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THE MEASUREMENT OF VASCULAR AND NEUROLOGICAL FUNCTION IN WORKERS EXPOSED TO HAND-TRANSMITTED VIBRATION

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ABSTRACT

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THE MEASUREMENT OF VASCULAR AND NEUROLOGICAL FUNCTION IN WORKERS EXPOSED TO HAND-TRANSMITTED VIBRATION

by Christopher John Lindsell

Four methods for measuring disorders of vascular function and neurological function associated with occupational exposure to hand-transmitted vibration have been defined by reference to the available literature. For measuring vascular function the methods are: i) measures of the finger systolic blood pressure (FSBP) response to local cooling and ii) measures of the finger skin temperature (FST) response to local cooling. For measuring neurological function the methods are: i) measures of vibrotactile thresholds at the fingertips and ii) measures of thermal thresholds at the fingertips.

Measures of the FSBP and the FST response to cold provocation were appraised in 109 dockyard workers. The FST test did not differentiate between 82 healthy subjects and 27 subjects with vibration-induced white finger (VWF) whilst the FSBP test was found to be sensitive, specific and responsive to VWF. Vibrotactile and thermal thresholds were found to be sensitive, specific and responsive to symptoms of numbness in another study of 104 dockyard workers, of whom 67 reported neurological disorders. It was concluded that whilst the above tests could be useful for monitoring the vascular and neurological disorders, a number of improvements to the measurement methods could be worthwhile. Further experiments were carried out to investigate these improvements.

The simultaneous measurement of FSBPs on multiple test fingers was developed to improve the practicality of this test when measuring FSBPs on more than one test finger. Increased central sympathetic activity was hypothesised to result from increasing the stimulus by cooling more fingers. In two experiments on 12 healthy subjects, it was found that FSBPs measured simultaneously on four test fingers gave similar results to FSBP measurements on one test finger. Simultaneous FSBP measurements on four test fingers had comparable repeatability to measurements on one test finger. It was concluded that measuring FSBPs on multiple test fingers is a useful improvement to this test.

When measuring FSBPs, changing the order of presentation and the period of recovery between thermal stimuli was hypothesised to influence the results by altering central sympathetic activity. In 12 healthy subjects it was found that the order of presentation of thermal stimuli was not important but that inter-subject variability increased when recovery was allowed between thermal stimuli. It was concluded that minimising the time interval between successive applications of thermal provocation reduces undesirable inter-subject variability. Another study on 12 healthy subjects showed that different reference measurement locations give different results. It was concluded that the thumb is suitable location for making reference measurements.

The FSBP test and the FST test both involve application of cold provocation. The two tests are sometimes performed in succession but multiple thermal provocations may have cumulative effects on central sympathetic activity. When the two vascular tests were performed in succession on 36 subjects, including 12 subjects with VWF, any effects of the order of test presentation were small although a test performed first tended to be more repeatable. It was concluded that if both tests are performed consecutively, greater emphasis should be placed on the test performed first. The data for the FST test were reanalysed and showed that the sensitivity and specificity to VWF of this test is improved by changing the method of interpreting the results. Three methods of interpreting the FST response to cold provocation that represent an improvement to the test are suggested.

The two vascular tests have been shown in the literature to be repeatable for healthy subjects but not for subjects with VWF. The repeatability of the vascular tests was assessed in 36 subjects (12 manual workers, 12 office workers and 12 subjects with VWF). The repeatability of both tests was found to be low amongst workers with VWF; some of these subjects showed a negative test result on one occasion and a positive test result on another occasion. It was concluded that a repeat test may be required when a false negative result is obtained.

For the vibrotactile threshold test, the skin-stimulus contact force is usually controlled. Controlling the skin indentation would simplify measurement equipment. An experiment on ten healthy subjects investigated the relationship between skin-stimulus contact force, skin indentation and vibrotactile thresholds. It was concluded that the vibrotactile threshold test could be improved by implementing control of skin-indentation. Skin indentations giving comparable vibrotactile thresholds to those obtained using controlled contact forces were identified.

It is concluded that a test battery comprising the four test methods identified from the literature and subsequently developed during the course of this research can be used to monitor disorders of both vascular and neurological function associated with occupational exposure to hand-transmitted vibration. A number of recommendations are made for further improvements that might be achievable as a result of further work.

ACKNOWLEDGEMENTS

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CHAPTER 1 INTRODUCTION

1.1 INTRODUCTION

Exposure to hand-transmitted vibration can cause a variety of disorders that are collectively termed the hand-arm vibration syndrome (HAVS). The syndrome includes vascular, neurological and musculo-skeletal components that may occur together or independently (Gemne 1997). The condition is compensatable in the United Kingdom as well as several other countries. The cardinal vascular component of HAVS is vibration-induced white finger (VWF) which manifests as episodic blanching of the fingers in response to cold (Taylor and Pelmear 1975). The neurological disturbance is a diffusely distributed neuropathy that is most commonly reported as numbness, sensations of tingling are also reported (Brammer *et al.* 1987).

The vascular and neurological disorders resulting from vibration exposure are complex and, due to their nature, are rarely observed by a clinician (e.g. Maricq *et al.* 1996). Currently, the onset of any disorder is often detected by a combination of workers' own report of their condition, a medical examination and clinical tests. However, workers exposed to hand-transmitted vibration might wish to exaggerate or belittle symptoms as this may result in compensation or retention of their job, respectively. Measures of vascular and neurological function could be used to provide supporting evidence of reported symptoms. Such measures could also be useful in epidemiological investigations, and for monitoring vascular and neurological function in workers exposed to hand-transmitted vibration in the workplace.

Two measures are currently in use to detect vascular disorders associated with hand-transmitted vibration: finger systolic blood pressures measured following thermal provocation and the response of FSTs to cold provocation (e.g. Bovenzi 1998, Gautherie *et al.* 1997). Measurements of vibrotactile thresholds and thermal thresholds are commonly advocated for detecting neurological disorders associated with exposure to hand-transmitted vibration (e.g. Lundström 1998b, Virokannas and Virokannas 1995). Methods of making the measurements have not yet been standardised. This has resulted in conflicting opinions concerning the validity of the measurements, and a scarcity of comparable data from epidemiological surveys and normative studies.

The scope of this thesis is: i) the definition of criteria that can be used to appraise measurement methods, ii) the appraisal of measurement methods using these criteria, iii) improvement of measurement methods with respect of the criteria, and iv) the definition of methods that can be used to monitor vascular and neurological function in workers exposed to hand-transmitted vibration.

1.1.1 Measures of vascular function

Vibration-induced white finger is a secondary form of Raynaud's phenomenon. The characteristic blanching of the fingers in response to cold results from the cessation of blood flow in the affected phalanges of the fingers (Lewis 1929). The mechanism of cessation of blood flow is unclear although it is believed that attacks are mediated partly centrally by the central sympathetic nervous system and partly locally by a lesion in the digital arteries (e.g. Gemne 1997, Olsen 1988). A test for vibration-induced white finger should assess the response of the peripheral vasculature to cold.

Finger systolic blood pressure (FSBP) measured following local thermal provocation provide an indication of the response of the digital arteries to cold. It has been suggested that this is the most accurate method for diagnosing and quantifying VWF; a drop in blood pressure after local cooling is indicative of exaggerated cold-induced vasoconstriction (e.g. Bovenzi 1993, Olsen 1998). The measurement is primarily an assessment of vasomotor tone, a higher vasomotor tone results in increased cold-induced vasoconstriction (Nielsen and Lassen 1977).

Finger skin temperatures (FSTs) measured in well controlled environments can correlate with blood flow (Bovenzi 1987, Gautherie *et al.* 1992a). Measures of the response of FSTs to cold provocation provide information on the effects of cold provocation on the peripheral circulation; a prolonged decrease in FSTs as a result of cooling suggests prolonged vasoconstriction, a sign of VWF (Bovenzi 1987). Measures of the FST response to cold provocation differ from measures of FSBPs in that they tend to reflect the release from vasoconstriction, and not the extent of vasoconstriction (Virokannas and Rintamäki 1991).

1.1.2 Measures of neurological function

The neurological disorders reported in HAVS are due to a diffusely distributed disorder in the peripheral nervous system (Gemne 1997). The measurement of vibrotactile thresholds provides an indication of the function of the mechanoreceptors, and of the large diameter myelinated A_β fibres that supply these nerve endings (e.g. Lundström 1984). There are thought to be four main types of mechanoreceptor in the glabrous skin, two quickly adapting receptors (FAI and FAII) and two slowly adapting receptors (SAI and SAII). The quickly adapting receptors are sensitive to vibration; lower frequencies of vibration (e.g. 10 Hz - 65 Hz) are detected by the FAI receptors (Meissner's corpuscles) and higher frequencies (e.g. 45 Hz - 400 Hz) are detected by FAII receptors (Pacinian corpuscles) (Vallbo and Johansson 1984). High vibrotactile thresholds can be indicative of damage to the peripheral tactile sensory system resulting from exposure to hand-transmitted vibration (e.g. Brammer *et al.* 1987, Lundström *et al.* 1995).

The measurement of thermal thresholds is considered a useful indicator of the function of the temperature receptors and the unmyelinated C-nerve fibres and thin myelinated Aδ-nerve fibres that supply the hot and cold temperature receptors, respectively (e.g. Dyck *et al.* 1993, Verdugo and Ochoa 1992). A low cold threshold, high hot threshold or wide neutral zone (the difference between the hot threshold and the cold threshold) can be indicative of dysfunctions of the peripheral thermal sensory system resulting from exposure to hand-transmitted vibration (e.g. Ekenvall *et al.* 1986, 1989, Hirosawa *et al.* 1992, Lundström *et al.* 1998, Virokannas and Virokannas 1995).

1.2 CRITERIA FOR APPRAISING MEASURES OF VASCULAR AND NEUROLOGICAL FUNCTION

To systematically appraise the methods for measuring vascular and neurological function reported in the literature, several criteria have been defined. These criteria are used to define measurement methods that can be recommended for monitoring workers exposed to hand-transmitted vibration. The criteria are:

- The measurement should be repeatable (i.e. consecutive measurements made on the same subject should be similar).
- The measurement should be specific to the presence of a disorder (i.e. measurements should minimise false positive results).
- The measurement should be sensitive to the presence of a disorder (i.e. measurements should minimise false negative results).
- The measurement should be responsive (i.e. measurements should reflect changes in the severity of the disorder).
- The measurement should be practical within the constraints of cost, expertise required and time taken to perform.

Further to these criteria, factors influencing the results of measurements need to be identified so they may be considered when interpreting results, or controlled when performing measurements.

1.3 DETERMINATION OF TRUE POSITIVE AND TRUE NEGATIVE CASES

For appraising the sensitivity and specificity of the measures to disorders arising from occupational exposure to hand-transmitted vibration, a method of determining true positive and true negative cases is required, i.e. a gold standard. An international working group has suggested that a medical interview is the best method for diagnosing VWF (Anonymous 1995b). Another working group reported that current neurological tests are neither sensitive nor specific enough to be definitive (Anonymous 1995a).

It has been shown that a simple four-question self-administered questionnaire tends to agree with clinicians' opinion as to the presence or absence of vascular disorders, although it can underestimate the severity of symptoms (Brennan *et al.* 1993). This would suggest that a questionnaire can be useful in detecting the presence or absence of the disorder. An experimenter led questionnaire can form the basis of a structured interview that, although not conducted by medical personnel, might be considered the best method for use as a 'gold standard' against which to appraise the sensitivity and specificity of measures of vascular and neurological function. For experimental work performed in this thesis, the questionnaire given in Appendix B has been used.

1.4 GRADING THE SEVERITY OF COMPONENTS OF HAVS FOR ASSESSING RESPONSIVENESS

The severity of components of HAVS is usually given as a staging on the Stockholm Workshop vascular and neurological scales. Various deficiencies in the Stockholm vascular scale have been noted. By combining the frequency of occurrence of symptoms with the extent of symptoms, the classification of a subject can become difficult. Furthermore, the extent of symptoms and the frequency of occurrence of symptoms may not always be related (Palmer and Coggon,1997). These authors suggested a scoring system based upon extent of symptoms can be a useful alternative for grading the severity of VWF for research purposes.

To assess the responsiveness of measures of vascular and neurological function to disorders arising from hand-transmitted vibration in this work, the severity has been scored using the method reported by Griffin (1990). The scoring system quantifies the extent of symptoms on the fingers; numbers correspond to areas of the fingers affected (Figure 1). The scores can be given for individual fingers, or combined to give a score for a hand, or an overall score.

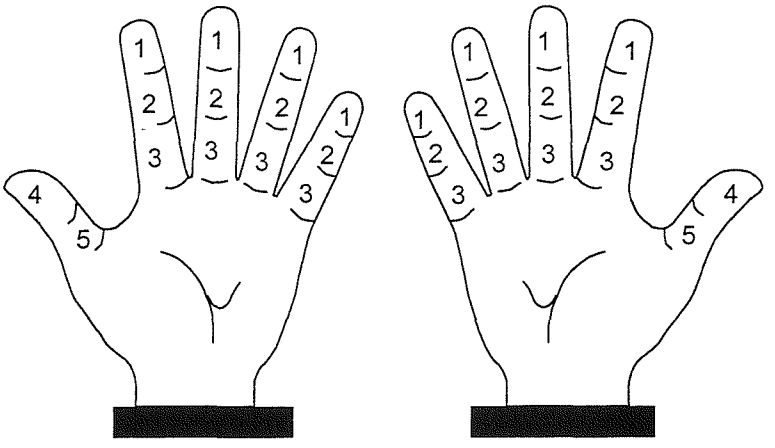


Figure 1 Scoring system for grading the severity of symptoms (after Griffin 1990). The numbers indicate the score given when symptoms occur on that phalanx.

1.5 APPRAISING THE VASCULAR AND NEUROLOGICAL MEASUREMENTS

Further to establishing criteria for appraising measurement methods, a procedure has been developed for performing the appraisal (Figure 2). Briefly, a method for making a measurement is defined, which is then appraised using each criterion in turn. At each stage of the appraisal, failure to meet a criterion results in a repeat of the investigative loop; the measurement method is redefined and is then systematically reappraised.

For the measurements under investigation here, the appraisals have been partially performed and reported in the literature. The first stage of this work is to clarify from the literature those criteria that have been considered, and to define measurement methods that may currently be considered optimal with respect to the criteria. These defined measurement methods are then appraised using the criteria and improvements are made. Measurement methods that have been demonstrated to satisfy the criteria can then be defined for monitoring workers exposed to hand-transmitted vibration.

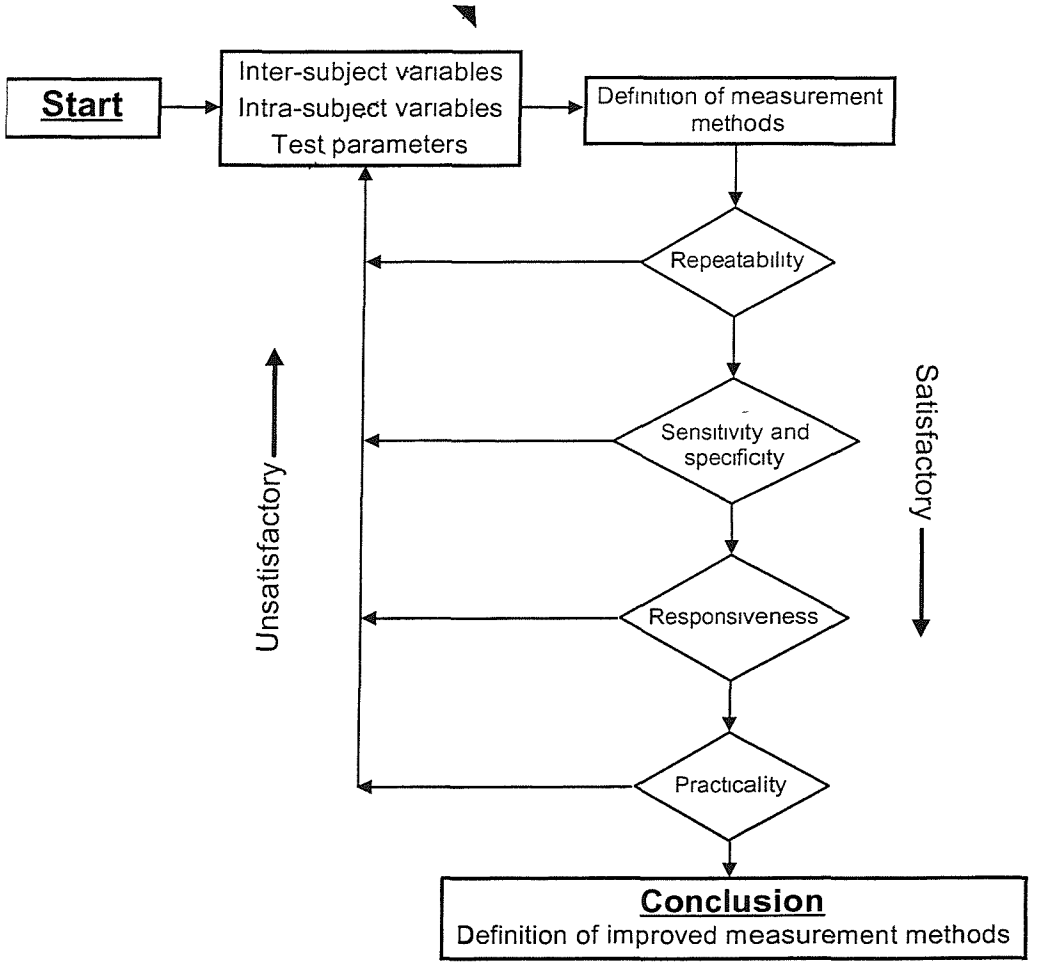


Figure 2 Procedure for appraising the methods of measuring vascular and neurological function in workers exposed to hand-transmitted vibration.

CHAPTER 2 METHODS FOR PERFORMING MEASUREMENTS OF VASCULAR AND NEUROLOGICAL FUNCTION

2.1 INTRODUCTION

Measures of finger systolic blood pressures (FSBPs) and of the response of finger skin temperatures (FSTs) to cold provocation have been recommended for detecting vibration-induced white finger (VWF). Measures of thermal thresholds and of vibrotactile thresholds have been suggested for detecting disorders of the peripheral nervous system. This chapter reviews some of the literature concerning the measurements. The methods for making measurements and the factors influencing results are discussed. Measurement methods are defined that are appraised in Chapter 3 using the criteria given in Section 1.2. Results obtained using these methods are compared to results reported in the literature in Chapter 3 and in subsequent chapters.

2.2 FINGER SYSTOLIC BLOOD PRESSURES

2.2.1 Introduction

The measurement of FSBPs following local cooling provides an indication of the response of the digital arteries to changes in temperature. Nielsen and Lassen (1977) proposed a technique for the measurement of FSBPs using a pressure cuff and a cooling cuff. The procedure was later adapted to incorporate local cooling of the digit into the pressure cuff itself (Nielsen *et al.* 1980). The method has been widely adopted for the measurement of FSBPs. The measurement method and factors known to influence FSBPs are discussed.

2.2.2 Measurement of FSBP

The method of measuring FSBPs defined by Nielsen and Lassen (1977) uses strain-gauge plethysmography. The principal of the measurement is to detect arterial inflow distal to a pressure cuff during gradual release from supra-systolic pressure applied by the pressure cuff. Inflow is detected as a volume change by means of a mercury-in-elastic strain gauge placed around the fingertip.

To compare the response of the digital arteries to different intensities of cold provocation, Nielsen and Lassen (1977) measured the FSBPs after cooling the medial phalanx of a test finger for 5 to 7 minutes using a water-perfused cuff with the water controlled at different temperatures. Water-perfused cuffs were thin-walled, rectangular, plastic bags secured with Velcro™, sized 24 mm by 80 mm (Figure 3).

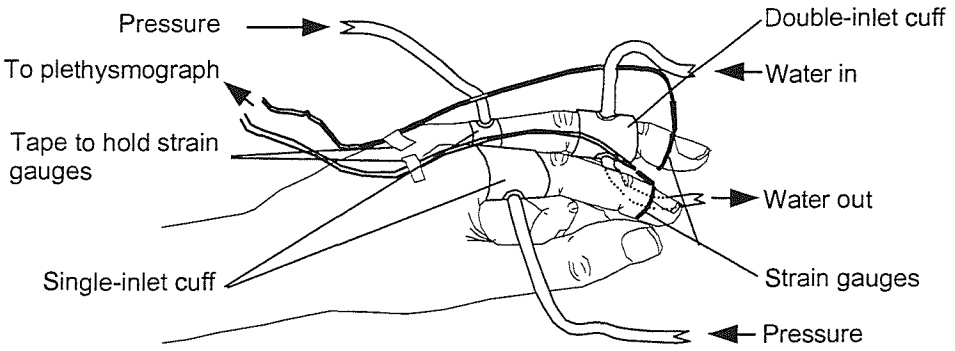


Figure 3 Placement of transducers and pressure cuffs for measurement of FSBP after local cold provocation.

During the cooling period, the test finger and a reference finger were held in an ischaemic state by means of air-inflated pressure cuffs (10 mm x 80 mm, test finger; 24 mm x 80 mm, reference finger) placed around the proximal phalanx of the test finger and the medial phalanx of the reference finger (Figure 3). The FSBP in the reference finger served as a control and was obtained without cooling.

Prior to application of supra-systolic pressure, the fingers were emptied of venous blood by light external compression. During cooling, the apex of the test finger was heated with a lamp; Nielsen and Lassen (1977) suggest this was required to obtain a reasonable volume signal from the strain gauge when blood flow returned following ischaemia. Subsequent studies have shown that warming of the finger tips during a measurement is not necessary (e.g. Bovenzi *et al.* 1995).

At the end of the cooling period, the FSBP was measured in the test finger and, simultaneously, in the reference finger. The FSBP was defined as the highest cuff pressure at which arterial inflow resulted in an increase in the volume of the distal phalanx of the finger, as indicated by the strain gauge (Figure 4). Blood pressures were assessed several times with a stepwise reduction in temperature between each measurement.

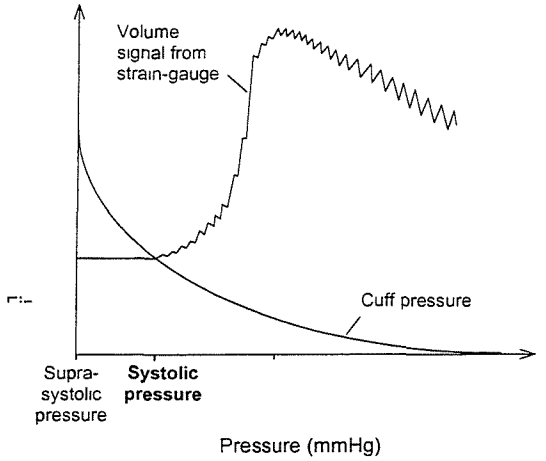


Figure 4 Volume - Pressure plot for a measurement of FSBP. Arterial inflow is permitted when cuff pressure equals, or is less than, systolic pressure. Inflow is detected by an increase in volume indicated by the strain gauge signal.

Concern about the influence of the measurement procedure on the vasomotor tone was expressed by Nielsen and Lassen (1977); the myogenic vasomotor tone might be lowered by ischaemia and the deprivation of stretch stimuli. These authors stated their concerns did not appear to be justified, a rise in vasomotor tone was observed in all cases studied.

The technique described above involves placing a cuff on the proximal phalanx of the test finger to act as a tourniquet during cooling. Nielsen *et al.* (1980) described a technique for controlling the temperature of water perfusing a double-inlet cuff in a pressurised system. Pressurising the water-perfused cuff simplifies the measurement procedure considerably.

2.2.2.1 Alternative methods for measuring FSBPs

A number of alternative methods for indirectly measuring the arterial blood pressure in the fingers have been reported in the literature. For example, Yamakoshi *et al.*, (1982) describe an oscillometric method for determining blood pressure. These authors suggest that, based on the principal of detecting maximum pulsations, it is theoretically possible to accurately detect the mean and the systolic arterial blood pressure. The technique has not been evaluated *in vivo* for detecting VWF. A measurement technique that operates to maintain the digital arteries in an 'unloaded state' by application of an external pressure equal to the intra-arterial pressure has also been described (Yamakoshi 1980). This technique has not been widely adopted and in the original article was validated only on ten subjects. Neither of these techniques were considered further here as no information was found in the literature about their usefulness in detecting VWF.

2.2.3 Apparatus for the measurement of FSBP

2.2.3.1 Plethysmograph

The plethysmograph has a direct effect on the measured FSBPs and their interpretation. Equipment that is highly sensitive to small electrical changes in the transducers will give a plethysmographic trace which is difficult to interpret as there will be measurement artefacts present (e.g. movement, signal noise). Insensitive equipment will require a greater volume change before signals are recordable, giving artificially low FSBPs. Some mention has been made of the efficiency of various digit cooling systems (Kurozawa *et al.* 1992, Nielsen *et al.* 1980); if the water temperatures are not sufficiently controlled the FSBPs may not reflect the desired effects.

2.2.3.2 *Transducers*

When measuring blood pressures using the technique described above, blood flow in the distal phalanges of the test and reference fingers is monitored using mercury-in-elastic strain gauges. A change in finger volume is recorded as a change in the resistance of the mercury, and hence a voltage drop across the transducer. This voltage drop is interpreted as a volume change and recorded as such by the plethysmograph.

Several other types of transducer have also been used for monitoring blood flow in the distal phalanges. Photoelectric cells have been used to note changes in tissue colour; a change in tissue colour is indicative of changes in digital circulation (e.g. Maricq *et al.* 1996). Doppler methods that use the principal of frequency shifts when electromagnetic or sound waves are reflected by red blood cells are also used (e.g. Kurozawa *et al.* 1992). It is possible that the use of different transducers will result in different values of FSBP. For example, the strain-gauge primarily monitors blood flow in the main digital arteries whereas some photoelectric cells detect blood flow in the skin.

Kurozawa *et al.* (1992) compared the simultaneous measurement of FSBPs made by strain-gauge plethysmography with that made by laser-Doppler flowmetry. They found that the laser-Doppler method was more sensitive to blood flow in patients exhibiting strong vasospasm than was strain-gauge plethysmography. Doppler shift methods, however, are likely to be more variable than the strain-gauge techniques. The photocell technique used by Maricq *et al.* (1996) gave practical problems; movement artefacts and low signal amplitudes resulted in loss of data. It was concluded that the strain gauge technique is preferable for use when appraising the measurement method for monitoring workers exposed to hand-transmitted vibration.

2.2.3.3 *Pressure cuffs*

2.2.3.3.1 Size

Measures of arm blood pressure by means of the ausculatory technique are dependent upon the width of the cuff; for an accurate measurement the width of the cuff should be at least 20% larger than the circumference of the limb (BS1060-1, 1996). If too narrow a cuff is used, artificially high blood pressures are recorded. A similar effect might be expected in the fingers.

Hirai *et al.* (1976) investigated the effect of cuff size on FSBPs. Finger systolic blood pressures and arm systolic blood pressures were compared in normal subjects; cuff widths of 24 mm placed on the medial phalanges of the index, middle and ring fingers gave systolic blood pressures similar to those on the arms. On the little finger, a 24 mm

cuff placed on the proximal phalanx, or a 20mm cuff placed on the medial phalanx, gave FSBPs similar to arm systolic blood pressures. Hirai *et al.*, (1976) concluded that the 20% rule should be applied to the fingers as well as to the arm. These authors also note that when using excessively wide cuffs, these would not maintain contiguity with the surface of the finger, resulting in variability in FSBPs.

2.2.3.3.2 Cuff material

The material from which a pressure cuff is made is likely to influence the test outcome. Too stiff a material prevents the cuff maintaining contiguity with the surface of the finger whilst softer cuffs adapt to finger shape in a more acceptable manner. Too elastic a material can result in loss of cuff shape and hence loss of control over variability caused by cuff size. Hirai *et al.* (1976) report that the adaptation of a thin-walled plastic cuff to finger shape is better than that of rubber cuffs.

The thermal conductivity of cuffs used to cool a finger is also important, the rate of attainment of thermal equilibrium of the finger is dependent upon the rate of energy flow through the cuff wall. This is important in determining the period of cold provocation. There are no known studies to compare the measurements of FSBPs after cold provocation with cuffs of different thermal characteristics.

When appraising the measurement method it was decided to use cuffs that were thin-walled and/or of high thermal conductivity and that they should be soft enough to maintain contiguity with the finger. A cuff width of 24 mm was selected.

2.2.3.4 Cold provocation

2.2.3.4.1 Temperature

For the detection of VWF, a series of FSBP measurements at decreasing temperatures allows the determination of the critical temperature at which closure of the digital arteries occurs. It has also been suggested that the temperature at which closure occurs is indicative of the severity of the condition in subjects with primary Raynaud's phenomenon (Nielsen and Lassen 1977).

Thulesius *et al.* (1981) investigated the blood pressures in 107 subjects with either secondary or primary Raynaud's phenomenon at 5°C intervals between 35°C and 5°C. They suggest that measurement at a single temperature is not sufficient for diagnosis of Raynaud's phenomenon; a complete temperature - pressure curve should be obtained to fully assess the vascular response to cold provocation. Maricq *et al.*, (1996) performed FSBP measurements at 30°C, 20°C, 15°C and then at 10°C amongst groups of patients

with Raynaud's phenomenon. They ceased performing measurements if complete closure of the digital arteries was elicited at any temperature, recording subsequent FSBPs as zero. Although ceasing the measurement following closure of the digital arteries is beneficial for practical reasons, it may not be correct to assume zero FSBPs at temperatures lower than the closure temperature; Thulesius *et al.* (1981) show that cooling below the critical temperature can result in an increase in the FSBP.

It has been reported that the sensitivity of FSBPs to VWF improves with a decreasing temperature of cold provocation (e.g. Bovenzi 1989). Nielsen (1978) suggests that the use of cold provocation at 15°C is the most suitable temperature for diagnosis of primary Raynaud's phenomenon; this showed the greatest difference between normal subjects and patient groups in experimental work. However, a temperature of 15°C may not result in abnormal FSBPs in subjects with only mild symptoms; the cold response of digital arteries has been shown to increase with increasing severity of VWF (Bovenzi 1997). Cooling below 15°C may be required to elicit a vasoconstrictive response in some subjects.

For measurements of the effects of cold on FSBPs to be meaningful, a minimum of two measurements must be made, one with the arteries in a state of vasodilation (i.e. basal vasomotor tone) and one with the arteries in a state of cold-induced vasoconstriction. In many studies, two or three temperatures of cold provocation have been used, generally 30°C to induce vasodilation and 15°C and/or 10°C to induce vasoconstriction. A procedure for the measurement of FSBPs at more than two or three temperatures might be considered prohibitively lengthy for use in monitoring workers exposed to hand-transmitted vibration. For further work, it was decided to make measurements at 30°C, 15°C and 10°C.

2.2.3.4.2 Duration

Nielsen and Lassen (1977) investigated the length of cold provocation during ischaemia that was required to equalise the temperature of the artery walls to that of the temperature of cold provocation. Initial experimentation was performed using a PVC tube (diameter 2.0 cm, wall thickness 1.2 mm) filled with a watery gel to represent the finger. Cold provocation was applied using a double-inlet, water perfused cuff. At the centre of the tube, the temperature was close to thermal equilibrium within 5 to 7 minutes. Digital arteries lie in the superficial subcutaneous tissue, hence a cold provocation of 5 to 7 minutes was considered adequate for the arterial walls to equalise to cuff temperature under ischaemic conditions.

Nielsen and Lassen (1977) also investigated the internal temperature of the finger during cooling using thermocouples inserted in the subcutaneous tissue. They found that after 5 minutes of cooling with ischaemia, the tissue temperature was within 1°C of the cuff temperature. After the cessation of cold provocation, the temperature of the tissue did not rise more than between 0.25°C and 0.5°C before blood was allowed to flow in the finger.

Kurozawa *et al.* (1991) compared 5 minutes of local cooling at 10°C with 10 minutes of local cooling combined with body cooling. They found that the first measurement only allowed a distinction between severe VWF and other subjects whereas the second measurement provided a distinction between patient groups with mild VWF and control subjects. The addition of body cooling during the second measurement at 10°C may have improved the sensitivity of the measure to VWF by increasing the sympathetic discharge to the digits (Nielsen 1978). Alternatively, cumulative effects of cold provocation may have contributed to this difference (Ekenvall and Lindblad 1989). It was concluded that five minutes would be a suitable duration of cold provocation for use in further work as this is sufficient to control the temperature of the arterial wall.

2.2.3.4.3 Duration between provocations

It is unknown whether a period of recovery is required between successive applications of thermal provocations. It is possible that there will be a cumulative effect of cold provocation on the fingers. For example, Ekenvall and Lindblad (1989) showed that with a fifteen minute recovery period between tests, subjects exhibited lower blood pressures at a second test compared to the first. The possibility of recovery effects requires further investigation.

2.2.4 Number of simultaneous measurements

Measurements of FSBPs may be finger specific, i.e. sensitive to vascular dysfunction in the test digit (Kurozawa *et al.* 1991). Measurements on more than one test finger, therefore, may improve the sensitivity of the test to VWF. Simultaneous measurements at multiple test sites would then be beneficial for practical reasons; the procedure for the measurement of FSBP after local cooling can be time consuming when measuring on more than one finger. However, effects of increasing the area of cold provocation on the central sympathetic nervous system, and hence vasomotor tone, should be investigated. When appraising the measurement method it was decided to consider measures on one test finger only.

2.2.5 Cuff location

The position of a pressure cuff and a cooling cuff in the measurement of FSBPs may be a cause of variability in FSBPs. The finger on which the measurement of FSBPs is performed is of particular importance; the sensitivity and specificity of the measurement to VWF may be dependent on the condition of an individual finger (Kurozawa *et al.* 1991). Table 1 gives a summary of measurement locations used in some investigations of FSBPs.

In normal subjects, the FSBPs tend not to differ between fingers (Hirai *et al.* 1976). Nielsen (1978) also reported that measurements made on a test finger and on a reference finger in air and at 30°C did not differ. These results indicate that in healthy subjects, any differences between the FSBPs measured in different fingers are small. Differences between fingers in subjects with VWF are likely to be influenced by the distribution of blanching on the fingers.

Table 1 Cuff positions used in investigations of FSBP using the strain gauge technique

Source	Test finger		Reference finger	
	Control group	Patient group	Control group	Patient group
Nielsen *et al* (1980)	Middle finger, left hand	Middle finger, left hand	Thumb, left hand	Thumb, left hand
Ekenvall and Lindblad (1982)	Ring finger, left hand	Ring finger, most affected hand	Index finger, left hand	Index finger, most affected hand
Ekenvall and Lindblad (1986)	Ring finger, left hand	Ring finger, most affected hand	Index finger, left hand	Index finger, most affected hand
Arneklo-Nobin *et al* (1987)	Middle finger	Most affected finger	Index finger	—
Bovenzi (1988)	Middle finger, left hand	Middle finger, left hand	Ring finger, left hand	Ring finger, left hand
Bovenzi (1989)	Middle finger, left hand	Most affected finger	Ring finger, left hand	Ring finger, same hand as test finger
Kurozawa *et al.* (1991)	Middle finger	Most affected finger, also measurements on bilateral index, middle and ring fingers of 14 subjects	Thumb, same hand as test finger	Thumb, same hand as test finger
Virokannas and Rintamaki (1991)	—	Middle finger, most affected hand	—	Same finger, contralateral hand.
Carnicelli *et al.* (1992)	Middle finger, right hand	—	Ring finger, right hand	—
Bovenzi (1993)	Middle finger, left hand	Most affected finger	Ring finger, left hand	Usually the ring finger
Bovenzi *et al* (1995)	Middle finger, left hand	Most affected finger	Ring finger, left hand	Usually the ring finger
Bovenzi (1997)	Middle finger, left hand	Most affected finger	Usually the ring finger	Usually the ring finger

2.2.5.1 Reference measurement location

The use of an affected finger as a reference finger might result in low FSBPs in the reference finger; vasoconstriction may occur in response to cold provocation of an adjacent test finger. The locations of reference measurements reported in the literature are variable (Table 1), and the condition of the reference finger rarely reported.

Ekenvall and Lindblad (1986) found that the calculation of %FSBPs was confounded by vasoconstriction in the reference finger brought about by general body cooling during the test procedure. They concluded that a better reference measurement could be made on the arm. They further suggested that as the change in systemic systolic blood pressure was small, it may not be necessary to correct for it.

Nielsen (1978) reported that the arm systolic blood pressures tended to be higher than FSBPs, the mean difference being 14 mmHg. This conflicts with Hirai *et al.* (1976) who reported similar blood pressures in the arm and in the fingers. This might be the result of a pressure drop between the arm and the fingers, differences in the accuracy of measurement techniques or the use of inappropriate cuff sizes. Whatever the cause, it is reasonable to assume that such differences may be reproducible elsewhere. The use of arm systolic blood pressure as a reference might have deleterious effects on the diagnostic value of FSBPs. For appraising the measurement of FSBPs, it was decided to use the middle finger as the test finger and the ring finger as the reference finger. Further work is required to determine if reference fingers are influenced by cold provocation of an adjacent test finger.

2.2.6 Posture

It is well known that the measurement of blood pressure is dependent upon the posture of the body. In the standing body the blood pressure of the feet can be as much as 90 mmHg higher than in the upper arm. To avoid this hydrostatic pressure effect, it was decided to perform measurements with the subject in the supine position after a period of habituation and with the hand supported at or near the level of the heart.

2.2.7 Interpretation of results

A subjective element to the measurement of FSBP exists in that an investigator must choose the criterion for the determination of systolic blood pressure from plethysmographic traces. Nielsen and Lassen (1977) suggest that the cuff pressure at which a volume increase is measured using the strain gauge is equal to the systolic intra-arterial pressure. These authors took this to be their criterion for the determination of systolic blood pressure. However, a pulse can sometimes be observed on the

plethysmographic trace prior to a volume increase. This shows that arterial inflow can occur at a higher pressure than the cuff pressure at which a volume increase is measured. It was concluded that both a volume increase and an observation of the pulse should be used here, the highest estimate of FSBP being taken as the true value.

2.2.7.1 Pressure indices

A measurement of FSBP is not meaningful in determining the cold response of the digital arteries without reference to a basal measurement. A calculation is usually performed to determine the percentage change in FSBPs. Several methods have been suggested to calculate the percentage change, usually involving a correction for systolic pressure changes measured at a reference location.

The pressure index most frequently reported is the percentage FSBP ($\%FSBP_{t°C}$). This index involves a correction for changes in the systolic pressure at a reference location between measurements. The usual calculation, as proposed by Nielsen (1978), is:

$$\%FSBP_{t°C} = \frac{FSBP_{test,t°C}}{FSBP_{test,30°C} - \left(FSBP_{ref,30°C} - FSBP_{ref,t°C}\right)} \cdot 100\% \qquad (1)$$

Where *%FSBP* is the percentage FSBP; $FSBP_{test,t°C}$ is the FSBP of the test finger after thermal provocation at 10°C or 15°C; $FSBP_{test,30°C}$ is the FSBP measured on the test digit after thermal provocation at 30°C; $FSBP_{ref,30°C}$ is the FSBP measured on the reference finger after thermal provocation of the test finger at 30°C; $FSBP_{ref,t°C}$ is the FSBP measured on the reference finger after thermal provocation of the test finger at 10°C or 15°C.

An alternative method for calculation of %FSBPs was suggested by Thulesius *et al.* (1981). The equation ensures that the percentage FSBP is 100% at the higher temperature of thermal provocation. The formula is given as:

$$\%FSBP_{t°C} = \frac{FSBP_{ref,30°C} \times FSBP_{test,t°C}}{FSBP_{test,30°C} \times FSBP_{ref,t°C}} \times 100 \qquad (2)$$

The digital pressure index (DPI) has also been implemented (e.g. Bovenzi 1993, Ekenvall and Lindblad 1986). It is the ratio between the FSBP and systemic systolic blood pressure (SSP), usually measured in the arm either immediately prior to, or immediately following, the measurement of FSBP:

$$DPI_{t°C} = \frac{FSBP_{test,t°C}}{SSP_{t°C}}\% \qquad (3)$$

Bovenzi (1993) showed the variability in %FSBP to be lower than that for DPI; it was concluded that the calculation of %FSBPs resulted in a more robust and repeatable index of digital circulatory function than the calculation of DPIs. Maricq *et al.* (1996) used both the DPI and the absolute FSBP for the detection of Primary Raynaud's Phenomenon and Raynaud's Phenomenon secondary to scleroderma. They demonstrated that both were useful parameters for detection of vascular disorders. Ekenvall and Lindblad (1986) argued that in patient groups the use of a reference finger in the calculation of %FSBPs could adversely influence results; general body cooling applied during the test can cause digital vasospasm in the reference finger.

Hirai *et al.* (1976) related the FSBPs to the systemic systolic blood pressure by subtracting the FSBP from the ASP. A similar index, the reduction in FSBP (R-FSBP) has also been calculated in some studies (e.g. Bovenzi 1989):

$$R - FSBP_{t°C} = FSBP_{test,30°C} - FSBP_{test,t°C} - \left(FSBP_{ref,30°C} - FSBP_{ref,t°C}\right) \quad (4)$$

The pressure index that results in the greatest repeatability and sensitivity and specificity to VWF is currently unknown. The most commonly used pressure index, the percentage FSBP calculating using equation (1), has been shown to be repeatable and sensitive and specific to VWF (e.g. Table 2). It was decided to use this index in further work.

2.2.8 Reported FSBPs

There is a wide range of %FSBPs reported in the literature for groups of subjects with VWF and for healthy workers. Table E1, Appendix E summarises some of the reported %FSBPs for healthy subjects. Table 2 summarises some of the reported sensitivities and specificities of the test to VWF. The variable nature of reported FSBPs may be due to differences in the response of digital arteries to cold provocation, different test parameters and conditions and different severities of symptoms in patient groups. This confirms the test methods require standardisation if results are to be reproducible.

Table 2 Some reported sensitivities and specificites of %FSBPs to VWF.

Study	Lower normal limit	Sensitivity	Specificity
Ekenvall and Lindblad (1986)	<65% (15°C) and < 60% (10°C)	74.0%	-
Bovenzi (1991, 1993)	< 60%	84.2%	100%
Kurozawa *et al.* (1991)	<90%	81.7%	90.3%
Virokannas and Rintamäki (1991)	<76%	50.0%	84.0%
Bovenzi (1997)	< 60%	85.8%	73.8%

2.2.9 Summary

It was decided that in appraisals of the measurement of finger systolic blood pressures following cold provocation the method suggested by Nielsen and Lassen (1977) and refined by Nielsen (1980) should be used. Finger systolic blood pressures would be measured on the medial phalanges of the fingers or on the proximal phalanx of the thumb.

Cuffs with a width of 24 mm were selected for use, with mercury in elastic strain gauges placed to detect the return of blood flow in the distal phalanx of a finger during deflation of pressure cuffs.

It was decided to make measurements after cold provocation of the test finger at 30°C, 15°C and 10°C using the ring finger as a reference.

Further work is needed to clarify the need for measurements of FSBPs on more than one test finger, and to determine if there are any effects of cold provocation of a test finger on reference finger FSBPs.

2.3 FINGER SKIN TEMPERATURE RESPONSE TO COLD PROVOCATION

2.3.1 Introduction

Several different methods are currently used for measuring the finger skin temperature (FST) response to cold provocation. There is little standardisation of the cold provocation procedures or of the reporting of results. The methods of measuring FSTs and the cold provocation procedures are discussed, a measurement method for further appraisal is suggested.

2.3.2 Transducers for measuring skin temperature

There are several types of transducer commonly available for the measurement of FSTs. Thermocouples and thermistors (point transducers) are often used as these are relatively inexpensive and simple to use. Thermal imaging devices have also been implemented, sometimes employing infra-red sensors (e.g. von Bierbrauer *et al.* 1998). These systems tend to be expensive and difficult to calibrate accurately compared to point transducers.

Dupuis (1987) compared measurements made by infra-red imaging and by 'thermo-sensors' following cold provocation at 15°C for 1 minute in 222 subjects. Both were considered to be useful transducers for measuring FSTs, but it was concluded that measurements along the finger length by means of infra-red imaging yielded added useful information about the temporal and spatial changes in FSTs.

A difficulty in recording thermal images continuously, and the extra equipment required to convert thermal images to temperatures for analysis, may be considered impractical for routine monitoring of workers exposed to hand-transmitted vibration. Point transducers were considered preferable for use here if several precautions are taken: i) transducers would have a low heat capacity and be of small contact area to avoid influencing temperature changes at the measurement location, ii) transducers would be placed so as to maintain good contact with the skin, iii) transducers would not be in contact with surfaces other than the skin at the measurement location and iv) transducers would be allowed to settle until the recorded FST stabilises (Pelmear and Taylor 1992).

2.3.3 Cold provocation

Different combinations of duration of cold exposure, temperatures of cold exposure and hand conditions during cold exposure have been reported in the literature. Exposure durations have varied between 1 minute and 20 minutes, water temperatures between 0°C and 20°C and hand conditions between wet or dry and ischaemic or non-ischaemic. The response of FSTs to cold provocation depends upon the amount of cold-induced vasoconstriction in the digits (Bovenzi 1987). The temperature, duration and conditions of cold provocation should be chosen so as to achieve maximal vasoconstriction with minimal subject discomfort (e.g. Pelmear and Taylor 1992).

2.3.3.1 Method of application of cold provocation

The hand is usually immersed in a temperature-regulated water bath for the application of cold provocation. Environmental chambers and cold air have also been suggested as possible methods of applying the stimulus (Greenstein *et al.* 1991, Nasu and Kurozawa 1995). Use of an environmental chamber may be considered impractical in the routine monitoring of workers exposed to hand-transmitted. A temperature-regulated water bath was considered preferable to cold air for use here since the flow of air across the hand can result in uneven cooling of the skin surface and can also result in increased evaporation at the skin surface.

2.3.3.2 Temperature of cold provocation

Table 3 summarises some of the different cold provocation temperatures reported in the literature. Too cold a temperature can cause a cold-induced vasodilation (Pelmear and Taylor 1992) and pain (Chang 1976, Futatsuka *et al.* 1990). Too high a temperature may not be sufficient to cause vasoconstriction in patients with VWF.

Several studies have compared the response of FSTs to different temperatures of cold provocation. Chang (1976) compared cold provocation at 5°C and 10°C in 16 students and 29 patients with VWF. A temperature of 10°C was shown to be sufficient for differentiating between patients and controls. Pain was more severe for cold provocation at 5°C compared to cold provocation at 10°C; 10°C was considered more acceptable, and safer, than cold provocation at 5°C. Hack *et al.* (1983, 1986) compared the effects of water temperatures of 10°C and 15°C on reactive hyperaemia following the removal of a tourniquet during cold provocation. Both temperatures inhibited reactive hyperaemia in 22 subjects with VWF although a significant difference between the VWF group and a control group was observed only at 10°C. Bovenzi (1987) summarised the results of a review by Montgomery (1974) of 20 reports of finger blood flow as functions of skin and room temperature. It was concluded that maximum vasoconstriction occurs at about 20°C. Gautherie *et al.* (1992a) recommend that water between 10°C and 18°C be used for cold provocation as it is in this range that minimum blood flow in the hand is observed.

These reports suggest that water temperatures between 10°C and 20°C may be suitable for the measurement of the FST response to cold provocation. Although a water temperature of 10°C appears to have the highest frequency of use, 15°C has been shown to have a similar specificity and sensitivity to VWF as 10°C (Table 3). A temperature of 15°C causes less discomfort and is easier to achieve. For implementation here, a water temperature of 15°C was considered suitable.

2.3.3.3 Duration of cold provocation

No studies were found that compared different durations of cold provocation on the response of FSTs to cold provocation. Howarth and Griffin (1989) showed that immersion times of between about 4 minutes and about 30 minutes were required to achieve FSTs below 17°C during immersion in water at 15°C for five subjects. They suggested that fixing the duration of cold provocation would simplify the measurement. In general, reported results show that FSTs tend to approach a minimum value after about 5 minutes of immersion (e.g. Chang 1976, Virokannas *et al.* 1990). Durations of cold provocation greater than 5 minutes have not been shown to improve the sensitivity and specificity of the test to VWF (Table 3) and can cause pain in older subjects (Spurr *et al.* 1955). For use here, 5 minutes of cold provocation was considered a sufficient duration to provoke cold-induced vasospasm whilst maintaining a reasonably short testing time and minimising subject discomfort.

Table 3 Examples of some methods of application of cold provocation reported in the literature and their corresponding sensitivity and specificity to VWF.

Author	Temperature (°C)	Duration (mins)	Ischaemia[1]	Sensitivity[2] %	Specificity[2] %
Hellstrom *et al* (1970)	5 ± 0.2	20	-	61	51
Gemne and Swensson (1975)	5	2	-	-	-
Chang (1976)	5 / 10	10	-	-	-
Harada and Matsumoto (1980)	10	10	-		
Juul and Nielsen (1981)	10	-	yes	100	-
Hack *et al* (1983, 1986)	5 - 7	15	no	73	74
Welsh (1983)	10	> 3	yes	-	-
Kurumatani (1984)	10	10	-	-	-
Pelmear *et al.* (1985)	10	10	½	70 - 80	35 - 85
Bovenzi (1986)	4	2	-	-	-
Brubaker *et al* (1986)	-	-	yes	76	61 - 65
Iki *et al* (1986)	10	10	-	-	-
Kurumatani *et al* (1986)	10	10	-	81 8 - 91 1	73 3 - 93.0
Niioka *et al* (1986)	10	10	-	80	100
Pyykko *et al.* (1986)	12 - 15	10	-	52 - 58	-
Taylor *et al.* (1986)	10 - 12	1	-	51.3	-
Welsh (1986)	10	3	yes	-	-
Bovenzi (1987)	5	5	yes	60	92
Dupuis (1987)	15	1	-	-	-
Harada (1987)	10	10	-	20 - 25	-
Laroche and Thériault (1987)	4	1	-	49.1	79.4
Pelmear *et al* (1987)	10	10	½	35 - 76	37 -89
Matoba and Sakurai (1987)	5/10	10	-	-	-
Olsen N (1988)	10	5	yes	35 - 80	80 - 98
Howarth and Griffin (1989)	15°C	4 - 30	no	-	-
Futatsuka *et al.* (1990)	5 / 10	10	-	-	-
Jansen and Schwarze (1990)	5	14	-	-	-
Kester *et al.* (1990)	5	1	-	97	-
Saito *et al.* (1990)	10	10	-	-	-
Virokannas *et al.* (1990)	10	10	-	57	-
Kent *et al* (1991)	5	1	-	97	-
Gautherie *et al.* (1992a)	15 ±1	3	-	95	-
Gautherie *et al.* (1992b)	15 ± 1	3	-	95	-
Bovenzi *et al.* (1994)	10	5	yes	-	-
Nasu and Kurozawa (1995)	5	10	-	5.9 - 50	69.8 - 97.7
	10 / 15	10	½	73	74
Von Bierbrauer *et al.*, (1998)	12	3	-	58.3 – 91.7	66 7 - 100

[1] ½ = Ischaemia was applied for the first half of the immersion period only.
[2] Sensitivities and specificities have been estimated from the reported data where necessary. For indices of recovery used to obtain the sensitivities and specificities see Table E2, Appendix E.

2.3.3.4 Area of application of cold provocation

Different areas of application of cold provocation have been reported. For example, Bovenzi (1987) cooled only one finger, Olsen (1988) immersed hands in cold water up to the middle of the palm whilst Pyykkö *et al.* (1986) immersed the arms up to the level of the shoulder. Some authors have cooled both hands simultaneously whilst others have cooled only one. One study used whole body cooling (Lau *et al.* 1995).

Most investigators have cooled one hand with immersion up to the wrist, this appears to be sufficient for inducing vasospasm in fingers affected with VWF (Table 3). Both hands can be immersed if required, although this involves loss of a reference location for the

measurement; Downey and Frewin (1973) show that there is a reduction in the blood flow in the contralateral hand during cold provocation of one hand. This may provide information useful to the objective assessment of VWF (Sakakibara *et al.* 1997). In further investigations here, it was decided to cool one hand only.

2.3.3.5 Hand conditions during immersion

2.3.3.5.1 Covering

Whether or not the hand is covered during cold provocation is not believed to affect immersion temperatures of the hand, provided the hand is not insulated against the cold. Removal of the hand whilst wet, however, will allow cooling by evaporation. This effect could be minimised by drying the hand. This may, however, affect FSTs or dislodge transducers. It might be concluded that preventing the hand becoming by wet by covering them during immersion is preferable. In this work, it was decided to use coverings that were thin-walled and/or of high thermal conductivity to minimise any insulation effects. The coverings were chosen to be loose enough so as not to restrict skin blood flow.

2.3.3.5.2 Ischaemia

The use of a tourniquet to induce ischaemia in the hand during cooling has been recommended by some authors (e.g. Bovenzi 1987, Juul and Neilsen 1981, Pelmear and Taylor 1992). Ischaemia of the hand allows more rapid reduction in both FST and internal hand temperature (Olsen 1988). The use of ischaemia during cooling, however, does not appear to affect the sensitivity and specificity of the test to VWF (Table 3).

The removal of a tourniquet can result in reactive hyperaemia (Kilgour *et al.* 1997). Some authors have used a cold-induced inhibition of reactive hyperaemia as a criterion for the diagnosis of VWF (Pelmear *et al.* 1985, Kent *et al.* 1991). Hack *et al.* (1983, 1986) compared the repeatability and diagnostic value of i) the hyperaemic temperature achieved on removal of a tourniquet at the wrist during cold provocation at 10°C or 15°C and ii) the FSTs measured at 1, 3, 5, 7, 10, 12.5 and 15 minutes after cold provocation of both hands at between 5°C and 7°C for 15 minutes. Both test methods were shown to be similarly repeatable and both exhibited similar sensitivities and specificities to VWF, about 60% of subjects being correctly classified as healthy or unhealthy.

Neither the use of ischaemia nor the criteria of abolished reactive hyperaemia appear to improve the sensitivity of the test to VWF (Table 3). The added complication of applying ischaemia is not obviously beneficial in the diagnosis of VWF and has therefore not been considered here.

2.3.3.5.3 Posture

During cooling, resting the hand in a comfortable position avoids muscle activity and the subsequent changes in blood flow. Positioning the hand to avoid compression of blood vessels might also be considered beneficial. Some authors have suggested that the hand should grip an iron bar during immersion to increase cold-induced vasoconstriction (Bovenzi *et al.* 1994, Juul and Nielsen 1981, Olsen 1988). Most authors have reported similar sensitivities and specificities to VWF as these authors without requiring a subject to grip a metal bar (Table 3). It is possible that the muscle activity required to grip the bar, and the difficulty in controlling contact area might be a cause of variability. For appraising the measurement method here, it was decided to position the hand so it is not thermally influenced by any surface that it contacts to reduce potential variability.

2.3.3.6 Hand conditions during recovery

For this work, it was decided to rest the hand in a comfortable position at the level of the heart using a support of low thermal conductivity (e.g. wood). This was not expected to thermally influence the hand. It was decided that the coverings used during immersion would be removed and compression of blood vessels would be avoided.

2.3.4 Parameters describing the FST response to cold provocation

Many different parameters have been used to describe the response of FSTs to cold provocation. The rewarming time, the rewarming rate and the recovery temperature have all been used, as have the immersion temperature and the hyperaemic temperature. The definitions of each of these parameters are variable but common use is suggested in Chapter 7. None of the parameters uniquely describe the response of FSTs to cold provocation for an individual. Table E2, Appendix E summarises some of the other parameters that have been used, and their lower normal limits reported in the literature.

Several studies have compared different parameters of the FST response to cold provocation. Howarth and Griffin (1989) investigated the repeatability of several different parameters and demonstrated that the time taken for FSTs to rise by 6°C following cold provocation was more repeatable than rates of temperature change, recovery rates and absolute FSTs before and during cooling. Carnicelli *et al.* (1992) also compared the repeatability of several different parameters: i) the immersion temperature reached during cold provocation at 15°C, ii) the time taken for FSTs to reach the lowest temperature, iii) the times taken for FSTs to rise by 3°C, 4°C, 5°C and 6°C from the lowest temperature, and iv) the final temperature. They found that the time take for FSTs to rise by 3°C and 4°C exhibited the greatest repeatability.

The times at which the FSTs reached 50%, 75%, 90% and 95% of initial temperature been shown to be insufficient to distinguish between workers with and without VWF (Pelmear *et al.* 1985). Four distinct patterns of response to cold were noted in this study, however. Based on the observations, Pelmear *et al.* (1985) concluded that the maximum hyperaemic temperature achieved after removal of a tourniquet provided the greatest sensitivity to VWF. Hack *et al.* (1983, 1986), however, showed that whilst the temperature of reactive hyperaemia 3 minutes after removal of a tourniquet could distinguish between groups of healthy subjects and patients with VWF, the predictive power of this parameter was low. When comparing the hyperaemic temperature with the FSTs measured at 1, 3, 5, 7, 10, 12.5, 15 and 20 minutes after cold provocation, they found no difference between hyperaemic temperatures and absolute temperature measurements for their sensitivity and specificity to VWF.

Based upon observations of 1800 subjects examined with a cold provocation test, Gautherie *et al.* (1992a,b) concluded that the rewarming curve, i.e. FSTs plotted continuously on a graph throughout the test, could be used to determine abnormalities in results. They suggested that calculated parameters could be used to quantify such abnormalities. They recommended the use of three parameters: i) the delay in rewarming, ii) the rate of recovery and iii) the FST after 15 minutes recovery compared to the initial temperature. Gautherie *et al.* (1997) suggest the use of 11 parameters that are combined in the calculation of a quantitative measure of the extent of vasoconstriction. These authors also suggest that asymmetry between hands and differences between fingers can distinguish between VWF and Raynaud's phenomena with other causes.

Chang (1976) reported a parameter calculated from the immersion temperature ($T_{immersed}$) and the FSTs at 1,2 and 3 minutes (T_{1min}, T_{2min}, T_{3min}) after cold provocation:

$$\text{Recovery activity} = \frac{1}{3}\left[(T_{1min} - T_{immersed}) + \frac{1}{2}(T_{2min} - T_{immersed}) + \frac{1}{3}(T_{3min} - T_{immersed})\right]$$

Chang (1976) suggested that this described the initial recovery activity and provided a greater sensitivity to VWF than the rewarming rate and the time taken for FSTs to recover to the initial temperature.

Absolute FSTs, differences between the FSTs in the coldest and warmest fingers and the mean FST for all fingers were compared by von Bierbrauer *et al.*, (1998). They found that the maximum difference between fingers did not show a significant difference between a group of patients with VWF and a control group. The mean FST across fingers, and the FSTs of individual fingers, were statistically significantly different between the two groups.

These authors used the data to calculate the time taken for the FSTs to reach their initial temperature and suggested this gave the greatest sensitivity and specificity to VWF. They concluded, however, that the parameters could not be used to provide an unequivocal diagnosis of VWF on an individual basis.

Since there are a number of different parameters reported, none uniquely identifying the patterns of FSTs during and after cold provocation, it was decided that the entire rewarming curve should remain of interest in this work. The various parameters discussed may be of use to highlight abnormalities of the curve and for statistical analyses, in this work the times to rise by 3°C, 4°C and 6°C were selected for use as they have been shown to be repeatable.

2.3.5 Measurement location

Measurements of the response of FSTs to cold provocation may be finger specific (e.g. Kester *et al.* 1990). Gautherie *et al.* (1997) suggest that the presence of asymmetry between the hands, and differences between the fingers, can be indicative of VWF whilst a symmetrical pattern of FSTs is more likely to be indicative of Raynaud's phenomenon with other causes. Kester *et al.* (1990) recommend the measurement of FSTs along the entire length of the fingers since the direction of rewarming, normally from the tip to the base of a finger, can be reversed in patients with VWF. In this work it is considered desirable to obtain measurements at as many sites as possible. It is not considered necessary to measure both the dorsal and volar surfaces of the fingers; they tend to exhibit a similar response to cold provocation (Dupuis 1987).

When cold provocation is applied to one hand only, the measurement of FST on the contralateral hand has been shown to provide a useful indicator of changes in sympathetic activity; these changes are significantly different when compared between healthy subjects and subjects with VWF (Sakakibara *et al.* 1997). Contralateral changes in FSTs have also been demonstrated by others (e.g. Falkenbach *et al.* 1997). Figure 5 illustrates possible transducer locations that may provide the greatest sensitivity to VWF with the fewest transducers. Combinations of these locations were chosen for further work.

2.3.6 Posture

The posture of a subject during a rewarming test has a direct effect on the blood flow in the fingers. To maintain resting blood flow, it was decided to position the subject comfortably, either seated or supine, with excessive movement not being permitted. It was decided to support the arm at about heart level during the settling and recovery periods of the test.

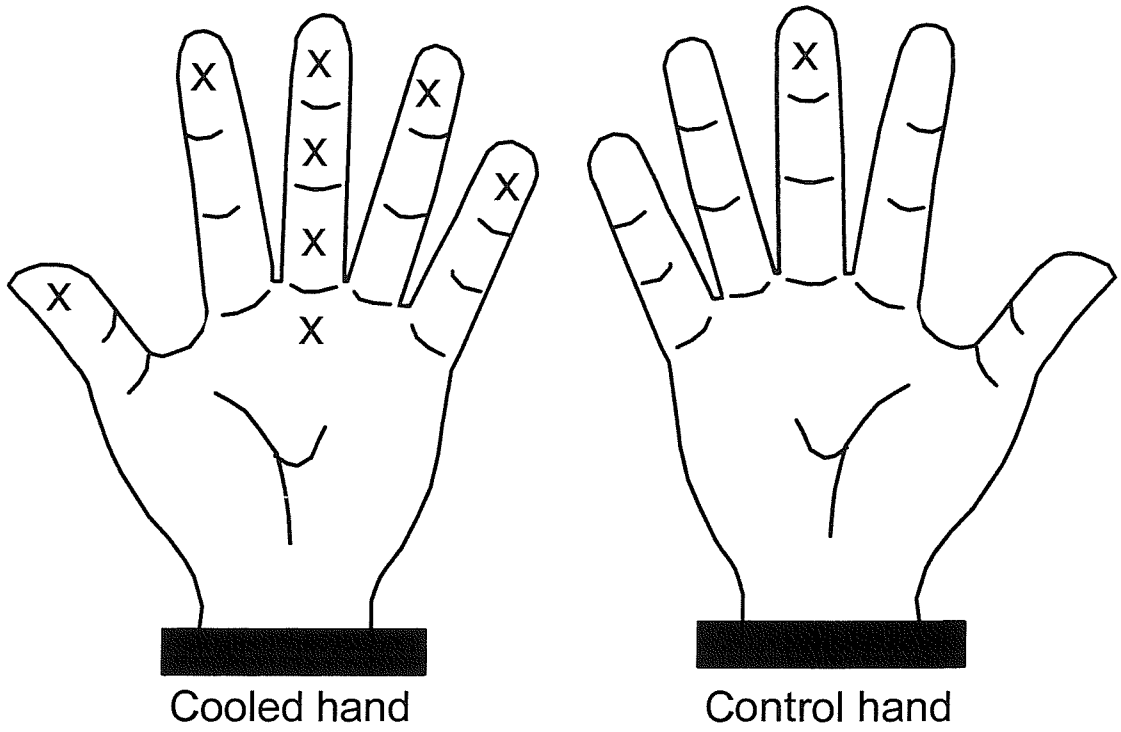


Figure 5 Positions for transducers in the measurement of the FST response to cold provocation when cooling one hand only.

2.3.7 Summary

It was decided that for appraisal of the measurement method, the response of FSTs to cold provocation should be measured using point transducers attached to the skin. A settling period was considered necessary, followed by immersion of the covered hand up to the wrist in water at 15°C for a duration of 5 minutes.

On removal from the water, it was concluded the hand would be uncovered and rested at heart level until the pre-immersion finger skin temperatures were reached or 15 minutes had elapsed, whichever was shorter. It was decided to record the rewarming curve for each measurement site from about 2 minutes before immersion to about 15 minutes after removal of the hand from the cold water.

Currently, the times taken for FSTs to rise by 3°C, 4°C and 6°C are considered useful parameters of the rewarming curve for use in statistical analyses. Further work is required to understand the patterns of the FST response to cold provocation observed in healthy subjects and subjects with VWF so appropriate parameters can be selected to more adequately describe the response of FSTs to cold provocation.

2.4 VIBROTACTILE THRESHOLDS

2.4.1 Introduction

Various equipment has been implemented for measuring vibrotactile thresholds. These include tuning forks (e.g. Hilz *et al.* 1998, Martina *et al.* 1998), commercially produced electronic devices (e.g. Vibrameter, Somedic A/S; Tactile Vibrometer, *HVLab*; Bio-Aethesiometer, Bio-Medical Instruments Co.), and devices developed by investigators (e.g. a modified audiometer used to control a shaker, Piette and Malchaire 1997).

Different devices are unlikely to give similar thresholds due to differences in the applied stimulus, the skin-stimulus contact conditions and the methods of calculating thresholds (e.g. Maeda and Griffin 1995). This section reviews some of the literature concerning the measurement of vibrotactile thresholds. A method for measuring vibrotactile thresholds is defined for further appraisal using the criteria of sensitivity, specificity and responsiveness.

2.4.2 Psychophysical methods for measurement of vibrotactile thresholds

Several different psychophysical algorithms have been used to determine vibrotactile thresholds. The more common methods are the method of limits (Lundström 1984, Ess and Dupuis 1992), the up-and-down method of limits (Gescheider *et al.* 1978, Hilz *et al.* 1998) and the two alternative forced-choice algorithm (Deng *et al.* 1993). No algorithm has been universally accepted for threshold measurements although it has been shown that vibrotactile thresholds are dependent upon the psychophysical algorithm used (Maeda and Griffin 1995).

The method of limits involves the application of a vibrating stimulus at sub-threshold levels. The magnitude of the stimulus is then incremented at a constant rate, when subjects perceive the vibration they respond and the vibration returns to a sub-threshold level. The test is repeated several times and the mean of the judgements is calculated. Using this method, the vibration appearance, or perception, threshold is measured (Hilz *et al.* 1998, Lundström 1984).

When using the up-and-down method of limits, also called the modified method of limits and the von Békésy tracking method, the magnitude of vibration is incremented at a constant rate from sub-threshold levels. When subjects perceive the vibration they respond. The stimulus magnitude is then decremented at a constant rate until subjects no longer perceive the vibration and respond again, this is the disappearance threshold. The direction of change of stimulus magnitude is again reversed and the cycle repeated. Several such cycles are recorded and the threshold is calculated as the average of the appearance threshold and the disappearance threshold.

A forced-choice method involves presenting a subject with a null stimulus and a vibrating stimulus, the vibrating stimulus being systematically varied until the subject can only just differentiate between it and the null stimulus.

Maeda and Griffin (1995) recommend the up-and-down method of limits; the method requires less time for threshold determination than forced-choice algorithms and thresholds measured in this way are sufficiently repeatable. The up-and-down method of limits is also relatively independent of reaction time compared to measuring the appearance threshold alone; the reaction time to the appearance threshold cancels out with the reaction time to the disappearance threshold. Furthermore, the up-and-down method of limits is simple to understand and faster to perform than forced-choice testing, aiding subject co-operation (Hilz *et al.* 1998). The up-and down method of limits was selected for use in this work.

2.4.2.1 Threshold calculation

Threshold peaks and troughs obtained using the up-and-down method of limits can be averaged by the arithmetic or the geometric mean (Verberk *et al.* 1985, Maeda and Griffin 1995). Results are not very different when the arithmetic and geometric means are compared, unless the peaks and troughs of thresholds vary by more than about 10dB. The current draft international standard for measuring perception of vibration requires peak or trough variations to be less than 10 dB (ISO-CD 13901, 1998).

It was decided to use the arithmetic mean here. It is calculated as the mean of the mean peak (ascending judgement or appearance threshold) and the mean trough (descending judgement or disappearing threshold). The first peak and first trough was ignored when calculating the mean threshold as these may have contained artefacts relating to short-term learning effects.

2.4.2.2 Vibrating stimulus

2.4.2.2.1 Pulsed vibration

An intermittent pure tone stimulus has sometimes been used to provide a quiescent interval between vibrating pulses. Such an interval may serve to contrast physiological noise with the applied stimulus (Brammer *et al.* 1987). This is claimed to result in improved threshold definitions, no empirical evidence has been found to confirm this hypothesis. Pulsed stimuli might reduce any TTS caused by suprathreshold vibrotactile stimulation (Section 2.4.2.2.3). However, it is difficult to control and repeat the quality of a pulsed stimulus (Verrillo 1966b). It was concluded that the difficulty in producing a clean signal when using pulsed stimuli, and the lack of data supporting any benefits of using a pulsed single, suggests the use of a continuous stimulus to determine vibrotactile thresholds in this work.

2.4.2.2.2 *Waveform distortion*

Distortion of the sinusoidal waveform may affect the vibrotactile thresholds (Maeda and Griffin 1994). Waveform distortion is more likely to occur when using a pulsed stimulus than when using a continuous stimulus (Section 2.4.2.2.1). Gescheider *et al.* (1992) studied the effects of waveform distortion by imposing noise on a sinusoidal vibration stimulus. At low stimulus magnitudes, noise caused masking of vibrotactile perception whereas at high stimulus magnitudes no such effect was observed.

It has been shown that at measurement frequencies between 25 and 200 Hz, there is a complex summation between the Pacinian corpuscle response and the Meissner's corpuscle response to suprathreshold stimuli. Although for low frequency vibration, the Meissner's corpuscles dominate the response and at higher frequencies, the Pacinian corpuscles dominate the response (Hollins and Roy 1996), waveform distortion may result in additional stimulation of the Meissner's or Pacinian corpuscles. It was decided to monitor and minimise waveform distortion when measuring vibrotactile thresholds.

2.4.2.2.3 *Duration*

The duration of application of a vibrating stimulus can influence vibrotactile thresholds. Exposure to suprathreshold stimuli during a measurement results in TTS. For example, Berglund and Berglund (1970) and Lundström and Lindmark (1982) found that the application of vibration at suprathreshold levels resulted in raised thresholds that took 2 to 3 minutes to return to pre-exposure values.

It is unknown whether a fatigue effect occurs during a single threshold measurement although some authors recommend that a lengthy test procedure should be avoided (e.g. Hilz *et al.* 1998). Hayward (1986) found that for five successive 45 second measurements using the up-and-down method of limits, each separated by one minute rest periods, no fatigue effect occurred. This would suggest that repeated measurements performed at one minute intervals are not influenced by fatigue. If many measurements are to be performed, it may be beneficial to provide a one minute interval between threshold measurements.

The measurement duration should be chosen to be of sufficient length to allow the vibrotactile threshold to converge on its true value without causing fatigue or a TTS. Maeda and Griffin (1994) show that the criterion of a minimum of six reversals using the up-and-down method of limits gives repeatable vibrotactile thresholds. In the example results presented by these authors (Figure 4 and Figure 5 in Maeda and Griffin 1994), the 6 reversals were only just completed within the 30 second period allowed for the measurement. To ensure 6 reversals could be completed during the measurement, 45 seconds was selected as the measurement duration for further work here.

2.4.2.2.4 Rate of stimulus increment and decrement

Rates of change of stimulus between 1 dB/s and 10 dB/s have been used to measure vibrotactile thresholds, step changes in stimulus intensity have also been reported (Table E3, Appendix E). An appearance or disappearance vibrotactile threshold may be increased or decreased, respectively, by a faster rate of change of vibration magnitude; there is a time lag between vibrotactile perception, subject response and the reversal of the direction of change of stimulus magnitude (e.g. Hilz *et al.* 1998). When calculating the mean threshold using the up-and-down method of limits, however, this is unlikely to significantly affect the results as this reaction time effect cancels out between the appearance and disappearance threshold. Thresholds found using a step change in stimulus intensity employing a fast rise time might be affected by ringing. They will also be limited by the resolution of the step change. Rates of increment and decrement of less than 5 dB/s were considered suitable for measuring thresholds in this work; there is no obvious benefit and possibly some detriment to using faster rates of change of stimulus.

2.4.2.2.5 Frequency

Vibrotactile thresholds can be frequency dependent. Very low frequencies (< 10 Hz) are believed to result in the stimulation of SAI mechanoreceptors (receptors sensitive to stretch and touch), frequencies below about 65 Hz stimulate the Meissner's corpuscles and frequencies above about 45 Hz stimulate the Pacinian corpuscles (e.g. Brammer and Piercy 1990).

Some studies suggest that thresholds mediated by Pacinian corpuscles may be affected before thresholds mediated by Meissner's corpuscles among persons exposed to hand-transmitted vibration (e.g. Brammer *et al.* 1987, Virokannas 1992). For diagnosing vibration-induced neuropathies, therefore, it might be suggested that mechanoreceptor specific thresholds are obtained.

There is some overlap between the vibration frequencies to which mechanoreceptor populations are sensitive, as illustrated in the literature by the range of frequencies for which mechanoreceptor specific thresholds have been obtained. The overlap between mechanoreceptor specific thresholds is further influenced by contact conditions and subject conditions. Harada and Griffin (1991) show that frequencies below 63 Hz are Meissner's corpuscle specific whilst those above 63 Hz are Pacinian corpuscle specific when using the contact conditions suggested for use in Section 2.4.4.

To obtain mechanoreceptor specific thresholds here, 31.5 Hz and 125 Hz were chosen. Data obtained with the same contact conditions to those selected here are available for these frequencies (e.g. Bovenzi *et al.* 1997, Hadlington 1991, Hayward 1986, Maeda and Griffin 1994).

2.4.3 Apparatus for stimulus application

2.4.3.1 Contactor

2.4.3.1.1 Size

The surface area of a contactor has a significant effect on the perception of a vibration stimulus (Goble *et al.* 1996, Harada and Griffin 1991, Verrillo 1962,1963). Increasing the contactor size reduces vibrotactile thresholds mediated by Pacinian corpuscles. This reduction is further influenced by the presence of a surround, and the gap between the surround and the contactor (e.g. Goble *et al.* 1996). It has been hypothesised that this change in thresholds is due to changing the number of Pacinian corpuscles being stimulated; Pacinian corpuscles exhibit spatial summation (Verrillo 1966a).

Verrillo (1962) and Gescheider (1978) have shown that for measurement frequencies below about 60 to 80 Hz, vibrotactile thresholds are independent of contactor area (contactor area > 0.02 cm^2). These results suggest that the Meissner's corpuscles do not exhibit spatial summation. Goble *et al.* (1996) did show an effect of contactor size on vibrotactile thresholds measured at 10 Hz, they suggest this may have been due to activation of the Merkel disks. Stimulation of the Merkel disks is unlikely at the lower frequency selected here for measurement of vibrotactile thresholds (Section 2.4.2.2.5).

Contactor areas less than 0.02 cm^2 (diameter 1.4 mm) have been shown not to give mechanoreceptor specific thresholds; with smaller contact areas frequency-independent thresholds are obtained (Verrillo 1962).

A contactor between about 2 mm diameter and 6 mm diameter might be recommended for use. Use of larger contactor sizes is limited by the use of a surround; increasing the contactor diameter may result in the hole in the surround being larger than the fingertip. A contactor diameter of 6 mm was chosen for use here as this has been shown to be repeatable (Maeda and Griffin 1994).

2.4.3.1.2 Material

There is no known evidence to suggest that the material from which a contactor is made influences vibrotactile thresholds. However, if receptors other than those being assessed are strongly stimulated, vibrotactile thresholds might be affected. A thermally neutral contactor material was chosen (i.e. of low thermal conductivity and low specific heat capacity) to minimise thermal sensations. The surface was selected to be smooth to minimise tactile sensations.

2.4.3.1.3 Cross-sectional Shape

Verrillo (1962) showed that vibrotactile thresholds were lower if the contactor cross-sectional shape was annular when compared to a solid, circular cross-section. Due to the difficulties in constructing an annular contactor and the possibility of affecting thresholds by stimulation of pain or stretch receptors when using a contactor with corners, a solid, circular contactor will be used. Although surface contours of the contactor have been shown not to influence vibrotactile thresholds (Verrillo 1963), a planar contact surface was selected for use here.

2.4.3.2 Surround

The use of a surround has the effect of decreasing the low frequency (< 40 Hz) thresholds and increasing the high frequency (> 80 Hz) thresholds (e.g. Goble *et al.* 1996, Harada and Griffin 1991). Pacinian corpuscles exhibit spatial summation; the ability to perceive vibration improves as vibration propagates through finger tissue and stimulates an increased number of Pacinian corpuscles (Gescheider *et al.* 1978). The use of a surround prevents wave propagation (Maeda and Griffin 1994). The effect of a surround on lower frequency thresholds is thought to be due to the edge receptive properties of the Meissner's corpuscles; the Meissner's corpuscles become more sensitive when there is an edge in their receptive field (e.g. Johansson *et al.* 1982, Verrillo 1979).

It was decided to use a surround in this work to localise the measurement to the skin-contactor interface and to simplify determination of Meissner's corpuscle specific thresholds. The use of a surround also simplifies control of skin-contactor interface conditions.

2.4.3.2.1 Gap

The gap between a contactor and a surround is of importance in the measurement of vibrotactile thresholds (Gescheider *et al.* 1978, Harada *et al.* 1995). For low frequencies, thresholds increase with an increasing gap; for high frequencies, the thresholds decrease with increasing gap (Verrillo 1962). This is consistent with results for measurements with and without a surround. A gap of about 2 mm can give mechanoreceptor specific thresholds (Harada and Griffin 1991) and was chosen for use here.

2.4.4 Contact conditions

Finger push force on a surround, contactor push force on the skin and skin indentation have all been shown to alter vibrotactile thresholds. To minimise variability caused by these parameters, they should be controlled (Maeda *et al.* 1997).

Vibrotactile thresholds decrease with increasing skin indentation (e.g. Makous *et al.* 1996, Verrillo 1962). Measuring thresholds without a surround, Lowensthal and Hockaday (1987) showed vibrotactile thresholds decreased as contact force increased up to 4 N. Using a surround, Harada *et al.* (1995) showed that increasing the magnitude of the contact force from 1 N to 2 N decreased thresholds at frequencies above about 125 Hz only; there was little difference in thresholds between contact forces of 2 N and 3 N. Individual variations in the mechanical properties of the skin make it impossible to control both skin indentation and skin contact force.

The relationship between skin indentation and skin contact force is complicated by the use of a surround. Push force on a surround is used to aid discrimination between mechanoreceptor specific thresholds (Section 2.4.3.2). The push force on a surround has rarely been considered. Maeda *et al.* (1998) suggests a push force on a surround of 1 N although this recommendation was based on subject comfort and not on the effects on vibrotactile thresholds.

The relationship between skin indentation and contact force with and without a surround was studied by Piercy and Brammer (1998). The effects of these parameters on vibrotactile thresholds were not reported, however. Further work is required to understand the combined relationship between skin indentation, skin contact force, push force on a surround and vibrotactile thresholds.

Using a skin contact force of 1 N whilst controlling the push force on a surround at 2 N results in repeatable, mechanoreceptor specific vibrotactile thresholds (Maeda and Griffin 1994) that are dependent upon the neurological function of workers exposed to hand-transmitted vibration (Lawson and Neville 1998). Based on this, these contact conditions were selected for use in this work.

2.4.5 Units for reporting thresholds

Different units have been used to report vibrotactile thresholds. Some measurement equipment gives thresholds in arbitrary units, such an approach is not considered useful in this work. Units of measurement for thresholds tend to be displacement (measures of peak displacement and peak-to-peak displacement) or r.m.s. acceleration. These units have sometimes been converted to decibels but different reference levels are specified. For ease of understanding, it was decided to use r.m.s. acceleration levels (i.e. ms^{-2} r.m.s.) here.

Lundborg *et al.*, (1986, 1992) suggest the use of the Sensibility Index for reporting vibrotactile thresholds. The sensibility Index combines information from measurements at 7 different frequencies between 16 Hz and 500 Hz. Using this parameter the authors report high sensitivity and specificity to various neurological disorders. However, they loose information about the individual mechanoreceptors; it has been shown that the mechanoreceptor pathways are not always similarly affected by exposure to hand-transmitted vibration (e.g. Virokannas 1992). Combining vibrotactile thresholds to form the Sensibility Index was not considered beneficial here.

Lundström *et al.* (1998a) have recently reported other measures of the vibrotactile stimulus, namely dynamic force and absorbed power. They suggest that measures of vibrotactile thresholds that include the dynamic force may be useful as they contain information about the mechanical coupling between stimulus and skin and the strain on the skin. Such an approach was not considered in this work, there is a scarcity of data against which to compare results obtained here.

2.4.6 Measurement location

Many different sites on the hand and fingers have been investigated for their vibrotactile sensitivity (e.g. Table E3, Appendix E). Although the magnitudes of thresholds differ between sites (e.g. Verrillo 1962), the frequency-dependence of the thresholds is similar at each site (e.g. Lundström 1984). The differences in threshold magnitudes are likely to be due to the differing densities of mechanoreceptor populations in the skin. The density of both Meissner's and Pacinian corpuscles increase from the palm distally to the fingertip for the area of the hand innervated by the median nerve. This increase is non-linear, the density in the fingertips is approximately three times that for the proximal and medial phalanges and the mechanoreceptor density of the medial and proximal phalanges is about one-and-a-half times that on the palm. The tip of the distal phalanx exhibits higher mechanoreceptor densities than the base of the distal phalanx (Johansson and Vallbo 1979).

For the purposes of this work, it was decided to assess the more sensitive parts of the finger will, i.e. the volar surface of the distal phalanx at the centre of the whorl. In this way, lower magnitudes of vibration are required to stimulate the mechanoreceptors. Also, it is at the fingertip that patients with VWF tend to first report neurological symptoms such as numbness.

2.4.6.1 Finger

Different neuropathies may be characterised by different vibrotactile thresholds measured on different fingers. For example Doezie *et al.* (1997) show greater dysfunction in the area innervated with the ulnar nerve than in the area innervated in the median nerve for medical transcriptionists. Compression of the median or ulnar nerve can also alter the perception of vibration at the fingertips (Goadsby and Burke 1994). Since the innervation of the fingers differ, it was decided that measurements should be made on at least two fingers, one finger innervated with the ulnar nerve and the other innervated by the median nerve, i.e. the little finger and the middle or index finger, respectively.

2.4.6.2 Hand

Similar vibrotactile thresholds are reported for the dominant and the non-dominant hand in normal subjects (Hilz *et al.* 1998, Lundström 1985, Halonen 1986b). Occupational exposure to vibration may give rise to a threshold shift which differs between hands due to an asymmetrical trauma to the hands (e.g. Wiles *et al.* 1990). It was concluded that measurements should be made on both hands here.

2.4.7 Posture

No studies have been found which address the effect of subject posture directly. Flexure or rotation of the wrist during threshold measurements might result in compression of the median or ulnar nerve and it was decided this would be avoided.

2.4.7.1 Finger posture

Verrillo (1962) hypothesised that finger movement could alter the vibrotactile threshold through masking by physiological noise. The author studied one subject in two conditions, once with a free finger and once with the finger held rigidly in place. Thresholds measured at frequencies between 25 Hz and 640 Hz were similar for the two conditions. Although Verrillo (1962) showed the results for only one subject, it was concluded that to improve the practicality of the measurement the finger need not be held rigidly in place.

2.4.8 Summary

Vibrotactile thresholds provide a measure of the function of mechanoreceptors and the large myelinated A_β nerve fibres that innervate the hand. Vibrotactile thresholds have been shown to be dependent upon skin-contactor interface conditions, vibration frequency and stimulus type. Table E3, Appendix E summarises some of the methods used to obtain vibrotactile thresholds and, where possible, mechanoreceptor specific thresholds for the Pacinian and Meissner's corpuscles. A similar table giving examples from other studies is given by Maeda and Griffin (1994, Table1).

The up-and-down method limits with a duration of 30 to 45 seconds and a rate of change of vibration intensity of 3 dB/s has been shown to provide repeatable thresholds that are useful in evaluating peripheral nervous function. These parameters were chosen for implementation here. It was decided that mechanoreceptor specific thresholds for the Meissner's and Pacinian corpuscles would be obtained at 31.5 Hz and 125 Hz, respectively.

The contactor was selected to have a 6 mm diameter circular tip that applies a force of 1 N to the skin. It was decided that a rigid surround to the contactor is required, leaving a gap of 2 mm between contactor and surround. The finger push force on the surround was selected as 2 N. Further work is required to understand the complex relationship between contactor force, push force on a surround, skin indentation and vibrotactile thresholds.

2.5 THERMAL THRESHOLDS

2.5.1 Introduction

Several different methods for measuring the threshold of warm and cold perception have been proposed. This section reviews some of the literature concerned with the measurement of thermal thresholds. The measurement methods are discussed and a measurement method is suggested for use in further work.

2.5.2 Psychophysical methods for measuring thermal thresholds

Several different psychophysical algorithms have been used to measure thermal thresholds in patient groups and in normal subjects. A commonly used method of threshold determination is the Marstock method. Using this method, a stimulus applicator is heated or cooled at a constant rate, the subject responding when warmth or cold is perceived. The direction of change of stimulus is reversed until a further feeling of cold or warmth is perceived. The process is repeated several times and the mean temperature difference between hot and cold perception, the neutral zone, is calculated.

The method of limits allows determination of the hot and cold thresholds independently, with respect to a reference temperature. A stimulus applicator is set to the reference temperature and it is placed in contact with the finger. The temperature of the applicator is then increased or decreased until a heating or cooling sensation is felt by the subject, who then responds (a judgement). This results in the return of the applicator to its reference temperature. This procedure is repeated a number of times to give a mean hot threshold and a mean cold threshold. The neutral zone can be calculated from the difference between the mean hot threshold and the mean cold threshold.

Bertelsmann *et al.* (1985) suggest using a forced choice stepping algorithm to measure thermal thresholds. A forced-choice method is less affected by response bias than the method of limits or the Marstock method (e.g. Claus *et al.* 1990, Jamal *et al.* 1985). Schady *et al.* (1991) conclude that the increased time taken for measurements using forced-choice algorithms (about 6 times longer than when using the method of limits, Claus *et al.* 1990) offsets any psychophysical advantage; a long measurement duration results in fatigue and increased distraction of a subject. Dyck *et al.* (1993a) developed a reproducible stepping algorithm for the measurement of thermal thresholds that reduces testing time by one quarter compared to conventional forced-choice algorithms. Such a method might be suitable for measurement of thermal thresholds but the measured thresholds are unlikely to be comparable to the method of limits or the Marstock method.

Claus *et al.* (1990) compared thresholds measured with the method of limits to those measured with a forced choice method. Thresholds were highest when measured using the method of limits. The authors stated, however, that discrimination between normal and pathological thresholds is more important than measuring low thresholds and that both psychophysical algorithms performed similarly in this respect. Dyck *et al.* (1993c) compared various psychophysical methods for measurement of thermal thresholds. These authors showed that with rates of change of temperature of 1°C/s or lower, thresholds were similar for forced choice methods and the method of limits.

Ruffell and Griffin (1995) investigated the repeatability of the method of limits and showed high correlation coefficients between days for hot thresholds, cold thresholds and the neutral zones. Using a reference temperature of 30°C to 34°C (Section 2.5.2.2), the percentage differences in warm and cool thresholds across three days were between 4.4% and 3.36%. The variability of forced choice algorithms has been shown to exhibit a similar pattern to that for the method of limits; the hot threshold is more variable than the cold threshold and the maximum intra-individual variability of thermal thresholds is about 5% (Jamal *et al.* 1985). Claus *et al.* (1990) compared the repeatability of thermal thresholds using a forced-choice method and the method of limits. These authors show that the repeatability of the two methods is similar, if not slightly higher using the method of limits. These results would suggest that neither algorithm has an advantage over the other with respect to repeatability.

A forced choice algorithm and the method of limits both appear useful for measuring thermal thresholds. To minimise testing time, the method of limits was considered the preferred psychophysical method for appraising measurements of thermal thresholds in this work.

2.5.2.1 *Number of judgements*

The number of threshold judgements during a measurement must be sufficient to converge on the true threshold. Levy *et al.* (1987) reported that between 30 and 50 stimuli were required to obtain a true threshold value when using a two alternative forced-choice method. Ruffell (1994) showed that five judgements were sufficient for threshold determination when using the method of limits, the mean of the final three judgements giving a good estimate of the true threshold value. Verdugo and Ochoa (1992) obtained thresholds with between 3 and 6 judgements and showed this was sufficient to detect various neuropathies. Schady *et al.* (1991) suggest that 10 reversals are sufficient when using the Marstock method if the threshold level is determined from reversals in the latter part of the test. It was concluded that three judgements would be the minimum number required, although more judgements would be preferable. Too many judgements result in increased testing time that should be avoided.

2.5.2.2 *Reference temperature*

The reference temperature is presented as the temperature from which a change is to be discriminated. When the Marstock method is used, the reference temperature has less influence upon the final threshold value compared to the influence of the reference temperature in the forced-choice method and the method of limits; the reference temperature is presented only as a starting temperature in the Marstock method.

Mito and Shimizu (1981) used finger skin temperatures to set reference temperatures and they showed positive correlations between neutral zones and warm thresholds and the reference temperatures. Comparing thresholds obtained with controlled reference temperatures of 28°C, 30°C, 32°C, 34°C and 36°C in ten healthy males, Ruffell and Griffin (1995) found that an increase in reference temperature resulted in an increase in both hot and cold thresholds, a marginal change in the neutral zone was also observed. Reference temperatures in the mid-range of those used (i.e. 30°C to 34°C) resulted in the most repeatable threshold determinations. Verdugo and Ochoa (1992) recommend a reference temperature of 32°C whilst Jamal *et al.* (1985) recommend a reference temperature of 34°C; complete adaptation to temperature sensation was said to occur quickly at these temperatures.

It is necessary that if hot and cold thresholds are to be assessed independently, the reference temperature is controlled. A reference temperature between 30°C and 34°C was considered suitable for use in this work.

2.5.2.3 *Rate of change of temperature*

The rate at which temperature is incremented and decremented during a threshold test has a significant effect on thermal thresholds (Verdugo and Ochoa 1992). The rate of change of temperature alters the peak discharge frequency, and the number of impulses, in the nerve fibres of finger skin. These changes have been stated to be greatest below 0.5°C and above 1.5°C (Jamal *et al.* 1985). Too fast a rate of change of temperature can also result in overshoots in threshold judgements that are dependent on response time (e.g. Dyck *et al.* 1993b, 1993c, Verdugo and Ochoa 1992). Such overshoots result in overestimation of hot thresholds and underestimation of cold thresholds. Ruffell (1994) showed that incremental rates set between 0.5°C/s and 2.0°C/s did not significantly effect thermal thresholds. These results are consistent with those of Kenshalo *et al.* (1968) where thresholds were shown to remain constant with incremental rates above 0.1°C. It was concluded that when using the method of limits, an incremental rate of 1°C/s would be suitable for further work.

2.5.2.4 *Duration at the reference temperature*

The duration for which a reference temperature is maintained at the test site, either prior to measurements or between judgements within a threshold determination, might affect the measurement of thermal thresholds. No studies have been found which investigate this hypothesis although it has been stated that holding a test site at a reference temperature between 30°C and 35°C allows quick and complete adaptation of the thermal receptors to that temperature (Jamal *et al.* 1985, Verdugo and Ochoa 1992). The duration at the reference temperature should be controlled although further work is required to determine an optimal duration. Three to five seconds was considered a suitable duration for use here.

2.5.2.5 *Hot thresholds, cold thresholds and the neutral zone*

Some authors have used the temperature neutral zone, the difference between the hot and the cold threshold, with some success in detecting peripheral neuropathies in workers exposed to hand-transmitted vibration (e.g. McGeoch *et al.* 1992). Lundström *et al.*, (1998b) suggest that the neutral zone shows evidence of a dose-response relationship with vibration exposure. The neutral zone may be considered a useful indicator of thermal sensory function but information about the hot and cold sensory pathways is lost (e.g. Verdugo and Ochoa 1992). There is evidence that one thermal pathway may be damaged before another during exposure to hand-transmitted vibration (e.g. Ekenvall *et al.* 1986, Hirosawa *et al.* 1983, Virokannas and Virokannas 1995). In this work, it was decided to consider the hot thermal threshold and the cold thermal threshold independently.

2.5.2.6 Learning effects

Several authors have reported learning effects when measuring thermal thresholds (e.g. Jamal *et al.* 1985). Ruffell and Griffin (1995) found that warm thresholds decreased and cool thresholds increased when measurements were made on consecutive days. Kenshalo (1986) found that in practice trials, effects of order of presentation of ascending or descending stimulus were evident but that during subsequent test trials the effects were no longer evident. It was decided to use practice trials in further work to reduce learning effects when measuring thermal thresholds.

2.5.3 Method of stimulus application

Mostly, thermal thresholds have been assessed using a single surface with a temperature controlled by a Peltier element or by a surface whose temperature is controlled using hot and cold water. For forced choice testing, both one and two plates have been used for comparison of temperatures. Use of a Peltier element appears to result in repeatable thresholds and a well controlled stimulus (e.g. Jamal *et al.* 1985, Ruffell and Griffin 1995, Verdugo and Ochoa 1992). This method was selected for use here.

2.5.3.1 Applicator size and skin contact area

The area of contact between the skin and the stimulus applicator is of importance in the assessment of thermal thresholds since the temperature receptors exhibit spatial summation (Ekblom and Hansson 1987, Verdugo and Ochoa 1992). Increasing the applicator area decreases thermal thresholds (Dyck *et al.* 1993c). Mito and Shimizu (1981) show that thermal thresholds measured using an applicator larger than a finger pad do not depend on the size of the finger pad. For measurements at the fingertip, the applicator was selected to be large enough so as to stimulate the entire finger pad. Further work is required to determine if a smaller applicator can be used, it is easier to accurately control the temperature of a smaller applicator than a larger applicator.

2.5.3.2 Applicator shape and material

No studies have been found that investigate the effects of applicator shape or material on thermal thresholds. These parameters may be of importance; the measured thermal thresholds may be masked by stimulation of mechanoreceptors if the applicator surface is not smooth and flat. A smooth, planar applicator was chosen for further work.

2.5.3.3 Contact force

The contact force between the skin and the applicator should be controlled (Jamal *et al.* 1985). Contact forces of about 2 N have generally been used (e.g. Bertelsmann *et al.* 1985, 200g, Ruffell and Griffin 1995, 2N, Schady *et al.* 1991, 240g). No studies have been found to compare thermal thresholds obtained with different contact forces. It was decided to use a contact force of 2 N here, further work is required to determine the effect of changing the contact force on thermal thresholds.

2.5.4 Measurement location

2.5.4.1 Finger

Many investigators have measured thermal thresholds on the foot, on the ankle, on the palm of the hand and on the thenar eminence, fewer have been performed on the fingers (Table E4, Appendix E). McGeoch *et al.* (1992) reported neutral zones measured on the index, middle, ring and little fingers of both hands in workers exposed to hand-transmitted vibration. They demonstrated differences between the neutral zones measured at each site and advise measurements be made on the index and little fingers. This may also allow the detection of neuropathies resulting from disorders (such as compression) of one or other of the median and ulnar nerves (Goadsby and Burke 1994).

In the appraisal of thermal thresholds to be performed here, it was decided to measure thermal thresholds at one site innervated by the median nerve (index or middle finger) and one site innervated by the ulnar nerve (little finger).

2.5.4.2 Hand

Hot thermal thresholds can be higher, and cold thresholds lower, on the dominant hand than on the non-dominant hand in workers exposed to hand-transmitted vibration (Ekenvall *et al.* 1986). This may be due to a different vibration exposure on the dominant and the non-dominant hand. It was decided to assess fingers on both hands.

2.5.4.3 Foot

In many studies reporting results of thermal threshold testing, measurements have been made on the foot (Table E4, Appendix E). These thresholds are not similar to those measured on the finger tips; there are significant differences between thresholds obtained on the hand and the foot (e.g. Jamal *et al.* 1985).

2.5.5 Posture

No studies were found that address the effect of posture on measurements of thermal thresholds. It is hypothesised, however, that flexure or rotation of the wrist during a measurement might result in compression of the ulnar or median nerve and hence a change in the measured thresholds. An uncomfortable arm or body posture might also affect thresholds by increasing fatigue. Movement artefacts are not expected if subjects are instructed to hold the test fingers still during testing. It was decided these precautions should be taken when making measurements here.

2.5.6 Summary

Thermal thresholds can be used to detect some of the neurological changes caused by occupational exposure to hand-transmitted vibration. Table E4, Appendix E, summarises some of the normal threshold values reported in the literature.

In this work, it was decided to assess hot thresholds and cold thresholds independently using the method of limits. A rate of change of temperature of 1°C/s was selected with a thermo-neutral reference temperature between 30°C and 34°C. The push force on the aplicator by the finger was chosen to be 2 N.

It was decided to measure thresholds on the palmar surface of the most distal phalanx of one finger innervated with the median nerve and one finger innervated with the ulnar nerve on both hands.

2.6 FACTORS INFLUENCING OBJECTIVE TEST RESULTS

Various factors that are not intrinsic to the methods of measuring vascular and neurological function have been found to have significant effects on the outcome of the tests. This section discusses some of the factors that may require consideration in further work.

2.6.1 Experimental conditions

2.6.1.1 Effects of temperature

Environmental temperature is an important factor in the thermo-regulation of the human body. This, in turn, has an effect on the blood flow in the peripheral circulatory system (e.g. Bovenzi 1987). Kurozawa *et al.* (1991) reported that the lowest ambient temperature at which a human body can maintain thermal equilibrium at the basal metabolic rate is 26°C, although this is influenced by clothing. In a cold environment the blood supply will be directed away from the extremities to the body core. In warmer environments blood flow to the extremities is increased. The change in blood flow is mediated by

vasoconstriction or vasodilation of the arteries. There are no known studies of the effects of humidity and air velocity on measures of FSBPs and the FST response to cold provocation or on vibrotactile thresholds and thermal thresholds.

The temperature of the environment in which measurements of thermal and vibrotactile thresholds are performed might affect finger skin temperatures (FSTs). Since FSTs can significantly alter neurological thresholds (Section 2.6.1.1.6), it was decided to control environmental conditions so as to be comfortable and sufficiently high to prevent undue reduction in FST.

2.6.1.1.1 Internal environmental temperature and vascular measurements

Bovenzi (1987) discussed the dependence of FSTs following cold provocation on environmental factors, concluding that strict control over these factors was required to produce repeatable measurements. Harada *et al.* (1997, 1998) measured the FST response to cold provocation in 6 healthy subjects at 6 different room temperatures between 10°C and 30°C. The colder rooms resulted in colder initial FSTs but little difference in the FSTs measured after 6 minutes immersion in water at 10°C. Slower recovery of the FST to its initial temperature was observed in the colder environments. Ishitake *et al.* (1998) show that a room temperature of 17°C results in significantly lower FSTs during recovery from cold provocation than a room temperature of 22°C, which in turn results in lower FSTs during recovery than a room temperature of 26°C. Cold environments might also result in the occurrence of the hunting phenomenon (cold-induced vasodilation), as demonstrated by Ekenvall and Lindblad (1986a).

Nielsen (1978) stated that the measurement of FSBPs is highly dependent upon environmental conditions and suggested that each laboratory should perform a study to determine a range of normal values for that laboratory. Cold environments may also cause vasoconstriction in the digital arteries of a reference finger in patients with VWF (Ekenvall and Lindblad 1986). Ekenvall and Lindblad (1982) compared the FSBPs measured in ten subjects with VWF and those of ten control subjects at two room temperatures, 17°C and 23°C. They found that four patients exhibited normal responses to cold provocation in the warmer room compared to only one with a normal response in the cooler room. Similarly, Virokannas and Rintamäki (1991) found that use of a room controlled between 20 and 23°C was not sufficiently cold to obtain a high sensitivity to VWF in patients with only mild VWF. Pelmear *et al.* (1985) recommend a room temperature of between 20°C and 23°C for the measurement of the FST response to cold provocation; they interpreted a low sensitivity of their measurements to VWF as resulting from controlling the room temperature at 30°C, a temperature inhibiting sympathetic activity.

Investigators who have found the measurement of FSBPs and of FSTs following cold provocation to be sensitive and specific to VWF (e.g. Table 2 and Table 3) have usually used room temperatures between 18°C and 25°C. An internal environmental temperature controlled between 20°C and 24°C was considered suitable for further work as it is comfortable and is unlikely to unduly influence the vascular response to cold provocation.

2.6.1.1.2 Local body cooling and warming

Body cooling increases central sympathetic activity whereas body heating effectively inhibits central sympathetic activity (Lau *et al.* 1995). The use of localised body cooling by means of water-perfused blankets or ice packs has been advocated to exaggerate cold-induced vasoconstriction when measuring FSBPs (e.g. Nielsen 1978). The use of body cooling is helpful if the investigator is trying to induce complete closure of the digital arteries (e.g. Olsen *et al.* 1985, Nielsen *et al.* 1980). Bovenzi (1993) stated that the use of body cooling was found to be uncomfortable and argued that the diagnostic sensitivity of the measurement of FSBPs was sufficient without the use of body cooling. In patients with only mild symptoms, however, body cooling may be required to elicit a vasoconstrictive response to cold provocation. For example, Kurozawa *et al.* (1991) found that body cooling was required when using FSBPs to distinguish between subjects with mild VWF and healthy subjects, but not for distinguishing between severe cases of VWF and healthy subjects.

A complication in the use of body cooling is possible in that the sudden application of cold can result in a transient increase in sympathetic discharge to the fingers (Nielsen 1978). Juul and Nielsen (1981) compared the effects of body cooling to the effects of body heating on the FST response to cold provocation. They found that body cooling resulted in delayed recovery of FSTs in normal subjects and that body heating decreased the variability of the test in 19 healthy subjects. Pelmear *et al.* (1985) also reported that the use of body warming efficiently inhibited sympathetic vasoconstrictor response, improving the reproducibility of the method and increasing the rewarming rate. Conversely, Falkenbach *et al.* (1997) report that cooling the feet during measurements of the FST response to cold provocation increases the speed of recovery of FSTs compared to when the feet were warmed.

Due to the added complexity, the possibility of increasing variability in the measurements and the possibility of influencing the false negative rate or the false positive rate, it was decided not to use body heating and cooling here.

2.6.1.1.3 Seasonal variations in vascular measurements

The results of vascular tests depend, in part, upon the season during which the test is performed. Harada *et al.* (1997) reported the FST response to cold for six healthy subjects measured during the spring, summer, autumn and winter. The results were obtained at three different room temperatures. For room temperatures of 20°C and 30°C, FSTs were higher in the summer than in the winter, spring and autumn and for room temperatures of 30°C, the FSTs measured in spring and autumn were higher than those measured in winter. At a room temperature of 10°C, there was less effect of season on FSTs. Several studies have recommended that measurements should be performed during the winter months only (Gautherie *et al.* 1992a, 1997, Jansen and Schwarze 1990, Ekenvall and Lindblad 1986). Gautherie *et al.* (1992b) suggest the criterion that external temperature should be below 15°C before measurements commence.

The influence of seasonal variations on measurements of the vascular response to cold are not fully understood. These variations are likely to be of importance and further work is required to investigate the effects.

2.6.1.1.4 Environmental conditions preceding objective tests

Several authors have suggested that subjects should not be exposed to uncomfortable environments prior to measurements of vascular function (e.g. Chang 1976, Hellstrøm 1970). Such exposures may result in lasting changes in central sympathetic activity. The environment in which a subject habituates immediately prior to measurements can also influence FSTs. The FST can affect thermal and vibrotactile thresholds. Slow warming or cooling of the fingers during the course of a threshold test might also be hypothesised as adding to the variability of the measurement. A period of adaptation to the environment in which tests are to be performed was considered necessary in this work. It was also decided to exclude exposures to extreme environmental conditions prior to measurements.

2.6.1.1.5 Local cold provocation preceding neurological tests

Local cold provocation alters FSTs which, in turn, influence neurological measurements. Niioka *et al.* (1986) found a negative correlation between FSTs following local cold provocation and vibrotactile thresholds in 34 chain-sawyers. Mito and Shimizu (1981) showed that local cold provocation raised both cold and hot thresholds. Ishitake *et al.* (1998) report results of vibrotactile threshold measurements during recovery from a cold provocation test and from their data it can be seen that the lower the FST, the higher the vibrotactile thresholds. The recovery of vibrotactile thresholds to their pre-immersion

values was dependent on room temperature; rapid recovery (less than five minutes) was observed for a room of temperature 27°C whilst recovery was incomplete after 15 minutes in temperatures of both 17°C and 22°C. When performing neurological tests and vascular tests in the same test session, it was decided to perform the neurological tests first to avoid these effects. Should subjects be exposed to local cold provocation of the hands prior to measurements, it was decided that complete recovery should be allowed before measurement of thermal or vibrotactile thresholds.

2.6.1.1.6 Finger skin temperature

It is not known whether starting FSTs have an affect on the outcome of the vascular tests. It may currently be assumed that the influence of cold provocation on the fingers overrides any effects of pre-provocation finger skin temperatures. For example, Harada *et al.* (1997) reported results of measurements of the response of FSTs to cold provocation at different room temperatures. With a colder room temperature, the starting FST was lower than at warmer room temperatures but after 6 minutes cold provocation at 10°C there was little difference between the FSTs measured in the different room temperatures. No conclusions were drawn as to the effect of starting FSTs on the FSTs measured during recovery because of the environmental influence over the FSTs measured during recovery.

Finger skin temperatures have been shown to influence thermal thresholds in patients with diabetes but not in normal subjects (Levy *et al.* 1987). Gelber *et al.* (1995) also reported that FSTs did not correlate with thermal thresholds in normal subjects. Bartlett *et al.* (1998), however, demonstrated a significant, but not clinically important, effect of FSTs on cold thresholds. It is unlikely that FSTs significantly affect measurements of thermal thresholds when a fixed reference temperature is used, the thermal receptors adapt rapidly to the reference temperature (Jamal *et al.* 1985). If FST is used as a reference temperature, however, thermal thresholds are likely to be dependent upon the FST (Mito and Shimizu 1981).

The FST has been shown to have a significant effect on the perception of vibration mediated by both the Meissner's and Pacinian corpuscles (e.g. Gescheider *et al.* 1997, Green 1977, Halonen 1986a). Below about 26°C, decreasing FSTs result in increasing vibrotactile thresholds. Decreasing the FST below approximately 22°C rapidly increases vibrotactile thresholds. When measuring vibrotactile thresholds, it is concluded the FST should be considered as having an influence on the results if it drops below about 26°C; measurements of vibrotactile thresholds when the FSTs are below 22°C are unlikely to be a true reflection of the function of mechanoreceptors.

2.6.1.2 Effects of noise

It has been reported that noise can trigger an attack of blanching (Bovenzi 1986) and hence might influence measurements of vascular function. Pyykkö *et al.* (1982) demonstrated a reduction in peripheral circulation during exposure to an auditory stimulus. It was decided that noise should be avoided in areas where measurements of vascular function are to be performed.

No studies have been found which address the effects of auditory noise levels on thermal or vibrotactile thresholds. It is hypothesised, however, that noise could mask the detection of thermal and vibrotactile thresholds by causing distractions or increasing fatigue. It has been shown that vibrotactile thresholds can be masked through a centrally mediated mechanism (Gilson 1969). In the case of vibrotactile thresholds, it has also been observed that the application of a vibration stimulus can provide an aural cue for the detection of thresholds. The use of hearing protection is considered beneficial and it was suggested this be worn by subjects during measurements of thermal and vibrotactile thresholds. An ambient noise level of 50 dB(A) was subjectively considered appropriate for implementation here.

2.6.2 Vibration

Effects of acute exposures to whole-body vibration on measures of vascular and neurological function are currently unknown. Ambient vibration during measurements of vibrotactile thresholds might alter the vibration stimulus applied to the finger. Ambient vibrations might also cause masking of vibrotactile and thermal thresholds. It was decided to avoid ambient vibration in this work.

Recent investigations have demonstrated significant changes in peripheral blood flow following acute exposure to hand-transmitted vibration. Bovenzi *et al.* (1995) showed that immediately after exposure to vibration, vasodilation occurred in the digital blood vessels, followed by a vasoconstriction. The vibration-induced vasoconstriction of the digital blood vessels resulted in significant decreases in FST between one and one and a half hours after vibration. The acute effects of exposure to hand-transmitted vibration on peripheral blood flow have been demonstrated repeatedly (e.g. Bovenzi *et al.* 1998). The duration of the effects are dependent on the frequency, magnitude and duration of vibration exposure (Bovenzi and Griffin 1997, Bovenzi *et al.* 1998). Any lasting effects of acute exposures to vibration on the response of the digital circulation to cold provocation are not currently known.

Various authors have reported temporary deterioration in the ability to perceive thermal and vibrotactile stimuli following acute exposures to hand-transmitted vibration (e.g. Hirosawa *et al.* 1992, Maeda 1994, Nishiyama and Watanabe 1981, Nishiyama and Taoda 1997). Such temporary threshold shifts were shown in these studies to have recovered within about 20 minutes of exposure to vibration. However, Bovenzi *et al.* (1997) showed a lasting temporary threshold shift in vibrotactile thresholds measured at the end of a work shift. Piette and Malchaire (1997) also show that recovery of the temporary shift in vibrotactile thresholds includes a more permanent component.

It was considered necessary to allow acute effects of exposures to hand-transmitted vibration on the peripheral circulation and the peripheral nervous system to recover before measures of neurological or vascular function are performed here. Further work is required to determine an optimal time interval without exposure to hand-transmitted vibration before measurements are performed, two hours is considered suitable here.

2.6.3 Disease and injury

2.6.3.1 Vascular measurements

There are many diseases and injuries known to result in abnormal peripheral blood flow or secondary Raynaud's phenomenon. Some examples are given by Arneklo-Nobin *et al.* (1987) and by Wigley (1993). No list of diseases or injuries that can influence measurements of vascular function is exhaustive. The occurrence of such conditions might have deleterious effects on the sensitivity and specificity of vascular tests to VWF and measurements should be interpreted with regard to the possibility of disease and injury.

2.6.3.1.1 Primary Raynaud's phenomenon

The constitutional condition known as primary Raynaud's phenomenon is of particular interest when attempting to diagnose VWF, VWF is a secondary form of Raynaud's phenomenon. Gemne (1997) suggests that before VWF can be diagnosed, primary Raynaud's phenomenon must be excluded. This is because of the high prevalence of the condition amongst the normal population. The reported prevalence of primary Raynaud's phenomenon ranges from 0.5% to 30% amongst different populations (Wigley 1993). When applying strict criteria to its diagnosis, the prevalence of primary Raynaud's phenomenon is more likely to be in the range 0.5% to 7.5% (e.g. Bartelink *et al.* 1992, Bovenzi *et al.* 1995, Bovenzi 1997, Wigley 1993).

Several studies have compared FSBPs between primary Raynaud's patients and VWF patients. Bovenzi (1993) showed digital vasoconstriction at 10°C was greater in subjects with primary Raynaud's phenomenon than in subjects with VWF. Similarly, Virokannas

and Rintamäki (1991) found that subjects with primary Raynaud's phenomenon tended to exhibit lower %FSBPs than subjects with VWF. The differences observed in these studies may have been due to milder symptoms in the VWF subjects than in the primary Raynaud's subjects. In a review of diagnostic methods for evaluating VWF, Ekenvall (1987) concluded that no test could distinguish between primary Raynaud's phenomenon and VWF. Gautherie *et al.* (1997), however, suggests that measurements of the FST response to cold provocation can be specific to VWF since the topography of dysfunction across the fingers and hands in VWF tends to be different to that found in primary Raynaud's phenomenon.

The vascular tests being investigated here may detect the occurrence of primary Raynaud's phenomenon and other forms of secondary Raynaud's phenomenon in addition to VWF. It was decided that an occupational and medical history would be used to determine if a measured hyperreactivity to cold provocation could be due to vascular disturbances resulting from vibration exposure, as suggested by Gemne (1997).

2.6.3.2 Neurological measurements

There are several diseases known to have a deleterious effect on the peripheral nervous system (e.g. Heijenbrok *et al.* 1992, Levy *et al.* 1987, Mito and Shimizu 1981, Schady *et al.* 1991). Injuries which result in compression of the median or ulnar nerve, such as carpal tunnel syndrome, or injuries or treatments which involve sympathectomies may also result in raised thresholds (e.g. Goadsby and Burke 1994, Lundborg *et al.* 1986, 1992). Exposure to neurotoxic agents in the workplace can also affect the peripheral nervous system (e.g. Kovala *et al.* 1997). Conditions of particular interest when monitoring neurological function in workers exposed to hand-transmitted vibration are peripheral alcoholic neuropathies, exposure to neurotoxic agents and diabetes mellitus. It was decided that the occurrence of neurological disorders with causes other than exposure to hand-transmitted vibration would be determined by obtaining a medical and occupational history.

2.6.4 Body size and mass

Body mass and size is known to influence systolic blood pressures (e.g. Hirai *et al.* 1976). The Body Mass Index (BMI), the ratio of weight to the square of the height, has been shown to influence FSBPs. This may be due to the amount of insulation being provided by adipose tissue differing between subjects with low and high BMIs (Hildegard *et al.* 1996). The effect may need to be considered but is unlikely to have a significant effect on the outcome of measurements performed in well controlled environments that do not require excessive thermo-regulation of the body.

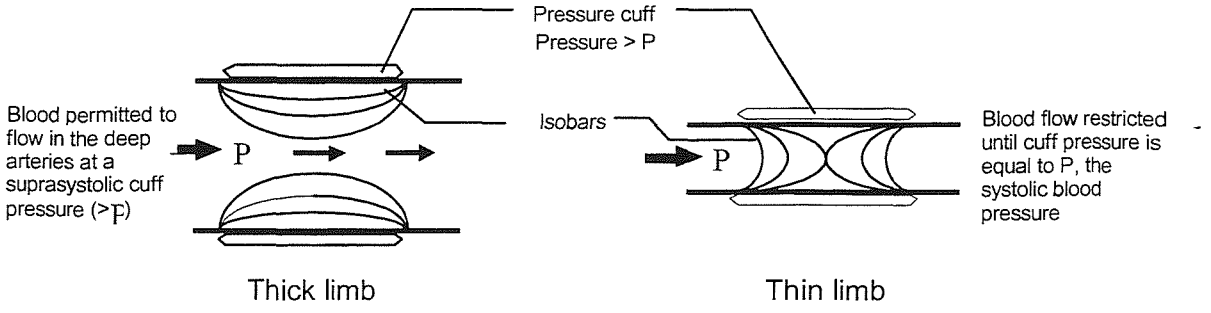


Figure 6 Simplified pressure distribution beneath occluding cuffs in a thick and thin finger.

Body size and mass do not significantly affect the results of neurological tests performed on the hand, although significant effects of height have been observed for neurological measurements on the toes (e.g. Bartlett *et al.* 1998). No such relationship exists for thermal or vibrotactile thresholds measured on the fingers (Hilz *et al* 1998, Gerr and Letz 1994). The height effect is most likely due to the longer axon going to the toe than to the finger (Skov *et al.* 1998). It was decided body size and mass need not be considered when measuring vibrotactile thresholds or thermal thresholds.

2.6.4.1 Finger and hand size

The relationship between finger size and the size of a pressure cuff has been shown to be important in the measurement of FSBPs (Hirai *et al. 1*976). This is because the variation of pressure beneath the cuff is not linear, but dependent upon the area of application of the pressure. Figure 6 shows a much simplified distribution of pressure in a thick and thin finger underneath the same sized pressure cuff. Hirai *et al.* (1976) showed that if a cuff width of 20% of finger diameter is used in preference to other sizes, the influence of finger size on pressure measurements is not observed. Finger size may need to be considered when selecting pressure cuffs for the measurement of FSBPs.

No studies have been found that investigate the effect of hand size on the FST response to cold provocation, although Bovenzi *et al.* (1995) demonstrated that finger blood flow was positively correlated with finger volume. It is possible that this is a cause of inter-subject variability, a large hand may require a longer period of cold provocation to reach the same temperature as a smaller hand. Current knowledge does not suggest that finger and hand size needs to be considered in this work when measuring the FST response to cold provocation.

It is possible that the size of the finger affects the distribution of mechanoreceptors within the skin. The total number of mechanoreceptors in each hand is constant at approximately 17,000 (Johansson and Vallbo 1984) and it might be hypothesised that in a

larger hand they are more dispersed. Since the Pacinian corpuscles exhibit spatial summation (Section 2.4.3.1.1), this could influence the vibrotactile thresholds. Any effects of the size of the finger or hand on thermal threshold are unknown. Further work could be performed to determine any influence of finger size over neurological measurements.

2.6.4.2 Finger skin thickness

It is unknown if finger skin thickness has an effect on measurements of vascular function. Levy *et al.* (1987) and Jamal *et al.* (1985) state that skin thickness affects thermal thresholds although Gelber *et al.* (1995) showed that neither vibrotactile thresholds nor thermal thresholds were different when measured on callused skin compared to smooth skin. It is likely that there is some inter-subject variability due to skin thickness so it was decided to avoid measurements on scarred or callused tissue in further work.

2.6.5 Age

An increase in peripheral circulatory and neurological insufficiencies is commonly observed in older subjects. Ageing may also influence vascular and neurological function directly. Changes in vascular function may be due to hardening of the digital arteries as a result of ageing. Reasons for age-related deterioration of nervous function have been suggested in the literature.

2.6.5.1 Vascular measurements

During measurements of the FST response to cold provocation, Saito *et al.* (1990) found older subjects reached lower immersion temperatures than younger subjects, little difference was observed between older and younger subjects during recovery of the FSTs. Spurr *et al.* (1955) demonstrated inhibition of the hunting phenomenon and slower recovery of FSTs from cold provocation in older subjects compared to younger subjects. Other authors have shown that age did not influence recovery of FSTs following cold provocation (Harada and Matsumoto 1981, Kurumatani *et al.* 1986).

For FSBPs, Bovenzi (1991) showed that age did not contribute significantly to variability in the measurement. Bovenzi (1993) studied 291 healthy males aged between 20 and 69 and found a difference only between the youngest and the eldest subjects. Older subjects showed higher FSBPs after thermal provocation at 30°C than younger subjects. Other authors have noted that FSBPs can be age-independent (Ekenvall and Lindblad 1982, Virokannas and Rintamäki 1991, Nielsen *et al.* 1980).

Whether there is an age effect on measures of FSTs and FSBPs following cold provocation remains inconclusive. It is likely, however, that there is a small effect that only becomes statistically significant when very old (>60 years) subjects are compared with very young (>25 years) subjects. Such a small effect may not be necessary to consider on a group basis.

2.6.5.2 Neurological measurements

The effects of age on vibrotactile thresholds are well documented. Vibrotactile thresholds for both the Meissner's and Pacinian corpuscles have been shown to increase with increasing age (e.g. Kenshalo 1986, Martina *et al.* 1998, Verrillo 1980). The ageing effect is non linear; above about 35 years, vibrotactile thresholds begin to deteriorate more rapidly than before that age (Bartlett *et al.* 1998, Halonen 1986a, Hilz *et al.* 1998, Skov *et al.* 1998). The cause of changes in vibrotactile thresholds with age is not fully understood (e.g. Elderson *et al.* 1989, Goble *et al.* 1996). Kenshalo (1986) hypothesised that the reasons for age-related changes in thresholds are: i) atrophy (up to 90% of Meissner's corpuscles can be lost due to age), ii) morphological changes, iii) diminishing mechanoreceptor densities and iv) histological changes in ageing skin. Goble *et al.* (1996) argue that the most likely of these mechanisms are changes in the density of the mechanoreceptors and morphological changes.

Reported ageing effects on thermal thresholds are contradictory (e.g. Bertelsmann *et al.* 1985, Dyck *et al.* 1984, Ekenvall *et al.* 1986b, Gelber *et al.* 1995, Gerr and Letz 1994, Levy *et al.* 1987, Merchut and Cone-Toleikis 1990). Kenshalo (1986) hypothesised that thermal thresholds were less likely to be affected by ageing than vibrotactile thresholds due to a lower susceptibility of the unmyelinated and small myelinated fibres to dystrophies of various types compared to the large myelinated fibres. Doeland *et al.* (1989) and Jamal *et al.* (1985) both demonstrate ageing effects in thermal thresholds and suggest these are due to a reduction in the number of nerve fibres with age, or to changes in the functional properties of the nerve fibres and associated end organs.

Whatever the reason for ageing effects in measures of vibrotactile and thermal thresholds, it was concluded age should be considered as a covariate in further work.

2.6.6 Gender

Nielsen *et al.* (1980) compared FSBPs measured in men and women and found no differences between the two groups. The influence of gender on the FST response to cold provocation was not identified from the literature. It remains inconclusive if there is an influence of gender on the vascular response to cold, further work is required. It was decided to use only male subjects in further work to avoid unknown variability.

Studies of the differences in neurological function between men and women are contradictory. Many studies have not revealed any significant gender differences (e.g. Claus *et al.* 1993, Halonen 1986a, Jamal *et al.* 1985, Kenshalo 1986). Halonen (1986b) and Hilz *et al.* (1998) both showed that the age-related changes in vibrotactile thresholds were different for men than for women. Lundström (1992) reported vibrotactile thresholds that were 1 dB to 2 dB lower for women than men. Using a tuning fork method, Martina *et al.* (1998) show lower vibrotactile thresholds at the internal malleolus for women than for men. Doeland *et al.* (1989) demonstrated lower thermal thresholds amongst women than amongst men. One possible reason for conflicting reports concerning gender effects may be the state of the menstrual cycle amongst women; vibrotactile thresholds have been shown to decrease during menstruation (Espritt *et al.* 1997).

The results of these studies suggest there may be some gender differences in neurological function but that these difference are small. Gender differences in neurological tests may need to be taken into account when forming normative data for thermal threshold measurements. In this work, it was decided to use only male subjects to remove added variability caused by using mixed gender subject groups.

2.6.7 Drug intake

There are several forms of medication that can significantly affect the peripheral circulation, and even some that can cause episodic blanching (e.g. Arneklo-Nobin 1987, Wigley 1993). There are also several prescribed medications that can alter neurological function and the peripheral circulatory system (e.g. Baldini *et al.* 1992, Elderson *et al.* 1989, Halonen 1986a). It was decided to exclude subjects who report the use of medications known to have effects on the peripheral circulation or on neurological function from further work.

2.6.8 Nicotine intake

Smoking is a risk factor in the development of peripheral vascular disease (e.g. artherosclerosis), as well as interfering with endothelial function and hence influencing vasospasm in response to cold (Ekenvall and Lindblad 1989). It has been suggested that the measurement of FSBPs in subjects with VWF may be more susceptible to the influence of nicotine on the vasomotor tone than measurements in healthy subjects (Ekenvall and Lindblad 1989). An increased response to cold has been observed amongst smokers compared to non-smokers in some studies (Bovenzi 1993, Arneklo-Nobin *et al.* 1987). Several authors, however, have found no influence of smoking status on either the FSBP response to cold provocation (Welsh 1986) or on

FSBPs (Bovenzi 1991, Ekenvall and Lindblad 1982, Maricq *et al.* 1996, Virokannas and Rintamäki 1991). It was decided that vascular measurements would continue to be interpreted with respect to chronic effects of nicotine intake on the vasculature.

Thermal thresholds measured on the fingers have been shown to be influenced by the smoking status of a subject, whilst vibrotactile thresholds are unchanged (Gerr and Letz 1994). The link between chronic effects of nicotine intake and neurological measurements is unclear but it may need to be considered when interpreting results.

The intake of nicotine has the result of inducing an immediate vasoconstriction in the cutaneous blood vessels. Such a change may favour an increased vasospasm in response to further vasoconstrictive stimuli such as cold. To determine the acute effects of tobacco consumption on cold-induced vasoconstriction, Ekenvall and Lindblad (1989) investigated the FSBPs in 30 healthy subjects: 10 smokers, 10 snuff users (oral intake of nicotine) and 10 non-users of tobacco products. Finger systolic blood pressures were measured after four hours without tobacco use. The subjects were re-examined after they had smoked a cigarette (smokers), taken snuff (snuff users) or rested (non-users). All subjects exhibited lower $\%FSBP_{15°C}$ and lower $\%FSBP_{10°C}$ in the second test. It was concluded that acute effects of nicotine intake would be avoided when measuring the vascular response to cold provocation by choosing either non-smoking subjects only, or by excluding its use for a period prior to measurements.

2.6.9 Alcohol intake

Available studies do not clearly indicate any chronic effects of alcohol intake on the measurement of vascular function. An immediate vasodilation following alcohol consumption, however, has a direct effect on the response of the digital arteries to cold provocation by abolishing or relieving exaggerated vasoconstriction (e.g. Ekenvall and Lindblad 1986, Nielsen and Lassen 1977). It was decided avoid acute effects of alcohol by excluding alcohol intake prior to measurements of vascular function.

Mild alcohol consumption has not been found to have long term effects on thermal or vibrotactile thresholds (Gerr and Letz 1994). Heavier alcohol consumption has been shown to result in raised vibrotactile thresholds at lower frequencies of measurement (Virokannas 1992). Raised thermal discrimination thresholds and vibrotactile thresholds resulting from polyneuropathies have been shown in cases of alcoholism (Gentile *et al.* 1993, Hilz *et al.* 1995). It may be necessary to consider chronic effects of excessive alcohol consumption as a possible cause of diminished thermal and vibrotactile sensibility.

2.6.10 Caffeine intake

No studies have been found that address the acute or chronic effects of caffeine consumption on the response of peripheral circulation to cold provocation. It might be hypothesised, however, that the vasoactive nature of caffeine may influence results of cold provocation tests.

The influence of caffeine on thermal thresholds measured at the thenar eminence was studied by Hilz *et al.* (1992). The authors found that after ingestion of a high dose of caffeine (0.5 g), hot thresholds were significantly lowered. There is no known effect of caffeine consumption on vibrotactile thresholds.

Further work is required to determine if acute effects of caffeine consumption do alter vascular and neurological measurements. Currently, it seems reasonable to avoid possible acute affects of caffeine by excluding its consumption prior to making measurements.

2.6.11 Time of day

It has been reported that the time of day has a direct influence over FSTs (Gautherie 1973). It is unknown whether these daily variations have a significant effect on the FST response to cold provocation or on FSBPs. It was decided that repeated measurements of the vascular response to cold should be made at the same times of day to prevent possible added intra-subject variability.

Ess and Dupuis (1992) reported results of measurements of vibrotactile thresholds made on 8 subjects at 2 hour intervals between 8 a.m. and 8 p.m. They found no systematic changes in thresholds during the course of the day. Strain *et al.* (1989) demonstrated that for both hot and cold thermal thresholds, no diurnal variations were evident for 11 young healthy men. Jamal *et al.* (1985) also report an absence of diurnal variations. It is concluded time of day need not be considered as an influencing factor when measuring thermal thresholds or vibrotactile thresholds.

2.6.12 Food intake

The intake of food prior to a vascular test might be hypothesised to change the response of the peripheral circulation to cold provocation; food intake increases the metabolic rate and might induce circulatory changes. Harada *et al.* (1997) investigated the effects of food intake on the FST response to cold provocation 1 hour after, 3 hours after and 13 hours after eating a meal. There were no differences between measurements made in the three conditions. These results suggest that acute effects of food intake on the circulation do not need to be taken into account when using vascular tests, food intake need not be considered in this work.

2.6.13 Pain

Pain can be experienced during objective tests of vascular function involving cold provocation (e.g. Arneklo-Nobin *et al.* 1987, Bovenzi 1993). Pain and discomfort, although subjective feelings, can result in physiological changes in the body, including the cardiovascular system. These feelings could be a cause of inter-subject variability. No studies have been found that address this subject directly.

Ekblom and Hansson (1987) reported results of thermal threshold measurements performed on subjects with acute pain from teeth or surrounding tissue, no effects of pain were found. It is possible, however, that the presence of pain during neurological threshold testing may cause masking if located at the site of threshold testing, or distraction.

In this work, it was decided that causing pain when measuring the peripheral vascular response to cold should be avoided where possible and that measurement of neurological function at sites that are painful should be avoided.

2.7 SUMMARY

A location with a low ambient noise level (less than about 50 dB(A)) and where sudden or loud noises are unlikely to occur would be suitable for performing the tests. Ear protection was considered beneficial for measurement of vibrotactile thresholds to avoid aural cues.

It was decided to control test environments at 20°C to 24°C with no noticeable air flow. Subjects would be habituated to the test environment before commencing measurements. The order of performing tests also has a direct influence over the interpretation of results, it was considered preferable to perform neurological tests first.

Results would be interpreted with respect to the health of the subject, the age and gender of the subject, and the intake of nicotine and alcohol prior to testing. It was decided to avoid acute effects of vaso-active and neuro-active substances.

Further work is required to more fully determine the influence of the time of day and seasonal variations over vascular measurements. Any effects of gender on the vascular tests should be investigated, as should acute effects of caffeine consumption on vascular and neurological tests.

2.8 CONCLUSIONS

It has been shown that measurements of FSBPs and the response of FSTs to cold provocation can be useful in detecting VWF. Thermal thresholds and vibrotactile thresholds can be useful in measuring peripheral neurological function. The literature shows that different measurement methods give different results. The measurement methods discussed in this chapter, and summarised below, have been shown by others to satisfy the criterion of repeatability and are considered practical to perform. Further work in this thesis will appraise the measurement methods using the criteria of sensitivity, specificity and responsiveness.

When appraising the measurement methods, it was decided they should be performed in a room of mean temperature 22°C (± 2°C) with an ambient noise level below about 50 dB(A). Control over vaso-active and neuro-active physical and chemical agents prior to measurements was recommended. Light indoor clothing was suggested as suitable, and subjects would be habituated to the test environment for 15 minutes before measurements begin, or until finger skin temperature was above 22°C.

When performed in the same session, it was considered preferable to perform neurological tests before vascular tests. It was decided some control over subject posture is required; subjects would be seated for neurological tests and seated or supine for vascular tests, the wrist would be held straight and the forearm and hand supported for both neurological and vascular tests. The measurement location has been shown to be of importance and it was concluded neurological tests would be performed on both hands using one finger innervated with the median nerve and one finger innervated with the ulnar nerve.

The method of limits with a rate of change of temperature of 1°C/s and a reference temperature between 30°C and 34°C was selected for measuring thermal thresholds. Application of the stimulus to the palmar surface of the most distal phalanx of the test finger by means of a smooth, flat surface contacting the finger with a force of 2 N was selected. The number of judgements made to determine thresholds would be sufficient to produce repeatable thresholds, three judgements was considered sufficient although five or six judgements was considered preferable.

It was decided to measure vibrotactile thresholds using the up-and-down method of limits with sinusoidal vibration at frequencies of 31.5 Hz and 125 Hz, a rate of change of vibration magnitude between 2 dB/s and 5 dB/s and a measurement duration of 45 seconds. A circular contactor, 6 mm diameter, concentric to a static annular surround,

allowing a gap of 2 mm between contactor and surround, was chosen for applying the vibration stimulus at the centre of the whorl on the most distal phalanx of the test finger. A finger push force on the surround of 2 N and a contactor force on the digit of 1 N were selected.

It was decided measurements of the FST response to cold provocation should be made on one hand with point transducers placed in good thermal contact with the skin. Provision of a settling period of a minimum of two minutes to allow the temperature of the test hand to stabilise in air was considered preferable. The test hand would then be placed within a thin waterproof covering before being immersed up to the wrist in stirred water controlled at 15 °C. After immersion of the hand for five minutes with no ischaemia, it would be removed from the water and the waterproof covering removed. It was decided to support the hand at heart level during a fifteen minute recovery period. Further work is required to determine the most accurate parameter of the rewarming curve in detecting vibration-induced white finger.

It was decided that finger systolic blood pressures would be obtained on one test finger simultaneously with a measurement on a reference finger, the latter measurement being obtained with an air-inflated pressure cuff. Water-perfused pressure cuffs were selected for measurements on the test finger, with all pressure cuffs being 24 mm wide. Mercury-in-elastic strain gauges were selected as the transducer for detecting blood flow, these being placed around the distal phalanges of the reference finger and the test finger. The chosen measurement procedure involves squeezing the tips of the fingers and then applying a supra-systolic pressure to all cuffs. Water, controlled at either 30°C, 15°C, or 10°C, would then perfuse the double-inlet cuffs for 5 minutes before all cuffs were gradually deflated. For analysis of the volume-pressure plot, it was decided to take the FSBP for a finger to be the cuff pressure at which the return of blood flow in that finger was first detected by the strain gauge.

The literature indicated that further work is required to investigate the relationship between skin indentation, contact forces and vibrotactile thresholds. For the measurements of FSBPs, any effects of cold provocation on the reference measurement, and effects of cooling more than one finger, are currently unknown and should be investigated. For both vascular tests, effects of exposure to local cold provocation immediately before measurements requires investigation.

CHAPTER 3 APPRAISAL OF MEASUREMENT METHODS IN DOCKYARD WORKERS EXPOSED TO HAND-TRANSMITTED VIBRATION

3.1 INTRODUCTION

An opportunity presented itself as part of an ongoing longitudinal study of vibration-induced white finger (VWF) in dockyard workers to carry out an experimental appraisal of the tests of vascular and neurological function. Methods for measuring finger systolic blood pressures (FSBPs), the finger skin temperature (FST) response to cold provocation, vibrotactile thresholds and thermal thresholds are defined in Chapter 2, Section 2.8. Before being able to recommend any particular test for measuring vascular and neurological function amongst workers exposed to hand-transmitted vibration, they should be appraised against the criteria specified in Chapter 1, Section 1.2 (repeatability, sensitivity, specificity, responsiveness and practicality).

3.1.1 Repeatability

The repeatability of the measurement methods has been studied by others. Several authors have suggested the measurement of FSBPs is repeatable: Bovenzi (1991) showed small coefficients of variation (CoV, 3.8% to 9.5%); Carnicelli *et al.* (1992) showed a slightly higher range (CoV, 5.4% to 29%) and Nielsen (1978) showed coefficients of variation of about 20%. The repeatability of the FST response to cold has been studied by Carnicelli *et al.* (1992), Howarth and Griffin (1989) and Hayward (1988), among others. Although coefficients of variation of between 14.9% and 91% have been reported (Hayward 1988 and Howarth and Griffin 1989 respectively), the authors concluded that the test was repeatable.

It is generally accepted that both of the neurological tests are repeatable; Carnicelli and Rice (1991) and Maeda and Griffin (1994) demonstrated the repeatability of vibrotactile threshold measurements using the method described in Chapter 2, whilst Ruffell and Griffin (1995) demonstrated the repeatability of the measurement method for thermal thresholds given in Chapter 2.

3.1.2 Sensitivity, specificity and responsiveness

The sensitivity and specificity of vascular measurements to VWF have been investigated by others (Table 2, Table 3). The different sensitivities and specificities reported allow different conclusions to be drawn about the validity of the tests with respect to the criteria of sensitivity and specificity. The sensitivity and specificity of a test is dependent upon the

severity of dysfunction amongst a patient group (Metz 1978); a difference in the severity of dysfunction in the study populations has been suggested as the cause of disagreement between authors (Pyykkö *et al.* 1986, Virokannas and Rintamäki 1991). This would suggest the tests exhibit responsiveness. Therefore, the methods of measuring the vascular response to cold proposed in Chapter 2 should be evaluated for their sensitivity, specificity and responsiveness within the same group of subjects.

The sensitivity and specificity of neurological test results to disorders associated with hand-transmitted vibration have been reported less often than the sensitivity and specificity of the cold provocation tests to VWF. For vibrotactile thresholds, Couto-Wakulczyk *et al.* (1997) found vibrotactile thresholds had a specificity of 61.7% to self-reported numbness. Wenemark *et al.* (1996) found sensitivities to reported numbness and problems with dexterity of 40 - 44% with specificities of 78 - 79%. Using data estimated from Ekenvall *et al.* (1986), the sensitivity to numbness, tingling or pain was 35% with a specificity of 93%. Lundborg *et al.* (1992) suggest a sensitivity to neuropathy resulting from vibration exposure of 80% with a specificity of 90%. Virokannas (1992) gives the sensitivity and specificity of the vibrotactile threshold test to 'indirectly evaluated vibration-induced nerve damage' as 68% and 90%, respectively. Kent *et al.* (1998) suggest that measurements of vibrotactile thresholds show a 'low' sensitivity and specificity to the hand-arm vibration syndrome (HAVS).

The range of reported sensitivities and specificities of vibrotactile threshold measurements is likely to have been influenced by several factors including: i) the equipment used to measure the vibrotactile thresholds (Wenemark *et al.* 1996), ii) the different indices of vibration perception used (e.g. *cf.* Sensibility Index, Lundborg *et al.* 1992 and peak-to-peak displacement at 100 Hz, Ekenvall *et al.* 1986), iii) the disorder under investigation (Couto-Wakulczyk *et al.* 1997) and iv) the cut-off value for distinguishing true positive and true negative cases (Virokannas 1992). Furthermore, the vibrotactile threshold test has been shown to be responsive both to the severity of neurological disorders and to vibration exposure (e.g. Bovenzi 1997, Ekenvall *et al.* 1989, Flodmark and Lundborg 1997, Lundström *et al.* 1995). The sensitivity, specificity and responsiveness of the measurement method defined in Chapter 2 should, therefore, be determined for the independent symptoms of blanching, tingling and numbness with reference to vibration exposure.

The sensitivity and specificity of thermal threshold tests to numbness and tingling have rarely been reported. Data from Ekenvall *et al.* (1986) suggest a sensitivity of 54% and a specificity of 98% to numbness, tingling or pain and data from Ekenvall *et al.* (1989)

suggest a sensitivity of 54% and a specificity of 92% to neurological symptoms above stage 1 on the Stockholm Workshop neurological scale. More commonly for thermal thresholds, differences between vibration exposed groups and controls, or between patient groups and controls, have been reported (e.g. Hirosawa *et al.* 1983a, 1983b, Lundström *et al.* 1998b, McGeoch *et al.* 1992). Hirosawa *et al.* (1983a, 1983b) also showed a strong relation between a staging of HAVS and thermal thresholds, implying responsiveness of this test to dysfunction. The lack of data concerning the sensitivity, specificity and responsiveness of measurements of thermal threshold requires its appraisal against these criteria.

By performing measurements of FSBPs, the FST response to cold provocation, vibrotactile thresholds and thermal thresholds on groups of manual workers with and without symptoms of HAVS, the sensitivity, specificity and responsiveness of the tests can be determined. This chapter outlines a longitudinal study that has been analysed in a cross-sectional manner to appraise the measurement methods using these criteria amongst groups of dockyard workers who have either i) not been exposed to hand-transmitted vibration, ii) been occupationally exposed to hand-transmitted but report no symptoms of HAVS or iii) been occupationally exposed to hand-transmitted vibration and report symptoms of HAVS.

3.2 SENSITIVITY, SPECIFICITY AND RESPONSIVENESS OF VASCULAR MEASUREMENTS

The sensitivity, specificity and responsiveness of vascular tests have been determined for a cohort of dockyard workers participating in a five year study designed to assess changes in neurological and vascular function with vibration exposure. During the third year of this study, FSBPs and the FST response to cold were measured using the methods defined in Chapter 2. These data have been analysed to appraise the sensitivity, specificity and responsiveness of the two vascular measurements to vibration-induced white finger (VWF).

It was expected that the two vascular tests would show both sensitivity and specificity to VWF. It was also hypothesised that the measurement of FSBPs would be more sensitive and specific to blanching when it occurs on the test finger than when it occurs on the test hand (Kurozawa *et al.* 1991). The results of the measurements were expected to be responsive to the severity of reported symptoms; an increased vasoconstrictive response to cold provocation was expected with increasing severity of VWF (e.g. Kurozawa *et al.* 1992).

3.2.1 Method

3.2.1.1 Subjects

One hundred and nine dockyard workers participated in the third year of the study. Of these, 45 were not exposed to vibration (unexposed control group), 37 were exposed to vibration but did not report blanching (exposed control group) and 27 were exposed to vibration and reported episodic blanching in response to cold (VWF group).

Subject characteristics, medical histories and vibration exposures were ascertained using an experimenter led questionnaire (Appendix B). Subjects characteristics and reports of symptoms related to vibration exposure are given in Table 4. There were significantly more smokers amongst subjects reporting blanching than amongst other workers ($p < 0.05$). Age and drinking habits were similar for controls and the VWF group ($p > 0.1$).

The vibrating tools that subjects reported having used during their work are summarised in Table 5. The estimated total duration of exposure to vibration, as reported by each subject, is shown in Figure 7. Vibration exposure was significantly higher for the workers reporting blanching than for the vibration-exposed control group (Table 4).

Table 4 Characteristics of subjects used to appraise the measurements of rewarming times and FSBPs.

	Overall	**Controls**		**VWF**
Number, N (%)	109 (100)	82 (75)		27 (25)
Age (years) median (IQR)	39 (17.5)	37.5 (16.5)		42 (18.0)
Smokers, N (%)	37 (33.9)	29 (35.4)		8 (29.6)*
Regular drinkers, N (%)	55 (50.5)	40 (48.8)		15 (55.6)
		Unexposed	**Exposed**	**Exposed**
Number, N (%)		45 (41)	37 (34)	27 (25)
Numbness, N (%)	40 (36.7)	0	14 (37.8)	26 (96.3)
Tingling, N (%)	34 (31.2)	0	16 (43.2)	18 (66.7)
Lifetime vibration exposure (hrs), median (IQR)	5855 (20550)	0	12024 (19806)	22809 (22755)**

Differences between controls and subjects reporting VWF, Mann-Whitney U: * $p < 0.05$; ** $p < 0.01$

Table 5 Tools used by subjects participating in the appraisal of objective tests of vascular function. The number of subjects using each tool is shown in brackets.

Caulking tools (13)	Drills (34)	Grinders (34)	Impact wrenches (13)	Nibblers (3)
Other tools (14)	Sanders (4)	Saws (28)	Scalars (1)	Riveting tools (4)

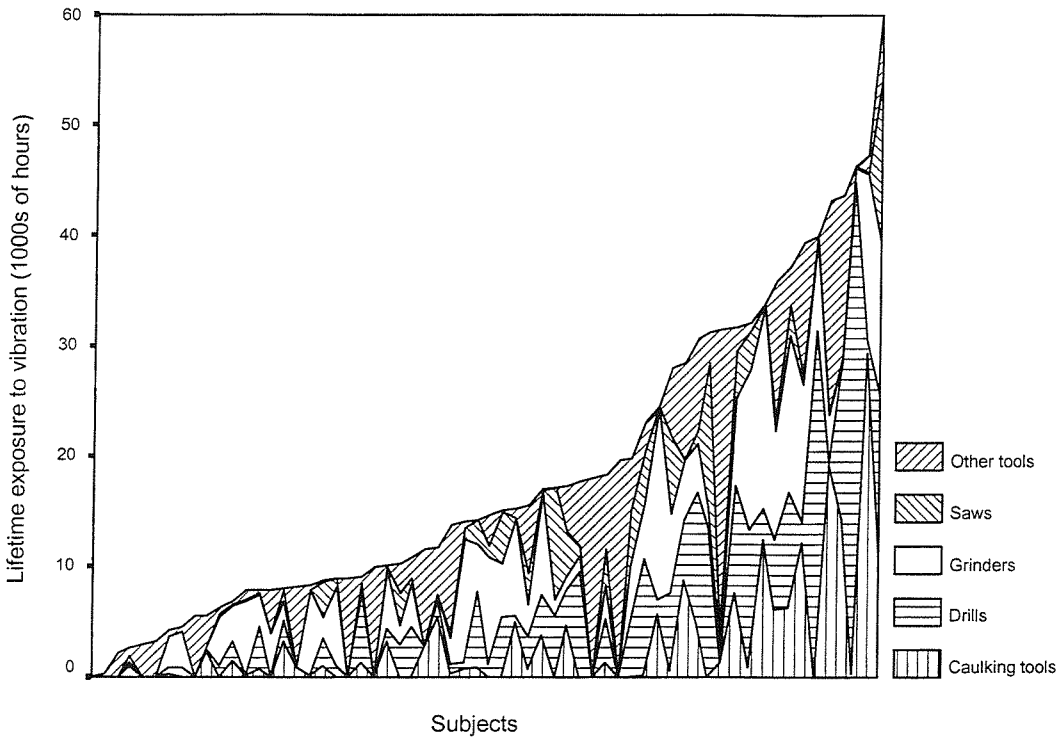


Figure 7 Lifetime exposure to hand-transmitted vibration for vibration exposed subjects participating in the appraisal of tests of vascular function. The area under the curve has been shaded to show the proportion of total exposure to caulking tools, drills, grinders, saws and other tools.

3.2.1.2 Experimental Procedure

Subjects were asked to refrain from smoking for one hour, and from drinking alcohol for 12 hours, prior to attending for examination. On arrival, they were acclimatised to the test environment (20°C to 25°C) until the skin temperature of the middle finger of the right hand was a minimum of 22°C. The FSBPs on the right hand were measured before the FST response to cold on the left hand. During testing, subjects were led through the questionnaire to determine their symptom history and vibration exposure history. Each session lasted approximately one and a half hours. In this year of the study, data were gathered by Mr. A Hadlington.

3.2.1.2.1 Finger systolic blood pressures

The FSBPs were measured using the method defined in Chapter 2, Section 2.8. Briefly, the right hand was instrumented; a double-inlet plastic bag type cuff was placed around the medial phalanx of the test finger (middle finger) and a single-inlet air cuff was placed around the medial phalanx of the reference finger (ring finger). Mercury-in-elastic strain gauges were placed around the distal phalanges of the test finger and the reference finger at the base of the nail. The fingers were squeezed and cuffs were inflated to a suprasystolic pressure of 250 mmHg. For the first measurement, water controlled at 30°C

perfused the double-inlet cuff at a pressure of 250 mmHg for five minutes. The pressure was subsequently reduced until blood flow was detected in the instrumented fingers. Blood flow was defined as the point at which a volume increase was observed, or the first pulse was observed, by means of the strain gauge (Section 2.2.2). The procedure was repeated for a water temperature of 15°C and then for a water temperature of 10°C. Percentage FSBPs were calculated using Equation 1, Section 2.2.7.1. Measurements were made using a Medimatic DM2000 plethysmograph with digit cooling unit. The apparatus is described in more detail in Appendix A.

3.2.1.2.2 Finger skin temperature response to cold provocation

The responses of the FSTs to cold provocation were measured using an *HVLab* 8-Channel Temperature Monitor (Appendix A). Thermocouples were taped to the palmar surface of the left (cooled) hand and the right (control) hand in the locations shown in Figure 8. Thermocouples on the distal phalanges were taped at the centre of the whorl on the finger pad. Thermocouples on the medial and proximal phalanx of the middle finger of the left hand were taped on the mid-axillary line midway between the inter-phalangeal joints. The thermocouple on the palm of the left hand was placed 1 cm below the base of the middle finger.

The FSTs were allowed to settle for two minutes with the subject seated and the arms rested at heart height. A thin-walled plastic bag was then placed over the left (cooled) hand and it was immersed to the level of the wrist on both the palmar and dorsal surface in water controlled at 15°C. A 5 minute period elapsed before the hand was lifted from the water and the bag removed. The hand and arm were rested at heart height for a further 15 minutes. The FSTs were monitored throughout.

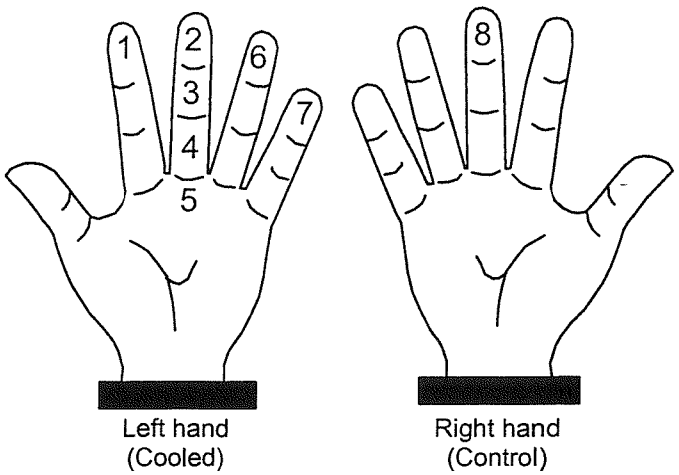


Figure 8 Thermocouple locations for the measurement of the FST response to cold provocation.

3.2.2 Results

3.2.2.1 Finger systolic blood pressures

The FSBPs measured after thermal provocation at 30°C, 15°C and 10°C, and the percentage FSBPs, are shown in Table 6. The FSBPs at 10°C and percentage FSBPs at 15°C and 10°C were significantly lower amongst the VWF group than amongst the control groups. Measurements made at 15°C were significantly positively correlated with measurements made at 10°C (Table 8).

3.2.2.1.1 Sensitivity and specificity

3.2.2.1.1.1 Receiver operating characteristics

One hundred and nine combinations of sensitivity and specificity to blanching on a test hand were calculated to obtain the ROC curves plotted in Figure 9. Each subject's percentage FSBP was used as a threshold value below which the results were said to positively indicate the presence of blanching. To determine if the tests were more sensitive and specific to blanching on the test finger than on the test hand, ROC curves have also been plotted for detecting blanching on the test finger (Figure 10). Of those reporting blanching, 22 subjects reported blanching of the test finger, 9 on the distal phalanx only, 10 on both the medial and distal phalanges and 3 along the entire length of the finger.

Table 6 Finger systolic blood pressures measured after thermal provocation of the middle (test) finger at 30°C, 15°C and 10°C. Medians (interquartile ranges) are shown for the test finger and the reference finger. Percentage FSBPs are also shown.

	All controls (N = 82)	Unexposed controls (N = 45)	Exposed controls (N = 37)	VWF (N = 27)
$FSBP_{30°C, test}$	138 (28)	137 (29)	138 (26)	134 (13)
$FSBP_{30°C, reference}$	138 (26)	139 (25)	138 (26)	135 (11)
$FSBP_{15°C, test}$	132 (34)	131 (36)	132 (33)	115 (48)
$FSBP_{15°C, reference}$	142 (25)	139 (24)	143 (27)	145 (19)
$FSBP_{10°C, test}$	125 (28)**	125 (30)*	126 (30)*	112 (27)
$FSBP_{10°C, reference}$	140 (23)	143 (27)	138 (22)	145 (22)
$\%FSBP_{15°C}$	92.3 (15.4)*	92.1 (18.4)*	92.8 (22.0)*	79.6 (21.9)
$\%FSBP_{10°C}$	89.6 (12.0)**	88.6 (10.3)**	93.1 (18.0)**	79.1 (18.0)

Mann-Whitney U, differences from VWF group: * $p < 0.05$; ** $p < 0.01$

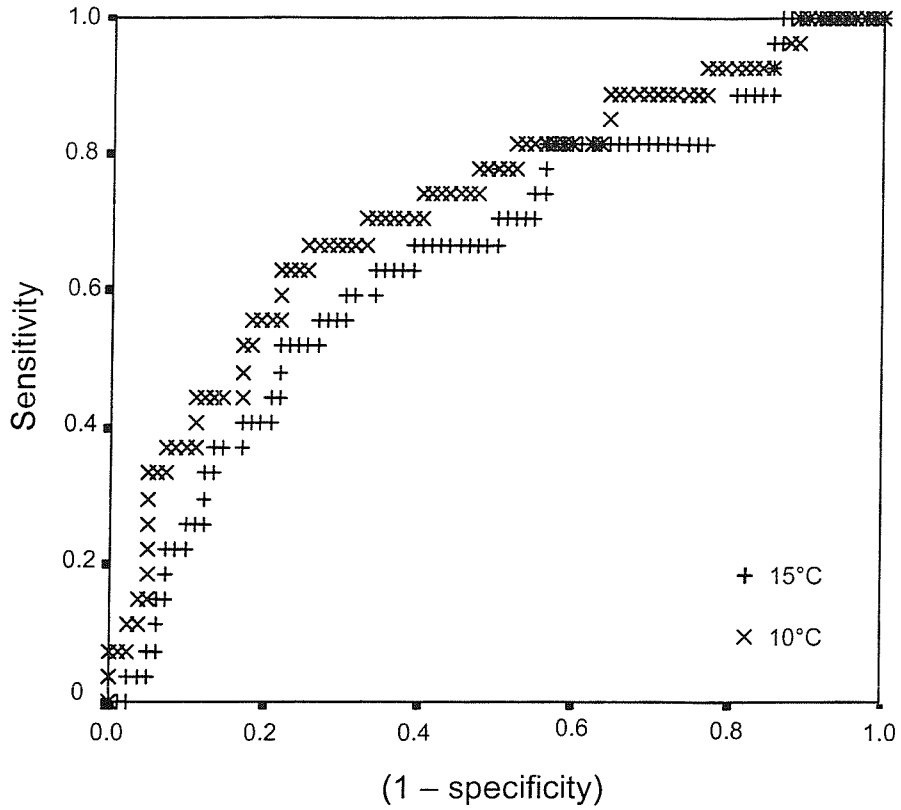


Figure 9 Receiver operating characteristic curves for percentage FSBPs at 15°C and 10°C for detecting the presence of blanching on the test hand of 109 subjects, 27 of whom reported symptoms of VWF.

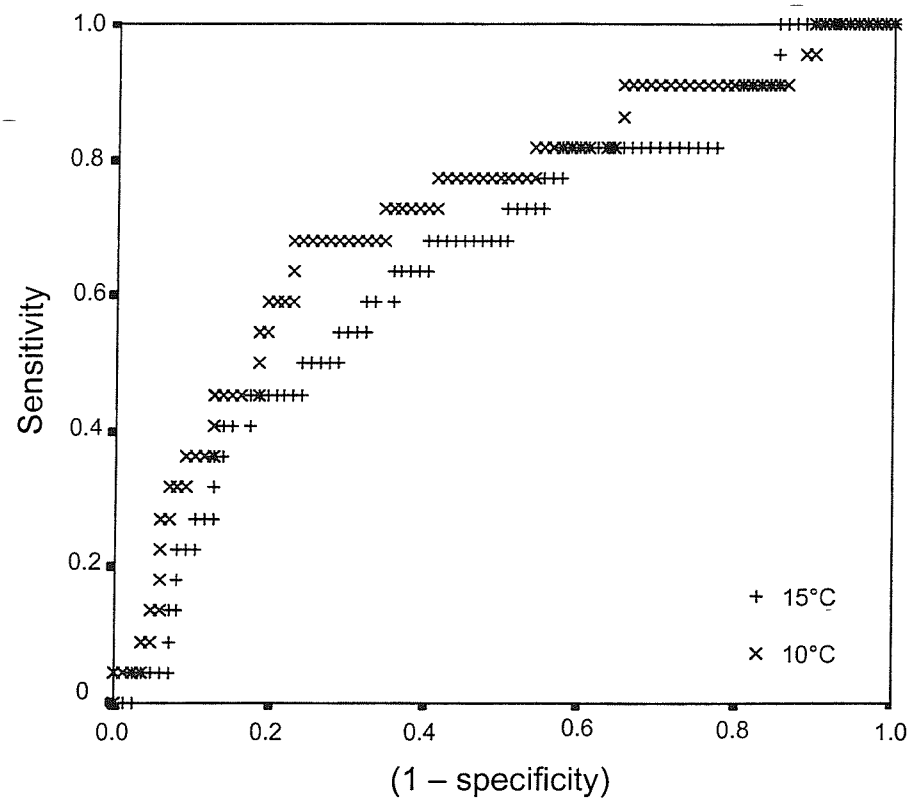


Figure 10 Receiver operating characteristic curves for percentage FSBPs at 15°C and 10°C for detecting blanching on the test finger of 109 subjects, 22 of whom reported symptoms of VWF on the test finger.

3.2.2.1.1.2 Lower normal limits

The lower normal limits, calculated as the mean minus two standard deviations of the percentage FSBPs at 15°C and 10°C, are shown in Table 7 for exposed controls, unexposed controls and for all controls. For a normal distribution, this is the lower limit above which 97.5% of data falls. The percentage FSBPs were normally distributed amongst the control group (Kolmogorov-Smirnov, $p > 0.073$) and hence this limit should correspond to a specificity of 97.5%. The calculated sensitivities and specificities are given in Table 7.

Table 7 Lower normal limits and corresponding sensitivities and specificities to the presence of blanching.

		Unexposed controls (N = 45)	Exposed controls (N = 37)	All controls (N = 82)
15°C	Lower normal limit (mmHg)	55.3	48.8	61.5
	Sensitivity (%)	1.2	0	3.6
	Specificity (%)	100	100	96.7
10°C	Lower normal limit (mmHg)	68.0	57.1	65.0
	Sensitivity (%)	2.4	0	2.4
	Specificity (%)	88.9	100	92.6

Table 8 Spearman's ρ correlation coefficients for the associations between percentage FSBPs, blanching scores and vibration exposure. The upper portion of the table shows coefficients for all vibration-exposed subjects (N=64) and the lower portion shows coefficients for subjects reporting blanching (N=27).

	%FSBP$_{10°C}$	%FSBP$_{15°C}$	Blanching score	Blanching score, test digit	Lifetime exposure to vibration (hours)	Lifetime exposure to vibration (years)	Exposure to vibration in preceding year (hours)
%FSBP$_{10°C}$	—	0.703**	-0.413**	-0.345**	-0.242*	-0.211*	-0.170
%FSBP$_{15°C}$	0.625**	—	-0.356**	-0.298**	-0.209*	-0.125	-0.107
Blanching score	-0.175	-0.285	—	0.885**	0.321**	0.198	-0.055
Blanching score, test digit	-0.051	-0.188	0.677**	—	0.199	0.110	-0.115
Lifetime exposure to vibration (hours)	-0.054	-0.142	0.031	-0.208	—	-0.550**	0.167
Lifetime exposure to vibration (years)	0.026	-0.189	0.046	-0.013	0.382*	—	-0.140
Exposure to vibration in preceding year (hours)	-0.401**	-0.224	0.105	-0.056	0.141	-0.105	—

Spearman's ρ: * $p < 0.05$; ** $p < 0.01$

3.2.2.1.2 Responsiveness

Correlation coefficients have been used to identify associations between percentage FSBPs, exposures to vibration and blanching scores. One-tailed tests of significance have been performed; it was expected that percentage FSBPs would decrease with both increasing duration of vibration exposure and with increasing blanching score, whilst blanching score would increase with increasing duration of vibration exposure. Table 8 shows two sets of correlation coefficients, one calculated for all vibration-exposed subjects (upper portion), and one calculated for subjects reporting blanching (lower portion). Three measures of vibration exposure have been investigated: i) the estimated duration of lifetime exposure measured in hours, ii) the number of years of vibration exposure, and iii) the duration of exposure to vibration in the year preceding the tests. Correlation coefficients have been calculated both for overall blanching score and for blanching score on the test digit.

3.2.2.2 Finger skin temperature response to cold provocation

The times taken for the FST to rise by 3°C, 4°C and 6°C from the temperature at the end of the immersion period have been used to evaluate the sensitivity, specificity and responsiveness of this test to VWF. These parameters were selected as they have been shown to be repeatable (Carnicelli *et al.* 1992, Howarth and Griffin 1989). Data for the three groups of subjects (exposed controls, unexposed controls and the VWF group), and for the two control groups combined, are shown in Table 9. Measurements made on the control hand are not shown; this site rarely exhibited temperature variations as great as 3°C. There were no significant differences between any of the groups of subjects for the parameters investigated.

The three parameters investigated were significantly positively correlated with each other at each measurement location ($p < 0.01$). Each parameter was significantly positively correlated between locations ($p < 0.05$) with two exceptions: i) the time to rise by 3°C on the medial phalanx of the middle finger was not related to the time to rise by 3°C on the distal phalanx of the little finger ($p = 0.132$), and ii) no measurements made on the medial phalanx of the middle finger correlated with measurements made on the palm ($p > 0.1$).

3.2.2.2.1 Sensitivity and specificity

3.2.2.2.1.1 Receiver operating characteristics

Receiver operating characteristics have been calculated for each thermocouple for the times for FSTs to rise by 3°C, 4°C and 6°C. The ROC curves shown in Figure 11 were calculated using 109 combinations of specificity and sensitivity for each curve. For each combination, the threshold values below which positive results were indicated corresponded to one subject's result for that measurement.

Table 9 Median (interquartile range) times taken for FSTs to rise by 3°C, 4°C and 6°C following cold provocation. There were no significant differences in the various measurements between the groups of subjects.

Location	Time to rise by	All controls (N = 82)	Unexposed controls (N = 45)	Exposed controls (N = 37)	VWF (N = 27)
Index	3°C	141 (136)	129 (108)	124 (113)	148 (94)
	4°C	228 (224)	168 (141)	170 (210)	235 (180)
	6°C	360 (577)	296 (333)	286 (267)	363 (446)
Middle, distal	3°C	134 (147)	117 (97)	128 (103)	128 (118)
	4°C	224 (266)	186 (138)	208 (185)	225 (251)
	6°C	418 (547)	349 (362)	280 (285)	369 (548)
Middle, medial	3°C	131 (228)	106 (166)	124 (229)	233 (326)
	4°C	262 (324)	262 (290)	256 (241)	380 (403)
	6°C	414 (564)	378 (518)	410 (373)	564 (560)
Middle, proximal	3°C	96 (243)	90 (135)	102 (331)	101 (305)
	4°C	234 (352)	204 (294)	232 (354)	321 (491)
	6°C	465 (369)	448 (622)	410 (408)	567 (546)
Middle, palm	3°C	63 (83)	62 (67)	50 (229)	84 (105)
	4°C	99 (188)	94 (92)	104 (416)	125 (161)
	6°C	233 (668)	166 (187)	236 (618)	289 (737)
Ring	3°C	141 (186)	141 (133)	90 (97)	121 (149)
	4°C	201 (296)	172 (207)	152 (205)	218 (186)
	6°C	397 (475)	350 (338)	296 (229)	415 (353)
Little	3°C	161 (121)	160 (103)	138 (85)	178 (103)
	4°C	272 (247)	207 (156)	210 (137)	259 (198)
	6°C	414 (592)	329 (302)	334 (235)	421 (531)

3.2.2.2.1.2 Normal limits

The normal limits for the times for FSTs to rise by 3°C, 4°C and 6°C have been calculated as the mean plus two standard deviations for unexposed controls, exposed controls and for the two control groups combined. The corresponding sensitivities and specificities are shown in Table 10.

3.2.2.2.2 Responsiveness

The association between the times for FSTs to rise by 3°C, 4°C and 6°C, blanching scores and the duration of vibration exposure were investigated using Spearman's ρ correlation coefficients. One-tailed tests of significance were used; the time for FSTs to rise by 3°C, 4°C and 6°C were expected to increase with increasing blanching score and with increasing duration of vibration exposure. The results are shown in Table 11. The relationship between duration of exposure to vibration and blanching is shown in Table 8.

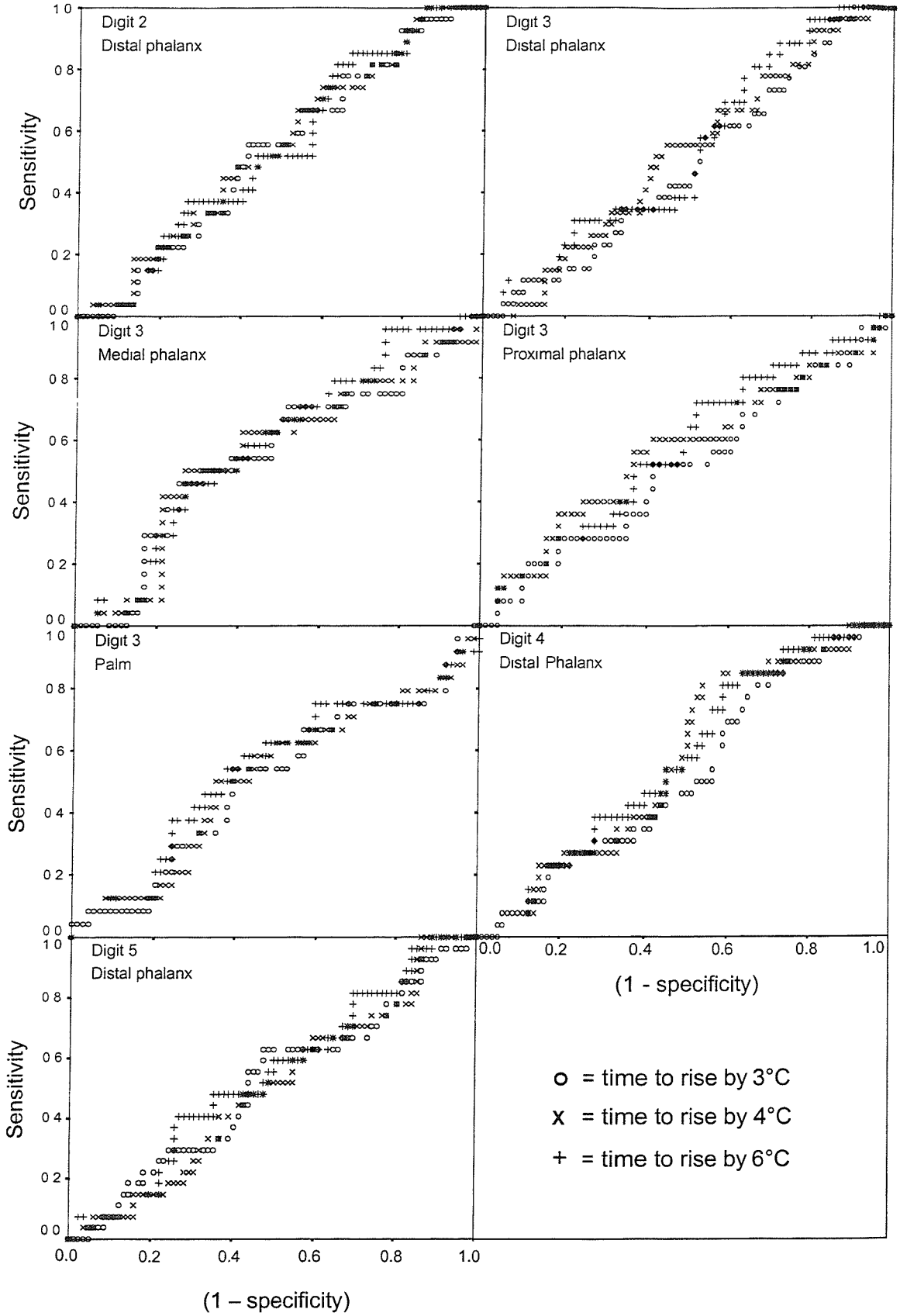


Figure 11 ROC curves for the detection of blanching by the response of FSTs to cold provocation. Curves are shown for the times taken for the FSTs to rise by 3°C, 4°C and 6°C for each measurement location. Of the 109 data points, 27 are for subjects reporting blanching.

Table 10 Normal limits and corresponding sensitivities and specificities for the time taken for FSTs to rise by 3°C, 4°C and 6°C.

Time to rise by	Location		Unexposed (N = 45)	Exposed (N = 37)	All (N = 82)
3°C	Index	Normal Limit (s)	228	350	413
		Sensitivity	23 2	14 6	11 0
		Specificity	77 8	88 9	96 3
	Middle, distal	Normal Limit (s)	311	334	428
		Sensitivity	11 1	9 9	9 9
		Specificity	88 5	92 4	92 4
	Middle, medial	Normal Limit (s)	438	582	587
		Sensitivity	16 9	12 7	12 7
		Specificity	87 5	100	100
	Middle, proximal	Normal Limit (s)	360	764	492
		Sensitivity	19 1	4 4	11 8
		Specificity	72	96 0	84 0
	Middle, palm	Normal Limit (s)	196	508	229
		Sensitivity	18 9	6 8	18 9
		Specificity	91 7	91 7	91 7
	Ring	Normal Limit (s)	407	284	513
		Sensitivity	12 5	22 5	10
		Specificity	92 3	76 9	92 3
	Little	Normal Limit (s)	366	308	403
		Sensitivity	12 2	13 4	11 0
		Specificity	92 6	85 2	92 6
4°C	Index	Normal Limit (s)	450	590	676
		Sensitivity	14 6	13 4	13 4
		Specificity	81 5	92 6	96 3
	Middle, distal	Normal Limit (s)	462	578	756
		Sensitivity	18 8	15 0	10
		Specificity	95 2	95 2	96 3
	Middle, medial	Normal Limit (s)	84 2	738	910
		Sensitivity	12 7	16 9	0
		Specificity	95 9	91 7	100
	Middle, proximal	Normal Limit (s)	792	940	938
		Sensitivity	14 7	0	0
		Specificity	84	100	100
	Middle, palm	Normal Limit (s)	278	936	475
		Sensitivity	23 0	0	18 9
		Specificity	83 3	100	87 5
	Ring	Normal Limit (s)	586	562	793
		Sensitivity	15 0	15	12 5
		Specificity	76 9	76 9	92 3
	Little	Normal Limit (s)	519	484	766
		Sensitivity	13 4	15 9	6 1
		Specificity	92 6	88 9	96 3
6°C	Index	Normal Limit (s)	962	820	1514
		Sensitivity	0	22 0	0
		Specificity	100	74 1	100
	Middle, distal	Normal Limit (s)	1073	850	1512
		Sensitivity	0	22 2	0
		Specificity	100	87 0	100
	Middle, medial	Normal Limit (s)	1414	1156	1542
		Sensitivity	0	0	0
		Specificity	100	100	100
	Middle, proximal	Normal Limit (s)	1692	1226	1203
		Sensitivity	0	0	0
		Specificity	100	100	100
	Middle, palm	Normal Limit (s)	540	1472	1569
		Sensitivity	33 8	0	0
		Specificity	54 2	100	100
	Ring	Normal Limit (s)	1026	754	1347
		Sensitivity	0	23 8	0
		Specificity	100	73 1	100
	Little	Normal Limit (s)	933	804	1598
		Sensitivity	0	25 6	0
		Specificity	100	74 1	100

Table 11 Spearman's ρ correlation coefficients for the associations between the times for FSTs to rise by 3°C, 4°C and 6°C, blanching scores and duration of vibration exposure. Correlation coefficients are given for all vibration-exposed workers and for subjects reporting blanching.

		Vibration exposed subjects (N=64)					Subjects reporting blanching (N=27)				
Location	Time to rise by	Blanching score	Blanching score, test digit	Lifetime exposure to vibration (hours)	Lifetime exposure to vibration (years)	Exposure to vibration in preceding year (hours)	Blanching score	Blanching score, test digit	Lifetime exposure to vibration (hours)	Lifetime exposure to vibration (years)	Exposure to vibration in preceding year (hours)
Index	3°C	0.050	0.059	0.168	0.145	-0.253*	-0.195	-0.004	0.192	0.014	-0.255
	4°C	0.109	0.104	0.218*	0.155	-0.253*	0.073	0.106	0.201	0.161	-0.320
	6°C	0.127	0.108	0.287*	0.190	-0.172	0.068	0.050	0.193	0.159	-0.267
Middle distal	3°C	0.021	-0.063	0.183	-0.102	-0.059	-0.089	-0.279	0.325	-0.189	-0.084
	4°C	0.133	0.055	0.218*	-0.006	-0.062	0.080	-0.114	0.292	-0.042	-0.080
	6°C	0.137	0.071	0.243*	0.051	-0.017	0.063	-0.055	0.259	0.016	-0.166
Middle medial	3°C	0.074	0.090	0.160	0.191	0.027	-0.110	0.038	-0.458*	-0.143	0.014
	4°C	0.040	0.061	0.263*	0.218	0.069	-0.337	-0.160	-0.220	-0.046	-0.028
	6°C	0.179	0.171	0.409**	0.195	0.009	-0.125	0.004	0.145	0.129	-0.292
Middle proximal	3°C	-0.014	0.035	0.217*	0.081	-0.008	0.179	0.143	0.132	0.022	-0.221
	4°C	0.119	0.140	0.279*	0.069	0.016	0.235	0.143	0.214	-0.033	-0.295
	6°C	0.194	0.207	0.384**	0.186	-0.051	0.169	0.193	0.238	0.073	-0.367*
Middle palm	3°C	-0.039	-0.044	-0.081	-0.126	-0.095	-0.021	-0.008	0.113	-0.104	-0.079
	4°C	-0.029	-0.019	-0.036	-0.130	-0.134	0.059	0.124	0.124	-0.140	-0.244
	6°C	-0.015	0.003	-0.031	-0.077	-0.216	-0.138	0.023	0.000	-0.106	-0.547**
Ring	3°C	0.137	0.085	0.145	-0.082	0.016	0.016	0.063	0.384*	-0.048	0.207
	4°C	0.194	0.111	0.216	0.021	-0.040	0.193	0.041	0.394*	0.121	0.037
	6°C	0.190	0.141	0.278*	0.112	-0.058	0.144	0.098	0.290	0.053	-0.114
Little	3°C	0.057	0.017	0.269*	0.081	-0.127	-0.079	-0.031	0.022	-0.151	-0.290
	4°C	0.049	0.045	0.295**	0.104	-0.075	0.005	0.042	0.079	-0.097	-0.238
	6°C	0.128	0.129	0.351**	0.067	-0.104	0.122	0.155	0.249	-0.041	-0.331*

Spearman's ρ: * $p < 0.05$; ** $p < 0.01$

3.2.3 Discussion

3.2.3.1 Finger systolic blood pressures

Measurements of FSBPs have been shown in the literature to be lower amongst subjects with VWF than amongst control groups without VWF (e.g. Bovenzi 1998, Olsen *et al.* 1981). This study showed similar findings, the FSBPs at 10°C were significantly lower amongst subjects reporting VWF than amongst the control groups (Table 6).

Decreasing the temperature of cold provocation has been shown to increase exaggerated cold-induced vasodilation (e.g. Kurozawa et al. 1991, Nielsen and Lassen 1977). Similarly in this study, FSBPs at 10°C were significantly lower amongst workers reporting VWF than amongst the control workers whilst cold provocation at 15°C was not sufficient to induce a significant difference between the VWF group and control subjects (Table 6).

The calculation of percentage FSBPs has the effect of decreasing the inter-subject variability of the measurement (Table 6); changes in systemic systolic blood pressure are taken into account in the results. Both percentage FSBPs at 15°C and those at 10°C were significantly lower amongst the VWF group than among the control group (Table 6). This implies the need to correct for changes in systemic systolic blood pressure. The calculation increased the difference between subjects with VWF and subjects without VWF. It is concluded that this correction is useful when interpreting measurements of FSBPs. However, differences in the effect of cold provocation of a test finger on the arm systolic blood pressure and the reference FSBP between groups with VWF and control groups have been reported (Ekenvall and Lindblad 1986, Nielsen 1978). Effects of cold provocation of a test finger on reference FSBPs is further investigated in Section 5.2, Chapter 5.

3.2.3.1.1 Sensitivity and specificity of percentage FSBPs

Comparison of the ROCs for percentage FSBPs at 15°C and 10°C show that the colder measurement is more sensitive and specific to VWF than the measurement at 15°C. This is consistent with other studies (e.g. Bovenzi 1993, Kurozawa *et al.* 1991, Olsen *et al.* 1981, Virokannas and Rintamäki 1991). Decreasing the temperature of cold provocation increased the digital vasoconstriction amongst the VWF group.

Nielsen (1978) suggests that the measurement of FSBPs could be simplified by making measurements after cooling to 15°C only. In the subjects used here, this would have resulted in a higher number of false negative outcomes (decreased sensitivity) than the 10°C measurement for a given specificity. If it is considered necessary to improve the practicality of the test by shortening test time, it might be reasonable to stop the test if exaggerated vasoconstriction is observed at 15°C. A further measurement at 10°C would then be required where expected confirmatory evidence of VWF was not found at 15°C.

The sensitivity and specificity of percentage FSBPs to blanching on the test finger was higher than the sensitivity and specificity to blanching on the test hand (*cf.* Figure 9 and Figure 10). This suggests that measurements of FSBPs are dependent on blanching on a test finger more so than on a test hand. Although the pathogenesis of VWF is not fully

understood, several mechanisms are thought to play a part in its development including: i) hyperreactivity of the central sympathetic nervous system, ii) local faults including morphological changes in the smooth muscle wall of affected blood vessels, iii) damage to the vasoregulatory function of vessel walls and iv) endothelial damage (e.g. Gemne 1994, Olsen 1987). The finding of this study agrees with the hypothesis that episodic blanching in response to cold is at least partly a local dysfunction. Measurements on more than one finger would be beneficial in determining the number of fingers affected with blanching in a subject with VWF, i.e. the severity of dysfunction. The measurement of FSBPs on more than one test finger is considered further in Chapter 4.

The ROCs for percentage FSBPs show that the measurement can be sensitive and specific to VWF. However, when the cut-off value between positive and negative test results was defined by calculation of normal limits (Table 7), the test did not appear useful for detecting VWF, even though the normal limits obtained were similar in this study to those reported by others (e.g. Ekenvall and Lindblad 1986, Bovenzi 1991). The normal limit for percentage FSBPs was calculated as 76% by Virokannas and Rintamäki (1991) using ROCs. Figure 12 compares the ROC curve obtained by these authors to the ROC curves obtained in this study. When applying a normal limit of 76% to the data presented here, the sensitivity was 37% for percentage FSBPs at 15°C and 10°C and the specificity was 89% at 15°C and 87% at 10°C; these results are similar to those reported by Virokannas and Rintamäki (1991).

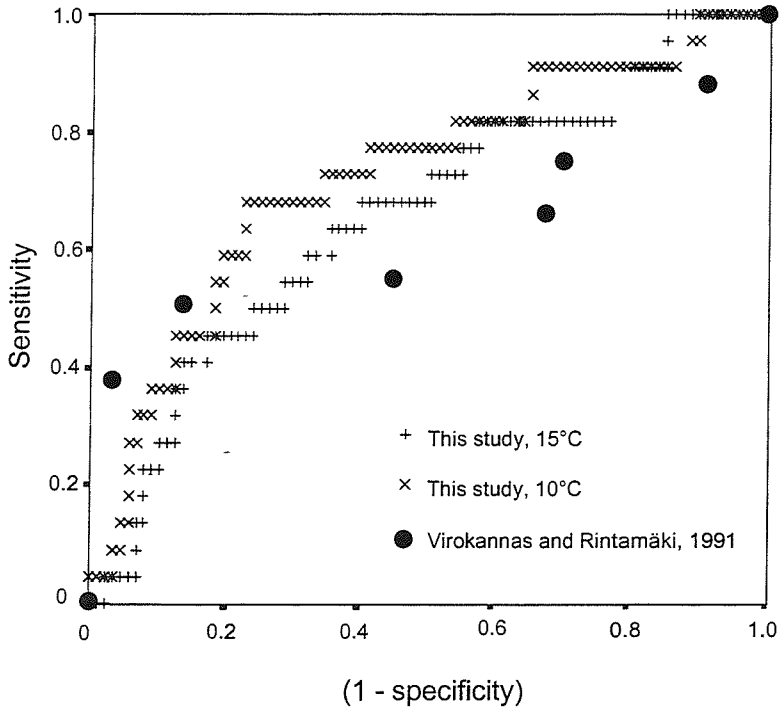


Figure 12 Receiver operating characteristics for percentage FSBPs at 15°C and 10°C for detecting blanching on the test finger. Data estimated from Virokannas and Rintamäki (1991) have been overlaid.

Pyykkö *et al.* (1986) suggested a low specificity to reported blanching in their study was due to using subjects with a low severity of VWF. Virokannas and Rintamäki (1991) also suggested this was the reason for the differences between their data and others. The subjects used in this study exhibited only mild VWF in comparison to the groups studied by authors reporting higher sensitivity and specificity; only 12 subjects would be classified as being at stage 2 or greater on the Stockholm Workshop vascular scale. This suggests that the measurement may be responsive to the severity of VWF and that subjects reporting severe VWF exhibit greater cold-induced vasoconstriction than do subjects with mild VWF.

3.2.3.1.2 Responsiveness of FSBPs

Table 8 shows the correlation coefficients for the relation between the severity of reported blanching, percentage FSBPs and duration of vibration exposure. The significant relation between percentage FSBPs and the duration of vibration exposure is most likely due to the positive correlation between duration of vibration exposure and blanching. This association was expected and is indicative of a dose-response relationship between the duration of vibration exposure and the severity of vibration-induced white finger, as suggested by others (e.g. Bovenzi *et al.* 1995, BS6842 1987, ISO5349 1986).

For the VWF group and the vibration-exposed control group combined, the correlation coefficients between blanching score and percentage FSBPs were negative and statistically significant. For the VWF group only, the correlation coefficients were still negative, although not statistically significant. This indicates the percentage FSBPs decreased with increasing severity of blanching on both the test hand and the test finger. These findings show that the measurement of FSBPs with local cold provocation was responsive to the extent of blanching reported by subjects in this study.

3.2.3.2 Finger skin temperature response to cold provocation

There were no significant differences in the times taken for the FSTs to rise by 3°C, 4°C or 6°C between the VWF group and other subjects (Table 9). The ROCs showed that these parameters did not satisfy the criteria of sensitivity and specificity; the curves were close to straight lines at an angle of 45° through the origin (Figure 11). Use of normal limits to calculate sensitivity and specificity showed very low sensitivity to VWF (0% to 23.2%) with specificities ranging from 54.4% to 100% (Table 10). There were no significant correlation coefficients for the association between these parameters and blanching scores; they were not responsive to the severity of VWF (Table 11).

These results suggest that the test was not sufficient to distinguish between subjects reporting VWF and subjects not reporting VWF. This is in agreement with some other authors (e.g. Harada 1987, Nasu and Kurozawa 1995, Olsen 1988). The ROC curves obtained here are also similar to those obtained by Tomida *et al.* (1998). However, relatively high sensitivities have also been reported in the literature (e.g. Hack *et al.* 1986, Kurumatani *et al.* 1984). The difference in opinion between authors may be due to differences in the cold provocation applied or the subject groups studied. Most likely, it is due to the different methods of interpreting test results. For example, Bovenzi (1987) interpreted the response of FSTs to cold provocation using percentage recovery 20 minutes after immersion and found the sensitivity of this test to be 60%. From Figure 2 in Bovenzi (1987), no differences would have been found between subjects with VWF and control subjects if the time for FSTs to rise by 3°C, 4°C or 6°C had been used. Different methods of interpreting the FST response to cold provocation have been investigated in Chapter 7.

An alternative cause for the poor sensitivity of the FST response to cold can be postulated from Ekenvall and Lindblad (1982). These authors observed a prolonged reduction in FSTs following cold provocation in symptom free subjects exposed to vibration. They suggested this phenomenon correlated with the duration of vibration exposure. The control subjects used in this study were either exposed to vibration, or were manual workers. They may have exhibited prolonged cold-induced vasoconstriction. This could have influenced the ROCs and the normal limits obtained. Furthermore, the prior application of a FSBP test on the contralateral hand may have contributed to the low sensitivity and specificity; there may have been a lasting effect on central sympathetic activity (Sakakibara *et al.* 1997). The response of FSTs to cold provocation and the effect of the order of presentation of the two cold provocation tests have been investigated using different control groups in Chapter 6.

3.3 SENSITIVITY, SPECIFICITY AND RESPONSIVENESS OF NEUROLOGICAL TESTS

Measurements of vibrotactile thresholds and thermal thresholds were made during the final year of a longitudinal study of vascular and neurological function in a cohort of dockyard workers (Section 3.2). Measurements were performed using the methods defined in Chapter 2. These data have been analysed to assess the sensitivity, specificity and responsiveness of thermal thresholds and vibrotactile thresholds to reported symptoms of blanching, numbness and tingling. Neurological function was expected to deteriorate with increased severity of numbness and tingling, i.e. hot thresholds and vibrotactile thresholds would increase and cold thresholds would decrease as the severity of numbness and tingling increased.

It was previously believed that sensory function, particularly vibrotactile function, deteriorated with increasing severity of VWF (e.g. Taylor and Pelmear 1975, Hayward and Griffin 1986). Current opinion, however, suggests that neurological symptoms can be independent of the vascular symptoms (e.g. Brammer *et al.* 1987, Ekenvall 1987). Virokannas (1992) showed that vibrotactile thresholds may not be related to VWF. Virokannas and Pyykkö (1992) and Hadlington and Griffin (1992) demonstrated the independence of vascular and neurological function in comparisons of measurements of FSBPs and vibrotactile thresholds; no relations were found between these tests. Ahrend *et al.* (1995) also suggest no correlation between vibrotactile thresholds and cold provocation test results, although they did not show cold provocation test results. It was hypothesised here, therefore, that the neurological tests would be more closely related to neurological symptoms than to vascular symptoms.

3.3.1 Method

3.3.1.1 Subjects

One hundred and seven dockyard workers participated in the longitudinal study in its final year. Of these, 76 were exposed to hand-transmitted vibration whilst 21 were manual workers who had not been exposed to hand-transmitted vibration in the work place (control subjects). Of the vibration-exposed subjects, 49 reported episodic blanching of the digits in response to cold.

Subject characteristics, medical histories and vibration exposure histories were obtained using an experimenter led questionnaire (Appendix B). Subjects details are shown in Table 12. Since VWF is a vascular dysfunction, this has not been used as the criterion for grouping subjects. Three subjects (two controls and one vibration exposed worker) were excluded from analyses, these subjects reported either a family history of Raynaud's phenomenon, drug treatment or neurological symptoms not associated with vibration exposure. Figure 13 shows the numbers of subjects reporting symptoms, or combinations of symptoms, of HAVS. The tools that had exposed the subjects to hand-transmitted vibration are summarised in Table 13 and the total duration of exposure to vibration, as reported by each subject, is shown in Figure 14.

3.3.1.2 Experimental procedure

Subjects attended for examination directly from the workplace, or from home, having not smoked tobacco for one hour or consumed alcohol for 12 hours. The median external temperature was 16.3°C (inter-quartile range, IQR, 6.25°C) and the median internal temperature was 24.5°C (IQR 1.95°C). Subjects were acclimatised to the test environment for fifteen minutes, or until finger skin temperature was above 20°C. Subjects were seated during acclimatisation and threshold measurements.

Table 12 Characteristics of subjects used to appraise the measurements of vibrotactile thresholds and thermal thresholds.

	Overall	Controls	Exposed
Number, N (%)	104 (100)	29 (27.9)	75 (72.1)
Age (yrs) median (IQR)	38 (13)	36 (14)	39 (13.5)
Smokers, N (%)	30 (28.8)	4 (13.8)	26 (34.7)**
Regular drinkers, N (%)	66 (63.5)	20 (69)	46 (61.3)
Lifetime vibration exposure (hrs), median (IQR)	6057 (14789)	0	10597.5 (13917.5)**

Differences between control group and exposed group, Mann-Whitney U: ** $p < 0.05$

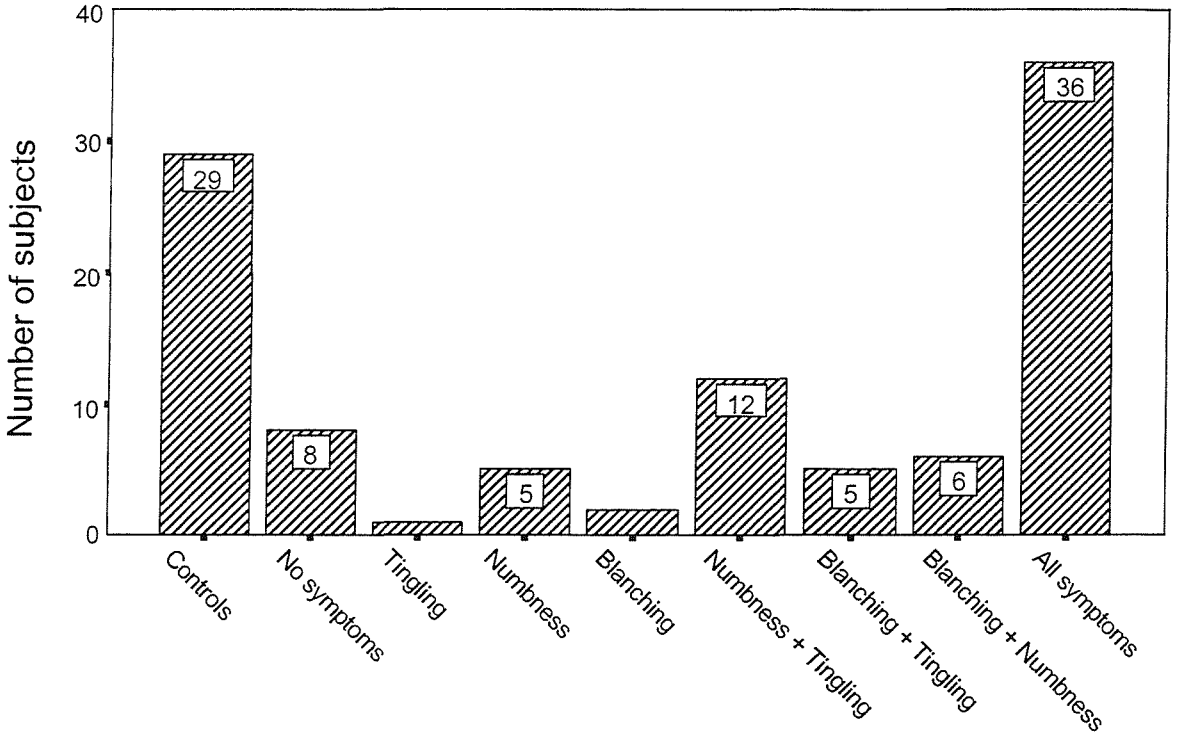


Figure 13 Number of subjects reporting symptoms, or combinations of symptoms of the hand-arm vibration syndrome.

Table 13 Tools that had been used by vibration-exposed subjects. The number of subjects using each tool is shown in brackets.

Caulking tools (44)	Etching pens (19)	Needleguns (5)	Road breakers (1)
Cengar saws (58)	Grinders (70)	Nibblers (17)	Sanders (17)
Chain saws (3)	Impact wrenches (54)	Pipe prepping machines (20)	Scalars (27)
Chipping hammers (4)	Milling machines (1)	Pop-rivet guns (3)	Shotblasters (3)
Drills (68)	Nailers (3)	Riveting tools (26)	Threading machines (1)

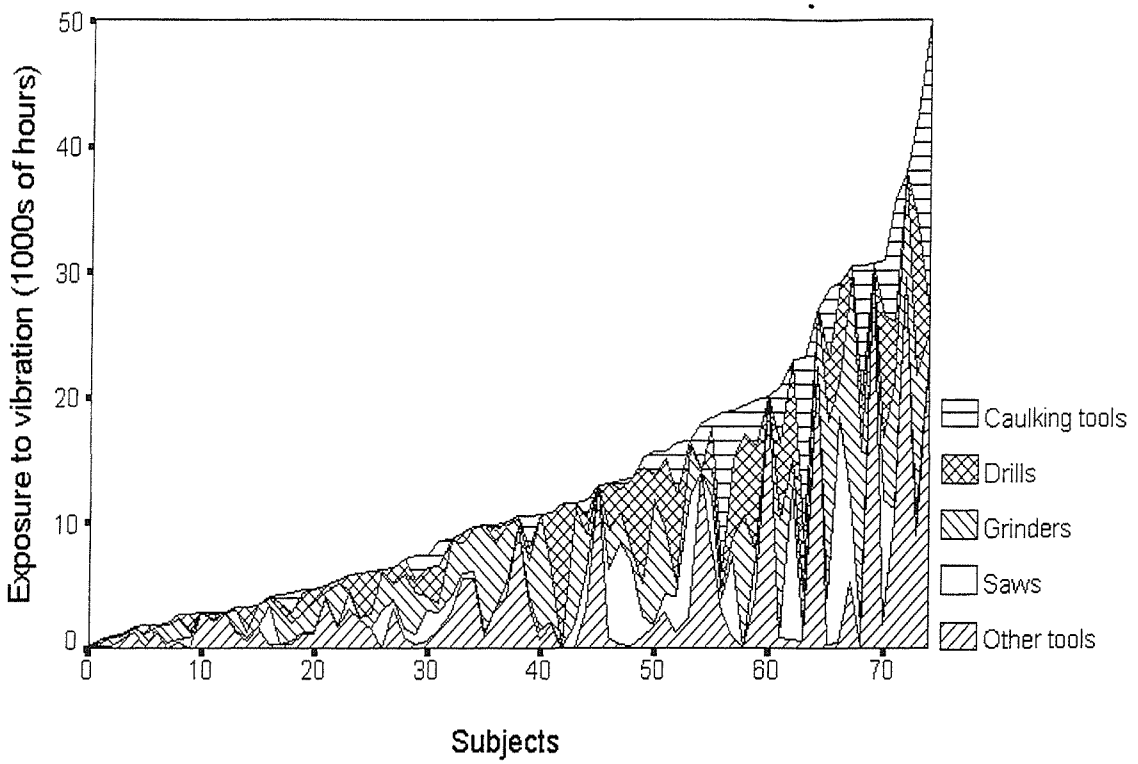


Figure 14 Lifetime exposure to hand-transmitted vibration for vibration exposed subjects participating in the appraisal of tests of neurological function.

Subjects underwent vibrotactile and thermal threshold tests on the middle finger and the little finger of both the right hand and the left hand. The order of presentation of tests, fingers and hands was balanced across the study population. Subjects were given written instructions for the two tests and completed a practice measurement on the index finger or the ring finger prior to beginning the tests.

3.3.1.2.1 Vibrotactile threshold measurements

Vibrotactile thresholds were measured using an *HVLab* Tactile Vibrometer (Appendix A). A downward force of 2 N was applied to the surround by the finger. A 6mm diameter probe protruded through a 10 mm diameter hole in the surround and exerted an upward force on the finger of 1 N. Thresholds were measured using the up-and-down method of limits with a 3 dB/s rate of change of stimulus magnitude and a measurement duration of 45 seconds. A minimum of six reversals were obtained during each measurement, the first reversal was ignored in threshold calculations.

Vibrotactile thresholds at 31.5 Hz and 125 Hz were obtained to reflect excitation of the Meissner's corpuscles and Pacinian corpuscles, respectively. The order of presentation of frequencies was balanced across the study population. Thresholds were measured at the centre of the whorl on the palmar surface of the distal phalanx.

3.3.1.2.2 Thermal threshold measurement

Hot and cold thresholds were obtained independently using an *HVLab* Thermal Aesthesiometer (Appendix A). The method of limits was used: the temperature of the applicator increased or decreased from a reference temperature of 30°C at a rate of 1°C/s. When subjects perceived a change in temperature, they responded and the direction of temperature change was reversed until the applicator returned to the reference temperature. The applicator was held at the reference temperature for about 3 seconds before further threshold judgements were made. The mean hot threshold and the mean cold threshold were determined from three judgements of each sensation. Limitations on the time for which a subject could be removed from the workplace prohibited further judgements.

The order of determining hot and cold thresholds was balanced across the study population. Thresholds were measured on the palmar surface of the distal phalanx. The fingers applied a force of 2 N to the applicator, feedback being provided by electronic scales. To prevent injury, the minimum applicator temperature was set to 5°C and the maximum to 55°C. If the applicator temperature reached either of these limits during a measurement, the threshold was given as the limit achieved (5°C or 55°C).

3.3.2 Results

Median (interquartile range) thermal thresholds and vibrotactile thresholds measured on digit 3 (middle finger) and digit 5 (little finger) of the right and the left hand are shown in Table 14. Cold thresholds were significantly lower, and vibrotactile thresholds and hot thresholds were significantly higher, amongst vibration-exposed workers than amongst subjects not exposed to hand-transmitted vibration. Further analysis has considered fingers independently; McGeoch *et al.* (1992) suggest that not considering fingers independently can result in erroneous conclusions.

Amongst vibration-exposed workers, hot thresholds and vibrotactile thresholds at both 31.5 Hz and 125 Hz tended to be significantly higher for fingers reported to blanch (N = 114) compared to fingers that were not reported to blanch (N = 186) ($p < 0.088$). Cold thresholds were significantly different between these groups ($p = 0.0.039$). Hot thresholds and vibrotactile thresholds at 125 Hz were significantly higher ($p < 0.026$) and vibrotactile thresholds at 31.5 Hz were marginally higher ($p = 0.094$) amongst fingers reported as exhibiting numbness (N = 155) compared to fingers not reported as exhibiting numbness (N = 145). Cold thresholds were not significantly different between fingers with and without numbness ($p > 0.197$). None of the threshold measurements were significantly different between fingers with and without tingling ($p > 0.372$).

Table 14 Median (inter-quartile range) thermal thresholds and vibrotactile thresholds measured amongst subjects exposed to hand-transmitted vibration and control subjects.

		Overall (N = 104)	Controls (N = 29)	Exposed (N = 75)
Hot threshold, Median (IQR)	Digit 3, right	41.6 (6.6)	39.9 (5.4)	42.1 (6.7)**
	Digit 5, right	41.7 (7.6)	40.1 (4.6)	42.6 (7.7)**
	Digit 3, left	40.1 (6.1)	38.0 (2.9)	41.3 (6.7)**
	Digit 5, left	41.1 (6.1)	39.8 (3.5)	42.3 (6.7)**
Cold threshold, Median (IQR)	Digit 3, right	23.7 (5.8)	25.9 (2.2)	22.5 (7.4)**
	Digit 5, right	24.3 (5.8)	25.8 (17.6)	23.6 (6.8)**
	Digit 3, left	22.7 (6.4)	24.9 (4.0)	21.9 (8.1)**
	Digit 5, left	22.2 (7.5)	24.8 (4.1)	21.0 (8.0)**
Vibrotactile threshold 31.5 Hz, Median (IQR)	Digit 3, right	0.21 (0.34)	0.13 (0.13)	0.26 (0.35)**
	Digit 5, right	0.25 (0.39)	0.15 (0.11)	0.58 (0.58)**
	Digit 3, left	0.20 (0.22)	0.15 (0.11)	0.23 (0.28)*
	Digit 5, left	0.22 (0.24)	0.18 (0.14)	0.27 (0.25)**
Vibrotactile threshold 125 Hz, Median (IQR)	Digit 3, right	0.43 (0.77)	0.28 (0.39)	0.56 (0.84)**
	Digit 5, right	0.53 (0.97)	0.40 (0.34)	0.77 (1.67)**
	Digit 3, left	0.36 (0.51)	0.26 (0.33)	0.43 (0.69)+
	Digit 5, left	0.49 (0.80)	0.39 (0.46)	0.59 (1.18)**

Differences from the control group, Mann-Whitney U: + $p < 0.1$ * $p < 0.05$; ** $p < 0.01$

3.3.2.1 Sensitivity and specificity

3.3.2.1.1 Receiver operating characteristics

Receiver operating characteristics have been calculated for vibrotactile thresholds and thermal thresholds for their sensitivity and specificity to blanching (Figure 15), numbness (Figure 16) and tingling (Figure 17). For thermal thresholds, the ROC curves were computed using increments or decrements of 0.5°C from the reference temperature as the cut-off value between healthy and pathological results. For vibrotactile thresholds, the ROC curves were computed by incrementing the cut-off value from zero in steps of (i) 0.05 m/s² r.m.s below 3.5 m/s² r.m.s or (ii) 0.5 m/s² r.m.s. above 3.5 m/s² r.m.s.

3.3.2.1.2 Normal limits

Four normal limits have been calculated for each threshold measurement: i) for the control group only, ii) for all subjects not reporting blanching, iii) for all subjects not reporting numbness and iv) for all subjects not reporting tingling. Normal limits were defined as the mean plus two standard deviations for vibrotactile thresholds and hot thresholds. For cold thresholds, the normal limit was defined as the mean minus two standard deviations. The corresponding sensitivities and specificities to blanching, numbness or tingling on the test finger are shown in Table 15.

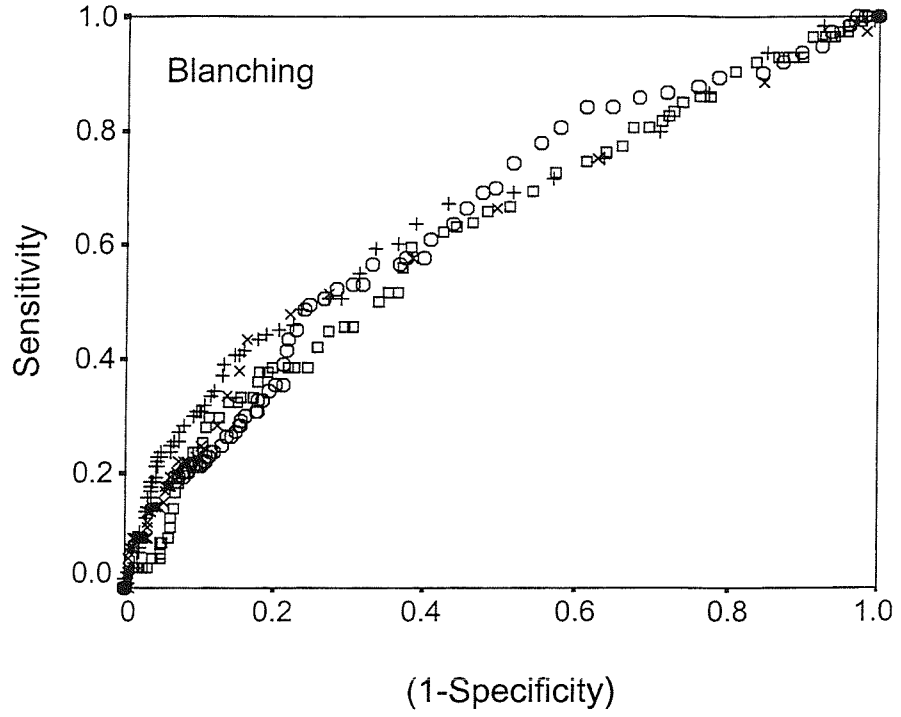


Figure 15 Receiver operating characteristics for the detection of blanching on a test finger by vibrotactile thresholds at 31.5 Hz (x) and 125 Hz (+) and by hot thresholds (□) and cold thresholds (○) (Test fingers with blanching = 114, test fingers without blanching = 302).

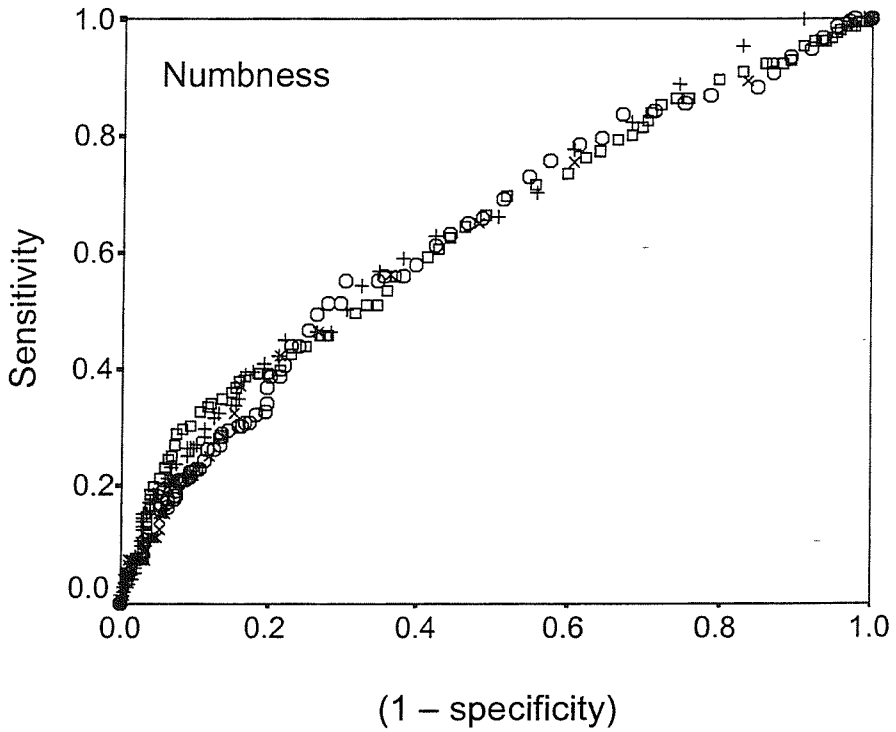


Figure 16 Receiver operating characteristics for the detection of numbness on a test finger by vibrotactile thresholds at 31.5 Hz (x) and 125 Hz (+) and by hot thresholds (□) and cold thresholds (○) (Test fingers with numbness = 155, test fingers without numbness = 261).

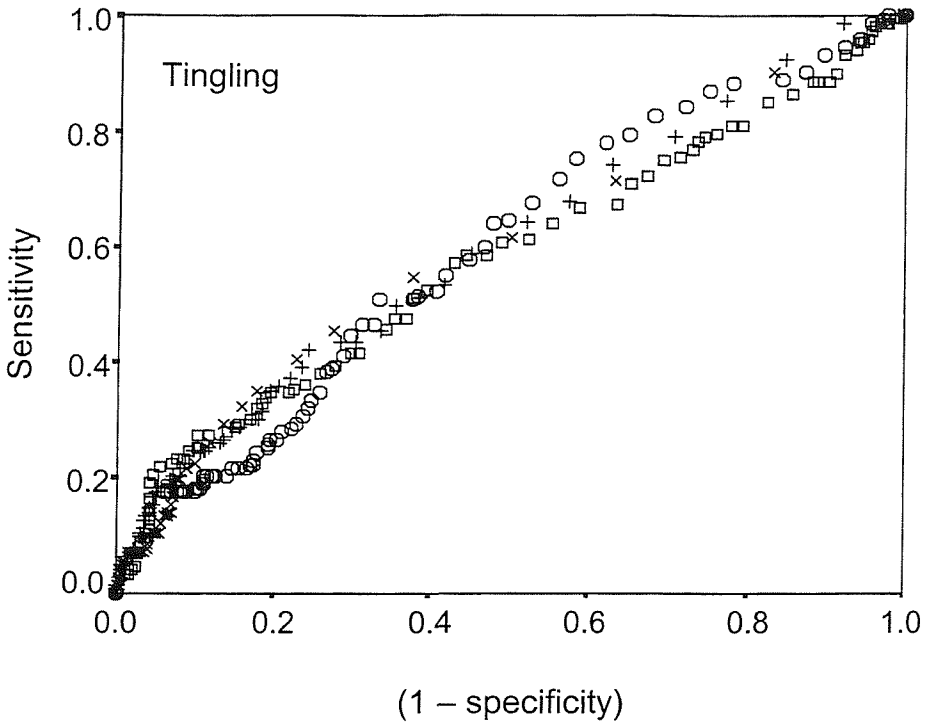


Figure 17 Receiver operating characteristics for the detection of tingling on a test finger by vibrotactile thresholds at 31.5 Hz (x) and 125 Hz (+) and by hot thresholds (□) and cold thresholds (○) (Test fingers with tingling = 247, test fingers without tingling = 269).

Table 15 Normal limits and corresponding sensitivities and specificities for the detection of blanching, tingling and numbness on the test finger using measurements of vibrotactile thresholds and thermal thresholds.

		Blanching		Numbness		Tingling	
		Control fingers	Fingers without blanching	Control fingers	Fingers without numbness	Control fingers	Fingers without tingling
		N = 116	N = 302	N = 116	N = 261	N = 116	N = 269
Vibrotactile threshold, 125 Hz	Normal limit (m/s²)	1.02	3.73	1.02	1.77	1.02	1.73
	Sensitivity	48.7	15.9	39.1	23.8	34.9	22.4
	Specificity	82.1	97.0	83.4	92.7	80.5	91.4
Vibrotactile threshold, 31.5 Hz	Normal limit (m/s²)	0.401	0.982	0.401	0.900	0.401	0.744
	Sensitivity	43.7	17.7	37.1	16.6	34.9	19.5
	Specificity	83.8	93.9	84.1	94.2	92.3	92.1
Cold threshold	Normal limit (°C)	17.0	10.9	17.0	12.9	17.0	10.9
	Sensitivity	29.2	20.4	28.3	18.4	22.2	17.4
	Specificity	84.6	92.3	84.4	93.0	82.7	92.1
Hot threshold	Normal limit (°C)	46.3	49.6	46.3	48.2	46.3	49.9
	Sensitivity	32.4	14.0	33.5	24.5	28.6	14.2
	Specificity	85.0	94.6	88.4	93.8	85.0	95.9

3.3.2.2 Responsiveness

The relation between thresholds, blanching scores, numbness scores, tingling scores and duration of vibration exposure were investigated using Spearman's ρ correlation coefficients. Correlation coefficients were calculated for all vibration-exposed subjects. One-tailed tests of significance were used; it was expected that neurological function would diminish with increasing severity of dysfunction and with increasing duration of exposure to vibration. The results are shown in Table 16

Table 16 Spearman's ρ correlation coefficients for the relation between thermal thresholds, vibrotactile thresholds, blanching score, numbness score, tingling score (total score for each subject and scores for each finger) and vibration exposure. Data for vibration-exposed subjects were included in the analysis (N = 75).

			Blanching score		Numbness score		Tingling score		Lifetime exposure to vibration (hours)	Exposure to vibration in the year preceding tests (hours)	Lifetime exposure to vibration (years)
	Hand	Finger	Total	Test finger	Total	Test finger	Total	Test finger			
Vibrotactile threshold 125 Hz	Right	3	0.188	0.181	0.149	0.210*	0.129	0.100	0.284**	0.152	0.228**
		5	0.209*	0.275*	0.142	0.278**	0.035	0.095	0.285**	0.097	0.307**
	Left	3	0.166	0.148	0.148	0.165	0.064	-0.070	0.309**	0.096	0.346**
		5	0.134	0.194*	0.140	0.154	0.060	0.087	0.241*	0.015	0.329**
	All		0.173**	0.155**	0.143**	0.157**	0.066	0.019	0.274**	0.082	0.300**
Vibrotactile threshold 31.5 Hz	Right	3	0.103	0.125	0.047	0.155	0.153	0.158	0.254*	0.106	0.266**
		5	0.149	0.216*	-0.022	0.201*	-0.025	-0.076	0.193*	0.087	0.201*
	Left	3	0.126	0.033	0.123	0.095	-0.023	-0.150	0.198*	0.145	0.135
		5	0.100	0.126	0.068	0.077	-0.003	0.025	0.306**	0.091	0.364**
	All		0.122*	0.105*	0.057	0.110*	0.028	0.012	0.241**	0.106*	0.244**
Cold threshold	Right	3	-0.139	-0.187	-0.016	-0.130	-0.057	-0.125	-0.112	0.009	-0.185
		5	-0.169	-0.132	-0.088	-0.256*	0.014	-0.086	-0.230*	-0.060	-0.259*
	Left	3	-0.072	0.022	-0.219*	-0.159	0.003	0.063	-0.279**	-0.130	-0.217*
		5	-0.085	-0.075	-0.066	-0.130	-0.025	0.005	-0.168	-0.049	-0.208*
	All		-0.117*	-0.092	-0.101*	-0.168**	-0.019	-0.031	-0.193**	-0.052	-0.219**
Hot threshold	Right	3	0.052	0.096	0.050	0.106	-0.039	-0.064	0.148	0.029	0.107
		5	0.127	0.177	0.167	0.133	-0.123	-0.050	0.240*	0.081	0.202*
	Left	3	0.101	0.179	0.148	0.203*	0.068	-0.025	0.170	0.093	0.111
		5	0.097	0.168	0.120	0.204*	0.044	0.157	0.209*	0.167	0.122
	All		0.088	0.142**	0.121*	0.161**	-0.022	-0.005	0.140**	0.094	0.129*

Spearman's ρ: * $p < 0.05$; ** $p < 0.01$

3.3.3 Discussion

Vibrotactile thresholds and thermal thresholds tended to indicate diminished sensory function in fingers with blanching and fingers with numbness compared to fingers without these symptoms (Section 3.3.2). This is in agreement with authors who have shown that in the same subjects, both vibrotactile and thermal sensory function diminishes with the onset of the hand-arm vibration syndrome (HAVS) (Ekenvall *et al.* 1989, Toibana *et al.* 1998, Virokannas and Virokannas 1995).

Neither vibrotactile thresholds nor thermal thresholds discriminated between fingers with tingling and fingers without tingling. No studies in the literature could be found that have considered tingling as an independent symptom of HAVS against which this finding could be compared. It might indicate that reported sensations of tingling are not due to the same dysfunction of the tactile and thermal sensory pathways as numbness.

Hot thresholds increased and cold thresholds decreased in fingers reported as blanching compared to fingers that were not reported as blanching. There was a significant increase in hot thresholds for fingers with numbness compared to fingers without numbness, but no difference in cold thresholds between fingers with and without numbness. Hirosawa *et al.* (1983a, 1983b) also reported that hot thresholds were affected more in VWF than cold thresholds. Ekenvall *et al.* (1986) and Virokannas and Virokannas (1995) showed that cold thresholds were more often affected than hot thresholds in subjects exposed to hand-transmitted vibration. Differences between the measurement methods may account for the discrepancy; Ekenvall *et al.* (1986) and Virokannas and Virokannas (1995) both used the Marstock method (Section2.5.2) for determining thresholds whilst Hirosawa *et al.* (1983a, 1983b) measured the hot and cold thermal thresholds independently, as was done in this study. It is likely that the hot and the cold sensory pathways are affected differently by vibration exposure. It remains unclear whether the unmyelinated C-nerve fibres that supply the hot receptors are more often affected by hand-transmitted vibration than the thinly myelinated Aδ-nerve fibres that supply the cold receptors.

Vibrotactile thresholds at 125 Hz were higher in fingers with blanching compared to fingers without blanching, and in fingers with numbness than in fingers without numbness. This increase was greater than for vibrotactile thresholds at 31.5 Hz (Section 3.3.2). This pattern has been observed by others. For example, Virokannas (1992) showed that high frequency thresholds deteriorated before low frequency thresholds in subjects exposed to hand-transmitted vibration whilst Brammer *et al.* (1987) showed that the Pacinian corpuscles were affected before the Meissner's corpuscles by exposure to hand-

transmitted vibration. These results support the suggestion that both the sensory pathway mediated by the Meissner's corpuscles and the sensory pathway mediated by the Pacinian corpuscles should be treated independently when screening for vibration-induced neuropathies.

3.3.3.1 Sensitivity and specificity

The receiver operating characteristics shown in Figure 15 and Figure 16 show that both vibrotactile thresholds and thermal thresholds can be sensitive and specific to blanching and numbness. Sensitivity and specificity to tingling was comparatively low and further suggests these measurements are not useful for detecting this symptom (Figure 17).

The ROCs indicate that the vibrotactile threshold at 125 Hz shows a slight improvement compared to the vibrotactile threshold at 31.5 Hz, and the hot threshold shows a slight improvement compared to the cold threshold, in the sensitivity and specificity to blanching and numbness. This difference supports the finding in the previous section that the hot threshold and the vibrotactile threshold at 125 Hz were affected before the cold threshold and the vibrotactile threshold at 31.5 Hz in workers exposed to hand-transmitted vibration.

Use of lower normal limits to determine sensitivity and specificity showed that vibrotactile thresholds and thermal thresholds tended to be more sensitive and specific to blanching than to numbness (Table 15). This result is surprising as it was expected that threshold measurements would be more closely related to neurological dysfunction than to vascular dysfunction. However, there is a complex relationship between symptoms of HAVS, vibration exposure and thresholds.

It has been shown that both vascular and neurological function deteriorate with increasing vibration exposure. Lundström *et al* (1995) demonstrated a correlation between duration of vibration exposure and vibrotactile thresholds. Wenemark *et al.* (1996) also show the sensitivity and specificity of vibrotactile thresholds is higher to vibration exposure than to neurological dysfunction alone. Lundström *et al.* (1998b) and Nillson *et al.* (1998) suggest thermal thresholds are influenced by vibration exposure. The dose-response relationships for the onset of VWF with vibration exposure given in ISO5349 (1986) and BS6842 (1987), and the epidemiological evidence that vascular function deteriorates with increasing vibration exposure (e.g. Bovenzi 1998, Ekenvall and Carlson 1987, Futatsuka *et al* 1989), suggest the development of vascular dysfunction with vibration exposure. Since vascular and neurological symptoms develop with increasing vibration exposure, it is not possible to consider their relation to neurological measurements independently of each other or independently of vibration exposure.

Table 17 Partial Pearson's correlation coefficients showing the relationship between neurological thresholds and numbness and blanching scores on each test finger.

		Blanching score		Numbness score	
	Correcting for:	vibration exposure	vibration exposure, numbness	vibration exposure	vibration exposure, blanching
Subjects exposed to vibration (N = 284)	Cold threshold	-0.1570**	-0.0137	-0.2599**	-0.2001**
	Hot threshold	0.1033*	-0.0276	0.2233**	0.1365**
	Vibrotactile threshold, 31.5 Hz	0.1224*	0.0779	0.1038*	0.0037
	Vibrotactile threshold, 125 Hz	0.1926**	0.1441*	0.1324*	-0.0079
Subjects with blanching and numbness (N = 152)	Cold threshold	-0.2304**	-0.0489	-0.3058**	-0.1751*
	Hot threshold	0.1086	-0.0177	0.1919**	0.1047+
	Vibrotactile threshold, 31.5 Hz	0.0824	0.0316	0.0914	0.0246
	Vibrotactile threshold, 125 Hz	0.1918**	0.1167+	0.1619*	0.0310

Pearson's partial correlation coefficents: +$p < 0.1$; *$p < 0.05$; **$p < 0.01$

Partial Pearson's correlation coefficients have been calculated to test the relation between symptoms and thresholds, correcting for the duration of vibration exposure. Blanching and numbness were related ($p < 0.0001$) so partial Pearson's correlation coefficients were calculated to test the association between numbness scores and thresholds, correcting for blanching score, and between blanching scores and thresholds, correcting for numbness score. The analyses were performed for all subjects exposed to vibration, and for those subjects reporting symptoms of both blanching and numbness. The results are shown in Table 17. Tingling was not correlated with measured thresholds when corrected for vibration exposure ($p > 0.1$) and has not been included in the table.

The results suggest that thermal thresholds were more closely related to symptoms of numbness than to symptoms of blanching, this was not true for vibrotactile thresholds. Due to the complexity of the combined relationship between vibration exposure, thresholds and symptoms of HAVS, it is uncertain if vibrotactile thresholds were directly related to symptoms of blanching. The literature suggests this is unlikely to be the case (e.g. Brammer *et al.* 1987, Ekenvall 1987, Hadlington and Griffin 1992, Virokannas 1992, Virokannas and Pyykkö 1992).

The ROCs obtained in this study for the detection of numbness have been compared to the sensitivities and specificities reported in the literature (Figure 18). For vibrotactile thresholds, the results reported by Wenemark *et al.* (1996) and by Ekenvall *et al.* (1986, 1989) correspond well with the ROCS reported here. Both of these authors used data from more than one measurement site to determine sensitivity and specificity; if one measurement deviated from normal the subject was classified as having a neurological disorder. When the data obtained here were treated similarly, i.e. when any of the four

measurements (middle and little fingers bilaterally) exceeded the lower normal limits for the unexposed control group (Table 15), the sensitivity of the vibrotactile thresholds at 125 Hz to numbness was 49% and the specificity 80%. This is an improvement on the sensitivity and specificity reported by both Wenemark *et al.* (1996) and Ekenvall *et al.* (1986, 1989). It might be concluded that although fingers should be treated independently (McGeoch *et al.* 1992), the efficacy of the test increases when the measurements at different sites for a subject are considered together.

In addition to absolute thresholds, Wenemark *et al.* (1996) used the Sensibility Index to obtain measures of sensitivity and specificity. The Sensibility Index is a measure of the area under the curve for measurements made at one-third octave band centre frequencies between 16 Hz and 500 Hz (Lundborg *et al.* 1992). It has the disadvantage of combining information about the Meissner's and Pacinian pathways (Virokannas 1992). Lundborg *et al.* (1992) reported a high sensitivity (80%) and specificity (90%) to neurological dysfunction using the Sensibility Index. When thresholds at 31.5 Hz and 125 Hz were considered together using data obtained in this study, the sensitivity to numbness was shown to be 57% and the specificity 76%. This is an improvement on the results reported by Wenemark *et al.* (1996) although the measurement does not appear to perform as well as the measurements reported by Lundborg *et al.* (1992).

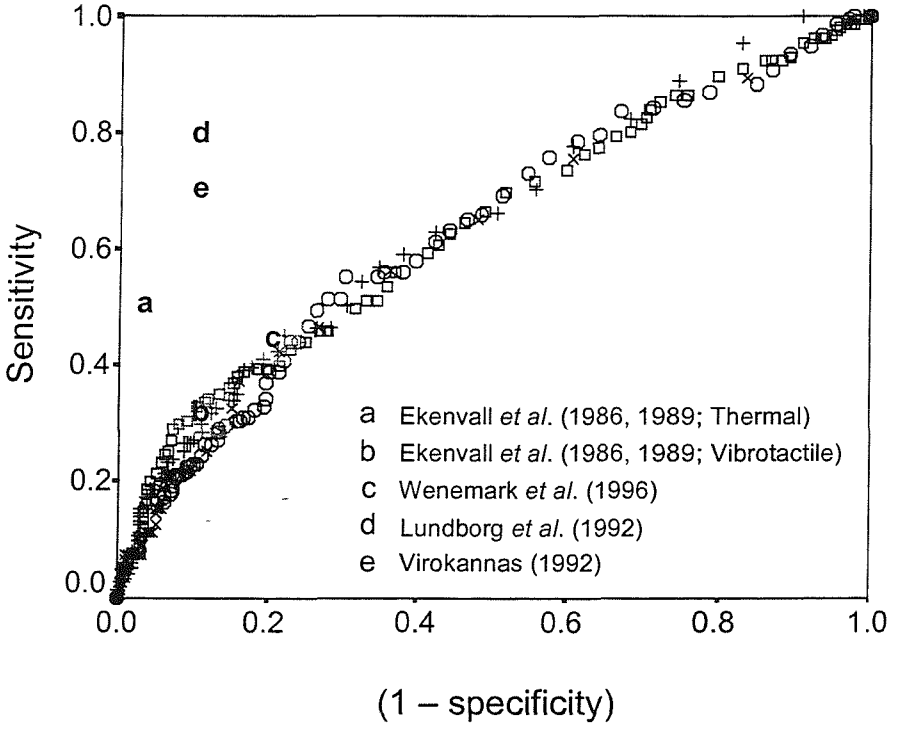


Figure 18 Receiver operating characteristics for the detection of numbness on a test finger by vibrotactile thresholds at 31.5 Hz (x) and 125 Hz (+) and by hot thresholds (□) and cold thresholds (○). The sensitivities and specificities estimated from the literature are overlaid.

The difference between the results reported here and those reported by Lundborg *et al.* (1992) is likely to have been due to the definition of true positive used in the two studies. Lundborg *et al.* (1992) used a patient group that had been referred for specialist investigations and had undergone clinical examinations in combination with radiological and neurophysiological tests in order to be classified as positive. The classification for the study reported here was based upon the answer to a single question on an experimenter led questionnaire (Do you experience numbness in your hands?, Appendix B). The patient group reported by Wenemark *et al.* (1996) are more comparable to that reported here, these authors also used a questionnaire response to classify true positives. It might be concluded that combining measurements for low and high frequencies can increase the sensitivity and specificity of vibrotactile thresholds to neurological disorders, although mechanoreceptor specific information is lost.

Virokannas (1992) showed higher sensitivity and specificity than that obtained here. In this study, the control workers were generally outdoor manual workers who were of similar age to the subjects exposed to hand-transmitted vibration. Virokannas (1992), however, used both male and female indoor workers who were younger than the patient group. Although Virokannas (1992) performed an age correction, the control group is unlikely to give similar results to the control group used in this study and this may have accounted for the difference. Furthermore, the subjects considered as true negatives in calculating the sensitivities and specificities in this study included vibration-exposed subjects. These subjects had not necessarily avoided exposure to vibration immediately prior to testing for practical reasons; they may have exhibited some temporary threshold shift (TTS) (e.g. Bovenzi 1997). A higher number of false positive results (i.e. decreased specificity) was likely to be obtained compared to when using subjects who had avoided exposure to vibration for a longer period of time before testing, as suggested by Ekenvall *et al.* (1989). It might be recommended that workers should avoid vibration-exposure for a period of time before measurements of vibrotactile thresholds are made. Further work is required to determine the length of time required before TTS fully recovers; Piette and Malchaire (1997) suggest that there is likely to be some residual TTS after exposure to hand-transmitted vibration.

For thermal thresholds, only two studies were found in the literature from which the sensitivity and specificity to disorders associated with hand-transmitted vibration could be estimated (Ekenvall *et al.* 1989, 1986). These authors showed that when combining measurements of the neutral zone made at the thenar eminence and measurements made on the index and middle fingers simultaneously, a sensitivity of about 50% with a specificity of about 95% was obtained. When the hot threshold and the cold threshold for

all measurement sites were considered together in this study, the sensitivity to numbness was 57% with a specificity of 70%. The sensitivity obtained here appears to be an improvement although the specificity was lower. Ekenvall *et al.* (1986, 1989) used patient groups (true positives) that had been referred for examination due to suspected vibration-induced disorders. These patients are likely to have reported more severe symptoms than those used in this study. Furthermore, their subjects were not exposed to vibration for at least 16 hours before measurements, whereas subjects used in this study may have come directly from the workplace where they had been exposed to hand-transmitted vibration. This could have resulted in a TTS in thermal thresholds (e.g. Hirosawa *et al.* 1992) and a greater likelihood of false positive results (i.e. decreased specificity). Given the likelihood of a decreased specificity in this study, the measurement method reported here may be considered to give similar results to the measurement method reported by Ekenvall *et al.* (1986, 1989).

It can be concluded from these results that the method of measuring vibrotactile thresholds and the method of measuring thermal thresholds used in this study can be both sensitive and specific to neurological disorders resulting from vibration exposure. The methods perform similarly to, or better than, other methods reported in the literature.

3.3.3.2 Responsiveness

The significant correlations between duration of vibration exposure and both vibrotactile and thermal thresholds agrees with suggestions of a dose-response relationship between thresholds and duration of exposure to vibration (e.g. Bovenzi 1997, Lundström *et al.* 1995, Lundström *et al.* 1998b, Virokannas 1992). When appraising thermal threshold and vibrotactile threshold measurements against the criteria of responsiveness, it is therefore necessary to consider vibration-exposure as a covariate. The analyses reported in Table 17 have been used to assess the responsiveness of vibrotactile thresholds and thermal thresholds to disorders associated with hand-transmitted vibration.

The significant correlations observed between both vibrotactile thresholds and thermal thresholds and numbness score, corrected for vibration exposure, suggest that the measurements are responsive to neurological disorders associated with hand-transmitted vibration. This is in agreement with other authors (e.g. Ekenvall *et al.* 1989). Thermal thresholds appear to be more closely related to neurological dysfunction than vibrotactile thresholds, as suggested by Virokannas and Virokannas (1995). Thermal thresholds were also significantly correlated with numbness when corrected for both vibration exposure and blanching score, suggesting thermal thresholds were responsive to neurological dysfunction but not to vascular dysfunction.

Due to the complexity of the combined relationship between vibration exposure, thresholds and symptoms, it is uncertain if the vibrotactile thresholds were directly related to symptoms of blanching. It is likely, however, that this correlation arises because of the increased exposure to vibration required to cause an increase in vibrotactile thresholds compared to the exposure to vibration required to diminish thermal sensory function (Virokannas and Virokannas 1995). Such an increase in vibration exposure is more likely to result in the development of vascular symptoms (e.g. Bovenzi 1998, BS6842 1987, ISO5349 1986).

These results suggest that both thermal thresholds and vibrotactile thresholds measured using the methods defined in Chapter 2 are responsive to neurological disorders arising from exposure to hand-transmitted vibration

3.4 CONCLUSIONS

The appraisal of vascular tests showed that the measurement of FSBPs and the subsequent calculation of percentage FSBPs could be sensitive and specific to VWF. Percentage FSBPs were shown to be responsive to the severity of VWF. The measurement was shown to be specific to the presence of blanching on the test finger, suggesting measurements on more than one finger would be beneficial in the detection of VWF.

The FST response to cold provocation was neither sensitive, specific nor responsive to VWF. The results for the FST response to cold provocation may have been influenced by the prior application of cold provocation during the FSBP test, the mild severity of symptoms reported amongst the subjects used in this study or the parameter of the rewarming curve chosen for analysis. Further work is required to determine if these factors adversely influenced the measurement.

Measurements of both vibrotactile thresholds and thermal thresholds were sensitive, specific and responsive to loss of sensation resulting from vibration exposure, they were not related to reports of tingling. It is uncertain if the vibrotactile thresholds were influenced by reported symptoms of blanching.

It is concluded that the methods of measuring FSBPs, thermal thresholds and vibrotactile thresholds defined in Section 2.8, Chapter 2 are useful for monitoring vascular and neurological function in workers exposed to hand-transmitted vibration.

CHAPTER 4 FINGER SYSTOLIC BLOOD PRESSURES: SIMULTANEOUS MEASUREMENTS ON FOUR TEST FINGERS AS OPPOSED TO ONE TEST FINGER

4.1 INTRODUCTION

Measurements of finger systolic blood pressure (FSBP) following cold provocation change with the condition of the test finger, i.e. FSBPs are lower in fingers affected with VWF than in unaffected fingers within the same subject (e.g. Kurozawa *et al.* 1991). Studies on the finger skin temperature (FST) response to cold have shown differences between fingers, and between hands, in subjects with VWF (e.g. Gautherie 1997, Lawson and Neville 1998). These results are consistent with theories of local dysfunction contributing to the pathogenesis of VWF (e.g. Lewis 1929, Olsen 1987).

The appraisal of the FSBP measurements reported in Chapter 3 provided further evidence that there is local dysfunction in VWF. It was shown that the sensitivity and specificity of measurements of FSBPs were higher to blanching on a test finger than blanching on a test hand, regardless of the test finger's true condition (Section 3.2.3.1). Measurements of the vascular response to cold for detecting VWF can therefore be qualified as finger specific, i.e. dependent on the condition of the test finger.

Since measurements are finger specific, to determine the extent of vascular dysfunction in a case of VWF, measurements would be required on each finger of both hands. Using the method defined in Section 2.8, Chapter 2, the time taken to perform measurements on eight test fingers, using the thumbs as a reference, would be approximately 1½ hours to 2 hours. This may be considered impractical. It would be useful to measure FSBPs simultaneously on more than one finger.

Commercially available equipment for the measurement of FSBPs with cold provocation (Medimatic DM2000 with digit cooling system, Appendix A) allows the simultaneous measurement of FSBPs on only one test finger and one reference finger. A new plethysmograph has been developed that is capable of the simultaneous measurement of the FSBPs of four test fingers and a reference finger (Lewis 1996, *HVLab* Multi-Channel Plethysmograph, Appendix A). In this chapter, two studies comparing the new plethysmograph with the commercially available machine are reported.

4.2 THE EFFECTS OF THERMAL PROVOCATION OF .FOUR TEST FINGERS COMPARED TO ONE TEST FINGER ON FINGER SYSTOLIC BLOOD PRESSURES

4.2.1 Introduction

When measuring FSBPs following cold provocation, increased vasoconstriction in mild cases of VWF is observed when cooling blankets are used to apply additional cold provocation (e.g. Kurozawa *et al.* 1991). The added cooling augments the stimulation of the sympathetic nervous system and exaggerates the cold response of the digital arteries (Lassen 1978). When making simultaneous measurements on more than one test finger, there is an increased area of thermal provocation. The increased area of the cold stimulus might result in an increased cold-induced vasoconstriction by increasing central sympathetic activity. Exaggeration of cold-induced vasoconstriction would be beneficial to the detection of mild VWF (Kurozawa *et al.* 1991, Olsen, personal communication). However, it is necessary that any effect be small in healthy fingers or false positive results may occur.

This study was performed to compare finger systolic blood pressures measured simultaneously on four test fingers with those measured on only one test finger amongst healthy subjects. Measurements made on one test finger have also been compared between the new *HVLab* Multi-Channel Plethysmograph and the Medimatic DM2000 plethysmograph. It was hypothesised that amongst healthy subjects the effects of cold provocation of four fingers compared to one finger would be negligible. No differences were expected between the two plethysmographs.

4.2.2 Method

4.2.2.1 Subjects

Twelve healthy, male volunteers participated in the study, mean age 23.1 years (standard deviation, SD, 1.98 years). All subjects were students or office workers with no history of occupational exposure to hand-transmitted vibration. Subject suitability was assessed by health questionnaire, none reported symptoms associated with peripheral vascular insufficiency, injuries to the upper extremities or a family history of episodic blanching. The mean weight of the subjects was 73.9 kg (SD 7.4 kg) and the mean standing height was 1.83 m (SD 0.07 m). All subjects were non-smokers.

4.2.2.2 Experimental conditions

Subjects attended in light indoor clothing having not consumed alcohol for 12 hours or caffeine for 4 hours. Subjects attended directly from the workplace, or from home. They were habituated in a room of mean temperature 24.0°C (SD 0.8°C) for at least fifteen

minutes before measurements were made. Mean external temperature, measured at the start of each session, was 8.4°C (SD 4.3°C). During the period of habituation, subjects lay supine on an examination couch. They remained supine until the end of each session.

4.2.2.3 Experimental procedure

Subjects attended three experimental sessions on consecutive days, each at the same time of day. During each session, subjects were presented with one of the three conditions shown in Table 18. The conditions were presented in a balanced order.

During the habituation period, the left hand was instrumented for measurements of FSBPs in air. Plastic bag type cuffs (Appendix A), were placed around the medial phalanges of the test finger or fingers and around the proximal phalanx of the thumb. Mercury-in-elastic strain gauges were placed around the distal phalanges of the test finger, or fingers, and around the thumb at the base of the nail (Figure 19).

Measurements of FSBP were performed using the technique defined by Nielsen and Lassen (1977). The method requires squeezing of the end of each finger to remove an amount of blood prior to cuff inflation (Section 2.2.2). For measurements made on one test finger, this was performed directly by the experimenter. To allow squeezing of the fingertips when measurements were made simultaneously on five fingers, the five-finger squeezer was developed (Appendix A).

Following squeezing, cuffs were inflated to a suprasystolic pressure of 250 mmHg. The pressure was subsequently reduced until blood flow was detected in each instrumented finger. The return of blood flow was defined as the point at which a volume increase was observed, or the first pulse was observed, by means of the strain gauge (Section 2.2.2).

Table 18 Conditions used for the measurement of FSBP.

Condition	Plethysmograph	Test finger(s)	Reference finger
1	Medimatic DM2000	Middle finger	Thumb
2	*HVLab*	Middle finger	Thumb
3	*HVLab*	Index finger, Middle finger, Ring finger, Little finger	Thumb

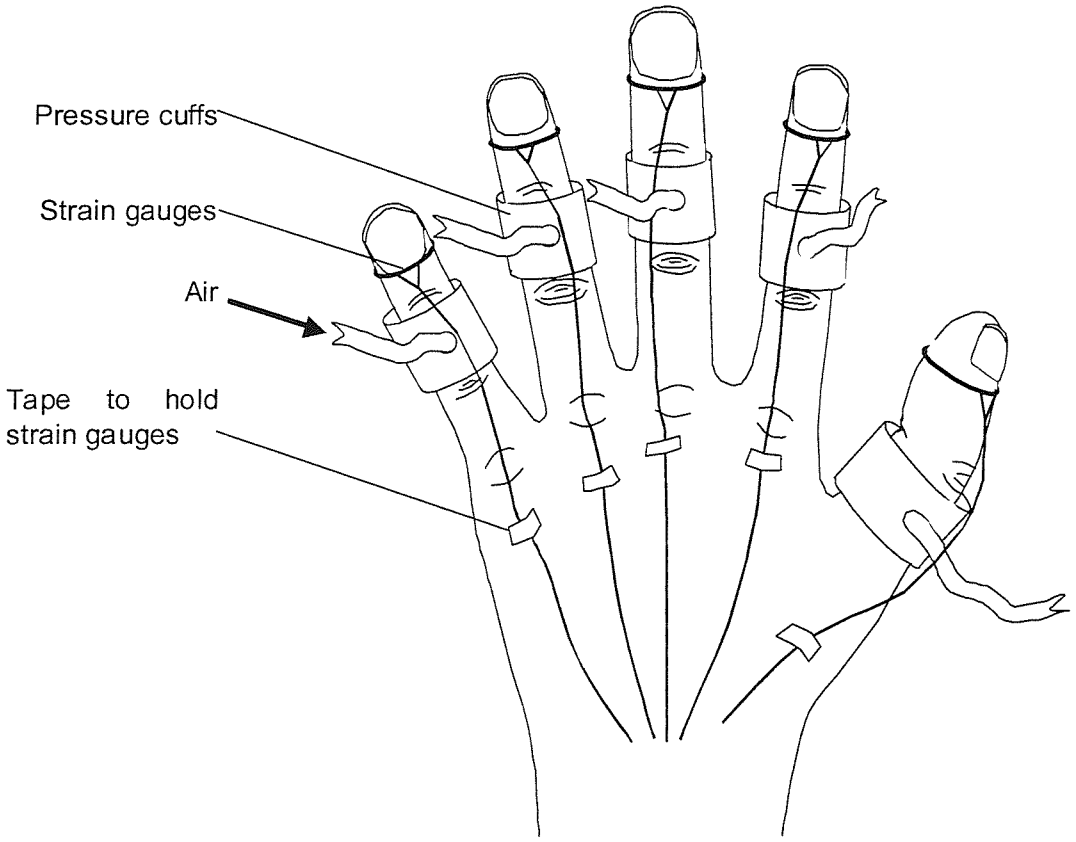


Figure 19 Placement of transducers and pressure cuffs for measurement of FSBPs on four test fingers and one reference finger. For measurements with thermal provocation the single inlet air cuffs were replaced with double-inlet, water-perfused cuffs connected in series. For measurements on one test finger, cuffs and strain gauges were not placed on the index, ring and little fingers.

The single-inlet cuffs on the test fingers, used for measurements of FSBP in air, were removed and replaced with double-inlet cuffs of the tube type (Appendix A) for both water perfusion and pressure application. The thumb retained a single-inlet cuff for air inflation only. For Condition 3, i.e. thermal provocation of four test fingers, the double-inlet cuffs were connected in series. This ensured that water flowed through each cuff, and that the temperatures and pressures were similar in each of the four cuffs. A pilot study showed that when cuffs were connected in series the maximum temperature difference between cuffs was 0.5°C.

For the first measurement following thermal provocation, water controlled at 30°C perfused the double-inlet cuffs at a pressure of 250 mmHg for five minutes before the measurement of FSBP. The procedure was repeated for a water temperature of 15°C and then for a water temperature of 10°C. A period of five minutes was allowed for fingers to recover between each thermal provocation. Percentage FSBPs were calculated using the formula given by Nielsen and Lassen (1978)(Section 2.2.7.1, Equation 1).

4.2.2.4 Analysis

Parametric statistics have been used; the measured data exhibited normality (Shapiro-Wilkes, $p > 0.1$). Repeated measures analysis of variance (MANOVA) has been used to test for significant effects of cold provocation and to test for differences between plethysmographs. Differences between subjects have been tested using independent samples *t*-tests; differences within subjects have been tested using paired samples *t*-tests. Pearson's correlation coefficients have been used as measures of association. A *p*-value of 0.05 has been chosen to indicate significance, with marginal significance being achieved when $p < 0.1$.

4.2.3 Results

Table 19 shows the mean values and standard deviations of the FSBPs measured in each of the three conditions. Percentage FSBPs are also shown. Age, body size and body mass were found not to influence FSBPs ($p > 0.1$). External temperature and internal temperature did not systematically influence the results.

Measurements made on the thumb and on the middle finger in air were not different between each condition ($p > 0.1$, Table 19). When using the *HVLab* Multi-Channel Plethysmograph, measurements made on the middle finger with thermal provocation were significantly higher than when measured using the Medimatic DM2000 plethysmograph ($p < 0.02$, Table 19).

The differences between plethysmographs for measurements made on the middle finger with thermal provocation were found to be due to a residual hydrostatic pressure in the double-inlet cuffs. This effect is discussed in Appendix A, Section A2.4.6.

Finger systolic blood pressures have been corrected for the residual hydrostatic pressure effect. The baseline for correction was found by subtracting the head of water in the *HVLab* Multi-Channel Plethysmograph from that in the Medimatic DM2000 plethysmograph to give the difference between the two machines. This difference was used to calculate corrected FSBPs for the *HVLab* Multi-Channel Plethysmograph referenced to the Medimatic DM2000 plethysmograph. A re-analysis of the data has been performed after correction for residual hydrostatic pressure, the corrected data are shown in Table 20. The corrected data have been used in further analyses.

Table 19 Mean values and standard deviations of FSBPs (mmHg) and percentage FSBPs (%) for the three measurement conditions.

		Air	$FSBP_{30°C}$	$FSBP_{15°C}$	$FSBP_{10°C}$	$\%FSBP_{15°C}$	$\%FSBP_{10°C}$
Condition 1 DM2000	Digit 1	101 5 (13 8)	98 2 (13 9)	104 8 (14 1)	104 7 (16 7)	-	-
	Digit 3	100 4 (12 2)	108 3 (10 3)	100 4 (15 2)	106 6 (12 9)	87 8 (13 3)	93 0 (8 2)
Condition 2 *HVLab*	Digit 1	106 9 (14 9)	106 5 (12 1)	102 7 (15 1)	111 0 (10 8)	-	-
	Digit 3	102 0 (14 2)	¨132 4 (15 7)	¨126 3 (25 4)	¨131 5 (17 9)	⁺95 9 (8 7)	98 2 (11 8)
Condition 3 *HVLab*	Digit 1	108 8 (16 8)	100 8 (11 3)	102 8 (12 5)	104 2 (10 3)	-	-
	Digit 2	87 9 (13 0)	113 9 (17 9)	110 5 (14 2)	115 9 (16 5)	95 1 (13 0)	91 8 (20 2)
	Digit 3	95 2 (15 3)	¨123 9 (15 5)	˙117 1 (22 4)	¨125 7 (17 9)	92 5 (20 4)	99 7 (13 7)
	Digit 4	112 0 (23 7)	125 2 (14 9)	115 8 (18 9)	124 4 (16 0)	90 1 (15 7)	97 5 (14 9)
	Digit 5	96 4 (17 5)	115 7(20 6)	108 0 (20 6)	113 8 (17 8)	90 9 (14 0)	99 8 (20 2)

Paired samples *t*-test, differences from Condition 1 $^{**}p < 0\ 01$, $^{*}p < 0\ 05$, $^{+}p < 0\ 1$

Table 20 Mean (standard deviation) of FSBPs (mmHg) and percentage FSBPs (%) measured on the thumb and middle finger corrected for residual hydrostatic pressure.

		Air	$FSBP_{30°C}$	$FSBP_{15°C}$	$FSBP_{10°C}$	$\%FSBP_{15°C}$	$\%FSBP_{10°C}$
Condition 1	Digit 1	101 5 (13 8)	98 2 (13 9)	104 8 (14 1)	104 7 (16 7)	-	-
DM2000	Digit 3	100 4 (12 2)	108 3 (10 3)	100 4 (15 2)	106 6 (12 9)	87 8 (13 3)	93 0 (8 23)
Condition 2	Digit 1	106 9 (14 9)	106 5 (12 1)	102 7 (15 1)	111 0 (10 8)	-	-
HVLab	Digit 3	102 0 (14 2)	115 4 (15 8)	109 3 (25 4)	114 5 (17 9)	98 0 (13 3)	95 4 (9 60)
Condition 3	Digit 1	108 8 (16 8)	100 8 (11 3)	102 8 (12 5)	104 2 (10 3)	-	-
HVLab	Digit 3	95 2 (15 3)	106 9 (15 5)	100 1 (22 4)	108 7 (17 9)	91 5 (23 7)	99 7 (15 9)

4.2.3.1 Comparison between plethysmographs

To compare measurements between the two plethysmographs, FSBPs measured in Condition 1 and Condition 2 have been compared.

For measurements made on the thumb, repeated measures analysis of variance indicated no difference between machines but a significant effect of temperature of thermal provocation. The interaction between plethysmograph and temperature of thermal provocation was not significant. Post hoc tests showed that for the Medimatic DM2000 plethysmograph, FSBPs measured on the thumb after cold provocation of the test finger at 10°C and at 15°C were higher than those after thermal provocation of the test finger at 30°C ($p < 0.016$).

For measurements made on the middle finger, there was a significant effect of plethysmograph in the repeated measures analysis of variance. Overall, measurements made using the *HVLab* Multi-Channel Plethysmograph were higher than those made using the Medimatic DM2000 plethysmograph. The temperature of thermal provocation also resulted in significant changes in FSBPs measured on the middle finger. The interaction between plethysmograph and temperature of thermal provocation was not

significant. Post hoc tests showed the *HVLab* Multi-Channel Plethysmograph only gave higher FSBPs than the Medimatic DM2000 plethysmograph for measurements made after thermal provocation at 30°C. This difference was marginally significant ($p = 0.082$).

For both plethysmographs, measurements made on the middle finger after thermal provocation at 30°C were higher than measurements in air ($p < 0.046$). For the *HVLab* Multi-Channel Plethysmograph, measurements made after thermal provocation at 10°C were marginally higher than those measured in air ($p = 0.082$). There were no other differences between FSBPs resulting from thermal provocation.

Percentage FSBPs were not different between machines, there were no differences between the percentage FSBPs at 15°C and 10°C ($p > 0.1$). Neither FSBPs nor percentage FSBPs were significantly correlated between plethysmographs, or between temperatures of cold provocation ($p > 0.05$).

4.2.3.2 Thermal provocation of four fingers compared to cold provocation of one finger

To assess the effects of cold provocation of four fingers as opposed to one finger, measurements made in Condition 2 and Condition 3 have been compared.

For measurements made on the thumbs, repeated measures analysis of variance indicated no significant differences when four fingers were cooled compared to when one finger was cooled. The interaction between number of fingers undergoing thermal provocation and the temperature of cold provocation was not significant. There was a marginal effect the temperature of thermal provocation ($p = 0.087$).

Post hoc analysis showed that following thermal provocation of one test finger, marginally higher FSBPs were observed at 10°C than at 15°C ($p = 0.070$). After thermal provocation of four test fingers, higher FSBPs were observed at 10°C than at 30°C ($p = 0.001$).

For measurements made on the middle finger, repeated measures analyses of variance showed no significant differences between FSBPs due to the number of fingers being cooled, the temperature of thermal provocation or the interaction between the two. Post hoc analysis showed measurements made at 30°C and at 10°C were marginally higher than measurements in air for both conditions ($p = 0.068$ and $p = 0.081$, respectively). For thermal provocation of four test fingers, FSBPs at 10°C were higher than FSBPs at 15°C ($p = 0.037$).

Percentage finger systolic blood pressures were not different between conditions. For measurements made with thermal provocation of four fingers, percentage finger systolic blood pressures were higher at 10°C than at 15°C ($p = 0.002$).

Measurements made at 30°C, 15°C and 10°C on both the thumb and the middle finger were positively correlated within conditions ($p < 0.062$). Measurements made on the middle finger at 30°C, 15°C and 10°C were positively correlated between the two conditions ($p < 0.047$). Percentage FSBPs after thermal provocation of four test fingers were correlated between measurements made at 15°C and at 10°C, they were not significantly correlated between measurements made in the two conditions.

4.2.4 Discussion

The results of this study show that when measuring FSBPs, artificially high FSBPs are obtained if there is a residual hydrostatic pressure in the pressure cuffs during the deflation period. The effect is dependent upon the difference in height between the pressure cuffs and the water level in the reservoir of the plethysmograph. For a difference in height of 20 cm, FSBPs are approximately 15 mmHg too high. This difference will decrease the sensitivity of the measurement method to VWF because subjects with mild VWF who exhibit FSBPs that are marginally pathological will have normal results.

The effect of residual hydrostatic pressure must be taken into account when making measurements of FSBPs. This can be done by measuring the pressure in the cuffs directly, by maintaining the cuffs at the height of the water in the pressure reservoir, or by performing a mathematical correction. To make a mathematical correction, the true cuff pressure can be obtained from the following equation:

$$\textit{True cuff pressure (mmHg)} = \textit{Measured pressure (mmHg)} - 0.0735 \times \textit{Height of water (mm)}$$

The height of water is the height of the pressure cuffs above the water level in the reservoir of the plethysmograph, measured in millimetres. The pressure is measured in millimetres of mercury.

4.2.4.1 Comparison between plethysmographs

Measurements of reference FSBPs made on the thumbs following thermal provocation of the middle finger were not different between the two machines, demonstrating reference measurements were unaffected by the plethysmograph used to measure them. The effect of thermal provocation on thumb systolic blood pressures might suggest a difference between the two plethysmographs: the effect was observed for the Medimatic DM2000 plethysmograph only. The repeated measure analysis of variance, however, did not show an interaction between machine and temperature of thermal provocation and so it might be concluded that such differences are negligible.

For measurements made on the middle finger, the *HVLab* Multi-Channel Plethysmograph gave higher finger systolic blood pressures overall. When the measurements were compared at each temperature, only measurements at 30°C differed, this difference only attaining marginal significance. The effect of thermal provocation was similar for the two machines as no interaction was seen between plethysmograph and the temperature of thermal provocation. The percentage FSBPs were also similar for the two machines. The differences between measurements made on the middle finger using the two plethysmographs were small and, since the effects of thermal provocation were similar for both machines, it is concluded that results from the two machines are comparable, provided the correction for residual hydrostatic pressure is made.

The lack of correlation between measurements made with the two plethysmographs, or between measurements made at different temperatures of thermal provocation with the same plethysmograph, indicates some degree of intra-subject variability in the measurements. The repeatability of the Medimatic DM2000 plethysmograph has been demonstrated by others (Bovenzi 1991, Carnicelli *et al.* 1992) but it would be beneficial to compare it to the intra-subject variability for the *HVLab* Multi-Channel Plethysmograph. The repeatability of measurements made with the *HVLab* Multi-Channel Plethysmograph is considered in Section 4.3.

4.2.4.2 Thermal provocation of four fingers compared to thermal provocation of one finger

Comparison of reference FSBPs in the thumb after thermal provocation of either one test finger or of four test fingers using the same apparatus showed no differences. There were significant effects of the temperature of thermal provocation on the reference FSBPs, but these did not differ between the two conditions; the interaction between temperature of thermal provocation and the number of fingers undergoing thermal provocation was not significant. These results show that the reference FSBPs were unaffected by the number of test fingers.

Measurements made on the middle finger showed similar results to measurements made on the thumb. There were no differences between FSBPs measured after thermal provocation of one finger or of four fingers. Furthermore, measurements after thermal provocation showed similar patterns for both conditions, higher FSBPs being observed at 10°C and 30°C than at 15°C and in air. The percentage FSBPs were also similar between conditions. These results show any differences in FSBPs due to thermal provocation of four fingers compared to thermal provocation of one finger were negligible amongst these subjects.

Table 21 Percentage FSBPs reported in the literature and those obtained in this study before correcting for residual hydrostatic pressure.

Literature		$\%FSBP_{15}$	$\%FSBP_{10}$
Thulesius et al (1981)	Mean (standard deviation)	98 (8)	97 (10)
Ekenvall and Lindblad (1986)	Median (Range)	86 (67-100)	83 (59-96)
Bovenzi, M (1989)	Median (Range)	100 (100-100)	96.3 (68-113)
Bovenzi, M (1991)	Mean (Standard deviation)	88.5 (10.1)	91.8 (13.8)
Virokannas and Rintamaki (1991)	Mean (Standard deviation)	90 (14)	90 (10)
Carnicelli *et al* (1992)	Mean (Standard deviation)	89.9 (9.4)	85.5 (8.3)
Bovenzi, M (1993)	Median (Range)	100 (65-114)	100 (61-115)
Bovenzi *et al* (1995)	Median (IQR)	-	100 (90 7-100)
Bovenzi (1997)	Mean (Standard deviation)	98.3 (8 7)	94.8 (11 8)
This study			
Condition 1	Mean (Standard deviation)	87.8 (13.3)	93.0 (8 23)
Condition 2	Mean (Standard deviation)	95 9 (8.7)	98.2 (11.8)
Condition 3, index finger	Mean (Standard deviation)	95.1 (13.0)	91.8 (20.2)
Condition 3, middle finger	Mean (Standard deviation)	92.5 (20 4)	99.7 (13.7)
Condition 3, ring finger	Mean (Standard deviation)	90.1 (15 7)	97.5 (14 9)
Condition 3, little finger	Mean (Standard deviation)	90.9 (14.0)	99.8 (20.2)

The data obtained in this study have been compared to measurements reported in the literature (Table 21). Since it is not possible to correct for the effect of residual hydrostatic pressure in the data obtained from the literature, only percentage FSBPs are shown; these did not exhibit the large differences due to effects of residual hydrostatic pressure.

The data in Table 21 show that the mean percentage FSBPs measured in this study were similar to those obtained by other authors. However, measurements made after thermal provocation of four fingers show a larger inter-subject variability than both the measurements reported in the literature and the measurements made after thermal provocation of one finger in this study.

High inter-subject variability does not necessarily imply high intra-subject variability. A higher degree of association was observed between conditions and temperatures of thermal provocation for the *HVLab* Multi-Channel Plethysmograph than was observed between plethysmographs. Subjects exhibiting high FSBPs on one occasion were more likely to exhibit high FSBPs on another occasion when both measurements were made using the *HVLab* Multi-Channel Plethysmograph compared to when measurements were made with different plethysmographs (*cf.* Section 4.2.3.1 and Section 4.2.3.2). The correlation between percentage FSBPs at 10°C and 15°C when thermal provocation was applied to four fingers, compared to the absence of correlation when thermal provocation was applied to one test finger (Section 4.2.3.2), also suggests increasingly consistent response to cold when the number of test fingers was increased.

The greater consistency within subjects, and the higher inter-subject variability observed when thermal provocation was applied to four test fingers compared to when thermal provocation was applied to one test finger, is most likely due to the exaggerated stimulus applied to the fingers. An exaggerated stimulus alters central sympathetic nervous system activity, and hence the response of digital arteries to thermal provocation (Lassen 1978).

The increased effects of thermal provocation of four fingers on the central sympathetic nervous system may be useful in detecting VWF (Kurozawa *et al.* 1991). However, the high inter-subject variability results in lower normal limits than those found in the literature when they are calculated as the mean minus two standard deviations. Further work is needed to compare the intra-subject variability between measurements of FSBPs with thermal provocation of four fingers and with thermal provocation of one test finger to determine if measurements made on four test fingers are as repeatable as measurements on one test finger.

4.2.5 Conclusions

The results of this study show that measurements made following thermal provocation of one finger can be compared between plethysmographs, provided a correction is made for the effects of residual hydrostatic pressure. The difference between the effects of thermal provocation of one finger compared to four fingers were negligible amongst healthy subjects, indicating that the increased stimulus would not cause a rise in false positive results when the measurements are used to detect VWF. However, it was shown that inter-subject variability was increased by increasing the number of test fingers, most likely due to exaggerating central sympathetic activity. The increase in inter-subject variability could result in lower normal limits and might increase the number of false negative results. Further work is required to investigate the intra-subject variability of measurements of finger systolic blood pressures on four test fingers.

4.3 REPEATABILITY OF SIMULTANEOUS FINGER SYSTOLIC BLOOD PRESSURE MEASUREMENTS ON FOUR TEST FINGERS COMPARED TO ONE TEST FINGER

4.3.1 Introduction

The newly developed *HVLab* Multi-Channel Plethysmograph and the commercially available Medimatic DM2000 plethysmograph were compared in Section 4.2. It was found that although similar results could be obtained with the two machines, the variability increased across normal subjects when thermal provocation was applied to four test fingers compared to one test finger. The effect was hypothesised as being due to the increased area of stimulus application affecting the central sympathetic nervous system.

It is likely that the intra-subject component of the variability of the measurement is affected by this change in central sympathetic activity. The data from the previous study indicated that measurements made with thermal provocation of four fingers were more consistent than measurements made with thermal provocation of one finger, despite the increase in inter-subject variability.

The repeatability of the Medimatic DM2000 plethysmograph has been reported by some investigators. For percentage FSBPs, Bovenzi (1991) showed coefficients of variation between 3.8% and 9.5% in healthy subjects. Carnicelli *et al.* (1992) showed coefficients of variation between 5.4% and 29%. It is suggested in the literature that measurements made using the Medimatic DM2000 plethysmograph with cold provocation of one test finger are repeatable.

The study reported here was performed to compare the repeatability of measurements using the *HVLab* Multi-Channel Plethysmograph to those made using the Medimatic DM2000 Plethysmograph. It was hypothesised that measurements made after thermal provocation of four test fingers exhibit greater repeatability than measurements made after thermal provocation of one test finger due to a more consistent effect of the increased thermal provocation on the central sympathetic nervous system.

4.3.2 Method

4.3.2.1 Subjects

Twelve healthy, male volunteers with a mean age of 23.8 years (standard deviation, SD 2.76 years) participated in the study. They were students, office workers or unemployed with no history of occupational exposure to vibration. None reported symptoms associated with peripheral vascular insufficiency, injuries to the upper extremities or a family history of episodic blanching. The mean height and the mean weight of the subjects were 1.79 meters (SD 0.07 m) and 71.2 kg (SD 6.6 kg), respectively.

4.3.2.2 Experimental conditions

Participants attended for testing wearing light, indoor clothing. They were instructed not to smoke for one hour, drink caffeine for 4 hours or alcohol for 12 hours before each session. Subjects were examined in a supine position after habituation for 15 minutes in a room of mean temperature 26.5°C (SD 1.3°C). Mean external temperature before each session was 12.6°C (SD 3.3°C). Room temperature was measured adjacent to the subjects' hands at the start of each session, the end of each session and during each measurement using a thermocouple connected to an *HVLab* 8-Channel Temperature Monitor (Appendix A). External temperature was measured at the start of each session using the free probe thermocouple of an *HVLab* Thermal Aesthesiometer (Appendix A).

4.3.2.3 Experimental procedure

Each subject attended four sessions, each on consecutive days. Measurements were made simultaneously on four test fingers and a reference finger during two sessions, and on one test finger and a reference finger during two sessions. The *HVLab* Multi-Channel Plethysmograph was used for measurements made on four test fingers, the Medimatic DM2000 plethysmograph was used for measurements made on one test finger. The order of presentation of conditions was balanced across subjects.

During the period of habituation, the left hand was instrumented as described in Section 4.2.2.3. For thermal provocation of four fingers, the index, middle, ring and little fingers were used as test fingers and the thumb was used as the reference finger. For thermal provocation of one finger, measurements were made on the middle finger (test finger) and the thumb (reference finger).

Arm systolic pressure (ASP) was measured in both arms. Finger systolic blood pressures were then measured in air using the method defined in Section 2.8. Following measurements in air, the single inlet cuffs on the test fingers were replaced with double inlet cuffs. The reference finger retained the single-inlet air cuff for measurement of changes in systemic systolic pressure (SSP). Ischaemia and thermal provocation at 30°C were applied to the test finger(s) for a period of five minutes, followed by a measurement of ASP in both arms and FSBPs on the left hand. The procedure was repeated for a temperature of 15°C and then for a temperature of 10°C.

4.3.2.4 Analysis

Parametric statistics have been used in the analysis; measurements were normally distributed (Shapiro-Wilkes, $p > 0.1$). Repeated measures analysis of variance has been used to compare results between plethysmographs. Post hoc tests have been performed using independent samples *t*-tests for differences between subjects; differences within subjects have been tested using paired samples *t*-tests. Root-mean-square differences, Pearson's correlation coefficients and limits of agreement have been used to assess repeatability of the two machines. A *p*-value of 0.05 has been chosen to indicate significance, with marginal significance being achieved at the 10% level.

Pearson's correlation coefficients provide a measure of association between two sets of measurements. The r.m.s. differences reflect the mean magnitude of changes between two sets of measurements (Maeda and Griffin 1994). The mean difference identifies systematic changes, or bias, between two sets of measurements.

Limits of agreement are calculated as the mean difference ± 2 standard deviations of the differences between two sets of measurements. The upper and lower limits of agreement indicate the maximum change expected in 95% of normal subjects in the increasing and decreasing direction, respectively. Thus, the limits of agreement quantify the extent of intra-subject variability (Bland and Altman 1986).

4.3.3 Results

Mean ASPs and of FSBPs are shown in Table 22. The ASPs were higher in smokers (N = 5) than in non-smokers (N = 7) ($p < 0.05$). There were no significant effects of smoking habits on FSBPs. Neither height nor weight were correlated with FSBPs or ASPs ($p > 0.05$). External temperature and internal temperature were not related to the results ($p > 0.1$). Finger systolic blood pressures and percentage FSBPs, after correcting for residual hydrostatic pressure (Section 4.2.3), are shown in Table 23.

Repeated measures analysis of variance indicated no significant differences between plethysmographs, sessions or conditions of thermal provocation for either FSBPs or percentage FSBPs. The interaction between plethysmographs and thermal provocation was significant for FSBPs ($p = 0.038$), no other interactions were significant. The Pearson's product moment correlation coefficients, r.m.s. differences, mean differences and limits of agreement for assessing repeatability are shown in Table 24.

Table 22 Mean ASPs and FSBPs (in mmHg), measured after thermal provocation of four test fingers in two sessions (*HVLab* Multi-Channel Plethysmograph) and after thermal provocation of one test finger in two sessions (Medimatic DM2000 plethysmograph).

			Thumb	Index finger	Middle finger	Ring finger	Little finger	Left Arm	Right Arm
HVLab Multi-Channel Plethysmograph	1st Session	Air	105	101	95	97	95	112	120
		30°C	94	120	100	114	94	110	119
		15°C	96	116	94	109	94	111	111
		10°C	96	119	102	112	102	111	121
	2nd Session	Air	104	102	97	99	99	112	117
		30°C	99	116	108	115	92	109	116
		15°C	98	116	98	108	89	112	120
		10°C	101	114	103	108	92	112	118
Medimatic DM 2000 Plethysmograph	1st Session	Air	115	116	-	-	-	114	116
		30°C	113	134	-	-	-	110	115
		15°C	112	126	-	-	-	112	117
		10°C	114	111	-	-	-	112	117
	2nd Session	Air	109	110	-	-	-	113	117
		30°C	111	130	-	-	-	112	114
		15°C	112	120	-	-	-	112	115
		10°C	118	116	-	-	-	113	117

Table 23 The mean (standard deviation) FSBPs measured on the thumb and the middle finger with either thermal provocation of one test fingers (Medimatic DM2000 plethysmograph) or four test fingers (*HVLab* Multi-Channel Plethysmograph), corrected for residual hydrostatic pressure. Percentage FSBPs measured on the middle finger are also shown.

Condition	Finger	Air	$FSBP_{30°C}$	$FSBP_{15°C}$	$FSBP_{10°C}$	$\%FSBP_{15°C}$	$\%FSBP_{10°C}$
DM2000	Thumb	115.4 (9.5)	112.2 (11.6)	111.0 (12.2)	113.6 (12.2)	-	-
Session 1	Middle	116.2 (8.8)	131.6 (31.3)	124.1 (25.6)	111.2 (34.9)	94.5 (16.9)	85.8 (23.8)
DM2000	Thumb	108.8 (14.5)	111.5 (25.8)	112.2 (26.7)	118.3 (26.3)	-	-
Session 2	Middle	109.8 (9.4)	130.2 (24.9)	119.8 (29.7)	116.5 (31.3)	92.3 (20.5)	91.5 (26.5)
HVLab	Thumb	115.7 (12.6)	104.5 (16.1)	105.9 (15.6)	106.6 (17.5)	-	-
Session 1	Middle	111.4 (10.4)	115.0 (15.8)	110.8 (18.8)	114.2 (22.6)	95.2 (21.2)	98.1 (20.3)
HVLab	Thumb	114.5 (19.5)	109.8 (14.0)	108.2 (16.0)	112.0 (16.2)	-	-
Session 2	Middle	112.9 (16.1)	110.4 (19.9)	110.7 (23.7)	108.5 (21.9)	103.6 (24.5)	99.9 (18.2)

For the Medimatic DM2000 plethysmograph, all the measurements of FSBP on the thumb tended to be positively correlated within sessions ($p < 0.099$). For measurements made on the middle finger, positive correlations were observed between FSBPs at 30°C and 15°C, and between FSBPs at 15°C and 10°C within session 1 ($p < 0.079$). No other significant correlations were observed for this plethysmograph.

For the *HVLab* Multi-Channel Plethysmograph, measurements made on the thumb during session 1 in air, at 30°C, at 15°C and at 10°C were significantly positively correlated with each other ($p < 0.028$). For session 2, measurements on the thumb made after thermal provocation of the test fingers were not correlated with measurements on the thumb without thermal provocation of the test fingers ($p > 0.16$). Measurements on the thumb at the different temperatures of thermal provocation of the test fingers were correlated with each other ($p < 0.083$). For the middle finger in session 1, there were positive correlations between measurements made with thermal provocation ($p < 0.091$), but not with measurements made in air ($p > 0.124$). For session 2, there was a correlation between measurements made on the middle finger at 10°C and measurements made on the middle finger at 15°C ($p = 0.037$).

4.3.4 Discussion

A comparison of the data given in Table 21, Section 4.2.4, with those in Table 23 show similar mean percentage FSBPs. The standard deviations for the measurements in this study, however, appear to be higher than those given in Table 21. This is due to a higher inter-subject variability amongst the subjects used here than has been reported by other investigators. This inter-subject variability is unlikely to influence the intra-subject variability.

Table 24 Pearson's product moment correlation coefficients. and their associated *p*-values, r.m.s. differences, mean differences and limits of agreement between two sessions for measurements of FSBP made on the thumb or middle finger using the *HVLab* Multi-Channel Plethysmograph or the Medimatic DM2000..

	Air	$FSBP_{30°C}$	$FSBP_{15°C}$	$FSBP_{10°C}$	$\%FSBP_{15°C}$	$\%FSBP_{10°C}$
HVLab Multi-Channel Plethysmograph, repeatability statistics for measurements made on the thumb						
Pearson's r	0.5696	0.0658	0.6768	0.6414	-	-
p	0.522	0.857	0.032	0.046	-	-
r.m.s. difference (mmHg)	15.9	19.8	12.3	14.5	-	-
Mean difference (mmHg)	1.2	-3.0	-1.1	-3.8	-	-
Lower limit of agreement (mmHg)	-33.4	-44.4	-26.9	-33.2	-	-
Upper limit of agreement (mmHg)	34.5	38.3	24.8	25.7	-	-
Medimatic DM2000, repeatability statistics for measurements made on the thumb						
Pearson's r	-0.0818	0.5470	-0.0983	0.4189	-	-
p	0.322	0.102	0.787	0.228	-	-
r.m.s. difference (mmHg)	17.9	20.8	30.2	26.1	-	-
Mean difference (mmHg)	6.6	0.8	-1.2	-6.2	-	-
Lower limit of agreement (mmHg)	-28.3	-42.7	-64.5	-59.4	-	-
Upper limit of agreement (mmHg)	41.4	44.2	62.1	47.0	-	-
HVLab Multi-Channel Plethysmograph, repeatability statistics for measurements made on the middle finger						
Pearson's r	0.2469	0.2273	-0.2145	0.4354	-0.4826	-0.2552
p	0.522	0.556	0.579	0.241	0.188	0.507
r.m.s. difference (mmHg)	15.4	21.5	31.0	19.2	38.9	27.9
Mean difference (mmHg)	-1.4	2.9	-2.2	-0.3	-7.8	-2.7
Lower limit of agreement (mmHg)	-33.7	-40.3	-67.4	-40.8	-88.6	-61.5
Upper limit of agreement (mmHg)	30.9	48.0	63.1	40.2	73.0	56.1
Medimatic DM2000, repeatability statistics for measurements made on the middle finger						
Pearson's r	0.5615	0.8741	-0.1468	0.7623	-0.4861	0.7113
p	0.190	0.010	0.758	0.046	0.269	0.048
r.m.s. difference (mmHg)	11.5	20.9	35.5	32.5	25.6	19.4
Mean difference (mmHg)	6.3	-1.1	4.4	-11.5	2.3	-6.0
Lower limit of agreement (mmHg)	-13.8	-44.9	-69.2	-76.1	-62.7	-45.5
Upper limit of agreement (mmHg)	26.5	42.7	77.9	54.3	67.3	33.6

4.3.4.1 Differences between plethysmographs

Repeated measures analysis of variance showed no differences between FSBPs measured with either plethysmograph. A significant interaction between the effect of cold provocation and the plethysmograph used for making measurements was found. The post hoc analyses were performed to investigate this interaction.

There was a decrease in thumb systolic blood pressures during measurements with thermal provocation compared to measurements in air during the first session using the *HVLab* Multi-Channel Plethysmograph. Within sessions, measurements on the thumbs made using both plethysmographs tended to be positively correlated. This indicates that inter-subject differences tended to remain similar over the thirty minutes it took to perform the measurements. Thus it is concluded that the observed difference in thumb systolic

blood pressure for the *HVLab* Multi-Channel Plethysmograph during session 1 is a true effect. A similar but insignificant trend was observed during the second session performed with the *HVLab* Multi-Channel Plethysmograph, and in the previous study when measurements were made on four test fingers and a reference finger (Condition 3, Table 20). The reason for this change is unknown but it is tentatively suggested it is caused by an increase in central sympathetic activity in response to the increased stimulus when thermal provocation was applied. Further work is needed to determine the cause of this effect, although for assessing the vascular response to thermal provocation it may not be considered important when measurements in air are not used as the baseline measurement for calculating percentage FSBPs.

The other factor found to influence the interaction between thermal provocation and plethysmograph was the increase in test finger FSBPs at 30°C compared to measurements in air when using the Medimatic DM2000 plethysmograph. This change was not directly observed for the *HVLab* Multi-Channel Plethysmograph. For the *HVLab* Multi-Channel Plethysmograph there was, however, a drop in systemic systolic blood pressure measured in the reference finger whilst the FSBP remained similar in the test finger between measurements in air and at 30°C. This would imply that relative to systemic systolic blood pressure, the test finger showed a rise in FSBP, a similar result to that observed for the Medimatic DM2000 plethysmograph. It can be concluded that there is no difference in the effects of thermal provocation at 30°C between the two plethysmographs. The increased FSBP at 30°C would be consistent with vasodilation occurring at 30°C compared to air temperature. No studies were found in the literature that have compared FSBPs measured in air to those measured at 30°C with which to support this finding.

These results would suggest little or no difference between FSBPs measured on four test fingers and a reference finger and FSBPs measured on one test finger and a reference finger. It can be concluded that the two plethysmographs compared in this study can be used interchangeably. The decrease in systemic systolic blood pressure observed when thermal provocation is applied to four test fingers compared to measurements in air requires some further investigation.

4.3.4.2 Repeatability of FSBP measurements

Repeated measures analysis of variance did not show a difference between the repeatability of the two plethysmographs. The mean difference between sessions for each measurement of FSBP showed no systematic changes for measurements made with the same machine. Nielsen (1978) showed mean differences between days of between 2.6 mmHg and 5.6 mmHg which are similar to those found here. These analyses suggest the measurements were repeatable with both plethysmographs.

4.3.4.2.1 *Measurements made on the reference finger*

The repeatability statistics given in Table 24 show that reference finger measurements were more consistent between sessions for the *HVLab* Multi-Channel Plethysmograph than for the Medimatic DM2000 plethysmograph; the correlation coefficients were generally higher and the r.m.s. differences smaller for measurements made using the *HVLab* Multi-Channel Plethysmograph than for measurements made using the Medimatic DM2000 plethysmograph.

To quantify the degree of intra-subject variation, the limits of agreement have been used (Table 24). The limits of agreement were influenced by the application of thermal provocation. The changes within subjects between sessions increased with the addition of thermal provocation for the Medimatic DM2000 plethysmograph but decreased for the *HVLab* Multi-Channel Plethysmograph. The correlation coefficients also suggest a much greater consistency of response of the reference FSBPs to cold provocation with the *HVLab* Multi-Channel Plethysmograph than with the Medimatic DM2000 Plethysmograph. This further suggests more repeatable reference finger measurements for the *HVLab* Multi-Channel Plethysmograph than for the Medimatic DM2000 plethysmograph.

These results are consistent with the hypothesis that a more repeatable effect on the central sympathetic nervous system is observed with cold provocation of four fingers than with cold provocation of one finger; changes in the FSBP measured on a reference finger are assumed to reflect changes in the systemic systolic blood pressure (Nielsen and Lassen 1978) which in turn are influenced by the central sympathetic nervous system (Nielsen 1981).

4.3.4.2.2 *Measurements made on the middle finger*

Measurements on the test fingers show a difference in repeatability between machines dependant on the temperature of thermal provocation. At all temperatures, the correlation coefficients are higher for the Medimatic DM2000 plethysmograph than for the *HVLab* Multi-Channel Plethysmograph. At 30°C and 15°C, the limits of agreement and r.m.s. differences were similar for the two plethysmographs, suggesting that intra-subject variability was similar. At 10°C, the r.m.s. differences and limits of agreement indicate a smaller intra-subject variability for the *HVLab* Multi-Channel Plethysmograph than for the Medimatic DM2000 plethysmograph.

For both plethysmographs, measurements made at 30°C and 10°C on the test finger gave more repeatable responses than measurements made at 15°C. For measurements made at 15°C on the middle finger, however, the correlations between sessions were negative. Negative correlation coefficients and wide limits of agreement imply that although intra-subject variability may be large, subjects with a low FSBP in one session

are likely to exhibit an increase in FSBPs in the next session whereas subjects with high FSBPs are likely to exhibit a decrease. In this case, the r.m.s. differences and the limits of agreement over-estimate the intra-subject variability. Because of the negative correlation coefficients, however, it can still be concluded that measurements made after thermal provocation at 15°C show a less consistent effect than thermal provocation at 10°C or at 30°C.

These results are consistent with the hypothesis of a more repeatable effect of thermal provocation when four test fingers are cooled than when one test finger is cooled due to a more repeatable response of the central sympathetic nervous system to the exaggerated stimulus. As the temperature of thermal provocation decreases, the central sympathetic discharge to the digits increases (Nielsen and Lassen 1978). As more fingers are cooled, the stimulus is exaggerated and this further increases central sympathetic activity (Section 4.2.4). The greater consistency of response with an exaggerated stimulus is possibly due to a dominance of the effect of the thermal provocation on the central sympathetic activity over the effects of other factors affecting sympathetic activity such as noise, environmental conditions and mental stress (Nielsen 1981).

4.3.4.2.3 Percentage finger systolic blood pressures

For measurements made with the *HVLab* Multi-Channel Plethysmograph, percentage FSBPs were more variable than the FSBPs (Table 20). With the Medimatic DM2000 plethysmograph, percentage FSBPs were less variable than the FSBPs. This difference between machines is probably caused by the direction of change in blood pressures for each individual, the widest limits of agreement being observed for measurements which were negatively correlated between sessions. Narrower limits of agreement were observed for the positively correlated measurements.

The r.m.s. differences and limits of agreement suggest the Medimatic DM2000 plethysmograph gave more consistent responses than the *HVLab* Multi-Channel Plethysmograph. This finding was not expected as the FSBPs tended to be more consistent between sessions with the *HVLab* Multi-Channel Plethysmograph than with the Medimatic DM2000 plethysmograph. The negative correlation coefficients for the *HVLab* Multi-Channel Plethysmograph, however, would suggest the limits of agreement overestimate the intra-subject variability.

From the interpretation of the repeatability data, it might be suggested that changes in FSBPs within subjects measured on different occasions can be large. However, the large changes tend to occur when a subject has exhibited a relatively high FSBP or a relatively

low FSBP on the first occasion of measurement; during the second measurement session, the subject is likely to show lower or higher FSBPs, respectively. It is concluded that that the measurement method is repeatable, although FSBPs do vary within individuals when measured on different occasions.

4.3.5 Conclusions

The method of measuring of FSBP by strain-gauge plethysmography has been shown to be repeatable although FSBPs vary within individuals between occasions. The repeatability of the measurement of FSBPs was slightly greater for the *HVLab* Multi-Channel Plethysmograph than the Medimatic DM2000 plethysmograph, although the reverse was seen for percentage FSBPs. The differences between machines were small and both machines gave similar results. It is concluded that the two plethysmographs both give repeatable measurements and can be used interchangeably.

When cold provocation of four fingers was employed, a small decrease in FSBPs was observed when compared to the cold provocation of one finger. This is consistent with an increase in sympathetic activity in response to an increase in the number of fingers being cooled.

CHAPTER 5 FINGER SYSTOLIC BLOOD PRESSURE MEASUREMENTS: INFLUENCE OF TEST PARAMETERS

5.1 INTRODUCTION

Finger systolic blood pressures may be inadvertently affected by the way they are measured. The method of correcting results for changes in systemic systolic pressures may further influence the outcome of this measurement. Two studies are reported in this chapter which address possible causes of variability due to the method of measuring and interpreting finger systolic blood pressures as described by Nielsen and Lassen (1977, 1978).

5.2 EFFECTS OF COLD PROVOCATION ON REFERENCE FINGER SYSTOLIC BLOOD PRESSURES

5.2.1 Introduction

Measurements of finger systolic blood pressure (FSBP) following thermal provocation of a test finger are often made in conjunction with simultaneous reference measurements obtained at a site not thermally provoked. These reference measurements are made so that changes in systemic systolic pressure (SSP) can be considered when explaining how the finger systolic pressure changes in response to thermal provocation (Section 2.2.7.1).

The reference measurement can be obtained from another finger (e.g. Bovenzi 1991, Nielsen and Lassen 1978, Virokannas and Rintamäki 1991) The arm systolic pressure is sometimes used (e.g. Ekenvall and Lindblad 1986, Thulesius *et al.* 1981). When using a FSBP measurement made on a reference finger to correct for changes in SSP, it is assumed that there is no effect of thermal provocation of a test finger on the reference finger. It is also assumed that a reference finger affected with VWF, or the arm systolic blood pressure if this is used as a reference, will reflect the systemic changes in a similar manner to healthy fingers.

Ekenvall and Lindblad (1986) showed that some subjects exhibit exaggerated vasoconstriction in a reference finger. The use of a reference finger to calculate percentage FSBPs was therefore questioned. If exaggerated vasoconstriction occurs in a reference finger, false negative results may be obtained when using the equation for calculating percentage finger systolic blood pressures quoted in the literature and in the studies reported in this thesis (Equation 1, Section 2.2.7.1) because increased vasoconstriction would result in a lower value for the denominator in the equation.

There are differences between FSBPs measured on different fingers, between the FSBPs measured along the length of a finger, and between measurements of SSP on the arm and the fingers (Hirai *et al.* 1976, Kurozawa *et al.* 1992, Nielsen 1978). Therefore, reference measurements made at different sites may not give comparable corrections for changes in SSP. It is also unlikely to be possible to measure SSP in the arm simultaneously with the FSBPs in the ipsilateral hand as occlusion of blood flow in the arm by the blood pressure cuff may result in incorrect measurements in the fingers.

This experiment investigated the effects of cold provocation of a test finger on the FSBPs of the other fingers on the same hand, and on the arm systolic blood pressure measured immediately before and immediately after removal of cold provocation. It was expected that the proximity of adjacent fingers to the cold provocation would result in increased vasoconstriction in these fingers, and therefore a decrease in FSBP. No effect was expected in the arms. Repeatability of the measurements was assessed.

5.2.2 Methods

5.2.2.1 Subjects

Twelve healthy male subjects participated in the study (mean age 22 years, standard deviation, SD 1.1 years; mean weight 73.7 kg, SD 11.7 kg; mean height 1.80 m, SD 0.07 m). Subjects were office workers, students or unemployed with no history of occupational exposure to vibration or of vascular disorders.

5.2.2.2 Experimental conditions

Subjects attended three identical sessions on three separate days. They wore light indoor clothing and did not smoke for one hour, or consume caffeine for four hours or alcohol for 12 hours before each session. Subjects rested supine in a room of mean temperature 21.7°C (SD 1.2°C) for 15 minutes prior to the commencement of measurements. Subjects remained supine for the duration of each session.

5.2.2.3 Experimental procedure

After the 15 minute adaptation period at the start of each session, arm systolic pressure (ASP) was measured on both arms using the ausculatory technique, as described in Appendix A. During measurement, the arms were horizontal at the side of the subject. The FSBPs of the thumb, index, ring and little fingers of both hands were measured in air using the method defined by Nielsen and Lassen (1978) (Section 2.2.2). The Medimatic DM2000 plethysmograph was used, the apparatus is described in Appendix A.

Table 25 Mean systolic blood pressures (millimetres of mercury, 12 subjects, each measured 3 times).

		Before Cooling		During Cooling		After Cooling	
		Mean	SD	Mean	SD	Mean	SD
Left	Arm	121	8.2	118	11.5	124	12.0
	Thumb	115	16.5	119	17.2	-	-
	Index finger	108	18.1	111	14.1	-	-
	Ring finger	113	16.2	115	15.5	-	-
	Little finger	106	15.9	107	16.4	-	-
Right	Arm	124	12.0	125	10.7	120	9.2
	Thumb	118	18.0	-	-	-	-
	Index finger	104	17.7	-	-	-	-
	Ring finger	117	16.3	-	-	-	-
	Little finger	109	16.5	-	-	-	-

Cold provocation at 10°C was applied to the medial phalanx of the middle finger of the left hand for a period of five minutes using a double-inlet cuff of the plastic bag type. A measurement of ASP was then made in each arm with the cold finger cuff still in place, followed by a measurement of FSBP in each of the uncooled fingers of the left hand. The cold finger cuff was then removed and a further measurement of ASP on both arms was made.

Restrictions imposed by the apparatus meant that only two measurements of FSBP could be obtained simultaneously. The FSBPs on the four fingers of each hand measured before finger cooling were therefore obtained with four separate measurements, the measurements were made in a random order. The FSBPs measured on the four uncooled fingers of the left hand at the end of finger cooling were obtained with two separate measurements, measurements being made in a balanced order. The FSBP in the cooled digit was not measured. The experimental procedure was identical on the three days.

5.2.3 Results

Table 25 shows the mean and standard deviations of the arm systolic blood pressures and the FSBPs measured before, during and after cold provocation. Weight and height were significantly correlated with pressure measurements. No other covariates were found to be significant. Weight has been used to correct for body size in analyses of variance.

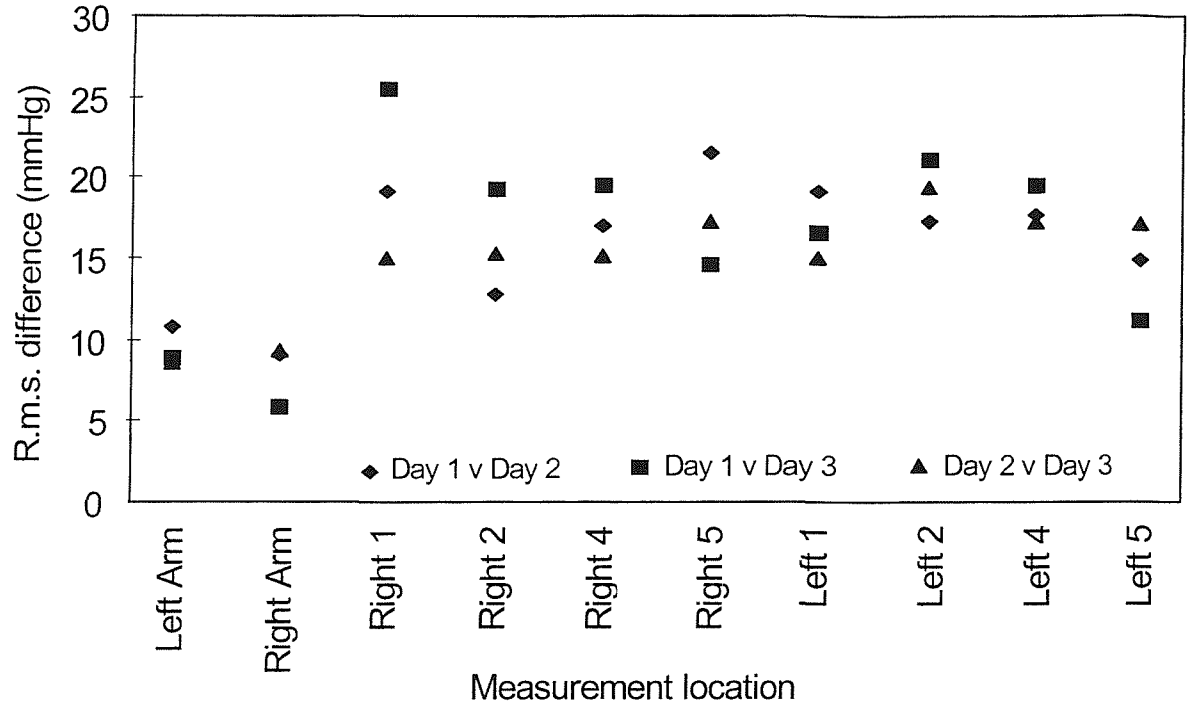


Figure 20 The root-mean-square differences between systolic blood pressure measurements in air obtained from individual subjects on different days prior to application of cold provocation to the middle finger.

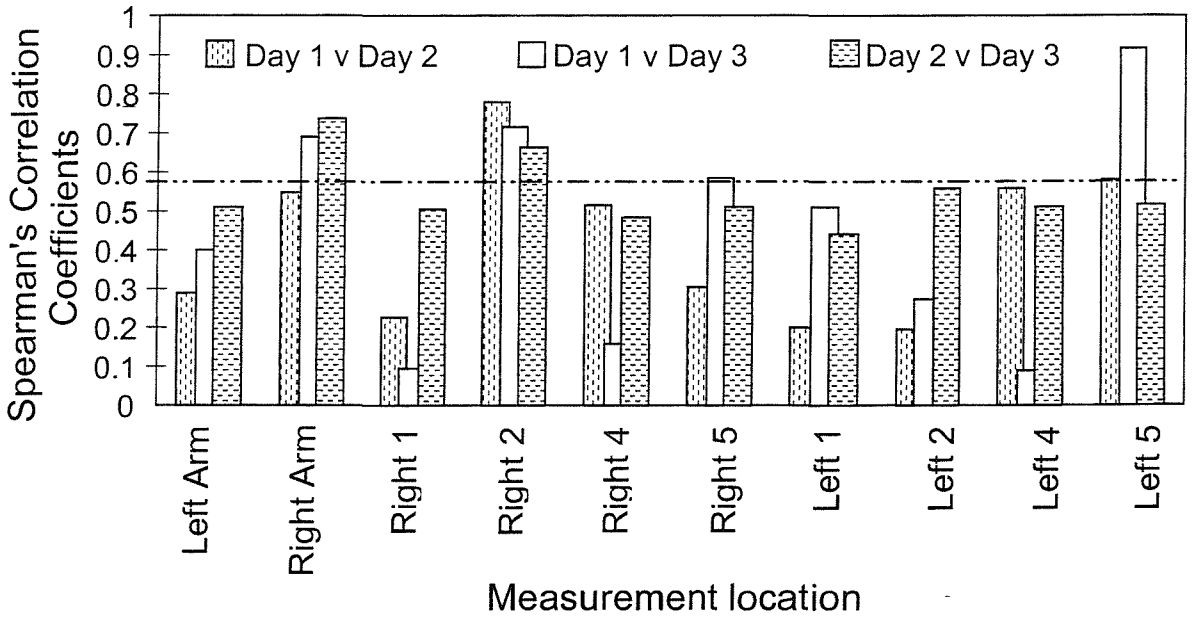


Figure 21 Spearman's rank correlation coefficients between systolic pressure measurements in air obtained on different days prior to application of cold provocation to the middle finger. Values attain significance when Spearman's $\rho = 0.57$ (shown by the dotted line).

5.2.3.1 *Repeatability of systolic blood pressure measurements in air*

Repeated measures analysis of variance showed no significant differences in FSBPs or ASPs between days for any of the measurements. The r.m.s. differences, in conjunction with correlation coefficients, have been used to assess the repeatability of the ASPs and FSBPs measured on different days. For high repeatability, the r.m.s. differences should be small and the correlation coefficients high (Maeda and Griffin 1994). Figure 20 and Figure 21 show the r.m.s differences and Spearman's correlation coefficients, respectively, for the systolic blood pressure measurements made before finger cooling.

The Spearman's correlation coefficients are generally positive and most are, or approach, statistical significance. Within the group of 12 healthy male subjects, a person with higher pressures measured on one day tended to have higher pressures relative to other subjects in the group when measured on another day.

5.2.3.2 *Effect of cold provocation on systolic blood pressures*

There were no significant changes in the ASP of either arm between measurements made before, during and after cooling of digit 3 of the left hand. Table 25 shows that in the thumb, index finger, ring finger and little finger of the left hand there was a mean increase in FSBPs measured at the end of a 5 minute period of cooling of the middle finger of the left hand. This was significant for the thumb and ring finger ($p < 0.1$) but insignificant in other fingers.

The difference between ASPs and FSBPs measured before, during and after cooling were calculated for each subject for each day to give an indication of the repeatability of the effects of cold provocation. Repeated measures analysis of variance indicated no significant differences in the effects of cold provocation between days. Figure 22 and Figure 23 show the r.m.s. differences and correlation coefficients for the changes, respectively.

The between-day r.m.s. differences of the changes in systolic blood pressures due to cold provocation were greater in magnitude than the changes due to cold provocation within each session; the mean (standard deviation) r.m.s. change in systolic blood pressures within each session was 11.1 (2.16) mmHg. This shows that the effects of cold provocation varied between days. The correlation coefficients between the changes in individual subjects on different days are low and variable. This suggests that the effects of cold provocation were not consistent on different occasions.

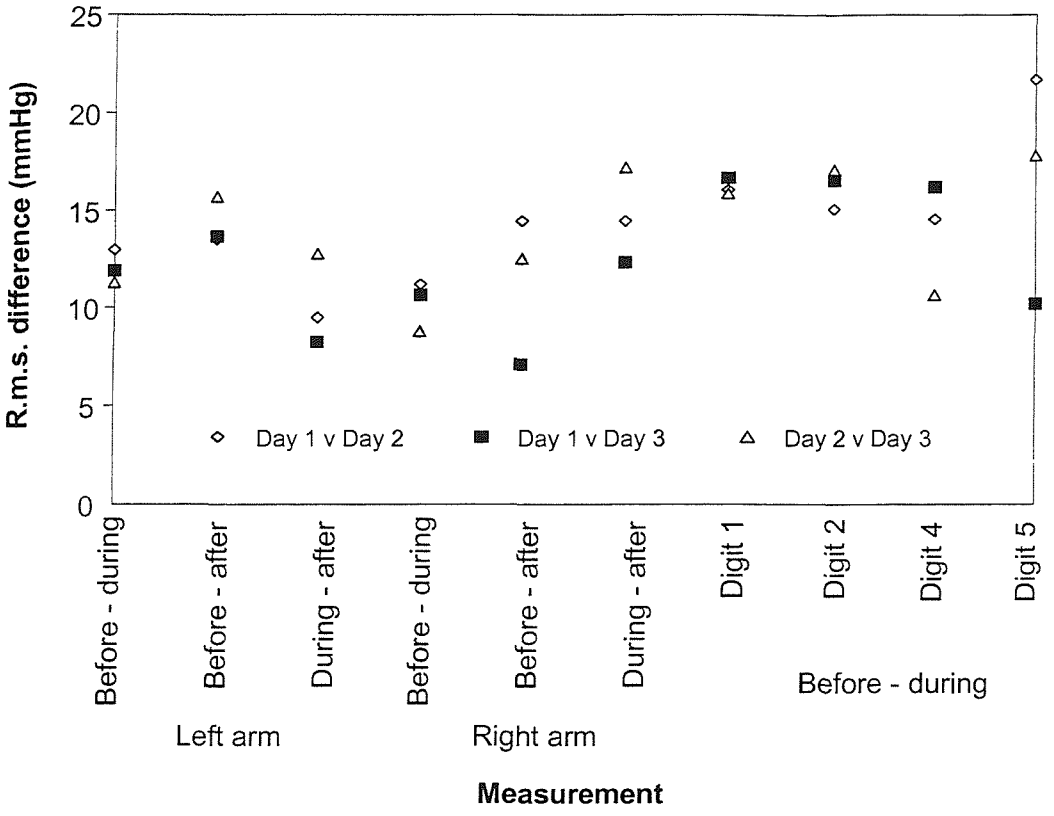


Figure 22 The root-mean-square differences of the changes in systolic blood pressures at different locations between measurements made before, during or after cooling of digit 3 of the left hand.

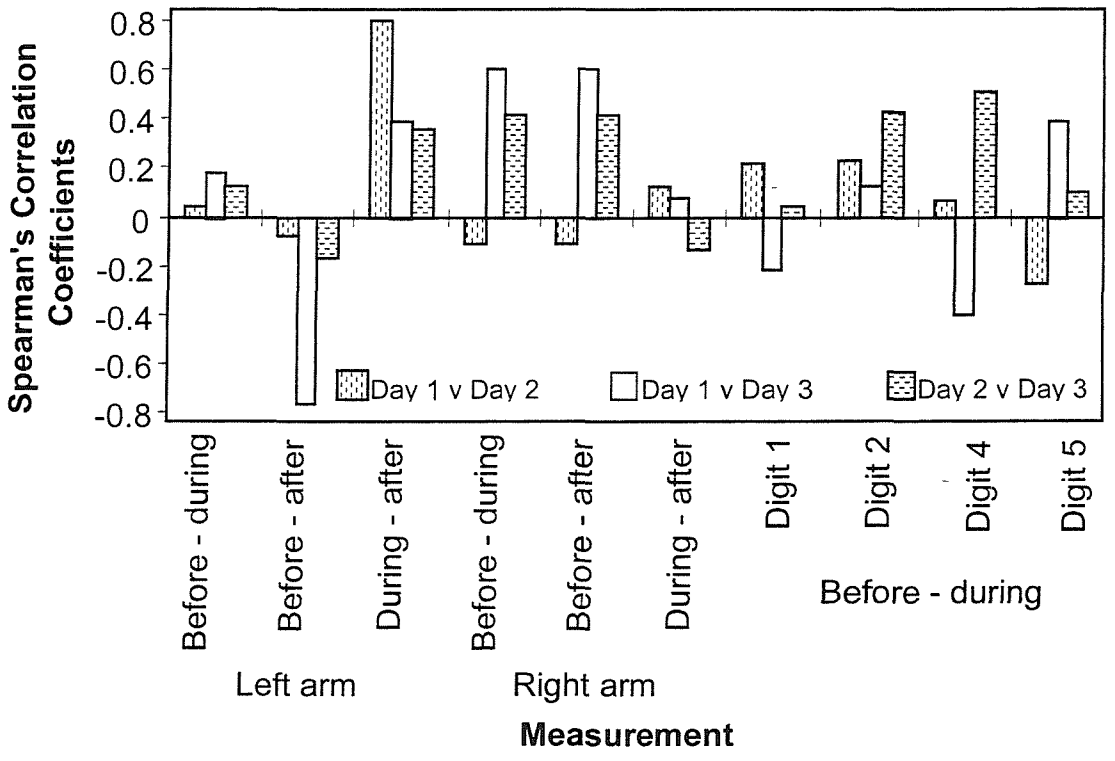


Figure 23 Spearman's correlation coefficients between changes in systolic blood pressures measured before, during and after cooling of digit 3. Values attain significance when Spearman's $\rho = \pm 0.57$.

Table 26 Statistical significance of differences between systolic blood pressures at different locations (Wilcoxon signed ranks test) (+ $p < 0.1$, * $p < 0.05$)

		Left					Right				
		Arm	Thumb	Index	Ring	Little	Arm	Thumb	Index	Ring	Little
Left	Arm		+	*	*	*	*	-	*	+	*
	Thumb			+	-	+	*	-	-	-	-
	Index				-	+	*	-	-	-	-
	Ring					*	*	-	-	+	-
	Little						*	-	-	-	-
Right	Arm							+	*	*	*
	Thumb								*	-	*
	Index									*	-
	Ring										*
	Little										

5.2.3.3 Effect of measurement location on systolic blood pressures

Table 26 summarises the results of statistical comparisons (Wilcoxon signed ranks test) between FSBPs measured on the different fingers and between ASPs and FSBPs before cooling of the middle finger. Measurements on the left arm were significantly lower than measurements on the right arm. Measurements made on the fingers were similar on the left and the right side, only the ring fingers showing a marginally significant difference; the FSBP measured on the right side tended to be higher than that measured on the left side. The FSBPs were significantly lower than the ASPs. Thumb systolic pressures were marginally lower than ASPs.

5.2.4 Discussion

5.2.4.1 Repeatability of systolic pressure measurements in air

Measurements of finger systolic blood pressures and arm systolic blood pressures in air may be considered to be repeatable: the r.m.s. differences between sessions were between 5 mmHg and 25 mmHg and the differences between days were statistically insignificant. The measurements made on different days also tended to be positively correlated. This suggests that although blood pressure is inherently variable, subjects who exhibit relatively high blood pressures one day also exhibit relatively high blood pressures on another day. The results of this study are consistent with those of the repeatability study reported previously (Section 4.3). The r.m.s. differences between days for measurements in air were of a similar magnitude to those previously obtained with the Medimatic DM2000 plethysmograph for measurements on the thumb and on the middle finger in air (Table 24). However, the higher correlations reported here than in Table 24 indicate a slightly greater repeatability than was previously found.

5.2.4.2 *Effects of cold provocation on reference measurements*

There were no significant changes in systolic blood pressures measured on any of the fingers, or the arms, due to cold provocation of a test finger. On a group basis, the requirement for a reference measurement of systolic pressure might be unnecessary since the observed change in systolic blood pressure was small. However, large changes were seen in individuals, and larger changes might be found with a less well-controlled environment or in persons with a vascular disorder. Some form of correction may then be desirable.

The low repeatability of the effects of cold provocation of a test finger on FSBPs measured on adjacent fingers without cold provocation is consistent with any systematic effects of cold provocation of a test finger on the FSBP of a reference finger being small and masked by other factors affecting the systemic systolic blood pressure.

Since the observed changes in FSBPs and ASPs due to the cold provocation were small compared to other factors influencing the SSP, it can be assumed that cold provocation of a test finger does not greatly influence the reference measurements in healthy subjects. However, in reference fingers affected with vibration-induced white finger the effect of cold provocation of the test finger on the systolic blood pressure of a reference finger might be greater. If there is a fall in the FSBP of the reference finger as an adjacent finger is cooled, or if body cooling is applied, the percentage FSBP should be interpreted with caution (Ekenvall and Lindblad 1986).

5.2.4.3 *Location of reference measurements*

Systolic blood pressures were different at the various locations on the fingers and arms, in agreement with studies cited in the literature (e.g. Hirai *et al.* 1976, Kurozawa *et al.* 1992, Nielsen 1978). Measures of the changes in SSP may not be comparable if different locations are used for the reference measurement. This suggests the need for standardisation of the location of reference measurements.

The least variable, and easiest systolic pressure to measure, is that measured on the arm. Measurements of FSBPs and ASPs would best be obtained simultaneously since there were changes in ASP between measurements made immediately before removal of cold provocation and those made immediately after removal of cold provocation (Figure 22), this would add to variability in the measurement. However, it is not possible to measure arm and finger systolic pressure simultaneously ipsilaterally; obstruction of the arteries proximal to the measurement point in the fingers is likely to affect measurements.

For FSBPs, the r.m.s. differences between different days were about double the r.m.s. differences seen for ASP measurements (Figure 20). This might reflect the greater precision with which FSBPs were measured (± 1 mmHg) than were ASPs (± 5 mmHg). This would result in the FSBPs being more susceptible to small changes within subjects than ASPs. The FSBPs may give a more accurate indication of changes not due to the cold provocation than the ASPs.

Thumb systolic blood pressure might be used as a reference measurement; this can be measured simultaneously with measurements on a test finger of the same hand and in this study it was not significantly different to the ipsilateral ASPs (Table 26). The thumb is preferable over other fingers in that it shows symptoms of VWF less often than other fingers (e.g. Olsen *et al.* 1981) and is therefore less likely to exhibited exaggerated cold-induced vasoconstriction when an adjacent test finger is cooled. Furthermore, measurements made using strain-gauge plethysmography are more precise than measurements made using the ausculatory technique. They are more likely to be representative of the change in systemic systolic blood pressure in the fingers than the arm systolic blood pressure.

5.2.5 Conclusions

In healthy subjects, any effects of cold provocation of the middle finger on the pressures measured elsewhere (i.e. those measured on the arm, the thumb, and the index, ring and little fingers) were small and not repeatable. The changes may be exaggerated in subjects with VWF. If this occurs, corrections for changes in SSP should be performed with caution; there is a possibility of false negative results. It is concluded that the thumb systolic blood pressures are preferred over other FSBPs for correcting for systemic variations in blood pressure. Variability in measurements are likely to be increased if the test and reference systolic blood pressures are not measured simultaneously.

5.3 EFFECTS OF ORDER AND RECOVERY BETWEEN SUCCESSIVE THERMAL PROVOCATIONS ON FINGER SYSTOLIC BLOOD PRESSURES

5.3.1 Introduction

Measurements of FSBPs for assessing the vascular response to cold are usually performed at a minimum of two temperatures, one temperature inhibiting cold-induced vasoconstriction and the other expected to result in cold-induced vasoconstriction in subjects with vibration-induced white finger (VWF). More commonly, measurements are made following thermal provocation at 30°C, then at 15°C and then at 10°C. The measurements at 15°C and 10°C are compared to that at 30°C, correcting for simultaneous measurements made on a reference finger (e.g. Bovenzi 1997, Ekenvall and Lindblad 1986, Nielsen and Lassen 1977).

The exaggerated vasoconstriction in response to cold provocation observed in subjects with VWF is believed to be mediated partly locally, by changes in the fingers, and partly centrally in response to the central sympathetic nervous system (e.g. Olsen 1987). The temperature, duration and area of cold provocation influence the degree of cold-induced vasoconstriction apparent in the blood vessels through both the local and central mechanisms (e.g. Bovenzi 1987, Nakamoto 1990, Virokannas and Rintamäki 1991).

Measurements of FSBPs at different temperatures are usually made in quick succession. Little consideration has been given to any lasting influence of thermal provocation on either the central sympathetic nervous system or the local response to thermal provocation. Lasting changes have, however, been noted. For example, measurements of FSBP at 30°C may not always release cold-induced vasoconstriction caused by prior body cooling (Ekenvall and Lindblad 1986) and changes in central sympathetic activity following applications of cold provocation have been shown (Nakamoto 1990, Sakakibara *et al.* 1997). It is known that the change in central sympathetic activity is enhanced in workers with VWF (Bovenzi 1990). This change in central sympathetic activity might be hypothesised as influencing consecutive measurements.

It was hypothesised that when measuring FSBPs, there is a cumulative effect of thermal provocation at 15°C and 10°C on central sympathetic activity, resulting in lower FSBPs during a consecutive measurement than would be observed if there was no prior cold provocation. Allowing recovery between applications of cold provocation would also be expected to result in different FSBPs during consecutive measurements as the central sympathetic nervous system recovers its resting state. If there is a cumulative effect of thermal provocation, the order of presentation of thermal stimuli would also influence measurements of FSBPs. This study was performed to investigate the effect of recovery between thermal provocations, and the effect of order of application of thermal provocation on FSBPs in healthy subjects.

5.3.2 Method

5.3.2.1 Subjects

Twelve healthy male office workers participated in the study. Subjects had a mean age of 23.4 years (standard deviation, SD, 2.4 years), a mean height of 180 cm (SD 4.6 cm) and a mean weight of 77.6 kg (SD 4.6 kg). No subjects reported a history of occupational exposure to hand-transmitted vibration or injuries to the upper extremities and none reported problems with cold hands. All subjects were non-smokers.

Table 27 Test conditions used in this experiment.

	Condition 1	Condition 2	Condition 3	Condition 4	Condition 5	Condition 6
Recovery period (mins)	0	5	15	0	0	0
Order of thermal provocations (°C)	30, 15, 10	30, 15, 10	30, 15, 10	30, 10, 15	15, 30, 10	10, 30, 15

5.3.2.2 Experimental conditions

The study was conducted over a 4-week period during which mean external temperature, measured at the start of each session, was 8.6°C (SD 2.4°C). Mean room temperature during the study was 22.5°C (SD 0.8°C). All subjects refrained from intake of caffeine for 4 hours and alcohol for 12 hours before each session. On arrival at the test centre, subjects lay supine and were habituated in the test environment for 15 minutes. Subjects remained supine for the remainder of each session.

5.3.2.3 Experimental procedure

Subjects attended six sessions, each on a different day. During three of the six sessions, FSBPs were measured first after thermal provocation at 30°C then after thermal provocation at 15°C and then after thermal provocation at 10°C with differing recovery periods between measurements in each session. During the remaining three sessions, the order of application of thermal provocations was varied with the recovery period minimised. The six experimental conditions are given in Table 27. The order of presentation of the six test conditions was balanced using a partial Latin-squares design.

The FSBPs were measured using the *HVLab* Multi-Channel Plethysmograph and tube type cuffs described in Appendix A. During the habituation period, the hands were instrumented. Double-inlet pressure cuffs (for pressure application and water perfusion) were placed around the medial phalanges of the index, middle, ring and little fingers of the right hand. A single-inlet cuff (for pressure application only) was placed around the proximal phalanx of the thumb of the right hand. Mercury-in-elastic strain gauges were placed around the distal phalanges of the five fingers of the right hand at the base of the nail (Figure 19, Section 4.2.2, the single-inlet pressure cuffs on the test fingers were replaced with the double-inlet cuffs throughout).

The tips of the fingers were squeezed and the five pressure cuffs inflated to 250 mmHg. Water, controlled at either 30°C, 15°C or 10°C, perfused the double-inlet cuffs for five minutes, following which the pressure in the five cuffs was reduced. The FSBP was defined as the point at which a volume change was observed in the finger, or the first pulse was observed (Figure 4, Section 2.2.2).

5.3.2.4 Analysis

Percentage FSBPs have been calculated using the formula given by Nielsen and Lassen (1978)(Equation 1, Section 2.2.7.1). The data were normally distributed (Shapiro-Wilkes, $p > 0.05$) and are described by their mean and standard deviation. Repeated measures analysis of variance has been used to test the effects of recovery duration and order of application of thermal stimuli. For testing the recovery effect, the three sessions where measurements were made at 30°C followed by 15°C and then 10°C were included. The four sessions where no recovery was permitted were included when testing for order effects. Post hoc analyses were performed using student's *t*-test for paired samples. Analyses were performed using SPSS for Windows version 7.5.

5.3.3 Results

One subject was excluded from analyses as this subject exhibited an abnormally variable response to cold provocation. For this subject, the within-subject coefficient of variation (CoV) between sessions for measurements made at 15°C and 10°C were between 16.8% and 78.7% whereas for all other subjects the coefficients of variation between sessions ranged from 6.8% to 30.9%.

Figure 24 shows the mean (± one standard deviation) FSBPs measured on the index, middle, ring and little fingers in each of the six conditions. Figure 25 shows the mean (± one standard deviation) percentage FSBPs measured on the index, middle, ring and little fingers in each of the six conditions.

Effects of age, height, weight and environmental temperatures on FSBPs and percentage FSBPs were tested using Pearson's correlation coefficients. Only six of the 144 correlations attained significance and these were randomly distributed. These variables have not been considered in further analysis.

5.3.3.1 Effects of recovery duration

At 15°C there was a significant decrease in both the FSBPs and the percentage FSBPs with increasing recovery duration (conditions 1, 2 and 3, Figure 24 and Figure 25). This reduction was accounted for by one subject who exhibited complete closure of the digital arteries on two fingers in this condition. When this subject was removed from the analyses, FSBPs at 15°C were not significantly different between sessions. Further analyses were performed without including data for this subject.

For FSBPs, repeated measures analysis of variance indicated effects of thermal provocation for the thumb ($p < 0.001$) and for the index finger ($p = 0.030$). There was a session by thermal provocation interaction for the ring finger ($p = 0.042$). The session by thermal provocation interaction was found to be due to a low mean FSBP on the ring finger at 15°C in condition 3. No differences were shown between the effects of thermal provocation at 30°C or 10°C between conditions.

For percentage FSBPs, there was a significant effect of session for the middle finger ($p = 0.027$) and the ring finger ($p = 0.001$), and a significant effect of thermal provocation on the little finger ($p = 0.021$). For the middle finger at both 10°C and 15°C, the percentage FSBPs were lower in condition 1 than in condition 2. Percentage FSBPs at 15°C were lower in condition 2 than condition 3 for the middle finger. The percentage FSBPs at 15°C were lower in condition 3 than in both condition 1 and condition 2 for the ring finger. At 10°C on the ring finger, the percentage FSBPs were lower in condition 3 than in condition 2.

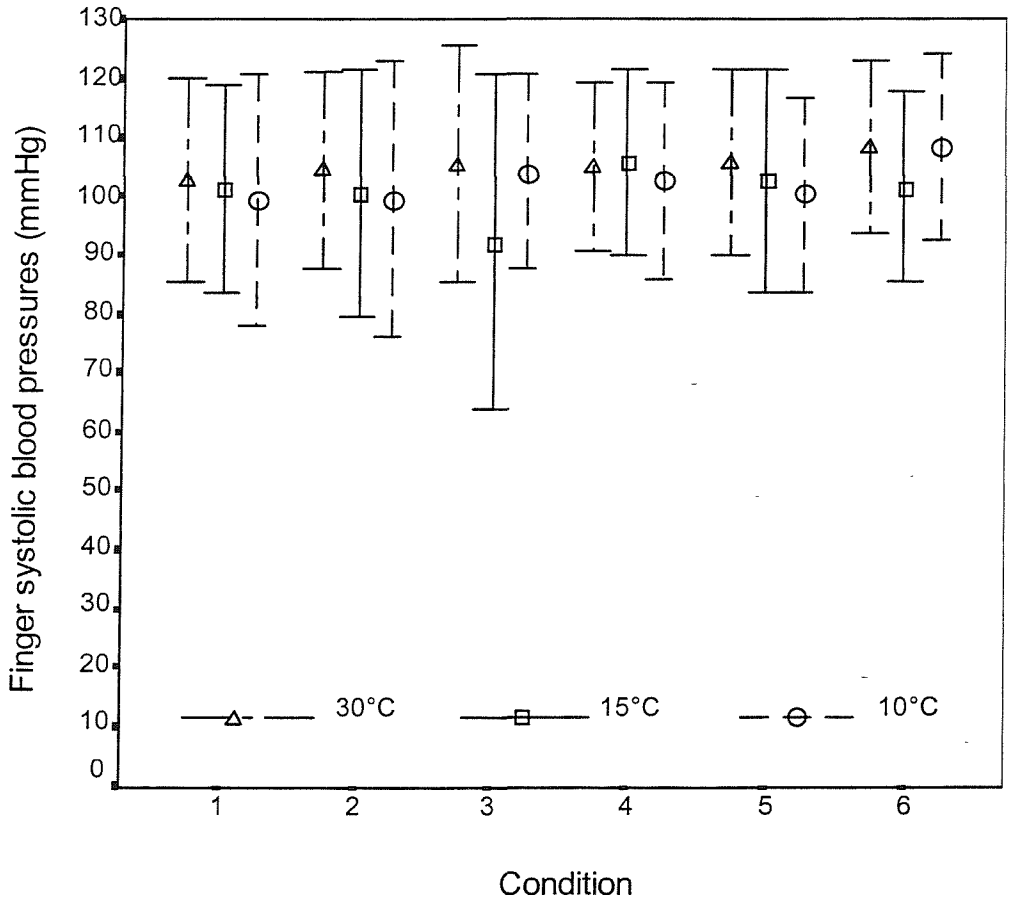


Figure 24 Mean (± 1standard deviation) FSBPs measured on the index, middle, ring and little fingers in each of six experimental conditions. Experimental conditions are given in Table 27.

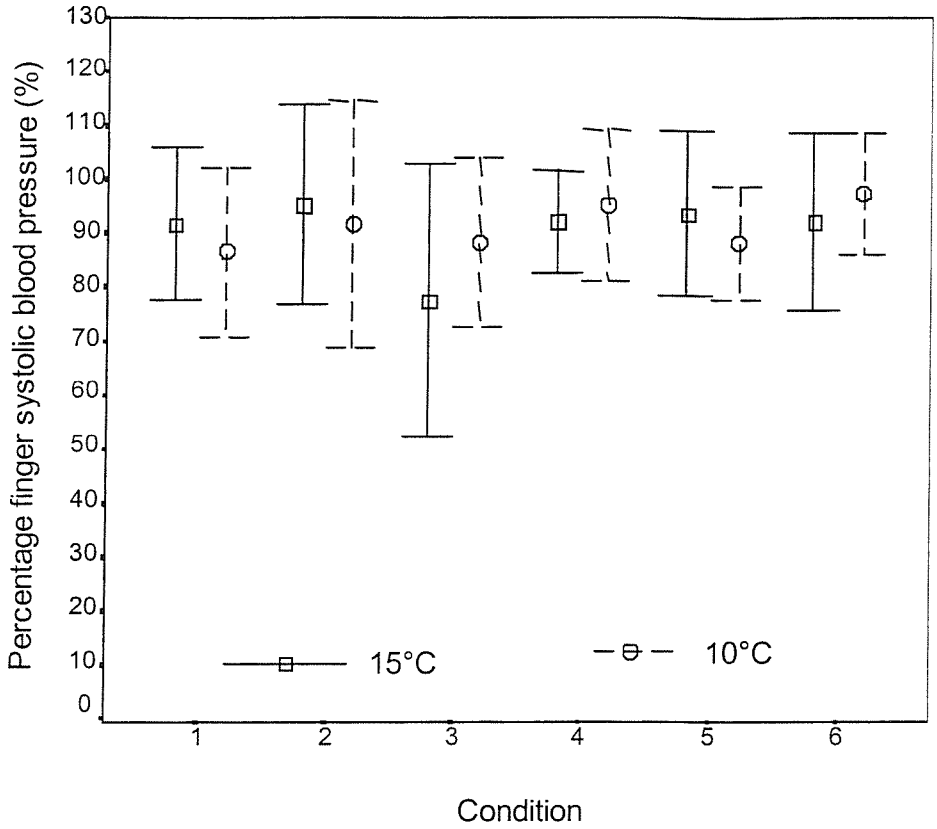


Figure 25 Mean (± 1 standard deviation) percentage FSBPs measured on the index, middle, ring and little fingers in each of six experimental conditions. Experimental conditions are defined in Table 27.

5.3.3.2 Effects of order of presentation of thermal provocation

The repeated measures analysis of variance showed no differences between the four sessions for either the FSBPs or the percentage FSBPs when the order of presenting thermal provocations was varied. There was a significant effect of the temperature of thermal provocation on FSBPs measured on the thumb ($p < 0.001$) and the index finger ($p = 0.016$), but no effect of thermal provocation on the percentage FSBPs. There was no interaction between the temperature of thermal provocation and the order of presenting thermal provocations for either FSBPs or percentage FSBPs.

5.3.4 Discussion

5.3.4.1 Recovery effects

The repeated measures analysis of variance indicated no consistent changes in FSBPs or percentage FSBPs due to the recovery duration. The post hoc analyses suggested the recovery duration effect differed between the fingers for which significant effects were observed. This might indicate that any differences between conditions were small and not repeatable. However, the data appear to show that as the duration of recovery increased, the inter-subject variability in blood pressures also increased.

The coefficients of variation (CoV) for between-subject variability within the three conditions were calculated and are shown in Figure 26. The figure shows that for both FSBPs and percentage FSBPs at 15°C the CoV increased as the recovery duration increased. At 10°C, the change was smaller and only observed when the recovery duration increased from 0 minutes to 5 minutes.

The changes in the CoVs are most likely due to changes in central sympathetic activity. Some subjects exhibited rapid recovery in central sympathetic activity and showed less cumulative effects of thermal provocation than those who exhibited slow recovery. This would be consistent with the hypothesis of cumulative effects of thermal provocation on the central sympathetic nervous system.

It is likely that any recovery effects will be exaggerated in workers with VWF; Bovenzi (1989) showed that subjects with VWF exhibit exaggerated cardiac sympathetic tone. Furthermore, Nielsen *et al.* (1978) suggest that in cases of Raynaud's phenomenon some time, from minutes to hours, must elapse between thermal provocations for a second attack of blanching to occur. In their study, it was hypothesised a sudden release of norepeniphrine from the sympathetic nerve terminals was required to produce the blanching phenomenon. This would further suggest exaggerated effects of recovery duration when performing measurements of FSBPs amongst patient groups.

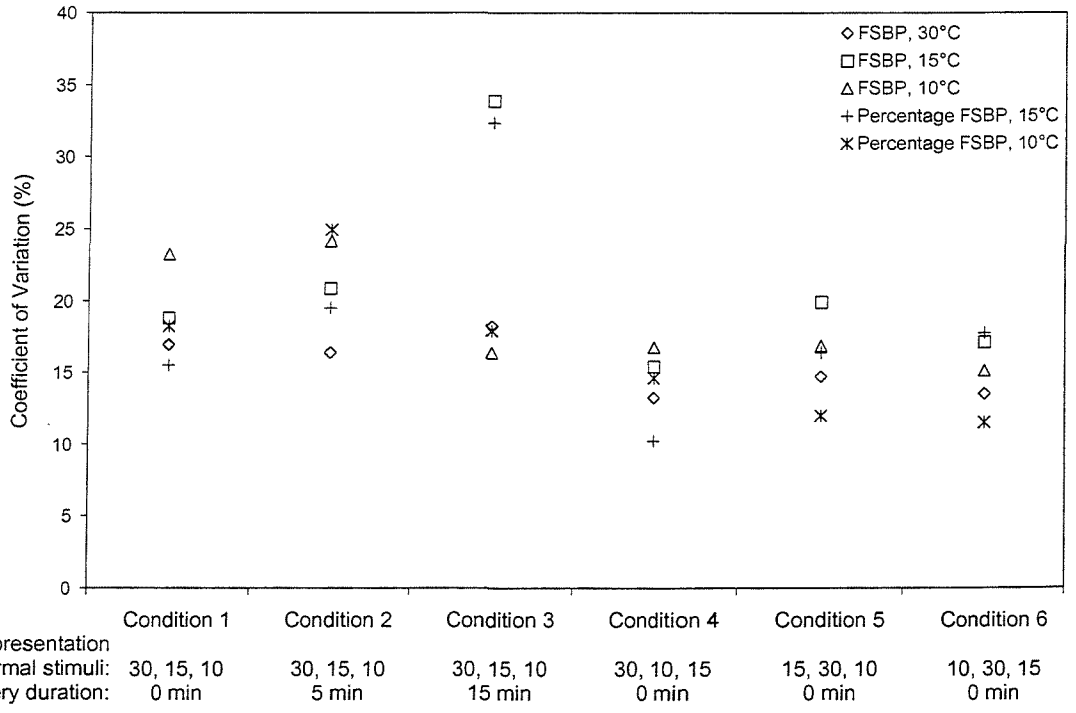


Figure 26 Coefficients of variation for between-subject variability in finger systolic blood pressures and percentage finger systolic blood pressures measured in 6 conditions.

For monitoring vascular function in workers exposed to hand-transmitted vibration, it is preferable that undesirable inter-subject variability is minimised. In addition, the criterion for deciding whether a FSBP is normal can depend on inter-subject variability; lower normal limits are sometimes calculated as the mean of normative data minus a multiple of the standard deviation. The results of this study suggest there is little advantage, and possibly some disadvantage, in allowing recovery between measurements.

5.3.4.1.1 Order effects

The order in which thermal provocations were presented did not significantly affect the FSBPs or the percentage FSBPs. The coefficients of variation for between-subject variability were also not altered perceptibly by changing the order in which measurements were made (Figure 26). It is concluded that the order in which thermal provocation is applied is not of great importance when performing the measurements amongst healthy subjects.

When investigating the effects of recovery duration on FSBPs, it was observed that any effects of recovery duration were dependent on the temperature of thermal provocation. It is inevitable that there is some delay between consecutive applications of thermal provocation when measuring FSBPs so it is tentatively suggested that measurements be made at progressively lower temperatures. This will ensure that any temperature dependent effects of recovery duration remain consistent between subjects. Furthermore, when using measurements of FSBPs for monitoring vascular function in workers exposed to hand-transmitted, it has been suggested that following detection of a pathological result at 15°C a further measurement at 10°C may not be required (e.g. Maricq *et al.* 1996, Nielsen 1978). To improve the practicality of the measurement in this way requires the FSBPs to be measured at progressively lower temperatures.

5.3.5 Conclusions

Increasing the recovery period between successive applications of thermal provocation resulted in increased inter-subject variability amongst office workers. Minimising any recovery period between consecutive measurements of FSBPs will help to reduce inter-subject variability. The order of presentation of thermal provocation did not significantly affect results, it may be more practical to measure FSBPs at progressively lower temperatures.

CHAPTER 6 COLD PROVOCATION TESTS: ORDER EFFECTS AND REPEATABILITY

6.1 INTRODUCTION

6.1.1 Repeatability

The repeatability of measures of finger systolic blood pressures (FSBPs) and measures of finger skin temperatures (FSTs) following cold provocation have been reported in the literature. Bovenzi (1998), Carnicelli *et al.* (1992), Nielsen (1978) and Olsen *et al.* (1981) concluded that the repeatability of measures of FSBPs is acceptable whilst Carnicelli *et al.* (1992), Howarth and Griffin (1989) and Hayward *et al.* (1988) concluded that the repeatability of measures of FSTs is acceptable. Some variability in measures of FSBPs has been shown previously in this work (Section 4.3), although the variability was subjectively considered normal. Apart from the study reported by Olsen *et al.* (1981), the investigations cited above have used groups of healthy office workers to determine repeatability, and some have included female subjects. These samples may not be representative of the worker populations amongst whom the tests are likely to be applied.

6.1.1.1 Finger systolic blood pressures

For percentage FSBPs at 10°C measured in five healthy subjects on five consecutive days, Bovenzi (1998) showed coefficients of variation (CoVs) between 3.8% and 9.3%. Carnicelli *et al.* (1992) found CoVs amongst ten healthy male subjects to range between 5.4% and 29%. The subject exhibiting the CoV of 29% in their study also exhibited relatively low mean percentage FSBPs (70.0% at 15°C and 67.2% at 10°C). The authors demonstrated that CoVs were negatively correlated with mean percentage FSBPs, implying more repeatable measurements amongst subjects not exhibiting exaggerated vasoconstriction. Ekenvall and Lindblad (1986) performed repeat testing on 15 male patients with VWF who had exhibited a normal response to cold provocation during a measurement of FSBP. They found 13 of the patients exhibited pathological results during the repeated test. The study population used by Olsen *et al.* (1981) to determine repeatability comprised a random sample of 10 subjects from a population of 39 chain-sawyers, of which one-third had symptoms of VWF at either stage 2 or stage 3. These authors showed significant differences between repeated measurements of percentage FSBPs at 6°C. It is therefore questionable if it is possible to infer from studies on healthy office workers that measures of FSBPs following thermal provocation are repeatable amongst a population with VWF.

6.1.1.2 Response of finger skin temperatures to cold provocation

For measures of the response of FSTs to cold provocation, the repeatability has rarely been reported to be high, although the test has been extensively used. The different methods of performing the measurement, and the different parameters used for interpretation, also result in different repeatabilities. For various parameters describing the response of FSTs to cold provocation, Hayward *et al.* (1988) showed CoVs between 18.5% and 103% whilst Howarth and Griffin (1989) showed CoVs between 13.9% and 70.6%. Carnicelli *et al.* (1992) showed normalised r.m.s. differences between sessions of between 0.1 and 0.62 for similar parameters, these authors did not show within-subject CoVs. Nielsen (1981) quotes a CoV of about 30% for measurements of FSTs following cold provocation. Bovenzi (1987) suggests that measurements of FST in air, as occurs during the recovery period of the test, is an inadequate indicator of finger blood flow as it is highly dependent on many other factors. Since the repeatability of measurements of FSTs following cold provocation has not been shown to be high and, as has been suggested for FSBPs, the repeatability of the measurement may be influenced by the subject group, further knowledge of the variability of this measurement is required.

6.1.2 Order effects

When used for the objective measurement of the vascular response to cold, it sometimes occurs that both FSBPs and FSTs following cold provocation are measured in the same session (e.g. Ekenvall and Lindblad 1986, Pyykkö *et al.* 1986, Virokannas and Rintamäki 1991). Exposure of the hand to cold provocation increases central sympathetic activity (Nakamoto 1990, Sakakibara *et al.* 1997). It is likely that this change in central sympathetic activity can influence the results of a cold provocation test if it is performed subsequent to another cold provocation test.

It was found in Chapter 5, Section 5.3, that after the application of cold provocation during a measurement of FSBP, the inter-subject variability of consecutive measurements can increase. In cases of VWF, the intra-subject variability may also be expected to increase; Nielsen *et al.* (1978) suggest that in cases of Raynaud's phenomenon, some time can elapse before the same temperature of thermal provocation leads to a similar vasoconstrictive response.

In this study, the repeatability of the methods for performing measurements of FSBPs and FSTs following cold provocation defined in Chapter 2, Section 2.8, have been investigated amongst groups of i) vibration-exposed workers reporting VWF, ii) manual workers not reporting VWF and iii) healthy office workers. It was hypothesised that the repeatability of

measurements of FSBPs would be acceptable amongst the two healthy groups of workers, but lower amongst the group of workers with VWF. The measurement of FSTs following cold provocation was not expected to show repeatable results amongst any group of subjects. It was also hypothesised that when performing two cold provocation tests consecutively, the response of the digital arteries to cold provocation during a second test would differ from when it was performed first due to a cumulative effect of thermal provocation; the intra-subject variability was expected to increase in measurements performed subsequent to a prior cold provocation test.

6.2 METHOD

6.2.1 Subjects

Thirty-six male subjects participated in the study: (i) 12 office workers not exposed to vibration, (ii) 12 subjects currently employed in manual work who did not report symptoms of VWF, and (iii) 12 subjects exposed to hand-transmitted vibration who reported symptoms of VWF. Subject details and reported exposure to hand-transmitted vibration are given in Appendix D. There were no significant differences in age, smoking habits, drinking habits or handedness between the groups; duration of vibration exposure was significantly greater in the VWF group than in the manual worker group (Table 28).

Table 28 Characteristics of the three groups of subjects used in the study.

	Office workers	Manual workers	VWF
Age (yrs), mean (SD)	44.0 (8.2)	44.3 (10.0)	45.7 (8.9)
Non-smokers, N(%)	5 (41.7)	3 (25.0)	3 (25)
Smokers, N(%)	1 (8.3)	5 (41.7)	6 (50)
Ex-smokers, N(%)	6 (50)	4 (33.3)	3 (25)
Non-drinker, N(%)	0 (0)	1 (8.3)	0 (0)
Occasional drinker, N(%)	1 (8.3)	4 (33.3)	3 (25)
Regular drinker, N(%)	11 (91.7)	7 (58.3)	9 (75)
Right handed, N(%)	10 (83.3)	9 (75)	10 (83.3)[a]
Left handed, N(%)	2 (16.7)	3 (25)	1 (8.3)[a]
Vibration exposure (yrs), mean (SD)	0.4 (1.3)	11.3 (11.9)	18.9 (8.3)
Vibration exposure (hrs), mean (SD)	164 (568)	9848 (17414)	23907 (18008)
Blanching score, median (IQR)	0 (0)	0 (0)	16.5 (19.3)
Blanching frequency[b], median (IQR)	0 (0)	0 (0)	17.5 (42.8)
Numbness score, median (IQR)	0 (4.5)	0 (0)	12.0 (32.3)
Numbness frequency[b], median (IQR)	0 (0.75)	0 (0)	22.5 (277)
Tingling score, median (IQR)	0 (3)	0 (0)	11.0 (23.0)
Tingling frequency[b], median (IQR)	0 (0.75)	0 (0)	25.0 (39.0)

[a] One subject reporting VWF was ambidextrous.

[b] Frequency was defined as the number of episodes of blanching, numbness or tingling occurring in the year preceding the study.

6.2.2 Experimental conditions

Subjects were requested to avoid intake of nicotine for 2 hours, caffeine for 4 hours and alcohol for 12 hours prior to attending for testing. Mean daily external temperature during the study was 17.1°C (SD 2.7°C). On arrival, subjects were habituated for 15 minutes in the test environment, mean temperature 23.4°C (SD 1.3°C), prior to measurements. Subjects lay supine for measurements of FSBPs and were seated for measurements of FSTs.

6.2.3 Experimental procedure

Subjects attended four sessions, each on a different day but at the same time of day. During each session, both the FSBPs and the FST response to cold were measured on the same hand. In two sessions, the FST response to cold provocation was measured first (condition 1) and in two sessions FSBPs were measured first (condition 2). The order of presentation of test conditions was balanced within subject groups.

For subjects reporting VWF, the hand that was reported to have the greatest blanching score was selected as the test hand. For office workers and manual workers, the test hand was selected as the test hand of the VWF subject with the nearest age. Within each group, 8 left hands and 4 right hands were tested.

6.2.3.1 Finger skin temperature response to cold provocation

Thermocouples were attached to the distal phalanx of each finger and the thumb of the test hand, and on the medial and proximal phalanges of the middle finger of the test hand, using a porous surgical tape. A further thermocouple was attached to the distal phalanx of the middle finger of the contralateral hand. Thermocouples were placed on the palmar surface along the midaxilliary line (Figure 5, Section 2.3.5).

The test hand was placed in a waterproof covering and the monitoring of skin temperature begun. After a two minute baseline reading, the test hand was immersed to the level of the wrist on both the palmar and dorsal surfaces in water controlled at 15°C. After five minutes of immersion, the test hand was removed from the water, the waterproof covering removed and the hand rested at about heart height for 15 minutes. The FSTs were monitored throughout the settling, immersion and recovery periods using an *HVLab* 8-Channel Temperature Monitor (Appendix A).

6.2.3.2 Finger systolic blood pressures

The FSBPs were measured simultaneously on the five fingers of the test hand with the thumb being used as the reference finger. The *HVLab* Multi-Channel Plethysmograph was used, the plethysmograph and associated apparatus is described in greater detail in Appendix A. Double-inlet, water-perfused cuffs of the tube-type were placed around the medial phalanges of the test fingers (index, middle, ring and little fingers) and a single-inlet air cuff of the plastic bag type was placed around the proximal phalanx of the thumb (e.g. Figure 19, Section 4.2.2.3). Mercury-in-elastic strain gauges were placed around the tips of the fingers and the thumb at the base of the nail in order to detect the return of blood flow. The tips of the fingers were squeezed and a pressure of 250 mmHg was applied to all the cuffs. Water perfused the double-inlet cuffs at 30°C for five minutes, following which the pressure in the cuffs was released at a rate of 2 mmHg/s. The procedure was immediately repeated for a water temperature of 15°C and then for a water temperature of 10°C.

6.2.4 Analysis

Finger systolic blood pressures at 15°C and 10°C were expressed as a percentage of the systolic blood pressure measured at 30°C, corrected for changes in the reference finger using Equation 1, Section 2.2.7.1. The FSTs measured at four minutes during immersion and at five minutes during recovery were used for analyses. Although the times to rise by 3°C, 4°C and 6°C have previously been used in this work, they were shown to give low sensitivity and specificity to VWF (Section 3.2.3.2).

Repeatability and order effects have been tested using multivariate repeated measures analysis of variance, the designs used are shown in Table 29. Pearson's correlation coefficients, r.m.s. differences and limits of agreement have been used to quantify repeatability.

Table 29 Designs used for repeated measures analysis of variance.

Cold provocation test	Dependent measures	Repeated condition	Within-subject design
Finger systolic blood pressures	Digit 2, Digit 3, Digit 4, Digit 5	Identical	Cold, Session, Cold * Session
		Order varied	Cold, Order, Cold * Order
Finger skin temperatures	Digit 1, Digit 2, Digit 3 distal, Digit 3 medial, Digit 3 proximal, Digit 4, Digit 5	Identical	Session
		Order varied	Order

6.3 RESULTS

6.3.1 Repeatability

Mean (standard deviation) data for each of the four sessions are given in Table 30. The repeatability statistics and results of the repeated measures analyses of variance are presented in Appendix C for both percentage FSBPs and FSTs following cold provocation. Repeatability data are given for measurements made in each experimental condition (i.e. for FSTs measured before FSBPs, condition 1, and for FSBPs measured before FSTs, condition 2).

6.3.1.1 Finger systolic blood pressures

6.3.1.1.1 Condition 1: FSTs measured before FSBPs

Repeated measures analysis of variance indicated no significant differences between the two sessions for percentage FSBPs measured in this condition, no interactions involving session were significant (Table C11, Appendix C). There was a significant group effect; percentage FSBPs were lower for VWF subjects than for both groups of control subjects. There was also a significant group by cold interaction; vasoconstriction of the digital arteries was greater at 10°C than at 15°C amongst the VWF group but not amongst the two groups of control subjects.

The correlation coefficients between percentage FSBPs measured during the two sessions were positive for both office workers and manual workers (Table C1, Appendix C). Measurements had higher correlation coefficients at 10°C than at 15°C. More measurements were significantly correlated between sessions for office workers than for either manual workers or for the VWF group.

The r.m.s. differences were lower for office workers and manual workers than for the VWF group. The r.m.s differences for the VWF group were large. The limits of agreement were narrower (i.e. the lower limit was higher and the upper limit was lower) for the office workers and manual workers than for the VWF group (Table C1, Appendix C).

6.3.1.1.2 Condition 2: FSBPs measured before FSTs

Repeated measures analysis of variance showed no differences between percentage FSBPs measured during the two sessions in this condition (Table C10, Appendix C). There was a marginal session by group interaction; measurements made on subjects with VWF varied more between sessions than measurements made on the two groups of healthy subjects. The interaction between group and cold was not significant. There was a significant group effect; percentage FSBPs were lower for VWF subjects than for control subjects.

Table 30 Mean (standard deviation) percentage FSBPs and FSTs measured twice in each of two conditions for the three groups of subjects used in this study.

		Controls (office)				Controls (manual)				VWF			
		Condition1 Session 1	Condition1 Session 2	Condition 2 Session 1	Condition 2 Session 2	Condition1 Session 1	Condition1 Session 2	Condition 2 Session 1	Condition 2 Session 2	Condition1 Session 1	Condition1 Session 2	Condition 2 Session 1	Condition 2 Session 2
$\%FSBP_{15°C}$	Digit 2	96 (9)	98 (12)	103 (17)	97 (15)	95 (14)	97 (15)	92 (12)	100 (10)	64 (35)	77 (33)	63 (35)	80 (27)
	Digit 3	99 (10)	97 (9)	100 (17)	95 (11)	92 (12)	96 (7)	98 (12)	96 (6)	70 (27)	89 (21)	81 (30)	80 (26)
	Digit 4	99 (12)	98 (12)	99 (19)	95 (10)	95 (13)	90 (9)	97 (7)	97 (13)	65 (39)	86 (26)	72 (36)	87 (29)
	Digit 5	97 (13)	100 (9)	102 (13)	102 (15)	99 (14)	97 (7)	100 (6)	98 (8)	85 (36)	92 (26)	90 (35)	87 (29)
$\%FSBP_{10°C}$	Digit 2	95 (9)	94 (7)	103 (14)	97 (9)	90 (11)	99 (14)	91 (10)	99 (17)	63 (39)	69 (34)	63 (36)	84 (28)
	Digit 3	100 (13)	95 (5)	94 (30)	91 (16)	95 (10)	99 (10)	95 (6)	99 (9)	68 (34)	80 (27)	77 (38)	82 (27)
	Digit 4	97 (13)	95 (10)	98 (11)	93 (8)	92 (11)	95 (10)	92 (9)	97 (15)	57 (46)	73 (35)	76 (38)	80 (38)
	Digit 5	97 (11)	96 (7)	99 (16)	98 (12)	99 (11)	107 (8)	98 (9)	99 (14)	81 (30)	90 (33)	91 (35)	91 (30)
FSTs at 4 minutes of immersion	Digit 1	23 (5)	23 (5)	23 (3)	22 (4)	23 (3)	25 (4)	23 (4)	22 (3)	21 (3)	23 (3)	23 (5)	23 (3)
	Digit 2	22 (5)	21 (5)	21 (3)	21 (5)	22 (3)	25 (5)	23 (4)	25 (3)	19 (3)	22 (3)	19 (3)	22 (4)
	Digit 3 dist[1]	23 (6)	23 (5)	23 (4)	23 (6)	24 (4)	27 (4)	24 (5)	24 (4)	21 (4)	24 (4)	22 (4)	23 (4)
	Digit 3 med[2]	22 (5)	22 (5)	23 (4)	23 (5)	22 (3)	24 (3)	23 (5)	24 (2)	20 (3)	23 (3)	21 (3)	23 (3)
	Digit 3 prox[3]	22 (5)	23 (5)	22 (3)	22 (4)	21 (3)	22 (3)	22 (3)	23 (2)	21 (3)	22 (2)	21 (3)	22 (2)
	Digit 4	21 (5)	21 (5)	21 (4)	20 (4)	23 (4)	25 (4)	21 (4)	23 (3)	20 (3)	23 (4)	20 (4)	23 (4)
	Digit 5	22 (6)	21 (5)	22 (5)	22 (6)	23 (4)	26 (5)	23 (5)	24 (5)	20 (4)	23 (5)	20 (5)	23 (4)
	Digit 3 ref[4]	35 (2)	35 (3)	36 (0.5)	36 (1)	36 (1)	36 (1)	35 (2)	35 (3)	35 (1)	36 (1)	35 (2)	35 (2)
FSTs at 5 minutes of recovery	Digit 1	32 (5)	31 (6)	34 (1)	34 (2)	32 (5)	34 (4)	33 (4)	34 (2)	28 (7)	31 (6)	30 (6)	32 (5)
	Digit 2	31 (6)	31 (7)	33 (5)	32 (5)	32 (5)	34 (4)	34 (3)	35 (1)	26 (8)	30 (7)	29 (7)	33 (5)
	Digit 3 dist[1]	31 (6)	30 (7)	34 (2)	33 (4)	32 (6)	35 (3)	32 (6)	34 (2)	27 (8)	30 (7)	29 (8)	32 (6)
	Digit 3 med[2]	30 (6)	30 (7)	33 (3)	32 (4)	30 (6)	34 (4)	31 (6)	33 (3)	27 (7)	30 (7)	28 (7)	31 (6)
	Digit 3 prox[3]	30 (6)	30 (7)	33 (3)	32 (4)	30 (5)	33 (4)	30 (5)	32 (3)	27 (6)	31 (5)	28 (6)	31 (6)
	Digit 4	30 (6)	29 (6)	32 (3)	31 (5)	31 (6)	34 (3)	32 (5)	33 (4)	27 (7)	31 (7)	28 (8)	31 (6)
	Digit 5	31 (6)	30 (7)	33 (3)	32 (4)	31 (7)	34 (4)	32 (6)	34 (4)	28 (8)	30 (7)	28 (8)	31 (7)
	Digit 3 ref[4]	36 (1)	35 (3)	36 (0.5)	36 (1)	36 (1)	36 (1)	35 (2)	36 (1)	36 (1)	36 (1)	35 (2)	36 (1)

[1] Dist = distal phalanx;[2] Med = medial phalanx;[3] Prox = proximal phalanx;[4] ref = reference finger

Correlation coefficients (Table C2, Appendix C) were significant and positive between the two sessions for office workers. For manual workers, no correlation coefficients were significant. For the VWF group, correlation coefficients tended to be positive and two of the eight measures were significantly positively correlated.

The r.m.s. differences were lower for office workers and manual workers than for the VWF group, and the limits of agreement were narrower (Table C2, Appendix C). For the VWF group, the r.m.s. differences were large and the limits of agreement relatively wide.

6.3.1.2 Finger skin temperature response to cold provocation

6.3.1.2.1 Condition 1: FSTs measured before FSBPs

Repeated measures analysis of variance indicated no significant differences in the data between the first and second session in this condition (Tables C4 and C6, Appendix C). For the measurement of FSTs at the fourth minute of immersion, there were no differences between the three groups of subjects. For the measurement made at 5 minutes of recovery, the VWF group showed marginally lower FSTs than the control groups.

For office workers, all correlation coefficients between the two sessions in this condition (Table C1, Appendix C) were positive and 44% of the dependent measurements showed significant correlations between the two sessions. For manual workers, there were no significant correlations between sessions. For the VWF group, measurements made in the two sessions tended to be positively correlated and 44% of the dependent measures were significantly positively correlated between sessions.

At the fourth minute of immersion, the r.m.s. differences between the two conditions for measurements of FSTs were similar for the three groups whereas five minutes after immersion, the r.m.s. differences tended to be lower for the office works than for the manual workers and the workers with VWF.

The limits of agreement were narrower for the VWF group than for office workers and manual workers during immersion, the latter two groups showed similar limits. At five minutes after immersion, the limits of agreement were narrower for the VWF group than for the office workers who, in turn, exhibited narrower limits than the manual workers.

6.3.1.2.2 Condition 2: FSBPs measured before FSTs

In this condition, repeated measures analysis of variance showed no differences between FSTs measured during the two session for any of the groups (Tables C5 and C7, Appendix C). Post hoc tests showed that FSTs measured after 5 minutes of recovery were marginally lower in the VWF group than in other groups.

For office workers, the correlation coefficients for measurements made during the two sessions were positive, and correlations for 63% of the dependent variables were significant (Table C2, Appendix C). There were no significant correlations between measurements made on the test hand during the two sessions for either the manual workers or the VWF group.

At the fourth minute of immersion, the r.m.s. differences were smaller and the limits of agreement narrower for office workers than for the manual workers and the VWF group, the manual workers and the VWF group gave similar results. After 5 minutes of recovery, the r.m.s. differences were larger and the limits of agreement wider for the VWF group than the office workers and the manual workers. The r.m.s. differences were larger and the limits of agreement wider for the manual workers than the office workers.

6.3.2 Effects of order of presentation of cold provocation tests

The means of the two measurements made in each condition have been calculated. These means have been compared between conditions using repeatability statistics (Table C3, Appendix C) and repeated measures analyses of variance (Tables C8, C9 and C12, Appendix C). Repeated measures analyses of variance showed a marginally significant order effect for FSTs measured at 4 minutes of immersion and a significant order effect for FSTs measured at 5 minutes of recovery; the FSTs tended to be lower in condition 1 than in condition 2 (i.e. they were lower when measured first). For FSBPs, there were no differences between measurements made in the two conditions.

There were significant group effects for both percentage FSBPs and FSTs; lower values were recorded for subjects with VWF than for office workers and manual workers. There were no group by session interactions, however, suggesting that any order effects were similar for the three groups.

The correlation coefficients showed that for the office workers, the manual workers and the VWF group, there was a tendency for subjects measured high in one condition to be measured high in the other, and for subjects measured low in one condition to be measured low in the other. The r.m.s. differences tended to be smaller between conditions than within conditions, the limits of agreement tended to be narrower (Tables C1, C2 and C3, Appendix C); averaging within conditions reduces the variability.

6.3.2.1 Repeatability

To compare the repeatability between the two conditions, the data in Table C1 and Table C2 (Appendix C) have been compared. Table 31 shows the mean r.m.s. difference, the mean range of the limits of agreement (the mean of the difference between the upper limit of agreement and the lower limit of agreement) and the mean correlation coefficient for percentage FSBPs at 15°C and 10°C and for FSTs at four minutes of immersion and at five minutes of recovery for the three groups of workers in the two conditions.

Table 31 Mean r.m.s. differences, mean limits of agreement and mean correlation coefficients for percentage FSBPs at 15°C and 10°C and for FSTs at four minutes of immersion and at five minutes of recovery for three groups of workers in two conditions.

		Office workers		Manual workers		VWF workers	
	Condition[d]:	1	2	1	2	1	2
%FSBP (15°C)[a]	Correlation coefficient	0.30	0.74	0.20	0.12	0.21	0.32
	R.m.s difference (%)	12.3	12.4	14.6	15.3	44.9	36.6
	Limits of agreement (%)[c]	50.5	45.9	53.6	60	166.0	145.5
%FSBP (10°C)[a]	Correlation coefficient	0.49	0.68	0.32	0.11	0.11	0.29
	R.m.s difference (%)	10.4	12.8	13.5	13.1	41.9	36.8
	Limits of agreement (%)[c]	42.8	49.5	56.4	49.9	160.8	146.1
FST at 4 minutes of immersion [b]	Correlation coefficient	0.51	0.68	0.05	-0.28	0.38	0.16
	R.m.s difference (°C)	4.2	3.1	4.7	5.6	4.0	4.8
	Limits of agreement (%)[c]	9.0	6.3	9.0	11.6	6.9	10.0
FST at 5 minutes of recovery [b]	Correlation coefficient	0.52	0.60	-0.01	0.06	0.56	0.26
	R.m.s. difference (°C)	5.2	2.6	6.6	4.9	6.2	7.8
	Limits of agreement (%)[c]	10.1	5.0	12.9	9.5	8.7	15.4

[a] Mean of the statistics for the four measurement sites
[b] Mean of the statistics for the eight measurement sites
[c] Range of the limits of agreement, i.e. the difference between the upper limit of agreement and the lower limit of agreement
[d] Condition 1: FSTs measured before FSBPs; Condition 2: FSBPs measured before FSTs

For office workers, the intra-subject variability for percentage FSBPs tended to be similar in the two conditions, as shown by the r.m.s. differences and limits of agreement. The correlations between sessions were much higher when FSBPs were measured first. The measurements of the response of FSTs to cold provocation exhibited less intra-subject variability, and the between-session correlation coefficients tended to be higher, when measured after FSBPs.

For the manual workers, the intra-subject variability of percentage FSBPs tended to be similar for the two conditions whilst the correlation coefficients tended to be higher when the FSBP response to cold was measured last. For FSTs measured at 4 minutes of immersion, the intra-subject variability was higher when this test was performed first. At the fifth minute of recovery, however, the intra-subject variability decreased when FSTs were measured last compared to when the FSTs were measured first. These differences in intra-subject variability were small.

For both measurements, the workers reporting VWF showed more consistent responses when a test was performed first than when a test was performed after a prior cold provocation test. The correlations between sessions were higher when a test was performed first than when a test was performed after another.

6.4 DISCUSSION

6.4.1 Repeatability

For FSBPs, the data from office workers generally showed greater repeatability than the data from manual workers. Both groups of healthy subjects showed greater repeatability than the data from subjects with VWF. The r.m.s. differences and limits of agreement showed large variability for the VWF group when compared to the two groups of healthy workers. This was because a subject with VWF who exhibited an exaggerated response to cold provocation on one occasion did not necessarily exhibit an exaggerated response on the second occasion. This resulted in the large r.m.s. differences and wide limits of agreement for these subjects. The results are consistent with Ekenvall and Lindblad (1986) who showed that of 15 patients exhibiting a normal response to a finger systolic blood pressure on one occasion, 13 exhibited exaggerated vasoconstriction on a retest.

For FSTs measured during and following cold provocation, data for the office workers tended to be more repeatable than the data for the other two groups, although differences in the repeatability between the three groups of subjects were small. The repeatability statistics suggest this test is similarly repeatable amongst the three groups.

To compare the repeatability of measurements made in this study with the repeatabilities reported in the literature, the coefficients of variation (CoV) across all four sessions were calculated, the CoV was the most common repeatability statistic found in the literature. Although any intra-subject variability due to order effects will have been introduced into the CoVs calculated from the data in this study, this will only be important to consider if the CoVs calculated here are much greater than those reported in the literature. The mean and range of CoVs are shown in Table 32 for this study and for those found in the literature.

For FSBPs measured in healthy office workers and healthy manual workers, the data are similar to those in the literature and confirm that for these subjects the test is sufficiently repeatable for use. For workers reporting VWF, however, this is not the case. The coefficients of variation are between three and four times higher than those shown in the literature. The low repeatability of this test for workers reporting symptoms of VWF has not previously been reported, although it is consistent with the data found in the literature. When using FSBPs in the diagnosis or screening of VWF, the possibility of false negative results should be considered (e.g. Olsen 1998).

Table 32 Mean, minimum and maximum coefficients of variation for measurements of FSBPs and FSTs following cold provocation reported in the literature and for this study.

Study	Test procedure	Subjects	Parameter[§]	CoV (%) Min	Max	Mean
Bovenzi (1988, 1998)	FSBPs at 30°C, 15°C and 10°C during 5 sessions, one test finger (middle)	5 healthy subjects	$\%FSBP_{15°C}$	4.3	9.5	6.5
			$\%FSBP_{10°C}$	3.8	9.2	6.3
Carnicelli *et al.* (1992)	FSBPs at 30°C, 15°C and 10°C during 5 sessions, one test finger (middle)	10 healthy males	$\%FSBP_{15°C}$	5.4	26.2	10.5
			$\%FSBP_{10°C}$	6.0	29.0	13.3
Current study	FSBPs at 30°C, 15°C and 10°C during 4 sessions, 4 test fingers (index, middle, ring, little)	12 healthy male office workers	$\%FSBP_{15°C}$	1.6	27.4	9.0
			$\%FSBP_{10°C}$	1.8	26.8	9.5
		12 healthy male manual workers	$\%FSBP_{15°C}$	2.3	24.9	8.3
			$\%FSBP_{10°C}$	1.7	26.8	9.7
		12 males with VWF	$\%FSBP_{15°C}$	2.6	200.0	36.1
			$\%FSBP_{10°C}$	1.6	200.0	44.4
Hayward *et al.* (1988)	Immersion of one hand in water at 15°C for five minutes, 5 sessions, measurement location not reported	5 healthy subjects	A	18.5	81.8	49.9
			B	19.4	99.5	53.5
			E	0.2	91	44.8
			F	20.6	103.0	56.2
			G	0.2	60.7	37.4
Howarth and Griffin (1989)	Immersion of left hand in water at 15°C until skin temperature was below 17°C for 1 minute, 5 sessions, measurement location not reported	5 healthy female subjects	A	17.5	50.0	35.7
			B	13.9	56.5	38.5
			E	15.9	41.1	30.9
			F	14.8	55.1	42.2
			G	25.0	44.8	33.2
Current study	Immersion of one hand in water at 15°C for 5 minutes, 4 sessions, measurements on the distal phalanges of digits 1 to 5 and on medial and proximal phalanges of the middle finger	12 healthy male office workers	C	15.2	165.8	71.4
			D	8.3	168.1	72.2
			E	10.3	150.2	68.7
			H	3.3	33.7	12.6
			I	0.3	30.6	8.4
		12 healthy male manual workers	C	19.2	191.6	86.2
			D	10.8	185.7	81.5
			E	12.8	164.5	74.5
			H	3.0	28.1	11.1
			I	0.1	30.0	10.0
		12 males with VWF	C	26.6	185.3	92.2
			D	22.1	181.5	85.9
			E	9.4	167.7	74.7
			H	3.0	26.3	13.0
			I	0.8	37.0	15.4

[§] For the response of FSTs to cold provocation, the parameters are: A) time to recover by 50% of fall during cooling; B) time to recover by 80% of fall during cooling; C) time to rise by 3°C from the lowest temperature; D) time to rise by 4°C from the lowest temperature; E) time to rise by 6°C from the lowest temperature; F) time to change of slope; G) initial slope of the curve; H) temperature at 4 minutes of immersion; I) temperature at 5 minutes of recovery.

The findings of this study might be due to the relatively mild symptoms reported by subjects; no subject would have been placed at higher than stage 2 on the Stockholm Workshop vascular scale or the Taylor-Pelmear scale. In a previous study presented here (Section 3.2.3.1), it was suggested that the sensitivity and specificity of this test to VWF was lower amongst subjects with mild VWF than amongst subjects with more severe symptoms. This would suggest that in a suspected case of mild VWF, several tests might be required before a negative finding can be considered correct. This is in agreement with Gemne (1997) who suggests that the existence of VWF cannot be excluded by a negative test result.

The CoVs for the times to rise by 3°C, 4°C and 6°C were calculated for comparison with previous data (Parameters C, D and E, Table 32). These parameters were found by others to be the more repeatable parameters of the rewarming curve (Hayward *et al.* 1988, Howarth and Griffin 1989, Carnicelli *et al.* 1992). The CoVs for these three parameters in this study were much higher than those reported previously. These parameters would not be considered repeatable in this study since large differences were observed between sessions for some subjects in each of the three groups.

The times to rise by 3°C, 4°C and 6°C were found to have a low sensitivity and specificity to VWF in a previous study presented here (Section 3.2.2.2.1). This may have been due to a low repeatability of these parameters, as found here. Retests may be necessary to obtain confirmatory evidence of an expected cold-induced vasoconstriction in subjects reporting symptoms of VWF (Gautherie, personal communication, Gemne 1997).

For FSTs following cold provocation, the parameters selected for analysis in this study were more repeatable than those previously reported in the literature. The repeatability of the parameters may be considered to be acceptable for all three groups of subjects; they show a similar range of CoVs to FSBPs and the measurement of FSBPs has been considered repeatable (e.g. Bovenzi *et al* 1998, Carnicelli *et al.* 1992).

The results of the analyses presented here show that there are differences between repeatabilities of the various parameters used to interpret the response of FSTs to cold provocation. The different parameters used to interpret the FST response to cold provocation are considered further in Chapter 7.

6.4.2 Order effects

There were no significant effects of prior cold provocation during measurements of FSTs on the results of a FSBP test. This may be due to complete recovery of the central sympathetic nervous system to its original state during the recovery period of the

measurement of the response of FSTs to cold provocation. This would be consistent with the literature, 15 minutes after cold exposure changes in the central sympathetic activity tend to have recovered (Nakamoto 1990, Sakakibara *et al.* 1997).

For FSTs, the order of test presentation had a significant effect. When measured first, the FSTs were lower than when measured second. This might suggest that prior application of thermal provocation during the FSBP test resulted in a conditioning effect; there was less cold-induced vasoconstriction when FSTs were measured second. This would be consistent with the suggestion of Nielsen (1978), that some recovery is required before repeated vasoconstriction can be elicited.

6.4.2.1 Effects of order on repeatability

The repeatability of the two tests was affected by the order in which they were performed. For the office workers, both tests were more repeatable when the FSBP test was performed first. For workers reporting symptoms of VWF, when a test was performed first it was more repeatable than when it was performed subsequent to a prior cold provocation test. For the manual workers, the repeatability of the tests appeared unaffected by the order in which they were performed.

For office workers, the results of this study appear to be consistent with the experiment presented in Section 5.3; not allowing recovery between successive thermal provocations resulted in a more consistent response. This strengthens the hypothesis that one cause of intra-subject variability seen in measurements of FSBPs and FSTs is a variation in the initial state of the central sympathetic nervous system.

The intra-subject variability was similar between the two test conditions for the manual workers. These subjects are likely to be more accustomed to the application of cold provocation through their work and may provide a more consistent response of the central sympathetic nervous system to the cold provocation, regardless of test order.

For workers reporting VWF, one reason for the repeatability of the tests being higher when performed first compared to when performed second can be supposed from the literature. Nielsen *et al.* (1978) suggest that exaggerated vasoconstriction may be due to the release of norepinephrine from sympathetic nerve terminals, this release requiring some period of recovery before a subsequent test can elicit a similar response to the first.

The cause of the inconsistent test results amongst subjects with VWF should be further investigated to ascertain the principal causes of intra-subject variability. This would also provide information on factors contributing to closure of the digital arteries in response to cold amongst subjects reporting blanching.

6.4.3 Recommendations for performing the tests in a single test session

When performing the two tests in the same test session, it would be beneficial to minimise intra-subject variability whilst maximising the distinction between healthy subjects and subjects with VWF.

For manual workers, it does not seem to be necessary to control the test order. For office workers, performing the FSBP test first appeared to result in less variable measurements, and in higher FSTs measured in response to cold provocation. If lower normal limits are calculated from data from office workers using the mean minus two standard deviations, higher lower normal limits will be obtained. This is less likely to result in a false negative result when screening workers exposed to hand-transmitted vibration (i.e. a greater sensitivity to VWF). It is concluded that this test order (FSBPs measured before the FST response to cold provocation) can be used when making measurements on office workers with the purpose of formulating normative data. For making measurements on subjects reporting VWF, it is concluded that greater emphasis should be placed on the test that is performed first; this is the test that shows the greatest repeatability.

6.5 CONCLUSIONS

The results of this study show that the repeatability of measurements of FSBPs and measurements of the response of FSTs to cold provocation can be acceptable for the tests to be of use amongst subjects reporting no symptoms of VWF.

For measurements of FSBPs in subjects with VWF, the intra-subject variability was greatly increased relative to both the office workers and the manual workers; some subjects gave a normal response to cold provocation on one occasion and an abnormal response on another. Where the test gives a negative result and a positive result is expected from a worker's own report of a condition, a retest may be necessary. Further work is required to ascertain the causes of this intra-subject variability amongst subjects reporting symptoms of VWF.

For manual workers, the repeatability of the tests was unaffected by the order of presentation and there was no effect of the order of presentation. Amongst office workers, the effects of the order of presentation of the tests on both the repeatability and the measured results suggest that when both tests are to be performed in the same session and the data are to be used to form normal limits, it is preferable to measure FSBPs before FSTs. For subjects with VWF, the test performed first was shown to be the most repeatable; it is concluded that when both tests are to be performed in the same session, greater emphasis should be placed on the first test than on the second test.

CHAPTER 7 INTERPRETATION OF THE FINGER SKIN TEMPERATURE RESPONSE TO COLD PROVOCATION

7.1 INTRODUCTION

The finger skin temperature (FST) response to cold provocation has been widely used for detecting vibration-induced white finger (VWF), but with varying degrees of success. Reported sensitivities of the test to VWF have been between 20-25% (Harada 1987) and 100% (Juul and Nielsen 1981); Pelmear *et al.* (1985) reported a lower limit of specificity of 35% whilst Niioka *et al.* (1986) reported a specificity of 100%. In Chapter 3 of this thesis, use of lower normal limits to calculate sensitivity and specificity showed very low sensitivity to VWF (0% to 23.2%) with specificities between 54.4% to 100% (Table 10).

The measurement methods reported in the literature differ widely. However, even when the same methods have been used, different specificities and sensitivities have resulted. For example, Kurumatani *et al.* (1986), Niioka *et al.* (1986), Harada (1987) and Virokannas and Rintamäki (1991) used whole hand immersion at 10°C for 10 minutes without ischaemia of the hand in room temperatures between 20°C and 23°C. The sensitivities ranged between 20% and 91% whilst the specificities ranged between 70% and 100%.

Pelmear *et al.* (1985) used whole hand immersion at 10°C for 10 minutes with ischaemia for the first five minutes of the immersion period and showed sensitivities between 70% and 80% with specificities between 35% and 85%. In a report in 1987, the same authors showed sensitivities from 30% to 80% with specificities between 37% and 89%.

One reason for the discrepancies in the sensitivities and specificities of this test is likely to be the method of interpreting the results. Generally, one or more parameters of the rewarming curve are selected and used for analysis. The various parameters are unlikely to give the same results. For example, Pelmear *et al.* (1985) used the temperature of reactive hyperaemia following removal of a tourniquet as their diagnostic criterion whereas Pelmear *et al.* (1987) used the FST during immersion and the time it took for the FST to recover to within 1% of its initial temperature (Figure 27). In Chapter 6 of this thesis, it was also shown that different parameters exhibit different repeatabilities (Table 32), this is likely to further influence the sensitivity and specificity of this test to VWF. Differences between the physiological mechanism that some of the parameters are measuring is likely to contribute to the differences between parameters.

The response of FSTs to cold provocation when plotted as a rewarming curve and when measured under controlled conditions after a period of habituation in the absence of vasoactive agents other than cold provocation, can be divided into three sections which provide differing information: (a) the FST before cold provocation (the settling period) provides information about the state of blood flow in the fingers at rest, (b) the FST during the immersion period provides information about the extent of vasoconstriction, and (c) the FST during the recovery period provides information about the extent of subsequent vasodilation.

The state of blood flow during the settling period is important in indicating poor capillary blood flow or obstructive disorders of the peripheral circulation. A low blood flow in the finger skin at rest can result in a low FST (Bovenzi 1987). It may be beneficial to interpret measurements of FST during immersion and recovery with some reference to the state of resting FST; VWF is observed as a cold-induced episode, a low settling period FST can also indicate low blood flow due to some other peripheral vascular disorder.

Vasoconstriction during immersion results in the reduction of the heat source to the fingers, i.e. the blood. This results in lower FSTs and, the greater the vasoconstriction, the greater the reduction in FST during cooling. It has also been shown that exaggerated vasoconstriction can inhibit the occurrence of reactive hyperaemia (Hack *et al.* 1986, Kilgour *et al.* 1997, Pelmear *et al.* 1985). Exaggerated cold-induced vasoconstriction may also inhibit the occurrence of the hunting phenomenon, a cyclical rise and fall of temperature that occurs in healthy hands during cold exposure (Jepson 1954, Spurr *et al.* 1955). Therefore, very low FSTs during the immersion period may be indicative of exaggerated cold-induced vasoconstriction.

The vasodilation process is less well understood in VWF. Nielsen (1981) suggests it is the gradual release of arterial vasospasm. Virokannas and Rintamäki (1991) suggest that the process has two components: i) passive vasodilation by release of cold-induced vasoconstriction and ii) active vasodilation through, for example, the regulation of the arterio-venous anastamoses by the β-adrenergic receptors. Measurement of FSTs during the recovery period may be considered representative of the extent of blood flow resulting from a combination of these mechanisms. A low FST during recovery can indicate dysfunction of either mechanism.

The various parameters used to describe the rewarming curve in the literature are illustrated in Figure 27 and Table 33. The parameters fall into three main categories: i) measurements of the resting state of FST, ii) measurements of the extent of vasoconstriction during cooling, and iii) measurements of the extent of vasodilation following cooling. Combinations of two or more parameters are sometimes used.

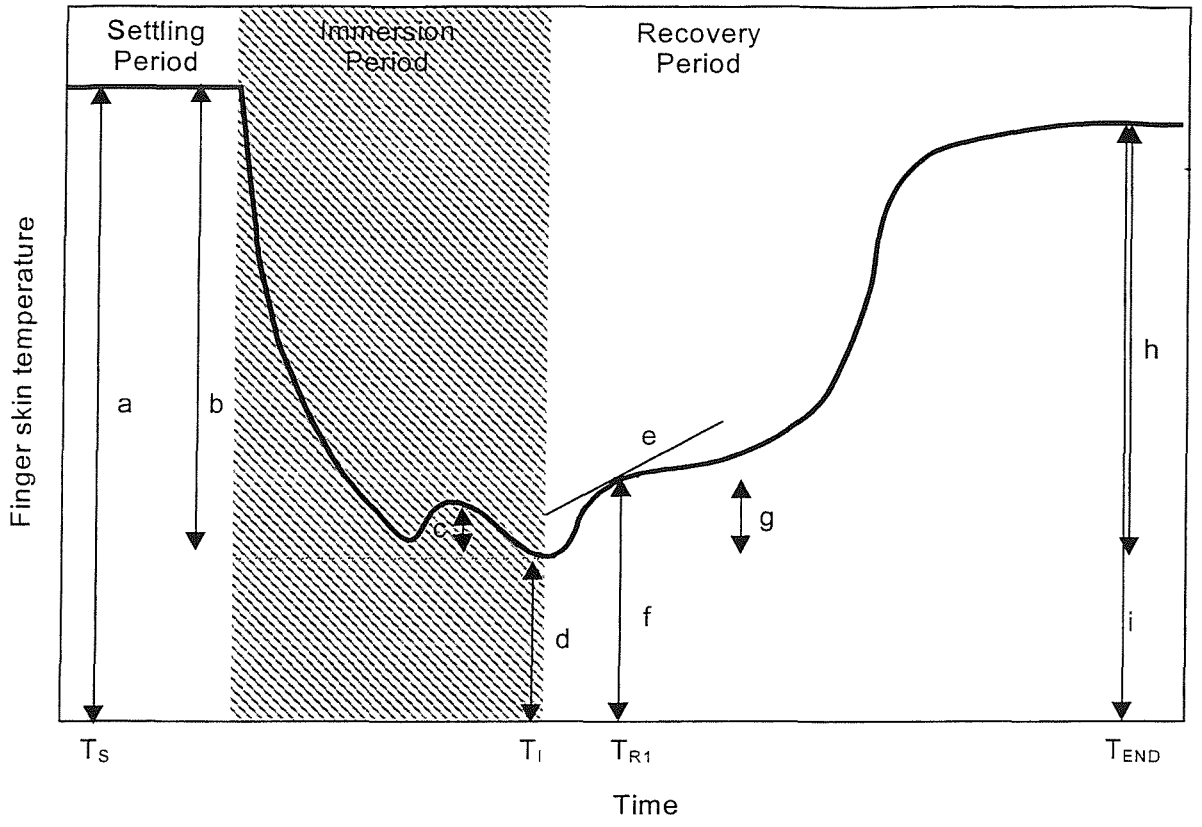


Figure 27 A rewarming curve showing finger skin temperature response to cold and the various parameters used to interpret results. The meanings of the parameters are given in Table 33.

Table 33 Commonly used parameters for interpreting the response of finger skin temperature measurements to cold provocation

Parameter	Description
a	Settling period temperature
b	Decrease in temperature during immersion
c	Hyperaemic temperature or occurrence of hyperaemia
d	Minimum temperature or temperature during immersion measured at time T_I
e	Rate of change of temperature at time T_{R1}
f	Temperature at time T_{R1}
g	Increase in temperature at time T_{R1}
h	Change of temperature during recovery
i	Recovery temperature or maximum temperature
$T_{R1} - T_I$	Time to rise by g°C
d/a x 100	Percentage decrease in temperature
f/a x 100	Percentage recovery at time T_{R1}
$g/(T_{R1} - T_I)$	Rate of change of temperature to time T_{R1}
g/b x 100	Percentage of temperature change recovered at time T_{R1}

Some comparisons between different parameters have been reported. For example Howarth and Griffin (1986) and Carnicelli *et al.* (1992) compared parameters amongst healthy subjects in studies designed with the aim of suggesting repeatable measurement parameters. In 121 workers with and without VWF, Pelmear *et al.* (1985) compared the times it took for the FST to reach 50%, 75%, 90% and 95% of initial temperature and the hyperaemic temperature following removal of a tourniquet during cooling. It was concluded that the recovery times were not as useful as the hyperaemic temperature in detecting VWF. However, four distinctly different patterns of rewarming were noted in these subjects. This might suggest that the entire rewarming curve should be used to interpret the results of this measurement.

Lawson and Neville (1997) stated that subjective judgement of the whole rewarming curve was the best method of interpreting this measurement. Juuls and Nielsen (1981) also used subjective judgement of the entire rewarming curve in forming their conclusions. Gautherie (1997) suggests that the entire rewarming process should be taken into account; using a complex calculation from 11 different parameters of the rewarming curve this author suggests the test can give sensitivities and specificities greater than 90%).

Two previously unused parameters that might address the rewarming process more completely than the parameters discussed here are i) the area under the curve and ii) the area above the curve (Figure 28). A relatively small area under the curve during the immersion period would be suggestive of suppression of reactive hyperaemia or exaggerated cold-induced vasoconstriction or both. During the recovery period, a relatively small area under the curve would be indicative of delayed release from cold-induced vasoconstriction or absence of active vasodilation or both. The opposite is true for areas above the curve, larger areas indicating an exaggerated response to cold provocation. However, the area above the curve, when calculated as the area between the curve and the settling period temperature, would also take into account the state of resting FST.

An analytical investigation of data previously collected on healthy subjects and subjects reporting symptoms of vibration-induced white finger has been performed to compare different parameters of the rewarming curve with the area under the curve and the area above the curve. It was hypothesised that the areas under and above the curve would show greater sensitivity and specificity to vibration-induced white finger than the parameters more commonly reported in the literature.

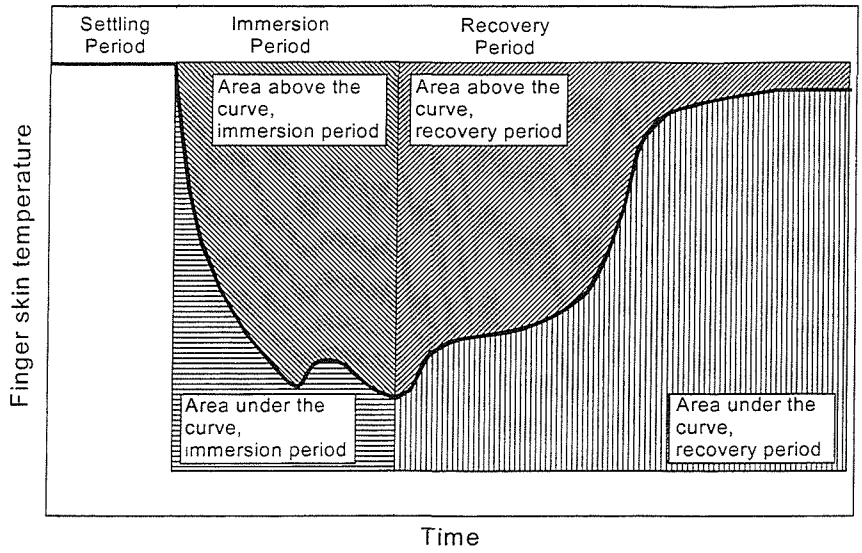


Figure 28 Diagramatic representation of areas above and below the curve. The area above the curve is that between the skin temperature and the settling period temperature. The area under the curve is that between the finger skin temperature and the temperature of cold provocation.

7.2 METHOD

7.2.1 Data

Data have been taken from measurements made on 36 subjects during an experiment to determine effects of the order of presentation of, and the repeatability of, cold provocation tests. Subject details are given in Section 6.2.1 and in Appendix D. The experimental procedure is described in Section 6.2.3. For each subject, the data from the first session in which the FST response to cold was measured before FSBPs have been used.

Data were available for measurements made at the fingertips and for the medial and proximal phalanx of the middle finger of the test hand. Only data for the fingertips are included here; it has been suggested that there are differences in the FST response to cold provocation between different sites along the length of a digit (Kester *et al.* 1990). Data have been grouped according to the reported presence or absence of blanching on the distal phalanx of the finger on which the measurement was made; measurements of the vascular response to cold are most likely finger specific (Section 3.2.3.1, Gautherie 1997, Lawson and Neville 1998). There were 147 healthy fingers and 33 fingers reported as exhibiting blanching.

The data were obtained using a sampling interval of 0.55 seconds throughout a two minute settling period, five minutes immersion in water at 15°C and a fifteen minute recovery period. Figure 29 shows the mean (± one standard deviation) rewarming curves for the healthy fingers and for the fingers reported as having VWF. For subjects not reporting VWF, recovery of the initial FST sometimes occurred before the end of the fifteen minute period and for practical reasons recording ceased at the tenth minute of recovery, the curves have been drawn to the tenth minute of recovery.

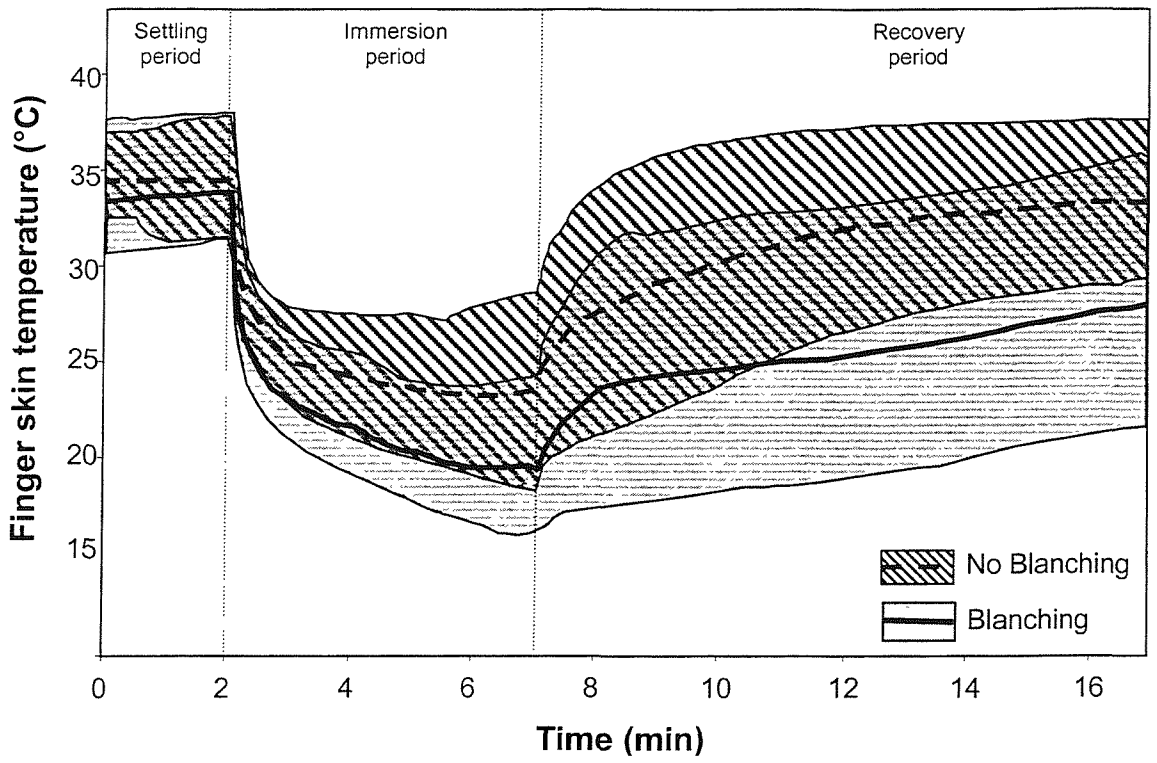


Figure 29 Mean (± 1 standard deviation) rewarming curves for fingers with blanching (N = 33) and fingers without blanching (N = 147).

7.2.2 Analysis

The rewarming curves were smoothed using a five sample triangular averaging window prior to calculation of parameters of the rewarming curves. This has the effect of smoothing the rewarming curve by reducing the effect of signal noise. Data have been compared between fingers reported as blanching and fingers not reported as blanching using the Mann-Whitney *U* test.

The sensitivity and specificity of the parameters have been compared using receiver operating characteristics (ROCs). The ROC curve is a plot of sensitivity against (1 – specificity) and is calculated by determining the sensitivity and specificity of a test for a range of threshold values, i.e. the test result beyond which the presence of a disease is indicated. From such a curve it is possible to select a threshold value which balances the benefits of a correct classification and the detriment of an incorrect classification (Lusted 1978). The ROC curve has several advantages for comparing the diagnostic efficacy of a test: i) it is independent of what is measured so the sensitivity and specificity of several parameters can be compared, ii) it is independent of the prevalence of the condition being assessed and iii) it is independent of a decision making threshold value (Metz 1978).

7.3 RESULTS

Twenty one parameters have been calculated, representing the range of parameters reported in the literature. The parameters have been grouped as: a) areas above the curve, b) areas under the curve, c) times to rise by T°C, d) percentage recovery, e) absolute temperature measurements and e) rates of change of temperature. Table 34 shows the median (inter-quartile range, IQR) values for each of these parameters for fingers reported as blanching and for fingers not reported as blanching. The ROCs for detection of blanching are shown in Figure 30.

Some of the parameters are derived using the settling period temperature. The median (IQR) settling period temperature was 35.4°C (2.2°C) for fingers with blanching and 35.3°C (2.45°C) for fingers without blanching. The settling period temperature was not significantly different between fingers with and fingers without blanching (p = 0.94).

Table 34 Median (inter-quartile range) values for 21 parameters describing components of the FST response to cold in 147 healthy fingers and 33 fingers reported as blanching. The parameters are explained in Figure 27, Figure 28 and Table 33.

Parameter		Digits without blanching (median, IQR)	Digits with blanching (median, IQR)
Area above the curve during the recovery period	°C.s	4896 (1670)	5691 (1489)**
Area above the curve during the immersion period	°C.s	2545 (4400)	6445 (11017)**
Area above the curve during the immersion and recovery period	°C.s	7243 (5577)	12814 (11906)**
Area under the curve during the recovery period	°C.s	11036 (4480)	7209 (8281)**
Area under the curve during the immersion period	°C.s	2834 (1689)	2391 (1167)*
Area under the curve during the immersion and recovery period	°C.s	13891 (6075)	8708 (8723)**
Time to rise by 3°C (T_{R1} - T_I, g=3)	s	34.3 (117.7)	40.9 (325.3)
Time to rise by 4°C (T_{R1} - T_I, g=4)	s	52.5 (172.2)	79.4 (479.1)
Time to rise by 6°C (T_{R1} - T_I, g=6)	s	116.3 (239.8)	198.8 (9544.3)
Percentage of initial temperature at 10th minute of recovery (f/a x 100, T_{R1}=10)	%	97.4 (4.7)	95.3 (35.1)*
Percentage of initial temperature at 5th minute of recovery (f/a x 100, T_{R1}=5)	%	95.5 (12.1)	76.1 (37.7)**
Percentage of temperature drop recovered by the 10th minute of recovery (g/b x 100, T_{R1}=10)	%	91.4 (13.1)	89.1 (68.8)$^{+}$
Percentage of temperature drop recovered by the 5th minute of recovery (g/b x 100, T_{R1}=5)	%	84.9 (38.8)	50.4 (72.8)**
Temperature at 10 minutes of recovery (f, T_{R1} = 10)	°C	34.9 (3.1)	34.3 (14.1)*
Temperature at 5 minutes of recovery (f, T_{R1} = 5)	°C	34.5 (5.6)	26.0 (15.1)**
Minimum temperature during immersion (d)	°C	22.2 (6.9)	18.4 (5.0)*
Maximum temperature during recovery (i)	°C	35.4 (2.6)	33.0 (14.3)**
Rate of rewarming in 10 minutes of recovery (g/10)	°C/min	1.06 (0.54)	1.00 (0.89)
Rate of rewarming in 5 minutes of recovery (g/5)	°C/min	1.81 (1.18)	1.43 (1.77)*
Rate of rewarming during the 10th minute of recovery (e, T_{R1}=10)	°C/min	0.11 (0.48)	0.25 (0.46)*
Rate of rewarming during the 5th minute of recovery (e, T_{R1}=5)	°C/min	0.33 (0.53)	0.24 (0.27)$^{+}$

Mann-Whitney U: $^{**}p < 0.01$; $^{*}p < 0.05$; $^{+}p < 0.1$

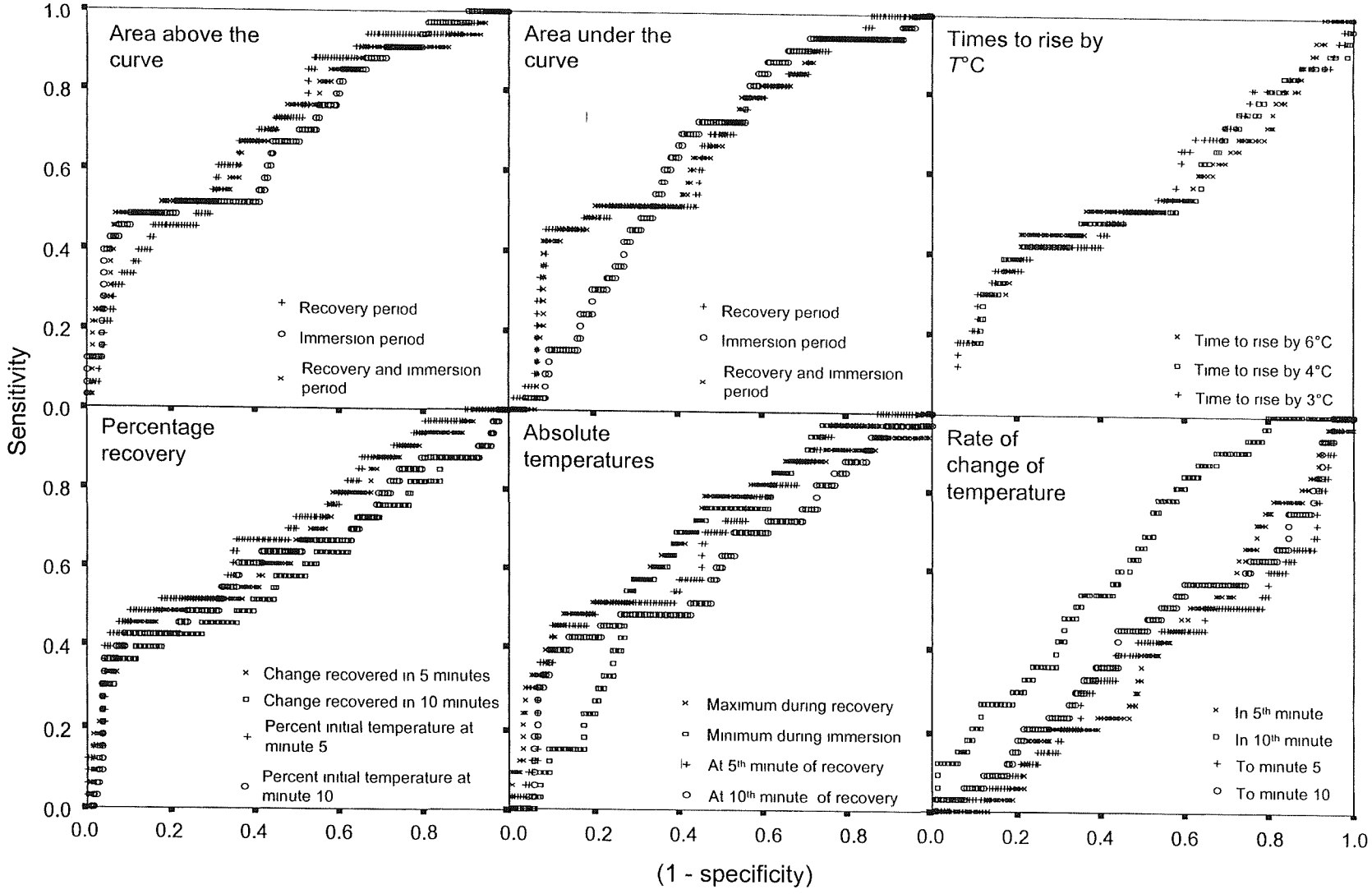


Figure 30 Receiver operating characteristics for the detection of VWF using 21 different parameters of the rewarming curve.

7.4 DISCUSSION

The response of finger skin temperatures (FSTs) to cold provocation can differentiate between groups of subjects with and without VWF but it is sometimes suggested the measure is unsuitable for diagnosing VWF on an individual basis (e.g. Bovenzi 1987). Analysis of the data here showed that whilst some parameters could distinguish between groups of fingers with blanching and groups without blanching, some of the parameters that are in use did not distinguish between the two groups. The ROC curves suggest that some parameters of the rewarming curve are more useful for detecting the presence of blanching on an individual basis than others. These results support the call for consideration of the parameter used to interpret the FST response to cold provocation (Tomida *et al.* 1998).

To interpret the ROC curves, some discussion is necessary. In general, the further the apex of the curve moves upwards and to the left, the better the measure is performing in distinguishing between fingers with VWF and healthy fingers. When the ROC curves cross over, however, it is not as simple to determine which test is performing best. When the prevalence of disease is low, or the consequences of a false positive decision are deleterious, use of the lower left region of the ROC curve is recommended, i.e. maximising the specificity (true negative fraction) at the expense of the sensitivity (true positive fraction). If the disease prevalence is high and the need to find true positive cases is of the greatest importance, then the upper right portion of the curve should be used, i.e. maximising sensitivity at the expense of specificity (Metz 1978).

In the case of VWF, the prevalence of disease is dependent upon the worker population of interest. However, the reason for performing the measurement is to decrease the prevalence of the condition in the workplace and hence it might be assumed that when the test is in use, the prevalence of the condition being investigated will be low. Also, the consequences of a false positive decision may be considered detrimental in some circumstances; the data may be used to support the removal of an employee from the workplace. This would suggest that the lower left region of the ROC curve is of greater importance than the upper right portion of the curve. Bovenzi (1987) however, suggests that the sensitivity of the test should be maximised, i.e. the upper right portion of the curve should be used. This conclusion was based upon requirements for insurance and medico-legal purposes where the need to find supporting evidence of disease for actually positive cases is high, and where a false positive will not necessarily result in a worker being removed from employment. For the results reported here, greater emphasis is placed upon the lower left portion of the curve for choosing parameters suited for monitoring vascular function in workers exposed to hand-transmitted vibration.

7.4.1 Areas above the curve

The areas above the curve were significantly greater during the recovery period, the immersion period and both periods combined in the fingers with VWF than the fingers without VWF. The ROC curves indicate that for a high specificity (true negative fraction), use of the area above the curve during the immersion period performs better than the area above the curve for the recovery period. For a high sensitivity the opposite is true. The combined area above the curve appears to perform well over the whole ROC curve. This is as expected since it incorporates measures of both vasodilatative and vasoconstrictive function. The area above the curve during the recovery and immersion periods combined is considered the better of the three parameters.

7.4.2 Areas under the curve

The area under the curve was significantly smaller during the recovery period, the immersion period and both periods combined for the fingers with VWF than for the fingers without VWF. The area under the curve during the immersion period showed more overlap between the two groups than the other two parameters, as shown by the median values and interquartile ranges given in Table 34. This parameter also performs poorly in the lower left region of the ROC curve. The area under the curve during the immersion period is not considered a useful parameter for detecting VWF. The results also suggest there is little advantage of combining immersion period areas and recovery period areas. Measuring only the recovery period temperatures simplifies the data collection and enables a wider range of transducers to be used since these will not require immersion in water. The area under the curve during the recovery period is considered the most suitable of the three parameters calculated for areas under the curve; it is the most practical of these parameters to measure. However, this parameter does not appear as useful as the area above the curve. This may be because no consideration is given to the state of resting FSTs.

7.4.3 Times to rise by *T*°C

The times to rise by 3°C, 4°C and 6°C were not significantly different between fingers with VWF and fingers without VWF. The ROC curves are of a similar shape to those calculated for 104 dockyard workers in a previous study reported in this thesis (Section 3.2.2.2.1.1) and confirm that these parameters do not perform well in detecting VWF. These parameters have also been shown to be less repeatable than some others (Table 32, Chapter 6). Other parameters calculated here seem to be more suitable for monitoring vascular function in workers exposed to hand-transmitted vibration.

7.4.4 Percentage recovery

The percentages of the initial temperature at five and ten minutes after immersion were significantly lower for fingers with VWF than for fingers without. The percentages of the change in temperature during immersion were also lower in the fingers with VWF than the fingers without although the difference was only significant at 5 minutes during recovery. Receiver operating characteristics suggest that the percentage recovery at 10 minutes of recovery is not as useful as the percentage recovery at 5 minutes for detecting VWF. The percentage of initial temperature generally performed better than the percentage of change during immersion.

Tomida *et al.* (1998) also showed significant differences between a group of subjects reporting VWF and healthy office workers for the percentage of the change in FST during immersion that had recovered after five and ten minutes although these authors showed ROC curves approaching a straight line. Bovenzi (1987) showed a sensitivity of 60% and a specificity of 92% to VWF for the percentage of initial temperature recovered after 20 minutes. A similar parameter has been reported by von Bierbrauer *et al.* (1998), they found that using a criterion of 100% of initial temperature at 20 minutes gave a sensitivity of 66.7% and a specificity of 75% to VWF. These results support the suggestion that the percentage of initial temperature is a better diagnostic parameter than the percentage of the change during immersion.

7.4.5 Absolute temperatures

All absolute FST measurements analysed were significantly lower in the fingers with VWF than in the fingers without. For the ROC analysis, the maximum temperature during the ten minute recovery period showed the best performance of these parameters. The FSTs measured at the fifth minute of recovery exhibited only slightly poorer performance than the maximum temperature during recovery. The FSTs at the tenth minute of recovery performed well in the lower left region of the curve but poorly in comparison to other absolute FSTs in the upper right region of the curve. The FSTs measured during immersion did not perform well in the lower left region of the ROC curve although they performed similarly to other measures of FST in the upper right portion of the curve. The maximum temperature during recovery is considered the best of the parameters calculated here for detecting VWF.

Laroche and Thériault (1987) report the sensitivity and specificity of the recovery temperature at 15 minutes of recovery. The results are plotted in Figure 31 and support the results obtained here for absolute temperature measurements.

Tominaga (1998) showed the diagnostic sensitivity and specificity of absolute FST measurements made during immersion (mean of the 6th to tenth minute during immersion), at the fifth minute of recovery and at the tenth minute of recovery. The ROC curves reported by this author suggest that the FST measured at 5 minutes of recovery performed better than the other parameters, as found here.

Virokannas and Rintamäki (1991) showed a ROC curve for the maximum temperature during 20 minutes of recovery, they suggested an optimal limit of approximately 70% specificity and 70% sensitivity could be obtained. Although these values are higher than the sensitivity and specificity obtained here, they support the suggestion that the maximum temperature during recovery is a useful parameter for monitoring vascular function in workers exposed to hand-transmitted vibration.

Hack *et al.*, (1983, 1986), Pelmear *et al.*, (1985) and Brubaker *et al.* (1986) reported sensitivities and specificities for measurements of hyperaemic temperature. Their results are plotted in Figure 31 and suggest a better performance than the absolute temperature measurements reported here. However, these authors used longer periods of thermal provocation with colder water temperatures to elicit their desired responses, and the parameter is calculated as the difference between the minimum immersion temperature and a temperature of hyperaemic response subjectively decided by the investigator. The results of these studies are unlikely to give similar results to the data reported here. Furthermore, the hyperaemic response tends to be diminished in older subjects (Jepson 1954), suggesting an increasing false positive rate for this measure with increasing age. The hyperaemic temperature is not considered a useful indicator of VWF.

7.4.6 Rate of change of temperatures

The rate of change of temperature within the tenth minute of recovery, and the rate of change of temperature to the end of the fifth minute of recovery were both lower for fingers with VWF than for fingers without VWF. The ROC curves, however, suggested that these measures did not perform as well as other parameters. Nasu and Kurozawa (1995) reported the sensitivity and specificity of the rate of change of temperature to the fifth and tenth minute of recovery. Their results are shown in Figure 31 (parameter i) and do not support the use of these parameters for detecting VWF.

7.4.7 Selection of parameters for detecting VWF

The results reported here show that of the 21 parameters calculated, those that distinguish between fingers with and without blanching most often are the area above the curve during the immersion and recovery period, the percentage of initial temperature at the fifth minute of recovery and the maximum temperature during recovery. The ROC curves for these parameters are shown together in Figure 31. The curves do not show much distinction between the three parameters, suggesting any can be used for detecting VWF.

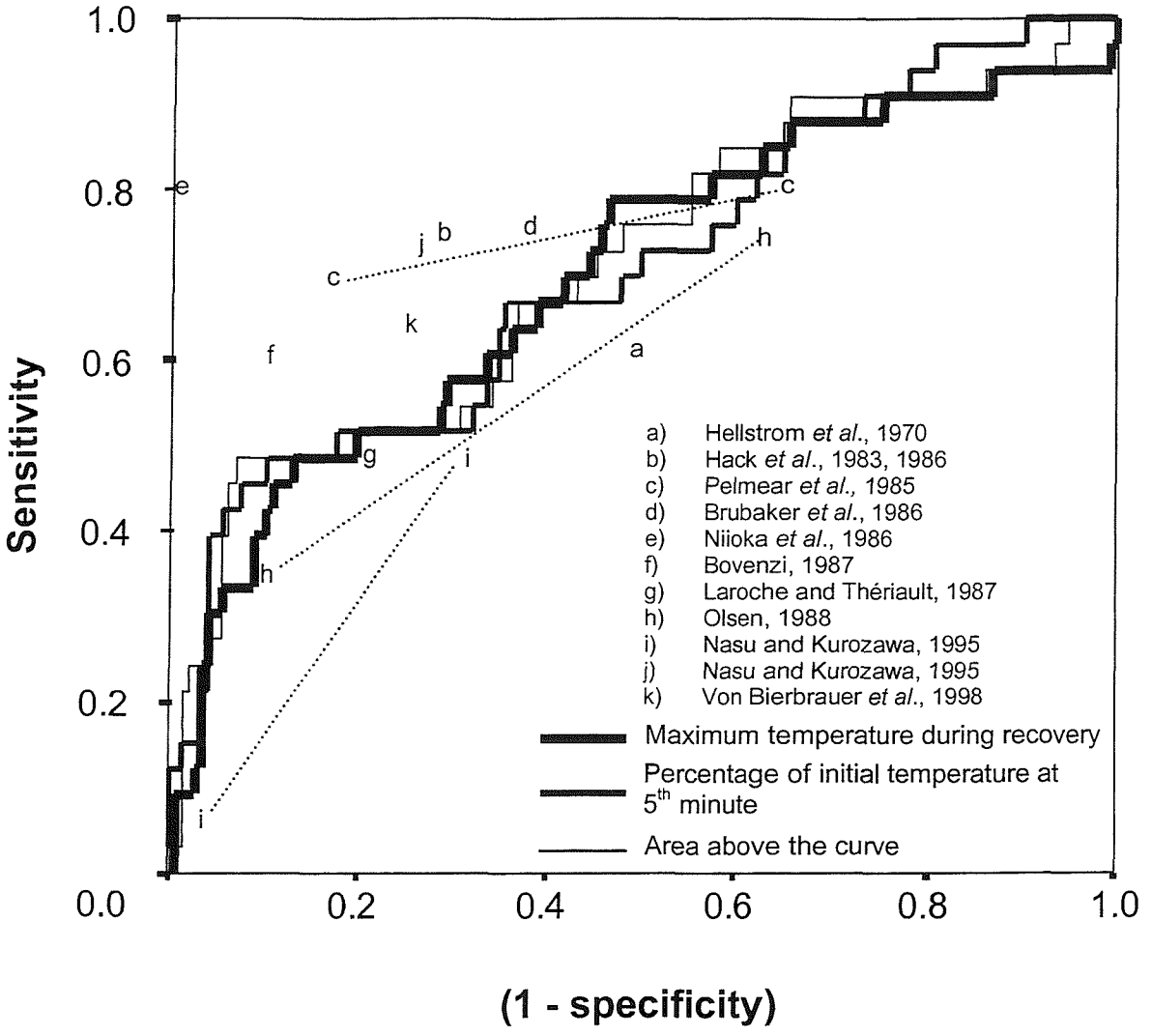


Figure 31 Receiver operating characteristics for three parameters found to give the greatest distinction between fingers with and without VWF across a range of threshold values. Sensitivities and specifities reported by other authors are also shown

When selecting a parameter for routine use in monitoring peripheral vascular function in workers exposed to hand-transmitted vibration, the practicality of obtaining the parameter should be considered. Of the three parameters shown to be the most useful, the percentage of initial temperature at five minutes of recovery is the simplest to calculate. Only two measurements are required, one prior to cold provocation and one at the end of the fifth minute of recovery. The maximum recovery temperature requires the monitoring of the FST throughout the recovery period and the area above the curve requires monitoring of the FST immediately before immersion, throughout immersion and throughout the recovery period. The area above the curve requires more extensive computation than both of the other parameters.

The data sampling rate will affect the area above the curve and the maximum temperature during recovery; too low a sampling rate may result in missing the maximum recovery temperature or in course estimates of the area above the curve whilst too high a sampling rate will result in unnecessarily large data files. The percentage of initial temperature at five minutes of recovery might be considered the most practical to calculate. Furthermore, for calculating this parameter a wider range of transducers may be used as these will not need to be immersed in water for monitoring FST during the immersion period.

The physiological mechanism which is being measured by each parameter is of importance when selecting the parameter for use. Virokanas and Rintamäki (1991) suggest that there is no evidence to support a vasodilatative dysfunction in VWF; the mechanism of dysfunction is not fully understood. They recommend that vasoconstriction should be considered. Of the three parameters reported here, only the area above the curve considers the vasoconstrictive mechanism. However, the area above the curve if given as a single number would not allow the distinction between several possible mechanisms of dysfunction; different shapes of the rewarming curve have been reported that might indicate different disorders (Pelmear *et al.* 1985). Neither the percentage of initial temperature nor the recovery temperature address the shape of the rewarming curve either. The area above the curve, although not permitting distinction between the various rewarming patterns, does at least incorporate some measure of shape of the rewarming curve.

The resting FST, when measured in well controlled conditions, is considered a useful indicator of peripheral vascular disorders not attributable to an exaggerated reponse to thermal provocation (Bovenzi 1987). It was suggested in the introduction to this chapter that the response of FSTs to cold provocation should be interpreted with respect to the initial temperature. Although the percentage of initial temperature at five minutes of recovery and the area above the curve during the immersion and the recovery periods do reflect the state of resting FST, the maximum recovery temperature does not. This may be important in differentiating between a cold provoked reduction in peripheral blood flow, as occurs in VWF, and a reduction in peripheral blood flow caused by some other disorder. When using maximum recovery temperature, therefore, it would be useful to measure the initial FST to discount false positive results.

The final consideration when selecting a parameter for use in interpreting the response of FSTs to cold provocation is how it is affected by the measurement procedure. All three parameters are affected by the amount of cold-induced vasoconstriction which is determined by the immersion temperature, the immersion period and the hand conditions during immersion. The area above the curve and maximum recovery temperature are also

influenced by the duration of the recovery period. A longer recovery period will give larger areas above the curve and higher maximum recovery temperatures in some subjects. For the maximum recovery temperature, as the duration of the recovery period increases there is a greater likelihood of false negative results as fingers that have exhibited exaggerated cold-induced vasoconstriction recover. Although the area above the curve is also affected by the duration of the recovery period, the effect is of less importance since this parameter is a measure of the entire rewarming process and hence includes the region of the curve indicating dysfunction.

7.5 CONCLUSIONS

The data analysed in this chapter have shown that the choice of parameter used to interpret the FST response to cold provocation affects the ability of the test to detect VWF. The percentage of initial temperature at 5 minutes of recovery, or the area above the curve during the immersion and recovery period were found to be the most suitable parameters for monitoring VWF in workers exposed to hand-transmitted vibration. The maximum recovery temperature was also useful but it may be necessary to interpret this parameter with consideration of the length of recovery period and the state of resting blood flow prior to cold provocation.

CHAPTER 8 VIBROTACTILE THRESHOLD MEASUREMENTS

8.1 EFFECTS OF MEASUREMENT DURATION WITH DIFFERENT SKIN-STIMULUS CONTACT CONDITIONS

8.1.1 Introduction

When making measurements of vibrotactile thresholds, the stimulus is applied by a vibrating probe contacting the finger, the probe sometimes protrudes through a rigid surround. The conditions of contact between the vibrating probe, the surround and the skin are known to alter the threshold of perception of vibration (Harada and Griffin 1991, Makous *et al.* 1996, Verrillo 1962).

Studies that have investigated the effects of increasing the force with which the vibrating probe contacts the skin have shown that vibrotactile thresholds mediated by the Pacinian corpuscles tend to decrease. A smaller reduction in vibrotactile thresholds mediated by the Meissner's corpuscles is also observed. The use of a rigid surround to the vibrating probe increases thresholds mediated by the Pacinian corpuscles and decreases thresholds mediated by the Meissner's corpuscles (Gescheider *et al.* 1978, Harada and Griffin 1991).

In the apparatus used in this work, the *HVLab* Tactile Vibrometer (Appendix A), the probe contact force is controlled by mounting the shaker generating the vibration on a balance beam. Similar set-ups have been reported in the literature (e.g. Piercy and Brammer 1998, Maeda and Griffin 1994). These arrangements are necessarily more complex than a fixed shaker mounting; they make the measurement equipment cumbersome and difficult to produce and they limit the application of vibration to a vertical direction.

The current draft International Standard for the measurement of vibrotactile thresholds at the fingertips (ISO/CD13091-1) allows for measurements using a controlled skin indentation as an alternative to a controlled probe contact force. However, vibrotactile thresholds measured using the two different contact conditions may be differentially affected by the duration of the measurement; when using a constant skin indentation, the force between the probe and the skin reduces over time as the subcutaneous tissue deforms (Lundström 1997, personal communication). No studies were found in the literature that have investigated how the skin contact force varies over time when a constant skin indentation is maintained.

Before selecting contact conditions between stimulus and skin for measuring vibrotactile thresholds, it is desirable to determine if any changes in vibrotactile thresholds occur during the period of stimulus application, and if these changes differ when the skin indentation is controlled compared to when the probe contact force is controlled. If the vibrotactile thresholds are primarily dependent on the probe contact force, then it may be reasonable to assume that vibrotactile thresholds will decrease if the probe contact force decreases when using a controlled skin indentation.

The study presented in this section was performed to compare the effect of measurement duration on vibrotactile thresholds obtained using a controlled skin indentation to those obtained using a fixed probe contact force. The thresholds for both the Pacinian corpuscles and the Meissner's corpuscles were expected to increase during the period of stimulus application when using a controlled skin indentation but not when using a controlled probe contact force.

8.1.2 Method

Ten healthy male subjects took part in the study. Their mean age was 27.8 years (standard deviation, SD 8.7 years). All subjects were office workers who had not been exposed to hand-transmitted vibration in the workplace, none were smokers and none reported injuries to the upper extremities or symptoms of vascular or neurological disorders. Finger skin temperature was measured at the start of each session using a thermocouple pinched between the thumb and index finger of the right hand. No subject exhibited a skin temperature below 30°C.

Subjects attended for testing in a quiet room of mean temperature 23.7°C (SD 1.3°C). Before measurements began, subjects were acclimatised to the test environment for a minimum of 10 minutes. During this period, they received written instructions on how to perform the vibrotactile threshold test and underwent a practice measurement on the middle finger of the right hand. Hearing protection was worn during all further measurements to prevent distractions.

An *HVLab* Tactile Vibrometer (Appendix A) was used to measure vibrotactile thresholds at the centre of the whorl on the distal phalanx of the index finger of the right hand. For all measurements, subjects maintained a downwards force on the surround of 2 N. Vibrotactile thresholds were measured at 31.5 Hz and 125 Hz to elicit responses from the Meissner's corpuscles and the Pacinian corpuscles, respectively. Two measurements were made at each frequency, one with a constant probe contact force of 1N and the other with a constant probe height relative to the surround of -0.5 mm (i.e. the surface of the probe was 0.5 mm below the level of the surround). Pilot investigations suggested a

probe contact force of 1 N with a 2 N push force on a surround gives a skin indentation of the order of 2 mm in young, healthy office workers when the probe and surround diameters are 6 mm and 10 mm, respectively. Setting the probe height relative to the surround at –0.5 mm resulted in skin indentations of approximately this magnitude. The order of presenting the conditions was balanced across the study population.

Measurements were made using the up-and-down method of limits with a rate of change of vibration magnitude of 3 dB/s. The measurement duration for each condition at each frequency was five minutes. Between each measurement, a rest period of a minimum of one minute was provided; threshold measurements repeated at one minute intervals have been shown not to change over time (Hayward 1986). Thresholds were calculated as the mean of the mean peak r.m.s. acceleration and the mean trough r.m.s. acceleration, ignoring the first cycle of the measurement. Vibrotactile thresholds were calculated for each consecutive minute of a measurement (running mean thresholds) and for the first minute, first two minutes, first three minutes, first four minutes and for the entirety of each measurement (cumulative mean thresholds).

8.1.2.1 Analysis

Results have been analysed using parametric statistics. The cumulative thresholds and the running thresholds were both normally distributed for all measures (Shapiro-Wilkes; $p > 0.081$) except for the running mean thresholds during the fourth and fifth minute measured with a fixed contactor height at 125 Hz. The use of parametric statistics for analysis was considered justified. Means and standard deviations have been used as measures of central tendency and dispersion, respectively. Repeated measures analysis of variance has been used to check for the effects of duration, contact conditions, frequency and their interactions. Post hoc comparison tests (paired sample *t*-tests) have been used to identify factors influencing significance in the repeated measures analysis of variance.

8.1.3 Results

The mean (standard deviation, SD) vibrotactile thresholds for each frequency and for each contact condition are shown in Table 35. Figure 32 shows the mean running thresholds for each frequency and each contact condition. One subject exhibited thresholds that could be considered abnormal (31.5 Hz threshold > 0.3 m/s² r.m.s.; 125 Hz threshold > 0.7 m/s² r.m.s.) and was excluded from analyses. The effects of room temperature, finger skin temperature and age were shown to be negligible when included in the analyses of variance ($p > 0.05$), these were not included in the final analyses.

For the running mean threshold, there was a significant frequency effect and marginal time and frequency by time effects (p = 0.008; p = 0.059; p = 0.058, respectively). There were no significant differences between thresholds measured using a fixed probe height and those measured using a fixed probe contact force. For the cumulative mean threshold, there were significant effects of frequency, time and frequency by time (p = 0.001; p = 0.006; p = 0.018, respectively). There were no significant effects of contact conditions.

Post hoc tests showed that thresholds measured at 125 Hz were higher than those measured at 31.5 Hz ($p < 0.05$). There were no differences between 125 Hz thresholds over time ($p > 0.1$). Thresholds measured at 31.5 Hz increased significantly over time ($p <$ 0.05, threshold in minute 1 v threshold in minute 5).

Although it appears that 125 Hz thresholds measured using a fixed probe height were systematically higher than those measured using a fixed probe contact force, this difference was not statistically significant. Power calculations showed that with the given sample size of 9 and a standard deviation of 0.1 m/s², the difference between mean values would have to be greater than 0.1 m/s² before statistical significance was achieved. The mean threshold at 125 Hz during minute 4 of the measurement exceeded this difference, however the standard deviations of the measurements were higher than 0.1 m/s².

Table 35 Mean (standard deviation) vibrotactile thresholds obtained using either a fixed contact force or a fixed probe height. Thresholds for each minute of the measurement (running threshold) and thresholds from the beginning of the measurement to the end of each minute of the measurement (cumulative threshold) are shown (N = 9).

		31.5 Hz		125 Hz	
		Force	**Height**	**Force**	**Height**
Running thresholds (m/s²)	Min 1	0.147 (0.066)	0.158 (0.036)	0.316 (0.075)	0.395 (0.107)
	Min 2	0.191 (0.045)	0.202 (0.051)	0.356 (0.130)	0.390 (0.093)
	Min 3	0.222 (0.079)	0.212 (0.060)	0.340 (0.114)	0.410 (0.158)
	Min 4	0.241 (0.092)	0.226 (0.077)	0.325 (0.122)	0.426 (0.281)
	Min 5	0.260 (0.107)	0.229 (0.065)	0.318 (0.124)	0.407 (0.216)
Cumulative threshold (m/s²)	1 Min	0.147 (0.066)	0.158 (0.036)	0.316 (0.075)	0.395 (0.107)
	2 Mins	0.170 (0.051)	0.180 (0.043)	0.337 (0.099)	0.392 (0.097)
	3 Mins	0.188 (0.057)	0.190 (0.046)	0.338 (0.102)	0.397 (0.117)
	4 Mins	0.201 (0.064)	0.198 (0.051)	0.335 (0.106)	0.402 (0.141)
	5 Mins	0.213 (0.071)	0.205 (0.053)	0.333 (0.109)	0.403 (0.153)

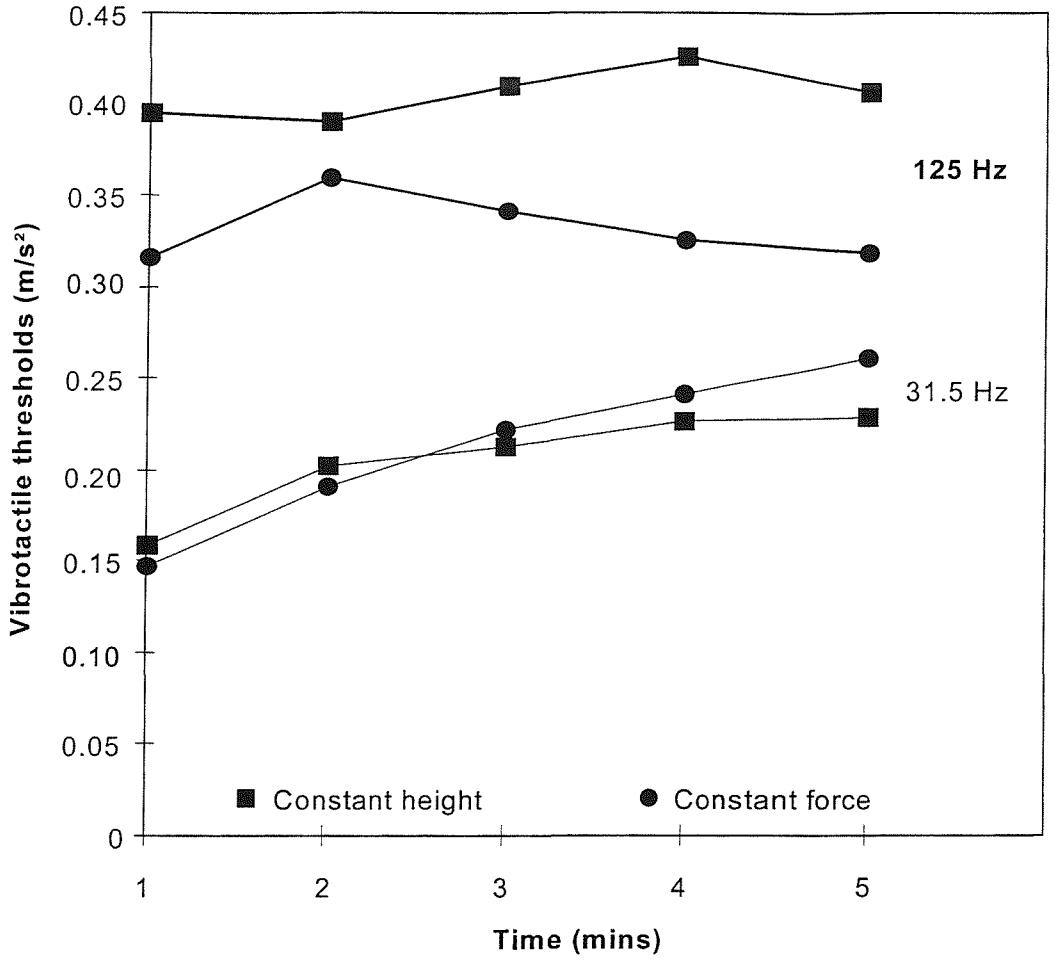


Figure 32 Mean vibrotactile thresholds at 31.5 Hz and 125 Hz measured using either a fixed probe height or a fixed probe contact force. The means for each minute of the measurement (running thresholds) are shown (N=9).

8.1.4 Discussion

The results show a different effect of duration on vibrotactile thresholds between the two afferent pathways. For the Pacinian pathways there was no evidence of a duration effect; for the Meissner's pathways, vibrotactile thresholds increased as the measurement duration increased. It is possible that this increase in thresholds over time could be due to cognitive fatigue or to a temporary threshold shift during the measurements (e.g. Lundström and Lindmark 1982). Since the effect was observed for the Meissner's pathways only, it is more likely there is some physiological process involved that affects the two mechanoreceptor pathways differently.

The observed duration effect at 31.5 Hz was similar for both fixed probe height and fixed probe contact force; no significant interaction was observed between the time effect and the effect of contact conditions on vibrotactile thresholds. It is therefore unlikely the increase in thresholds was due to changes in the probe-skin contact conditions over time. It is possible, however, that the skin and subcutaneous tissue were deforming over time due to maintaining a constant push force of 2 N on the surround.

Changes in the mechanical properties of the skin and subcutaneous tissue resulting from this deformation of tissue might influence the sensitivity of the Meissner's corpuscles; it has been suggested that the sensitivity of the Meissner's corpuscles increases when there is a discontinuity in stimulation induced by a surround (Harada and Griffin 1991, Johansson *et al.* 1982, Lamoré and Keemink 1988). The abruptness of any discontinuity will be affected by the conditions of contact. This would be unlikely to influence the sensitivity of the Pacinian corpuscles; the Pacinian corpuscles do not exhibit the same dependence on stimulus gradients as the Meissner's corpuscles (e.g. Verrillo 1979).

The apparent, but insignificant, difference between 125 Hz thresholds measured in the two conditions is most likely due to differences in the skin indentation; the effect of increasing skin indentation is to increase the sensitivity of the mechanoreceptors, the effect being greater for the Pacinian corpuscles than for the Meissner's corpuscles (Makous *et al.* 1996). Further work is required to determine a skin indentation that gives similar mechanoreceptor specific thresholds to those measured using a probe contact force of 1 N with a 2 N push force on a surround.

8.1.5 Conclusions

The measurement duration did not influence vibrotactile thresholds elicited from the Pacinian pathways. Meissner's corpuscle specific thresholds increased as the measurement duration increased. It is thought that this is due to changes in the mechanical properties of the finger tissue over time caused by maintaining a constant push force on the surround. A relatively short measurement duration (less than one minute) might minimise this effect.

8.2 RELATIONSHIP BETWEEN SKIN INDENTATION, SKIN-STIMULUS CONTACT FORCES AND VIBROTACTILE THRESHOLDS

8.2.1 Introduction

Increasing the static skin indentation caused by a vibrating probe, or increasing the probe contact force, has been shown to decrease vibrotactile thresholds (e.g. Craig and Sherrick 1969, Lamoré and Keemink 1988, Makous *et al.* 1996). Use of a surround decreases vibrotactile thresholds obtained for the Meissner's corpuscles whilst increasing vibrotactile thresholds obtained for the Pacinian corpuscles compared to when not using a surround (e.g. Harada and Griffin 1991).

When selecting skin-stimulus interface conditions for measuring vibrotactile thresholds, the effects of skin indentation, probe contact force and push force on a surround should be considered together as they are inter-dependent. Increasing probe contact force will increase skin indentation, and vice versa. Increasing push force on a surround stiffens the

skin (Piercy and Brammer 1998) and so will either increase the push force for a given skin-indentation, or decreases the skin indentation for a given push force. Differences in the mechanical properties of skin between individuals mean that it is not possible to control both the skin indentation and the probe contact force.

A relationship between skin-indentation and probe contact forces both with and without a surround has been reported in the literature; skin indentations resulting from different probe contact forces were measured to determine equivalent skin-stimulus contact conditions for measurement of vibrotactile thresholds (Piercy and Brammer 1998). The skin indentation to probe contact force relationship was evaluated without consideration of the vibrotactile thresholds.

Probe size has been shown to influence the effect of skin indentation on vibrotactile thresholds; for both Meissner's and Pacinian corpuscle specific thresholds, increasing skin indentation using a 1 mm diameter probe decreased vibrotactile thresholds more than similar increases in skin indentation using a 20 mm diameter probe (Makous *et al.* 1996). When determining skin indentations equivalent to probe contact forces for measuring vibrotactile thresholds, the size of the probe must be considered.

Piercy and Brammer (1998) used a 4 mm diameter probe both with and without a 7 mm diameter surround, and a push force on the surround of 1 N. These results may not be applicable to the skin-stimulus contact conditions used in this thesis (probe and surround diameters of 6 mm and 10 mm, respectively, with a probe contact force in the region of 1 N and a push force on a surround of 2 N).

Maeda *et al.* (1998) showed that increasing the push force on a surround from 0.25 N to 3 N resulted in a small increase in the Pacinian corpuscle specific thresholds when measured with a 1 N probe contact force and a probe diameter of 6 mm protruding through a 10 mm surround. These authors, however, did not measure skin indentation, or identify the effects of changing the push force on a surround on the Meissner's corpuscle specific thresholds. The interaction between skin indentation, probe contact force and push force on the surround, and their effects on vibrotactile thresholds, were not identified from the literature.

This study was performed to investigate the relationship between contact conditions at the skin-stimulus interface and their effects on vibrotactile thresholds for both the Meissner's and Pacinian corpuscles. It was hypothesised that increasing the push force on a surround would decrease the vibrotactile thresholds for the Meissner's corpuscles and increase vibrotactile thresholds for the Pacinian corpuscles. Increasing the skin indentation and increasing the probe contact force were expected to decrease the vibrotactile thresholds obtained for both the Meissner's and the Pacinian corpuscles.

8.2.2 Method

Ten healthy male subjects participated in the experiment; their mean age was 29.7 years (standard deviation, SD 6.2 years). All subjects were non-smokers and all were office workers. The mean finger skin temperature, measured at the start of each session using a thermocouple pinched lightly between the thumb and index finger, was 31.9°C (SD 3.2°C). Each subject attended one session during which static skin indentation and vibrotactile thresholds were measured for varying combinations of finger push force and probe contact force.

8.2.2.1 Skin indentation

Skin indentation was measured using the apparatus shown in Figure 33. Displacement transducers (RDP Electronics, type D2/200A) were placed under either end of a balanced beam. The transducer sensitivity was 140 mV/mm with an input voltage of 6V, they were placed so that they were operating within their linear range. A 6 mm diameter probe was mounted on one end of the balance beam, the probe was concentric to a 10 mm diameter hole in a strain gauged plate (the cover of an *HVLab* Tactile Vibrometer, Appendix A).

Each subject was asked to place the tip of the middle finger over the probe so that the probe was positioned at the centre of the whorl. Subjects applied a push force on the surround of either 1 N, 2 N or 3 N, feedback being provided by an analogue force meter. The probe was held so as not to touch the skin and was then raised until the subject could just feel it. This was considered an acceptable method of determining skin-probe contact; Makous *et al.* (1996) reported that the point at which a subject just felt a contactor touch the skin usually corresponded to the point at which contact was established by means of electrical continuity. For each push force, this procedure was repeated three times. The mean of the two transducer readings for each of the three repeats was recorded as the skin contact height for that push force.

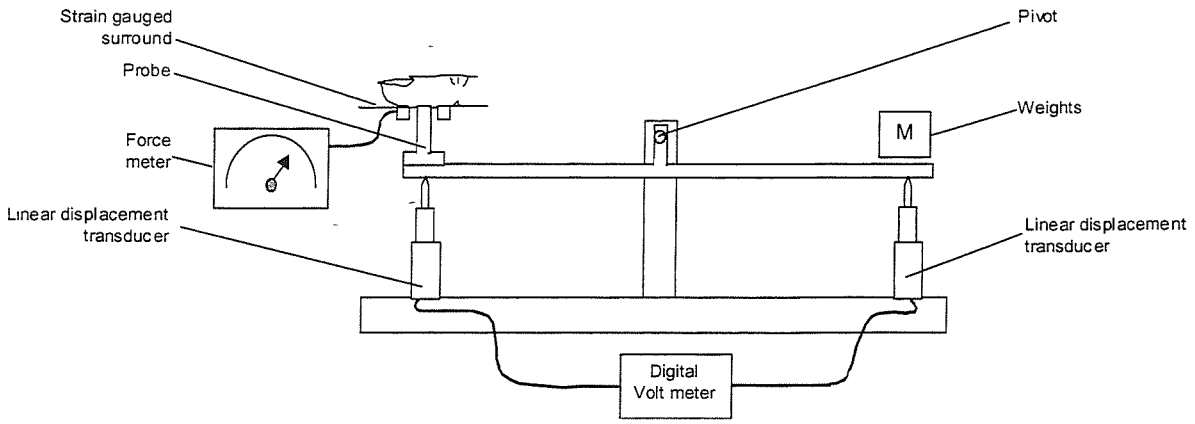


Figure 33 Apparatus used for the measurement of skin indentation whilst controlling probe contact force and finger push force.

Weights of either 50g, 100g, 150g or 200g were then placed on the end of the balance beam opposite to the probe so as to produce probe contact forces of either 0.5 N, 1 N, 1.5 N or 2 N (Figure 33). The probe was raised to the skin contact height and the balance beam gently released. When the displacement readings had settled, the probe height was recorded. Skin indentation was defined as the difference between the skin contact height and the probe height following addition of the masses. The skin indentation for each probe contact force was measured three times for each of three different push forces applied to the surround, 1 N, 2 N and 3 N. Skin indentation was calculated from the mean of the three repeats from the two displacement transducers. The order in which skin indentations were measured was balanced across the study population.

8.2.2.2 Vibrotactile thresholds

Vibrotactile thresholds were measured using an *HVLab* Tactile Vibrometer (Appendix A) for each combination of push force on the surround and probe contact force. Measurements were made at both 31.5 Hz and 125 Hz using the up-and-down method of limits. The rate of change of vibration magnitude was 3 dB/s and the measurement duration for each vibrotactile threshold was 45 seconds. A rest of at least 15 seconds was given between each threshold determination. The order of presentation of threshold tests was balanced across the study population.

8.2.2.3 Analysis

Data have been analysed using parametric statistics and are described by their mean and standard deviation. Vibrotactile thresholds tended to be normally distributed (Shapiro-Wilkes: $p > 0.05$ for 16 measures; $0.01 < p < 0.05$ for 7 measures), the use of parametric statistics was considered justified. General factorial analyses of variance have been used to model the effects of push force and probe contact force on vibrotactile thresholds, controlling for known covariates. The F-ratios and their respective significance levels are given. Linear regression has been used to assess the relationship between skin stiffness, skin indentation and vibrotactile thresholds, regression coefficients and their respective standard differences and significance levels are given. Spearman's correlation coefficients have been used to identify significant relationships between vibrotactile thresholds and covariates.

8.2.3 Results

The means and standard deviations of the skin indentation, the probe height relative to the surround, and the vibrotactile thresholds for each combination of probe contact force and push force are shown in Table 36. Figure 34 shows the skin indentation for each combination of contact conditions and Figure 35 shows the vibrotactile thresholds. Figure 36 shows the relationship between vibrotactile thresholds and skin indentation relative to point of contact.

Table 36 Mean (standard deviation) skin indentation, probe height relative to the surround and vibrotactile thresholds for each combination of push force and probe contact force used in this study (N = 10).

	Push Force	Probe contact force			
		0.5 N	1 N	1.5 N	2 N
Skin indentation (mm)	**1 N**	2.02 (0.35)	3.28 (0.51)	3.79 (0.57)	4.4 (0.74)
	2 N	1.61 (0.21)	2.78 (0.30)	3.59 (0.52)	4.05 (0.58)
	3 N	1.55 (0.58)	2.40 (0.39)	3.33 (0.67)	3.81 (0.71)
Probe height relative to surround (mm)	**1 N**	-0.48 (0.36)	0.78 (0.46	1.30 (0.60)	1.90 (0.78)
	2 N	-1.12 (0.36)	0.19 (0.50)	0.86 (0.70)	1.32 (0.77)
	3 N	-1.36 (0.51)	-0.52 (0.50)	0.42 (0.66)	0.90 (0.73)
Threshold, 31.5Hz (m/s^2)	**1 N**	0.22 (0.15)	0.19 (0.09)	0.18 (0.09)	0.15 (0.07)
	2 N	0.19 (0.10)	0.19 (0.13)	0.17 (0.09)	0.18 (0.11)
	3 N	0.20 (0.14)	0.19 (0.14)	0.19 (0.12)	0.16 (0.10)
Threshold, 125Hz (m/s^2)	**1 N**	0.47 (0.63)	0.46 (0.61)	0.30 (0.30)	0.25 (0.24)
	2 N	0.43 (0.39)	0.44 (0.49)	0.31 (0.23)	0.29 (0.21)
	3 N	0.49 (0.53)	0.46 (0.42)	0.34 (0.23)	0.29 (0.25)

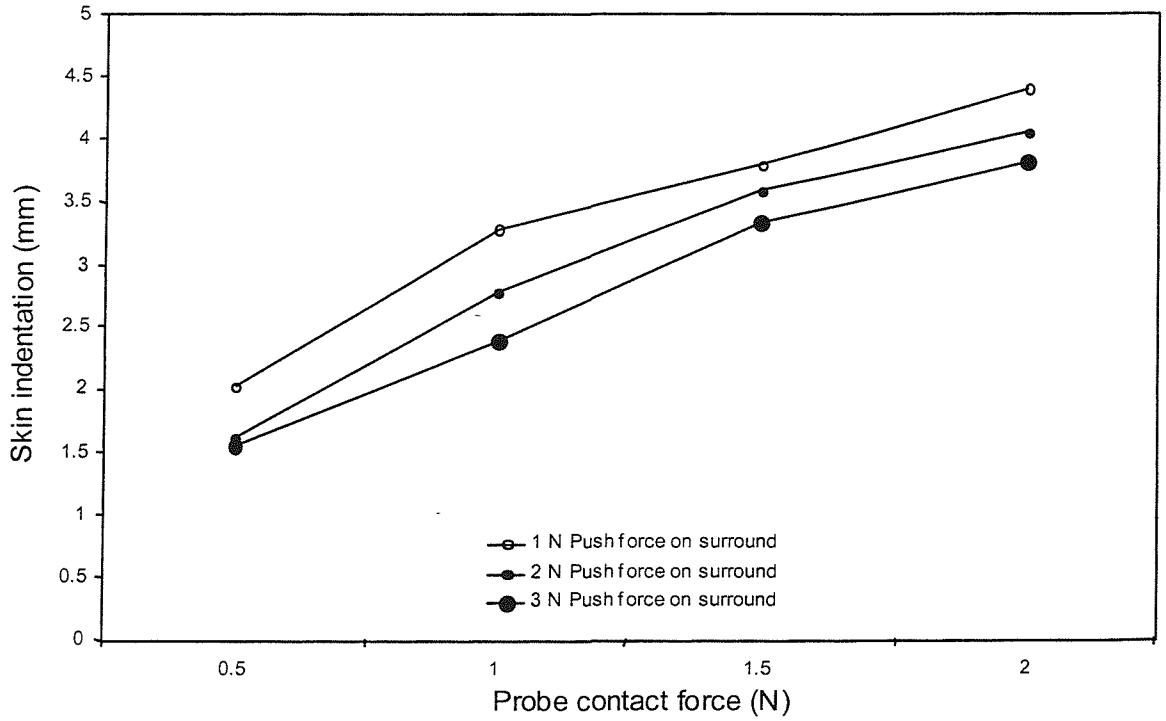


Figure 34 Mean skin indentation as a function of probe contact force for each of the three push forces on the surround.

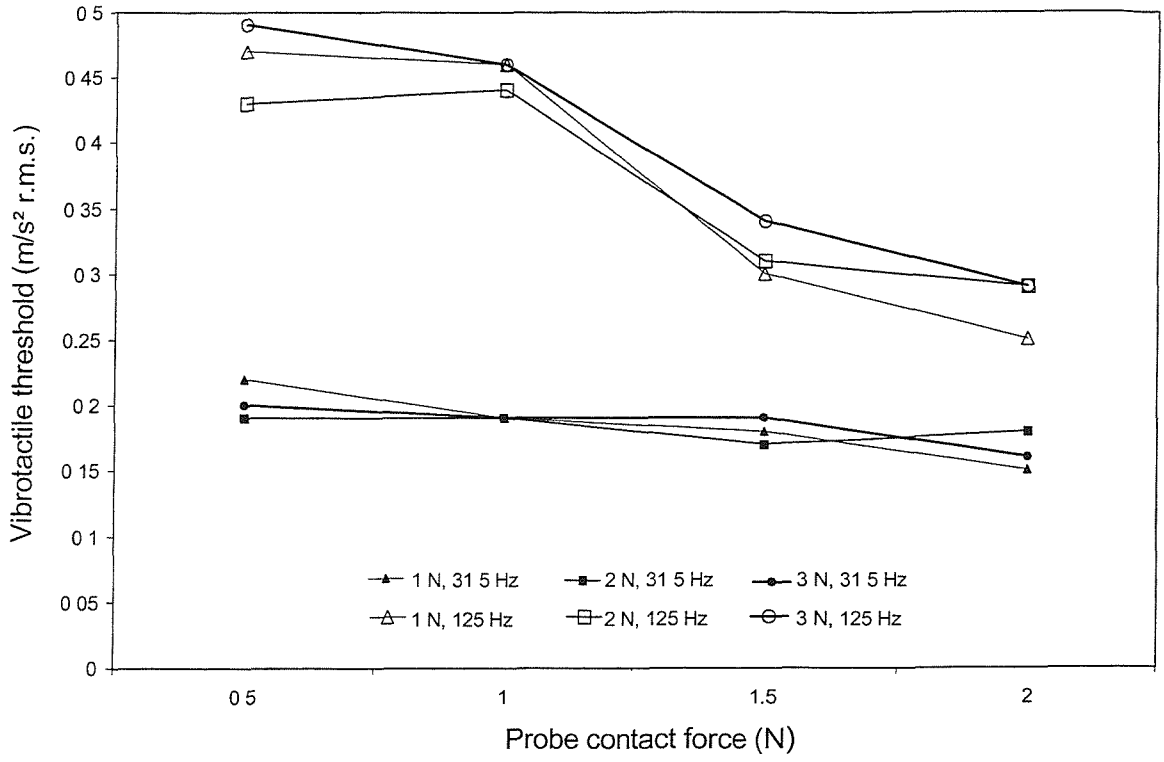


Figure 35 Mean vibrotactile thresholds at 31.5 Hz and 125 Hz as a function of probe contact force, lines are plotted for each push force on the surround.

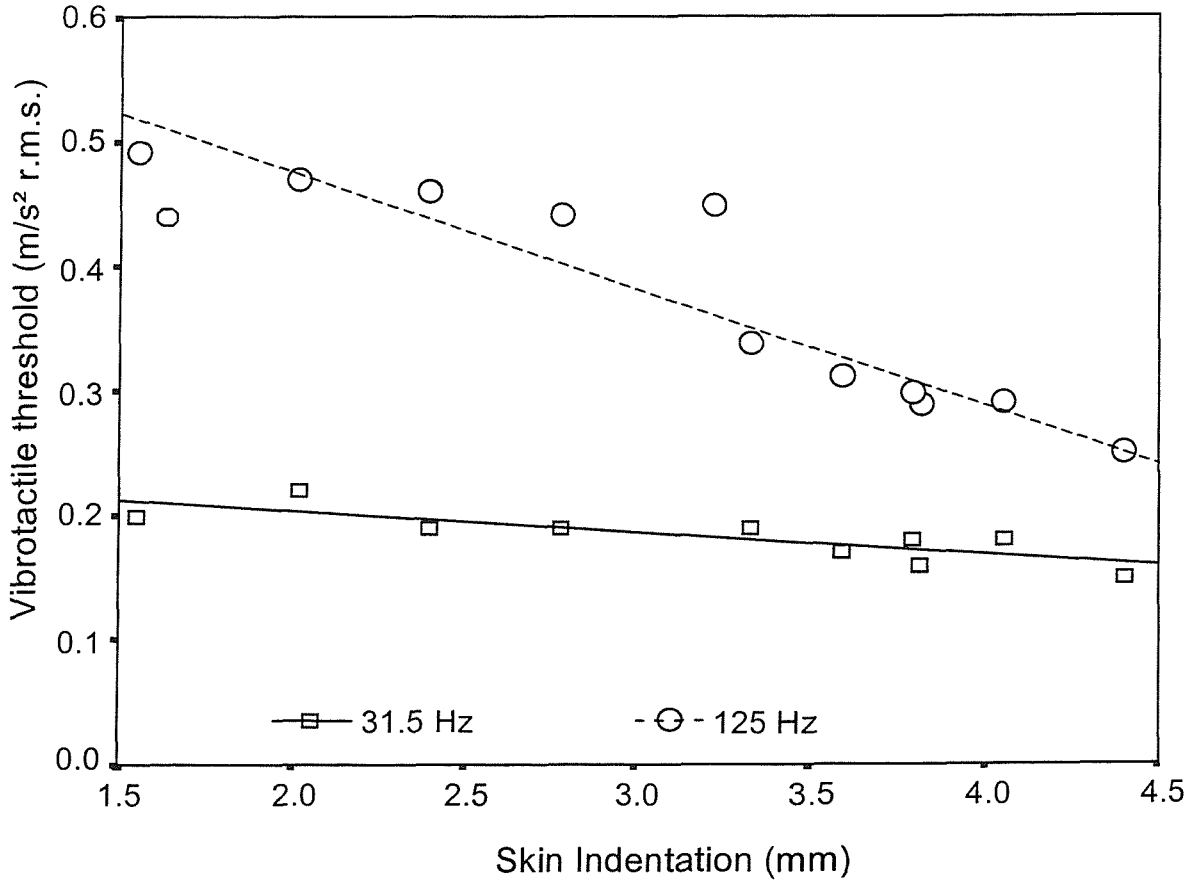


Figure 36 Mean vibrotactile thresholds at 31.5 Hz and 125Hz as a function of skin indentation. Best fit lines are also shown (linear fit).

8.2.3.1 Skin indentation and contact forces

Skin indentation increased with increasing probe contact force and decreased with increasing push force (Figure 34; $F_{Contact(3,112)}$= 112.14, p<0.001; $F_{Push(2,112)}$= 12.69, p<0.001). The effect was greater for the probe contact force than for the push force on a surround. The interaction between probe contact force and push force on a surround was not significant for the range of contact conditions employed in this experiment. The height of the probe relative to the surround exhibited similar variation with contact conditions (Table 36; $F_{Contact(3,112)}$= 91.22, p<0.001; $F_{Push(2,112)}$= 29.92, p<0.001).

8.2.3.2 Vibrotactile thresholds

Increasing age resulted in increasing thresholds for both of the mechanoreceptor populations (125 Hz, ρ=0.3529, p<0.001; 31.5 Hz, ρ=0.1566, p=0.088). Increasing finger skin temperature resulted in decreasing thresholds (125 Hz, ρ=-0.3555, p<0.001; 31.5Hz, ρ=-0.3795, p<0.001). These variables were included in the analyses of variance.

Both the probe contact force and the push force on a surround had significant or marginally significant effects on vibrotactile thresholds measured at 125Hz ($F_{Contact(3,112)}$=6.98, p<0.001; $F_{Push(2,112)}$=2.61, p=0.078; $F_{Regression(2,112)}$=19.71, p<0.001). Only the probe contact force had a marginally significant effect on vibrotactile thresholds measured at 31.5Hz ($F_{Contact(3,112)}$=2.22, p=0.090; $F_{Push(2,112)}$=0.24, p=0.783; $F_{Regression(2,112)}$=4.29, p=0.036). There was no significant effect of the interaction between the probe contact force and the push force.

Vibrotactile thresholds measured at 125 Hz were lowest for a high contact force and a low push force; they were highest with a low probe contact force and a high push force. Probe contact force only appeared to affect thresholds above about 1 N. Thresholds at 31.5 Hz were lowest for a high contact force and a high push force and highest with a low contact force and low push force, although the changes were small and not significant.

Vibrotactile thresholds at both 31.5 Hz and 125 Hz decreased with increasing skin indentation (31.5 Hz, β=-0.40238, SE(β)=0.1973, p=0.0437; 125 Hz β=-.8817, SE(β)=0.2673, p=0.0013). Figure 36 shows the mean thresholds for each condition of probe contact force and push force as a function of the mean skin indentation.

8.2.4 Discussion

8.2.4.1 Contact forces and skin indentation

In this study, increasing the push force on a surround resulted in a decreased skin indentation for a given probe contact force. Increasing the probe contact force increased skin indentation for a given push force on a surround (Figure 34), in agreement with Piercy and Brammer (1998) (see Figure 37).

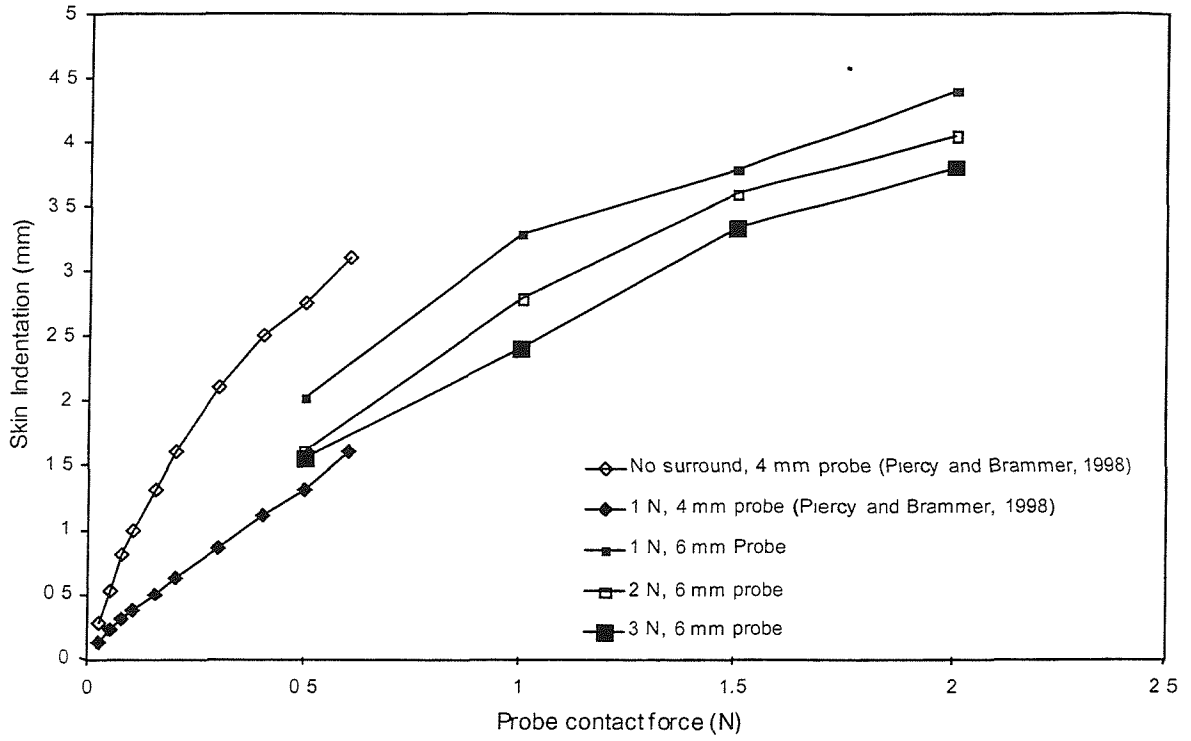


Figure 37 Skin indentation as a function of probe contact force for different push forces on a surround. Data from Piercy and Brammer (1998) have been estimated and plotted.

A relationship between probe contact force and skin indentation would enable probe contact force to be inferred from skin indentation, and vice versa. From Figure 37, it appears that the relationship between probe contact force and skin indentation is approximately linear between about 0.1 N and 2 N when using a surround. The linear relationship may be an indication that Hook's Law (Force = Stiffness x Displacement) is being obeyed for this range of forces and displacements. Calculation of the stiffness of the skin and subcutaneous tissue, therefore, would characterise the relationship between probe contact force and skin indentation. However, there is a discrepancy between data collected here and that reported by Piercy and Brammer (1998). The stiffness in this study population, estimated from Figure 37, was about 0.6 N/m whilst it was about 0.4 N/m for the subjects used by Piercy and Brammer (1998).

The probe used by Piercy and Brammer (1998) was 4 mm in diameter with a surround of 7 mm diameter. The probe used in this work was 6 mm diameter whilst the surround was 10 mm diameter. The stiffness of the tissue is likely to depend on the area of tissue being deformed, the size of the surround and the size of the annulus of skin and tissue between the surround and the probe. These factors most likely explain the difference between the data obtained here and the data obtained by Piercy and Brammer (1998). Further work is required to investigate how the probe size, surround size, and size of annulus affects the stiffness of the skin and subcutaneous tissue.

The slope of the curves in Figure 37 show that for low contact forces, below about 0.4 N, the tissue stiffness measured by Piercy and Brammer (1998) without a surround was lower than that for measurements using a surround. However, at higher probe contact forces the lines appear to have similar slopes, the stiffness for probe forces above 0.4 N was calculated as 0.35 N/m. This would suggest that after initial deformation, the tissue stiffness remains approximately constant, regardless of the presence of a surround. The effect of the probe may not be to increase skin stiffness, as suggested by Piercy and Brammer (1998), but to influence the extent of indentation by changing the boundary conditions.

8.2.4.2 Contact conditions and vibrotactile thresholds

The contact conditions between stimulus and fingertip were shown to affect the measured vibrotactile thresholds. In agreement with previously cited studies, increasing probe contact force or increasing skin indentation resulted in an increased sensitivity of the mechanoreceptors to vibration.

Increasing the push force on a surround had the effect of increasing the Pacinian corpuscle specific thresholds. Maeda *et al.* (1998) also showed this to be the case, although the differences reported were not significant among their study population. Increasing the push force on a surround did not significantly affect the sensitivity of the Meissner's corpuscles.

It has been suggested that use of a surround prevents propagation of surface waves travelling through the skin to stimulate sites other than those being contacted by the stimulus (e.g. Harada and Griffin 1991). The increased push force may act to further reduce the transmission of vibration through the finger tissue to sites other than those being directly stimulated, this would result in the increased thresholds observed with increasing push force. However, increasing the push force on a surround results in decreasing skin indentation for the same probe contact force (Figure 37), and decreasing the skin indentation results in significantly increased thresholds for the Pacinian pathways but not for the Meissner's pathways (Figure 36 and Makous *et al.* 1996). Since skin indentation was changing while the probe contact force remained the same, the skin indentation may be the parameter that contributed most to altering the perception of vibration through the Pacinian pathways.

In this study the effect of increasing push force on a surround resulted in no significant change in the Meissner's corpuscle specific thresholds. The results shown in Figure 36 suggest that there was a trend for Meissner's corpuscle thresholds to increase with decreasing skin indentation, however. For the changes in skin indentation resulting from

changing the push force on the surround (less than 0.8 mm for all probe contact forces), it is unlikely that a significant effect would have been seen here. This agrees with studies that show the Meissner's corpuscle specific thresholds show a small effect of skin indentation (e.g. Lamoré and Keemink 1988).

8.2.4.3 Contact conditions for measuring vibrotactile thresholds

Two criteria may be defined when selecting contact conditions for the measurement of vibrotactile thresholds: i) it should be possible to obtain mechanoreceptor specific vibrotactile thresholds and ii) small variations in the contact conditions should not contribute significantly to variability in vibrotactile thresholds. The first of these criterion allows the identification of dysfunctions specific to a mechanoreceptor pathway; it has been shown that the Pacinian pathways and Meissner's pathways are not always similarly affected by exposure to hand-transmitted vibration (e.g. Brammer *et al.* 1987). The second criterion allows vibrotactile thresholds measured with different equipment to be similar when there are small differences in contact conditions.

8.2.4.3.1 Skin indentation and probe contact force

In the previous section, it was suggested that the skin indentation may be the primary factor influencing vibrotactile thresholds. The skin-stimulus contact conditions might then be chosen to control skin indentation. Controlled contact forces did not produce the same skin indentation in each subject due to variations in the mechanical properties of finger tissue between the subjects used in this study; the difference between the 5th percentile and 95th percentile skin indentation relative to the point of contact of skin and probe was as large as 3mm for one combination of push force and probe contact force (Table 36, 5th percentile $\approx$ mean - 2SD, 95th percentile $\approx$ mean + 2SD). The mechanical properties of the skin also change with age (Kenshalo 1986), a more diverse study sample representative of the worker population amongst whom the measurements are to be made is likely to have increased the variability in skin indentation for a controlled probe contact force. If skin indentation is the primary factor affecting the vibrotactile thresholds, it would be appropriate to consider controlling the skin indentation in preference to controlling the probe contact force.

Figure 36 shows vibrotactile thresholds at 125 Hz and 31.5 Hz plotted as functions of skin indentation. Although the best fit lines plotted show steadily decreasing thresholds with increasing skin indentation, a quadratic function would be a better fit; for skin indentations below about 3 mm, there is a relatively small change in vibrotactile thresholds. A skin indentation in the region 1.5 mm to 3 mm may be appropriate for measuring vibrotactile thresholds.

8.2.4.3.2 Push force on a surround

The two criteria defined for the selection of contact conditions for measurements of vibrotactile thresholds imply the use of a surround should be recommended. Without using a surround and controlling skin indentation between 1.5 mm and 3 mm, small changes in probe contact force can result in large changes in skin indentation (Figure 37). Also, without a surround it is difficult to obtain mechanoreceptor specific thresholds (Harada and Griffin 1991, Maeda and Griffin 1994).

The data in this study are not sufficient to recommend a push force on a surround. However, to allow comparison between data collected using parameters recommended here and data available elsewhere, it might be suggested that use of a push force on the surround of 2 N is continued until further work is performed to determine if there is a more appropriate push force.

Skin indentation can be controlled either by setting the height of the probe relative to a surround or by setting its height relative to the point of contact between probe and skin (Makous *et al.* 1996). With a push force on a surround of 2 N and a probe of 6 mm diameter protruding through a 10 mm diameter surround, probe heights relative to the surround that correspond to skin indentations of between 1.61 mm and 2.78 mm are in the range -1.21 mm to 0.19 mm (Table 36). A probe height relative to the surround between these two limits may be suitable.

8.2.5 Conclusions

Increasing the probe contact force decreased vibrotactile thresholds, increasing the push force on a surround increased Pacinian corpuscle specific thresholds. These findings agree with other studies. The effects of probe size, surround size and the size of the annulus between probe and surround on the stiffness of the skin and subcutaneous tissue require further investigation.

The results show that the skin indentation may be the principal parameter influencing vibrotactile thresholds. Control of skin indentation may be preferable to control of probe contact forces. A skin indentation relative to the point of contact between the probe and the skin of 1.5 mm to 3 mm, with a push force on a surround of 2 N, can result in mechanoreceptor specific thresholds that are independent of small changes in contact conditions. It is concluded that these parameters are suitable for use when monitoring vibrotactile thresholds in workers exposed to hand-transmitted vibration.

CHAPTER 9 THE MEASUREMENT OF VASCULAR AND NEUROLOGICAL FUNCTION IN WORKERS EXPOSED TO HAND-TRANSMITTED VIBRATION

9.1 INTRODUCTION

Four tests have been recommended for monitoring peripheral vascular and neurological function in workers exposed to hand-transmitted vibration: finger systolic blood pressures (FSBPs) and the finger skin temperature (FST) response to cold provocation for monitoring vascular function, and vibrotactile thresholds and thermal thresholds for monitoring neurological function. The aims of this thesis were i) to appraise the measurement methods using predefined criteria (repeatability, sensitivity, specificity, responsiveness and practicality), ii) to improve the measurement methods with respect to the criteria, and iii) to define improved measurement methods for use in monitoring vascular and neurological disorders associated with hand-transmitted vibration. Table 37 provides an overview of the work that has been performed in this thesis to achieve these aims. In Chapter 2, measurement methods and test conditions were defined that were then appraised in Chapter 3. Chapter 4 to Chapter 8 presented studies performed to improve the measurement methods. This chapter revises the measurement methods and the test conditions to include the work performed in this thesis. Recommendations for further work are given.

9.2 GENERAL MEASUREMENT PROCEDURE

In Chapter 2, a controlled environment was suggested. It was shown the measurement methods could be repeatable, sensitive, specific and responsive to vascular and neurological disorders associated with hand-transmitted vibration when performed under these conditions (Chapter 3, Chapter 7).

Following a period of habituation in the controlled environment, measuring the finger skin temperatures (FSTs) and taking corrective action if necessary reduces the influence of FSTs on the neurological measurements (Section 9.3.2). Performing the neurological tests before the vascular tests avoids the acute effects of local cold provocation on the outcome of neurological measurements (Section 2.6.1.1.5).

In Chapter 6 it was found that if both of the vascular tests are performed in the same test session, there can be a carry over effect of cold provocation. The conclusions of the study suggested that the vascular test on which the greater emphasis is to be placed should be performed first. Performing the two vascular tests on different hands may help to minimise potential carry over effects when they are performed in the same session. If the test performed first is to have the greatest emphasis placed on it, the sensitivity of the measurement may be improved by performing it on the hand most affected with VWF.

Table 37 An overview of work performed to appraise and improve measures of vascular and neurological function for monitoring workers exposed to hand-transmitted vibration.

<table>
<tr><th>Finger systolic blood pressures</th><th>Finger skin temperature response to cold provocation</th><th>Vibrotactile thresholds</th><th>Thermal thresholds</th></tr>
<tr><td colspan="4">Definition of appraisal criteria: repeatability, sensitivity, specificity, responsiveness, practicality</td></tr>
<tr><td colspan="4">Definition of measurement methods from the literature (Chapter 2)</td></tr>
<tr><td colspan="4">Appraisal of measurement methods amongst workers exposed to hand-transmitted vibration with and without symptoms of the hand-arm vibration syndrome (Chapter 3)</td></tr>
<tr><td>Application of simultaneous measurements on four test fingers as opposed to one (Chapter 4)</td><td rowspan="3">Interpretation of the FST response to cold provocation (Chapter 7)</td><td rowspan="2">Effects of measurement duration with different skin-stimulus contact conditions (Chapter 8)</td><td></td></tr>
<tr><td>Effects of cold provocation of a test finger on a reference finger (Chapter 5)</td><td></td></tr>
<tr><td>Effects of order or presentation of thermal stimuli and of recovery between successive thermal stimuli (Chapter 5)</td><td rowspan="2">Relationship between skin indentation, contact forces and vibrotactile thresholds (Chapter 8)</td><td></td></tr>
<tr><td colspan="2">Repeatability amongst workers exposed to hand-transmitted vibration with and without VWF (Chapter 6)</td><td></td></tr>
<tr><td colspan="4">Definition of improved measurement methods for monitoring vascular and neurological function in workers exposed to hand-transmitted vibration (Chapter 9 and Appendix F)</td></tr>
</table>

9.3 TEST CONDITIONS

9.3.1 Environmental conditions

The environment in which measurements are performed affects the results of both vascular and neurological tests; controlling room temperature and noise levels can minimise these effects. In Section 2.6.1, Chapter 2, several suggestions were made: i) measurements should be performed in a room of temperature 22°C ± 2°C, ii) the ambient noise level should be low, iii) sudden and loud noises should be avoided, iv) hearing protection should be worn when conducting thermal thresholds tests and vibrotactile threshold tests, v) subjects should wear light indoor clothing and vi) subjects should be habituated to the test environment for 15 minutes. The experimental studies reported here met these recommendations.

The results shown in Sections 4.2.3, 4.3.3, 5.3.3, 8.1.3 show that measurements of both vascular and neurological function were not significantly influenced by the internal temperature when controlled within the suggested range. Fifteen minutes habituation was sufficient to avoid the influence of external temperatures on results in these studies (Sections 4.2.3, 4.3.3, 5.3.3). When appraising the vascular and neurological tests using the criteria of sensitivity, specificity and responsiveness (Chapter 3, Chapter 7), or the

criterion of repeatability (Section 4.3, Chapter 6), the measurement methods performed similarly to, or better than, measurement methods reported in the literature. It is concluded that the suggested environmental conditions were suitable for monitoring workers exposed to hand-transmitted vibration, they were also practical to achieve.

This thesis has not considered effects of air flow. Air flow can influence FSTs (Bovenzi 1987) and may need to be controlled. The test environments used here were controlled so air flow was not noticeable (less than about 0.2 ms^{-1}). This might be recommended until further work is performed to determine maximum permissible air flow.

9.3.2 Finger skin temperature

Finger skin temperatures influence measurements of vibrotactile thresholds. The recommendation made in Section 2.6.1.1.6 was that FSTs should be considered as having an affect on vibrotactile thresholds below 26°C, and that vibrotactile thresholds measured on fingers with an FST below 22°C were unlikely to be representative of the true threshold.

When making measurements on healthy subjects here, the FSTs were all above 26°C. In Section 8.1.3, it was shown that FSTs above 30°C did not significantly influence vibrotactile thresholds. However, in Section 8.2.3.2 it was shown that the FSTs did significantly influence vibrotactile thresholds; the mean FST was 31.9°C with a standard deviation of 3.2°C. This might suggest that even when above 26°C, the FSTs can still influence vibrotactile thresholds. This agrees with the results reported by Green (1977), small effects being observed above 26°C. The effect of FSTs above 26°C on vibrotactile thresholds is small when compared with inter-subject variability; they may not need to be considered for monitoring workers exposed to hand-transmitted vibration.

Obtaining FSTs above 26°C can be difficult in some subjects. In Section 3.3.1.2 the minimum FST measured on workers exposed to hand-transmitted vibration with symptoms of HAVS was reported as 20°C, even after habituation in the test environment for 15 minutes. Artificial warming of the hands could have been performed, e.g. by running them under hot water or providing a heat source. Following artificial warming of the hands, however, a progressive reduction in temperature has been observed by this author as the hands cool to their original temperature. Since there appears to be a small influence of FSTs even above 26°C, it might be concluded that artificial warming is not advantageous; it may result in added intra-subject variability during the course of measurements while the hands cool. Warming of the hands by natural means (e.g. using a warmer test environment or a longer habituation period) avoids this possibility.

Effects of starting FSTs on thermal thresholds have been shown in the literature but have not been assessed here, they are not believed to affect results when the method of limits is used with a reference temperature between 30°C and 34°C (Section 2.6.1.1.6). Any effects of starting FSTs on the vascular tests also remain unknown. It was shown in Chapter 7, however, that when the response of FSTs to cold provocation were interpreted using calculated parameters, the parameters tended to perform better against the criteria of sensitivity and specificity when they incorporated some measure of the starting FST. Reporting the FST with test results will allow measurements to be interpreted with respect to the influence of FST where this is shown to be important.

9.3.3 Exclusions

Several factors have been shown to have acute effects on vascular and neurological function. Alcohol consumption, nicotine consumption and vibration exposure appear to be the principal factors having acute effects (Sections, 2.6.8, 2.6.9). Some medications may also influence results (Section 2.6.7). The acute effects of these factors can normally be avoided by excluding them for a period of time prior to measurements. Caffeine consumption has been hypothesised as having an acute effect on vascular and neurological function although studies reported in the literature are not conclusive (Section 2.6.10). It is considered reasonable to suggest the exclusion of caffeine consumption prior to testing. Food intake does not appear to influence vascular or neurological tests (Section 2.6.12).

The duration prior to measurements for which the exclusions are necessary to avoid their effects could not be surmised accurately from the literature. In this work, nicotine consumption was excluded for a minimum of one hour prior to measurements, caffeine for 4 hours and alcohol for 12 hours. This was considered practical and may be reasonable to suggest.

Acute effects of vibration exposure on vascular function are magnitude, duration and frequency dependent (Bovenzi and Griffin 1997, Bovenzi *et al.* 1998). In their experiments, finger blood flow had not always returned to its resting state after 45 minutes recovery from vibration exposure. The duration of exclusion of vibration exposure prior to vascular tests cannot be stated explicitly although 2 hours may be considered reasonable to avoid potential effects. Prior to neurological tests, it has generally been shown that any temporary threshold shifts have recovered within 30 minutes of the end of exposure (Section 2.6.2). This may be a more suitable exclusion period to avoid acute effects of vibration exposure when performing neurological measurements only.

9.4 TESTS OF NEUROLOGICAL FUNCTION

9.4.1 Subject conditions

In Section 2.8 a measurement procedure was suggested that involved control over subject posture: subjects should be seated comfortably for neurological tests, the forearm and wrist should be supported and the wrist should be held straight to prevent compression of the ulnar or median nerve (Section 2.4.7 and 2.5.5). Implementation of these controls was practical to achieve in experimental work reported here and they remain as recommendations. It was also recommended subjects should practice neurological tests prior to measurements to reduce learning effects (Section 2.5.2.6). The American Diabetes Association (1992) suggests that all subjects should be made familiar with the testing procedures prior to making psychophysical measurements.

9.4.2 Measurement location

It was suggested in Sections 2.4.6 and 2.5.4 that measurements should be made on one finger innervated with the ulnar nerve and one finger innervated with the median nerve to distinguish nerve compression disorders from the more diffuse vibration-induced neuropathy. It was also suggested measurements were made on both hands because different effects of vibration were observed on the dominant and non-dominant hands. These suggestions are supported by the results reported in Section 3.3.3.1; it was shown that making measurements at the four sites could help to increase the sensitivity and specificity of the test to neurological disorders arising from exposure to hand-transmitted vibration.

Measurements made at the centre of the whorl on the palmar surface of the distal phalanx of the test finger were sensitive, specific and responsive to numbness (Section 3.3) and are repeatable (Maeda and Griffin 1994, Ruffell and Griffin 1995). It is concluded that measurement at the finger tips is useful for detecting neurological disorders arising from exposure to hand-transmitted vibration.

9.4.3 Skin-stimulus interface

The test finger must rest on, or have rested upon it, a contactor by which the thermal or vibration stimulus is presented. The conditions of contact between the skin and the stimulus should be controlled. In Sections 2.4.3, 2.4.4 and 2.5.3, conditions of contact were suggested that had been shown to be repeatable. When measurements of vibrotactile thresholds and thermal thresholds were made amongst a group of dockyard workers using these contact conditions, they were shown to be sensitive, specific and responsive to neurological disorders resulting from exposure to hand-transmitted vibration (Section 3.3).

The contact area between stimulus and skin is a cause of variability in measurements of thermal thresholds (Section 2.5.3.1). Effects of changing the stimulus contact area on the finger tips are not currently known. In this work, a contactor that encompassed the entire finger pad was used. Thermal control of smaller contact areas may be more practical to achieve. Further work could identify if smaller contact areas can result in an improvement in the test using the criteria of repeatability, sensitivity, specificity and responsiveness.

To improve the practicality of the vibrotactile threshold test, it was suggested that skin indentation might be controlled instead of probe contact force (Section 2.4.4). In Section 8.2, a study was reported that investigated the relationship between contact forces and skin indentation, and the effects of skin indentation on vibrotactile thresholds. It was found that it may be preferable to control skin indentation rather than probe contact force. A skin indentation was found that gave similar results to the probe contact forces used to appraise the measurement method in Chapter 3. Implementation of controlled skin indentation in preference to probe contact force would improve the practicality of the measurements. Further work is required to determine if controlling skin indentation gives repeatable results that are sensitive, specific and responsive to neurological dysfunction.

Contact conditions for the interface between a stimulus and the skin for measurements of thermal thresholds and vibrotactile thresholds used in this thesis are given in Table 38. It is concluded that these contact conditions can be useful when monitoring workers exposed to hand-transmitted vibration.

9.4.4 Thermal threshold test

When the hot and cold thresholds have been assessed independently, the hot and cold receptors have been shown to be differentially affected by exposure to hand-transmitted vibration (Section 3.3, Section 2.5.2.5). The neutral zone (i.e. the difference between the hot and the cold threshold) has also been reported to be a useful indicator of peripheral neurological function (e.g. Lundström *et al.* 1998, McGeoch *et al* 1992). Use of both the hot and the cold thresholds was shown here to improve the sensitivity and specificity of the measurement to numbness compared to when using one or the other (Section 3.3.3). It is concluded that the neutral zone may be useful but that assessing the hot and the cold thresholds independently can be beneficial.

The data in Table E4, Appendix E show that results obtained using different psychophysical methods may not be comparable. To obtain the hot and cold thresholds independently, the method of limits was used here for reasons discussed in Section 2.5.2. The temperature of a contactor was increased (hot thresholds) or decreased (cold thresholds) from a reference temperature until the subject perceived a change in temperature. The subject then made a judgement and the contactor returned back to the reference temperature. This cycle was repeated several times.

The parameters of the psychophysical test that were suggested in Section 2.5.2 and implemented in this thesis are summarised in Table 38. Using these parameters, thermal thresholds were shown to be sensitive, specific and responsive to numbness, even though three judgements were performed instead of the suggested six (Section 3.3). The method has also been shown to be repeatable (Ruffell and Griffin 1995). The measurement can, however, be time consuming to perform at four measurement sites. Care should be taken to avoid fatigue effects (e.g. Schady *et al.* 1991).

The parameters given in Table 38 are concluded to be suitable for measuring thermal thresholds using the method of limits to detect neurological disorders in workers exposed to hand-transmitted vibration. Further work is required to investigate reasons for differences between thermal thresholds obtained using different psychophysical methods and to investigate effects of contact area between the stimulus and the skin.

Table 38 Parameters for the measurement of thermal thresholds and vibrotactile thresholds used in this thesis.

	Parameter	Value
Thermal thresholds	Push force	2 N
	Contactor area	Larger than the finger tip
	Contactor surface	Smooth and planar
	Psychophysical method	Method of limits
	Reference temperature	30°C
	Rate of change of temperature	1°C/s
	Number of judgements	Minimum of six
Vibrotactile thresholds	Push force on surround	2 N
	Contactor shape	Cylindrical, 6 mm diameter
	Contactor surface	Smooth and planar
	Surround surface	Smooth and circular
	Gap	2 mm
	Skin indentation †	2 mm
	Psychophysical method	Up-and-down method of limits
	Frequency	31.5 Hz; 125 Hz
	Rate of change of stimulus	3 dB/s
	Measurement duration	30 - 45 seconds
	Number of reversals	Minimum of six

† Skin indentation OR contactor force can be controlled. If probe contact force is to be controlled, a force of 1 N ± 0.5 N can give similar results to the stated skin indentation.

9.4.5 Vibrotactile threshold test

It was recommended that vibrotactile thresholds were measured at 31.5 Hz and at 125 Hz using a fixed frequency, variable amplitude, sinusoidal vibration (Section 2.4.2). This could provide information about the function of both the Meissner's and Pacinian afferent pathways (Section 2.4.2.2.5). Measuring vibrotactile thresholds at both frequencies was shown to be beneficial in increasing the sensitivity and specificity of the test to neurological disorders (Section 3.3.3).

The up-and-down method of limits was used here due to its simplicity of implementation and short duration of measurements (Section 2.4.2). The vibration magnitude was increased from zero until a subject perceived the vibration, and responded. The vibration magnitude was then decreased until the subject no longer perceived the vibration, and responded again and the stimulus magnitude began to rise. This cycle was repeated several times. Using this psychophysical method with the parameters suggested in Section 2.4.2 and summarised in Table 38, the measurement has been shown to be repeatable (Maeda and Griffin 1994) and sensitive, specific and responsive to neurological disorders resulting from exposure to hand-transmitted vibration (Section 3.3).

Measurements of vibrotactile thresholds can be made with either a fixed skin indentation or a controlled probe contact force (Section 2.4.4, 9.4.3). In Section 8.2 it was shown that measurements using a fixed skin indentation may be preferable to measurements using a controlled probe contact force. It was hypothesised, however, that vibrotactile thresholds measured using a fixed skin indentation would be susceptible to changes in the probe contact force over the duration of a measurement due to mechanical variations in the skin-stimulus interface over time (Section 8.1.1). It was demonstrated in Section 8.1 that there is a duration effect when measuring vibrotactile thresholds elicited from the Meissner's corpuscles, but not when measuring those elicited from the Pacinian corpuscles. The duration effect occurred both when a controlled probe contact force and when a controlled skin indentation were used. This was tentatively concluded to due to the edge receptive properties of the Meissner's corpuscles being influenced by the push force on a surround (Section 8.1.4). Minimising the length of each measurement will minimise this duration effect. About 30 seconds may be suitable for healthy subjects, although longer (up to a minute) may be required for thresholds to converge on their true value for subjects with neurological dysfunction. In the studies reported here, most subjects gave reliable results, i.e. more than six cycles were completed and the peaks and the troughs varied by less than 10 dB within themselves (ISO-CD13901), when a 45 second duration was used.

The results shown in this thesis suggest that the parameters given in Table 38 are suitable for monitoring vibrotactile function in workers exposed to hand-transmitted vibration; they satisfy the criteria defined in Section 1.2. Further to the methods for performing measurements suggested in Section 2.8, limiting the duration of vibrotactile threshold measurements will help to minimise the duration effects observed when obtaining Meissner's corpuscle specific thresholds.

9.5 TESTS OF VASCULAR FUNCTION

9.5.1 Subject conditions

In Sections 2.2.6 and 2.3.6, it was recommended that to avoid influencing circulatory function during FSBP measurements and during the measurement of the FST response to cold provocation, subjects should be sitting or lying comfortably and excessive movement should be avoided. The hands should be supported at the level of the heart to reduce hydrostatic pressure influences on blood flow in the hands. The wrists should be held straight to prevent interrupting circulation due to compression of the blood vessels. Support for the hands should avoid thermally influencing the skin whenever possible (Section 2.3.3.6). When these recommendations were implemented in this thesis, measurements of FSBPs were shown to be repeatable among healthy subjects (Section 4.3, Chapter 6) and sensitive, specific and responsive to vascular disorders in a group of dockyard workers (Section 3.2).

The measurement of the FST response to cold provocation did not satisfy the criteria of sensitivity, specificity and responsiveness when appraised amongst dockyard workers in Section 3.2, even though the repeatability of this test had been shown to be acceptable by others (e.g. Carnicelli *et al.* 1992, Hayward *et al.* 1986). Further work demonstrated that the low sensitivity, specificity and responsiveness was most likely due to the method of interpreting the results (Chapter 7) and not the test conditions.

These recommendations for controlling subject posture and activity during vascular tests are considered practical to achieve. Both of the vascular tests can be repeatable when implementing these conditions (Chapter 6).

9.5.2 Finger systolic blood pressures

The FSBPs reported in Chapter 3 were measured according to the method defined by Nielsen and Lassen (1977) and refined by Nielsen (1980) (Section 2.2.2). Using this method, the results reported here were similar to those obtained by other authors; the measurements were repeatable amongst healthy subjects (Section 4.3, Chapter 6) and sensitive, specific and responsive to VWF (Section 3.2).

Briefly, the method involves simultaneous measurements of FSBP on a test and a reference finger. Pressure cuffs are placed around the medial phalanges of the fingers (proximal phalanx of the thumb and little fingers) and a mercury-in-elastic strain gauge is placed around the finger tip. The pressure cuffs are inflated to suprasystolic pressure while water at a controlled temperature perfuses the cuff on the test finger for a period of time. The pressure in the cuffs is then reduced and the return of blood flow is detected by the strain gauge. The test parameters used in Chapter 3 are given in Table 40.

When the method of measuring FSBPs was appraised using the criteria of sensitivity, specificity and responsiveness, it was found that the measurement performed better when performed on a finger affected with VWF than on an unaffected finger on a hand affected with VWF (Section 3.2). Measurements on more than one test finger would improve the sensitivity, specificity and responsiveness of the test. However, this might be considered impractical when measuring only one test finger at a time as the measurement duration can become prohibitively lengthy. The simultaneous measurement of FSBPs on multiple test fingers was therefore suggested.

Two experiments were performed to investigate making simultaneous measurements on four test fingers. The first experiment showed that measurements made with thermal provocation of four test fingers could give similar results to measurements made on one test finger (Section 4.2). However, the inter-subject variability was increased when measuring on four test fingers compared to when measuring on one finger. The repeatability of the two methods was then investigated (Section 4.3). The results demonstrated that measurements on four test fingers were similarly repeatable to measurements on one test finger; the criterion of repeatability had not been compromised. The repeatability was further demonstrated amongst healthy workers and the FSBPs were shown to be significantly different between subjects with VWF and subjects without VWF in Chapter 6.

Simultaneous measurements on four test fingers may be considered preferable to measurements on one test finger; complete appraisal of simultaneous measurements of FSBPs on four test fingers using the criteria of sensitivity, specificity and responsiveness is still required. Where it is not possible to make simultaneous measurements on more than one test finger, suggestions for the choice of measurement locations are given in Table 39 for both healthy subjects and for subjects reporting VWF.

Table 39 Suggested sites for the measurement of FSBPs. It is preferable to measure at as many as locations as possible.

	Healthy subjects	Subjects reporting VWF
Test sites		
Least preferable	Middle finger, dominant hand	The finger most affected with blanching, not including the thumb
	Middle and ring fingers, dominant hand	The two most affected fingers on the most affected hand, not including the thumb
	Index, middle and ring fingers, dominant hand	The three most affected fingers on the most affected hand, not including the thumb
	All fingers of the dominant hand, not including the thumb	All fingers of the most affected hand, not including the thumb
Most preferable	All fingers of both hands, not including the thumbs	All fingers, both hands not including the thumbs
Reference sites	Thumb of test hand	Thumb of test hand
		An unaffected finger on the test hand (only if the thumb is missing).

When measuring FSBPs with thermal provocation, the use of a reference measurement allows interpretation of results with respect to whole body changes in systolic blood pressures (Section 2.2.7.1). In Section 2.2.5.1 it was suggested that the reference measurement might be influenced by cold provocation of an adjacent test finger. A study was performed to investigate effects of cold provocation of a test finger on the reference finger systolic blood pressures (Section 5.2). The conclusions of this study were that effects of cold provocation of a test finger on reference FSBPs were small, but that different reference locations gave different results. The thumb was suggested as being a suitable reference measurement location (Section 5.2.5).

The increase in inter-subject variability found when making measurements on four test fingers compared to when making measurements on one test finger was hypothesised to be due to differing effects on central sympathetic activity between subjects (Section 4.2.4). Other effects of the measurement on central sympathetic activity were also hypothesised, namely effects of the order of presentation of thermal provocations and effects of the time interval between successive thermal provocations. It was shown that amongst healthy office workers, the order of presenting measurements had little effect on FSBPs but that providing a period of recovery between measurements increased inter-subject variability (Section 5.3). It was recommended that to minimise this inter-subject variability, measurements should be performed in quick succession. Although the order of making measurements did not significantly affect the FSBPs, to improve the practicality of measurements of FSBPs it was suggested in Section 2.2.3.4.1 that measurements at 10°C need not be made if a measurement at 15°C gave an expected pathologic result. This implies that the thermal provocation is applied at progressively lower temperatures.

Table 40 Test parameters for the measurement of FSBPs and the FST response to cold provocation used in this thesis.

	Parameter	Value
Rewarming test	Water temperature	15°C
	Settling period	2 minutes
	Immersion period	5 minutes
	Recovery period	15 minutes
	Hand conditions during immersion	Dry, non-ischaemic
Finger systolic blood pressure test	Cuff size	Width 24 mm
	Cuff properties	Thin walled, contiguous with surface of finger
	Cuff location	Medial phalanx (proximal phalanx of the thumb and little finger)
	Transducer location	Distal phalanx
	Transducer	Strain gauge
	Cooling period	5 minutes
	Cuff deflation rate	< 3 mmHg/s
	Water temperature	30°C, 15°C, 10°C

Further to the test procedure presented in Section 2.8, minimising any recovery between measurements can reduce inter-subject variability. Performing the measurement at progressively lower temperatures improves the practicality of the test. The measurement of FSBPs using the method defined here has been shown to satisfy the criteria defined in Section 1.2. Simultaneous measurements on multiple test fingers using the thumb as a reference is considered beneficial. It is concluded that the method is suitable for monitoring vascular function in workers exposed to hand-transmitted vibration.

9.5.3 Finger skin temperature response to cold provocation

In this thesis, measurements of the FST response to cold provocation have been performed on one hand only. Both hands could have been tested simultaneously. Although this would have resulted in the loss of useful reference finger information (Section 2.3.5), cooling two hands may also be beneficial in detecting VWF (Gautherie *et al.* 1997). It is unknown if the results reported here will be similar to measurements made on both hands because the increased area of cold stimulus may alter central sympathetic activity (e.g. Sections 4.1, 6.1).

Measurements of FSTs in the work reported here were made on the palmar surface of the hand. Measurements on the dorsal surface and the palmar surface of the fingers have been shown to exhibit a similar response to cold provocation (Dupuis 1987); results obtained here are likely to be applicable to measurements made on the dorsal surface.

Measurements made on the palmar surface of the hand were shown to be sensitive and specific to VWF (Chapter 7) so measurements made on the dorsal surface may not be necessary unless the condition of the hand makes it so (e.g. in cases of Dupuytrens contracture).

Some authors have recommended infra-red thermal imaging techniques to obtain a thermal scan of the hand (e.g. von Bierbrauer *et al.* 1998). Measurements in this thesis show that the FST response to cold provocation can be repeatable amongst healthy workers (Chapter 6), and sensitive and specific to VWF (Chapter 7), when point transducers (thermocouples) are used. The added complexity and cost of thermal imaging using infra-red techniques (Section 2.3.2) may make measurements less practical to perform and could not be justified here.

The need for recording of FSTs throughout the test, as suggested in Section 2.3.4, is dependent on the method used to interpret the rewarming curves. In Chapter 7 it was shown that different methods of interpreting the results of the test requires different data. If measurements made at single time points are used for interpretation, then data need not be recorded continuously. However, the results reported in Chapter 7 are not conclusive and further work is required to demonstrate the repeatability, sensitivity and specificity of the suggested parameters. It is currently recommended, therefore, that it is still useful to record the FSTs continuously during the test, commencing at the start of the settling period and finishing at the end of the recovery period.

In Section 2.3 the various methods for measuring the FST response to cold provocation were discussed and in Section 2.8 a method was proposed for use. Point transducers, positioned at locations shown in Figure 5, Section 2.3.5, are allowed to settle for two minutes prior to immersing a covered hand to the level of the wrist on both the palmar and the dorsal surfaces into water controlled at 15°C ± 1°C for a period of five minutes. At the end of this immersion period, the hand is removed from the water and the waterproof covering is removed. The hands are then allowed to recover for fifteen minutes. Using this method, which is summarised in Table 40, the repeatability of measurements was shown to be acceptable for healthy subjects (Chapter 6) and the measurement was shown to be sensitive and specific to VWF (Chapter 7). It is concluded the measurement method defined in Section 2.8 is suitable for use when monitoring vascular function in workers exposed to hand-transmitted vibration.

9.6 INTERPRETATION OF RESULTS

9.6.1 Confounding factors

Various factors that cannot always be controlled have been identified as influencing results of vascular or neurological tests, or both. These factors are age, gender, disease, injury and the seasonal environment (Section 2.6). Although these factors cannot always be controlled, they can be taken into account when interpreting results.

Age and gender specific normative data are required to allow interpretation of results with respect to these factors. The data obtained in this thesis are specific to males but they are not age specific. Larger groups of healthy subjects of differing ages need testing to obtain age related normative data. For female specific normative data, it may also be necessary to identify the phase of the menstrual cycle in which measurements are made, this has been shown to influence vibrotactile thresholds (Espritt *et al.* 1997). Effects of the menstrual cycle on thermal thresholds and the vascular response to cold are not currently known, further work is required.

The influence of disease, injury and long term medication intake on test results was discussed in Section 2.6.3. Of particular interest when assessing the vascular response to cold provocation is primary Raynaud's phenomenon, or secondary Raynaud's phenomenon with a cause other than vibration exposure. A questionnaire was used to determine the occurrence of disease, injury and medication intake in individuals in the studies reported here (Appendix B). This was found to be an appropriate method of determining the occurrence of these factors although medical examinations may still be required in some instances.

Time of day does not influence neurological tests, it is unknown if time of day affects the vascular response to cold provocation (Section 2.6.11). In this work, repeated measurements have been performed at the same time of day. This may not have been necessary, further work is required to determine if there are diurnal variations in vascular measurements. When making measurements for monitoring vascular and neurological function amongst workers exposed to hand-transmitted vibration, it is beneficial to avoid acute effects of vibration exposure that might occur during the work shift (Section 2.6.2).

Seasonal conditions have been shown to influence test results (Section 2.6.1.1.3). Further work is required to fully investigate this phenomenon and to determine if the season in which measurements are performed should be considered when monitoring workers exposed to hand-transmitted vibration.

9.6.2 Interpretation of the finger skin temperature response to cold provocation

The sensitivity and specificity of the response of FSTs to cold provocation was shown in Chapter 7 to be greatly influenced by the method of interpreting the results. Three parameters were shown to have greater sensitivity and specificity to VWF than the others that were calculated: i) the area above the curve, ii) the percentage of initial temperature at 5 minutes of recovery and iii) the maximum recovery temperature. These parameters might be suitable for interpreting the response of FSTs to cold provocation, the advantages and disadvantages of each were discussed in Section 7.4. Whichever parameter is used, it seems that interpreting the results with respect to the state of initial FST measured during the settling period of the test is beneficial.

In Section 2.3.4 it was stated that the entire rewarming curve should remain of interest to an investigator but that parameters of the rewarming curve could be used to highlight abnormalities of the response of FSTs to cold provocation, and for statistical analysis. Further work is required to determine the repeatability of the parameters found to exhibit the greatest sensitivity, specificity and responsiveness. Their sensitivity, specificity and responsiveness to VWF amongst a larger group of subjects should be determined before they are used in place of the entire rewarming curve.

9.6.3 Percentage FSBPs

In Section 2.2.7.1 it was suggested that several different calculations could be performed to correct for changes in systemic systolic blood pressure when measuring FSBPs. The most commonly used index, the percentage FSBP, was used in studies reported here as this index had previously been shown to have a high sensitivity and specificity to VWF (Table 2, Section 2.2.8). The calculation of percentage FSBPs was shown here to decrease unwanted intra-subject variability in the measurement (Section 3.2.3.1). The percentage FSBPs were calculated using the formula:

$$\%\text{FSBP} = \frac{FSBP_{TEST,t°C}}{FSBP_{TEST,30°C} - \left(FSBP_{REF,30°C} - FSBP_{REF,t°C}\right)}$$

Where *%FSBP* is the percentage FSBP; $FSBP_{TEST,t°C}$ is the FSBP of the test finger after thermal provocation at 15°C or 10°C; $FSBP_{TEST,\ 30°C}$ is the FSBP measured on the test digit after thermal provocation at 30°C; $FSBP_{REF,\ 30°C}$ is the FSBP measured on the reference digit (e.g. thumb) after thermal provocation of the test digit at 30°C; $FSBP_{REF,t°C}$ is the FSBP measured on the reference digit after thermal provocation of the test digit at 15°C or 10°C. Care should be taken when interpreting results using this formula if blanching is reported on the reference finger (Section 2.2.7.1).

9.6.4 Repeatability

When interpreting test results for monitoring vascular and neurological function in workers exposed to hand-transmitted vibration, it is necessary for the tests to be repeatable so that measurements made over time indicate changes in vascular and neurological function and not normal intra-subject variability. The methods of measuring vibrotactile thresholds and thermal thresholds used in this thesis have both been shown to be repeatable (Maeda and Griffin 1994, Ruffell and Griffin 1995). It is concluded that changes in neurological thresholds over time are likely to be due to changes in neurological function.

The vascular tests were previously considered to be repeatable (Section 6.1.1) but it was shown in Chapter 6 that neither of the tests is repeatable amongst workers reporting VWF. Although this lack of repeatability might cause concern, the tests were considered repeatable amongst healthy workers. It is concluded that when interpreting results of vascular tests, a positive test results can be indicative of the presence of VWF whilst a negative test result, unless repeated several times, cannot be assumed to be indicative of the absence of VWF. Where a positive test result is expected but not observed, retests may be necessary.

9.6.5 Sensitivity and specificity

Normal limits can be used to define a threshold value beyond which test results are considered pathological. Normative data are limited in application to the measurement methods and conditions with which they were defined. They should be obtained from a suitably matched group of healthy subjects. The choice of normal limits also has some influence over the interpretation of results.

Normal limits can be defined as the mean of normal data plus or minus a multiple of the standard deviation (e.g. Sections 3.2.2.1.1.2 and 3.2.2.2.1.2). When calculating the normal limit in this way, the true negative rate (i.e. specificity) is set. For example, if the mean plus or minus two standard deviations is used then about 95% of normal subjects will have results between these limits. An alternative method of defining the normal limits is to use receiver operating characteristics (ROCs, e.g. Chapter 7). Using this method, both the sensitivity and the specificity are known for a range of normal limits. This allows an investigator to choose a threshold value for pathological results so as to maximise the sensitivity or the specificity.

Since results are to be used to detect a vascular or neurological pathology, it is important to know the probability of an incorrect result. Therefore, it is suggested that the sensitivity and specificity relating to a chosen normal limit be reported with results.

9.7 CONCLUSIONS

Four methods for measuring disorders of vascular function and neurological function associated with occupational exposure to hand-transmitted vibration have been defined by reference to the available literature (Chapter 2). For detecting vascular disorders the methods are: i) measures of the finger systolic blood pressure (FSBP) response to local cooling and ii) measures of the finger skin temperature (FST) response to local cooling. For detecting neurological disorders the methods are: i) measures of vibrotactile thresholds at the fingertips and ii) measures of thermal thresholds at the fingertips.

Measures of the FSBP response to cold provocation and the FST response to cold provocation were appraised in 109 dockyard workers (45 manual workers not exposed to hand-transmitted vibration and 64 workers exposed to hand-transmitted vibration of whom 27 reported symptoms of VWF) (Section 3.2). The FSBP test was found to be sensitive, specific and responsive to VWF, the FST test was found not to differentiate between healthy subjects and subjects with VWF. Vibrotactile threshold measurements and thermal threshold measurements were appraised in 104 dockyard workers (29 manual workers not exposed to hand-transmitted vibration and 75 vibration-exposed workers of whom 65 reported a neurological disorder) (Section 3.3). Both of these tests were found to be sensitive, specific and responsive to symptoms of numbness but not to symptoms of tingling. It was concluded that a test battery comprising all of the above tests could be useful for monitoring vascular and neurological disorders associated with exposure to hand-transmitted vibration. However, a number of improvements to the measurement methods could be worthwhile. Further experiments were carried out to investigate these improvements.

In Chapter 4, the simultaneous measurement of FSBPs on more than one test finger was developed to improve the practicality of this test; when the sensitivity of this test to VWF was calculated for the detection of symptoms on the test finger compared to when the sensitivity was calculated for the detection of symptoms on the test hand, regardless of the condition of the test finger, the sensitivity was shown to increase (Section 3.2.3.1.1). Increased central sympathetic activity was hypothesised to result from increasing the stimulus by cooling more than one finger. This was studied in two experiments, each on 12 healthy subjects. It was found that FSBPs measured simultaneously on four test fingers gave similar results to measurements on one test finger (Section 4.2) and that FSBPs measured simultaneously on four test fingers had comparable repeatability to measurements on one test finger (Section 4.3). It was concluded that measuring FSBPs on multiple test fingers is a useful improvement to this test.

The FSBP test was further investigated in Chapter 5. It was hypothesised that changing the order of presentation of thermal stimuli when measuring FSBPs, and changing the period of recovery between successive applications of thermal stimuli, would influence the results by altering central sympathetic activity. The results showed that the order of presentation of thermal stimuli was not important, although for practical reasons it was concluded that a progressive reduction in temperature is desirable when measuring FSBPs (Section 5.3.4.1.1). It was also shown that inter-subject variability increased when recovery was allowed between thermal stimuli. It was concluded that minimising the time interval between successive applications of thermal provocation helps to reduce undesirable inter-subject variability (Section 5.3.4.1). Another study on 12 healthy subjects showed that different reference measurement locations give different results (Section 5.2). It was concluded from this study that the thumb is a suitable location for making reference measurements.

The FSBP test and the FST test both involve application of thermal provocation and they were performed in succession when appraising the vascular tests (Chapter 3). Multiple thermal provocations were hypothesised to have had cumulative effects on the central sympathetic nervous system. The results of the study reported in Chapter 6 showed that when the two vascular tests were performed in succession on 36 subjects, including 12 subjects who reported symptoms of VWF, any effects of the order of test presentation were small, although the test that was performed first tended to be more repeatable. It was concluded that if both vascular tests are to be performed during a single session, greater emphasis should be placed on the test performed first. The data for the response of FSTs to cold provocation obtained in this study were reanalysed and the results in Chapter 7 show that the sensitivity and specificity to VWF of the FST response to cold provocation is improved by changing the method of interpreting the results. It was concluded that three of the methods of interpreting the results of this test represented an improvement in the sensitivity and specificity of the test.

The two vascular tests have been shown in the literature to be repeatable (Section 3.1.1), but the repeatability of these tests had not been demonstrated for subjects with VWF. In the study reported in Chapter 6, the repeatability of the vascular measurements was assessed in 36 subjects: 12 manual workers, 12 office workers and 12 subjects with VWF. The repeatability of the vascular tests was found to be low amongst workers reporting VWF; some of these subjects showed a negative test result on one occasion and a positive test result on another occasion. It was concluded that a repeat test may be required when a suspected false negative result is obtained.

For the vibrotactile threshold test, the skin-stimulus contact force was controlled in the study reported in Chapter 3. Controlling the skin indentation would simplify measurement equipment. Ten healthy subjects were studied to investigate the relationship between skin-stimulus contact force, skin indentation and vibrotactile thresholds. The results showed that controlling the skin indentation would be preferable. Skin indentations giving comparable vibrotactile thresholds to those obtained using controlled contact forces were identified. It was concluded that the vibrotactile threshold test could be improved by implementing control of skin indentation.

A further investigation of the vibrotactile threshold test on ten healthy office workers showed that the duration of a measurement significantly influenced Meissner's corpuscle specific thresholds; as the measurement duration increased the sensitivity of the Meissner's corpuscles decreased (Section 8.1). It was concluded that the measurement duration should be minimised to minimise this effect.

It is concluded that a test battery comprising the four test methods identified from the literature and subsequently developed during the course of this research can be used to provide a reliable basis for monitoring disorders of both vascular and neurological function associated with occupational exposure to hand-transmitted vibration. The recommended measurements are summarised in Appendix F. It is important to note that the four tests (with the possibility of repeat tests where appropriate) must be used in the context of all other information available to the clinician because none of the tests were shown to be 100% reliable on their own. A number of recommendations are made for further improvements that might be achievable as a result of further work.

9.7.1 Recommendations for further work

Further work is required to determine the maximum permissible air flow before measurements are affected. The influence of starting FSTs on vascular measurements and the acute effects of caffeine consumption on measurement results should be investigated. Seasonal conditions have been shown to influence the outcome of objective tests (Section 2.6.1.1.3), further work is required to understand this phenomenon. Any effects of menstrual cycle on the normal response to measurements, and any effects of diurnal variations on the normal response to vascular tests should also be investigated.

The simultaneous measurement of FSBPs on four test fingers developed in this thesis was shown to be repeatable and to differentiate between groups of subjects with VWF and subjects without VWF (Chapter 6). The measurement should be appraised using the criteria of sensitivity, specificity and responsiveness amongst a larger group of subjects.

The repeatability, sensitivity and specificity of the measurement of the FST response to cold provocation have been shown to be dependent on the parameters used to interpret the results (Section 6.4.1, Chapter 7). Three parameters have been shown to perform better than other parameters calculated when appraised using the criteria of sensitivity and specificity (Chapter 7). These parameters should be appraised using the criteria of repeatability and responsiveness.

It was shown in the literature that measurements of thermal thresholds made with different psychophysical algorithms are not comparable (Section 2.5). Further experimentation is required to better understand the reason for this difference. Further work is also required to determine the most suitable contact area between skin and stimulus for the measurement, minimising contact area may make thermal control of the applicator more practical to achieve.

In Chapter 8 its was shown that measurements of vibrotactile thresholds made using a controlled skin indentation may be preferable to measurements made using a controlled probe contact force. A skin indentation that gave equivalent results to the previously recommended controlled contact force was determined. Measurements made using this controlled skin indentation should be appraised using the criteria of repeatability, sensitivity, specificity and responsiveness.

For interpreting the results of measurements of vascular and neurological function amongst workers exposed to hand-transmitted vibration, the range of normal responses to the tests should be known. In this thesis, some normative data has been obtained that may be used to aid interpretation. However, the population for which the results are valid is limited. Data from larger groups of subjects that is both age and gender specific should be obtained.

APPENDIX A APPARATUS

CONTENTS

A1 INTRODUCTION

This Appendix details the apparatus used for measuring finger systolic blood pressures, the finger skin temperature response to cold, vibrotactile thresholds and thermal thresholds. Apparatus and methods for making miscellaneous measurements are also described.

A2 APPARATUS

A2.1 Finger systolic blood pressures

A2.1.1 Plethysmograph

A plethysmograph is primarily a machine for measurement or recording of volume changes. The two plethysmographs used in studies reported here were capable of pressure application and the control of water temperature as well as recording volume changes in the finger. The plethysmographs were a dual-channel plethysmograph (Digitmatic DM2000, Medimatic A/S, Copenhagen) and a prototype *HVLab* Multi-Channel Plethysmograph. The main characteristics of the two machines are shown in Table A1. The Medimatic DM2000 plethysmograph was a free-standing machine. The *HVLab* Multi-Channel Plethysmograph required a personal computer for equipment control and data acquisition. The *HVLab* Multi-Channel Plethysmograph was interfaced to the computer by means of an Avantech PCL812-PG analogue to digital and digital to analogue conversion card. The computer was running *HVLab* Multi-Channel Plethysmograph software (version 1.0).

Table A1 Characteristics and available test parameters for the two plethysmographs used in the current studies.

Parameter	*HVLab* Multi-Channel Plethysmograph	Medimatic DM2000
Pressure Reservoir	1 litre	None
Water Reservoir	250 ml	50 ml
Digit Cooling System	Integrated	Separate
Air Outlets	1	1
Water Outlets	1	1
Transducer Inputs	5	2
Pressure Range	0 - 400 mmHg	0 - 300 mmHg
Deflation Rate	1 - 5 mmHg/s, linear	Time to reduce pressure from 120 mmHg to 100 mmHg set at 7 seconds, non-linear
Water Temperature	3 - 40°C, continuous	30°C, 15°C, 10°C, pre-set
Duration of Cold Provocation	Unlimited	0 - 9 minutes
Output	Graphical and numerical, generated by computer	Graphical, paper

A2.1.2 Hydrostatic pressure effects

In Chapter 4, Section 4.2, a difference between finger systolic blood pressures (FSBPs) measured with two plethysmographs during cold provocation was found. It was observed that during the deflation period, the cuffs and connecting pipes remained full of water. This resulted in a pressure difference between the pressure sensor, situated in the air pressure system above the water in the reservoir, and the cuffs (Figure A1). The hydrostatic pressure was directly proportional to the height of the cuff above the water reservoir (pressure = height of water x acceleration due to gravity x density of water). The hydrostatic pressure caused the cuff pressure to be lower than the pressure measured by the transducer. Measured FSBPs, therefore, were higher than the actual FSBPs. The height of water was higher in the *HVLab* Multi-Channel Plethysmograph than the Medimatic DM2000 plethysmograph, resulting in the higher FSBPs measured by the former machine compared to the latter. Using the line shown in Figure A2, a correction for the hydrostatic pressure effect can be calculated. The true pressure in the cuffs is found by subtracting the hydrostatic pressure from the measured pressure.

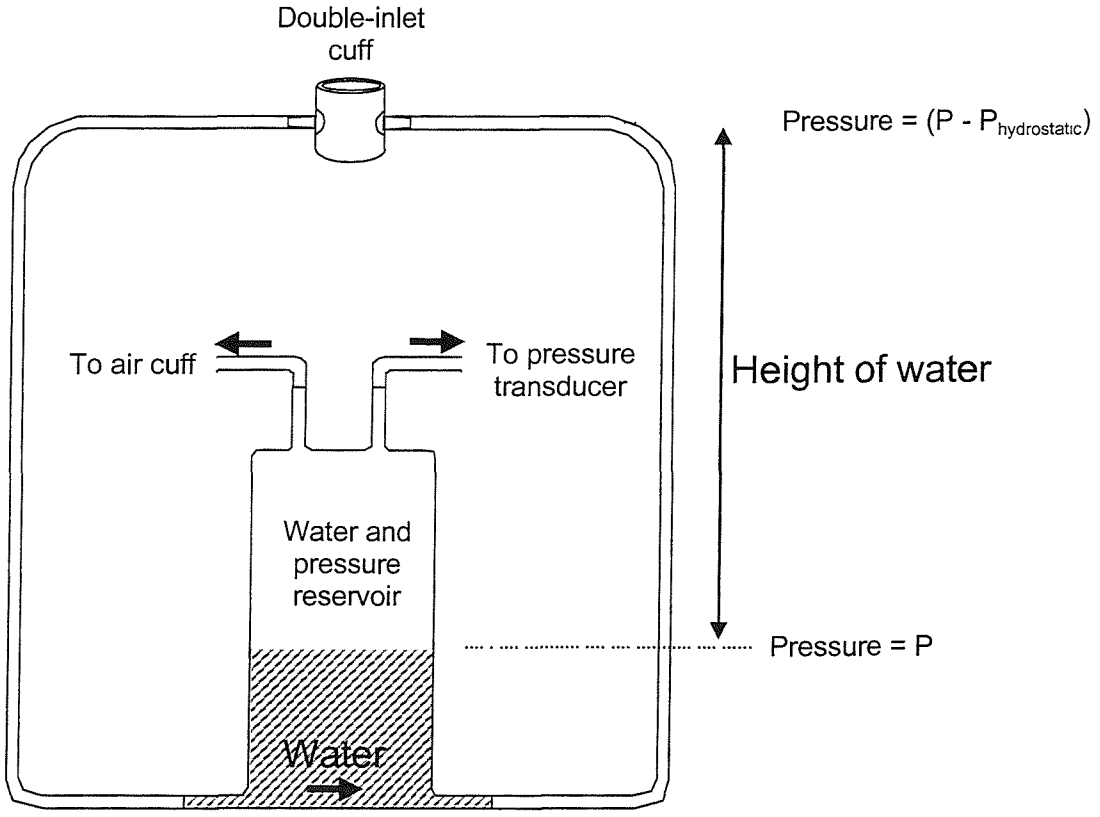


Figure A1 A schematic diagram showing the reduction in cuff pressure due to hydrostatic pressure.

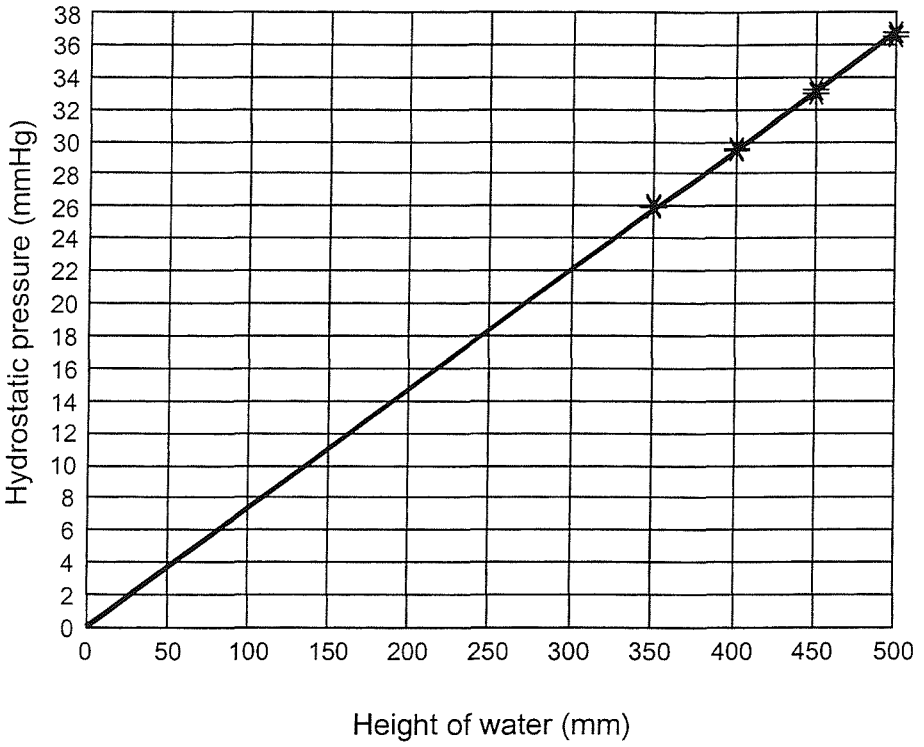


Figure A2 Graph used to obtain the correction for hydrostatic pressure effects. Measurements of the hydrostatic pressure are shown with the theoretical hydrostatic pressure. The gradient of the line is 0.0735 mmHg/mm

A2.1.3 Pressure cuffs

Two designs of pressure cuffs were used in experimentation, a plastic bag type cuff and a tube type cuff. The plastic bag type cuffs consist of thin-walled, rectangular plastic bags (Figure A3). The cuff was wrapped around the finger so as to be tight, but not tight enough to impair the circulation. The cuff was fastened in position by means of Velcro™ tabs. Double-inlet cuffs were used for water perfusion (as shown in Figure A3), and single-inlet cuffs were used for used for air inflation. Cuffs of the plastic bag type were 24 mm wide and between 90 and 130 mm in length. The length was chosen so the cuff fitted comfortably around the test phalanx.

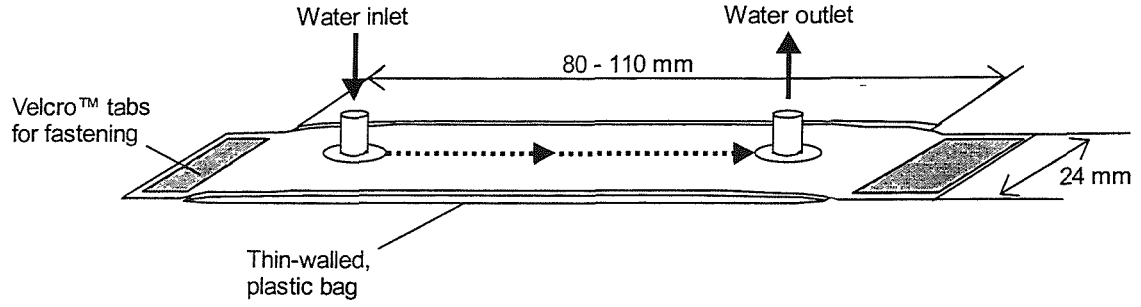


Figure A3 Plastic bag type cuffs. The cuff is wrapped around the finger to be tested and fastened in position by means of the Velcro™ covering. Water perfuses through the plastic bag. Single inlet cuffs are used for air inflation.

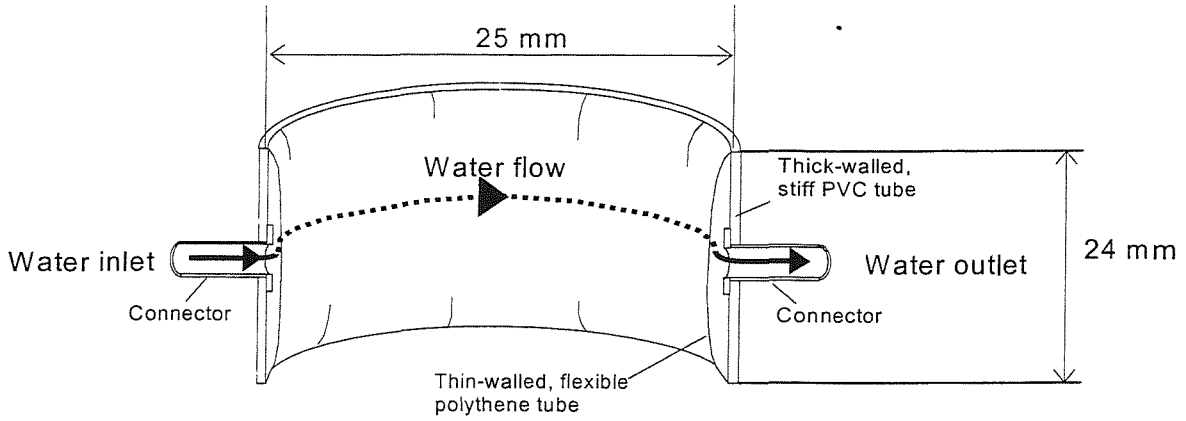


Figure A4 Tube type cuffs. Water perfuses the cuff between the thick-walled tube and the flexible inner membrane. Single inlet cuffs are used for air inflation.

The plastic bag type cuffs were constrained from fully adapting to the finger contour by the Velcro™ cover and by the stiffness of material. Placement of the cuffs was also time consuming and could result in partial occlusion of the digital circulation when placed too tight. These cuffs also resulted in occlusion of water flowing through them when connected in series, resulting in inadequate temperature control of the water at the finger skin surface.

For these reasons, a new cuff was developed consisting of a thick-walled, rigid PVC tube (internal diameter 25 mm, width of cuff 24 mm) lined with a thin-walled, flexible, PVC membrane (Figure A4). Water perfused the cuff between the flexible membrane and the rigid tube.

The rigid cuff was simpler to place on the finger. The inner membrane readily adapted to the finger contours. Occlusion of finger circulation was minimised since the cuff was loose around the finger until pressure was applied. In a trial study, three subjects were investigated twice with each cuff type. No differences in finger systolic blood pressures were found between cuffs for measurements made in air. It was assumed that the two cuff types were interchangeable.

Further developments of the tube type cuff have been made due to problems experienced during experimentation; the flexible inner membrane showed signs of fatigue after twenty to thirty pressure cycles. The fatigue resulted in leakage. The flexible PVC inner was replaced with a two layered membrane consisting of a latex bladder restricted by a fine gauged nylon net covering (Figure A5). The new tube type cuffs were not used in studies reported here.

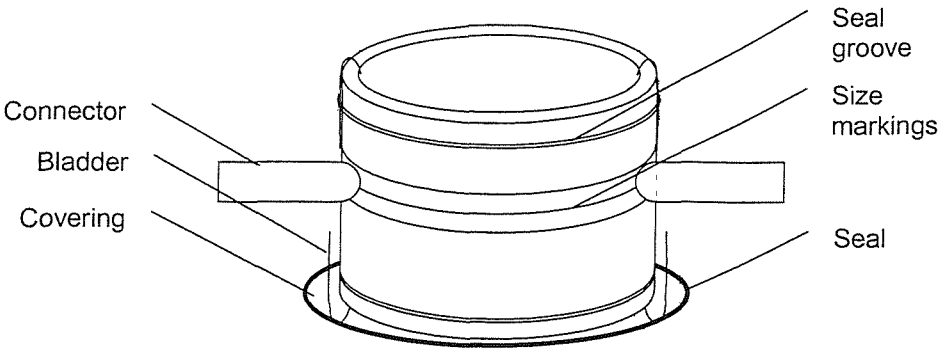


Figure A5 Tube type cuffs incorporating the two layered membrane consisting of a fine-gauged nylon net covering restricing a latex bladder.

A2.1.3.1 Influence of the nature of water circulation through pressure cuffs

The Medimatic DM2000 plethysmograph employed a peristaltic pump that operated by pushing water through a flexible pipe. Due to the nature of the pump, the water in this system was pulsated. Concern was expressed that the pulsation might result in an immediate vasoactive effect; it has been shown that there are changes in the digital circulation during exposure to vibration (Bovenzi *et al.*, 1995; Bovenzi and Griffin, 1997).

The maximum magnitude of vibration, measured at the cuff-finger interface, was found to be about 0.065 m/s^2 r.m.s. at a frequency of 10 Hz. This order of vibration magnitude is not believed to result in either vasoconstriction or vasodilation of the finger blood vessels (Bovenzi *et al.*, 1995; Bovenzi and Griffin, 1997).

A2.1.4 Strain gauges

Strain gauges were of the mercury-in-elastic type i.e. a thin silicone tube (internal diameter 0.5 mm) filled with mercury (Figure A6). The flexibility and stretch properties of the silicon tubing allowed the strain gauge to mould around the finger. The mercury within the silicon tube exhibited normal strain gauge properties; a change in stretch results in a change in the resistance of the mercury. The change in resistance is measured as a voltage drop, the voltage signal being acquired and amplified by the plethysmograph.

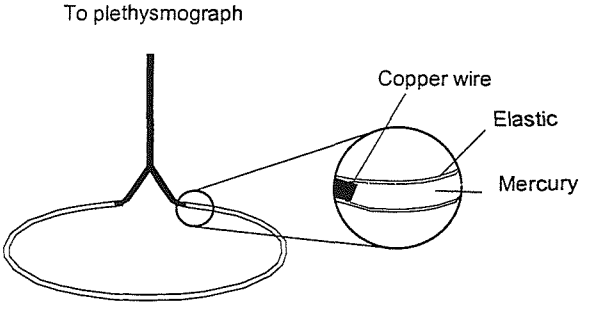


Figure A6 A mercury-in-elastic strain gauge.

A2.1.5 Pipe work

Pipe work connecting pressure cuffs to plethysmographs consisted of flexible polythene or silicone tubing, internal diameter 4.0 mm - 5.0 mm. Connections between pipes were made using either T-pieces, Y-pieces or straight couplers with a minimum internal diameter of 4.0 mm.

A2.1.6 Five finger squeezer

The procedure for measurement of finger systolic blood pressure involves the application of pressure to the distal phalanges prior to applying cuff pressure (Nielsen and Lassen, 1977). When performing measurements using the dual-channel plethysmograph, experimenters can apply this pressure by squeezing the patient's fingertips using their own fingers. For measurements made simultaneously on five fingers such a procedure is not possible. A device was manufactured to facilitate the squeezing of up to five fingers. A sphygmomanometer bulb was attached to five air cuffs, each of which was sewn into a loop, as shown in Figure A7. The cuffs are placed over the distal phalanges of the fingers and pressure applied by inflating the cuffs using the sphygmomanometer bulb.

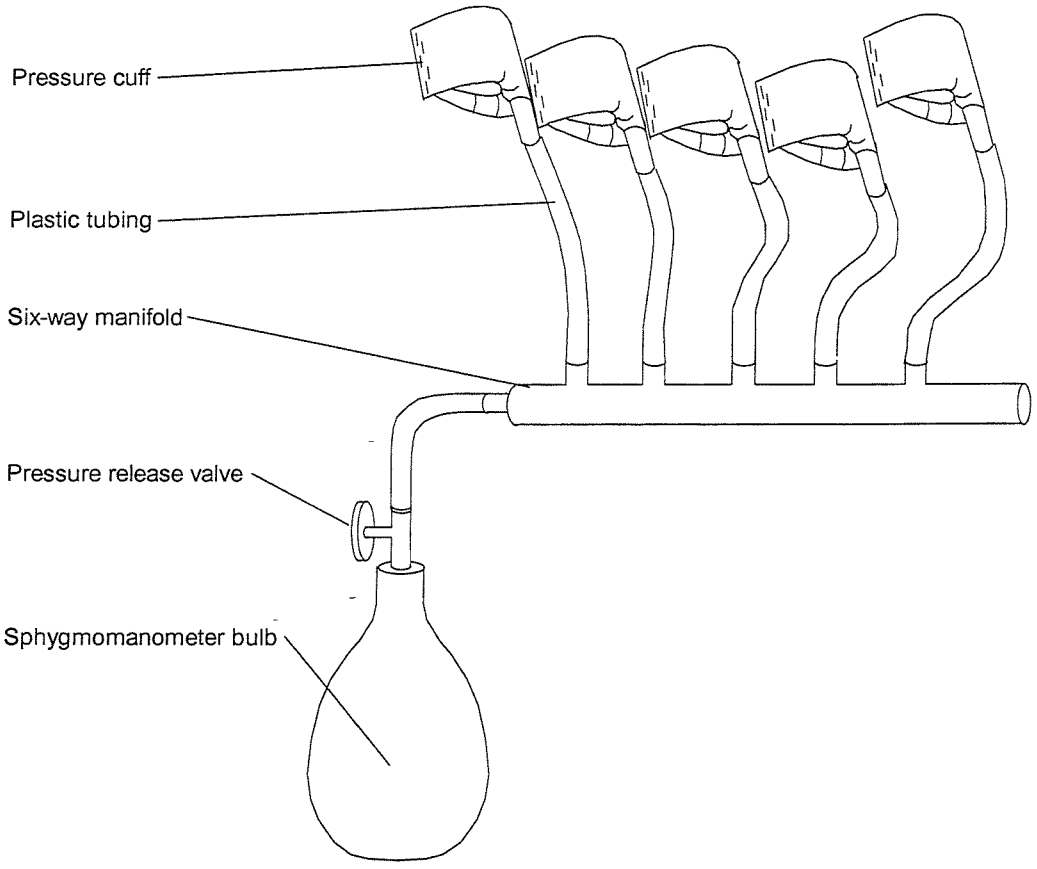


Figure A7 Diagram of the 5-finger squeezer

A2.2 Finger skin temperature response to cold provocation

An *HVLab* 8-Channel Temperature Monitor was used for measuring finger skin temperatures (FSTs). The temperature monitor was connected to a personal computer by means of an Avantech PCL812-PG interface card for analogue to digital conversion. The temperature monitor consisted of eight thermocouples connected to isolation amplifiers housed with the signal conditioning circuitry. The temperature monitor was powered by the personal computer through the interface card. The FSTs were logged using *HVLab* Data Acquisition and Analysis software or *HVLab* 8-Channel Temperature Monitor software (version 2.x). The system was calibrated daily during experimentation.

Water temperature was controlled in a Grant W38 water bath fitted with a Grant ZD heater/stirrer unit and a Grant CZ1 cooler unit, the Grant equipment is manufactured by Cambridge Instruments. The cooler unit operated constantly whilst the heater was thermostatically controlled to maintain water temperature at 15°C ± 0.2°C. The calibration of the Grant heater/stirrer unit was checked prior to and following experiments and at regular intervals during experiments. Figure A8 shows the set-up of the equipment used in experimentation.

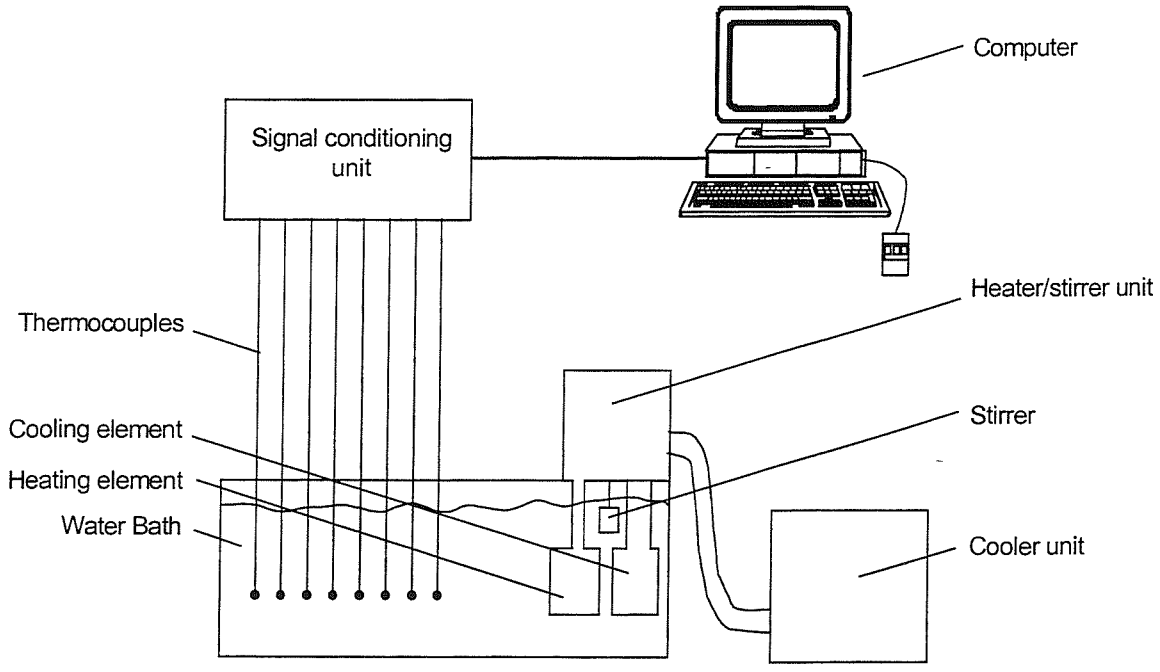


Figure A8 Set-up for the measurement of finger rewarming times

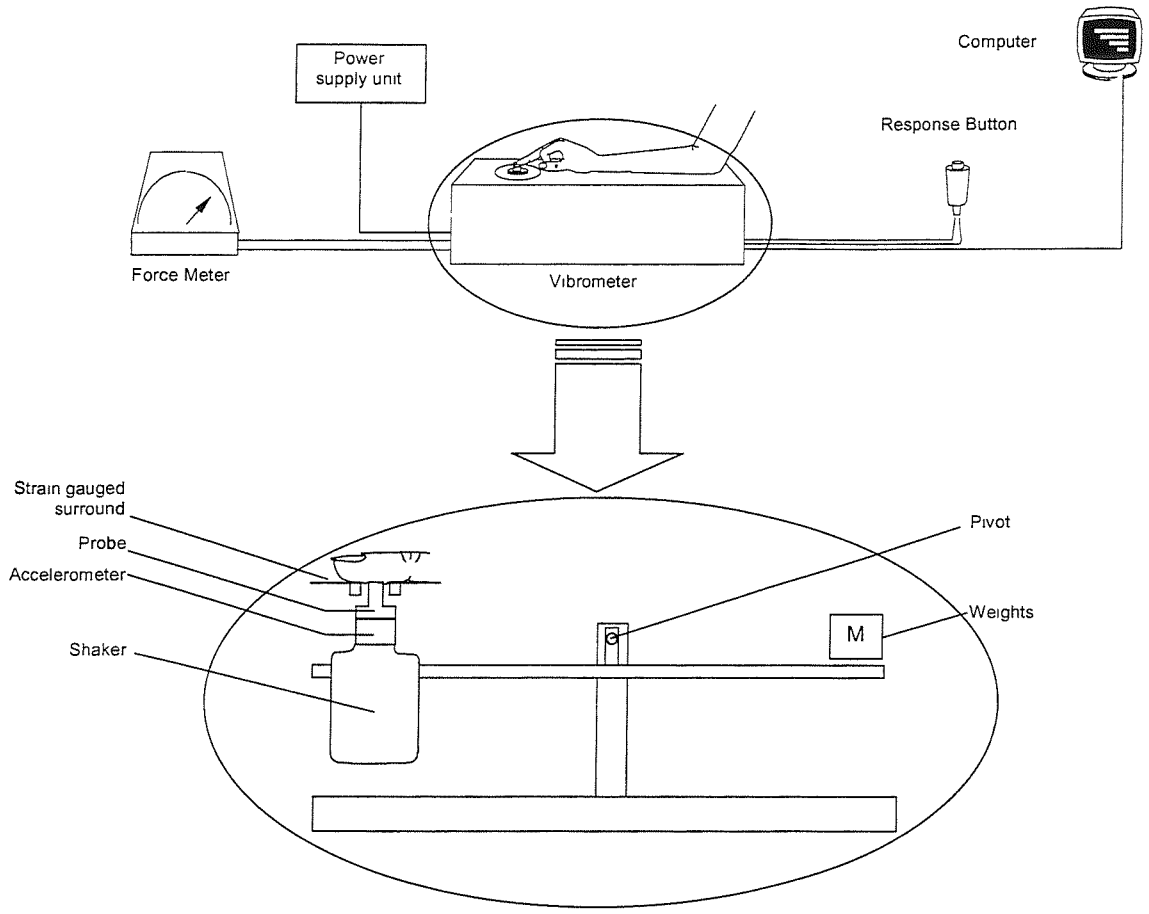


Figure A9 Set-up for the measurement of vibrotactile thresholds.

A2.3 Vibrotactile thresholds

An *HVLab* Tactile Vibrometer was used, connected to a personal computer fitted with an Avantech PCL812-PG interface card for analogue to digital and digital to analogue conversion. The computer was running *HVLab* Tactile Vibrometer software (versions 3.0 to 4.1) for equipment control and data acquisition. The *HVLab* Tactile Vibrometer hardware consisted of a power supply unit, the vibrometer unit, a force meter and a subject response button (Figure A9). The *HVLab* Tactile Vibrometer was capable of producing a clean sinusoidal vibration stimulus between 0.02 m/s^2 r.m.s. and 30 m/s^2 r.m.s. at a frequency of 31.5 Hz and between 0.02 m/s^2 r.m.s. and 50 m/s^2 r.m.s. at a frequency of 125 Hz.

The *HVLab* Tactile Vibrometer incorporated means for controlling both probe contact force and finger push force. Probe contact force was controlled by mounting a shaker (used to provide the vibration stimulus) on a beam, counter-balanced to produce a

constant upward force of at the shaker end of the beam. Finger push force was controlled using a strain gauged plate through which a cylindrical, nylon probe mounted on the shaker protruded. The probe was 6mm in diameter and the gap between probe and surround was 2mm. Subjects placed their finger over the probe and pushed on the instrumented plate. The strain gauge signals were output to the force meter for visual feedback of push force. The vibration stimulus was monitored using an accelerometer mounted between the shaker and the probe.

Vibration magnitude was calibrated before each experiment using a Brüel and Kjær Type 4294 Calibration Exciter which produces a frequency of 159.2 Hz with a r.m.s. acceleration of 10m/s². The maximum allowable error was 0.025 m/s² r.m.s. Push force and probe contact force were calibrated using standard weights. Calibration was checked before, at periodic intervals during, and after experimentation

A2.4 Thermal thresholds

An *HVLab* Thermal Aesthesiometer was used, connected to a personal computer fitted with an Avantech PCL812-PG interface card for analogue to digital conversion. The computer was running *HVLab* Thermal Aesthesiometer software (version 2.0) for equipment control and data acquisition. The *HVLab* Thermal Aesthesiometer hardware consisted of a control unit, an applicator (maximum contact area 23.76 cm²) and a subject response button. Figure A10 shows the set-up used in experimental work. Equipment was calibrated before each experiment to give a maximum temperature error of ± 0.2°C at the reference temperature. Calibration was checked before, at periodic intervals during and after experimentation.

Thermal control of the applicator was achieved with a Peltier element sandwiched between an aluminium cylindrical base, which acted as a heat sink, and a circular aluminium plate (1.6 mm thick, diameter 55 mm). A thermocouple was used to monitor plate temperature and provide feedback to the aesthesiometer control unit. The thermocouple was mounted in a groove 1.1 mm deep on the underside of the circular plate (Figure A11). During tests, the applicator was placed on a set of electronic scales to provide visual feedback of push force to the subject (Figure A10).

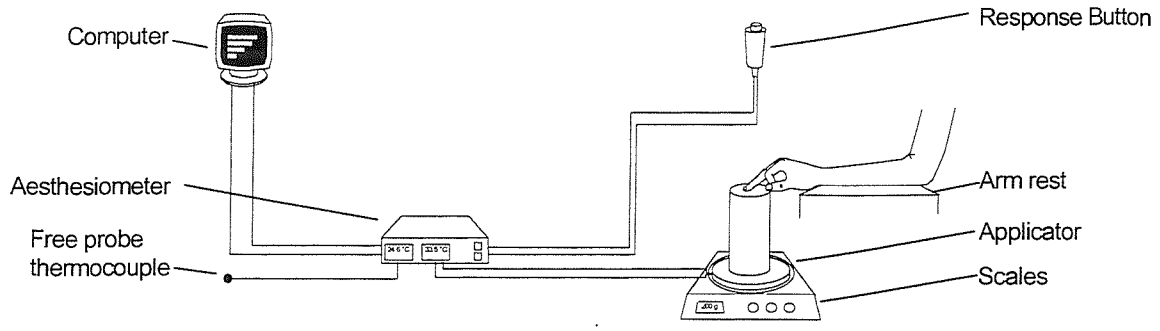


Figure A10 Set-up for the measurement of thermal thresholds.

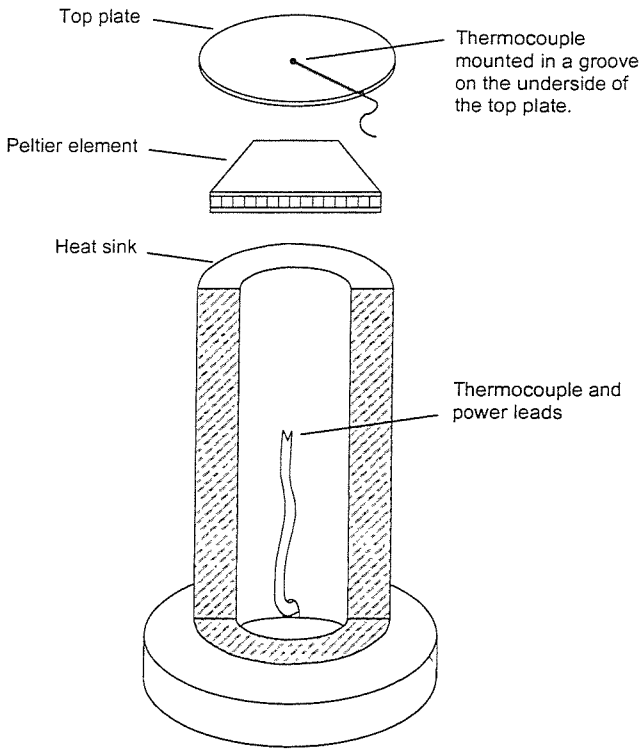


Figure A11 A diagram showing the components of the *HVLab* Thermal Aesthesiometer applicator.

The aesthesiometer control unit housed the power and control electronics. A free probe thermocouple was connected to the control unit for monitoring temperatures other those at the surface of the plate (e.g. finger skin temperature). The subject response button was also connected to the control unit. Visual feedback on the progress of tests was provided for the experimenter by means of temperature displays on the control unit and progress indicators in the software. Test progress indicators and temperature displays were shielded from the subject's field of view during tests.

A3 METHODS FOR PERFORMING MISCELLANEOUS MEASUREMENTS

A3.1 Finger skin temperature

Finger skin temperatures were measured using a k-type thermocouple connected to an *HVLab* Thermal Aesthesiometer (Section A2.4). For single measurements, the thermocouple was pinched lightly between the thumb and forefinger or between thumb and middle finger until the indicated skin temperature stabilised. For repeated measurements, the thermocouple was taped to the dorsal surface of the medial phalanx of the middle finger.

A3.2 Arm systolic blood pressure

Arm systolic blood pressure was measured using the standard ausculatory technique. Briefly, a pressure cuff was placed around the arm just above the elbow; the cuff was inflated to a suprasystolic pressure. The cuff pressure was slowly released whilst a stethoscope, placed over the point where the brachial artery divides into the radial and ulnar arteries, was used to monitor for Koroktoff sounds.

Koroktoff sounds result when compression of an artery is released and occur in five phases. The first phase, a clear tapping sound, is heard when the cuff pressure has fallen to the peak systolic pressure. The fifth phase, when the sounds become muffled and disappear, corresponds closely to the true diastolic pressure. These two phases have been used to determine arterial systolic and diastolic pressure.

For most measurements of arm systolic blood pressure, a standard mercury sphygmomanometer (Accoson, Dekamet Mk3) was used. In one study, an aneroid sphygmomanometer was used (BOSO-Med II). The cuff size for both sphygmomanometers was 14 cm by 24 - 33 cm (internal bladder 12 cm by 22 cm).

A3.3 Environmental temperatures

Room temperature and external temperatures were measured using mercury thermometers accurate to at least ± 0.5°C unless otherwise stated. External temperature was measured at the start of an experimental session. Room temperature was measured at a location close to the subject's hands and at the same height as the subject.

A3.4 Finger dimensions

Finger dimensions were measured using vernier callipers to an accuracy of 0.5 mm. Measurements of finger breadth and depth were made at the interphalangeal joints. Finger and phalangeal lengths were measured using the criteria given by Garrett (1970). Finger volumes and surface areas were calculated assuming the finger took the form of an elliptical cylinder.

APPENDIX B SYMPTOM HISTORY AND VIBRATION EXPOSURE QUESTIONNAIRE

Medical In Confidence

[Q101] (D)
[Q102] (M)
[Q103] (Y)

Date

		19

Serial Number

SN

ASSESSMENT OF THE EFFECTS OF HAND-ARM VIBRATION IN DEVONPORT DOCKYARD

Name .....

[Q104] Pay No .....

[Q105] Grade .....

[Q112] Trade .....

[Q106] Centre .....

[Q107] (D)
[Q108] (M)
[Q109] (Y) Date of birth

		19

[Q110] Gender

M	F
1	2

[Q111] Ethnic Group

- Caucasian		1
- Asian		2
- Negroid		3
- Mongoloid		4

[Q113] Are you left handed or right handed?

L	R	Both
1	2	3

SOCIAL HISTORY

Smoking History

[Q201] Do you smoke or have you ever smoked?

No	Yes
1	2

If yes:

[Q202] How much did/do you smoke?

Cigarettes per day (including rolling tobacco)			
under 20	20 or more	cigars	pipe

[Q210] Have you smoked in the past hour?

No	Yes
1	2

[Q203] When did you start smoking regularly? 19

[Q204] Do you still smoke?

No	Yes
1	2

If no:

[Q205] When did you give up smoking? 19

Alcohol Consumption

[Q206] Do you drink alcohol?

No	Yes
1	2

[Q207] Do you drink regularly (at least once a week)?

1	2

If yes:

[Q208] units per week

(1 unit = 1/2 pint beer
= single spirit
= glass wine)

[Q209] Have you drunk any alcohol in the past 12 hours?

No	Yes
1	2

MEDICAL HISTORY

Present Medical History

[Q301] Are you under medical supervision at present?

No	Yes
1	2

If yes:
What is the condition being treated?

[Q302] Are you taking any tablets or other medications at the present time?

No	Yes
1	2

If yes:

a) What is the condition being treated?
b) What tablets or other medications are you taking?

[Q303] Have you had any serious illness or injury requiring hospital attendance as an Outpatient?

No	Yes
1	2

If yes:
What clinic did you attend and when?

[Q304] Any aspect of medical history considered relevant?

No	Yes
1	2

Injury to Fingers, Hand, Arm, Shoulders or Neck

Have you ever injured any of the following?

Nature and location of injury	Date of injury	Treatment received	Specify any after effects
a) Fingers			
b) Hand			
c) Arm			
d) Shoulders			
e) Neck			

[Q401] Any of the above?

No	Yes
1	2

[Q402] Any of above considered relevant?

No	Yes
1	2

Related Medical Conditions

Have you ever suffered from any of the following (give details)?	No	Yes	Date of first occurrence		Still receiving treatment		Details (after effects, location)
			Month	Year	No	Yes	
a) Heart or circulation trouble?							
eg 1 Coronary thrombosis							
2 Angina							
3 Pain in calves of legs when walking							
4 High blood pressure							
5 Cold injury (eg frostbite)							
6 Other ( )							
b) Neurological disease (that is problems with nervous system)							
eg 1 Polio							
2 Stroke							
3 Carpal Tunnel Syndrome							
4 Other ( )							
c) Connective Tissue Disease							
eg 1 Dupuytrens Contracture							
2 Arthritis							
3 Other ( )							
d) Degenerative Disease							
eg 1 Arthritis of hands, arms and neck							
2 Other ( )							
e) Endocrine Disease							
1 Diabetes							
2 Other ( )							

[Q501] Any of the above?

No	Yes
1	2

[Q502] Any of above considered relevant?

No	Yes
1	2

HAND SYMPTOMS

[Q601] Have cold hands been more of a problem for you than for other people (those not using vibrating hand tools)?

No Yes Uncertain

1 2 3

[Q602] Have cold feet been more of a problem for you than for other people?

No Yes Uncertain

1 2 3

[Q603] Have you had chilblains in the last ten years?

No Yes

1 2

[Q604] Do any members of your family experience white fingers or Raynaud's phenomenon? (Answer 'yes' only for blood relatives, i.e. not wife/husband)

No Yes Uncertain

1 2 3

If yes:

[Q605] Do they use vibrating tools?

No Yes

1 2

[Q606] May I see your hands?

Significant Presence | No Significant Presence

1 2

BLANCHING

[Q701] Do any of your fingers ever go white?

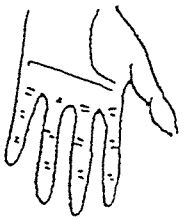
No	Yes
1	2

If no:
Go to next page.

Please indicate those areas on your fingers that go white.

Right Hand

Left Hand



[Q704-Q715] (Across page)

	Th	1	2	3	4	Total
Right Hand						

4	3	2	1	Th	Total	
						Left Hand

(Shade in parts of fingers affected and enter score for each finger)

	Month	Year
[Q702](M) [Q703](Y) When did you first notice this?		
[Q724](M) [Q725](Y) When did you last notice this?		
	1	2

[Q728] How often have your fingers appeared white in the past twelve months?

Times

Fingers go white for a number of reasons.
Are your fingers made to go white:

	No	Yes
[Q717] by cold conditions		
[Q718] by handling cold objects		
[Q719] when feeling the vibration from vibrating tools		
	1	2

[Q720] Do attacks occur only in cold conditions?

No	Yes
1	2

[Q721] Do the attacks occur in the Summer, Winter or both?

Summer	Winter	Both
1	2	3

[Q722] Does the condition interfere with any leisure activities?
Specify which:

No	Yes
1	2

[Q723] Does the condition interfere with any work activities?
Specify which:

No	Yes
1	2

BLUENESS

[Q801] Do any of your fingers ever go blue?

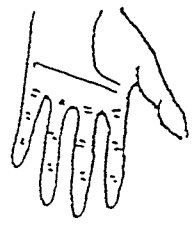
No	Yes
1	2

If no:
Go to next page.

Please indicate those areas on your fingers that go blue.

Right Hand

Left Hand



[Q805-Q816] (Across page)

	Th	1	2	3	4	Total
Right Hand						

	4	3	2	1	Th	Total
Left Hand						

(Shade in parts of fingers affected and enter score for each finger)

[Q802](M) [Q803](Y) When did you first notice this?

Month	Year
	19

[Q804] For those with blanching:

Was this before or after they first went white?

Before	After	Same Time
1	2	3

[Q823](M) [Q824](Y) When did you last notice this?

Month	Year
	19

[Q825] How often have your fingers appeared white in the past 12 months?

Times

[Q817] What is the longest period your hands have appeared blue?

Minutes

For those with blanching

Do your fingers go blue?

	No	Yes
[Q818] only before they go white?		
[Q819] only after they go white?		
[Q820] without going white?		
	1	2

[Q801] Does blueness only occur in cold conditions?

No	Yes
1	2

[Q822] Does blueness occur in the Summer, Winter or both?

Summer	Winter	Both
1	2	3

NUMBNESS

[Q901] Do you ever get numbness (that is, loss of feeling) in the fingers?

No	Yes
1	2

If no:
Go to page 11.

Please indicate those areas on your fingers that are affected by numbness.

Right Hand

Left Hand

[Q910-Q919] (Across page)

	Th	1	2	3	4	
Right Hand						

	4	3	2	1	Th	
Left Hand						

(Shade in parts of fingers affected and enter 0 or 1 in appropriate boxes)

[Q902] Does numbness occur only at night?

No	Yes
1	2

If yes:
Go to page 11.

[Q903] Does numbness occur immediately after using vibrating tools?

No	Yes
1	2

[Q904] For those with blanching:

Does numbness occur together with whitening of the fingers?

No	Yes
1	2

[Q905] Does numbness occur at other times?

No	Yes
1	2

(i.e. other than at night, immediately after using vibrating tools and without whitening of the fingers)

If yes:

[Q906](M) [Q907](Y) When did you first notice this?

Month	Year
	19

[Q908] For those with blanching:

Was this before or after they first went white?

Before	After	Same Time
1	2	3

[Q920] When did you last notice this?

Month	Year
	19

[Q922] How often have your fingers been numb in the past twelve months?

Times

[Q909] Does numbness occur only in cold conditions?

No	Yes
1	2

TINGLING

[Q1001] Do you ever get tingling in the fingers?

No	Yes
1	2

If no:
Go to page 13.

Please indicate those areas on your fingers that are affected by tingling.

Right Hand

Left Hand

[1010-1019] (Across page)

	Th	1	2	3	4	
Right Hand						

	4	3	2	1	Th	
Left Hand						

(Shade in parts of fingers affected and enter 0 or 1 in appropriate boxes)

[Q1002] Does tingling occur only at night?

No	Yes
1	2

If yes:
Go to page 13.

[Q1003] Does tingling occur immediately after using vibrating tools?

No	Yes
1	2

[Q1004] For those with blanching:

Does tingling occur together with whitening of the fingers?

No	Yes
1	2

[Q1005] Does tingling occur at other times?

No	Yes
1	2

(i.e. other than at night, immediately after using vibration tools and without whitening of the fingers)

If yes:

[Q1006](M) [Q1007](Y) When did you first notice this?

Month	Year
	19

[Q1008] For those with blanching:

Was this before or after they first went white?

Before	After	Same Time
1	2	3

[Q1020](M) [Q1021](Y) When did you last notice this?

Month	Year
	19

[Q1022] How often have you had tingling in your fingers in the past 12 months?

Times

[Q1009] Does tingling occur only in cold conditions?

No	Yes
1	2

OTHER SIGNS

[Q1101] Do you have problems with your grip?

No	Yes
1	2

If yes give details:

[Q1102] Do you have any other problems with your fingers or hands?

No	Yes
1	2

If yes:

Sign	Location	Other Details

VIBRATION EXPOSURE

Where have you worked with vibrating tools since leaving school?

Employer and Trade	Starting Date	Finishing Date

[Q1201](M) [Q1202](Y) When did you first start working with vibrating tools?

Month	Year
	19
1	2

Have you in the course of your work, used any of the following tools? (Please include tools used in any previous jobs)

Caulking hammers		Grinders	
Scalers/nobblers		Sanders	
Riveting hammers/holderons		Nailers/staplers	
Drilling machines		Saws	
Impact wrenches		Nibblers	

Have you ever used any other type of pneumatic or vibrating tools at work?

Details: .....

.....

Please indicate in as much detail as possible, your periods of use of the tools indicated previously.

Tn 1	Tn 2	Tn 3	Tn 4	Tn 5	Tn 6	Tn 7
Tool Type	Start Date	Finish Date	Hours/Day Holding Tool	Days/ Week	Weeks/ Year	Total Exposure (Hours)

Have you used any of the following regularly, for more than two hours per week when not at work?

		No	Yes	
[Q1401]	Power tools			1
	Motor cycle			2
	Motor mower			3

HTn 1	HTn 2	HTn 3	HTn 4	HTn 5	HTn 6	HTn 7
Tool Type	Start Date	Finish Date	Hours/Day Holding Tool	Days/ Week	Weeks/ Year	Total Exposure (Hours)

APPENDIX C COLD PROVOCATION TESTS: ORDER EFFECTS AND REPEATABILITY

REPEATABILITY STATISTICS

Repeatability statistics are given for measurements of percentage finger systolic blood pressures at 15°C and 10°C compared to measurements made at 30°C, and for finger skin temperatures measured at 4 minutes of immersion in cold water at 15°C and at 5 minutes of recovery from cold provocation. Results are given for manual workers, office workers and for subjects reporting symptoms of VWF. Measurements were made twice in two different conditions: i) finger systolic blood pressures measured before the FST response to cold provocation (Table C1) and ii) the FST response to cold provocation measured before finger systolic blood pressures (Table C2). Repeatability statistics are also shown for comparison between conditions using the mean of the two measurements made in each condition (Table C3). Analysis of variance tables for comparisons between and within conditions are also shown.

ANALYSIS OF VARIANCE TABLES

Table C4 Analysis of variance table for testing repeatability of finger skin temperatures during cold provocation measured 4 minutes after immersion in cold water at 15°C.

Table C5 Analysis of variance table for testing repeatability of finger skin temperatures during cold provocation, 4 minutes after immersion, when cold provocation was applied after a finger systolic blood pressure test had been performed.

Table C6 Analysis of variance table for testing repeatability of finger skin temperature measurements 5 minutes after removal from cold water.

Table C7 Analysis of variance table for testing repeatability of finger skin temperature measurements 5 minutes after immersion in cold water. Cold provocation was applied after a finger systolic blood pressure test had been performed.

Table C8 Analysis of variance table for testing for differences between two measurements of finger skin temperatures at 4 minutes of immersion in two conditions: before a finger systolic blood pressure test and after a finger systolic blood pressure test.

Table C9 Analysis of variance table for testing for differences between measurements of finger skin temperatures 5 minutes after immersion in cold water in two conditions: before a finger systolic blood pressure test and after a finger systolic blood pressure test.

Table C10 Analysis of variance table for testing repeatability of finger systolic blood pressures.

Table C11 Analysis of variance table for testing repeatability of percentage finger systolic blood pressures when measured after the response of FSTs to cold provocation.

Table C12 Analysis of variance table for testing for differences between percentage finger systolic blood pressures measured in two conditions: before measuring the FST response to cold provocation and after measuring the FST response to cold provocation.

Table C1 Repeatability statistics for when the FST response to cold provocation was measured before finger systolic blood pressures.

Statistic	Group	Percentage finger systolic blood pressures								Finger rewarming times													
		15°C				10°C				After 4 minutes of immersion								After 5 minutes of recovery							
		Dig 2	Dig 3	Dig 4	Dig 5	Dig 2	Dig 3	Dig 4	Dig 5	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]
Pearson's Correlation Coefficient[1]	Office	0.40	0.28	0.27	0.25	**0.62**	0.22	**0.65**	0.47	***0.73***	0.01	***0.74***	**0.69**	***0.83***	0.42	0.55	0.11	0.47	0.37	0.57	***0.77***	***0.82***	0.48	**0.61**	0.03
	Manual	0.05	**0.64**	0.03	0.09	0.55	0.50	0.14	0.07	0.04	0.01	0.11	0.15	0.15	0.25	-0.10	-0.20	-0.08	-0.12	-0.13	-0.23	-0.04	-0.08	-0.14	-0.02
	VWF	-0.01	0.00	***0.82***	0.03	0.16	-0.24	0.41	0.10	**0.71**	-0.12	0.33	0.12	0.23	0.51	**0.70**	0.54	***0.86***	-0.14	**0.61**	**0.69**	***0.77***	**0.70**	0.51	0.50
r.m.s. error	Office	8.7	15.7	13.9	10.7	9.2	11.4	9.6	11.4	3.4	7.0	4.0	3.7	2.8	5.1	4.9	3.2	5.8	7.3	5.8	3.7	3.6	6.4	5.8	3.0
	Manual	19.1	9.4	14.9	14.8	14.1	11.2	14.8	13.9	5.0	5.7	5.6	4.4	3.8	5.2	7.1	0.9	6.4	7.3	7.6	8.1	6.4	7.7	8.6	1.0
	VWF	50.1	43.1	28.7	43.1	43.8	41.0	42.0	40.7	3.3	5.3	5.8	4.6	3.4	4.3	4.4	1.1	4.2	11.0	7.6	6.3	5.2	6.2	7.6	1.3
Upper Limit of Agreement	Office	19.0	36.0	30.4	22.8	15.9	24.9	20.7	21.2	3.1	8.4	4.5	3.4	3.8	5.7	5.9	3.6	7.4	8.5	6.9	4.4	0.7	7.9	5.9	3.9
	Manual	23.3	12.6	26.8	17.8	24.4	16.3	33.9	29.2	2.4	3.3	2.9	1.9	2.9	3.6	3.4	0.4	3.8	5.0	3.8	4.1	3.4	4.5	4.9	0.7
	VWF	97.9	74.8	38.0	77.7	75.4	56.3	52.2	77.5	0.5	1.8	1.6	1.8	1.6	0.8	0.7	0.5	1.0	-2.7	2.3	1.8	0.7	2.1	4.8	1.0
Lower Limit of Agreement	Office	17.4	26.8	27.6	22.0	20.9	22.7	19.3	25.6	3.9	6.0	3.7	4.2	3.8	4.9	4.3	3.0	4.4	6.7	5.1	4.4	3.5	5.3	4.3	1.1
	Manual	43.8	21.8	34.0	34.2	32.4	26.1	33.9	29.2	7.0	7.9	7.7	6.1	4.9	6.8	9.8	1.3	8.7	9.6	10.4	11.3	8.8	10.5	11.7	1.3
	VWF	110.0	98.4	66.4	97.5	100.2	94.9	97.0	90.5	4.7	7.6	8.4	6.4	4.6	6.2	6.3	1.5	6.0	4.5	10.9	9.0	7.5	8.9	10.0	1.6

[1] Values in bold are significant at the 5% level, values in bold italics are significant at the 1% level
[2] Dist = distal phalanx
[3] Med = medial phalanx
[4] Prox = proximal phalanx
[5] ref = reference finger

Table C2 Repeatability statistics when finger systolic blood pressures were measured before the FST response to cold provocation.

Statistic	Group	Percentage finger systolic blood pressures								Finger rewarming times													
		15°C				10°C				After 4 minutes of immersion								After 5 minutes of recovery							
		Dig 2	Dig 3	Dig 4	Dig 5	Dig 2	Dig 3	Dig 4	Dig 5	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]
Pearson's Correlation Coefficient[1]	Office	***0.74***	***0.86***	***0.75***	**0.62**	***0.88***	***0.75***	***0.78***	0 34	**0.70**	0 60	**0.72**	***0.80***	***0.86***	0 56	**0.71**	0 46	0 36	0 32	**0.68**	***0.85***	***0.83***	***0.83***	***0.88***	0 04
	Manual	0 44	-0 02	0 03	0 03	0 08	0 35	-0 44	0 46	-0 17	-0 58	-0 24	-0 40	-0 29	-0 10	-0 26	-0 19	0 31	-0 42	0 16	0 10	0 02	0 28	0 05	0 00
	VWF	0.09	**0.66**	0 39	0 14	**0.68**	0 16	0 50	-0 20	-0 21	-0 15	0 37	0 23	0 16	0 17	-0 09	***0.81***	0 30	0 22	0 22	0 18	0 15	0 03	0 12	***0.88***
r.m.s. error	Office	10 7	17 8	8 7	12 4	9 6	12 1	13 3	16 1	2 8	4 0	4 0	3 0	1 9	3 9	3 9	0 9	1 8	5 4	2 8	2 6	3 2	2 8	1 7	0 8
	Manual	16 8	11 1	17 4	15 7	16 6	11 1	17 1	7 5	5 2	5 7	6 9	5 6	4 4	5 7	7 6	3 7	3 9	3 0	6 0	6 2	6 0	5 4	6 6	2 1
	VWF	37 1	27 8	40 6	40 8	30 0	34 9	34 9	47 2	6 1	6 0	4 7	4 6	3 3	5 5	6 9	1 5	6 7	8 5	9 2	8 8	7 6	10 4	9 9	1 2
Upper Limit of Agreement	Office	24 4	39 4	19 9	26 2	21 8	28 1	30 6	33 7	3 8	3 7	4 1	3 2	2 2	5 0	4 3	1 2	2 1	6 9	3 7	3 5	4 5	3 9	2 4	1 0
	Manual	23 5	16 2	30 1	31 7	19 5	23 1	35 1	12 7	4 5	4 5	6 5	5 5	3 4	4 1	6 9	3 6	2 6	1 6	3 6	3 8	3 2	4 3	5 1	1 3
	VWF	43 5	52 8	79 4	86	35 5	73.3	51 2	101 2	5 8	4 8	3 5	2 1	2 5	2 4	4 6	0 9	3 8	3 7	5 6	6 1	5 6	7 1	7 7	0 7
Lower Limit of Agreement	Office	12 4	34 6	1 1	25 5	10 2	17 5	22 2	33 9	1 6	4 7	4 3	3 0	1 8	3 0	3 9	0 6	1 7	3 9	1 5	1 3	1 1	1 1	0 8	0 7
	Manual	38 9	25 8	39 9	33 9	38 1	23 3	35 2	12 7	6 3	7 1	8 5	6 1	5 4	7 3	8 9	4 2	5 2	4 2	8 0	8 2	7 9	6 7	7 1	2 8
	VWF	84 9	62 0	89 0	84 4	68 9	72 2	80 8	101 2	6 8	8 2	9 1	6 3	4 3	7 6	9 0	2 1	9 0	11 9	12 2	11 5	9 8	13 7	12 5	1 9

[1] Values in bold are significant at the 5% level, values in bold italics are significant at the 1% level
[2] Dist = distal phalanx
[3] Med = medial phalanx
[4] Prox = proximal phalanx
[5] ref = reference finger

Table C3 Repeatability statistics for between conditions (mean of two measurements in each condition).

Statistic	Group	Percentage finger systolic blood pressures								Finger rewarming times													
		15°C				10°C				After 4 minutes of immersion								After 5 minutes of recovery							
		Dig 2	Dig 3	Dig 4	Dig 5	Dig 2	Dig 3	Dig 4	Dig 5	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]	Dig 1	Dig 2	Dig 3 dist[2]	Dig 3 med[3]	Dig 3 prox[4]	Dig 4	Dig 5	Dig 3 ref[5]
Pearson's Correlation Coefficient[1]	Office	0 52	0 26	**0.58**	0 50	***0.82***	0 37	***0.89***	0 27	0 46	0 20	***0.79***	***0.82***	***0.86***	***0.82***	***0.75***	0 56	0 20	-0 37	0 51	0 47	**0.58**	0 40	**0.59**	0 17
	Manual	0 45	0 36	0 16	0 00	0 52	0 12	-0 06	**0.64**	0 57	-0 13	0 55	**0.63**	0 53	0 29	**0.59**	0 23	**0.62**	0 52	**0.63**	***0.74***	***0.75***	***0 79***	***0.78***	0 39
	VWF	**0.69**	***0.76***	**0.70**	0 32	***0.79***	***0.72***	0 59	**0.63**	0 07	0 15	0 46	0 20	0 29	0 56	0 39	0 51	0 36	0 00	**0.65**	**0.59**	0 52	0 56	***0.74***	**0.68**
r.m.s. error	Office	10 7	21 3	8 2	10 8	9 6	12 0	6 4	13 0	4 1	4 4	3 2	2 7	2 3	2 4	3 4	1 9	5 0	6 4	5 9	6 1	5 2	5 6	5 7	1 7
	Manual	10 9	8 7	10 8	11 3	10 8	11 1	11 5	6 0	2 2	3 2	2 9	1 9	1 9	3 7	2 9	1 7	2 3	2 8	2 7	2 2	2 0	2 2	2 2	0 9
	VWF	21 7	19.5	30 2	27 1	17 6	14 2	24 3	17 9	3 6	2 8	3 5	3 1	2 3	2 7	3 8	1 6	6 2	6 9	5 2	5 2	4 8	5 5	4 3	1 5
Upper Limit of Agreement	Office	3 1	26 4	9 3	-1 1	6 2	12 9	8 2	9 8	4 8	5 7	3 0	1 8	2 7	2 8	3 3	0 5	2 6	6 0	1 8	2 4	3 0	2 8	2 0	0 8
	Manual	9 9	8 7	10 2	14 5	10 3	6 0	5 4	4 5	2 9	2 7	4 1	1 7	1 7	5 0	3 9	2 5	1 8	1 4	2 7	2 1	2 3	2 5	2 2	0 1
	VWF	13 7	13 7	17 0	22 1	15 2	14 3	25 0	18 9	3 0	2 4	3 4	2 7	2 5	3 0	4 1	2 2	4 6	4 3	3 8	4 0	4 2	5 1	3 8	2 0
Lower Limit of Agreement	Office	15 3	16 8	7 8	3 1	12 8	12 1	4 8	16 7	3 8	3 3	3 6	3 5	2 1	2 2	3 7	2 7	7 0	7 4	8 4	8 6	7 0	7 4	8 2	2 4
	Manual	12 9	9 5	12 4	8 1	12 3	14 6	16 0	7 7	1 5	3 9	1 3	2 3	2 3	2 0	1 5	0 7	3 0	4 0	2 9	2 6	1 7	2 0	2 4	1 7
	VWF	28.7	25 3	41 2	33 3	21 1	15 5	26	18 5	4 4	3 4	3 8	3 7	2 2	2 6	3 9	1 0	8 0	9 1	6 6	6 6	5 6	6 3	5 0	0 8

[1] Values in bold are significant at the 5% level, values in bold italics are significant at the 1% level
[2] Dist = distal phalanx
[3] Med = medial phalanx
[4] Prox = proximal phalanx
[5] ref = reference finger

Table C4 Analysis of variance table for testing repeatability of finger skin temperatures during cold provocation measured 4 minutes after immersion in cold water at 15°C.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				1.586	0.126
Session	Digit 1	45.3	1	45.3	7.014	0.014
	Digit 2	339.0	1	39.0	2.074	0.162
	Digit 3, distal	47.9	1	47.9	3.772	0.063
	Digit 3, medial	43.5	1	43.5	5.305	0.030
	Digit 3, proximal	34.5	1	34.5	7.301	0.012
	Digit 4	28.4	1	28.4	2.620	0.118
	Digit 5	59.7	1	59.7	4.206	0.051
	Multivariate				1.381	0.296
Session * Group	Digit 1	2.8	2	1.4	0.220	0.804
	Digit 2	39.7	2	19.8	1.055	0.363
	Digit 3, distal	23.6	2	11.8	0.930	0.408
	Digit 3, medial	2.6	2	1.3	0.157	0.856
	Digit 3, proximal	1.5	2	0.7	0.153	0.859
	Digit 4	5.5	2	2.8	0.254	0.777
	Digit 5	29.1	2	14.6	1.025	0.373
	Multivariate				0.430	0.955
Error (Session)	Digit 1	161.4	25	6.5		
	Digit 2	470.4	25	18.8		
	Digit 3, distal	317.8	25	12.7		
	Digit 3, medial	205.1	25	8.2		
	Digit 3, proximal	118.1	25	4.7		
	Digit 4	271.0	25	10.8		
	Digit 5	354.8	25	14.2		

Table C5 Analysis of variance table for testing repeatability of finger skin temperatures during cold provocation, 4 minutes after immersion, when cold provocation was applied after a finger systolic blood pressure test had been performed.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				1.317	0.235
Session	Digit 1	0.012	1	0.012	0.001	0.978
	Digit 2	36	1	36	2.366	0.135
	Digit 3, distal	6	1	6	0.348	0.560
	Digit 3, medial	8	1	8	0.676	0.418
	Digit 3, proximal	2	1	2	0.292	0.593
	Digit 4	8	1	8	0.572	0.456
	Digit 5	9	1	9	0.397	0.534
	Multivariate				0.512	0.816
Session * Group	Digit 1	7	2	4	0.259	0.774
	Digit 2	14	2	7	0.448	0.644
	Digit 3, distal	5	2	2	0.142	0.869
	Digit 3, medial	17	2	8	0.732	0.490
	Digit 3, proximal	4	2	2	0.341	0.714
	Digit 4	45	2	23	1.670	0.206
	Digit 5	15	2	8	0.335	0.718
	Multivariate				0.740	0.724
Error (Session)	Digit 1	391	28	14		
	Digit 2	426	28	15		
	Digit 3, distal	458	28	16		
	Digit 3, medial	321	28	11		
	Digit 3, proximal	172	28	6		
	Digit 4	378	28	14		
	Digit 5	647	28	23		

Table C6 Analysis of variance table for testing repeatability of finger skin temperature measurements 5 minutes after removal from cold water.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				0.757	0.708
Session	Digit 1	35	1	35	2.502	0.125
	Digit 2	51	1	51	1.211	0.280
	Digit 3, distal	115	1	115	4.982	0.034
	Digit 3, medial	113	1	113	6.155	0.019
	Digit 3, proximal	92	1	92	8.139	0.008
	Digit 4	90	1	90	4.409	0.045
	Digit 5	85	1	85	3.186	0.085
	Multivariate				1.291	0.300
Session * Group	Digit 1	40	2	20	1.422	0.258
	Digit 2	64	2	32	0.762	0.476
	Digit 3, distal	71	2	36	1.549	0.230
	Digit 3, medial	44	2	22	1.193	0.318
	Digit 3, proximal	47	2	24	2.085	0.143
	Digit 4	52	2	26	1.281	0.294
	Digit 5	47	2	23	0.871	0.430
	Multivariate				0.674	0.787
Error (Session)	Digit 1	391	28	14		
	Digit 2	1178	28	42		
	Digit 3, distal	646	28	23		
	Digit 3, medial	513	28	18		
	Digit 3, proximal	317	28	11		
	Digit 4	572	28	20		
	Digit 5	749	28	27		

Table C7 Analysis of variance table for testing repeatability of finger skin temperature measurements 5 minutes after immersion in cold water. Cold provocation was applied after a finger systolic blood pressure test had been performed.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				1.126	0.362
Session	Digit 1	21	1	21	1.808	0.190
	Digit 2	23	1	23	1.293	0.265
	Digit 3, distal	30	1	30	1.312	0.262
	Digit 3, medial	22	1	22	0.984	0.330
	Digit 3, proximal	12	1	12	0.614	0.440
	Digit 4	16	1	16	0.565	0.459
	Digit 5	16	1	16	0.540	0.469
	Multivariate				0.634	0.723
Session * Group	Digit 1	20	2	9.8	0.852	0.437
	Digit 2	85	2	42	2.336	0.115
	Digit 3, distal	54	2	27	1.184	0.321
	Digit 3, medial	32	2	16	0.174	0.498
	Digit 3, proximal	43	2	22	1.133	0.336
	Digit 4	53	2	27	0.955	0.397
	Digit 5	23	2	12	0.405	0.671
	Multivariate				1.166	0.332
Error (Session)	Digit 1	323	28	12		
	Digit 2	509	28	18		
	Digit 3, distal	639	28	23		
	Digit 3, medial	637	28	23		
	Digit 3, proximal	532	28	19		
	Digit 4	778	28	28		
	Digit 5	810	28	29		

Table C8 Analysis of variance table for testing for differences between two measurements of finger skin temperatures at 4 minutes of immersion in cold water in two conditions: before a finger systolic blood pressure test and after a finger systolic blood pressure test.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				1.866	0.062
Order	Digit 1	0	1	0	0.017	0.897
	Digit 2	0	1	0	0.007	0.933
	Digit 3, distal	0	1	0	0.000	0.997
	Digit 3, medial	10	1	10	2.549	0.123
	Digit 3, proximal	1	1	1	0.389	0.539
	Digit 4	1	1	1	0.198	0.660
	Digit 5	0	1	0	0.007	0.932
	Multivariate				2.02	0.106
Order * Group	Digit 1	4	2	2	0.347	0.710
	Digit 2	8	2	4	0.559	0.579
	Digit 3, distal	6	2	3	0.513	0.605
	Digit 3, medial	1	2	0	0.124	0.884
	Digit 3, proximal	1	2	0	0.121	0.887
	Digit 4	1	2	0	0.091	0.913
	Digit 5	4	2	2	0.295	0.747
	Multivariate				0.752	0.711
Error (Order)	Digit 1	157	25	6		
	Digit 2	185	25	7		
	Digit 3, distal	144	25	6		
	Digit 3, medial	97	25	4		
	Digit 3, proximal	70	25	3		
	Digit 4	124	25	5		
	Digit 5	172	25	7		

Table C9 Analysis of variance table for testing for differences between measurements of finger skin temperatures 5 minutes after immersion in cold water in two conditions: before a finger systolic blood pressure test and after a finger systolic blood pressure test.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig.
Group	Multivariate				1.033	0.442
Order	Digit 1	26	1	26	2.104	0.159
	Digit 2	31	1	31	1.637	0.212
	Digit 3, distal	21	1	21	1.950	0.174
	Digit 3, medial	16	1	16	1.481	0.234
	Digit 3, proximal	2	1	2	0.224	0.640
	Digit 4	2	1	2	0.150	0.702
	Digit 5	9	1	9	1.262	0.271
	Multivariate				4.103	0.006
Order * Group	Digit 1	2	2	1	0.067	0.936
	Digit 2	14	2	7	0.379	0.689
	Digit 3, distal	6	2	3	0.295	0.747
	Digit 3, medial	5	2	2	0.208	0.813
	Digit 3, proximal	4	2	2	0.203	0.817
	Digit 4	2	2	1	0.070	0.933
	Digit 5	2	2	1	0.148	0.863
	Multivariate				0.372	0.976
Error (order)	Digit 1	320	26	12		
	Digit 2	490	26	19		
	Digit 3, distal	279	26	11		
	Digit 3, medial	284	26	11		
	Digit 3, proximal	235	26	9		
	Digit 4	293	26	11		
	Digit 5	178	26	7		

Table C10 Analysis of variance table for testing repeatability. of finger systolic blood pressures.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig
Group	Multivariate				2 756	0 012
Session	Digit 2	1149	1	1149	3 192	0 084
	Digit 3	0 023	1	0 023	0 000	0 998
	Digit 4	262	1	262	0 455	0 505
	Digit 5	14	1	14	0 016	0 899
	Multivanate				1 522	0 224
Session * Group	Digit 2	3378	2	1689	4 691	0 017
	Digit 3	154	2	77	0 180	0 836
	Digit 4	1079	2	540	0 937	0 403
	Digit 5	21 2	2	11	0 013	0 988
	Multivariate				1 783	0 100
Error (Session)	Digit 2	10802	30	360		
	Digit 3	12882	30	429		
	Digit 4	17273	30	576		
	Digit 5	25277	30	843		
Cold	Digit 2	45	1	45	1 236	0 275
	Digit 3	199	1	199	1 867	0 182
	Digit 4	208	1	208	1 399	0 246
	Digit 5	15	1	15	0 222	0 641
	Multivariate				1 345	0 79
Cold * Group	Digit 2	64	2	32	0 866	0 431
	Digit 3	131	2	66	0 616	0 547
	Digit 4	4 6	2	2	0 015	0 985
	Digit 5	235	2	118	1 738	0 193
	Multivariate				0 661	0 724
Error (Cold)	Digit 2	1103	30	37		
	Digit 3	3199	30	107		
	Digit 4	4453	30	148		
	Digit 5	2028	30	68		
Session * Cold	Digit 2	15	1	15		0 493
	Digit 3	206	1	206	2 570	0 119
	Digit 4	2	1	2	0 025	0 874
	Digit 5	44	1	44	0 648	0 427
	Multivariate				0 602	0 664
Session * Cold * Group	Digit 2	11	2	6	0 178	0 838
	Digit 3	5	2	2	0 031	0 970
	Digit 4	453	2	227	2 453	0 103
	Digit 5	14	2	7	0 104	0 902
	Multivariate				0 627	0 752
Error (Session * Cold)	Digit 2	938	30	31		
	Digit 3	2407	30	80		
	Digit 4	2773	30	92		
	Digit 5	2045	30	68		

Table C11 Analysis of variance table for testing repeatability of percentage finger systolic blood pressures when measured after following the measurements of the response of FSTs to cold provocation.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig
Group	Multivariate				2 847	0 010
Session	Digit 2	1270	1	1270	1 509	0 228
	Digit 3	1607	1	1607	3 025	0 092
	Digit 4	1100	1	1100	2 694	0 111
	Digit 5	298	1	298	0 489	0 489
	Multivariate				1 141	0 358
Session * Group	Digit 2	547	2	274	0 325	0 725
	Digit 3	2723	2	1361	2 563	0 093
	Digit 4	2657	2	1329	3 254	0 052
	Digit 5	75	2	37	0 062	0 940
	Multivariate				1 434	0 202
Error (Session)	Digit 2	26090	31	842		
	Digit 3	16466	31	531		
	Digit 4	12659	31	408		
	Digit 5	18835	31	608		
Cold	Digit 2	292	1	292	3 945	0 056
	Digit 3	82	1	82	1 494	0 231
	Digit 4	711	1	711	2 858	0 101
	Digit 5	4	1	4	0 072	0 790
	Multivariate				1 647	0 190
Cold * Group	Digit 2	52	2	26 2	0 354	0 705
	Digit 3	544	2	272	4 958	0 014
	Digit 4	1017	2	509	2 044	0 17
	Digit 5	458	2	229	3 823	0 033
	Multivariate				2 418	0 025
Error (Cold)	Digit 2	2297	31	74		
	Digit 3	1700	31	55		
	Digit 4	7715	31	249		
	Digit 5	1857	31	60		
Session * Cold	Digit 2	31	1	31	0 413	0 525
	Digit 3	159	1	159	1 460	0 236
	Digit 4	2	1	2	0 033	0 857
	Digit 5	61	1	61	0 813	0 374
	Multivariate				0 504	0 733
Session * Cold * Group	Digit 2	314	2	157	2 082	0 142
	Digit 3	110	2	55	0 505	0 608
	Digit 4	339	2	170	3 138	0 057
	Digit 5	164	2	82	1 087	0 350
	Multivariate				1.540	0 164
Error (Session * Cold)	Digit 2	2337	31	75		
	Digit 3	3370	31	109		
	Digit 4	1676	31	54		
	Digit 5	2338	31	75		

Table C12 Analysis of variance table for testing for differences between percentage finger systolic blood pressures measured in two conditions: before measuring the FST response to cold provocation and after measuring the FST response to cold provocation.

Effect	Measure	Sum of Squares	Degrees of Freedom	Mean square	F	Sig
Group	Multivariate				2.380	0.029
Order	Digit 2	483	1	483	2 416	0 131
	Digit 3	31	1	31	0 139	0 712
	Digit 4	278	1	278	0 910	0 348
	Digit 5	258	1	258	1 074	0 309
	Multivariate				0 756	0 564
Order * Group	Digit 2	94	2	47	0.234	0 793
	Digit 3	166	2	83	0 373	0 692
	Digit 4	313	2	157	0 512	0 605
	Digit 5	207	2	104	0 431	0 654
	Multivariate				0 447	0.887
Error (Order)	Digit 2	5601	28	200		
	Digit 3	6244	28	223		
	Digit 4	8567	28	306		
	Digit 5	6729	8	240		
Cold	Digit 2	17	1	17	0.627	0.435
	Digit 3	120	1	120	2.633	0 116
	Digit 4	463	1	463	2.581	0 119
	Digit 5	14	1	14	0 444	0.511
	Multivariate				1.266	0.310
Cold * Group	Digit 2	8	2	4	0.154	0.858
	Digit 3	125	2	62	1.365	0.272
	Digit 4	282	2	141	0 787	0.465
	Digit 5	177	2	89	2.781	0.079
	Multivariate				1.387	0.224
Error (Cold)	Digit 2	750	28	27		
	Digit 3	1280	28	46		
	Digit 4	5024	28	179		
	Digit 5	891	28	32		
Order * Cold	Digit 2	84	1	84	3.606	0 068
	Digit 3	11	1	11	0.276	0.604
	Digit 4	54	1	54	2.636	0 116
	Digit 5	3	1	3	0.112	0.740
	Multivariate				1.471	0.241
Order * Cold * Group	Digit 2	14	2	7	0.309	0.737
	Digit 3	152	2	76	1.899	0.169
	Digit 4	466	2	233	11.322	0.000
	Digit 5	248	2	124	1.050	0.029
	Multivariate				2.651	0.016
Error (Order * Cold)	Digit 2	655	28	23		
	Digit 3	1119	28	40		
	Digit 4	577	28	21		
	Digit 5	858	28	31		

APPENDIX D COLD PROVOCATION TESTS: ORDER EFFECTS AND REPEATABILITY

SUBJECT DETAILS AND VIBRATION EXPOSURE

Group	Current trade	Age	Smoker	Drinker	Blanching score	Numbness score	Tingling score	Exposure to hand-transmitted vibration in the work place	Total duration of exposure (hours)
Office workers	Researcher	50	No	Yes	0	0	0	-	0
	Researcher	42	Ex	Occasional	0	0	0	-	0
	Researcher	47	No	Yes	0	0	0	-	0
	Researcher	60	No	Yes	0	0	0	-	0
	Researcher	32	Yes	Yes	0	0	0	-	0
	Academic	49	Ex	Yes	0	0	0	-	0
	Researcher	37	No	Yes	0	0	0	-	0
	Academic	50	Ex	Yes	0	0	48	-	0
	Administrator	50	Ex	Yes	0	0	0	-	0
	Social work	40	Ex	Yes	0	0	0	-	0
	Computer engineer	50	Ex	Yes	0	0	0	-	0
	Researcher	37	No	Yes	0	0	0	-	0
Manual workers without VWF	Sheet metal worker	38	Ex	Yes	0	0	0	Drill, grinder, impact wrench, riveting tool, sander, saw,	8030
	Electrical technician	52	Yes	Yes	0	0	0	Drills	50
	Scaffolder	58	Ex	Yes	0	0	0	Drill, grinder, heavy breaker, Kango hammer, Nibbler, saw, scalar	8428
	Refuse collector	22	Yes	Occasional	2†	66	4	-	0
	Industrial cleaner	53	Yes	Yes	0	0	0	Motorbike	19,000
	Industrial cleaner	34	No	Occasional	0	0	0	Floor polisher, lawn mower	1180
	Industrial cleaner	58	Ex	Occasional	0	0	0	Drill, grinder, meat mincer, nailer, nibbler, saw, scalar, sander	53904
	Riveter	54	No	Occasional	0	0	0	Drill, nibbler, riveting tool	37296
	Milkman	39	No	Yes	0	3	3	Motorbike	468
	Industrial cleaner	49	Yes	Yes	0	0	0	Grinder	1152
	Baker	38	Yes	Yes	0	0	0	Jack hammer	706
	Painter and decorator	36	Yes	No	0	0	6	Drill, grinder, impact wrench, nailer, nibbler, scalar	7836
Workers exposed to hand-transmitted vibration reporting symptoms of VWF	Landscape gardener	40	No	Yes	42	42	42	Chainsaw, disk cutter, grinder, jackhammer, mower, rotivator, strimmer, vibroplate	4209
	Bricklayer	60	Yes	Yes	12	12	12	Augers, chipping hammers, compacting machines, drills, jack hammers, nailers, rock drill, saws	10622
	Diver	50	Ex	Yes	14	7	6	Rock drills (underwater)	3775
	Bricklayer	39	Yes	Yes	11	11	32	motorbike	7644
	Forest craftsman	45	Yes	Yes	7	7	7	Chainsaw, Kango-hammer, strimmer	28680
	Riveter	61	No	Yes	28	48	0	Caulking hammer, drill, jackhammer, Kango-hammer, nibbler, riveting tool	55935
	Riveter	41	Ex	Occasional	5	8	21	Drill, grinder, nibbler, riveting tool	44833
	Riveter	44	Ex	Yes	12	12	8	Chainsaw, drill, polishing machine, riveting tool	33343
	Groundsman	42	Yes	Occasional	25	12	16	Chainsaw, hedge trimmer, lawnmower, strimmer	12165
	Riveter	40	No	Yes	19	2	14	Drill, grinder, riveting tool	33056
	Metal polisher	50	Yes	Occasional	48	48	48	Drills, flexible shaft polishing tool, grinder, sander, nibbler, nailer, saw	35955
	Riveter	44	Ex	Yes	1	0	6	Drill, grinder, riveting tool, sander	27617

† Symptoms were not on the test hand and were most likely due to injury This subject showed normal responses to cold provocation on the test hand

APPENDIX E NORMATIVE DATA

This appendix contains tables of reported finger systolic blood pressures, finger skin temperatures following cold provocation, vibrotactile thresholds and thermal thresholds. The data have been estimated from the literature and were obtained from groups of healthy office workers, healthy manual workers and workers exposed to hand-transmitted vibration not reporting symptoms associated with exposure to vibration.

Table E1 Some of the percentage finger systolic blood pressures for normal subjects reported in the literature.

Study	Test finger	Reference finger	Comments	$\%FSBP_{15}$	$\%FSBP_{10}$
Nielsen *et al* (1980)	Middle finger, left hand	Thumb, left hand			
Thulesius et al. (1981)			Mean (standard deviation)	98 (8)	97 (10)
Ekenvall and Lindblad (1982)	Ring finger, left hand	Index finger, left hand	Reported graphically only	-	-
Ekenvall and Lindblad (1986)	Ring finger, left hand	Index finger, left hand	Median (range), unexposed controls	86 (67-100)	83 (59-96)
Arneklo-Nobin *et al.* (1987)	Middle finger	Index finger	Reported graphically only		
Bovenzi (1988)	Middle finger, left hand	Ring finger, left hand			
Bovenzi, M (1989)	Middle finger, left hand	Ring finger, left hand	Median (range)	100 (100-100)	96.3 (68-113)
Bovenzi, M (1991)			Mean (standard deviation)	88.5 (10.1)	91.8 (13.8)
Kurozawa *et al.* (1991)	Middle finger	Thumb, same hand as test finger	Reported graphically only	-	-
Virokannas and Rintamäki (1991)	—	—	Mean (standard deviation)	90 (14)	90 (10)
Carnicelli *et al.* (1992)	Middle finger, right hand	Ring finger, right hand	Mean (standard deviation)	89.9 (9.4)	85.5 (8.3)
Bovenzi, M (1993)	Middle finger, left hand	Ring finger, left hand	Median (range)	100 (65-114)	100 (61-115)
Bovenzi *et al.* (1995)	Middle finger, left hand	Ring finger, left hand	Median (inter-quartile range)	-	100 (90.7-100)
Bovenzi (1997)	Middle finger, left hand	Usually the ring finger	Mean (standard deviation)	98.3 (8.7)	94.8 (11.8)
Olsen (1998)	—	—	Median (IQR)	74 (63 – 97)	

Table E2 Some reported measurements of the FST response to cold provocation reported in the literature, the indices of recovery and the suggested lower normal limits for these indices are given.

Author	Temperature (°C)	Duration (mins)	Ischaemia[1]	Room temperature (°C)	Index of rewarming	Normal Limit
Hellstrom *et al.* (1970)	5 ± 0.2	20	-	25 – 28	Rewarming curve	-
Gemne and Swensson (1975)	5	2	-	-		
Chang (1976)	5 / 10	10	-	20.5 – 22.5	Recovery activity	-
Harada and Matsumoto (1980)	10	10	-	20		
Juuls and Nielsen (1981)	10	-	yes	22 – 24	Rewarming time and rewarming curve	-
Welsh (1983)	10	> 3	yes	-		-
Kurumatani (1984)	10	10	-	20 – 23		-
Hack *et al.* (1983,1986)	5 - 7	15	no	20 – 22	Hyperaemic temperature	Immersion temperature + 0.2°C
Pelmear *et al.* (1985)	10	10	½	30	Hyperaemic temperature	-
Brubaker *et al.* (1986)	-	-	yes	-	Hyperaemic temperature	Immersion temperature + 0.2°C
Bovenzi (1986)	4	2	-	22.5 (SD 0.4)		-
Iki *et al.* (1986)	10	10	-	-		-
Kurumatani *et al.* (1986)	10	10	-	20 – 23	Immersion temperature, recovery temperature	Immersion temperature 11.4°C Temperature 5 minutes after immersion of 21.6°C
Niioka *et al.* (1986)	10	10	-	-		-
Pyykkö *et al.* (1986)	12 - 15	10	-	18 – 22	Colour of digits	-
Taylor *et al.* (1986)	10 - 12	1	-	-	Colour of digits	-
Welsh (1986)	10	3	yes	-		
Bovenzi (1987)	5	5	yes	22 – 24	Percentage recovery at 15 minutes after immersion	86%
Dupuis (1987)	15	1	-	22 – 24	Recovery temperature 15 minutes after immersion	28°C
Harada (1987)	10	10	-	20 – 23		
Laroche and Thériault (1987)	4	1	-	24	Recovery temperature at 15 minutes after immersion	Initial temperature minus 3°C

Author	Temperature (°C)	Duration (mins)	Ischaemia[1]	Room temperature (°C)	Index of rewarming	Normal Limit
Matoba and Sakurai (1987)	5/10	10	-	20 – 23	Recovery activity, rate of rewarming	30% at 15 minutes, 60 % at 20 minutes
Pelmear *et al.* (1987)	10	10	½	20 – 23	Rewarming time to 1% of initial temperature, Immersion temperature	-
Olsen N (1988)	10	5	yes	18	Finger colour	-
Howarth and Griffin (1989)	15	4 - 30	no	28°C	Initial temperature, fall of temperature, minimum temperature, recovery period (to 50% and 80% of initial), rewarming time for 6°C, time to change of slope, initial slope, secondary slope	-
Futatsuka *et al.* (1990)	5 / 10	10	-	-		
Jansen and Schwarze (1990)	5	14	-	30 / 14		
Kester *et al.* (1990)	5	1	-	25 ± 1	Direction of rewarming and rewarming curve	Rewarming from tip to base is normal
Saito *et al.* (1990)	10	10	-	-		
Virokannas *et al.* (1990)	10	10	-	20 – 23	Rewarming temperature and rewarming rate	-
Kent *et al.* (1991)	5	1	-	25± 1		
Gautherie *et al.* (1992a,b)	15 ±1	3	-	21 ± 1	Recovery rate and immersion temperature	-
Bovenzi *et al.* (1994)	10	5	yes	21		
Nasu and Kurozawa (1995)	5	10	-	24	Recovery rate at 5 and 10 minutes after immersion and rewarming curve	30% at 5 minutes, 60% at ten minutes
Nasu and Kurozawa (1995)	10 / 15	10	½	20 – 22		
Gautherie *et al.* (1997)					11 parameters coded and combined to produce quantitative evaluation of degree of vasoconstriction	-
von Bierbrauer *et al.* (1998)	12	3	-	22	Time to complete rewarming	15 or 30 minutes for complete rewarming
Ishitake *et al.* (1998)	10	10	-	17 – 27	Absolute temperatures, final temperature	-

[1] ½ = ischaemia was applied for the first half of the immersion period only

Table E3 Some vibrotactile thresholds reported for Meissner's and Pacinian corpuscle specific thresholds obtained using different measurement methods. Further examples are given by Maeda and Griffin (1994, Table 1).

Author	Measurement location	Psycho-physical method[1]	Skin indentation (mm)	Contactor push force (N)	Contactor size (area = cm²) (ø = mm)	Gap[2] (mm)	Push force on surround (N)	Stimulus type	Rate of change of continuous stimuli[3]	Meissner's corpuscle specific[4] thresholds (20 Hz – 40 Hz)	Pacinian corpuscle specific thresholds[4] (100 Hz - 125 Hz)
Yacorzynski and Brown (1941)	Fingertip	-	-	-	ø 5	X	-	-	-	-	-
Verrillo (1965)	1st metacarpal	MOL	-	-	0.32 - 0.29	-	-	Pulsed	1 ms	-	-
Verrillo (1966b)	1st metacarpal	-	0.5	-	0.002 - 6	1	-	Pulsed	100 ms	-	-
Franzén (1969)	Fingertip	UDMOL	-	-	ø 8	2	-	Pulsed	10 ms	-	-
Franzén and Nordmark (1975)	-	-	0.5	-	ø 2 ?	-	-	Pulsed	-	-	-
Green (1977)	-	Békésy	1	-	0.008	X	-	Pulsed	10 ms	80 μm pk-pk	1.3 μm pk-pk
Gescheider *et al.* (1978)	Thenar	Békésy	1	-	0.2 - 3.0	1 - 250	-	Pulsed	-	15 dB (re 1μm)	(-7) - 5 dB (re 1μm)
Nishiyama and Watanabe (1981)	Fingertip	MOL	-	-	-	-	-	Continuous	2.5 dB/step	-	-
Lundström and Lindmark (1982)	Fingertip	MOL	-	0.8 N/m²	0.6	?	-	Continuous	10 dB/s	0.5 m/s²	0.35 m/s²
Lundström (1984)	Fingertip	MOL	-	-	-	-	-	Continuous	10 dB/s	3.98 m/s²	1.12 m/s²
Lundström (1985)	Fingertip	MOL	-	0.8 N/m²	0.6	X	-	Continuous	3 dB/s	0.06 m/s²	0.19 m/s²
Verberk *et al.* (1985)	Fingertip	UDMOL	-	3.5	ø 12	X	-	Continuous	5 - 10%/ step	-	0.3 μm pk-pk
Halonen (1986a,b)	Fingertip	MOL	-	Constant	ø 13	X	-	Continuous	-	-	-
Lowenthal *et al.* (1987)	Fingertip	-	-	2 - 8	-	X	-	Continuous	-	-	-
Lamoré and Keemink (1988)	Fingertip	FC	-	-	1.5	1	-	Pulsed	30 ms	-	1 dB (re 1 μm)
Elderson *et al.* (1989)	1st metacarpal	MOL	-	Controlled	ø 13	X	-	Continuous	-	-	-
Fucci *et al.* (1989)	Thenar	ME	-	-	0.128	1	-	Pulsed	50 ms	-	-
Gerr *et al* (1990)	Fingertip	MOL	-	-	-	X	-	continuous	-	-	-
Grunert *et al* .(1990)	Fingertip	UDMOL	-	-	5 mm²	-	-	Continuous	-	-	-

Author	Measurement location	Psycho-physical method[1]	Skin indentation (mm)	Contactor push force (N)	Contactor size (area = cm²) (ø = mm)	Gap[2] (mm)	Push force on surround (N)	Stimulus type	Rate of change of continuous stimuli[3]	Meissner's corpuscle specific[4] thresholds (20 Hz – 40 Hz)	Pacinian corpuscle specific thresholds[4] (100 Hz - 125 Hz)
Wiles *et al.* (1990)	Fingertip	MOL	-	-	-	X	-	Continuous	-	-	-
Harada and Griffin (1991)	Fingertip	-	-	1, 2, 3	-	1.5, 3, X	-	Continuous	-	-	-
Ess and Dupuis (1992)	Fingertip	MOL	-	-	-	X	-	Continuous	-	-	≈ 0.05 m/s² r.m.s.
Lundström (1992)	Fingertip	Békésy	-	≈1	ø 6	X	-	Continuous	3 dB/s	-	-
Gescheider *et al.* (1992)	Thenar	FC	0.5	-	2.9	1	-	Pulsed	-	-	-
Virokannas (1992)	Fingertip	MOL	-	0.2 N	ø 2.6			Continuous	3 dB/s	0.31 m/s²	0.47 m/s²
Deng *et al.* (1993)	Fingertip	FC and MOL	-	-	-	X	Note 5	Continuous	-	-	1.32 Vibration units
Maeda and Griffin (1994)	Fingertips	Békésy	-	1	ø 6	2	2 N	Continuous	3 dB/s	0.11	0.16 m/s²
Bovenzi *et al.* (1998)[6]	Fingertip	Békésy	-	1	ø 6	2	2 N	Continuous	3 dB/s	0.285 m/s²	0.42 m/s²
Doezie *et al.* (1997)	Fingertips	-	-	-	5 mm²	-	-	-	-	0.22 – 0.35 m/s²	0.16 – 0.4 m/s²
Piette and Malchaire (1997)	Fingertips	-	-	-	-	-	-	-	-		0.06 m/s²
Lundström *et al.* (1998a)	Fingertip	FC	-	-	-	-	-	5 second pulse	1 dB/step	0.501 m/s²	0.126 m/s²
Maeda *et al.* (1998)	Fingertip	UDMOL	-	1	ø 6	2	1	Continuous	2.5 dB/step		≈ 0.11 m/s²

[1] MOL = method of limits; UDMOL = up-and-down method of limits; FC = forced choice method; ME = magnitude estimation

[2] X indicates no surround

[3] For pulsed stimuli, rise and fall time is given

[4] Results reported graphically have been approximated.

[5] Smaller than that required to cause finger blanching

[6] Mean of 6 digits for male workers

Table E4 Some reported hot thresholds, cold thresholds, neutral zones and thermal discrimination thresholds obtained using different measurement methods.

Study	Psychophysical algorithm[1]	Reference temperature (°C)	Rate of change of temperature (°C/s)	Measurement location	Minimum discriminable temperature[3] (°C)	Suggested normal cold thresholds[2] (°C)	Suggested normal hot thresholds[2] (°C)	Suggested normal neutral zones (°C)
Mito and Shimizu (1981)	MOL	FST	0.2	Finger tip	-	26.4	32.9	6.5
Hirosawa *et al.* (1983)	MOL	FST	0.12 - 0.2	Finger tip	-	24.5 (SD 2.7)	31.2 (SD 4.2)	6.6 (SD 3.8)
Bertelsmann *et al.* (1985)	MOL	FST	-	Dorsum of hand	0.15 - 0.3	-	-	-
Jamal *et al.* (1985)	FC	34	1	Wrist		33.85 (SD 0.05)	34.23 (SD 0.06)	-
Bertelsmann *et al.* (1986)	FC	FST	-	Dorsum of foot	0.25 - 0.5	-	-	-
Ekenvall *et al.* (1986)	Marstock	-	1.0	Finger tips (digits 2 and 3)				
Kenshalo (1986)	FC	33	1.0	Thenar eminence	-	32.74 (SD 0.2)	33.32 (SD 0.9)	-
Newrick *et al.* (1986)	FC	-	-	Dorsum of foot	9.0 (SD 9.0)	-	-	-
Ekblom and Hanson (1987)	Marstock	34 - 35	0.8	Dorsum of hand	-	-	-	4.8 - 5.5
Goran *et al.* (1987)	FC	FST	1.0	Volar surface of wrist	-	0.16 (SD 0.05)*	0.23 (SD 0.07)*	-
Levy *et al.* (1987)	FC	30	-	Dorso-lateral surface of foot	0.7	-	-	-
Zeigler *et al.* (1988)	Marstock	30	-	Thenar eminence	1.2 (SD 0.5)	29.4 (SD 0.1)	31.3 (0.4)	-
Ekenvall *et al.* (1989)	Marstock	-	-	Finger tips (digits 2 and 3)	-	-	-	5.2 (SD 2.5)
Strain *et al.* (1989)	Modified Marstock	30	1.0	Thenar eminence, day 1	-	28.86 (SD 0.54)	31.92 (SD 1.23)	-
				Thenar eminence, day 2		28.82 (SD 0.46)	31.68 (SD 0.89)	
Claus *et al.* (1990)	MOL	35	1	Right medial malleolus		31.24–0.05xage	39.73+0.07xage	-
Claus *et al.* 91990)	FC	35	1			32.15–0.04xage	39.21+0.06xage	-
Merchut and Cone-Toleikis (1990)	FC	25	-	Finger tip	0.9	-	-	-
Jensen *et al.* (1991)	Marstock	FST	0.7	Thenar eminence	-	-	-	0.5 - 1.8
Schady *et al.* (1991)	Marstock	31	1.0	Thenar eminence	-	-	-	-
Hirosawa *et al.* (1992)	MOL	Thermoneutral temperature	-	Finger tip	-	-	-	-
Verdugo and Ochoa (1992)	MOL	32	2	Thenar eminence		30.6 (SD 0.4)	33.5 (SD 1.2)	

Study	Psychophysical algorithm[1]	Reference temperature (°C)	Rate of change of temperature (°C/s)	Measurement location	Minimum discriminable temperature[3] (°C)	Suggested normal cold thresholds[2] (°C)	Suggested normal hot thresholds[2] (°C)	Suggested normal neutral zones (°C)
Claus *et al* (1993)	MOL	35 ± 0 5	1 0	Ankle	-	33 1 (SD 1 9)	40 1 (SD 1 6)	-
Dyck *et al* (1993c)	FC	FST	0 5	Dorsum of Hand (10cm² contactor)	-	0 12 (SD 0 07)	0 34 (SD o 20)	
				Dorsum of Hand (2 9cm² contactor)	-	0 53 (SD 1 16)	1 16 (SD 1 42)	
Ruffell (1994)	MOL	32 5	0 5 - 2 5	Finger tip	-	27 4	42 5	15 1
Maeda (1994)	MOL?	FST	0 2	Finger tip	-	21 5	38 0	16 5
Ruffell and Griffin (1995)	MOL	28 - 36	1 0	Finger tip	-	2 48 - 5 48	4 22 – 9 11	9 7 - 11 59
Bartlett *et al* (1998)	UDMOL	32	1	Thenar eminence	-	31	33 4	-
Lundstrom *et al* (1998)	Modified Marstock	-	-	Two finger tips, right hand	-	32 8 (SD 1 6)	36 5 (SD 1 6)	3 7 (SD 1 2)
				Two finger tips, left hand		33 0 (SD 1 4)	36 4 (SD 1 4)	3 4 (SD 1 0)
Nilsson *et al* (1998)	Modified Marstock	-	-	Finger tip	-	25 1	34 2	9 1
Tolbana *et al* (1998)	MOL	FST	0 2	Finger tip (right hand)	-	27 2 (SD 4)	36 1 (SD 2 5)	8 9 (SD 5 4)
				Finger tip (left hand		28 6 (SD 3 3)	35 9 (SD 1 9)	7 3 (SD 3 6)

[1]MOL = method of limits; UDMOL = up-and-down method of limits; FC = two-alternative forced-choice stepping algorithm

[2]Where possible, thresholds reported as a temperature change have been converted into absolute temperatures by subtraction or addition of the reference temperature. Results marked with an asterisk are minimum discriminable temperatures in the relevant direction.

[3]The smallest temperature difference in either the positive or negative direction which can be detected.

APPENDIX F A PROCEDURE FOR MEASURING VASCULAR AND NEUROLOGICAL FUNCTION IN WORKERS EXPOSED TO HAND-TRANSMITTED VIBRATION

F1 INTRODUCTION

This appendix summarises a procedure for measuring finger systolic blood pressures, the finger skin temperature response to cold provocation, thermal thresholds and vibrotactile thresholds to enable an investigator to obtain results similar to those in this thesis. The methods have been defined from the literature and improved using the results of work performed in this thesis. The procedure can be used for monitoring vascular and neurological function in workers exposed to hand-transmitted vibration.

F2 TEST CONDITIONS

Measurements of vascular and neurological function should be performed in a room of temperature 22°C (± 2°C), air flow should not be noticeable (< 0.2 ms^{-1}). Subjects should be dressed in light indoor clothing (e.g. shirt and trousers) and they should be habituated to the environment of the test room for at least 15 minutes before tests begin. Ambient noise level should be below about 50 dB(A), sudden and loud noises should be avoided. Hearing protection is recommended when conducting thermal thresholds tests and must be worn during vibrotactile threshold tests.

It is recommended that the finger skin temperature (FST) should be stable and above 26°C before tests begin. The FSTs, measured when tests begin, should be reported with results. Warming of cold fingers should be performed by natural means. If FSTs above 26°C cannot be achieved naturally, results should be interpreted with consideration of the influence of FSTs over neurological function.

Acute effects of exposure to hand-transmitted vibration or extreme environments should be avoided. Caffeine, alcohol and nicotine should not be consumed immediately prior to testing; 4 hours, 12 hours and 2 hours, respectively, are considered appropriate periods of exclusion. Any current medication and diseases or injuries should be reported with results. The neurological tests should be performed before the vascular tests.

F2.1 Tests of neurological function

Subjects should be seated comfortably for neurological tests. The forearm and wrist should be supported, the wrist should be held straight. Measurements should be made on both hands using at least one finger innervated with the median nerve and one finger innervated with the ulnar nerve. Measurements should be made on the fleshy part of the palmar surface of the most distal phalanx of the test digit (i.e. at the centre of the whorl on the distal phalanx). The test digit should rest on, or have rested upon it, a contactor or applicator by which the stimulus is provided; the recommended contact conditions are given in Table 38, Chapter 9. Subjects should practice neurological tests before measurements are made.

F2.1.1 Thermal thresholds

For thermal thresholds, the applicator should be larger than the finger tip and the finger should apply to it a force of 2 N. The hot and cold thresholds should be measured independently using the method of limits, a minimum of six judgements of temperature for each threshold measurement is recommended. The neutral zone can be reported. The rate of change of temperature should be controlled at 1°C/s (± 0.5°C). The reference temperature should be controlled at 32°C (± 2°C), a delay between temperature judgements of 3 or more seconds at this reference temperature is beneficial.

F2.1.2 Vibrotactile thresholds

Vibrotactile thresholds should be measured at 31.5 Hz and at 125 Hz using a fixed frequency, variable amplitude, sinusoidal vibration. The probe providing this stimulus should be 4 mm (± 2 mm) in diameter and it should protrude through a rigid surround. The gap between probe and surround should be 2 mm (± 0.5 mm). The probe should indent the skin by 2 mm ± 0.5 mm or it should apply a force in the finger of 1 N (± 0.5 N). The finger should push on the surround with a force of 2 N (± 0.5 N). The up-and-down method of limits is recommended with a controlled rate of change of stimulus magnitude of 3 dB/s – 5 dB/s. A minimum of six cycles should be completed with the peaks and troughs varying by less than 10 dB within themselves. The test duration at each frequency should be fixed at between 30 seconds and 45 seconds. The threshold should be calculated from the mean of the average peak and the average trough.

F2.2 Tests of vascular function

Subjects should be sitting or lying comfortably during vascular tests. The hands should be supported at the level of the heart, with the wrists held straight during blood pressure measurements and during the settling and recovery periods when measuring the finger skin temperature response to cold provocation. Support for the hands should not thermally influence the skin. If both vascular tests are performed during a single session it is necessary to be aware that there may be a carry-over effect from one application of cold provocation to the next. The test performed first should be that on which greatest emphasis is to be placed, this should be performed on the hand most affected with symptoms for subjects with VWF, or the dominant hand in healthy subjects. The second test performed should be on the other hand.

F2.2.1 Finger systolic blood pressures

Finger systolic blood pressures (FSBPs) may be measured on one test digit and one reference digit, measurement on as many fingers (not including the thumbs) is preferable. Simultaneous measurements on four test fingers can be made. A single-inlet air-inflated cuff should be placed around the proximal phalanx of the thumb (reference digit). If the

thumb is damaged or is missing, the medial phalanx of an alternative finger on the same hand may be used as the reference. If the thumb is reported as having blanching, it should still be used as the reference site but this should be reported. Double-inlet, water-perfused cuffs should be placed around the medial phalanges of the test digits (proximal phalanx of the little finger). Transducers should be attached to the distal phalanges of both the reference and the test digits so as to measure the return of blood flow.

Pressure cuffs should be 24 mm wide. They should fit around the finger so as not to interfere with circulation when deflated. The inner surface of the cuff should remain contiguous with the entire surface of the test site throughout the pressure cycle. Double-inlet cuffs should be thin-walled or of high thermal conductivity. The transducers used should be sensitive to the return of blood flow in the digital arteries during cuff deflation, a strain gauge is recommended. Transducers should not interfere with the circulation, mercury-in-elastic strain gauges are recommended.

Suprasystolic pressure (e.g. 250 mmHg) should be applied simultaneously to all cuffs whilst the tips of the fingers are being squeezed. Water, controlled at the required temperature, should then perfuse the double-inlet cuffs for five minutes. After thermal provocation, water should cease circulating whilst the cuffs are slowly deflated (< 3 mmHg/s) and the transducers detect the return of blood flow in the fingers.

Finger systolic blood pressure should be measured after thermal provocation at 30°C (± 1°C) and then after thermal provocation at 15°C (± 1°C). Where a pathological result is expected but not elicited at 15°C, a further measurement should be made after thermal provocation at 10°C (± 1°C). Measurements should be performed in quick session.

Percentage FSBPs should be calculated using the formula:

$$\%\text{FSBP} = \frac{FSBP_{TEST,t°C}}{FSBP_{TEST,30°C} - \left(FSBP_{REF,30°C} - FSBP_{REF,t°C}\right)}$$

Where *%FSBP* is the percentage FSBP; $FSBP_{TEST,t°C}$ is the FSBP of the test finger after thermal provocation at 15°C or 10°C; $FSBP_{TEST,\ 30°C}$ is the FSBP measured on the test finger after thermal provocation at 30°C; $FSBP_{REF,\ 30°C}$ is the FSBP measured on the reference finger (e.g. thumb) after thermal provocation of the test finger at 30°C; $FSBP_{REF,t°C}$ is the FSBP measured on the reference finger after thermal provocation of the test finger at 15°C or 10°C. Care should be taken when interpreting results using this formula if blanching is reported on the reference finger.

F2.2.2 Finger skin temperature response to cold provocation

The finger skin temperature response to cold provocation can be measured on either one or two hands. The hand(s) to be tested should have thermocouples (or similar transducers) attached at the sites suggested in Figure 5, Chapter 2. Skin temperatures should be recorded continuously throughout the test.

Measurements should commence with a settling period of a minimum of two minutes. When the FSTs are stable, the test hand(s) should be immersed into water controlled at 15°C ± 1°C for a period of five minutes. The hand(s) should be submerged to the level of the wrist on both the palmar and the dorsal surfaces. The hand(s) should be kept dry during immersion by means of a waterproof covering. The covering should provide little or no thermal insulation between the hand(s) and the water. The hand(s) should not be maintained in an ischaemic state during immersion and the waterproof covering should not be tight enough to interrupt blood supply to the skin.

The covering should be removed simultaneously with removal of the hand(s) from the water after the period of cold provocation. The hands should be allowed to recover for a period of 15 minutes. The entire rewarming curve for each measurement location from the beginning of the settling period to the end of the test should be reported. The area above the curve, the percentage of initial temperature or the maximum recovery temperature may be useful parameters to highlight pathological results.

F2.3 Interpretation of results

Interpretation of results should be carried out with respect to the nature of the dysfunction reported by the subject, the presence of disease or injury, and the intake of medications or other vaso-active or neuro-active substances. Normal limits can be used to differentiate between healthy and pathological results, the false positive rate and false negative rate of normal limits used should be known. Repeat vascular tests may be required when it is believed false negative results are obtained. Comparison against normative data should take into account age and gender. Normal data presented in Chapter 3 and Chapter 6 can be applied to populations of male workers but the data is not age specific.

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