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DECLARATION OF AUTHORSHIP AND PUBLICATIONS

The work presented in this thesis is the work of the author who, whilst working in Southampton and under the supervision of Professor John Warner, Professor Janet Stocks and Dr Eleanor Main, devised the methods used to measure force and respiration during chest physiotherapy. The author defined the specifications of all the force-sensing mats, conducted the force-sensing system validation procedures and devised the data collection protocols during pilot studies conducted in the Paediatric Intensive Care Unit at Southampton General Hospital. During this time she defined the analysis variables required for characterising the forces, and commissioned the production of analysis software discussed below.

Dr Martin Browne[1] operated the Instron during equipment validation testing, giving advice on the capabilities of the dynamic testing unit. Dr Graham Petley[2] supervised Rupa Jagannathan[2] and participated directly in the writing of the force analysis software and the respiratory-force overlay software. He also gave invaluable technical advice and support during the validation of the force-sensing system. This work is all contained in Chapter 2.

The clinical study described in Chapter 3 was conducted at Great Ormond Street Hospital for Children NHS Trust, London where the author was awarded a Research Fellowship. However, because award of the study funding coincided with her relocation to Belfast, the study was delayed until a research assistant was appointed. The author commenced training Harriet Shannon in January 2005; Harriet subsequently undertook all the data collection and data management for the clinical study between March 2005 and October 2006, which the author then statistically analysed. In addition, while the author undertook the repeatability studies, these data were analysed by Harriet Shannon, who was the principal author on the repeatability publication (Chapter 2). The footage on the accompanying compact disc (CD) includes children monitored both in Southampton and in London. The earlier study footage from Southampton was taken by Rachael Gregson and the later footage from London was taken by Dr Eleanor Main, for use as part of her teaching material.

[1] School of Engineering Sciences, University of Southampton
[2] Department of Medical Physics and Bioengineering, Southampton University Hospitals NHS Trust

I Rachael Gregson declare that the thesis entitled 'Characterisation of manual chest physiotherapy and respiratory response in mechanically ventilated children' and the work presented in the thesis are both my own, and have been generated by me as a result of my own original research. I confirm that:

- This work was done wholly or mainly while in candidature for a research degree at this University
- No part of this thesis has previously been submitted for a degree or any other qualification at this University or any other institution
- Where I have consulted the published work of others, this is always clearly attributed
- Where I have quoted from the work of others, the source is always given. With the exception of such quotations, this thesis is entirely my own work
- I have acknowledged all main sources of help
- Where the thesis is based on work done by myself jointly with others, I have made clear exactly what was done by others and what I have contributed myself
- Parts of this work have been published as:

Gregson, R. K., Petley, G. W., Browne, M., Pickering, R. M., & Warner, J. O. 2003, "A new method to quantify manual chest physiotherapy techniques", *Physiotherapy*, vol. 289, pp. 611-612.

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Full copies and additional media coverage in APPENDIX A

Signed: …… Date: ……

ABBREVIATIONS

Abbreviation	Definition
ARDS	Acute respiratory distress syndrome
ANOVA	Analysis of variance
CF	Cystic fibrosis
CICU	Cardiac intensive care unit
CP	Chest physiotherapy
CI	Confidence interval
C_{rs}	Respiratory system compliance
CV	Coefficient of variation
CWV	Chest wall vibrations
ECMO	Extra-corporeal membrane oxygenation
FiO_2	Inspired oxygen concentration
Fmax	Maximum force
Fmean	Mean force
GOSH	Great Ormond Street Hospital for Children NHS Trust, London
ICC	Intra-class correlation
ICU	Intensive care unit
ICP	Intracranial pressure
Minf	Manual lung inflations
OI	Oxygenation index
$PaCO_2$	Partial pressure of carbon dioxide
PaO_2	Partial pressure of oxygen
PEEP	Positive end expiratory pressure
PEF	Peak expiratory flow
PICU	Paediatric intensive care unit

PIF	Peak inspiratory flow
PIP	Peak inflation pressure
PRISM	Paediatric risk of mortality scale
R_{rs}	Respiratory system resistance
RR	Respiratory rate
SD	Standard deviation
SE	Standard error
SaO_2	Oxygen saturation in arterial blood
SPSS®	Statistical Package for Social Sciences
tE	Expiratory time
tI	Inflation time
UCL	University College, London
VE	Expired volume
VI	Inflation volume

OBJECTIVES AND OVERVIEW OF THESIS

Chest physiotherapy is integral to the management of mechanically ventilated children and previous research has confirmed that chest wall vibrations are the manual techniques used most frequently by physiotherapists in this population. Chest wall vibrations involve the application of a compressive force to the chest during expiration, with the aim of removing accumulated secretions and improving lung aeration. However, these techniques are largely unquantified and may vary greatly between practitioners and clinical units, with any significance of such variability remaining unknown.

In order to evaluate the effectiveness of any therapy it is important to have a means of quantifying the treatment. It is challenging to measure techniques which involve manual contact between the therapist and patient, and at the inception of this project no means existed of directly measuring the force applied through the hand during treatments. The effectiveness of chest physiotherapy in mechanically ventilated patients is likely to be influenced by the interactions between different treatment components, such as the magnitude and pattern of the chest wall vibrations and the accompanying lung inflations. It is therefore essential to assess both the forces applied during the vibrations with the *simultaneous* changes in air flow, recording the ventilatory pattern throughout the treatment.

The study hypotheses were:

1. *It is possible to create a technique to measure chest wall vibration forces during clinical treatments, and to relate such forces to simultaneous changes in respiratory flows, volumes and pressures*
2. *Maximum and mean force applied during chest wall vibrations increase with the size and age of the child*
3. *Manual lung hyperinflations with chest wall vibrations result in an increase in peak expiratory flow above that observed during baseline mechanical ventilation*
4. *After adjusting for inflation volume, application of chest wall vibrations result in an increase in peak expiratory flow above that obtained during manual lung inflations alone*

The primary objectives of this research were to:

1. Develop a method of quantifying chest wall vibration forces and a means of evaluating simultaneous changes in force with those of respiratory flow and pressure in ventilated infants and children of all ages
2. Estimate the variability over time, within and between individual physiotherapists when treating the same and different subjects with chest wall vibrations
3. Conduct a study to:

i) Assess the feasibility of measuring force and respiration in a population of critically ill, mechanically ventilated children

ii) Characterise the magnitude and pattern of forces applied during chest wall vibrations and evaluate the direct effects of these manoeuvres on flow and pressure changes in the lungs

iii) Determine the relative contribution of manual lung inflations and chest wall vibrations to any observed increase in expiratory airflow

A secondary objective was to explore the short term effects of chest physiotherapy, by recording changes in ventilation, respiratory system mechanics and blood gases following treatment.

The thesis comprises four chapters:

Chapter 1 contains a comprehensive literature review of published studies demonstrating the current knowledge base of the respiratory problems of mechanical ventilation in children, chest physiotherapy in intensive care and the relationship of chest physiotherapy to normal mechanisms of airway clearance.

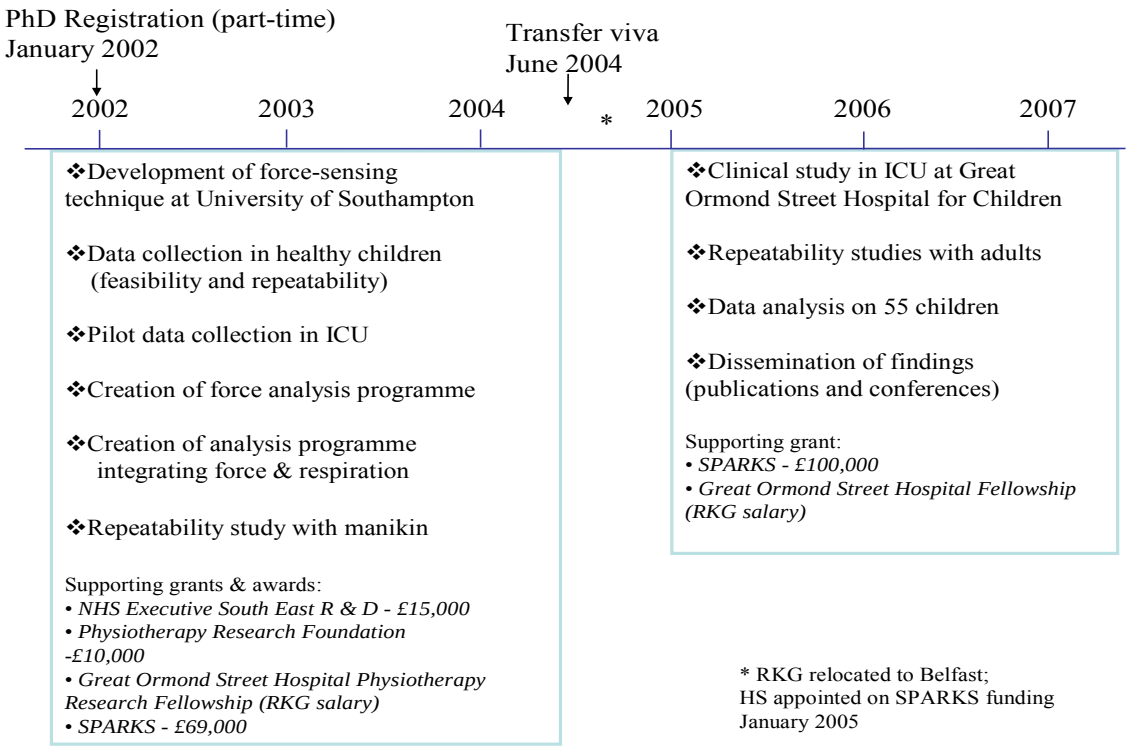
Chapter 2 describes the process of creating a dynamic force-sensing technique to characterise manual chest physiotherapy, detailing protocol and analysis refinement during pilot force and respiratory data collection. Assessment of the variability within and between physiotherapists is also assessed.

Chapter 3 details a clinical study undertaken in intensive care units at Great Ormond Street Hospital for Children NHS Trust, London. The results are presented and interpreted.

Chapter 4 discusses the findings of the thesis in relation to earlier research, highlights the strengths and limitations of the current study, interprets the clinical implications of the research and suggests future work.

The timeframe of this research is summarised below, detailing the main research tasks and the funding stream awarded to the author to support the research.

Timeline detailing the programme of research presented in this thesis



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Chapter 1 Literature review

1.1 Introduction

Over 14,000 children require admission to an intensive care unit in the UK every year (PICANet 2007), many receiving mechanical ventilation during their admission. Chest physiotherapy is considered an important component in the management of these ventilated patients (Ferdinande 1997;American College of Critical Care Medicine of the Society of Critical Care Medicine 1999). In the UK, physiotherapy treatments often involve either manual or ventilator-generated inflations of the patient's lungs, interspersed with the application of manual forces called chest wall vibrations (CWV). A primary purpose of these compressive vibrations is to mobilise secretions centrally into the large airways for removal by suction or cough (McCarren et al. 2006a). Although respiratory physiotherapy and treatments involving the application of compressive forces to the chest wall were first documented several decades ago (MacMahon 1915;Opie & Spalding 1958), the techniques remain largely unquantified and their direct effects on respiratory function have not been evaluated.

This review focuses initially on the heightened vulnerability of children to respiratory compromise and problems associated with mechanical ventilation. Chest physiotherapy is described and available research is reviewed. Studies evaluating the various modalities used in the paediatric intensive care unit (ICU) are discussed. Measures previously used to investigate chest physiotherapy in the ICU, and available options for monitoring outcome are evaluated. The normal mechanisms of airway clearance are then discussed. The chapter concludes with a summary of the current knowledge base of chest physiotherapy in mechanically ventilated children, and a statement of the resulting research hypotheses and objectives.

The review was informed by conducting computerised searches of Medline® from 1960 and Embase® from 1974 to the present. Additionally, the ISI Web of Knowledge® facilitated linkage between relevant articles. Keywords included: Physical Therapy Modalities / Techniques, Chest Wall Oscillation, Respiratory Therapy, Intensive care, Child, Repeatability, Respiratory Function Tests, Measurement Technique, Cough, Airway clearance, Lung inflations, Adverse events.

1.2 Developmental changes in lung function and children's increased vulnerability to respiratory compromise

Neonates and young children are particularly susceptible to airflow obstruction. The immaturity, both structurally and functionally, of the diaphragm and the instability of the thoracic cage reduce the infant's ability to cope with additional respiratory loads and result in impaired gas exchange compared with adults. Their heightened vulnerability relates to important differences in their anatomy and physiology as described below.

1.2.1 Upper airways obstruction

The anatomy of the upper airway allows infants to feed and breathe simultaneously until approximately 3-4 months of age. During this time, infants are preferential nose-breathers, and nasal obstruction can lead to periods of apnoea (Rodenstein et al. 1987). The combination of a proportionately larger tongue, higher placement of the larynx and enlarged lymphatic tissue (tonsils and adenoids) may lead to upper airway obstruction. In addition, the airways of pre-term infants and young children are highly compliant, with proportionately more mucus glands than in older subjects, factors which further increase their tendency to close during inspiration (Reid 1984;Shaffer et al. 1989;Penn et al. 1989).

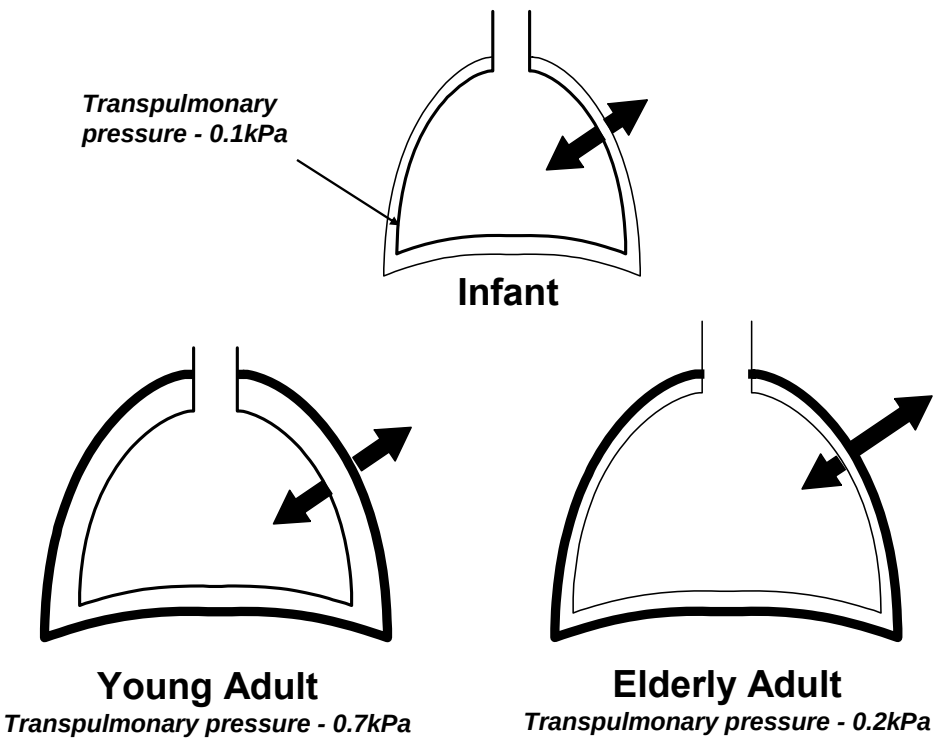
1.2.2 Diminished alveolar surface area and reduced collateral ventilation

Development of the conducting airways is complete by the end of the first trimester of pregnancy (Bucher & Reid 1961). However, alveolar development lags behind, with rapid alveolar multiplication during the last trimester and first two years of life, this process being virtually complete by the age of three years and continuing more slowly until the age of eight (Thurlbeck 1982;Reid 1984). This diminishes the surface area for gaseous exchange in young children, and lung damage during the time of alveolar growth can reduce respiratory function in the longer term (Hislop & Haworth 1989). It also means that there is less alveolar tissue to support small airways, resulting in airway closure even within the tidal breathing range during expiration in young infants. Decreased numbers of pores of Kohn exist in infancy and collateral ventilation is poorly established until 2-3 years of age, further predisposing to atelectasis (Allen et al. 1993;Stocks & Hislop 2002). The reduced lung compliance in pre-term infants (who lack normal surfactant levels) further hinders gaseous exchange.

1.2.3 Decreased chest wall compliance and chest-lung interactions

Respiratory function studies show that lung volumes increase dramatically through infancy, childhood and into adolescence. There is substantial increase in the size of the thoracic cage during growth and an increasing ability to support the lung more effectively. The chest wall has a major influence on the underlying lung (**Figure 1.1**). The arrows represent the relative magnitude of the inward lung and outward chest wall recoil. Outward recoil is reduced in the infant and young child (Turner et al. 1968;Gerhardt & Bancalari 1980). This is due to the increased thoracic cage compliance, with ribs being less mineralised than in older subjects. When compared with the young adult, transpulmonary pressure is reduced in both the infant, due to decreased chest wall recoil, and in the elderly, due to loss of lung recoil.

Figure 1.1 Maturational changes in lung and chest wall recoil and transpulmonary pressure at end expiration

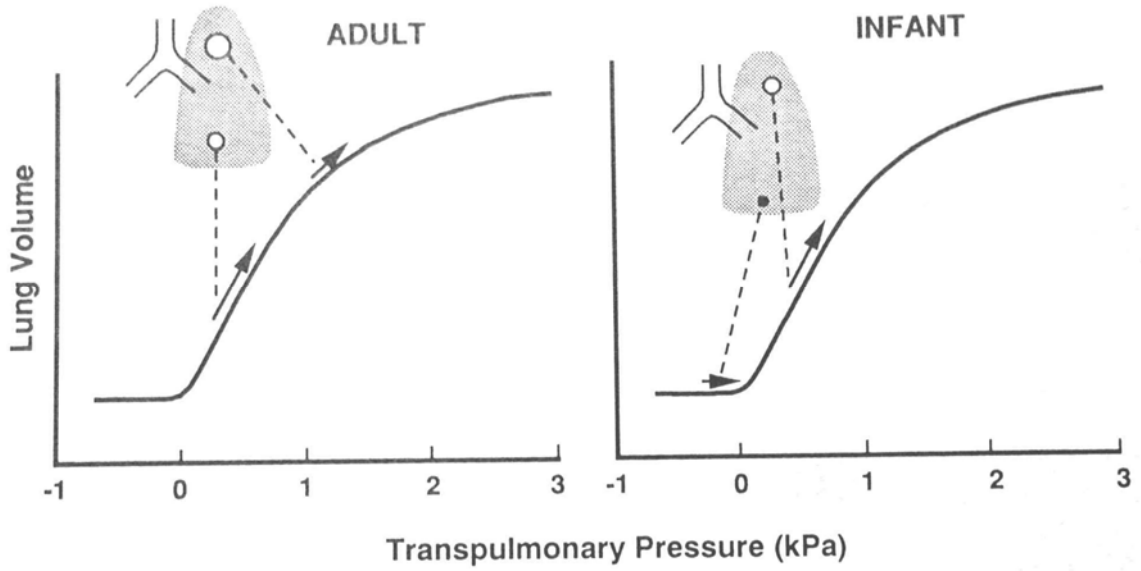


At end-expiration, transpulmonary pressure is less negative in both the infant and in the elderly than in the young adult. In the elderly this is caused by emphysematous changes with loss of lung recoil. By contrast, in the infant, lung recoil is similar to an adult's but the extremely compliant thoracic cage results in less outward recoil with which to keep the lungs and airways distended.

Illustration reproduced with permission from J Stocks

The ribs are at right-angles to the spine in recumbent infants. There is therefore limited capacity with rib movement to raise intra-thoracic volume, diaphragmatic contraction tending to distort the rib cage, further limiting volume changes. The low outward recoil allows the lung to deflate to low volumes, where peripheral airway function and gas exchange may be impaired (**Figure 1.2**).

Figure 1.2 Idealised lung pressure-volume relationships in a young healthy adult and normal infant



Transpulmonary pressure is relative to the atmosphere and the typical vertical lung pressure gradient is shown. Note that in the adult the lung apex is relatively over-distended, whereas the base is relatively compressed, although it is on the ideal portion of the volume/pressure curve. In the infant, the lung base is within the closing volume range, whereas the apex is on the ideal portion of the curve. *Illustration reproduced with permission from Taussig and Helms, 1996*

To overcome the tendency of the lung to collapse to very low volumes, the young infant adopts a strategy of modulating expiratory flow by a combination of laryngeal braking and post-inspiratory diaphragmatic braking, prolonging the expiratory time constant (τ) and sustaining an adequate resting lung volume or end-expiratory volume until the chest wall stiffens with maturity (Kosch & Stark 1984;Mortola et al. 1985;Kosch et al. 1988). Transition to a more relaxed pattern of expiratory flow occurs between 6 and 12 months of age (Colin et al. 1989;Ratjen et al. 1989). In young mechanically ventilated patients the presence of a tracheal tube prevents this laryngeal braking. However, use of positive end-

expiratory pressure (PEEP) helps maintain the end-expiratory volume above the closing volume of the airways.

The large central airways are supported by cartilage to resist collapse during expiration, whereas the small peripheral airways have no such support and remain patent by relying on the transpulmonary distending pressure, together with the surface-tension reducing properties of surfactant (Shaffer et al. 1989). In early infancy this distending pressure at end expiration is approximately 0.15 kPa, rising towards 0.75 kPa in early adult life (Helms et al. 1981). These low transpulmonary distending pressures and the accompanying tendency to airway closure in the small intrapulmonary airways render the infant and very young child vulnerable to airway obstruction, as shown in **Figure 1.2**. In the infant, peripheral airways may account for a significant proportion of the resistance of the conducting airways. This is in contrast to the young adult and adolescent where they account for a negligible proportion of total resistance to airflow (Helms & Stocks 1982). Nevertheless, because airway development precedes the development of alveoli in utero, at birth the airways are relatively large in proportion to the gas exchanging region of the lung in later life. This is associated with a relatively low airway resistance at birth. The subsequent rapid increase in lung volume in relation to airway size is referred to as dysanaptic growth (Doershuk et al. 1974;Tepper et al. 1986).

The increased tendency of the peripheral airways to close and the reduced alveolar surface area also result in relatively low arterial oxygen tension in infants and very young children (Gaultier et al. 1978). As in the adult, perfusion is greatest in the dependent lung area which, in upright subjects, is the lung bases (Bhuyan et al. 1989). However, because of poor lung support by the compliant chest wall, basal ventilation is reduced, preferential ventilation occurring in the uppermost lung regions (**Figure 1.2**), resulting in a significant ventilation-perfusion mismatch (Davies et al. 1985). Arterial oxygen tension reaches adult values by the age of four to five years, leading some to suggest the adult pattern of matched ventilation and perfusion at the lung bases is achieved in early childhood (Gaultier et al. 1978), whilst others believe the difference may persist until at least 10 years of age (Allen et al. 1993). These are important considerations when treating infants and young children with unilateral disease who require both gravity-assisted lung drainage and optimisation of ventilation, as positioning the affected lung uppermost to optimise lung

drainage may worsen ventilation. Clinical practice suggests the pattern is highly variable and must be assessed on an individual basis.

1.2.4 Ineffective response to increased respiratory loading

The high compliance of the rib cage also affects its stability and allows it to distort with increased respiratory loading (Muller & Bryan 1979). In addition to the distribution of airflow resistance towards the lung periphery in infancy and the greater predisposition to obstruction, the young child's ability to cope with added respiratory loads is further reduced by the respiratory pump configuration already described. In older children and adults, the 'bucket handle' movement of the ribs results in thoracic expansion. Such expansion cannot occur in young children because of the horizontal rib placement (Openshaw et al. 1984). The combination of a compliant chest wall, horizontal ribs and poorly developed intercostal muscles results in the diaphragm assuming even more prominence. However, diaphragmatic excursion is reduced because of its direct, horizontal angle of insertion which is less efficient than the domed adult diaphragm. To maintain minute volume, the infant must therefore increase respiratory rate rather than depth. In addition, the young infant has fewer type I, fatigue-resistant muscle fibres (slow twitch, high oxidative fibres) and is therefore at a greater risk of developing respiratory fatigue (Muller & Bryan 1979). Neonates have approximately 25% type I fibres (half the adult proportion of fibres) and pre-term infants may have less than 10% fatigue-resistant fibres.

The upper lobes of infants are more prone to atelectasis than the bases, a feature which is believed to be due both to the restricted movement of the upper thorax and the diaphragmatic, abdominal pattern of respiration (Rees 1958). In addition, in infants the heart and other organs including the thymus are relatively large in comparison with the lungs, occupying proportionately more thoracic volume.

1.2.5 Proportionately higher basal metabolic rate

In healthy adults, the resting energy expenditure of the respiratory pump is very low, equivalent to two lumps of sugar for a whole 24 hour period (Otis 1964). By contrast, infants have a high basal metabolic rate, increasing dramatically to nearly half the daily energy intake in infants with severe upper airways obstruction, as for example in Pierre Robin syndrome (Crosfill & Widdicombe 1961). Further demands for oxygen can

therefore rapidly cause hypoxaemia and studies have shown the detrimental effects on critically ill children of any handling procedure (Harding et al. 1994;Cohen et al. 1996;Horiuchi et al. 1997), as discussed in **section 1.5.2**. In contrast to the hypoxaemia-induced tachycardia of adults, infants respond to hypoxaemia with bradycardia (<100 beats per minute).

1.2.6 Respiratory patterns in pre-term infants and neonates

Pre-term infants and neonates sleep for up to 20 hours a day and may have irregular respiratory patterns, including periods of apnoea. Neonates may spend up to 80% of sleep time in rapid eye movement (REM) sleep, compared with 20% in adults. Rapid eye movement sleep causes decreased postural tone and a drop in functional residual capacity, thereby increasing the work of breathing (Muller & Bryan 1979).

1.2.7 Tracheal intubation

Since the cricoid cartilage is a complete ring, infants and young children have been preferentially intubated with uncuffed tubes to avoid trauma to the mucosa, which can result in scarring and subglottic stenosis. Although it is considered desirable to maintain a small tracheal leak to prevent mucosal damage, moderate or large tracheal leaks result in inconsistent delivery of ventilation and inaccurate monitoring of respiratory function (Kuo et al. 1996;Main et al. 2001). Furthermore, research suggests cuffed tubes can be used safely if monitored appropriately (Deakers et al. 1994;Khine et al. 1997;Newth et al. 2004).

1.2.8 Infants' response to bronchodilators

The use of bronchodilators in young infants may diminish the tone of the airway muscle, further reducing airway stability and resulting in a paradoxical response (Zach et al. 1981;Oberwaldner 2000).

1.3 Respiratory complications of mechanical ventilation

Patients may require mechanical ventilation for a variety of reasons including respiratory support following a neurological insult, or surgery or for a primary respiratory disorder. Although the patient's lungs may be healthy at the time of commencing ventilatory support, it is now widely accepted that mechanical ventilation itself may result in secondary lung injury. Possible causes include over-distension of aerated alveoli by inappropriately large tidal volumes [volutrauma (Dreyfuss et al. 1988)], repetitive shear stresses generated during the recruitment and de-recruitment of lung units at the junction of aerated and collapsed lung segments [atelectotrauma (Taskar et al. 1997)], inflammation secondary to the mechanical injury induced by volutrauma and atelectotrauma [biotrauma] and infective or ischaemic necrosis of persistently collapsed lung tissue (Tremblay et al. 1997;Slutsky & Tremblay 1998;Dos Santos & Slutsky 2000).

1.3.1 Effects of intubation on airway clearance

The use of an artificial airway during mechanical ventilation provides both opportunities and challenges to clinicians concerned with airway clearance. For example, it provides direct access to the airways for catheter suctioning of secretions and a direct route for delivery of medications that promote secretion mobilisation. However, the presence of the airway bypasses the filtering mechanisms and immune defences in the nose and pharynx as well as impairing the upper airways' natural mechanisms of airway clearance of cough and mucociliary function, as discussed in **section 1.6**. In addition, the more vertical alignment of the right main bronchus leaves children susceptible to upper lobe collapse which can occur if the tracheal tube extends into the right main bronchus, beyond the bifurcation for the right upper lobe.

The clearance of pulmonary secretions is a complex process that requires the integration of mucus production, ciliary movement and cough (Wanner 1977). By preventing glottic closure during intubation, cough is compromised, leaving the airway more susceptible to infection. Furthermore, mucus transport appears to cease at the tip of the tracheal tube and regular suction is required (Konrad et al. 1992;Konrad et al. 1994;Muscedere et al. 2008). Mucosal inflammation, erosions and reflex hyper-secretion caused by the tube's movement may also reduce mucus transport and alter airway reactivity (King et al. 1985b). In addition, disease processes may alter the rheology of the mucus, increasing secretion visco-elasticity (Rubin 2007). Drugs used for muscle relaxation, anaesthesia, analgesia and

sedation further impair respiratory function, compromising normal airway clearance (Pavia et al. 1983b;Pavia 1990;Ledowski et al. 2008). Mucociliary function may also be affected by the delivery of dry gases and the maintenance of a reduced body temperature.

1.3.2 Atelectasis, hypoxaemia and pneumonia

In an intubated, immobile patient, pulmonary atelectasis and accumulation of mucus occur in the dependent lung zones (Gamsu et al. 1976). During mechanical ventilation in the supine position, the passive movement of the diaphragm results in less excursion dorsally where opposing pressure from the abdominal contents is greatest (Muller & Bryan 1979). The abdominal contents push in a cephalic direction, decreasing the functional residual capacity and augmenting pooling of secretions in the dorsal areas of the upper and lower lung zones. Complete or partial closure of the alveoli will result in lowering of their compliance, requiring a greater level of opening pressure to restore alveolar patency. Despite the lung's response of hypoxic pulmonary vasoconstriction, atelectasis may result in hypoxaemia due to the development of a shunt (the perfusion of non-ventilated alveoli), pooled and stagnant secretions acting as a focus for bacterial proliferation and culminating in ventilator-associated pneumonia (van Kaam et al. 2004).

As a result of these factors, despite regular suctioning patients receiving mechanical ventilation have a tendency to retain secretions, promoting atelectasis, bacterial colonisation and pneumonia, hypoxaemia and possible fibrosis (Gamsu et al. 1976;Glauser et al. 1988;Bowton 1999;Members of the European Task Force et al. 2001;Muscedere et al. 2008). Post-operatively, the complexity of maintaining a patent airway is further confounded by the problems of anaesthesia, surgery and pain (Gamsu et al. 1976). The common occurrence of pneumonia in adult, paediatric and newborn patients admitted to ICU has led to an increased mortality rate, especially when complicated by systemic sepsis leading to septic shock (Bonten et al. 1996;Bonten et al. 1997;Vincent 1999;Grohskopf et al. 2002). Minimum standards of airway care have been proposed to reduce the incidence of ventilator-associated pneumonia (Dodek et al. 2004;Muscedere et al. 2008).

1.3.3 Principles of mechanical ventilation

Whilst tidal volumes in normal subjects at rest are in the range of 7 to 8 ml per kilogram, traditional approaches to mechanical ventilation used volumes of 10 to 15 ml per kilogram

of body weight (Marini 1996). These larger volumes were frequently necessary to achieve normal values for the partial pressure of arterial carbon dioxide and pH. However, research suggested that this traditional approach may delay healing of the injured lung. In animals, ventilation with large tidal volumes caused the disruption of pulmonary epithelium and endothelium, lung inflammation, atelectasis, hypoxaemia and the release of inflammatory mediators, increasing lung inflammation and causing injury to other organs (Dreyfuss et al. 1988;Marini 1996;Tremblay et al. 1997;Slutsky & Tremblay 1998). It was therefore suggested that the traditional approach to mechanical ventilation might exacerbate or perpetuate damage in ventilated patients with acute lung injury and acute respiratory distress syndrome (ARDS), increasing the risk of non-pulmonary organ or system failure (ARDSnet 2000). These findings led to a growing trend to explore the use of lower inflation volumes, placing a high emphasis on preventing excessive lung stretch during adjustments to mechanical ventilation (Muscedere et al. 1994;Marini 1996). As a result, the first priority of ventilation shifted from optimising oxygen exchange, oxygen delivery or respiratory system compliance to ensuring adequate lung protection and avoiding lung injury.

Although controversial, levels of peak inspiratory pressure greater than 35cm$H_2$0 are generally associated with increased risk of barotrauma (Dreyfuss et al. 1988;ARDSnet 2000). In addition to being caused by excessive stretch, lung injury may also result from repeated opening and closing of small airways or from stretch at the margins between aerated and atelectatic regions of the lungs (Tremblay et al. 1997). It has been shown that these types of lung injury may be prevented by the use of higher levels of positive end expiratory pressure (PEEP) to maintain the patency of the airways (Dreyfuss et al. 1988). High pressure recruitment manoeuvres have been advocated to open up the lung (Hammer & Newth 2005). Most involve the transient use of sustained inflations with high inflation pressures and the application of PEEP to maintain ventilation above the critical closing pressure of the lung.

Recent studies offer further insights into ventilator-induced injury and atelectotrauma. For example, it has been suggested that a sustained lung inflation followed by early nasal continuous positive airway pressure (through a nasopharyngeal tube) may offer an efficient and less injurious form of intervention in very preterm infants than conventional ventilation strategies of repeated manual lung inflations through a face mask (te Pas & Walther 2007).

It has also been postulated that the optimal combination of tidal volume and PEEP stabilises alveoli, thus diminishing recruitment / derecruitment and reducing ventilator-induced lung injury. Using ventilated piglets as an animal model of acute respiratory distress syndrome, Halter et al. used in-vivo microscopy to visualise directly the effect of high and low tidal volume and PEEP on alveolar mechanisms, correlating alveolar stability with lung injury (Halter et al. 2007). Their observations supported the suggestion that a ventilatory strategy employing high tidal volume and low PEEP causes alveolar instability. By contrast, low tidal volume and high PEEP worked synergistically to stabilise alveoli; increased PEEP appeared more effective at stabilising and 'protecting' alveoli than reduced tidal volume. The accompanying minimal changes in cytokines and proteases led the authors to suggest that the mechanism of lung injury in the high tidal volume /low PEEP group was mechanical, not inflammatory in nature. Alveolar derecruitment was defined as the difference in lung volume measured at a fixed airway pressure (15 cmH_2O) on pressure-volume curves performed at PEEPs of 15 and 0 cmH_2O. Such PEEP-induced lung derecruitment can be assessed at the bedside by the pressure-volume curve method and the measurements have been shown to be tightly correlated with computed tomography scan measurements (Lu et al. 2006).

Despite the respiratory vulnerability of infants and young children (**section 1.2**), laboratory data suggest that children may be more resilient than adults to any harmful effects of mechanical ventilation (Copland et al. 2004;Kornecki et al. 2005). A recent case series of children with ARDS suggested that, within observed limits, incremental increases in tidal volume might not have the major impact on outcomes that occur with adults (Flori et al. 2005). Although ventilator settings must be monitored carefully in all patients, mechanical ventilation may simply cause less injury to children. If so, it may be far more difficult to demonstrate the impact of varying ventilation strategies in children than in adults (Kavanagh 2005).

It can be seen that the young child is acutely vulnerable to respiratory compromise, a situation which is made worse by the process of mechanical ventilation. Chest physiotherapy is given to ventilated children to replace the normal mechanisms of airway clearance (**section 1.6**) and optimise ventilation. These treatments require a thorough knowledge of the anatomical and physiological development of children (Zach et al. 1981;Oberwaldner 2000).

1.4 Chest physiotherapy in ventilated children

The management of airway function in ventilated patients involves appropriate ventilatory control, regular suction, chest physiotherapy and pharmacotherapy. Primary aims of physiotherapy in these patients include secretion removal, restoration or maintenance of lung volume and optimisation of ventilation with perfusion, thereby improving oxygenation, decreasing lung resistance and increasing compliance. In the UK, physiotherapy often involves cycles of several treatment components including positioning, manual chest physiotherapy with lung hyperinflations (**Figure 1.3**) and suction which may be preceded by saline instillation. Clinical techniques and protocols for chest physiotherapy vary greatly from one intensive care unit to another (Lewis et al. 1992;Hodgson et al. 1999;Stiller 2000;Norrenberg & Vincent 2000;Chaboyer et al. 2004) and may vary between practitioners within the same unit.

Figure 1.3 Multimodality physiotherapy in a ventilated child

The intubated child is receiving chest wall vibrations from the therapist's left hand, combined with lung inflations from her right hand; suction with saline was also used (not shown).

1.4.1 Chest wall vibrations

Manual chest physiotherapy can broadly be divided into percussive (intermittent chest clapping with a cupped hand or face mask) or compressive techniques (Sutton et al. 1985), **Figure 1.4**. Whilst chest percussions may have a role in spontaneously breathing infants, they would not generally be the treatment of choice in mechanically ventilated infants and children, physiotherapists predominantly favouring chest wall compressions (Main et al. 2004;McCarren et al. 2006a;McIlwaine 2007).

Figure 1.4 A newborn baby receiving percussions with a face mask (left) and finger-tip chest wall vibrations (right)

Terms used in the literature to describe chest compressions have included vibrations, shaking and expiratory flow increase techniques (Sutton et al. 1985;Wong et al. 2003;Almeida et al. 2005). Since the techniques may overlap and have not been objectively defined, the general term 'chest wall vibrations', or CWV, will be used in this thesis to encompass all compressive manoeuvres applied during expiration. The vibrations are believed to aid secretion clearance and involve the application of a rapid extra-thoracic compressive force at the beginning of expiration, followed by oscillatory compressions until expiration is complete. At bronchoscopy, secretions have been seen to move into the upper airways when vibrations are applied to the chest wall (Ciesla 1996).

A number of physiological mechanisms have been proposed regarding the way in which chest physiotherapy may aid secretion clearance. The work is based largely upon research in simulated models or animals, and proposed mechanisms include:

1) increasing absolute peak expiratory flow (PEF) to move secretions towards the oropharynx (King et al. 1985a;Webber & Pryor 1989;van der Schans et al. 1999;McCarren et al. 2006a)

2) improving the expiratory bias of airflow to increase the annular flow of mucus towards the oropharynx, which occurs when the peak expiratory flow is at least 10% greater than peak inspiratory flow (PIF), i.e. PEF/PIF ratio ≥ 1.1 (Clarke et al. 1970;Chang et al. 1984;Kim et al. 1987;Benjamin et al. 1989;King et al. 1990)
3) increasing mucus transport by decreasing the viscosity of mucus and improving expiratory flow due to the effects of oscillation of airflow at frequencies ranging from 3–17 Hertz [Hz], some suggesting an optimal frequency of 13 Hz (King et al. 1984;Gross et al. 1985;King 1998)
4) eliciting spontaneous coughs via the mechanical stimulation of the airways (Mellins 1974)
5) improving mucociliary interaction [ciliary stimulation, alteration in the rheological properties of airway mucus] (King et al. 1974;King et al. 1985a).

1.4.1.1 Quantification of CWV

It is challenging to measure treatments which involve manual contact between the therapist and patient and at the outset of this research programme there had only been limited attempts to characterise the forces applied during chest physiotherapy (Rivingtonlaw et al. 1984;Blazey et al. 1998). Rivingtonlaw used a blood pressure cuff to measure the physiotherapist's hand pressure during CWV, a technique which is liable to inaccuracies and likely to have affected the therapist's routine treatment by impairing normal feedback mechanisms. Blazey et al. studied chest percussions by indirectly measuring the force applied to a healthy adult's chest, through load cells in the bed beneath the patient. Mean (SD) frequency and force of percussions were 7 (1) Hz and 58 (15) Newtons [N], respectively. The rate and force of percussions varied amongst the physiotherapists, and no relationship was found between the physical stature of the therapist and the force applied.

More recently, McCarren et al. used a similar instrumented plinth to monitor CWV (McCarren et al. 2006a;McCarren et al. 2006b), as summarised in **Table 1.1**. While these methods successfully assessed force application by therapists on healthy volunteers, they did not directly measure the force applied through the hand and it is likely that some of the force would be dissipated and absorbed by the subject's thorax or by the treatment couch. Furthermore, this method cannot easily be used in clinical environments such as intensive care.

Table 1.1 Recent studies exploring force, airflow and/or pressure during chest wall vibrations

Attached as separate file as landscape

McCarren et al. derived mean and peak force from the directional force vectors. The physiotherapists were asked to i) perform CWV and ii) separate their techniques into chest oscillations and compressions. Such division yielded valuable information as to the relative contributions of the component parts of chest compression and oscillation. However, it could be argued that the separation was artificial, encouraging the participants to consider their treatment styles in terms of the compressive and oscillatory components, this perhaps influencing their normal treatment style. The data obtained were limited in that only one force trace from a single CWV was included for publication, despite significant between-physiotherapist variability (mean resultant force 74.4 N [SD 47.1 N]) (McCarren et al. 2006a). No data on within-subject variability were presented. The large amplitude oscillations were more clearly presented in the publication exploring intra-pleural pressure, where the amplitude was approximately 50% maximum force applied, occurring at approximately 6 Hz (McCarren & Alison 2006;McCarren et al. 2006a;McCarren et al. 2006b). There was significant between-subject variability in the oscillatory component, and no data were presented on the repeatability of the treatments. By contrast Jones et al. measured the intra-class correlation (ICC) of transmitted forces in healthy adults using a Kistler™ force platform (Jones et al. 2005). They observed marked variation between physiotherapists in the delivery of CWV (ICC 0.082), but reported no absolute values for force.

1.4.1.2 Respiratory changes during CWV

At the outset of this research, limited data were available on respiratory changes during CWV. Maclean et al. reported an increase in PEF in 9 ventilated adults treated with CWV, expiratory flow increasing further when an abdominal binder was additionally applied during the physiotherapy (Maclean et al. 1989); force was not measured. Flows and volumes were also measured in the recent studies exploring CWV in spontaneously breathing healthy adults and young adults with cystic fibrosis (CF) who were clinically stable and whose lung function ranged from normal to severely abnormal, **Table 1.1** (McCarren et al. 2006a;McCarren et al. 2006b). A calibrated, heated pneumotachograph was used for all studies, and PEF during chest physiotherapy (PEF_{CP}) exceeded that during a relaxed expiration from total lung capacity, but was significantly less than that obtained during cough (PEF_{COUGH}). The authors concluded that CWV should only be used in situations where the patient's ability to cough was compromised, as is the case in mechanically ventilated patients. Peak expiratory flow was higher during CWV than other

physiotherapy interventions used to treat those with CF, and the oscillation frequency (mean 8.4 Hz, SD 0.4 Hz) fell within the range which is believed to increase mucus transport (**section 1.6**). The authors also commented that obtaining a PEF:PIF ratio > 1.1 to aid secretion clearance during CWV was dependent upon the instruction given, which needed to encourage a slow breath in, rather than a gasp-like maximal inspiration (an important consideration for physiotherapy in spontaneously breathing subjects).

The lower flows obtained during CWV compared to cough are unsurprising since there was neither a compressive phase of muscle activity against a closed glottis nor an expiratory effort during the expulsive phase, the latter being replaced by the physiotherapist's manual compressive force (**section 1.6.1**). Interestingly, in those with CF, although PEF_{COUGH} was three-fold greater than that during the CWV (mean (SD) 4.7 (1.9) l/s and 1.6 (0.7) l/s, respectively), PEF_{COUGH} was considerably less than that recorded in the healthy subjects, who showed an eight-fold increase from PEF_{CP} (mean (SD) 8.1 (0.92) l/s and 1 (0.27) l/s, respectively). The cough values obtained in those with CF were also lower than the 6-20 l/s reported elsewhere in healthy subjects (McCool 2006). Since all McCarren's studies involved the same method for measuring flow, and values of PEF_{CP} were comparable or greater in those with CF, the lower values obtained during cough in the CF patients may reflect muscle weakness or reduced lung recoil, related to the subjects' underlying disease state with an associated poor nutritional status.

The authors reported that changes in intrapleural pressure and PEF during CWV appeared to be the sum of those changes due to lung recoil, and the compressive and oscillatory components of CWV, suggesting all three components were required to optimise PEF_{CP}. They commented that the relative contributions of the three components might differ according to airway resistance and chest wall compliance. Whilst it is feasible that the large amplitude oscillations recorded in their studies of healthy adults would independently influence PEF and intrapleural pressure, it remains unclear whether similar results would be obtained with vibrations involving smaller amplitude oscillations, and in young children with more compliant chest walls.

1.4.2 Manual lung inflations

Lung hyperinflations are used to prevent and treat pulmonary complications in ventilated patients by lung volume recruitment and mobilising pulmonary secretions towards the larger, central airways for removal by suction, resulting in improved oxygenation, increased lung compliance and decreased resistance (Mead et al. 1967;Mackenzie 1989;Stiller 2000;Paratz et al. 2002;Ntoumenopoulos 2005). In Clement's original description in the 1960s, a large inflation volume was delivered at slow flows via a resuscitation circuit (Clement & Hubsch 1968). The slow inspiration was followed by an inspiratory pause and a rapid release of the inflation reservoir ('bag') to increase expiratory airflow. Hyperinflations may be used in isolation or combined with CWV to augment expiratory airflow (Clement & Hubsch 1968;Denehy 1999). Hyperinflations to re-expand areas of atelectasis rely upon the collateral ventilatory systems in the lung, the age-dependence of which was described in **section 1.2.2**.

While no research appears to have been conducted to explore lung inflations during CWV, studies of manual hyperinflations per se have been conducted using test lungs, adults and animals. Debate concerning the use of manual lung inflations must additionally include the more extensive research available on mechanical ventilation and lung injury which informs paediatric ventilation strategies and was discussed in **section 1.3.3**.

1.4.2.1 In-vivo studies of manual hyperinflation

Lung 'hyperinflation' has been defined as the delivery of a breath that is at least 50% greater than baseline tidal volume, generating an increase in elastic recoil and an increased expiratory airflow (Glass et al. 1993;Singer et al. 1994). However, Singer's research in ventilated adults suggested that the increase was frequently not achieved. They also demonstrated a correlation between an increase in tidal volume and a fall in cardiac output. Change in cardiac output was not related to peak inflation pressure (PIP). Recent research involving manual lung hyperinflation of healthy sheep also found that an increased intra-thoracic pressure applied during a prolonged inspiration significantly decreased cardiac output and was accompanied by compensatory vasoconstriction, with increased vascular resistance and mean arterial pressures (Anning et al. 2003). The authors concluded that a decreased cardiac output may result from positive inflation pressure in subjects with normal cardiac and respiratory function, suggesting that, in patients with compromised

cardiac output, a long inspiratory phase with an end-inspiratory pause may be contra-indicated.

Clarke et al. sought to relate peak airway pressure, tidal volume and lung injury scores in 25 ventilated adults during manual hyperinflations. They found an average increase of 170% tidal volume delivered but with wide variation, and a correlation between PIP and lung injury, PIP ranging from 37 to 74 cmH_2O with a mean (SD) of 51.5 (7.6) cmH_2O (Clarke et al. 1999) They also reported a correlation between lung injury score, inflation pressure and tidal volume, suggesting that more diseased lungs were subjected to a higher inflation pressure per unit inflation volume. These findings suggest an increased potential for barotrauma or volutrauma in susceptible lungs. A recent study documented the pattern of ventilation during manual lung inflations in 18 adults who were treated by the same physiotherapist on two consecutive days using the Mapleson-F® circuit (Maxwell & Ellis 2007). Eleven junior physiotherapists took part and the researchers explored the inspiratory and expiratory flows, volumes, pressures and times using a heated pneumotachometer and pressure transducers. The authors concluded that all the physiotherapists achieved an increase in volume within a "safe and effective pressure range", 26 of the 34 sessions comprising techniques "recommended for enhancing secretion clearance" by creating an appropriate expiratory flow bias. However, a wide range of volumes was delivered (0.64 to 2.16 litres), PEF varied considerably (1.06 to 7.18 l/s) and whilst mean PIP was 36 cmH_2O it ranged from 19 to 57 cmH_2O.

Berney and Denehy proposed that hyperinflations could be performed equally well using a manual circuit or by mechanical ventilation, both methods producing similar volumes of secretion clearance and improvements in static compliance in 20 ventilated adults (Berney & Denehy 2002). Others have suggested that whilst both manual and ventilator hyperinflations had equal benefit, ventilator hyperinflations produced less metabolic disturbance, perhaps by avoiding lung trauma from a loss of PEEP or lung over-inflation during manual inflations (Savian et al. 2006). Differences in secretion clearance have also been found when different manual lung inflation circuits were used (Hodgson et al. 2007). However, as mentioned by the authors, this study of 20 subjects was underpowered to draw clinical conclusions.

In a randomised cross-over design study of 20 ventilated adults, PEF and sputum removal increased during manual lung hyperinflations when patients were treated in a head-down position compared to treatments in a horizontal position (Berney et al. 2004). The use of gravity to assist secretion drainage is discussed further in **section 1.4.4**.

1.4.2.2 In-vitro studies of manual hyperinflation

Rusterholz and Ellis used a test lung to monitor the techniques of students and experienced staff (Rusterholz & Ellis 1998). Predictably, they found that respiratory compliance had a significant effect on the tidal volumes and pressures generated. Both groups allowed PIP to rise significantly in order to generate a large enough inspired volume when compliance was low. While some have shown consistency in physiotherapists' techniques when using a test lung, and that the physiotherapists were able to modify their technique according to changes in the simulated lung's characteristics (Patman et al. 2001), others have shown significant variability between practitioners (McCarren & Chow 1996). Variability may in part be due to the use of different hyperinflation circuits (Maxwell & Ellis 2003;Maxwell & Ellis 2007). Rapid release of the manual hyperinflation increased PEF more than slow release and a longer inspiratory time was associated with a lower peak inspiratory flow.

1.4.3 Suction and the use of saline

Although tracheal suction is acknowledged as essential in maintaining upper airway patency during mechanical ventilation, the technique itself is associated with negative side-effects. These include airway trauma, bronchospasm, atelectasis, hypoxaemia, reflux, apnoea, pneumothorax, cardiac arrhythmias and bradycardia, increased infection and raised intra-cranial pressure (Shim et al. 1969;Cordero & Hon 1971;Ninan et al. 1986;Graff et al. 1987;Durand et al. 1989;Kerem et al. 1990;Demont et al. 1991;Shah et al. 1992;Gemma et al. 2002;Van de Leur et al. 2003;Morrow et al. 2004;Morrow et al. 2006). Airway trauma may include mucosal lesions, damaged cilia and the stimulation of mucus hyper-secretion, all of which may slow mucociliary transport. In addition, the process of disconnecting a patient from ventilatory support for suctioning may potentially cause lung collapse and shear trauma due to the re-opening of closed lung units, which result from the loss of PEEP. Such adverse events may occur even before any negative suction pressure has been applied. Clinical practice guidelines to reduce these adverse effects have been drawn up and include the use of hyper-oxygenation, improved catheter designs, improved suction

techniques and closed suction systems (Young 1984;Glass & Grap 1995;Wainwright & Gould 1996;Morrow & Argent 2008). Since suction results in a reduction of air within the lung, some recommend the use of lung re-recruitment measures prior to recommencing mechanical ventilation. However, the guidelines are in general based on low quality research and further high quality studies are required to explore the various components of suction procedures in children (Woodgate & Flenady 2001;Pritchard et al. 2003;Spence et al. 2003;Morrow & Argent 2008).

In ventilated subjects, saline may be instilled prior to suction to reduce sputum viscosity or stimulate a cough to help mobilise tenacious secretions. However, some authors suggest that, at best, saline instillation may be ineffective, and at worst it is deleterious, causing a reduction in oxygen saturation (Ackerman & Mick 1998). It has been suggested that routine use of normal saline in ventilated patients should be discontinued until more evidence is available to substantiate its role (Blackwood 1999;Morrow & Argent 2008). However, saline is still widely used as an adjunct to physiotherapy treatment.

1.4.4 Positioning strategies to optimise respiratory function in ventilated children

Paediatric chest physiotherapy may at its simplest involve repositioning the infant or child to optimise ventilation and perfusion. Postural drainage involves repositioning the child so gravity assists drainage of secretions from the bronchial tree. This is particularly beneficial where mucociliary action is impaired, as in cystic fibrosis and primary ciliary dyskinesia syndrome, and the efficacy of gravity-assisted drainage has been well described in spontaneously breathing subjects with chronic sputum production (Wong et al. 1977;Sutton et al. 1982;Sutton et al. 1983;Selsby & Jones 1990). However, some suggest the time taken for effective drainage may be excessive, studies in ventilated adults reporting drainage requirements of up to an hour to obtain an increase in respiratory compliance (Mackenzie et al. 1980).

Treatment positions may require modification, for example in cases of raised intra-cranial pressure or gastro-oesophageal reflux (Prasad & Tasker 1990;Button et al. 1997). The head-down position is rarely adopted in young infants as loading the diaphragm may cause further respiratory compromise, and spontaneously breathing infants show improved oxygenation when nursed head-up (Thoresen et al. 1988). However, recent research in

sheep suggests that this position may encourage mucus flow towards the lungs, increasing the risk of bacterial colonisation and ventilator-associated pneumonia (Bassi et al. 2008). Any re-positioning of a critically ill child is likely to incur an additional physiological cost, as shown in a study of ventilated children following cardiac surgery, where greater oxygen de-saturation occurred in children who were turned during physiotherapy than in those treated in-situ (Hussey et al. 1996).

More than 30 years ago, Bryan reasoned that the shape of the diaphragm and the weight of the mediastinum would be better aligned when prone (Bryan 1974). In this position, lung regions poorly ventilated in the supine position would become functional. Bryan's physiological reasoning has proved sound, both in humans and in animal models, resulting in a more homogenous distribution of strain within the lung parenchyma and equalising the dorsal-ventilation perfusion gradients in the lung (Albert et al. 1987;Deakers et al. 1994;Khine et al. 1997;Albert 1999;Newth et al. 2004;Valenza et al. 2005;Lee et al. 2005). However, despite any potential ventilatory advantages of the prone position, parents should always be encouraged to place infants to sleep on their back once at home due to the greatly reduced risk of sudden infant death syndrome in this position (Mitchell et al. 2007).

Nursing critically ill children in the prone position may be logistically difficult, labour-intensive and associated with a risk of adverse events, including haemodynamic instability and tracheal tube obstruction. However, a recent study has shown that prolonged nursing in prone (up to 7 days) was feasible in children and was not associated with increased adverse events (Fineman et al. 2006). A recent Cochrane review showed the prone position to be significantly superior to the supine position in terms of oxygenation in infants and children with ARDS (Wells et al. 2005). However, this meta-analysis predominantly included ventilated, pre-term infants, and the conclusions may therefore be only relevant to these children. The findings of improved oxygenation in mechanically ventilated neonates who were nursed prone was confirmed in another recent Cochrane review, but there was no evidence as to whether any particular body position was effective in producing sustained and clinically relevant improvements (Balaguer et al. 2006). Several clinical studies have shown no improvement in ventilator dependency, recovery from lung injury or patient survival by using prone positioning (Gattinoni et al. 2001;Guerin et al. 2004;Curley et al. 2005). For this reason, intermittent prone positioning

has generally been recommended more as a recruitment manoeuvre for the treatment of a child with severe hypoxaemia or to improve the child's comfort.

In summary, many inter-related factors may influence the success or otherwise of a physiotherapy treatment, including the child's pathophysiology, the position in which the child is treated, the forces and combination of techniques used and the way in which suction is given. It is therefore important to devise methods for quantifying these individual treatment components and to explore the resulting treatment effects.

1.5 Clinical studies evaluating chest physiotherapy

Healthcare decisions are increasingly based upon the availability of high quality research to substantiate the use of a particular intervention, and there is widespread interest in the evaluation of clinical strategies to reduce healthcare costs, including physiotherapy (Alexander et al. 1996;Scally & Donaldson 1998;Merenstein et al. 2005). Double-blind, randomised, placebo-controlled trials remain the 'gold standard' medical model to evaluate treatment efficacy, the results of which are summarised in Cochrane reviews and meta-analyses. Reviews of chest physiotherapy studies have been undertaken for specific patient groups, including those with bronchiectasis, chronic obstructive pulmonary disease or cystic fibrosis (Thomas et al. 1995;Jones & Rowe 2000;van der Schans et al. 2000). Although conflicting results have been found, evidence exists in support of physiotherapy treatment for specific conditions including acute lobar atelectasis and cystic fibrosis (Marini et al. 1979;Hammon & Martin 1981;Stiller et al. 1990;Stiller et al. 1996;McIlwaine 2007). However, findings from studies in spontaneously breathing subjects are unlikely to be directly transferable to ventilated children, either in terms of the applicability of the techniques used, treatment effects or the measurement tools selected.

Reviews investigating physiotherapy in ventilated patients suggest that in general the physiotherapy treatments are poorly described (Kiriloff et al. 1985;Krause & Hoehn 2000;Stiller 2000;Clini & Ambrosino 2005). To illustrate, a study exploring the use of kinetic therapy and percussion therapy in ventilated adults contained detailed descriptions of the bed movements which contrasted with the description of conventional physiotherapy as "percussion therapy every 2 hours by the nursing staff" (Raoof et al. 1999). As with the studies in spontaneously breathing subjects, some studies in ventilated adults have reported

beneficial effects, whilst others have shown no significant or deleterious treatment effects (Mackenzie et al. 1980;Sutton et al. 1985;Mackenzie & Shin 1985;Gallon 1991;Eales et al. 1995;Ntoumenopoulos et al. 2002;Unoki et al. 2005). In the case of the recent Japanese studies by Unoki et al., first in anaesthetised rabbits with induced atelectasis and then in 31 adults, no lung hyperinflations were given during or after expiratory rib cage compressions (Unoki et al. 2003;Unoki et al. 2004;Unoki et al. 2005). The researchers concluded in all three studies that alveolar and airway collapse was not improved and was probably exacerbated by rib cage compression. This finding was unsurprising, since any lung units which were emptied during manoeuvres to increase expiratory flow would not have been re-recruited by lung hyperinflations. Regarding study design in published research, it would appear that the term 'conventional chest physiotherapy' embraces a wide range of treatments which are not standardised and are often incorrectly assumed to be a homogenous treatment package. In addition, the use of a valid placebo equivalent to active treatment is problematic in studies evaluating manual physiotherapy techniques.

1.5.1 Clinical studies in mechanically ventilated children

Additional problems specific to research in ventilated children include the ethics of obtaining parental consent in a highly stressful family situation, the limited availability of large numbers of children of similar ages and disease characteristics, the generally short duration of stay in ICU compared with adults and children's rapidly changing clinical condition (Beardsmore 1998;Randolph et al. 2003). Rapid changes due to growth and development may further influence interpretation of results. For example, forces applied to the chest during physiotherapy may vary not only according to the child's clinical status, as with older subjects, but according to the maturity, age and size of the child. Furthermore, the measurement of treatment outcome over time is limited by the child's requirement for other interventions which may occur in quick succession in the ICU. Thus the challenges of optimising clinical practice in this group are compounded.

Table 1.2 Summary of physiotherapy studies conducted in mechanically ventilated children

Table 1.2 summarises paediatric physiotherapy studies conducted in ICU since the 1960s, examples of outcome measures selected, an indication of the overall findings and the quality of the research. It is likely that patient management has progressed considerably since the early research was undertaken, which focussed predominantly on neonates. Some investigators attempted to standardise treatment by limiting the number of physiotherapists delivering the treatment or providing subjective technique descriptions (Finer & Boyd 1978;Finer et al. 1979;Tudehope & Bagley 1980). As with the example in mechanically ventilated adults (Unoki et al. 2005), some treatments did not reflect clinical practice (Fox et al. 1978;Reines et al. 1982). In others, few or no treatment details were given (al Alaiyan et al. 1996;Bernard-Narbonne et al. 2003). Control groups were frequently omitted, and multiple subgroup analyses reduced study power (Galvis et al. 1994;Hussey et al. 1996). Baseline periods of monitoring before an intervention were rarely included to assess normal, biological variability in the outcome measures and sample size has generally been too small for meaningful conclusions to be reached. Among the few studies that have attempted to assess baseline stability, Sasse et al. measured arterial blood gas variability over one hour in 28 adults in ICU, in whom all other variables of patient management remained stable (Sasse et al. 1994). They found a mean intra-individual variation of 6% for PaO_2 and 5% for $PaCO_2$. Similarly, Main et al. assessed spontaneous variability of respiratory mechanics and tidal volume in 33 paralysed and ventilated children, prior to exploring physiotherapy treatment effects (Main et al. 2004). Recordings between 15 minute epochs were highly reproducible, coefficient of variability (CV) being highest for respiratory resistance measures (4.2%) and lowest for compliance (0.9%).

A recently revised Cochrane review exploring the role of physiotherapy in reducing morbidity following extubation in ventilated neonates provided no guidelines for practice due to the poor study design in the reviewed research (Flenady & Gray 2004). The review emphasised the continuing problems of the quality of research, highlighting a need to define both the treatments applied and their specific effects, identifying the patient populations in whom the effects are beneficial.

1.5.2 Clinical studies exploring adverse events associated with chest physiotherapy

Critically ill patients are routinely subjected to interventions including physiotherapy that acutely increase oxygen demand and require increased output of the cardiac and respiratory systems. Providing tissues with an adequate supply of oxygen requires integration and close regulation of the pulmonary, cardiac, neural and circulatory systems. In healthy subjects, these systems work in complimentary fashion to meet the ever changing demands for oxygen. By contrast, in many critically ill patients, organ function may be compromised and adversely affected by the responses to increases in the oxygen demand (Klein et al. 1988;Weissman & Kemper 1991;Harding et al. 1994;Weissman et al. 1994;Cohen et al. 1996;Horiuchi et al. 1997). The majority of studies investigating haemodynamic and metabolic variables have involved chest percussions in patients with a wide range of respiratory problems, numbers were small, comparative treatments or control groups were not included and the rationale for physiotherapy intervention was often not provided or questionable (Britton et al. 1985;Selsby 1989).

1.5.2.1 Cardiac arrhythmias, blood pressure alterations and bronchospasm

Cardiac arrhythmias have been reported following suction and following chest percussion (Hammon et al. 1992). A study of percussion in adults found significant and at times dramatic increases in heart rate, systolic and mean blood pressure, cardiac output, oxygen consumption, carbon dioxide production and arterial carbon dioxide levels following treatment (Horiuchi et al. 1997). Use of the lateral decubitus position for bronchial drainage (without application of manual chest physiotherapy techniques) has been shown to alter blood pressure in healthy subjects (White & Mawdsley 1983). Neither the adoption of head-down positions nor the addition of percussion caused significant additional changes. Chest percussions and suction have independently been reported to cause bronchospasm in adults with chronic lung disease (Wollmer et al. 1985).

1.5.2.2 Oxygen consumption

Energy expenditure is an important outcome measure in evaluating airway clearance regimes in critically ill patients, since such patients have increased resting oxygen consumption (Weissman & Kemper 1993;Weissman et al. 1994). While some studies have shown stable oxygen consumption during chest physiotherapy (Berney & Denehy 2003),

others have recorded an increase ranging from 13% to 73% (Klein et al. 1988;Cohen et al. 1996;Horiuchi et al. 1997). In general, detrimental effects occurred during or within half an hour of physiotherapy treatment, and were lessened or prevented by pre-dosing with sedative medications. The administration of midazolam before physiotherapy lessened or prevented haemodynamic and metabolic responses compared with placebo medication (Harding et al. 1994). Others have reported that the patient's response to an increase in oxygen demand during multi-modality physiotherapy was related to the patient's baseline oxygen resting condition (Weissman et al. 1994). Dallimore et al. demonstrated increased oxygen consumption during expansion exercises with and without manual percussions compared to quiet breathing in 7 healthy subjects (Dallimore et al. 1998). Horiuchi et al. observed that while vecuronium suppressed increased metabolic demands seen during physiotherapy treatments preceded by midazolam, this did not alter haemodynamic responses (Horiuchi et al. 1997). This led them to conclude that increased metabolic demand during multi-modality physiotherapy was an exercise-like response resulting from increased muscular activity, whereas the increased haemodynamic responses are probably attributable to a stress-like response associated with an increased sympathetic output.

1.5.2.3 Intracranial pressure and cerebral perfusion pressure

In children with acute illness, rapid elevations in intracranial pressure (ICP) and falls in cerebral perfusion pressure have been associated with the development of significant neurological impairment and death due to poor cerebral blood flow, brain tissue herniation and brain stem compression (Brown et al. 1973). Raised ICP represents an increase in the volume of the intracranial contents, normal values being below 15 mmHg. The driving pressure of cerebral perfusion lies within the range of 50-70 mmHg and is defined as the difference between mean arterial blood pressure and ICP. Guidelines have been suggested for physiotherapy treatment of acutely ill children with raised ICP (Prasad & Tasker 1990;Paratz & Burns 1993). These important guidelines could further be strengthened by the availability of methods to explore the effects of quantified physiotherapy treatments in such children.

Studies of multi-modality physiotherapy have shown increased ICP following physiotherapy, although cerebral perfusion pressure was usually maintained at adequate levels due to parallel increases in blood pressure (Parsons & Shogan 1984;Imle et al. 1988;Ersson et al. 1990). In a study exploring multi-modality physiotherapy in patients

with severe head-injury, patients were continuously connected to the ventilator, and suction was performed via a port to minimise the effects of apnoea and a loss of PEEP on intra-thoracic pressure and ICP (Shapiro 1975). Ventilator-generated or manual hyperinflations were used as required during the suction period to help reduce ICP, according to strict guidelines drawn up by the medical team. Intracranial pressure rose in both groups over the 15 minutes of treatment, but was greater in the head down group. Specifically, ICP rose during the suction but not during the percussion or vibrations. Cerebral perfusion pressure changes were similar in both groups, falling during suction but always remaining above 60 mmHg. The authors concluded that patients with severe brain injury tolerated head-down treatment when treated according to strict guidelines, recommending cerebral perfusion pressure over ICP as a more valuable tool to assess patient response. In this study, the treatments were standardised according to procedure time and by a single physiotherapist performing treatments. In addition to adopting the authors' treatment guidelines, these 'safe' treatments could have been generalised and replicated had the physiotherapy forces and lung inflation techniques also been characterised. Useful additional information would have been gained by the inclusion of control groups receiving i) position change only and ii) position change and suction only, especially since ICP during treatment only rose during the suction.

1.5.3 Evaluation of outcome measures used to assess chest physiotherapy in ventilated patients

There is no single pulmonary function measure that satisfactorily describes the complete respiratory physiology of ventilated patients, and there appears currently to be no 'gold standard' method for examining short-term effects of physiotherapy in the intensive care unit (Hanekom et al. 2007). In the paediatric ICU, the measurement of respiratory function has a potential role in documenting the course of a disease process, assessing treatment efficacy and optimising ventilation settings (ARDSnet 2000;Main et al. 2001;Stocks 2006b). The marked improvement in microprocessor technology and the development of respiratory equipment for bedside monitoring offer new opportunities in the assessment of treatment effects, including chest physiotherapy. Awareness of the factors influencing bedside respiratory measurements and knowledge of the intrinsic limitations and assumptions underlying such measurements are crucial for correct interpretation of data collected in ICU; these include consideration of tracheal tube leak, spontaneous ventilatory effort and selection of a valid site of pressure measurement (Kuo et al. 1996;Kondo et al.

1997;Main et al. 2001;Hammer & Newth 2005). International consensus standards exist to ensure an acceptable degree of safety, precision and reproducibility when measuring respiratory function in spontaneously breathing infants, potentially improving the quality of clinical investigations and facilitating multi-centre collaborative studies (Stocks et al. 2000;Frey et al. 2000;Stocks 2006a;Stocks 2006b). However, measurement conditions in the intensive care environment differ substantially from those encountered in the laboratory, and such guidelines have yet to be extended to measurements in the neonatal and paediatric ICU. While the large variety of ventilation modes and the different strategies used in ICU result in many more variables that must be considered than when studying non-ventilated patients, it may be possible to control measurement conditions more closely in intubated children who are heavily sedated or paralysed.

1.5.3.1 Short-term evaluation of treatment outcomes

In the early studies of ventilated children there was a trend to monitor predominantly arterial blood gases to reflect gas exchange, as shown in **Table 1.2**. Arterial sampling is logistically easier in ICU, where the majority of patients have indwelling arterial lines. While there is a linear relationship and close correlation between arterial and transcutaneous oxygen readings, there is a tendency for transcutaneous values to be a few percentage points higher than arterial values. Less common outcome measures included sputum measurements and chest radiography. More recent studies measured respiratory mechanics (as reflected by respiratory compliance and resistance), end tidal carbon dioxide and deadspace, as discussed in **section 1.5.3.1.1**.

1.5.3.1.1 Respiratory mechanics

The dynamic mechanics of the respiratory system describe the mechanical behaviour of the lungs, airways and chest wall throughout the breathing cycle. Short-term changes in respiratory mechanics and oxygenation following physiotherapy have been measured both in adults and children, the basis of using these measures being that an increase in compliance and a decrease in resistance might reflect improvement in lung aeration and reduced airway obstruction from secretion removal. Researchers who have explored respiratory mechanics in ventilated adults variously reported an improvement (Mackenzie et al. 1980;Mackenzie & Shin 1985;Hodgson et al. 2000) or no difference (Eales et al. 1995) in these measures following physiotherapy. Potential reasons for the differing

responses to physiotherapy may include the patient group investigated. For example, the absence of a beneficial response in the study by Eales et al. may relate to the fact that the population studied had undergone open heart surgery, rather than having a primary diagnosis of obstructive lung disease.

In pharmacologically paralysed subjects, since no muscular activity is occurring static compliance can be assessed by measuring changes in pressure and volume during stepwise inflation/deflation manoeuvres of the lungs. Whilst demonstrating an improvement in total thoracic compliance (reflecting lung volume recruitment), a limitation in Mackenzie et al.'s study was that they were unable to make direct measurements, deriving their values of expired lung volume from the inspired volume and the ventilator circuit's 'compressible volume'.

More recently, valuable insight has been gained from the CO_2SMO® respiratory monitor, which provides bedside measurements including tidal breathing, respiratory mechanics, and capnography, and which has been validated for clinical research in ventilated children (Main & Stocks 2004;Main et al. 2004;Almeida et al. 2005). In a randomised cross-over trial in children, Main et al. compared the effects of chest physiotherapy versus suction in 100 mechanically ventilated, paralysed children, 83 of whom were included in the final analysis. The physiotherapy treatment was preceded by a period of baseline monitoring to explore the normal variability of the outcome measures selected. Although the researchers reported differences in treatment length and suction parameters between the groups, there was no significant difference in expired tidal volume or respiratory compliance following treatment. However, there was a tendency for respiratory resistance to fall following chest physiotherapy, the change being significant in patients on volume-preset ventilation. Within individuals, resistance tended to fall in twice as many children following physiotherapy as following suction alone. Both treatments induced an immediate transient respiratory deterioration in almost a third of patients. These and other authors have commented on the variability observed in the delivery of physiotherapy techniques, calling for quantification and detailed analysis of the profiles delivered during manual chest physiotherapy, and for further research into treatment effects and appropriate patient selection (App et al. 1998;van der Schans et al. 1999;Stiller 2000).

1.5.3.1.2 Direct sputum measurement

Direct quantification of secretion removal has included the measurement of sputum volume and wet and dry weighing (Bateman et al. 1981;Hasani et al. 1994;Berney & Denehy 2002). Although simple to perform, weighing expectorated sputum (wet or dry) is not precise or reproducible, nor do the values provide meaningful data about the biophysical properties of secretions (Rubin 2007). Data involving quantification of sputum have predominantly related to the effectiveness of physiotherapy in spontaneously breathing subjects with chronic lung diseases (van der Schans et al. 1999). In such conditions of long-term sputum expectoration, the trial design must control for variables including circadian variation in mucus production. In spontaneously breathing subjects, saliva may contaminate the sample and individuals may inhibit expectoration or swallow secretions. The association between sputum removal and change in respiratory function therefore remains unclear, resulting in a divergence of opinion as to the value of sputum collection (Bradley et al. 2006). In young, ventilated children, the tracheal tubes are of small diameter and may easily be obstructed, saline frequently being used to aid secretion removal (Main et al. 2004), which creates the problem of variable dilution of the sample with saline. Furthermore, wet-to-dry weight calculations may vary according to the hydration of expectorated secretions which may be influenced both by the disease process and ventilatory humidification (Houtmeyers et al. 1999;Bye & Elkins 2007).

More recent studies have assessed changes in sputum viscosity and visco-elasticity, termed the rigidity index (App et al. 1998;Kellett et al. 2005). Kellett et al. aimed to evaluate the use of nebulised hypertonic saline as an adjunct to physiotherapy in adults with stable bronchiolitis. The rationale for measuring sputum viscosity related to the researchers' hypothesis that hypertonic saline could increase mucociliary function and alter the visco-elasticity of sputum. They reported that since a rheometer was not available, viscosity was graded on a 5-point scheme assessing sputum 'pourability'. No further details of viscosity assessment were presented, but the authors quoted that a close correlation has been reported between rheometry and the grading system (Lopez-Vidriero et al. 1973). Measurement of change in viscosity would appear to be a valid outcome in studies comparing the ability of different chest physiotherapy techniques to mobilise secretions since it is a measure believed to be influenced by physiotherapy chest wall vibrations. However, the reliability of such a subjective grading measurement is questionable, and likely to be dependent upon the assessor's previous experience. Since 'wet' sputum

samples were used for analysis, measurements in ventilated children could additionally have been diluted with saline.

1.5.3.1.3 Radiological and radio-aerosol measures

In children, immediate radiological evidence of lung clearance following physiotherapy is difficult to obtain and results have been conflicting (al Alaiyan et al. 1996;Bloomfield et al. 1998). Radio-aerosol clearance studies have been conducted in adults to monitor sputum mobilisation (Bateman et al. 1979;Oldenburg et al. 1979;Bateman et al. 1981;van der Schans et al. 1986;Conway et al. 1992). However, this technique has less application in intensive care and, in particular, in growing children due to the risks from irradiation. Additionally, the radio-aerosol studies tracers tend to deposit inhomogeneously and more centrally, so that in cases of severe airway obstruction the tracer does not reach poorly ventilated parts of the lungs. If mucus in the periphery of the lungs and areas of atelectasis are poorly labelled with the radioactive tracer, mucus movement may therefore not be reflected in the radioactive images but only in the volume of expectorated mucus, which could account for previously reported discrepancies between the two measures (Sutton et al. 1983;Sutton et al. 1985).

1.5.3.1.4 Other respiratory measures

Whilst change from pre-treatment values in functional respiratory capacity would directly measure changes in lung volume recruitment following physiotherapy, such measurements are currently not suitable for assessing the effects of physiotherapy in the paediatric ICU. Similarly, although electrical impedance tomography may potentially provide a measure of changes in lung volume and ventilation distribution this was not available at the inception of this research and is still undergoing development as a valid research tool (Hinz et al. 2003;Victorino et al. 2004;Dunlop et al. 2006).

1.5.3.2 Long-term outcome and morbidity in the intensive care unit

Long-term monitoring under controlled conditions following acute interventions such as physiotherapy is not logistically possible in the paediatric ICU due to the multiple interventions such children require. The ability of physiotherapy to facilitate weaning, to shorten the length of stay in intensive care or hospital, or decrease hospital morbidity or mortality has not been widely reported. An exception to this is a study which compared

chest physiotherapy with sham treatment in 60 patients and found a significant reduction in ventilator-associated pneumonia in those receiving physiotherapy (Ntoumenopoulos et al. 2002). The physiotherapy aimed to aid sputum clearance and included postural drainage with CWV and suction, but not manual lung hyperinflations. The sham treatment consisted of cardiopulmonary assessment and occasional musculoskeletal physiotherapy. By contrast, a recent study suggested that chest physiotherapy actually prolonged the time adults spent on mechanical ventilation by around four days [median 15 compared with 11 days] (Templeton & Palazzo 2007). These data were published 10 years after collection, and while this was described as a randomised, controlled study of a large sample (180 patients), the study was flawed in several aspects (Ntoumenopoulos 2007). For example, the sample populations were not matched in terms of severity of illness measures or disease characteristics (including tracheostomy usage) and no details of physiotherapy treatment were presented.

1.6 Principles of normal airway clearance

In order to consider the features required for effective secretion clearance, mucus composition and mechanisms of normal airway clearance are discussed in more detail below. Mucus comprises two distinct layers, a serous lower, peri-ciliary layer and an upper mucus layer, consisting of cross-linked glycoproteins. The serous layer bathes the cilia and the mucus flowing above the serous level is propelled in a helical fashion up the airway by ciliary beating (Pavia et al. 1983a;Foster 2002). Newtonian liquids respond to stress by deforming and flowing as long as stress is applied. Like many biological fluids, mucus is a non-Newtonian fluid and due to the cross-linked glycoproteins, the rheological behaviour of mucus is described as visco-elastic (i.e. with properties of both a solid and a liquid). In addition, mucus shows marked thixotrophy, meaning that its viscosity decreases significantly at high shear rates, the mucus behaving more like a liquid than a solid when it is flowing rapidly.

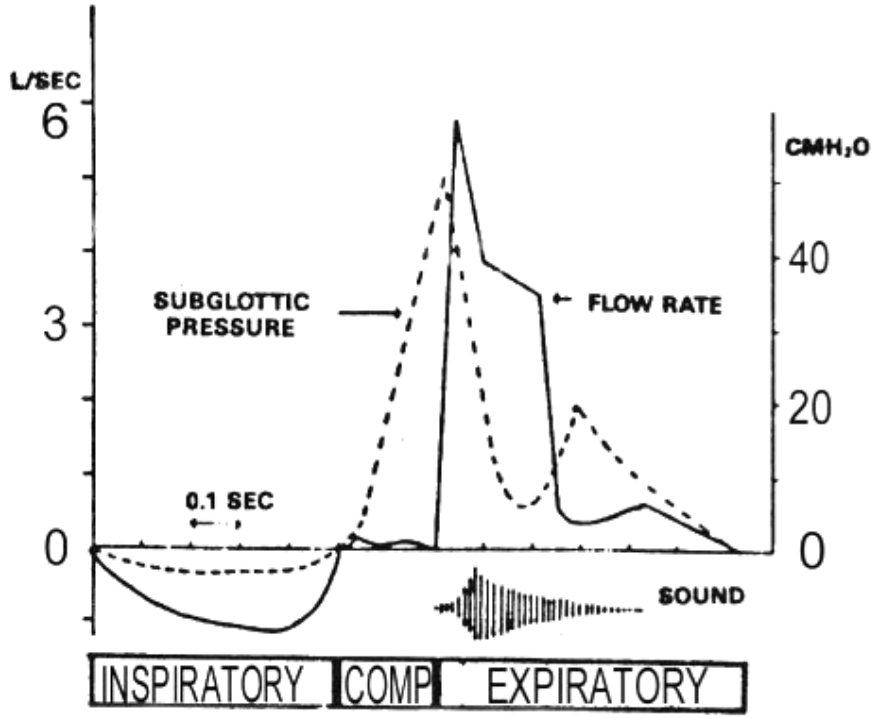
Airway secretions are removed by mechanisms including mucociliary clearance, peristalsis, alveolar clearance and cough (Houtmeyers et al. 1999). Clearance may be impaired in respiratory diseases including asthma, cystic fibrosis, and acute respiratory tract infections (App et al. 1998;Rubin 2007;Henke & Ratjen 2007;Bye & Elkins 2007). The structure, number, movement and co-ordination of the cilia present in the airways, as well as the amount, composition and rheological properties of the peri-ciliary and mucus layers are all determinants of mucociliary clearance (Sturgess et al. 1970;Lorenzi et al. 1992;Trout et al. 1998). In health, the ciliary escalator is usually sufficient to clear the normal amount of fluid reaching the airways by epithelial secretion (Wanner 1984a) but secretion retention may occur due to hyper-secretion of normal mucus, slower transport of the mucus or the presence of purulent secretions, called sputum (Rubin 2002;Rubin 2007). Under such conditions, airflow-dependent mucus clearance manoeuvres such as cough becomes critically important for airway hygiene (Scherer 1981;King et al. 1985b). The amount and rheological properties of mucus influence not only mucociliary clearance but also cough (Trout et al. 1998;Houtmeyers et al. 1999), a mechanism which will be affected by muscle weakness (Bach 1993;Chatwin et al. 2003;McCool 2006).

1.6.1 Cough

In healthy individuals cough may clear secretions from the 7th - 12th of the 23 airway generations, extending down to the respiratory bronchioles in the presence of excess mucus

production and low serous viscosity (Scherer 1981). An effective cough depends on the ability to drive gas at high linear velocities through the airways, and on an effective interaction between the flowing gas and mucus lining the airways (McCool 2006). These events rely upon the capacity of the respiratory muscles to increase intra-thoracic pressure and dynamically to compress the airways. **Figure 1.5** illustrates the three phases of cough: inspiratory, compressive and expiratory (Whittenberger & Mead 1952;McCool 2006).

Figure 1.5 Schematic diagram depicting the changes in flow and subglottic pressure during the phases of cough



(inspiratory, compressive or 'COMP', and expiratory airflow)

Illustration reproduced with permission from McCool 2006

- The initial, rapid inspiratory phase is not critical, an effective cough being accomplished even by inhaling small volumes
- After inhaling a volume of air, the glottis is closed and an expiratory effort ensues (the compressive phase). Glottic closure lasts for approximately 0.2s, maintaining lung volume as intra-thoracic pressures rise. The isometric contraction of the expiratory muscles puts the muscles at a mechanical advantage to generate greater positive intra-abdominal and intra-thoracic pressures, the latter rising to as much as 40 cmH_2O. These high pressures account for some of the adverse events associated with cough, including cardiovascular and neurological complications resulting from decreased venous return

- Once the glottis opens, the expiratory phase follows, as the high intra-thoracic pressures developed in the compressive phase result in high expiratory flows. There is a brief turbulent blast (30-50 ms) at up to 720 l/min (12 l/s) in adults. Although glottic closure enhances this phase of cough, it is not essential for an effective cough. For example, individuals with a tracheostomy or endotracheal tube can produce an effective cough by performing a huffing manoeuvre which is performed with an open glottis. Lower expiratory flows of 180-240 l/min (3-4 l/s) follow the initial cough blast. The velocity of the air stream increases from the periphery of the lungs to the central airways as the net cross-sectional area of the airways decreases.

The velocity of gas in the more central airways can be further enhanced by dynamic compression of these airways, which increases the kinetic energy, and is believed to enhance removal of mucus adhering to the walls. Dynamic compression during cough results from differences between intra-luminal and extra-luminal airway pressures, the transmural airway pressure. The point at which the extra-luminal pressure equals the intra-luminal pressure is called the equal pressure point, and is illustrated in **Figure 1.6**.

Figure 1.6 Dynamic airway compression during a forced expiration

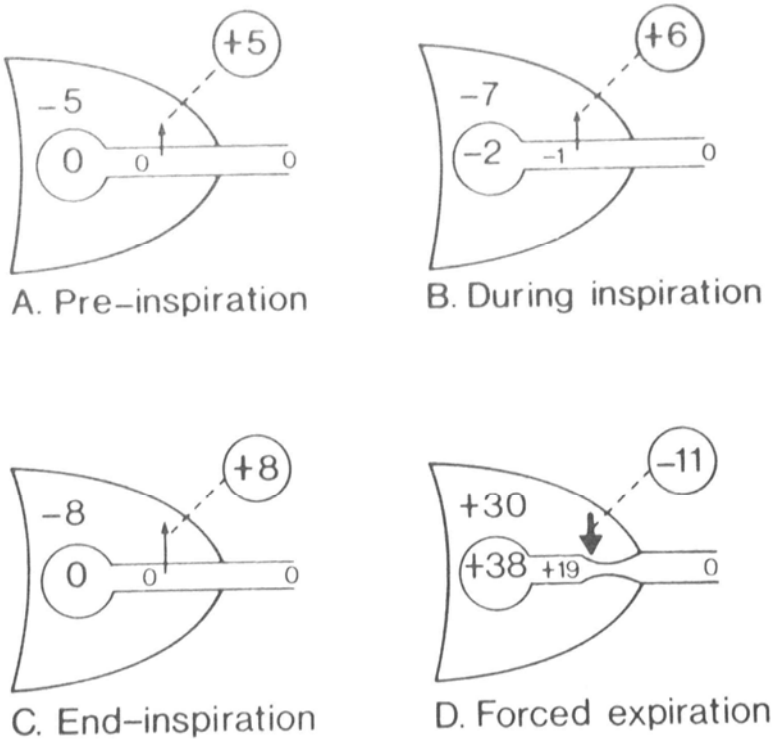


Illustration reproduced with permission from West 1992

During a forced expiration, the increase in pleural pressure is transmitted to the alveolus such that the trans-mural pressure at the alveolus is the same as the recoil pressure of the lungs (West 1992;McCool 2006). However, as expiratory flow continues, the intra-luminal pressure becomes lower, due to the viscous/resistive forces, while the extra-luminal pressure (pleural pressure) remains raised. Thus the airways downstream from the alveolus (nearer the mouth, which is at atmospheric pressure) are subject to dynamic compression. Normally, dynamic compression is initiated in the trachea and mainstem bronchi at high lung volumes, and travels to the more peripheral airways as lung volume decreases and the equal pressure point moves deeper into the lungs (described as 'upstream', towards the alveoli). This ensures that the whole length of the tracheobronchial tree is 'coughed', a prerequisite being that high intra-thoracic pressures are sustained throughout expiration. The high gas velocities generated during cough promote dispersion of liquid mucus into the air stream. Mucus is torn off and droplets are suspended within the airway lumen, a pattern termed *misty flow*. Waves of mucus are created, the waves enhancing particle clearance (Clarke et al. 1970;King et al. 1985a).

1.6.2 Two-phase gas-liquid interaction

Theoretically, when air (gas) flows over a thickly lined mucus layer (liquid), a shear force is developed on the interface of the mucus layer, in proportion to the square of the airflow velocity, called a two-phase gas-liquid interaction. Therefore, if the airflow velocity is maintained above a certain level at which the shear force on the mucus layer exceeds the resistive force in the mucus layer, the mucus layer starts to move in the direction of airflow (Clarke et al. 1970;Kim et al. 1986a;Kim et al. 1986b). The mucus can be transported steadily even against gravity with continuous airflow at flows expected from normal *tidal* breathing (Kim et al. 1986a), suggesting the extreme flow velocities of cough are not a requirement for mucus transport by this mechanism. During two-phase flow transport, mucus clearance is directly proportional to the depth of mucus and is inversely proportional to its viscosity and elasticity (Clarke et al. 1970;King et al. 1990;Rubin 2002). The interactions are strictly physical phenomena, meaning that they can occur in-vitro or in-vivo provided that there is both a sufficient amount of mucus (approximately 10-15% of airway diameter in large adult airways) and an asymmetrical airflow pattern which favours expiratory airflow (Kim et al. 1987;Sackner & Kim 1987;Benjamin et al. 1989). Kim et al. demonstrated that clearance could further be promoted by changing the rheological properties of mucus with an expiratory flow bias as low as 10% (ie a peak expiratory to

peak inspiratory flow ratio [PEF/PIF] ≥ 1.1). They commented that, in-vivo, there are many factors favouring two-phase flow transport. These include the airway orientation, an increase of the actual expiratory axial airflow velocity during expiration (as overall airway diameter and lung volume decrease), and the low-viscosity peri-ciliary fluid acting as a lubricating film such that movement of the mucus layer may occur at lower flows than predicted in in-vitro models. Furthermore, when excessive bronchial secretions are present, the mucus lining is likely to be irregular with local accumulation of secretions, which offers favourable conditions for eruption of large waves and subsequent triggering of mucus transport at lower airflows. Net outward wave motion of secretions from airways by two-phase gas-liquid transport favoured by a biased expiratory airflow was safely accomplished in sheep by inverse ratio ventilation (Benjamin et al. 1989). Two-phase flow clearance seemed less effective in the smaller airways, perhaps due to the low airflow velocities and plugging of the airways. Chang et al. showed increased mucociliary clearance with a combination of asymmetrical airflow and mechanical oscillations of 7-13Hz (Chang et al. 1988).

1.6.3 Mucus clearance by mechanical oscillations

Mechanical oscillators are believed to aid secretion clearance in humans and animals by promoting two-phase gas-liquid interaction, facilitating intrapulmonary gas mixing and improving mucociliary interaction (King et al. 1983;Gross et al. 1985;Chang et al. 1988;Rubin et al. 1989;King et al. 1990). Effective oscillations have been reported between frequencies of 3-17 Hz, several of the authors reporting an optimal frequency around 13 Hz, which is near the natural ciliary beat frequency (Rutland & Cole 1981). The mucociliary interactions are believed to be aided by ciliary stimulation and alterations in the rheological properties of airway mucus, by evoking the thixotropic nature of mucus and breaking the cross-links between the glycoproteins.

Improvement in ciliary activity may result from a mechanical effect such that vibrating frequencies approximating the intrinsic ciliary beat frequency produce resonance and therefore increased ciliary beat amplitude (Mead 1956;Mead 1969;Rutland & Cole 1981;Wanner 1984b). In an oscillating system, elastic and inertial forces operate in exact opposition and at a certain frequency, depending on their relative magnitudes, cancel each other out. This frequency is referred to as the resonant frequency of the system and for both healthy adults and infants occurs at approximately 5 Hz in the lungs and 7-14 Hz for

the cilia (Rutland & Cole 1981;Clary-Meinesz et al. 1997). Alternative mechanisms might include activation of chemical mediators causing cilio-stimulation. Lung inflation and hyperventilation have been shown to activate endogenous prostaglandin production (Said 1982) and it is believed chest wall vibrations may similarly release chemical mediators for cilio-stimulation into the airways (Wanner 1984a;Wanner 1984b). In vitro studies have demonstrated dose-dependent increases in ciliary beat frequency from prostaglandin E_1 and E_2 and leukotriene C_4, histamine additionally increasing mucociliary clearance (Iravani & Melville 1975;Verdugo et al. 1980a;Verdugo et al. 1980b;Wanner et al. 1983).

1.7 Summary of current knowledge of chest physiotherapy in ventilated children

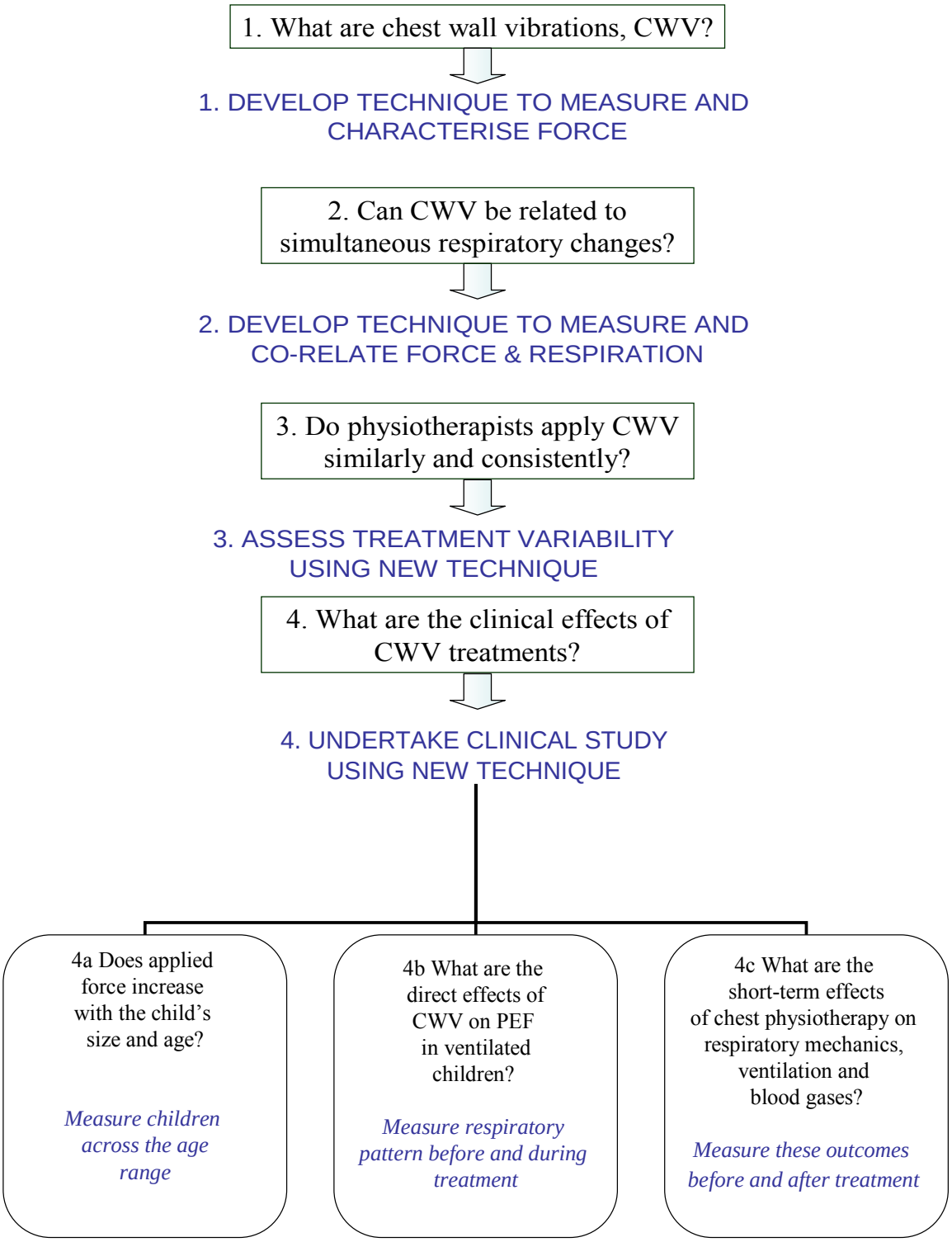
Young children are acutely vulnerable to respiratory distress and, although life-saving, management with mechanical ventilation may itself result in secondary lung injury. Chest physiotherapy comprises several inter-related treatment components, which have the ability to cause both beneficial and deleterious effects. Lung hyperinflations and manual chest vibrations are believed to restore lung volume and improve airway clearance in ventilated children. The vibrations are believed to simulate normal airway clearance by increasing expiratory airflow, by creating an expiratory bias of airflow and / or by vibratory effects on mucociliary clearance mechanisms. Clinical data are required to confirm these hypotheses.

The use of several techniques within a physiotherapy treatment session compounds the complexity of evaluating treatment effect. The effectiveness of chest physiotherapy in mechanically ventilated patients is likely to be influenced by the interaction between the chest vibrations and lung inflations. Ideally, it is therefore important to measure both the forces applied during CWV and the simultaneous changes in airflow. Whilst ventilatory measures have been recorded before and after treatment, at the start of this research no suitable method for force and respiratory measurements during treatment existed. Development of such a technique would provide a more fundamental insight, distinguishing between the direct effects on airflow resulting from the ventilatory pattern of the lung inflations and those resulting from the CWV forces. Patterns of treatment could then in turn be related to measures of lung volume recruitment and airway clearance following the physiotherapy.

Techniques may vary between individual physiotherapists, between institutions, between treatment occasions and between subjects according to underlying pathophysiology. Such variability may also be influenced by the age of the subject. In addition to changes in body mass, the chest wall becomes progressively stiffer (less compliant) with increasing age, this developmental change possibly influencing the compressive force that is required to increase airflow and mobilise secretions. The creation of a suitable measurement technique would allow both variability in treatment delivery and treatment effects to be objectively quantified and evaluated, providing an important tool with which to develop evidence based practice.

Questions were derived from observation of clinical practice and were defined following review of the literature. **Figure 1.7** summarises these questions and the actions required to address them. Since the CO_2SMO® respiratory profile monitor provides breath-on-breath data of ventilation and respiratory mechanics and has already been validated and successfully used in ventilated children, it was selected for use in the programme of research described in **section 1.9** in an attempt to assess respiratory monitoring during, as well as before and after, physiotherapy.

Figure 1.7 Questions posed in this thesis and actions required to address them



From these questions the following hypotheses and objectives were derived:

1.8 Research Hypotheses

1. *It is possible to create a technique to measure chest wall vibration forces during clinical treatments, and to relate such forces to simultaneous changes in respiratory flows, volumes and pressures*
2. *Maximum and mean force applied during chest wall vibrations increase with the size and age of the child*
3. *Manual lung hyperinflations with chest wall vibrations result in an increase in peak expiratory flow above that observed during baseline mechanical ventilation*
4. *After adjusting for inflation volume, application of chest wall vibrations result in an increase in peak expiratory flow above that obtained during manual lung inflations alone*

1.9 Research Objectives

The primary objectives of this research were to:

1. Develop a method of quantifying chest wall vibration forces and the means of evaluating simultaneous changes in force with those of respiratory flow and pressure in ventilated infants and children of all ages

2. Estimate the variability over time, within and between individual physiotherapists when treating the same and different subjects with chest wall vibrations

3. Conduct a study to:

i) Assess the feasibility of measuring force and respiration in a population of critically ill, mechanically ventilated children

ii) Characterise the magnitude and pattern of forces applied during chest wall vibrations and evaluate the direct effects of these manoeuvres on flow and pressure changes in the lungs, and

iii) Determine the relative contribution of manual lung inflations and chest wall vibrations to any observed increase in expiratory airflow

A secondary objective was to explore the short term effects of chest physiotherapy, by recording changes in ventilation, respiratory system mechanics and blood gases following treatment.

Chapter 2 Quantification of manual chest physiotherapy in ventilated children

This chapter describes the process of creating an appropriate technique to characterise manual chest physiotherapy forces and simultaneous respiratory changes. It details a pilot study to define a protocol and analysis format for relating changes in force to simultaneous changes in respiratory flow and pressure in a population of critically ill, mechanically ventilated children in the intensive care unit at Southampton General Hospital. The variability in physiotherapists' vibration techniques is then explored, as a precursor to undertaking a clinical study described in Chapter 3.

2.1 Characterisation of CWV

The author's initial concept was to create a sensing glove to measure the vibrations applied to a patient's chest directly through the physiotherapist's hand. This would facilitate measurements wherever the hand moved around the chest. An alternative solution was to create a thin sensing mat to lie over the chest wall, recording the CWV delivered through it. During the early development phase the proposed system was referred to as an 'interface sensing system', encompassing both alternatives.

An extensive search was undertaken to identify existing technologies available for measuring dynamic loading. This became focussed on equipment originally developed for in-shoe pressure measurement during gait analysis (Orlin & McPoil 2000). Systems used for measurement of physiotherapy spinal mobilisation techniques were also explored. However, it was found that research investigating these forces principally used instrumented treatment couches, which only allowed indirect measurement of the manual forces (Harms et al. 1995;Chiradejnant et al. 2001). Similarly, the author investigated measurements of both force and pressure. However, it became apparent that force was a more valid outcome measure since the contact area between the hand and chest varied during treatment, confounding pressure measurements during CWV.

The four requirements for devising a force measurement technique were:

- Definition of system requirements
- Sourcing and modification of appropriate technologies
- In-vitro and in-vivo evaluation of performance characteristics of the sensing system
- Definition of analysis variables to characterise the CWV forces

2.1.1 Definition of system requirements

At the outset of this research there were no data available regarding the range or pattern of forces delivered during CWV. Preliminary laboratory studies were therefore undertaken to define a likely force range for chest physiotherapy.

2.1.1.1 Methods

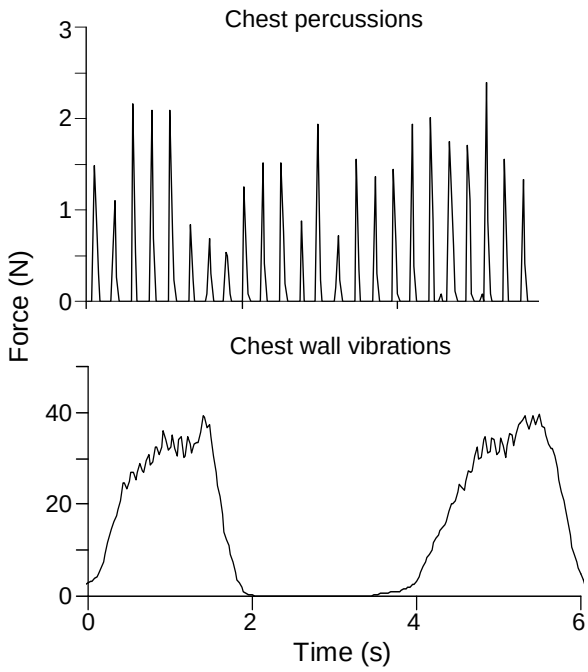
Six paediatric physiotherapists based at Southampton General Hospital were asked whether their clinical treatments of mechanically ventilated children predominantly comprised percussions or CWV. Both techniques were then measured in order to quantify the difference between the techniques.

Following a brief practice period, the physiotherapists mimicked their treatments of CWV and percussions for children, from babies through to teenagers. The magnitude and pattern of force were recorded using a force plate and dynamometer (Type UF2, Pioden Controls Ltd, Canterbury, England). A piece of firm foam was cut to simulate a child's convex chest wall, and positioned directly on top of the force plate. The therapists placed their hand on the foam and performed simulated treatments over a 30 second interval both for CWV and for percussions. The order of performing percussions and CWV was randomised and the underlying force plate and dynamometer recorded the magnitude, frequency and pattern of force delivered during the 'treatment'. These data were manually processed using Excel™ (v97) for force and Labview™ (v5.0) for frequency analysis.

2.1.1.2 Results

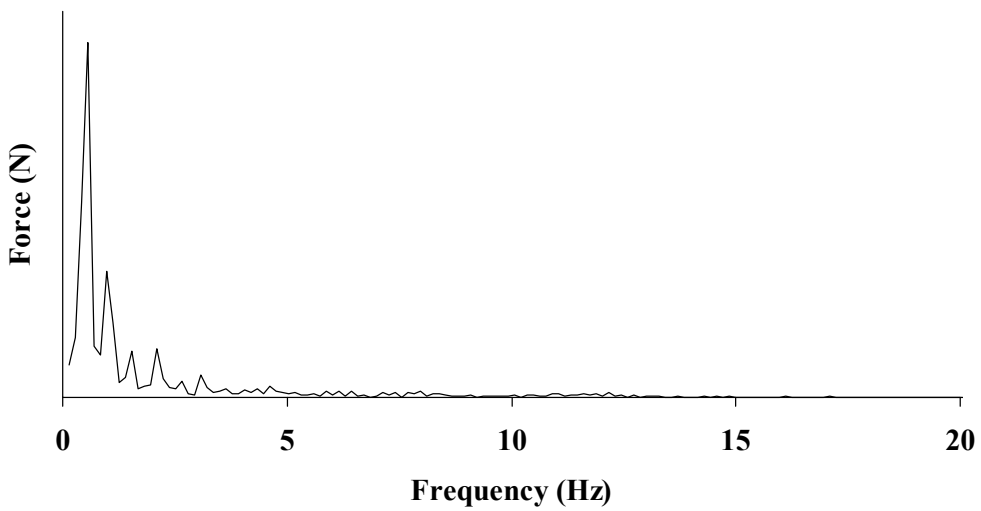
All six physiotherapists favoured CWV over chest percussions for treatment of ventilated children. Example traces of both techniques are included in **Figure 2.1**. Maximum vibration forces fell within 15-80 Newtons [N] (median 43 N) for simulated treatments of children. The force range recorded for percussions was 0.5 - 10 N (median 5 N).

Figure 2.1 Forces recorded during simulated chest percussions and chest wall vibrations



Frequency composition analysis for the CWV revealed that the vibration frequency was low, with minimal activity above 10 Hz as shown in **Figure 2.2**.

Figure 2.2 Frequency composition of chest wall vibration signal



It was decided that a sensing system to characterise CWV should be capable of measuring a force range at least twice the sampled range (i.e. 10-200 N). Sampling theory dictates an acquisition frequency of at least twice the highest frequency in the signal (Proakis & Manolakis 1992), the system therefore requiring a sampling frequency of $\geq$ 20 Hz. Additional specifications were that the system should be portable, the interface material being lightweight and thin to cause minimal interference to treatment, of a flexible material to accommodate the convexity of the chest wall and therapist's cupped hand, durable and suitable for use in a clinical environment (including being fully cleansable between subjects, hypoallergenic, electrically safe and minimally affected by changing temperature and humidity). The system needed to be acceptable to both the families and professionals working in the ICU.

2.1.2 Sourcing and modification of appropriate technologies

Three commercially available technologies were identified as possible alternatives for the measurement of dynamic load, namely Tekscan® (Tekscan Inc., South Boston, MA, USA), Paromed® (Paromed*gmbh*, Neubeuern, Germany) and the novel pliance® system (novel*gmbh*, Munich, Germany), as shown in **Table 2.1**.

Table 2.1 Comparison of the technologies available at the outset of the research programme

Product	Sensor type	Strengths / Limitations
Tekscan®	Resistance (ink based)	High inter-sensor variability & poor linearity* Short life of sensors
Paromed®	Hydrocell (piezoresistive sensor)	Good accuracy & linearity Embryonic stage of development
novel pliance®	Capacitance	Good linearity* Flexible, lightweight matrix Costly (approx. £30,000 currently)

* Xia 1994

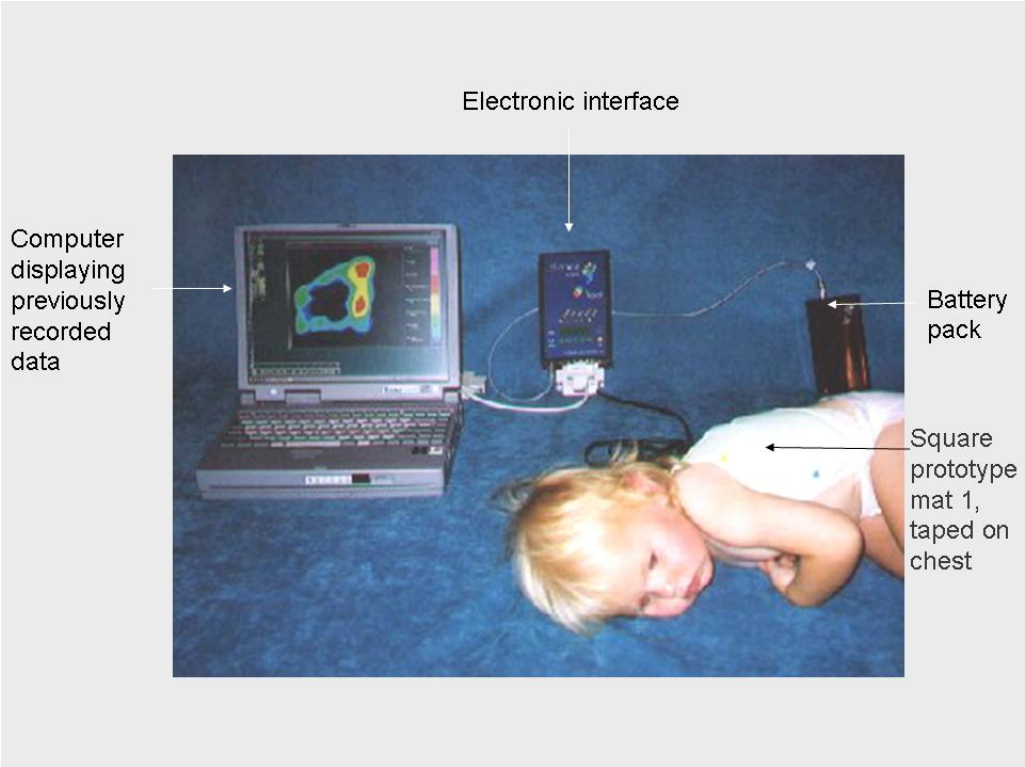
Research available on the various systems was reviewed, extensive discussions were conducted with the UK representative for Tekscan®, and both German bases were visited for detailed evaluation of the two companies' respective technologies. Advice was also sought from Professor Griffin in the Institute of Sound and Vibration Research, University of Southampton. Whilst the technology under development at Paromed® showed good accuracy and linearity, the system was in a very early stage of commercial production and was not suitable to measure forces applied around the chest wall. The novel pliance® system was also in an early stage of commercial release, as illustrated by the lack of any pliance® instruction manual. However, this system was based on other dynamic measurement systems already developed by the company for a variety of medical and non-medical applications. Medical applications included the production of inner soles for gait analysis and a large, flexible sensing mat suitable for seat measurements of pressure in, for example, wheelchair-users or horse-riders (the FTM® system).

The pliance® system was identified as a suitable commercially available technology upon which the new physiotherapy measurement technique could be based. This system measured dynamic pressure distribution and force by means of a number of individually calibrated capacitive sensors arranged in a matrix. The capacitive sensors comprised a compliant material sandwiched between two electrodes. When force was applied, the material was compressed bringing the electrodes closer together, which resulted in a change in capacitance. From the pressure values of the individual sensors and the area of these sensors the force component perpendicular to the surface could be then be calculated.

The company raised concerns that if a glove were developed, signal distortion and artefact would result as the sensors became creased in the physiotherapist's cupped hand during treatment. It was agreed that a sensing mat would therefore be developed, which could be moved and placed wherever necessary on the subject's chest, depending on both treatment approach and the age and clinical condition of the subject. Since no sensing mats of appropriate shape and size existed, a joint development agreement was established with the company to design and produce suitable mats.

The system consisted of three main components: an elastic, flexible sensing mat, the pliance® analyzer as electronic interface and a notebook or desktop computer running pliance® data acquisition software, as illustrated in **Figure 2.3**. An initial square prototype sensor mat was designed for recording the treatment of infants. It measured 15.5 cm x 15.5 cm, and was produced from a matrix of 16 x 16 sensors. Each of the 256 capacitive sensors measured 7.8 mm x 7.8 mm. The lightweight mat (weight 48g) was approximately 1.5 mm thick which allowed the physiotherapists to receive palpatory feedback from their patients during the treatment. The pliance® system sampled 10,000 sensors per second, resulting in a sampling frequency of 36 Hz for this initial prototype mat. The sensor matrix was encased in a plasticised leather material with heat-sealed seams, conforming to hospital hygiene requirements, and was cleaned with sodium hypochlorate spray.

Figure 2.3 Force-sensing system with the initial square prototype mat taped to the infant's chest



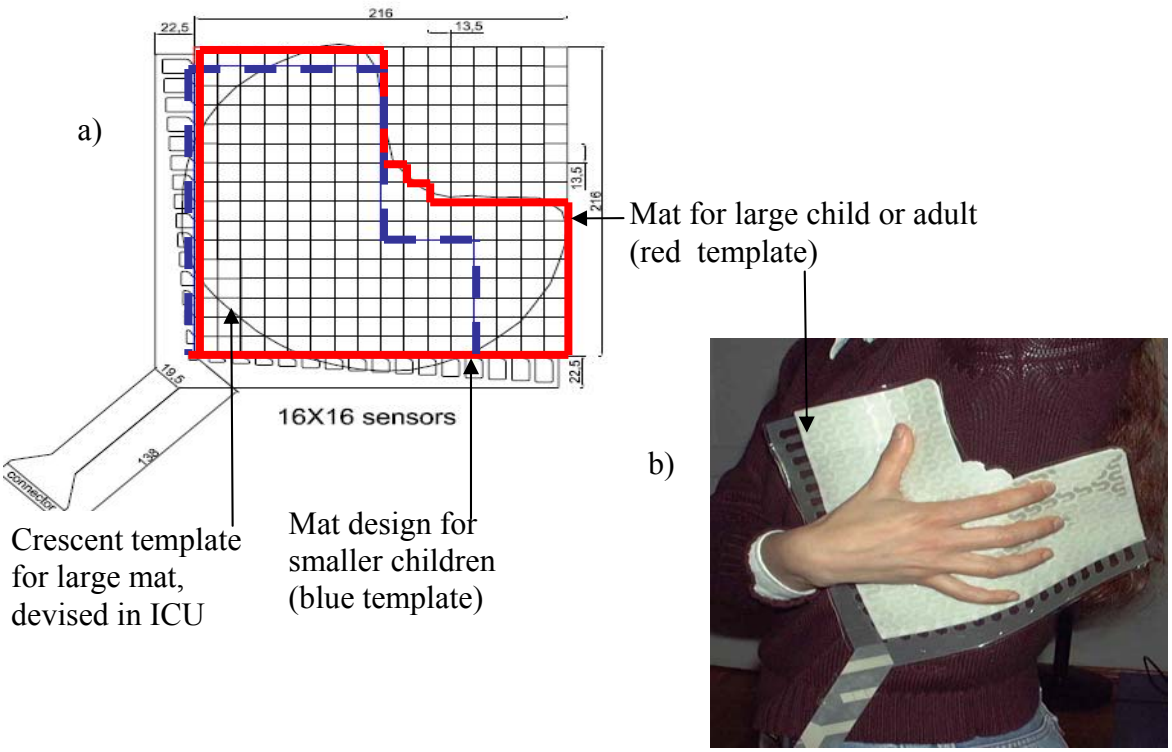
Twelve children (age range 1 month to 15 years) were monitored in Southampton General Hospital's paediatric ICU, during which time variables to analyse force were defined and protocols for data collection were modified (**section 2.2**). For many therapists, the initial square mat (designed for use in infants) was too small to accommodate their hand during

treatment. To define the shape of subsequent mats for use in older children, treatments were recorded with the square prototype and detailed observations were made of the physiotherapists' hand movements during treatment. To ensure the designs would be equally applicable for use with adults, templates were also drawn during physiotherapy in five adults (without the mat).

- It became apparent that a crescent was required so that the cut-away section of the mat could fit around the axilla, thereby allowing the therapist's hands access to the upper areas of the lungs.
- All mats were required to fit into the pliance trublu® calibration device.
- The shape and size of the final designs balanced the need to minimise the mat's size whilst accommodating hand movement during treatment. Flexibility of the mat was optimised (see below).

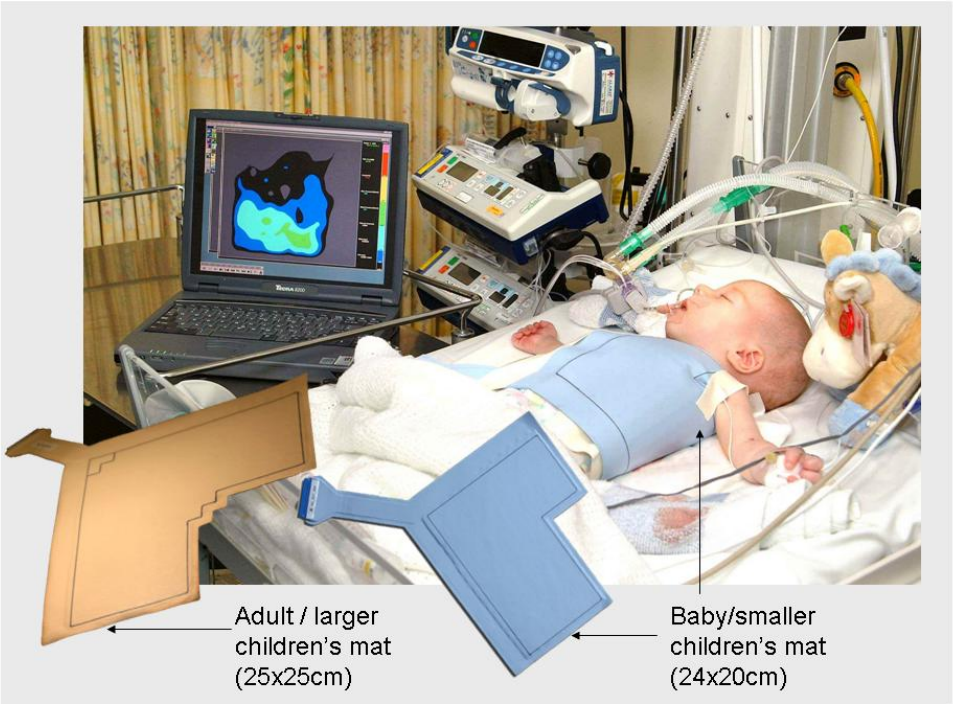
The manufacturer adapted their technology until suitable designs were available. Whilst it was not technically possible to create a crescent-shaped sensor matrix, two custom-made 'L-shaped' mats were designed to approximate closely to the templates and encompassed the whole hand, as shown in **Figure 2.4 (a)**. The photograph in **Figure 2.4 (b)** shows the snaking sensor wires and how the matrix edges were cut-away between the exiting sensor wires, thereby improving the flexibility of the mats' edges compared with the initial square prototype.

Figure 2.4 a) L-shaped mats based on crescent shaped template devised in ICU b) a partly-constructed prototype mat to monitor children over 8 years and adults



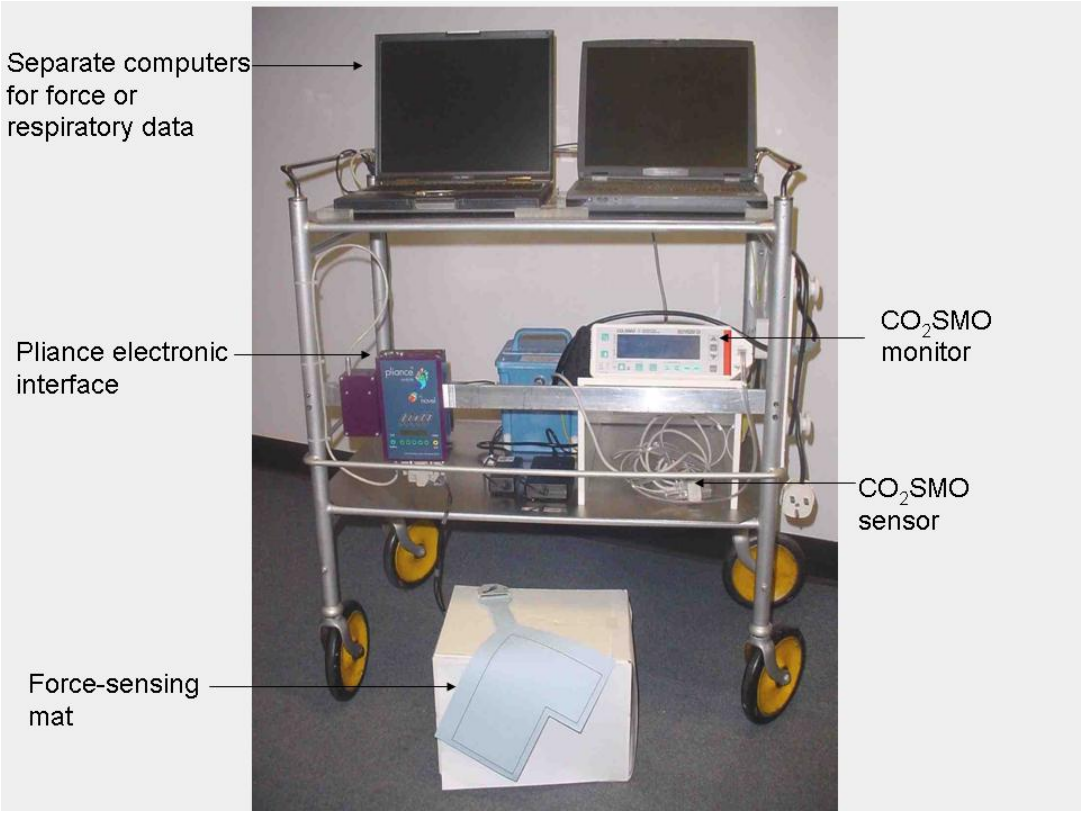
In the square prototype, the sensor lead and connector were heavy and cumbersome, emerging half way along the border of the mat, which tended to dislodge the mat during recordings. Operational characteristics of the later L-shaped mats were improved by re-locating the lead to the corner, as shown in **Figure 2.4 (b)**. The larger mat was designed for treatments of children over 8 years and adults, when the therapist's hand traversed a greater area of the chest. These 'L' shaped mats were used in the clinical study described in Chapter 3, and are shown in **Figure 2.5**. Review of the pilot data suggested that force was rarely concentrated over an area less than 4 cm x 4 cm. It was agreed that the size of each sensor element could therefore be increased without loss of information, the subsequent decrease in sensors in the matrix resulting in an increase in sampling frequency. The new sensors measured 13.5 x 13.5 mm (from 7.8 mm) and the total active sensors numbered 144 in the 24 x 20 cm mat and 195 in the larger 25 x 25 cm mat (compared with the square mat's 256 sensors). Sampling frequency of the new mats was set at 50 Hz during the research programme. The pressure calibration range was from 0.2 N/cm^2 to 15 N/cm^2, which equated to a force range between 10 N and 660 N when forces are applied by an average-sized hand with a contact area of 44 cm^2 (7.5 cm diameter).

Figure 2.5 A young ventilated child in intensive care with the second prototype mat taped in position, showing the third mat for larger children and adults



Due to competing commercial pressures at novelgmbh, a delay of several months occurred between the production of suitable mat templates and the receipt of the new prototypes in July 2003. However, this delay resulted in several new design features being incorporated into the technique used in the clinical study. These included the use of bluetooth™ telemetry, which removed any hard-wire connection between the sensor mats and either the computer or mains voltage. Two sensor mats could be used simultaneously to allow data collection when double-handed techniques required the therapist's hands to be placed at a distance from each other on the chest wall. Each mat was connected to a pliance® analyzer and the two were then synchronised to each other.

Figure 2.6 Trolley designed to accommodate force and respiratory equipment

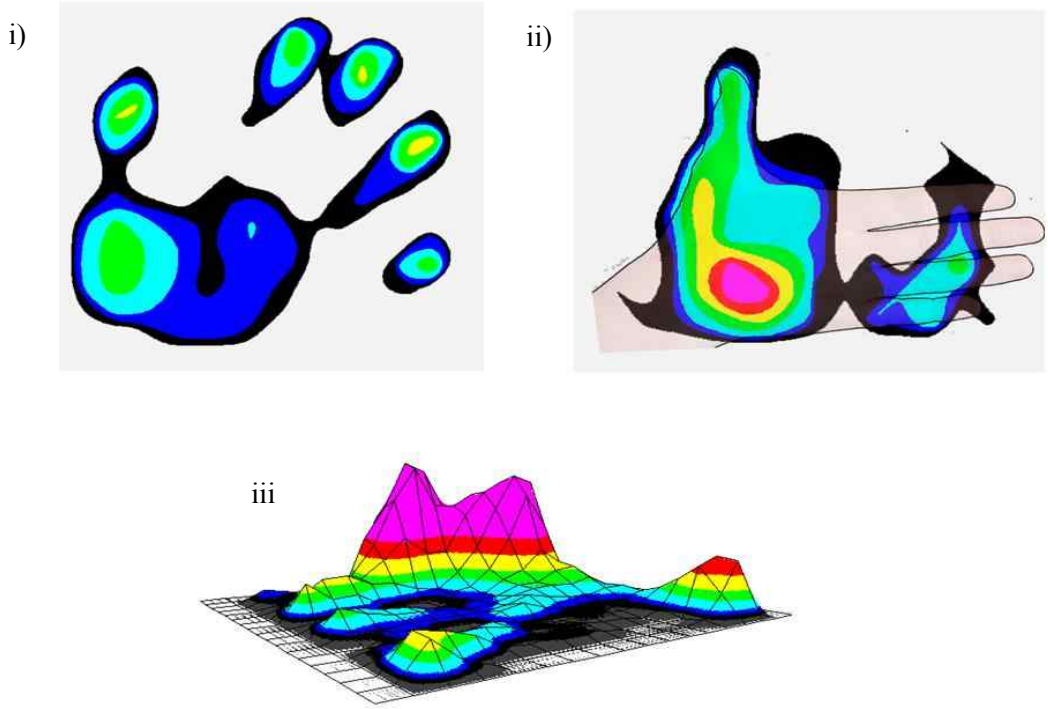


An electrically isolated trolley was designed to accommodate the testing equipment (**Figure 2.6**) including the respiratory equipment described in **section 2.2.2.2**. The trolley was safety tested by the Department of Medical Physics and Bioengineering, Southampton General Hospital and a risk analysis was undertaken for the evaluation and clinical data collection phases of the project. On initial delivery of the system, the manual supplied related to an earlier novel® system, and contained subtle operational differences. A basic

operational manual was therefore created specific to the pliance® system, which included the detailed process of calibration of the system. Feedback was given to the company regarding problems encountered with the data acquisition software, resulting in resolution of these problems and subsequent production by the company of a full operational manual.

The system also gave information regarding the spatial distribution of pressure by means of colour-coded displays which highlighted the area of most pressure, as shown in **Figure 2.7**. Sections ii) and iii) show images collected during physiotherapy treatments. Greatest concentration of pressure occurred in the heel of the hand (the red and pink areas) during the CWV. Whilst these displays were informative in so far as they indicated how physiotherapists delivered pressure, it was beyond the scope of this thesis to explore these changes in more detail, as the focus was on force measurements.

Figure 2.7 Colour-coded representations of spatial pressure distribution in the hand



i) pliance® profile from a hand print; ii) CWV profile superimposed onto a hand template (external to pliance® software) iii) pliance® isobar profile of CWV. Pressure code: greatest to least – pink to black

2.1.3 Evaluation of performance characteristics

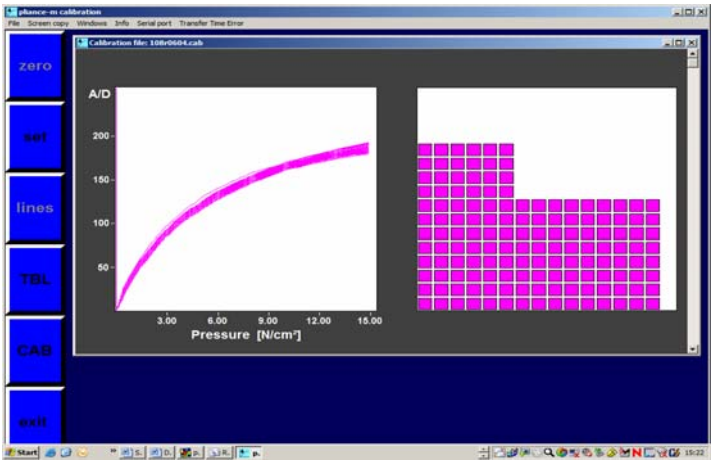
The novel pliance® system was subjected to laboratory evaluation for confirmation of dynamic and static performance characteristics, using the prototype square mat. The results are summarised under each procedure, together with comments on their clinical relevance.

2.1.3.1 Calibration

The sensor mat was calibrated according to the manufacturer's instructions using the novel trublu® calibration device, an airbladder system which applied air at a homogenous pressure. Each individual sensor was calibrated at step intervals of 1 N/cm^2 over the full calibration range 0.2-15 N/cm^2. The accuracy and stability of the mat's calibration was checked by applying known pressure signals over the full pressure range of the mat (0-15 N/cm^2): i) daily for a week and ii) weekly for a month.

Results: Figure 2.8 shows that the calibration traces for each of the 256 sensors covered the full A/D range in a smooth, regular manner. Calibration remained stable over the one month period (<5% variability).

Figure 2.8 novel pliance® calibration trace for each individual sensor

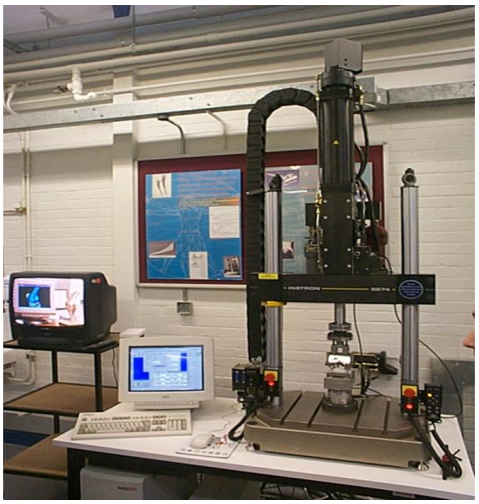


Clinical Relevance – Stability of calibration is dependent on the amount of mat usage. Prior to any data collection, the validity of the system's calibration was confirmed by applying a series of pressure signals of known amplitudes to the mats, covering the full calibration range (0.2 – 15 N/cm^2) at intervals of 1 N/cm^2. If measurement error exceeded 5% full scale deflection, the full recalibration process was performed according to the manufacturer's instructions. The system was additionally calibrated at monthly intervals.

2.1.3.2 Dynamic response

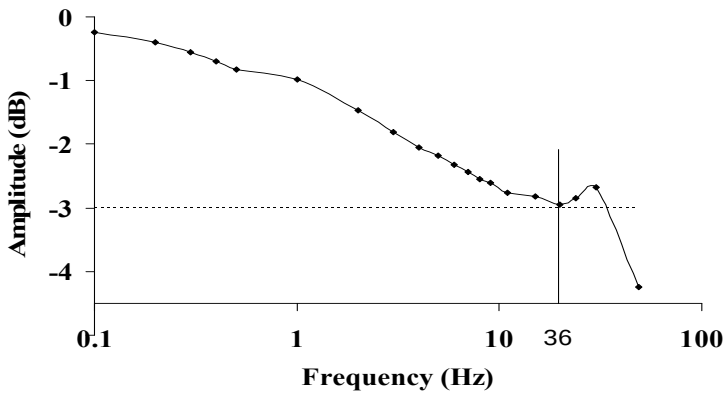
Dynamic response was investigated by imposing step and cyclic loading using a computer-controlled servo-hydraulic dynamic testing unit (Instron 8874™, Instron Ltd, Bucks, England), as shown in **Figure 2.9**. During Instron™ testing, the mat was loaded using a metal circular disc probe of 7.5cm diameter (44.2 cm^2 area) with milled surfaces and bevelled edges. The probe size was selected to simulate the area of the palm of the therapist's hand. The sensor mat and probe were in planar position, and a minimum of 4 sensors were simultaneously loaded. The sensor mat was cyclically loaded between 0 and 500 N at frequencies ranging from 0.1 Hz to 50 Hz.

Figure 2.9 Instron™ testing unit



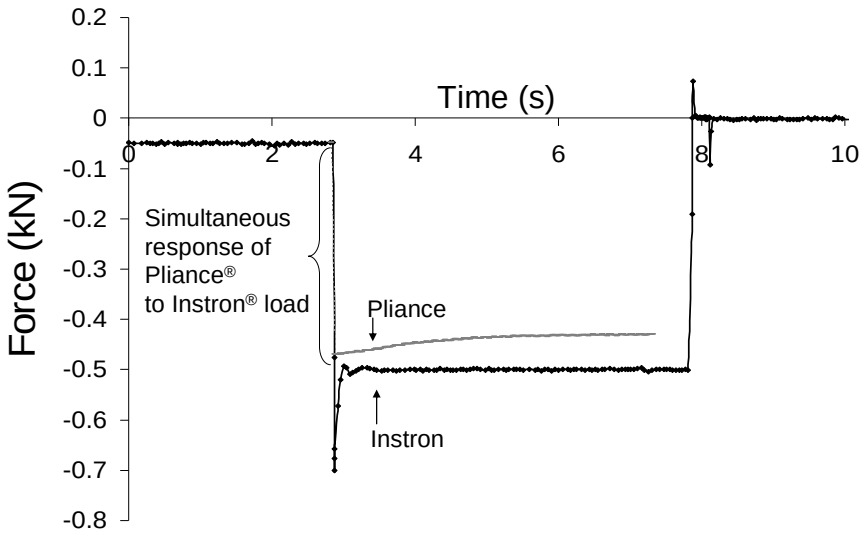
Frequency response: The initial square mat registered a frequency response up to 36 Hz (-3 dB), which agreed with the manufacturer's specifications, **Figure 2.10**.

Figure 2.10 Frequency response of the Pliance® system



Speed of sensors' response: The response of the sensors was essentially immediate (less than 0.1 s), following exactly the load applied by the Instron™, as shown in **Figure 2.11**.

Figure 2.11 Speed of response of the Pliance® system to 500N load



2.1.3.3 Static response

Static force characteristics were also assessed using the Instron™ to load the mat at increments of approximately 10 N up to 200 N, the estimated range of paediatric physiotherapy force application. Force was again applied over an area equivalent to the hand contact area during CWV (44.2 cm^2 area). To extend the test range towards the upper limits of the mat's calibration range (15 N/cm^2), measurements were continued up to 500 N, the possible loading range in adults (500 $N/44cm^2$ =11.4 N/cm^2).

Static Loading: Assessment of forces up to 500N with the Instron™ revealed that the novel pliance® system was linear in response, as shown in **Figure 2.12**. The measurement error was proportional to the applied force (**Figure 2.13**), and was therefore expressed as % differences. For the test range up to 200N, the mean % error (95% confidence intervals, CI) was -4.7% (-3.7, -5.7), the maximum error equating to -6.3%. Similarly, when loading was extended up to 500 N, mean % error was -4.5% (maximum -7.7%).

Figure 2.12 Response of the Pliance® system to loading from 0 N to 500 N

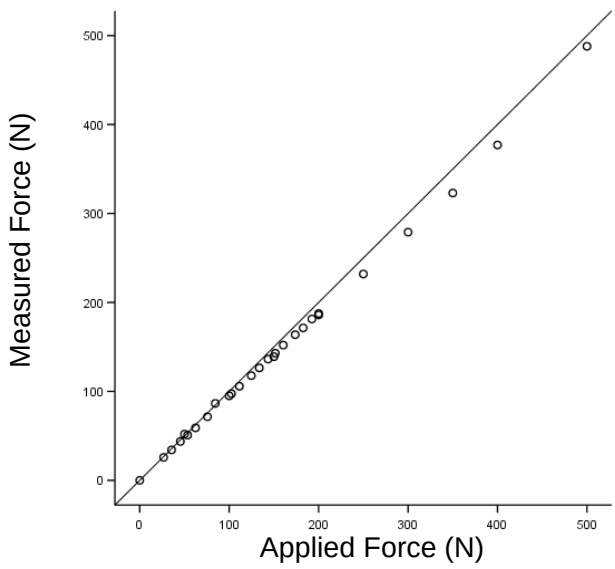
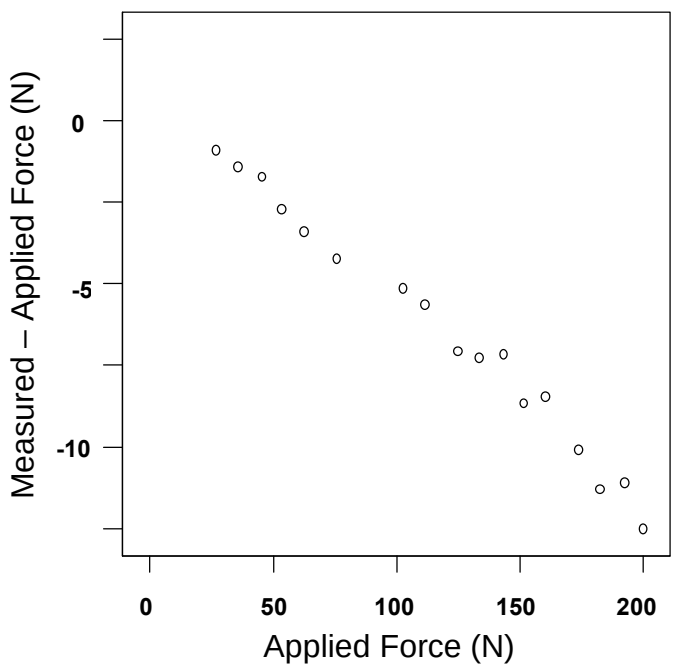


Figure 2.13 Relationship of measurement error to the force applied up to 200 N

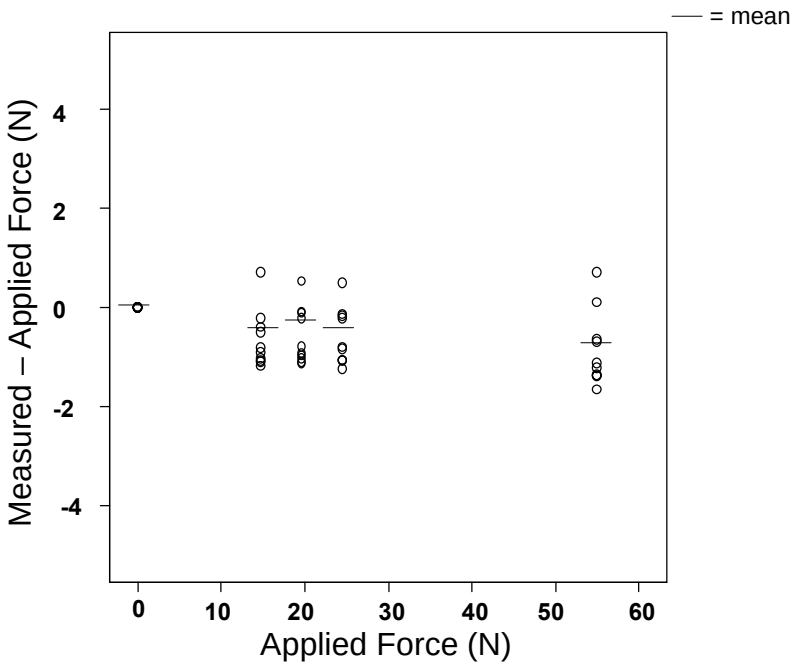


2.1.3.4 Accuracy and precision

The sensor mat was then evaluated by ten repeated, inhomogeneous random manual loadings of the mat, using 4 calibration weights, between 14.7 N and 54.9 N. The testing range was dictated by the availability of calibration weights. To improve conformity between the mat and the loading weight, the contact surface of the weights was interfaced with remnants of the plasticised leather material from the mat.

Accuracy and precision: During repeated, random loadings between 14.7 - 54.9N, the mean (95% CI) difference between measured and applied forces was -0.53N (-0.36, -0.7N), with a maximum error of -1.65N, as shown in **Figure 2.14**. The average coefficient of variation (CV) during these in-vitro assessments was 2.7% (range 1.4 to 4.1%).

Figure 2.14 The effect of repeated, random loading of the force mat with calibration weights



Clinical Relevance - The pliance® system was created to measure dynamic pressure distribution and is calibrated using homogenous pressure applied over all sensors by means of an airbladder system. Unlike pressure, force is independent of changes in contact area. Since force is a valid variable from the system and is appropriate for chest physiotherapy analysis, it was important to evaluate the pliance® system regarding the accuracy of force measurements. The small but systematic tendency for force underestimation when assessed by application of force using the Instron™ is likely to relate in part to the nature

of metallic rigid bodies, the surface of which does not conform fully to the mat. In the clinical environment, the hand's soft tissues produce good conformity with the mat, so that the force applied through the hand is distributed more evenly than occurs when force is applied using metal weights.

The ability of the mat to measure loads accurately is determined by the position of the load (weight) over the individual pressure sensors. During the random placing of each of the weights, at least 4 sensors would have been covered. In addition, adjacent sensors may have been partially loaded. Because of the averaging effects on the partially loaded sensors the output of these sensors might differ slightly from the applied force. Such partial loading of sensors may also occur clinically, but these results show the measurement error was small (< 5%).

2.1.3.5 Mat curvature

To explore the effect of laying the mat around the child's convex chest wall, the mat was subjected to extreme manual curvature (forming a cylinder of 6.5cm diameter) which was maintained for 15 minutes on 5 successive occasions.

Mat curvature: The maximum force generated by extreme curvature of the unloaded mat was mean 1 N (SD 0.1 N).

Clinical Relevance - The study protocol was designed to minimise further the already small effect of increasing forces by strong curvatures of the sensor mat. Prior to data collection, the mat was taped in position on the subject's convex chest wall and then 'zeroed' in-situ, while no load was being applied. This procedure negated any possible effect of static mat curvature. The pliance® system is only able to measure load applied perpendicular to the capacitance sensors. However, because the mat can be curved around the chest this is not a limitation, the mat measuring the compressive forces applied during CWV.

2.1.3.6 Stability

The margin of error resulting from factors including drift and creep was evaluated by sustained application of a 54.9 N force over a one hour period.

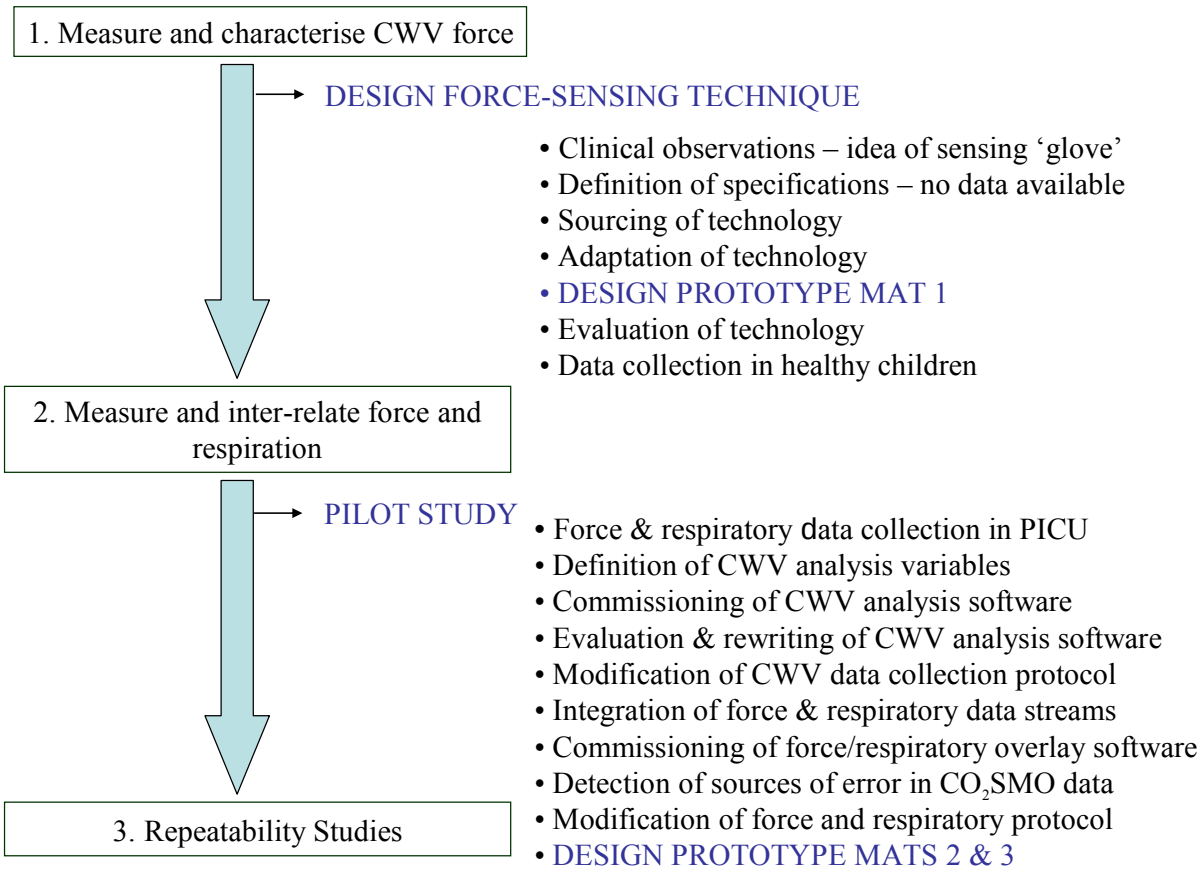
Stability: The margin of error for 54.9 N loading over 1 hour was 3%, the total force reading increasing by 1.6 N, from 54 N to 55.6 N.

Clinical Relevance - In the clinical study reported in **Chapter 3**, the median duration of a single CWV was 2 seconds (range 0.8s – 4.6 s) and the duration of whole treatment was 6 minutes (range 1.6 to 25 min). During the treatment there were lengthy periods when the mat was not loaded (during lung inflations and suction). In the clinical situation such sustained loading is therefore unlikely to occur, the margin of error again being small. The load applied approximated closely to the average force found in the clinical trial (median maximum force 41 N).

2.2 Pilot study of simultaneous measurement of force and respiration during chest physiotherapy

Figure 2.15 presents an overview of the inter-related and over-lapping tasks of technique development, validation and refinement required prior to the full clinical study (detailed in **Chapter 3**).

Figure 2.15 Overview of tasks required to devise a technique for measuring force and simultaneous changes in respiration



Having developed and validated the force-sensing technique, the feasibility of using the system was assessed by applying the technique to 11 healthy children (age range 7 month to 13 years) in order to gain experience prior to using the system in ICU and in an attempt to gain CWV repeatability data in children. The results of this preliminary data collection were published, which demonstrated that valid CWV force measurements in children were possible with the new tool, summarised the system's performance characteristics (**section 2.1.3**) and showed example force profiles (Gregson et al. 2003). The study also

demonstrated that valid repeatability data would be difficult to collect on healthy children under the age of 8 years due to movement artefacts during the chest physiotherapy.

The novel pliance® analysis packages were devised for analysis of gait and were therefore not directly transferable for characterisation of chest physiotherapy. No information existed regarding the most clinically useful variables to describe CWV force profiles and their respiratory effects, and a pilot study was therefore required. Approval for the study in healthy children and in ICU was granted by the Southampton and South West Hampshire Joint Research Ethics Committee (**Appendix B**).

2.2.1 Aims and Objectives of the pilot study

Objective 1. To develop a method of quantifying chest wall vibration forces and the means of evaluating simultaneous changes in force with those of respiratory airflow and pressure in ventilated infants and children of all ages

A pilot study was undertaken in Southampton General Hospital's paediatric ICU to:
1. Produce a protocol for simultaneous force and respiratory measurements *during* physiotherapy, prior to performing the full clinical study described in Chapter 3

2. Explore the force and respiratory output data and define the most valuable variables and analysis format to be included in the clinical study

2.2.2 Equipment

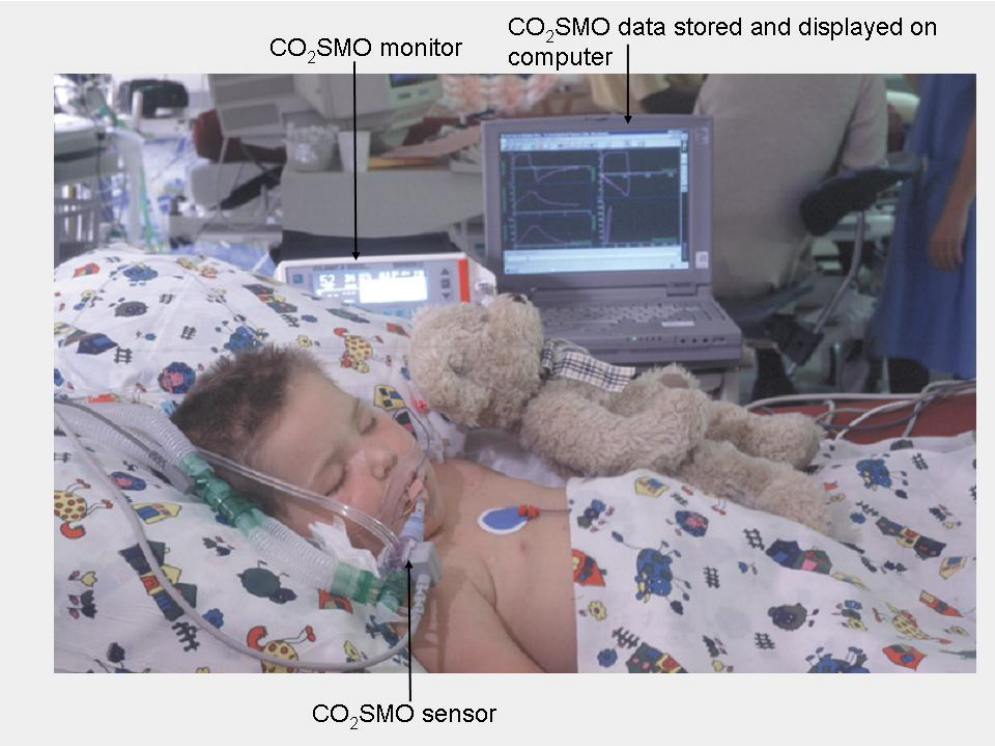
2.2.2.1 Force

The pliance® system and customised mats detailed in **section 2.1.2** were used to record force data.

2.2.2.2 Respiration

The CO_2SMO® Plus! Respiratory Profile Monitor (Respironics, Wallingford CT, USA) was identified as a suitable respiratory tool, and is shown in **Figure 2.16**. It provided non-invasive measurements of airflow and pressure at the airway opening continuously and in real-time via a low deadspace, fixed-orifice, differential flow and pressure sensor inserted between the endo-tracheal tube and the ventilator or manual inflation circuit. Volume was derived by integrating airflow over time (sampling frequency of 100 Hz).

Figure 2.16 CO_2SMO® attached to child's endotracheal tube to monitor ventilation prior to chest physiotherapy



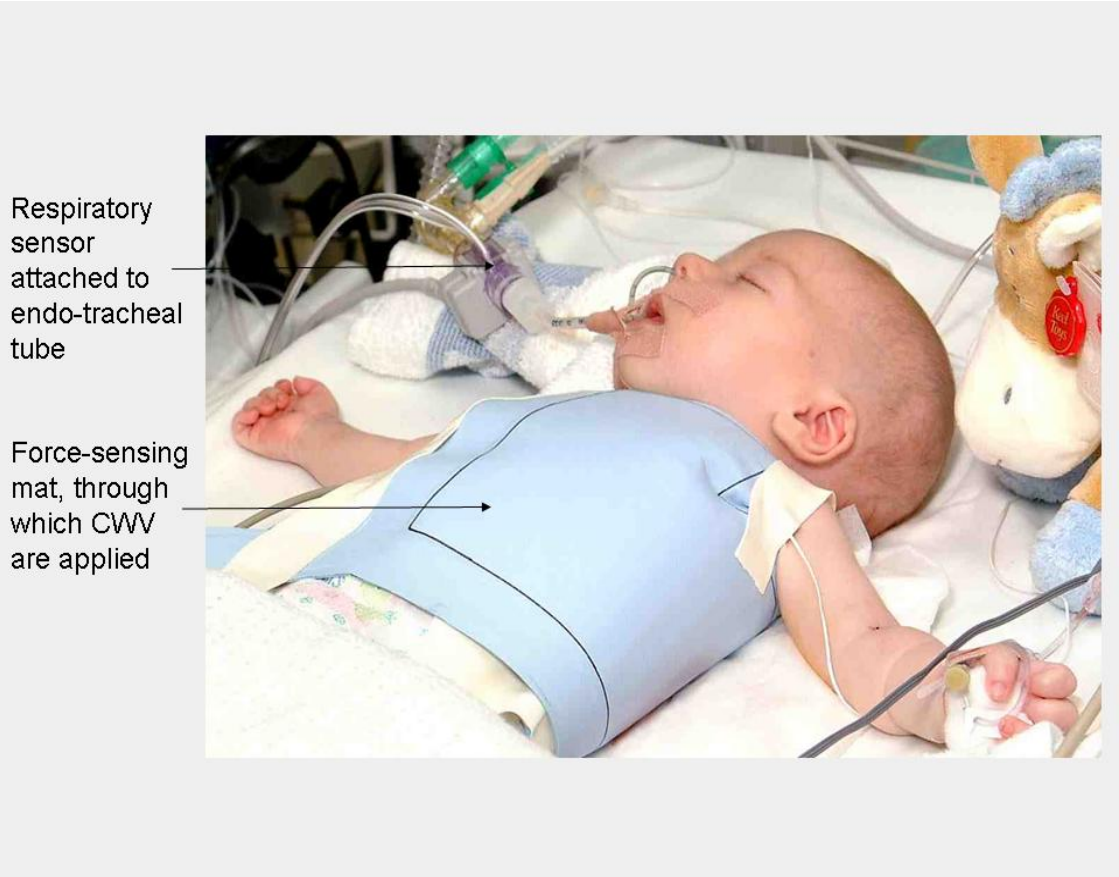
The CO_2SMO® also provided respiratory mechanics data (respiratory compliance and resistance) and capnography; both the neonatal and paediatric sensors for the CO_2SMO® had been previously validated in mechanically ventilated children (Main 2001;Castle et al. 2002;Main et al. 2004). The neonatal sensor was used for children less than two years of

age (where airflow was generally less than 25 l/min) and the paediatric / adult sensor (series 3) for older children. The CO_2SMO® sensors were calibrated by applying step increases of known volumes across their respective ranges of linearity using a Hans Rudolph® (Hans Rudolph Inc., Kansas City, MO., USA) calibration syringe.

2.2.3 Protocol

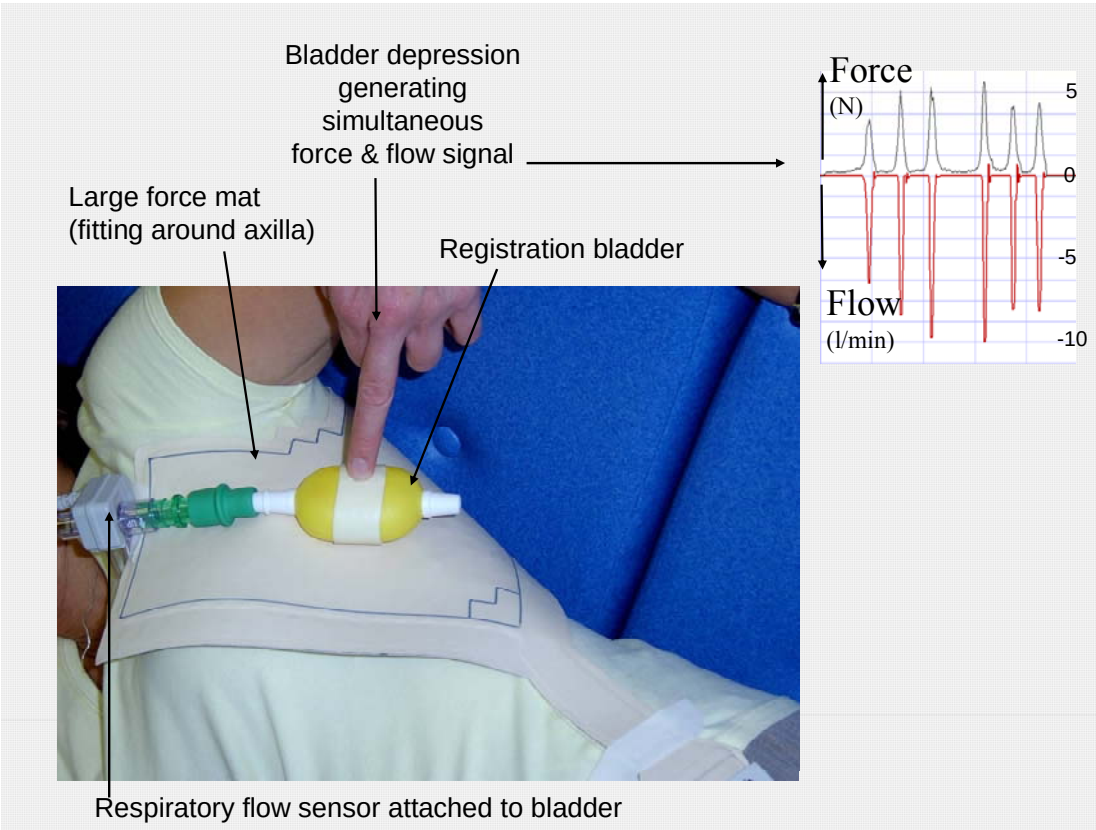
Informed, written consent was obtained from the families of the participating children. Children were eligible if they were receiving chest physiotherapy as part of their routine care. **Figure 2.17** shows the equipment used for the force and respiratory measurements in the ventilated children. Both systems were calibrated prior to each period of data collection, as detailed in **section 2.1.3.1** and **section 2.2.2**. To create a valid data collection protocol for the clinical study, the planned data collection conditions were simulated by including a brief five minute period of respiratory monitoring during normal mechanical ventilation before and after the physiotherapy treatment.

Figure 2.17 The equipment required for simultaneous force and respiratory measurements in mechanically ventilated children



The lightweight sensing mat was taped over the treatment area of the child's chest using elastic tape (Microfoam®). Since the force applied by the therapist and the respiratory data generated at the airway opening would be collected using independent systems and at different sampling frequencies (novel pliance® at 50 Hz and CO_2SMO® at 100 Hz), it was necessary to devise a means of synchronising the two data streams for analysis. Registration of force and flow (before and after physiotherapy) was accomplished using a small, re-inflating bladder (**Figure 2.18**). The bladder was placed over the sensing mat, with the CO_2SMO® sensor attached onto the mouth of the registration bladder. Repeated, swift depression of the bladder generated simultaneous force and flow signals.

Figure 2.18 Registration of the force and flow data streams by application of simultaneous signals to both recording systems.



Following data registration, the CO_2SMO® sensor was reconnected into the child's ventilator circuit and the entire physiotherapy session (comprising periods of manual lung inflations, CWV, saline instillation and suction) was continuously recorded using the sensing mat and CO_2SMO®. Suctioning and saline instillation was performed directly into the endotracheal tube, having first removed the CO_2SMO® sensor. Video footage available from the author demonstrates the protocol features.

2.2.4 Selection of outcome measures and data analysis procedure

The force variables were unknown at the start of pilot data collection. The following respiratory outcome measures were selected to describe the direct ventilatory effects of chest physiotherapy: Peak inflation pressure (PIP), positive end expiratory pressure (PEEP), inflation volume (VI), expired volume (VE), peak inspiratory flow (PIF) and peak expiratory flow (PEF). Although not available from CO_2SMO®, mean inspiratory and expiratory flows were manually calculated by dividing the respective volume by time, as it was felt that such measures could potentially describe additional effects of different CWV techniques.

Pilot force data were inspected and analysed using Excel™, and relevant variables were identified. Colleagues collaborating in this research (Dr Petley and Ms Jagannathan, Department of Medical Physics and Bioengineering) were then commissioned to write a suitable analysis programme to evaluate and store the extensive array of variables. Further software was then developed to inter-relate the simultaneous force and respiratory data to produce overlaid images.

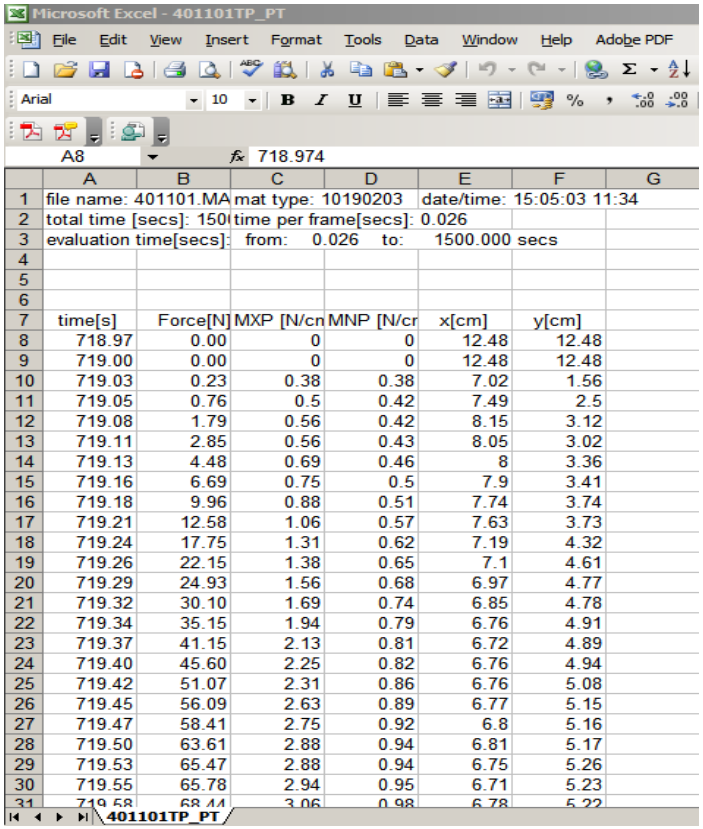
2.2.5 Results

Simultaneous measurements of force and respiration during physiotherapy were successfully collected in 14 of the 16 ventilated children studied (median age 2.3 years, range 6 weeks to 13.7 years). Three physiotherapists delivered the 16 treatments. The children tolerated the technique well, and the physiotherapists did not find that the mat interfered significantly with their normal treatment, palpatory feedback still being possible through the thin mats. Two early data sets were lost, which appeared to be due to interactions between the pliance® and CO_2SMO® data acquisition software. The data collection protocol was initially modified so that both programmes were opened and operated whilst each occupied half the computer screen. However, to avoid any risk of errors from parallel processing of the two data streams by one computer, data from the CO_2SMO® and pliance® systems were successfully collected via two separate computers in the final 10 children.

2.2.5.1 Force

The summary ASCII format file generated by the pliance® system comprised columns of data for time, force, pressure (maximum, mean and x-y co-ordinates for centre of pressure), as shown in **Figure 2.19**.

Figure 2.19 Novel® ASCII data exported into Excel®

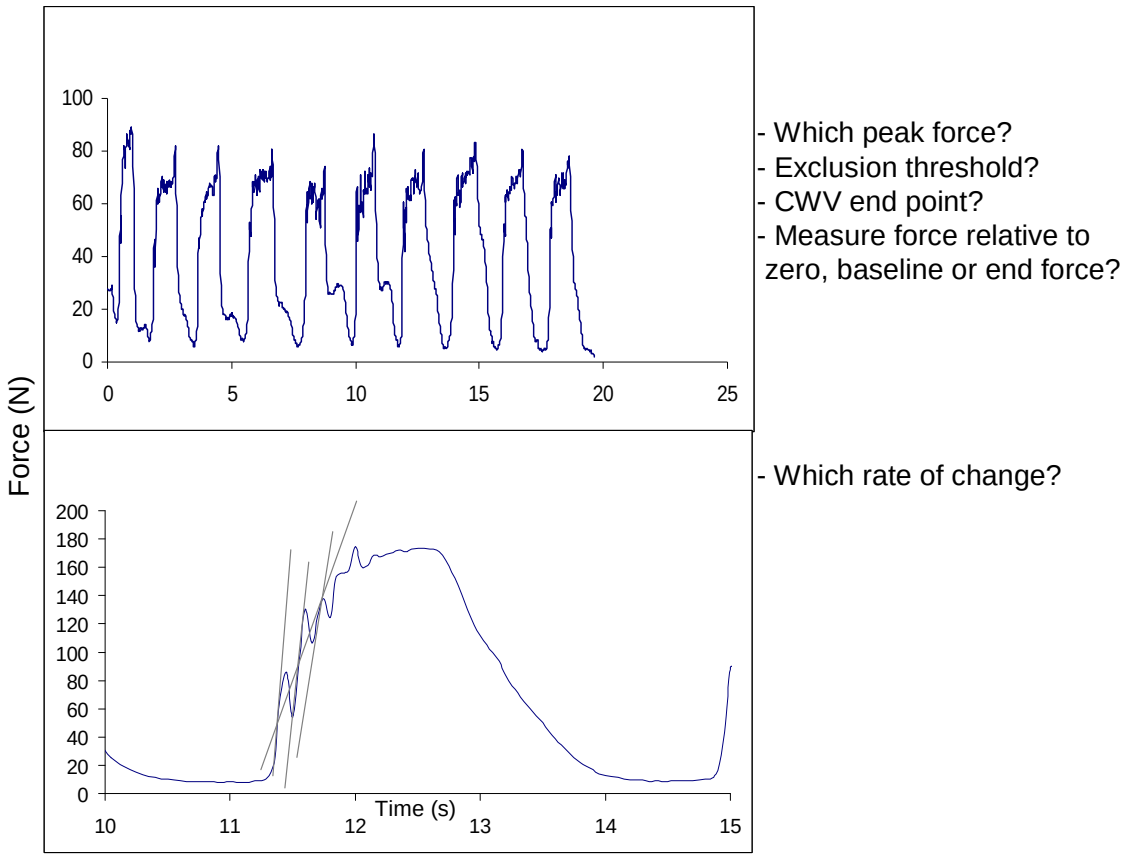


	A	B	C	D	E	F	G
1	file name: 401101.MA		mat type: 10190203		date/time: 15:05:03 11:34		
2	total time [secs]: 150		time per frame[secs]: 0.026				
3	evaluation time[secs]:		from: 0.026	to: 1500.000 secs			
4							
5							
6							
7	time[s]	Force[N]	MXP [N/cn	MNP [N/cr	x[cm]	y[cm]	
8	718.97	0.00	0	0	12.48	12.48	
9	719.00	0.00	0	0	12.48	12.48	
10	719.03	0.23	0.38	0.38	7.02	1.56	
11	719.05	0.76	0.5	0.42	7.49	2.5	
12	719.08	1.79	0.56	0.42	8.15	3.12	
13	719.11	2.85	0.56	0.43	8.05	3.02	
14	719.13	4.48	0.69	0.46	8	3.36	
15	719.16	6.69	0.75	0.5	7.9	3.41	
16	719.18	9.96	0.88	0.51	7.74	3.74	
17	719.21	12.58	1.06	0.57	7.63	3.73	
18	719.24	17.75	1.31	0.62	7.19	4.32	
19	719.26	22.15	1.38	0.65	7.1	4.61	
20	719.29	24.93	1.56	0.68	6.97	4.77	
21	719.32	30.10	1.69	0.74	6.85	4.78	
22	719.34	35.15	1.94	0.79	6.76	4.91	
23	719.37	41.15	2.13	0.81	6.72	4.89	
24	719.40	45.60	2.25	0.82	6.76	4.94	
25	719.42	51.07	2.31	0.86	6.76	5.08	
26	719.45	56.09	2.63	0.89	6.77	5.15	
27	719.47	58.41	2.75	0.92	6.8	5.16	
28	719.50	63.61	2.88	0.94	6.81	5.17	
29	719.53	65.47	2.88	0.94	6.75	5.26	
30	719.55	65.78	2.94	0.95	6.71	5.23	
31	719.58	68.44	3.06	0.98	6.78	5.22	

2.2.5.2 Definition of analysis variables to characterise the CWV forces

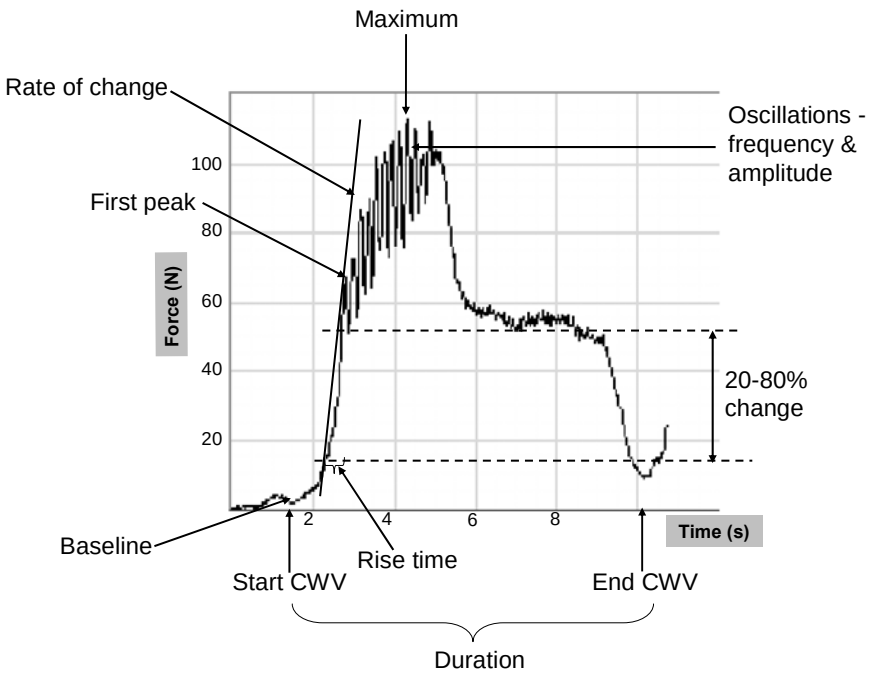
Figure 2.20 illustrates examples of two force profiles and decisions required on the relative importance of features within the trace.

Figure 2.20 Examples of decisions involved in defining appropriate force variables



The CWV analysis variables were derived by considering the theoretical effects of CWV on airflow, and deciding which features of the profile were likely to relate to airflow changes. **Figure 2.21** shows the measures initially selected for analysis.

Figure 2.21 Variables defined to characterise chest wall vibration force profiles

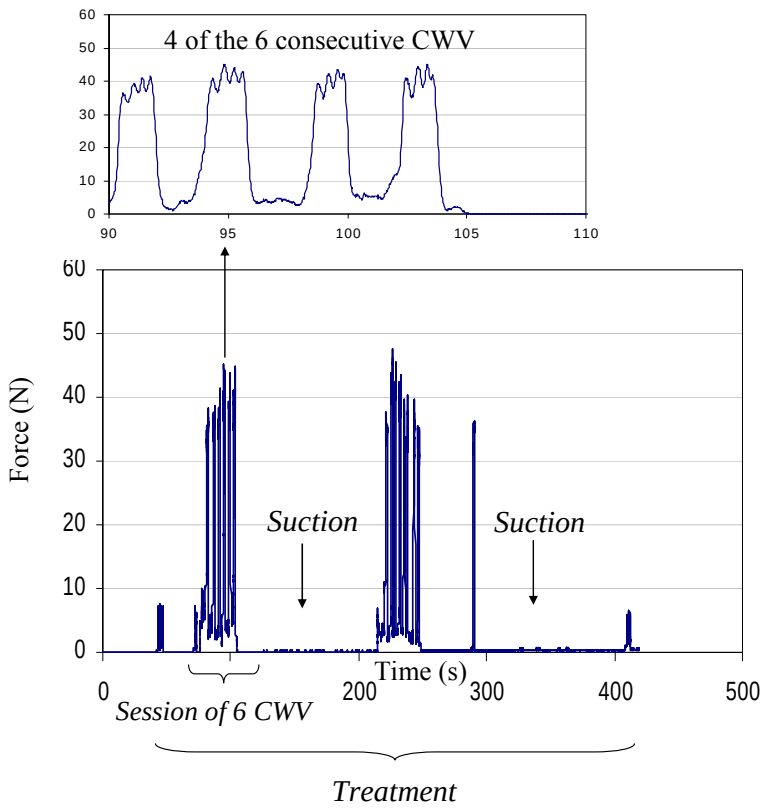


The key variables were defined as follows:

- Maximum force, Fmax (N) - *force occurring anywhere between the start and end of an individual CWV*
- Mean force over 1 second, Fmean (N) - *area under the curve divided by duration of CWV*
- Baseline (minimum) force (N) - *force applied at the start of a CWV*
- Baseline to maximum force (N) - *maximum – baseline force*
- Force at first peak (N) - *force at the end of the first inward compression, before oscillations occurred; used to calculate rate of change of force*
- Rise time (s) - *time for force to rise from start of CWV to first peak*
- Rate of change of force (N/s) - *slope derived over 20-80% baseline to first peak*
- Frequency (Hz i.e. cycles per second) and amplitude (N) of oscillations– *derived from the inward compressive oscillations*
- Duration of each vibration (s)

The duration (in minutes) of the whole treatment and the number of sessions of CWV in a treatment were also calculated, as illustrated in **Figure 2.22**. A series of consecutive CWV was termed a session, successive sessions being interspersed with other treatment techniques, such as suction. During the pilot phase, the data collection protocol progressed from storing each session in a separate data file to saving the whole treatment as a single, continuous data file.

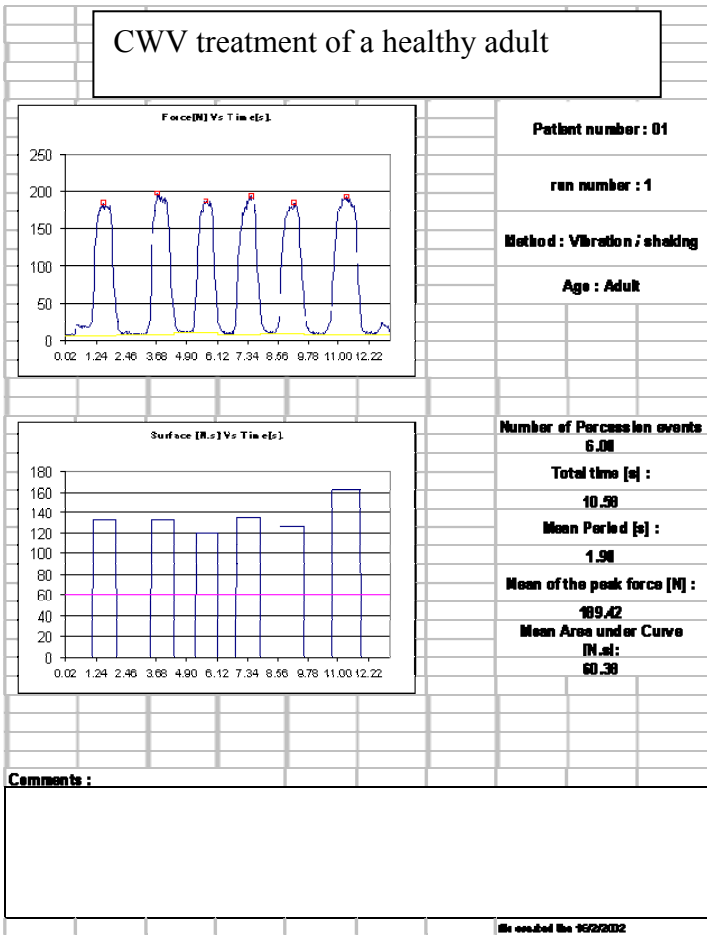
Figure 2.22 Definition of a session of chest wall vibrations within a treatment



It was noted, during preliminary trials, that some physiotherapists maintained a small positive baseline force through the mat between individual vibrations. Rate of change of force was therefore calculated over 20-80% of the gradient of the first inward chest wall compression (first peak force), thus lessening the impact of the point identified as the start of each CWV. Maximum force did not always occur at the point of the first inward compressive force – first peak force. Since first peak was used to calculate the rate of change of force, it was decided that two points of force should be identified, namely the first peak and the overall maximum force.

Analysis algorithms were devised initially in VEE Pro® and then in Labview®, the former programme proving insufficiently flexible for the task. An example of the initial VEE Pro® output is shown in **Figure 2.23**, the small red squares in the top graph identifying the maximum force, and the histograms represented the mean force, calculated from area under the curve.

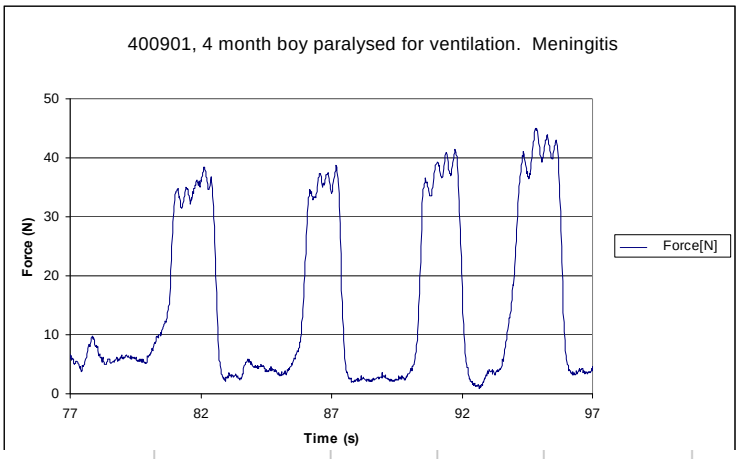
Figure 2.23 Original analysis programme written in VEE Pro®



The level of automation required from the analysis programme was carefully considered, as there was a trade-off between greater automation and the accuracy of the values obtained for each parameter. Since a primary aim of this research was to explore the data in great detail, it was important to maximise the accuracy of the information obtained. Data were therefore read into the software package, and the events were then manually identified by cursor placement at the beginning and end of each CWV event. These events were then used for automated analysis and the values were compared with those obtained by manual analysis in Excel™. The Labview® programme was validated by performing double analysis of the 14

data files, comparing the results generated by the programme with those obtained from manual analysis in Excel®, an example of which is shown in **Figure 2.24**. The iterative process resulted in the detection and resolution of any early programme errors. The last 5 of the 14 data files were analysed when the programme errors were fully resolved and revealed full agreement for maximum force values and CV < 3% for minimum (baseline) force.

Figure 2.24 Final chest wall vibration force analysis format



400901							
Vib	Event Label	Rate of Change	Max Forc	Min Force	Pk to Pk Forc	Duration	Rise Time
0	Vibrations	45.00	38.44	3.13	35.31	2.94	0.40
1	Vibrations	85.51	38.69	2.56	36.13	2.38	0.22
2	Vibrations	127.34	41.50	1.69	39.81	2.48	0.16
3	Vibrations	57.73	45.06	3.88	41.19	2.66	0.38
4	Vibrations	76.04	43.63	2.50	41.13	2.34	0.30
5	Vibrations	67.83	45.00	2.44	42.56	2.64	0.34
6	Vibrations	111.46	37.69	1.94	35.75	2.08	0.12
7	Vibrations	84.17	47.69	3.06	44.63	2.14	0.30
8	Vibrations	134.38	45.44	3.19	42.25	2.18	0.18
9	Vibrations	65.16	43.56	3.31	40.25	2.38	0.40
10	Vibrations	91.19	39.56	2.94	36.63	1.94	0.22
11	Vibrations	148.43	40.19	1.94	38.25	1.88	0.12
12	Vibrations	135.26	39.63	1.44	38.19	2.06	0.14
13	Vibrations	176.56	35.69	1.31	34.38	1.74	0.12
A	Suction Compression	47.34	36.19	0.63	35.56	2.28	0.40
Mean		100.43	41.55	2.52	39.03	2.27	0.24
SD		38.91	3.53	0.77	3.13	0.33	0.11
Max		176.56	47.69	3.88	44.63	2.94	0.40
Min		45.00	35.69	1.31	34.38	1.74	0.12
(Vib during Suction NOT included in summary)							

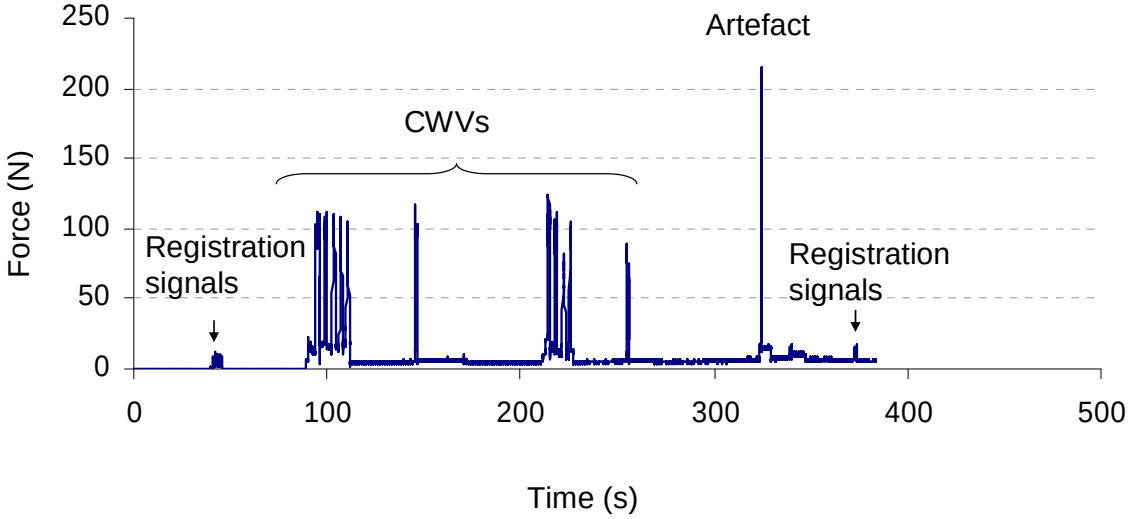
Upper section: Force-time profile produced manually in Excel (from Novel® ASCII data)
Lower section: corresponding data derived from analysis programme written in Labview®

The semi-automated nature of the programme facilitated removal or adjustment of any points in the trace which had been automatically but incorrectly identified by the programme, as discussed below.

2.2.5.2.1 Artefact in the force data

It was possible to create an artefact (a brief and abnormally high force) if the mat was creased, as shown in **Figure 2.25**. In this example, the artefact was created after the CWV treatment, during alterations to the patient's position. The analysis software allowed the operator to identify any individual CWV event which exhibited artefact and to exclude these from the analysis.

Figure 2.25 Identification of artefact within a force-time trace

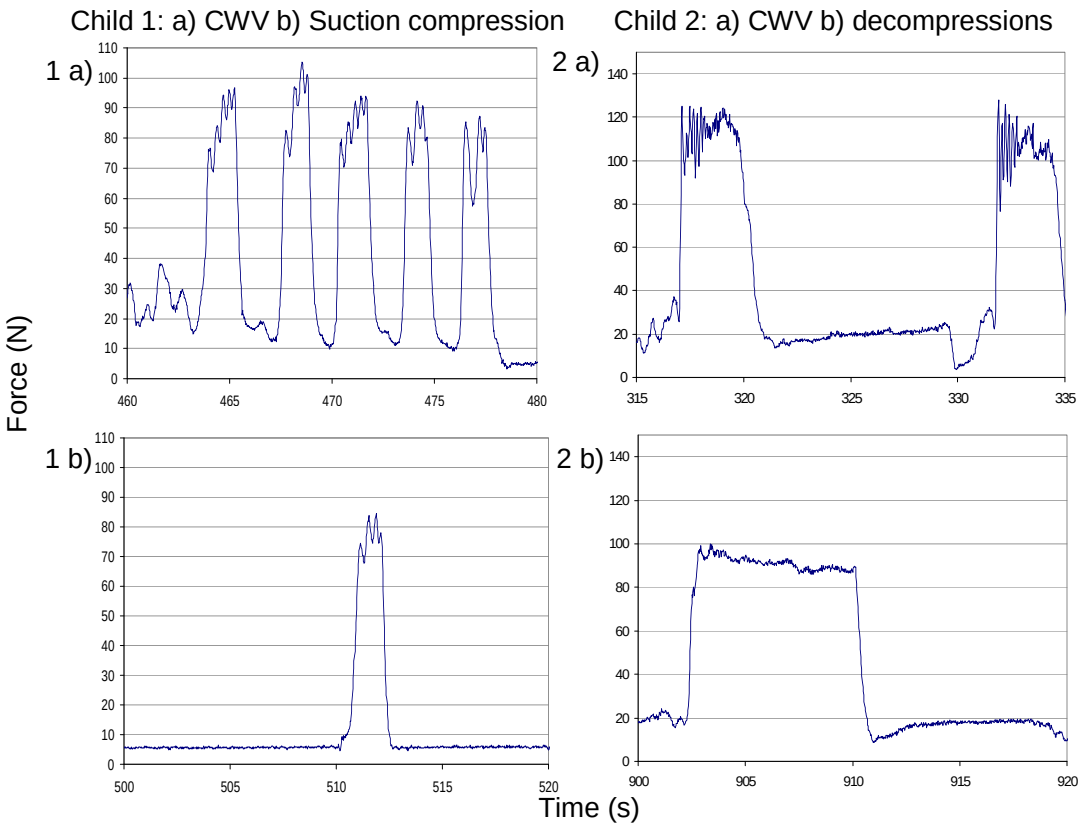


If a sensor in the pliance® mat became damaged, the particular sensor ceased to work, as indicated by an LED error light. This would result in the system's subsequent sampling frequency being halved for the remainder of the data file. This situation was encountered only once (at the beginning of the clinical study), and resulted from extreme creasing of the mat by the physiotherapist during her treatment preparation. The mat was repaired and the problem did not recur.

2.2.5.2.2 Categorisation of forces applied during treatment

In addition to applying CWV with manual lung inflations, some physiotherapists also compressed the child's chest during the suction procedure, to facilitate removal of secretions. On other occasions physiotherapists reported that they were decompressing the lung, to reduce the level of gas trapping. These forces were generally longer than the remaining CWV, and had little oscillatory component. **Figure 2.26** shows a child's treatment which comprised CWV and compressions during suction (Child 1) and another child's treatment which included CWV and chest decompressions (Child 2).

Figure 2.26 Categorisation of compressions applied during chest physiotherapy



Physiotherapists were routinely asked to report periods when they were delivering chest decompressions. Treatment notes to document periods of manual lung inflations, CWV, saline instillation, suction and decompressions were continuously timed and electronically entered into the $CO_2SMO^{®}$ during treatment. These allowed the forces and corresponding respiratory changes to be identified and differentially coded. Since the $CO_2SMO^{®}$ sensor was removed from the circuit during suction, suction compressions were further confirmed by the absence of respiratory data when force and respiration were overlaid (**section**

2.2.5.4). The remit of the current research was to focus on force and respiration during CWV (**Chapter 3**).

2.2.5.3 Respiration

The CO_2SMO® data were stored both as sequential files of real-time data (called snapshots, set to cover 10 minute periods of data) and as data files averaged over 1 minute periods (trended data). **Figure 2.27** contains an example of flow, pressure and volume being sampled continuously (at one hundredth of a second) throughout a breath. These data have been exported into Excel® for manual analysis. Upon completion of the analysis software, the real-time data files were imported into the programme designed in-house to overlay force and respiration (**section 2.2.5.4**).

Figure 2.27 Examples of (a) real time and (b) trended CO_2SMO® respiratory data exported into Excel®

(a)

Microsoft Excel - 401101ss10wa_MCPT

Name	ID	Date	Time	Seconds	Flow (lpm)	Pressure (	Volume (ml)	Volume-Exp (ml)	CO2 (kPa)
Christophe	401101 17	15/05/2003	11:11:52	0	-8.4	0.75	12	811.6	3.95
				0.01	-8.4	0.75	10	813	3.965
				0.02	-8.4	0.8	9	814.4	3.981
				0.03	-9.3	0.95	7	816	3.996
				0.04	-10.86	0.95	6	817.8	3.996
				0.05	-10.86	0.95	4	819.6	3.981
				0.06	-10.86	0.95	2	821.4	3.981
				0.07	-10.86	0.95	1	823.3	3.981
				0.08	-9.48	0.95	0	824.8	3.981
				0.09	-9.18	0.95	-2	826.4	3.981
				0.1	-9.18	0.95	-4	827.9	3.981
				0.11	-6.96	0.95	-5	829.1	3.981
				0.12	-6.96	1	-6	830.2	3.981
				0.13	-6.96	1.1	-8	831.4	3.981
				0.14	-6.96	1.2	-9	832.6	3.981
				0.15	-6.96	1.3	-10	833.7	3.996
				0.16	-6.78	1.3	-11	834.9	3.981
				0.17	-6.78	1.3	-12	836	3.965
				0.18	-4.5	1.65	-13	836.8	3.95
				0.19	-2.58	2	-14	837.2	3.95
				0.2	0	2.4	-15	837.2	3.965
				0.21	1.68	2.95	-15	836.9	3.981
				0.22	2.16	3.35	-15	836.5	3.996
				0.23	2.88	3.5	0	836.1	4.004
				0.24	2.88	3.8	0	835.6	3.981
				0.25	3.9	4.5	0	834.9	3.95
				0.26	7.08	5.65	0	833.7	3.942
				0.27	10.98	7.45	0	831.9	3.95
				0.28	16.8	9.85	0	829.1	3.95
				0.29	21.66	11.6	0	825.5	3.965

(b)

Microsoft Excel - 401401C trend

Name	ID	Date	Time	MV tot	MV alv t	RR total	Vt e spon	Vt e mech
401401	Robert	05/02/2004	10:43:59	1.13	0.13	22	23	109
			10:44:59	4.5	3.05	31	24	300
			10:45:59	5.4	3.93	18	75	313
			10:46:59	5.48	4.05	17	2	317
			10:47:59	5.41	4.07	17	0	318
			10:48:59	5.39	4.03	17	0	319
			10:49:59	5.43	4.01	17	0	308
			10:50:59	5.42	4.07	17	0	319
			10:51:59	5.28	3.96	16	0	318
			10:52:59	5.31	3.98	16	0	317
			10:53:59	5.4	4	17	0	312

However, on preliminary analysis in Excel® and following discussions with the manufacturers it was confirmed that the primary role of the volume columns displayed in **Figure 2.27a** was to detect and correct any 'zero volume' drift, caused if there was a difference between the inhaled and exhaled volume in a single breath. In this way the beginning of an inspiratory breath always started from zero on the volume axis. **Figure 2.28** relates flow, pressure and volume changes during mechanical ventilation, showing how disconnection from the ventilator produced a negative volume trace, because expired volume exceeded the inflation volume. The volume trace was then reset to zero for the start of the next breath. Similarly, if inflation volume exceeded expired volume (for example, if the physiotherapist was producing intrinsic PEEP during lung inflations), the volume trace would end above the zero baseline, and would then jump to the zero line for the start of the next breath. While this approach ensured the volume trace did not 'drift off' the screen during data collection, it can complicate identification of a leak, and invalidates the use of the data stored under the 'volume' columns [**Figure 2.27 (a)**]. The breath-by-breath and trended values for inflation and expiratory volume produced by CO_2SMO® [**Figure 2.27 (b)**] were actually derived from the flow signal once it had been processed using a series of internal validation calculations within the CO_2SMO® analysis software.

Figure 2.28 Relative changes in flow, pressure and volume during mechanical ventilation

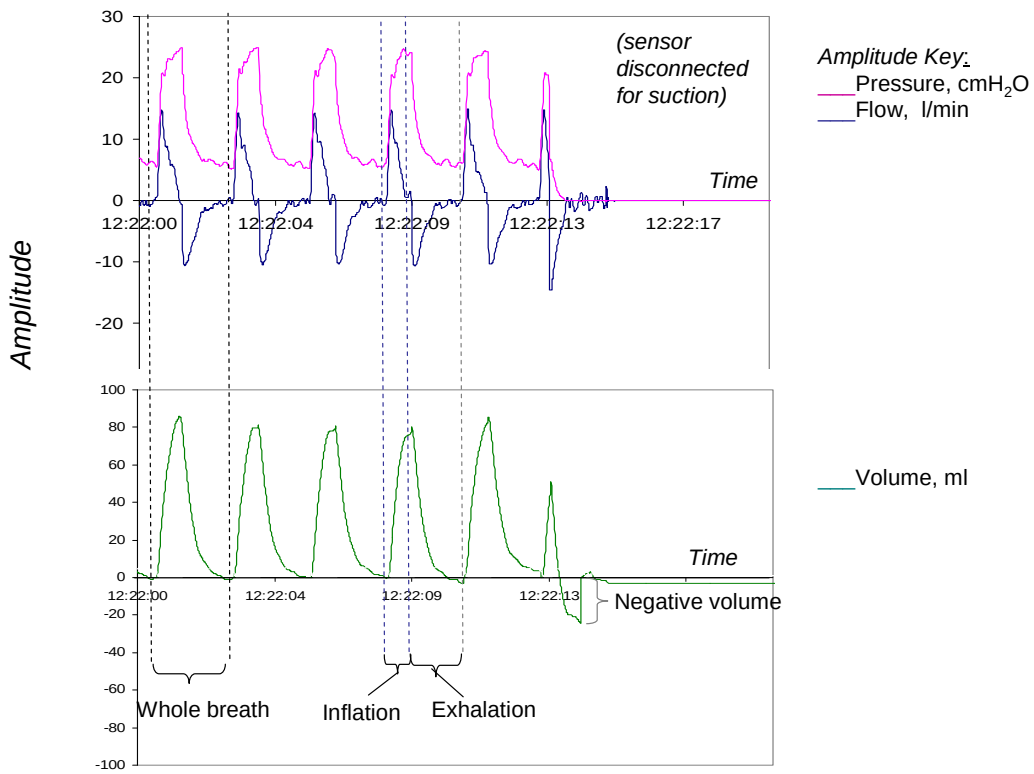
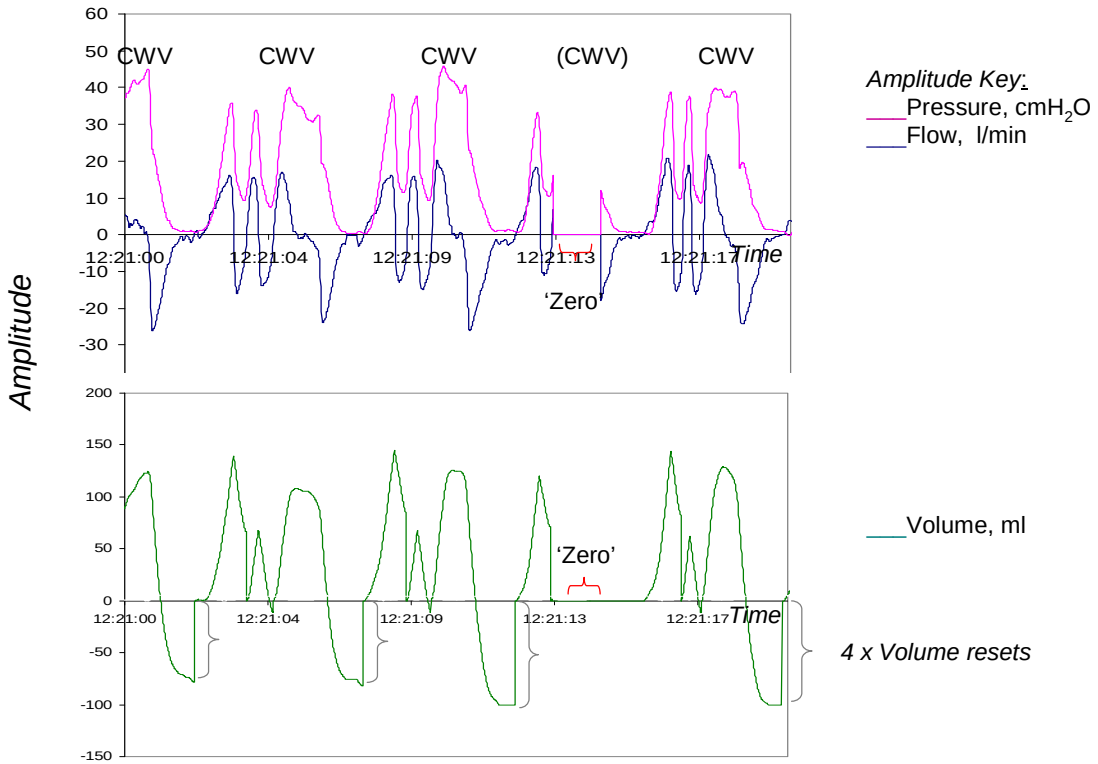


Figure 2.29 shows the respiratory traces during five CWV, with lung inflations interspersed between the vibrations. This figure again illustrates how the volume trace became negative and re-calibrated to zero when the expired volume exceeded the expected (inflation) volume. The trace additionally shows the sensor 'zeroing' (resulting in no data during the fourth CWV). It therefore became apparent that whilst the volume trace was helpful to view when inflation and expired volumes were roughly equal during baseline ventilation, the traces were less informative during physiotherapy treatments. Because the volume trace did not directly represent the values calculated by $CO_2SMO^{®}$, and because the amplitude scale required to display volume was significantly greater than the scales required to show flow, pressure and force (and therefore tended to obscure these traces) the decision was made to exclude volume when displaying the respiratory-force overlay traces, as discussed in **section 2.2.6.2**.

Figure 2.29 Relative changes in flow, pressure and volume during chest physiotherapy

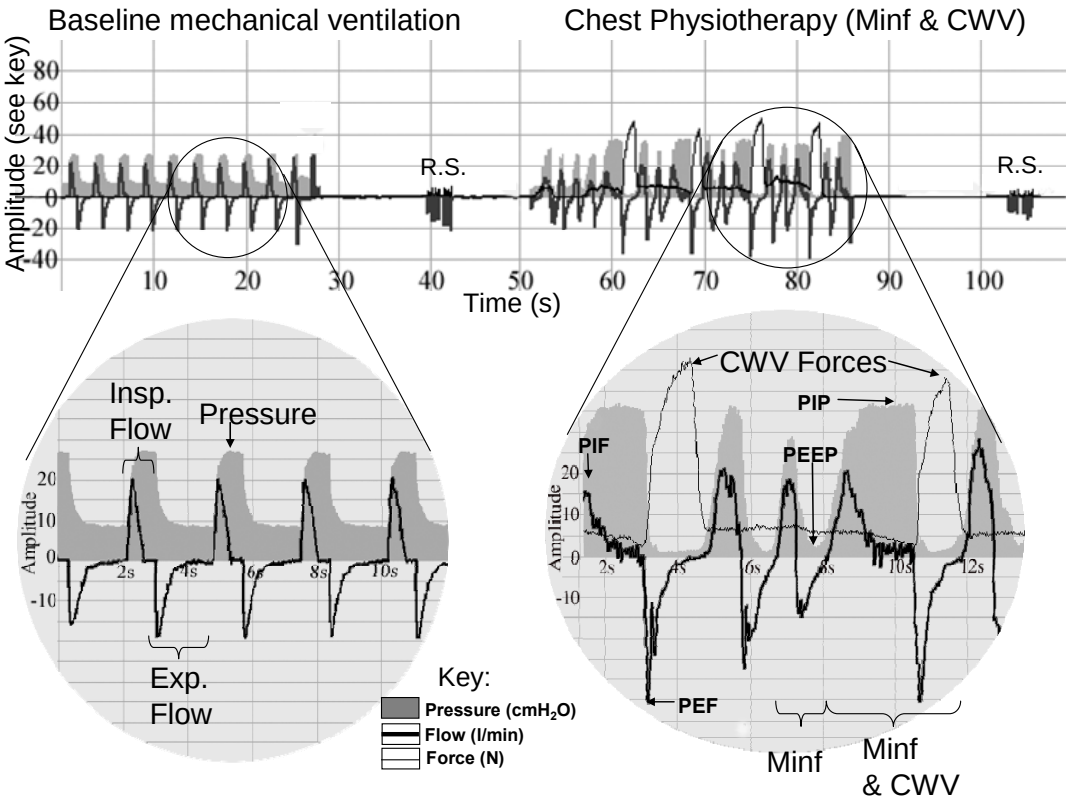


Volume trace 'saturated' at -100ml, to alert clinicians to a possible problem

2.2.5.4 Force and respiration during chest physiotherapy

It was possible to record force and respiratory recordings continuously during the entire physiotherapy session, with the exception of periods of suction and saline, when removal of the $CO_2SMO^{®}$ from the endotracheal tube was essential to prevent damage to the sensor. As can be seen in **Figure 2.30**, the respiratory data collected during physiotherapy were substantially different from that recorded during baseline mechanical ventilation.

Figure 2.30 Force and simultaneous respiratory changes aligned by the analysis software



Chest wall vibrations – CWV; Insp/Exp - inspiratory/expiratory; manual lung inflations – Minf; PEF - peak expiratory flow; PEEP – positive end-expiratory pressure; PIP - peak inflation pressure; R.S.- registration signals

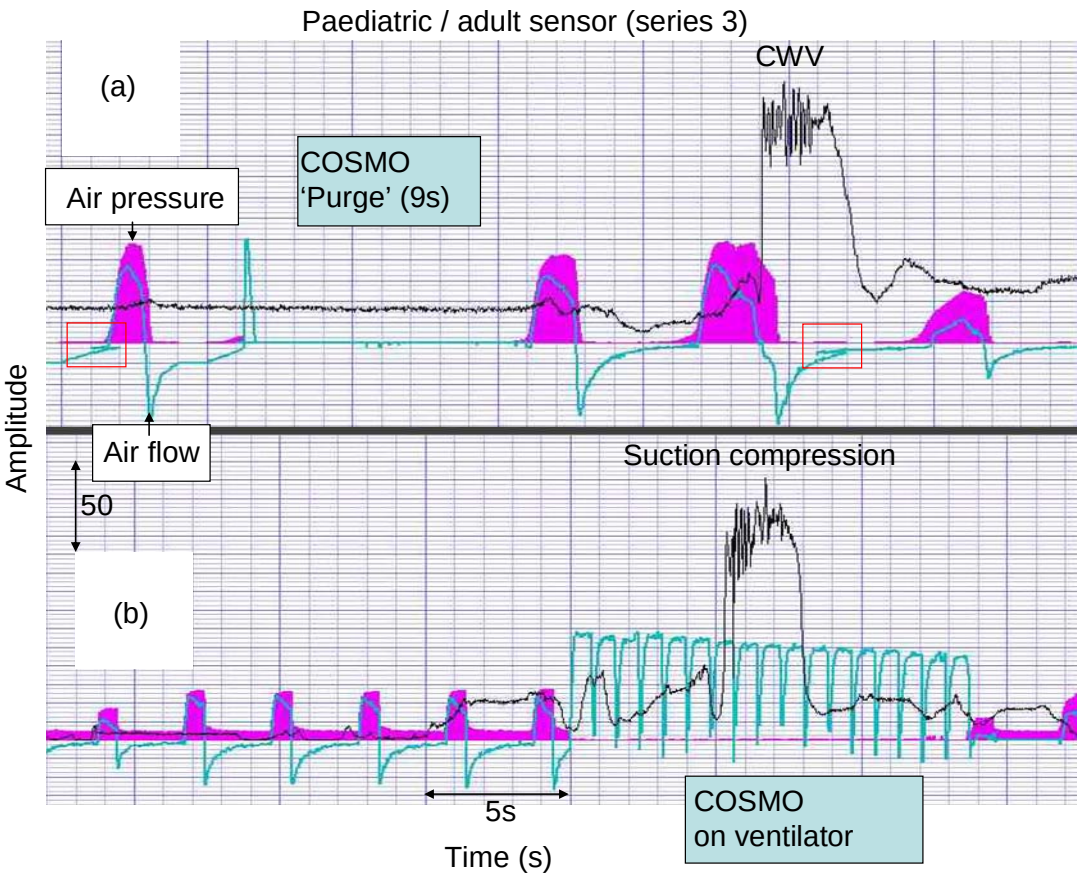
The upper panel shows representative data from a physiotherapy treatment of a child aged 5 years, including that recorded during baseline mechanical ventilation. Physiotherapy comprised manual lung inflations interspersed with CWV. The lower panels show in detail baseline ventilator respiration and the pressure and flow changes occurring during a 14 s snapshot of manual inflations with two CWV applied during expiration. The data were categorised into one of four monitoring periods, namely: i) before physiotherapy (during baseline mechanical ventilation) ii) during manual lung inflations iii) during lung inflations with CWV iv) after physiotherapy (during mechanical ventilation, not shown). The term

lung 'manual inflations' was adopted in preference to 'manual hyperinflations' as it became apparent that not all lung inflations resulted in breaths at least 50% greater than those delivered during baseline mechanical ventilation, concurring with earlier research (Singer et al. 1994). In **Figure 2.30** PEF doubled from 19 l/min during baseline ventilation to 40 l/min during the inflations for CWV. Peak inflation pressure also increased from 22 to 35 cmH_2O.

2.2.5.5 Data loss and subsequent technique modification

Use of the analysis programme which overlaid the force and respiratory data highlighted inconsistent timing errors between the two data streams in 9 of the 16 pilot data sets. Closer inspection of the data in Excel® resulted in the detection of a series of sources of error, which led to software and protocol modifications. On occasions the flow trace was seen to spontaneously loop back on itself (ie the time column went awry), as can be seen inside the red boxes in **Figure 2.31(a)**.

Figure 2.31 Multiple errors detected in CO_2SMO® data



Red boxes highlight errors in the CO_2SMO time data, causing flow trace to loop backwards

Sequential real-time $CO_2SMO^{®}$ data snapshots were also found to have overlapping data of varying duration. The force-respiration overlay analysis programme was rewritten to detect and delete duplicate data sections.

Considerable efforts were made to identify the circumstances causing erroneous data production, which continued into the early part of the clinical study. Investigations included detailed manual analysis of the raw $CO_2SMO^{®}$ data output in Excel™, and bench tests to recreate the $CO_2SMO^{®}$ errors and verify the accuracy of the pliance® data. Following these investigations and discussions with the manufacturer, several causes were identified, namely:

i) Frequent disconnections and reconnections of the $CO_2SMO^{®}$ sensor from the subject's respiratory circuit, resulting in sudden and unexpected re-zeroing

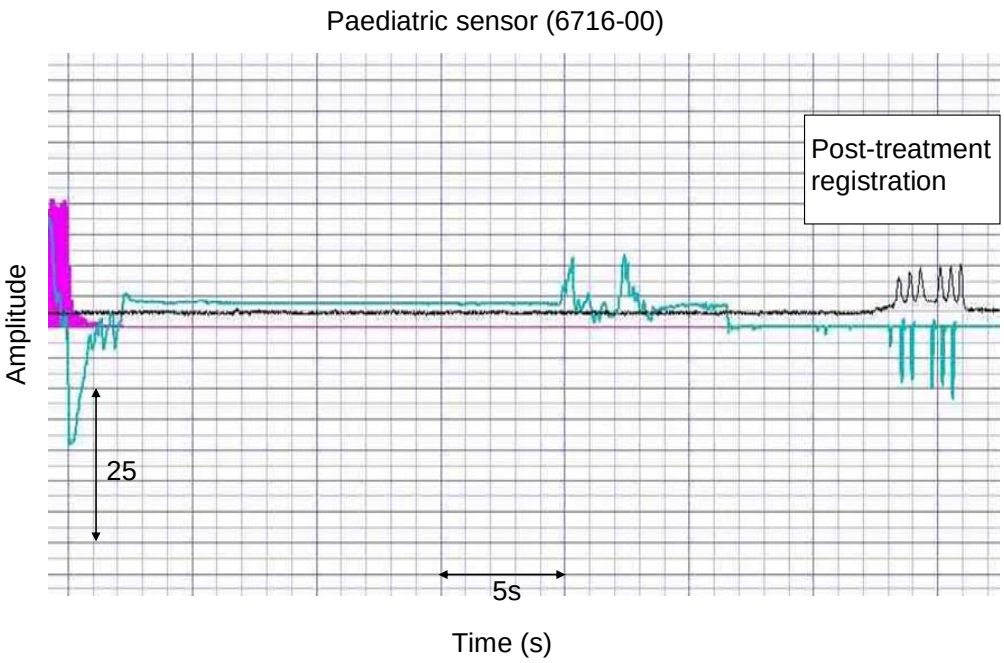
ii) Leaving the sensor attached to the ventilator circuit (with the distal end open to air) whilst suctioning the patient. As can be seen in **Figure 2.31(b)**, the sensor recorded the continuing positive airflow from the ventilator, without any compensatory negative airflow during respiration, leading to saturation of the transducer.

iii) Finally, several seconds of 'no data collection' occurred in subjects in whom the paediatric / adult sensor (series 3) was used, as shown in **Figure 2.31(a)**. This sensor frequently 'purged' or flushed through the sensor's pressure tubing and transducers, to remove any build-up of condensation.

In the majority of cases, the time delay created by the $CO_2SMO^{®}$ was under 3s. In one subject, sputum became lodged in the sensor itself during treatment of an asthmatic child with copious secretions, as indicated by an error message on the $CO_2SMO^{®}$ unit (reading 'check adaptor'). Although an isolated and extreme example, this event emphasised the need to be alert for such occurrences.

The sources of error were removed by implementing appropriate protocol modifications, as shown in **Figure 2.32**.

Figure 2.32 Data alignment following protocol modifications



These included:

a) Physically disconnecting the sensor from the $CO_2SMO^{®}$ monitor when not required for data collection (for example, during suction)

b) Using a paediatric sensor (model 6716-00), which did not 'purge', instead of the paediatric/adult sensor, for all subsequent studies in children above 2 years of age (PEF being roughly 25 l/min and above).

c) Finally, registration signals were performed frequently during the treatment to optimise data alignment. For example, data registration was performed when suction was completed, on recommencing respiratory data collection.

2.2.6 Selection of final outcome measures

2.2.6.1 Force

Pilot data were analysed to define the minimum number of variables which were robust, independent of each other and provided descriptors of the overall technique. This resulted in exclusion of variables including the force at first peak (which was closely related to maximum force and provided little additional information over and above that provided by maximum force) and rate of change of force (which showed a disproportionately high coefficient of variation), the profile shape being better described by the rise time.

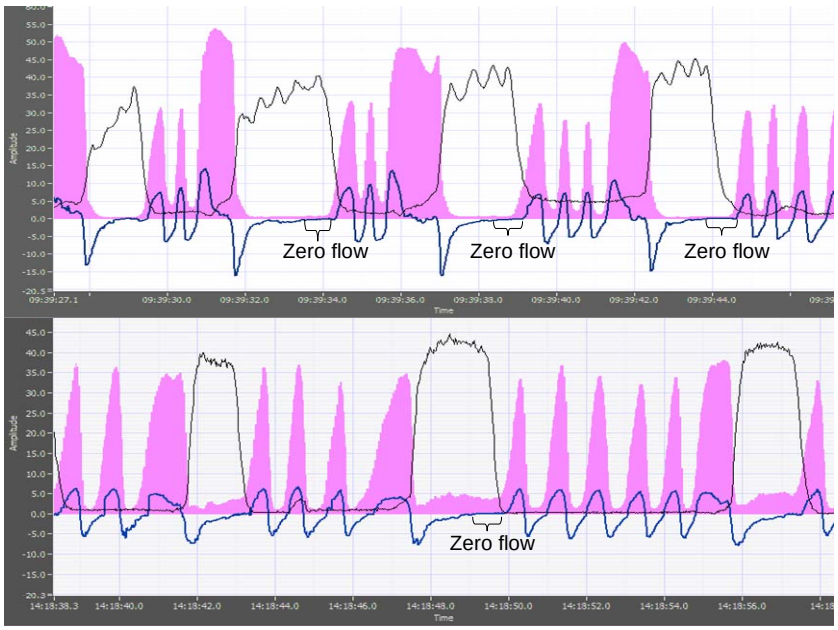
Maximum force was felt to be the most valid parameter to relate to changes in peak expiratory flow. Mean force was calculated with the intention of relating it to mean expiratory flow, since it represented the average force applied per second. However, mean expiratory flow was not calculated automatically by $CO_2SMO^{®}$ and manual calculations proved invalid (**section 2.2.6.2**). Nevertheless, calculation of the mean force relative to the maximum force was found to be a useful descriptor of the oscillatory component of a CWV, as will be discussed in **section 3.4.3**.

2.2.6.2 Respiration

All but one of the proposed respiratory measures was retained to quantify respiratory changes during chest physiotherapy in the clinical study. Manually calculated values of mean expiratory flow were found to be invalid because examination of the data revealed occasions where CWV continued for a significant time when expiratory flow had already ceased, as shown in **Figure 2.33.** Such periods of zero flow would be included within the recorded expiratory time (tE), artificially prolonging tE and underestimating mean expiratory flow as calculated by the formula VE/tE.

On questioning, some physiotherapists reported that they adopted this pattern of extended application of expiratory force to prevent retrograde transport of secretions resulting from an inspiratory airflow. However, others highlighted the possible danger of such a treatment pattern being used in young children, in whom it was possible to reduce lung volume to within the region of the child's closing volume.

Figure 2.33 Extended periods of zero flow recorded during expiration



2.3 Assessment of variability in physiotherapists' delivery of CWV

Objective 2. To estimate the variability over time, within and between individual physiotherapists when treating the same and different subjects with CWV

Little is known about the way in which physiotherapists make decisions regarding the delivery of CWV to patients in intensive care, the repeatability of an individual's technique, or the variability between physiotherapists. The stability of the physiotherapist's technique over time was evaluated as a precursor to the clinical trial, so that 'normal' variability in the application of CWV could be distinguished from significant alterations to the technique in response to specific clinical scenarios. Furthermore, an understanding of the control that physiotherapists have over the application of CWV could inform future teaching and training of the technique.

It is difficult to obtain repeatability data in children in the intensive care unit because their condition may fluctuate significantly over short time periods. As discussed in **section 2.2**, during earlier attempts to assess feasibility of data collection in healthy children it became apparent that repeated measures in such children would be difficult in those aged below 8 years due to movement artefact during chest physiotherapy. While this would be less of a problem in older children, chest wall compliance is then similar to that in adults, making it simpler and more ethical to limit investigations of variability of physiotherapists' technique to adults. A study was also undertaken at the Chartered Society of Physiotherapy Congress (2003, not reported in thesis) which aimed to investigate the repeatability of 10 physiotherapists' treatments using the force sensing mat and a cardio-pulmonary resuscitation manikin. These data were deemed invalid because it became apparent during data collection that physiotherapists were unable to treat the manikin in a realistic manner. They reported that the manikin's chest was unrealistic, because there was no thoracic excursion during the respiratory cycle and because of the absence of normal rib cage 'bucket handle' movement.

Using a healthy adult model, studies were therefore conducted to establish:

1. Repeatability of seven consecutive CWV, performed on a single test occasion
2. Repeatability of CWV between physiotherapists

3. Repeatability of CWV when applied to two healthy adult subjects
4. Between-test repeatability of CWV when applied 24 hours and 6 months apart

The potential importance of variability in the subject's breathing pattern was additionally investigated at the 6 month test by comparing tidal breathing with respiratory patterns during deep breaths both with and without force application.

2.3.1 Methods

The study was approved by the Great Ormond Street Hospital for Children NHS Trust and UCL, Institute of Child Health Research Ethics Committee (**Appendix A**). Written consent was obtained from the physiotherapists and the subjects who participated in the study.

2.3.1.1 Participants

Respiratory physiotherapists at Great Ormond Street Hospital for Children were recruited into the study. Recruitment, which was voluntary and unpaid, included both specialist respiratory and generalist rotating staff. This allowed for exploration of the differences in manual techniques between these two staff groups. Physiotherapists chose to participate in either the entire study (Tests 1, 2 and 3), or a part thereof (Tests 1 and 2) according to clinical commitments. Test 1 and Test 2 were within 24 hours of each other, with Test 3 six months later. Physiotherapists were assigned an identification number, which was used in all analyses to ensure anonymity of data. Two other members of the physiotherapy team volunteered to participate as Subjects A and B.

2.3.1.2 Equipment

Force was measured using the L-shaped pliance® mats previously described in **section 2.1.2** and shown in **Figure 2.34**. At Test 3, respiration was measured using a calibrated, adult CO_2SMO® sensor, which was attached to a mouthpiece. Prior to each test, the equipment was calibrated as detailed in **sections 2.2.2** and **2.2.3**. The subjects wore nose clips to prevent air leakage and encourage mouth-breathing.

2.3.1.3 Intervention

Each physiotherapist performed seven consecutive CWV manoeuvres on the two subjects, during each of the two or three test occasions (24 hours and 6 months apart). The 24 hour time period was selected because it reflected a clinically realistic interval; therapists regularly treat the same patient over consecutive days. The 6 month interval was chosen because this was the length of a clinical rotation and had the potential to provide an insight into the extent to which techniques are modified over the course of a rotation and of biological variation over longer time periods. The order in which physiotherapists performed CWV on each subject was randomised by tossing a coin. The order in which the physiotherapists were measured on each of the three test occasions was unstructured and dependent on their clinical commitments.

Figure 2.34 Equipment used for monitoring the repeatability of physiotherapists' chest wall vibrations

Subjects positioned themselves in right side lying on Akron™ treatment plinths, which were raised or lowered according to each physiotherapist's preference. Physiotherapists were asked to place their hands over the left side of the subject's chest as though they were treating the left lower lobe. The sensing mat was taped in position over the area of the

chest requiring 'treatment', according to each physiotherapist's hand position (**Figure 2.34**). The sensing mat was then unloaded and 'zeroed' to negate the effect of mat curvature around the chest. Following a brief practice period, subjects were instructed by the physiotherapist to take seven consecutive deep breaths, and the physiotherapist performed CWV during the expiratory phase of each breath. Physiotherapists provided verbal instructions to each subject as necessary, as would be done in a clinical setting, in order to co-ordinate their CWV with the subject's breathing. Subjects had at least 10 minutes of recovery time between each test and were told to inform researchers if they became light-headed.

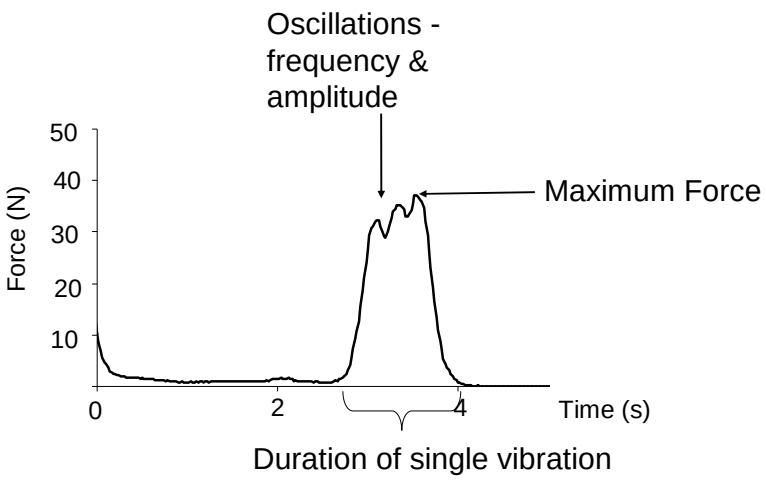
Increasing awareness of the potential impact of changes in the subjects' underlying respiratory pattern on the measured outcomes during physiotherapy resulted in an adaptation of the protocol during Test 3, such that the subjects were asked to perform a sequence of breathing manoeuvres which were then recorded. The subjects were instructed to breathe tidally for 30 seconds then to perform 4 sequential deep breaths, followed by normal tidal breathing for 1 minute, to allow time for respiration to return to its normal level (confirmed by inspecting the respiratory traces). Respiratory monitoring then continued during the usual protocol of deep breaths for CWV, the subjects continuing to breathe through the mouthpiece and sensor. This protocol allowed PEF to be measured in relation to breaths of similar magnitude with and without CWV. The researcher prompted the subjects when it was time to change between breathing patterns.

2.3.1.4 Outcome measures

As discussed in **section 2.2.5.1**, the real-time force data generated during CWV were exported in ASCII format to the custom-designed Labview® analysis programme, and the measures shown in **Figure 2.35** were derived:

1. Maximum force, Fmax (N)
2. Duration of each vibration (s)
3. Frequency (Hz) and amplitude (N) of oscillations

Figure 2.35 Variables used to define the force-time profile of a chest wall vibration



During Test 3, the variables used to explore the stability of respiration were: respiratory rate, RR (per min), inspired volume, VI (ml), expiratory time, tE (s) and peak expiratory flow, PEF (l/min).

2.3.1.5 Data analysis

Statistical analyses were conducted in SPSS® v 14.0 (Statistical Package for the Social Sciences, Chicago, Illinois USA). Data were summarised using the mean (SD), and force-time profiles of each set of 7 CWV. Four-way analysis of variance (ANOVA) was used to analyse the independent effects of chest wall vibration, physiotherapist, subject and test occasion on maximum force, duration, frequency and amplitude of oscillation. Interactions between each of the above were also calculated.

Between-test repeatability were examined using Bland-Altman plots, based on aggregated data for each test occasion (Bland & Altman 1986). Here the average forces applied between tests were plotted against the differences in forces applied between tests. Limits of agreement were calculated as +-2 SD from the mean difference.

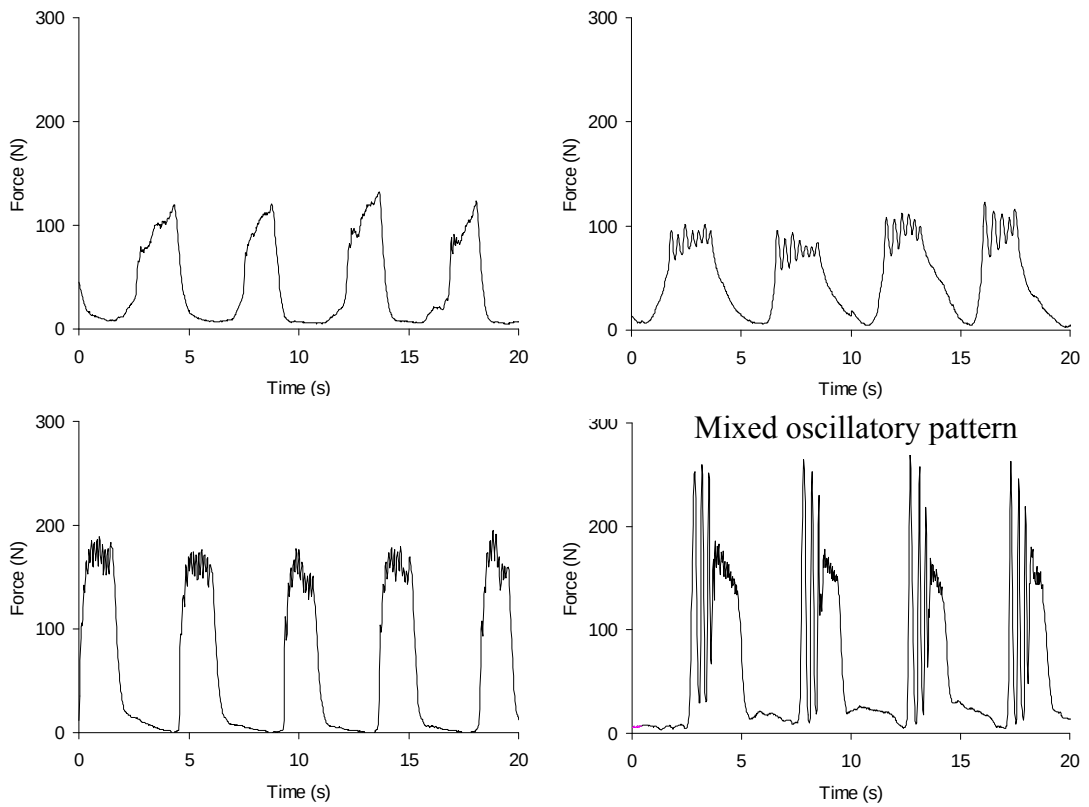
At Test 3, variability in each subjects' respiratory patterns was summarised using the mean (SD) ranges of the respiratory variables during the three breathing conditions (tidal, deep and deep with CWV). The volumes and times were plotted against PEF according to the measurement condition.

2.3.2 Results

Data were collected between July 2005 and January 2006. Eight respiratory physiotherapists (two specialist and six rotational staff) were recruited into the study. They had between 4 and 18 years post-qualification experience (median 7.5 y), and had worked in intensive care for between 1 month and 16 years (median 8 m). Subjects A and B were healthy females, aged 42 and 40 years respectively. All eight physiotherapists participated in Test 1 and Test 2, seven of whom also participated in Test 3, six months later. Forty-six individual sessions, each comprising seven CWV, were recorded in total (eight physiotherapists treating two subjects on two consecutive days and seven physiotherapists treating two subjects six months later).

Each physiotherapist demonstrated a unique and consistent force-time profile within each session of CWV (**Figure 2.36**). These profile shapes were preserved between subjects and between days for individual therapists even though the absolute force, duration and oscillation changed between tests.

Figure 2.36 Variation in force-time profiles applied by four physiotherapists to Subject A during single test occasions



However, force-time profiles varied markedly between physiotherapists even when treating the same subject, in terms of the characteristics of duration, oscillation and amplitude of forces applied (**Figure 2.36**). Within a single test occasion, and on a single subject, maximum force, duration, frequency and amplitude of oscillation varied considerably between therapists, with for example, maximum force ranging between 71 N and 222 N on Subject A, Test 1 (**Table 2.2**).

Table 2.2 Summary statistics of CWV profiles by physiotherapist, subject and test occasion

Therapist	Subject A				Subject B			
	Fmax (N)	**Duration** (s)	**Freq.** (Hz)	**Amp.** (N)	**Fmax** (N)	**Duration** (s)	**Freq.** (Hz)	**Amp.** (N)
1	102 (7)	5.2 (0.9)	3.5 (0.1)	29 (1.9)	132 (13)	4.5 (0.9)	3.3 (0.1)	29 (3.8)
2	173 (9)	3.2 (0.5)	8.1 (0.3)	29 (4.3)	131 (2)	2.2 (0.1)	8.9 (0.3)	12 (1)
3	222 (8)	2.3 (0.1)	3.9 (0.3)	62 (11)	178 (4)	1.9 (0.1)	6.2 (3)	7 (6.2)
4	198 (21)	3.4 (0.1)	6.3 (1)	59 (16)	200 (7)	2.3 (0.1)	6.5 (0.6)	54 (7)
5	105 (4)	2.7 (0.3)	6 (0.8)	6 (2.1)	137 (4)	2.1 (0.1)	6 (0.3)	13 (2.8)
6	178 (12)	3.4 (0.3)	7.5 (0.2)	29 (4.2)	173 (2)	2.2 (0.2)	8.4 (0.2)	26 (4.3)
7	129 (7)	2.6 (0.2)	8.1 (0.6)	14 (3.1)	135 (5)	2.2 (0.1)	8.5 (0.4)	18 (3)
8	71 (8)	2.7 (0.3)	8.9 (1.5)	2 (0.4)	83 (7)	2.7 (0.3)	11.4 (3.7)	3 (1.8)

Mean (SD) calculated for each session of 7 CWV by therapists 1 to 8, on Test 1.
Fmax – maximum force, Frequ. – frequency of oscillation, Amp. – Amplitude of oscillation

2.3.2.1 Repeatability of CWV

There were no significant differences in maximum force, duration or frequency and amplitude of oscillation within each set of seven CWV. This was demonstrated by a four-way ANOVA (therapist by subject by test occasion by individual chest wall vibrations). Since there were no significant main or interaction effects of individual chest wall vibrations, the ANOVA was limited to three-way for subsequent analysis (therapist by subject by test occasion).

2.3.2.2 Physiotherapist repeatability of CWV

There were significant differences between physiotherapists' techniques in terms of maximum force, duration and frequency and amplitude of oscillation. This was confirmed by three-way ANOVA, which showed highly significant main effects for physiotherapist ($p < 0.001$). Interactions (therapist by subject and therapist by test) were also significant

for maximum force, frequency and amplitude of oscillation ($p < 0.05$), suggesting that the differences between therapists were not systematic on each test occasion or when applied to each subject.

2.3.2.3 Subject repeatability

There were significant differences between the two subjects in terms of maximum force and duration and frequency of CWV applied ($p < 0.001$), while amplitude of oscillation was not significantly different (**Table 2.3**). There were also significant interactions between subject and test occasion for all four of the above parameters, suggesting that these differences were not systematic across the test occasions ($p < 0.001$). By contrast, the interaction between physiotherapist and subject for duration of CWV was not significant ($p=0.1$), with all physiotherapists consistently applying CWV over a longer time period to Subject A.

Table 2.3 Summary of 3-way analysis of variance
(of which Subject and Test are presented)

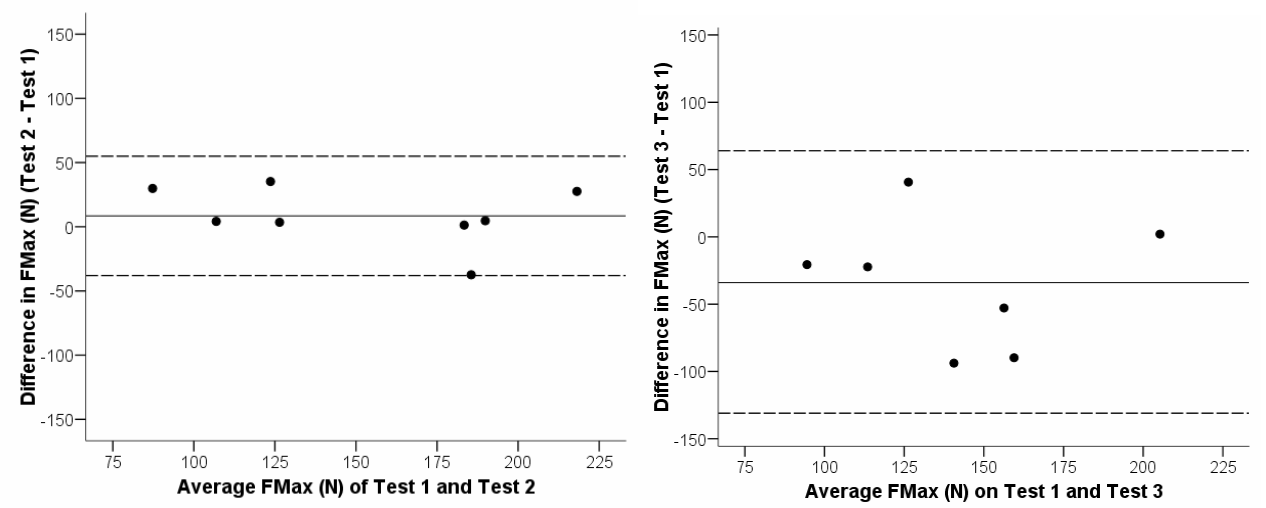
	Subject	**Test**			**SE**	**P**	**P**	**P**
		1	**2**	**3**		**Subject**	**Test**	**Interaction**
Fmax (N)	A	148	157	125	6.2	< 0.001	< 0.001	< 0.001
	B	149	160	152				
Duration (s)	A	3.2	3.3	2.6	0.1	< 0.001	< 0.001	< 0.001
	B	2.6	2.5	2.4				
Frequ. (Hz)	A	6.6	7.5	6.7	0.3	0.05	< 0.001	< 0.001
	B	7.6	7.3	6.7				
Amp. (N)	A	27.1	24.3	23.9	2.3	0.09	0.6	< 0.001
	B	25.9	21.5	28.2				

Results presented as mean values for each test occasion, and standard error (SE) across all tests, with significance for main and interaction effects
Fmax – maximum force, Frequ. – frequency of oscillation, Amp. – Amplitude of oscillation

2.3.2.4 Between-test repeatability

Maximum force, duration and frequency of oscillation differed significantly between test occasions ($p < 0.001$), while amplitude of oscillation did not ($p = 0.6$). All four measures had significant interaction effects between test and subject and test and physiotherapist, suggesting that physiotherapists applied CWV differently to the subjects on each test occasion. There was no systematic bias in maximum force between Tests 1 and 2 (an interval of 24 hours), but limits of agreement were wide (-38 to 55 N and -37 to 59 N applied to subjects A and B respectively, with mean differences of 8.6 and 11 N, **Figure 2.37**). There was also no systematic bias in maximum force between Test 1 and 3 (an interval of 6 months), but limits of agreement were even greater (-131 to 64 and -109 to 96 N applied to subjects A and B respectively, with mean differences of -34 and -6 N, **Figure 2.37**). Similarly, there was no systematic bias in the amplitude or frequency of oscillation applied between Tests 1, 2 or 3 and limits of agreement were wide for both amplitude and frequency of oscillation (data not shown).

Figure 2.37 Difference against average values for maximum force of CWV between Tests 1, 2 and 3, applied to Subject A



Mean difference and limit of agreement reference lines are presented

2.3.2.5 Within-session variability in respiratory pattern

Respiration was only measured on Test 3, once the possible influence of respiratory variation had become apparent. The within-session respiratory variability of each of the subjects was compared from: seven consecutive tidal breaths, four consecutive deep breaths and seven consecutive deep breaths with CWV, combining the data for all 7 physiotherapists' sessions (**Table 2.4**).

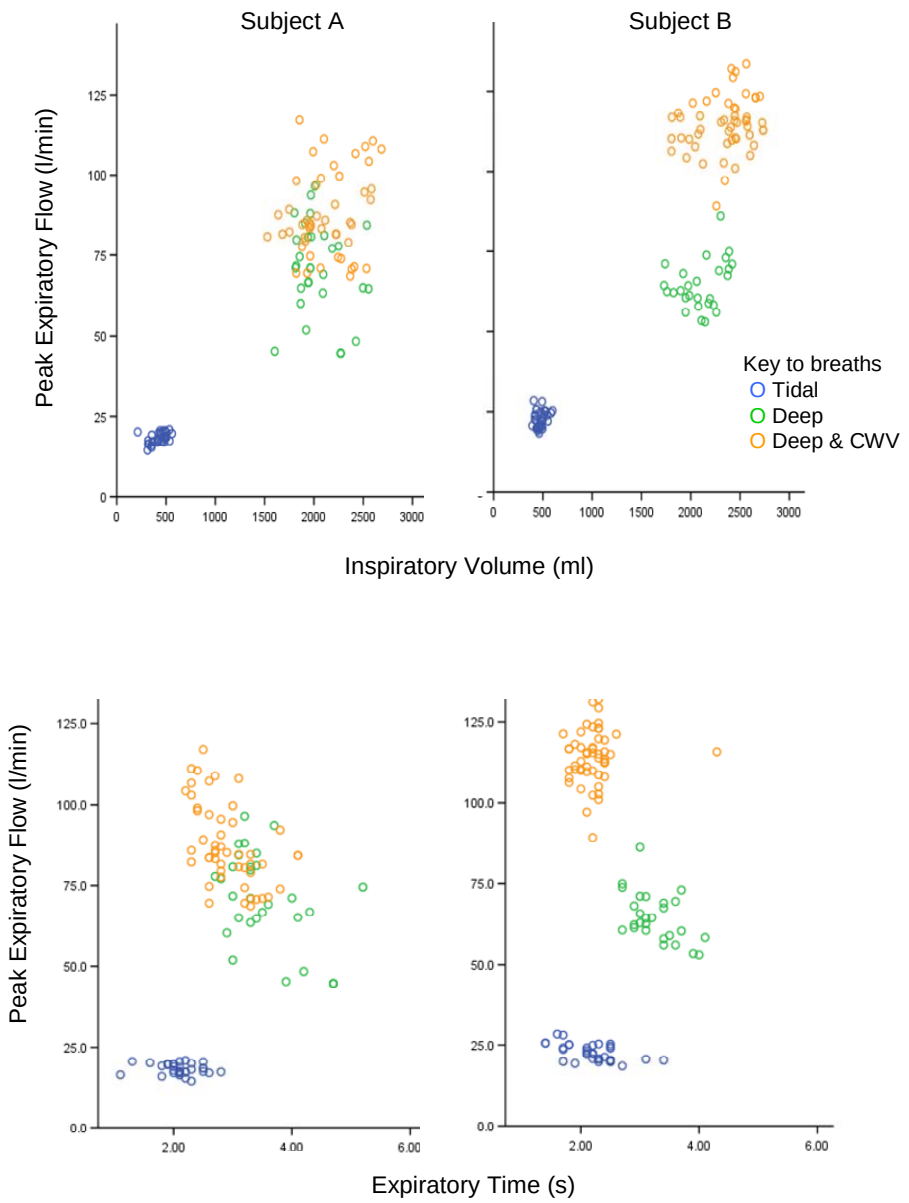
Table 2.4 Comparison of respiration according to subject and breath type

	Subject A			Subject B		
	Tidal breaths (n = 49)	**Deep breaths** (n = 28)	**Deep & CWV** (n = 49)	**Tidal breaths** (n = 49)	**Deep breaths** (n = 28)	**Deep & CWV** (n = 49)
RR (per min)	18 (1.8)	16 (1.5)	14 (1.4)	17 (1.9)	15 (1.6)	15 (2.3)
VI (ml)	427 (80.4)	2049 (237)	2129 (286)	476 (48)	2101 (211)	2342 (268)
tE (s)	2.1 (0.4)	3.6 (0.6)	2.9 (0.5)	2.2 (0.4)	3.3 (0.4)	2.2 (0.4)
PEF (l/min)	18 (1.6)	70 (15)	88 (13)	23 (2.6)	65 (7.5)	115 (8.6)

Values expressed as mean (SD)
RR – respiratory rate, VI – inspired volume, tE – expiratory time, PEF – peak expiratory flow

As expected, there were clear differences between the three measurement conditions in terms of the flows, volumes and timing indices recorded. However, there was also considerable variation within a measurement condition both within and between the two subjects, as illustrated in **Figure 2.38**. For example, Subject A's inspired volumes ranged from 212 ml to 560 ml during tidal breathing, variability increasing during both subjects' performance of deep breaths.

Figure 2.38 Variability in inspiratory volume and expiratory time and peak expiratory flow in Subjects A and B, according to the measurement condition



In some of the breaths recorded, there was a virtual doubling of inspiratory volume. Whilst Subject A's range of inspired volumes was similar for both sets of deep breaths, Subject B breathed deeper during the breaths for CWV. There was also a four-fold increase from tidal values in the subjects' inspired volumes during the deep breaths, which in turn was related to marked increases in PEF, even before CWV were applied (**Figure 2.38**). In Subject B, expiratory time was reduced during the CWV compared to deep breathing alone. This contrasted with Subject A, who showed more variability and overlap between the deep breaths with and without CWV. These data highlight the underlying variability of the subjects' respiratory pattern, and corresponding changes in PEF, the implications of which are discussed in **section 2.3.3**.

2.3.3 Discussion of repeatability findings

Contrasting findings in this study include the consistency in the delivery of CWV within each physiotherapist's treatment session and the wide variations in CWV force-time profiles between physiotherapists. The repeatability of physiotherapists' CWV within each treatment session suggests that therapists have fine control over the application of forces during CWV. There was wide variability within and between therapists' applications of CWV in response to different subjects or over time.

The variability of measurements within and between individual therapists, in response to both subject and test occasion, raises questions about the magnitude of measurement error, biological variation and the conscious or unconscious factors influencing the delivery of CWV. The equipment validation studies in **section 2.1.3** suggested measurement error over consecutive days would be < 5%, which therefore cannot explain the magnitude of difference observed. A primary purpose of repeatability studies is to provide data which identify clear limits of agreement between repeated measures as a benchmark against which 'clinically important' changes could be compared. Instead, this study has exposed considerable variability in physiotherapists' techniques over time, raising uncertainty about the similarities or differences in physiological effects that such variable treatments might produce. On the basis of these results, it appears unfeasible to predict with any accuracy whether, or to what extent, physiotherapists might vary their technique when treating the same patient on consecutive occasions. However, circumstances may be different in the clinical environment when the physiotherapist is receiving feedback from the patient's

lungs regarding the underlying pathophysiology. These issues can only be addressed by conducting a clinical study, as will be discussed in Chapter 3.

The significance of the various components of CWV (maximum force, oscillation and duration of CWV) and their role in treatment efficacy has yet to be established, and currently there is no defined 'optimum' method for the delivery of CWV. It was assumed at the outset of the repeatability study that there would be minimal between-subject difference in the healthy models, considering both subjects were female and of a similar age. However, the additional data collected in Test 3 confirmed the impression from the early tests that there was considerable and potentially important variability in the subjects' underlying breathing patterns. Moreover, between-subject differences might be expected to be far more discernible in patients of different ages and underlying pathology.
The fact that physiotherapists applied CWV for a significantly longer duration to Subject A than Subject B can be explained anecdotally and supported by the expiratory time data in **Figure 2.38**. Therapists reported that Subject A appeared to have a stiffer chest wall and tended to breathe abdominally, so that it was more difficult to anticipate the end of expiration. Consequently, therapists tended to continue CWV for longer in Subject A than in Subject B, suggesting that physiotherapists use feedback from the patient's breathing pattern to inform the timing and application of CWV. Similarly, PEF increased less during CWV in Subject A than B, suggesting Subject A's stiffer chest wall may have reduced the effect of the CWV on airflow.

The study suggests that it is valid to use the methodology described in **section 2.2.3** to assess the variability of CWV (in terms of the forces applied, the rate of force application and the oscillatory pattern of a treatment profile). However, the data show that variations in the underlying inflation pattern directly influence respiratory outcomes including PEF (**Figure 2.38**). It is therefore not possible to evaluate the respiratory effects of the different CWV techniques and the timing of force application during the respiratory cycle in healthy spontaneously breathing subjects unless they adopt a standardised breathing pattern. In the latter situation, use of a manikin ventilated with a constant inflation pattern may provide a useful alternative to patients or volunteers (**section 4.5**).

Since physiotherapists' hand size, degree of wrist extension and preferred standing posture varied, the position of the mat on the subject was not fully standardised. This may have

increased the variability of CWV between physiotherapists, but it was felt that there was a need to record the physiotherapists' 'own' application of CWV, rather than attempt to standardise the technique in a way which would not be clinically realistic.

In summary, the results of this study which aimed to investigate the repeatability of CWV suggested that, while each physiotherapist had control over their own technique, there was wide variation between therapists in terms of the magnitude and pattern of forces applied. The variability between tests performed by a single physiotherapist and between different therapists raises questions about the factors that influence the delivery of CWV. It is currently impossible to predict with any accuracy the extent to which physiotherapists might vary their technique when treating the same patient on consecutive occasions, even in the absence of clinical change. The inherent variability of the healthy adult subjects' breathing pattern must be taken into account when designing future repeatability and clinical studies. There is an urgent need to quantify the variability in current clinical practice and evaluate the importance of this variability in terms of corresponding physiological effects. Inspiratory volume appears to influence peak expiratory flow, even in the absence of CWV force application. Consideration should therefore additionally be given to the need to explore all ventilatory changes in flow, volume and pressure during chest physiotherapy.

2.4 Summary

- A new method for quantifying dynamic forces in real-time during chest physiotherapy has been successfully developed and is fully functional
- This technique has been shown to be accurate in the relevant loading range of paediatric chest wall vibrations (10-200 N), with a mean % error < 5%.
- The system was not suitable for characterising the much lower forces applied during chest percussions (1-10 N).
- Mats of different sizes have been created allowing monitoring in children of all ages, and in adults.
- Pilot data in the paediatric intensive care unit have been collected using the range of mats and respiratory profile monitor to record simultaneously force and respiration during treatment.
- Important protocol refinements have been implemented and an analysis framework has been produced.
- Exploration of the variability in CWV profiles within and between physiotherapists treating healthy adults has indicated that whilst an individual physiotherapist may demonstrate a single treatment style, there is wide variation between physiotherapists.
- These preliminary studies have prepared the way for a clinical study in mechanically ventilated children to explore current physiotherapy practice (**Chapter 3**).

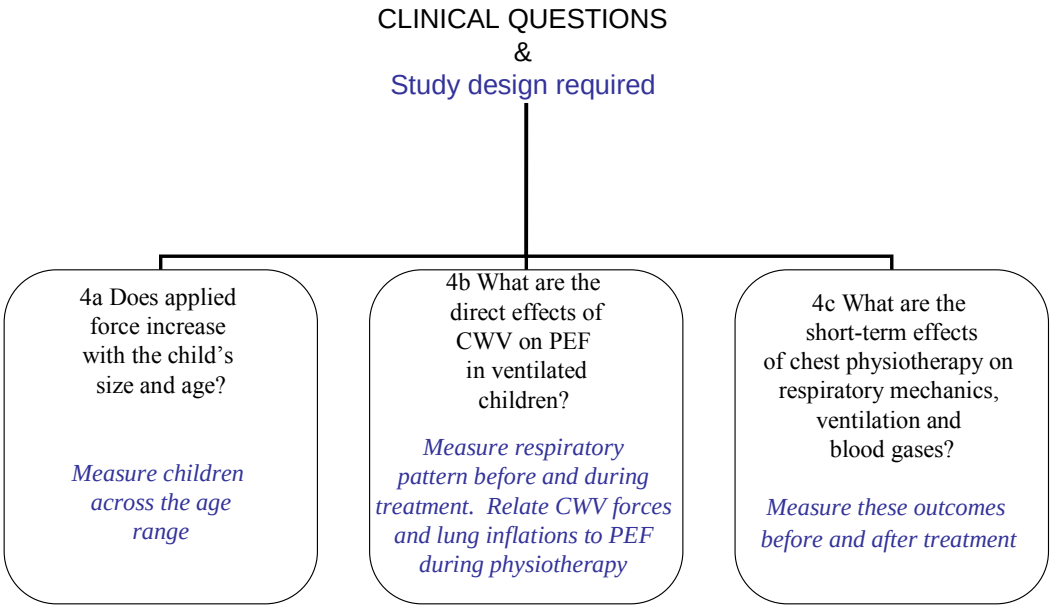
Chapter 3 Clinical evaluation of chest physiotherapy in mechanically ventilated children

A study was designed to assess the feasibility of quantifying current practice in two specialist intensive care units during chest physiotherapy for children of varying ages, body size and underlying pathology. The research also allowed specific hypotheses to be tested regarding the relationship between force profiles and resultant airflow, and the extent to which these are influenced by growth and development.

3.1 Introduction

Having successfully collected pilot data to optimise both the technique and analysis format for characterising force and respiration during chest physiotherapy, a clinical study was designed to address the questions broadly summarised in **Figure 3.1**.

Figure 3.1 Summary of key clinical questions regarding chest wall vibrations and their influence on study design



CWV – chest wall vibrations, PEF – peak expiratory flow

3.2 Research Hypotheses and Objectives

The following hypotheses were established and tested to explore chest physiotherapy and its underlying mechanisms in children:

1. Maximum and mean force applied during chest wall vibrations increase with the size and age of the child
2. Manual lung inflations with chest wall vibrations result in an increase in peak expiratory flow above that observed during baseline mechanical ventilation
3. After adjusting for inflation volume, application of chest wall vibrations result in an increase in peak expiratory flow above that obtained during manual lung inflations alone

The primary objectives of the clinical study were to:

1. assess the feasibility of measuring force and respiration in a population of critically ill mechanically ventilated children
2. characterise the magnitude and pattern of forces applied during chest wall vibrations and evaluate the direct effects of these manoeuvres on airflow and pressure changes in the lungs, and
3. determine the relative contributions of manual lung inflations and chest wall vibrations to any observed increase in expiratory airflow

A secondary objective was to explore the short term effects of chest physiotherapy, by recording changes in ventilation, respiratory system mechanics and blood gases following treatment.

3.3 Subjects and Methods

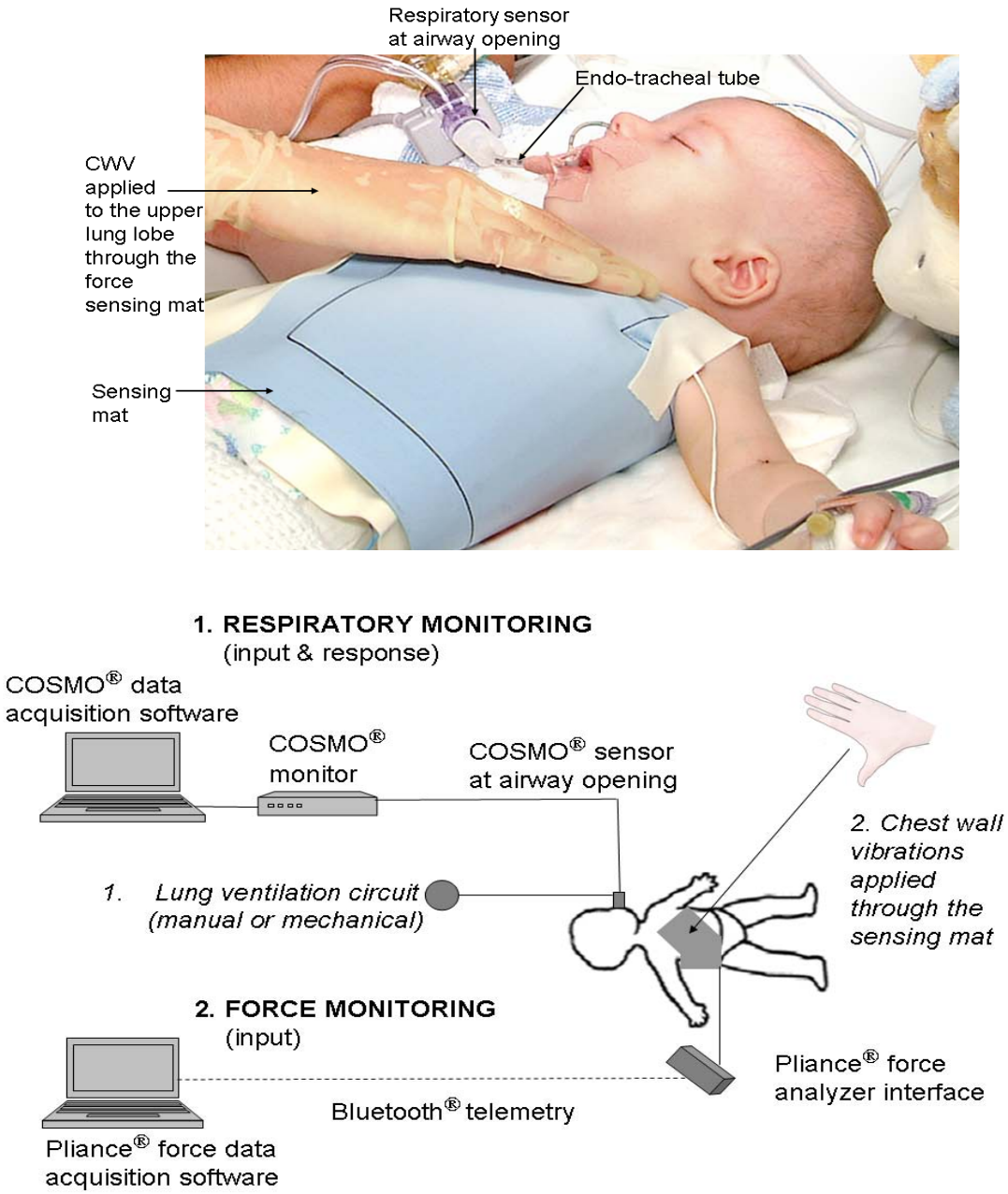
A clinical study was conducted in mechanically ventilated children requiring chest physiotherapy in the intensive care units of Great Ormond Street Hospital for Children NHS Trust, London. Approval for the study was granted by the Central Office for Research Ethics Committees (COREC, see **Appendix B**). Written, informed consent was obtained from all participating families and physiotherapists.

3.3.1 Equipment

The novel pliance® system and the customised mats described in **section 2.1** were used to record force data. The non-invasive CO_2SMO® Plus! Respiratory Profile Monitor

detailed in **section 2.2.1** measured airflow and pressure at the airway opening continuously and in real-time via a disposable, low deadspace sensor inserted between the endo-tracheal tube and the ventilator or manual lung inflation circuit (**Figure 3.2**).

Figure 3.2 Equipment required for simultaneous force and respiratory measurements in mechanically ventilated children



Inspired and expired volumes were derived by integrating flow over time. Respiratory compliance and resistance were calculated during each breath by least squares regression of

volume, pressure and flow data points throughout the breath cycle (Frey et al. 2000). Resistance values derived from the passive expiratory portion of the cycle were reported (Hjalmarson 1994). The values of all these respiratory variables were automatically calculated by the $CO_2SMO^{®}$, which has been previously validated in mechanically ventilated children (Main et al. 2001;Castle et al. 2002). A neonatal sensor (model 6720-00) was used for children less than 2 years of age (where airflows were generally < 25 l/min) and a paediatric sensor (model 6716-00) for older children. The final protocol detailed below resulted from the experience gained during the pilot study in Southampton General Hospital's paediatric ICU (**section 2.2**).

3.3.2 Selection Criteria

Mechanically ventilated children (0-16 years of age) were eligible for recruitment if they were cardiovascularly stable and were deemed, after assessment by the physiotherapist, to require chest physiotherapy. The study was designed to monitor clinical practice in a heterogeneous patient population. Clinical indications for physiotherapy therefore included signs of lung consolidation or atelectasis on chest radiograph, added or decreased breath sounds on auscultation, increased ventilatory requirements within the last 4 hours and/or deteriorating arterial blood gases. Children at risk of haemorrhage, those with osteoporosis or those whose medical instability precluded physiotherapy treatment were excluded, as were those children with a tracheal tube leak >20% (Main et al. 2001;Castle et al. 2002;Main & Stocks 2004). Leak was calculated as the percentage difference between the inspired and expired tidal volumes recorded using the $CO_2SMO^{®}$, and was assessed before and after physiotherapy.

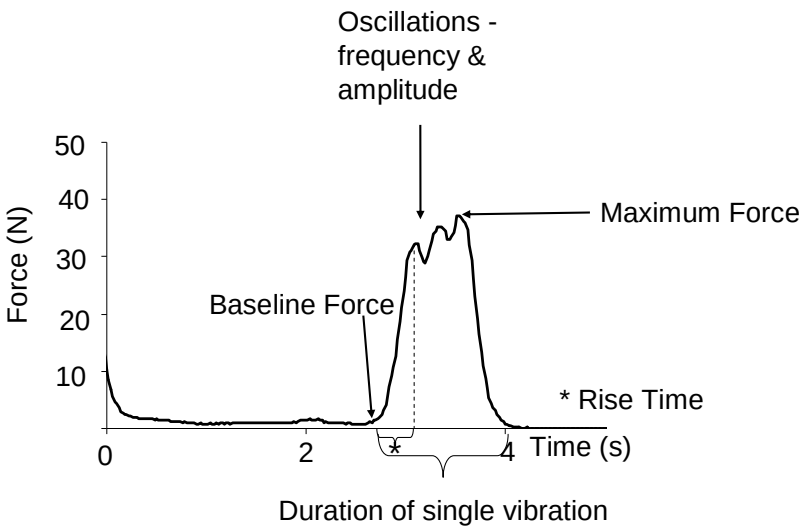
3.3.3 Outcome measures

3.3.3.1 Force variables

Force was characterised using the descriptors defined in **section 2.2.6.1**, as shown in **Figure 3.3**:

- Maximum force (N)
- Mean force [force over 1 second] (N)
- Baseline force (N)
- Rise time (s)
- Frequency (Hz) and amplitude (N) of oscillations
- Duration of each vibration (s) and whole treatment (mins)

Figure 3.3 Descriptors of chest wall vibration force profiles



3.3.3.2 Respiratory variables

The respiratory measures recorded for each breath throughout the monitoring period were: peak inspiratory and expiratory flow (PIF, PEF), peak inflation pressure and positive end-expiratory pressure (PIP, PEEP), inflation and expired volumes (VI, VE) and inspiratory and expiratory time (tI, tE). Expired volume has previously been reported as a valid respiratory outcome measure to reflect acute lung changes (Main et al. 2001;Main et al.

2004). However, this ceases to be of value if the child is on volume-controlled ventilation. Peak inspiratory pressure was therefore chosen as an alternative measure in these children. Peak expiratory flow was additionally monitored because it could be measured in all children, irrespective of their mode of ventilation. Respiratory mechanics (respiratory system compliance, Crs and resistance, Rrs) were measured in pharmacologically paralysed children during mechanical ventilation before and after the physiotherapy. Arterial blood gases were analysed in both sedated and paralysed children to measure oxygen saturation (SaO_2) and the partial pressures of oxygen and carbon dioxide (PaO_2, $PaCO_2$).

3.3.4 Protocol

Any water which had collected in the ventilator tubing was removed prior to commencing respiratory monitoring. Baseline respiratory data (flow, pressure and volume) during normal mechanical ventilation were recorded for a minimum of 15 minutes prior to the physiotherapy session, using the CO_2SMO®. The first five minutes of data from the CO_2SMO® were routinely discarded, to allow a period of stabilisation. Leak was assessed and data excluded if leaks remained above 20% despite repositioning the child (Main et al. 2001;Castle et al. 2002). The children were defined as clinically stable if no haemodynamic or ventilatory abnormalities were reported by the intensive care nursing staff. Blood samples from existing arterial lines were analysed immediately before and at 15 minute intervals during respiratory monitoring after the treatment.

The lightweight sensing mat was secured over the treatment area of the child's chest using Microfoam® elastic tape. Force and respiratory data streams (before, during and after physiotherapy) were synchronized using a small, re-inflating bladder, depression of which generated simultaneous force and flow signals (**section 2.2.2**). Following the initial data registration, the CO_2SMO® sensor was reconnected into the child's ventilator circuit and the entire physiotherapy session was continuously recorded using the sensing mat and CO_2SMO®. The CO_2SMO® sensor was removed from the patient circuit to avoid sensor damage during saline instillation and suctioning. It was also disconnected from the CO_2SMO® monitor during these periods to prevent the generation of CO_2SMO® data errors, as discussed in **section 2.2.5.5.** A CD available from the author contains video footage of a physiotherapy treatment, demonstrating the protocol features.

Appendix C contains an example treatment data sheet of all the recorded variables. Relevant treatment details relating to the child's diagnosis and pattern of underlying lung pathology (unilateral, segmental, diffuse), clinical stability, ventilatory support, and treatment delivery were documented. Severity of illness was assessed from: oxygenation index, Paediatric Risk of Mortality (PRISM) scores and the number of days since the onset of the acute episode of illness (Trachsel et al. 2005;Willson et al. 2005;Brady et al. 2006). Body weight was estimated from the last measurement upon or since hospital admission. Variables relating to the physiotherapy treatment included the child's position, mat position on the chest, and details regarding the physiotherapist's hand(s) used to deliver CWV (including hand dominance and size). Adverse events with respect to marked alteration in oxygen saturation, blood pressure or intracranial pressure during and after treatment were documented. A change in these measures of plus or minus 10% was considered significant, or less if a) the alarm limits set for an individual child were reached or b) remedial intervention was required.

Chest physiotherapy was delivered by the intensive care physiotherapists, who selected their treatment techniques based on assessment of clinical indications. Treatment notes to document periods of manual lung inflations, CWV, saline instillation and suction were continuously timed and electronically entered into the CO_2SMO®. Respiratory data collection continued for up to one hour following the chest physiotherapy, in the absence of any other interventions.

3.3.5 Data handling and statistical analysis

Statistical analyses were calculated using SPSS® v14 (Chicago, Illinois USA). Details are given in **section 2.2.4** of the process of deriving the descriptive variables for physiotherapy force characterisation, the creation of semi-automated programs in Labview® for force analysis and overlay of the force and respiratory data streams.

The CO_2SMO® produces both breath-by-breath data and data averaged over a 1 minute interval. Both outputs were required in this study for the two forms of analyses undertaken: the former to explore the breath-by-breath changes *during* physiotherapy, the latter to explore changes from baseline in the child's ventilatory pattern *following* treatment. The flows, volumes and compliance data were weight-corrected to allow comparison of data across the wide age range studied.

1. Force and ventilation during chest physiotherapy

Median values and ranges were used to describe any non-normally distributed data (as shown by a test of normality), using Spearman's rank correlation coefficient to assess the relationship between such variables. Mean values, standard deviations and Pearson's correlation coefficients were used to explore normally distributed data.

Respiratory data were summarised for statistical analysis by categorising each breath according to measurement condition (before, during and after physiotherapy), and aggregating these data. Manual lung inflations when CWV forces were applied were analysed separately from the remaining lung inflations, making a total of 4 measurement conditions as shown in **Figure 2.30.**

One-way repeated measures analysis of variance (ANOVA) compared respiratory data collected during baseline ventilation prior to treatment, with those obtained during manual inflations and CWV. Any data which did not meet the assumptions for normality were evaluated after appropriate adjustments (Greenhouse-Geisser and Huyn-Feldt tests). Differences between measurement conditions were considered significant when $p < 0.05$. Percentage changes in respiratory variables between baseline and manual lung inflations (Minf), with and without CWV, were calculated using the following equations:

i) $$\left[\frac{(M\inf) - Baseline}{Baseline}\right]*100$$

ii) $$\left[\frac{(M\inf + CWV) - Baseline}{Baseline}\right]*100$$

To explore the relative contribution of factors influencing PEF during manual lung inflations with and without CWV, initial univariable analyses on PEF were followed by multiple regression analysis, details of which are given in **section 3.4.6**.

2. Ventilatory changes following chest physiotherapy

The stability of the outcome variables (PEF, expired volume, respiratory compliance and resistance and arterial blood gases) was assessed during mechanical ventilation before physiotherapy, in the absence of any intervention.

Using data averaged over 15 minute intervals, one-way repeated measures ANOVA was used to assess short-term changes from baseline in PEF, expired volume (or peak inspiratory pressure if on volume-controlled ventilation), respiratory mechanics, oxygen saturation and arterial blood gases following physiotherapy.

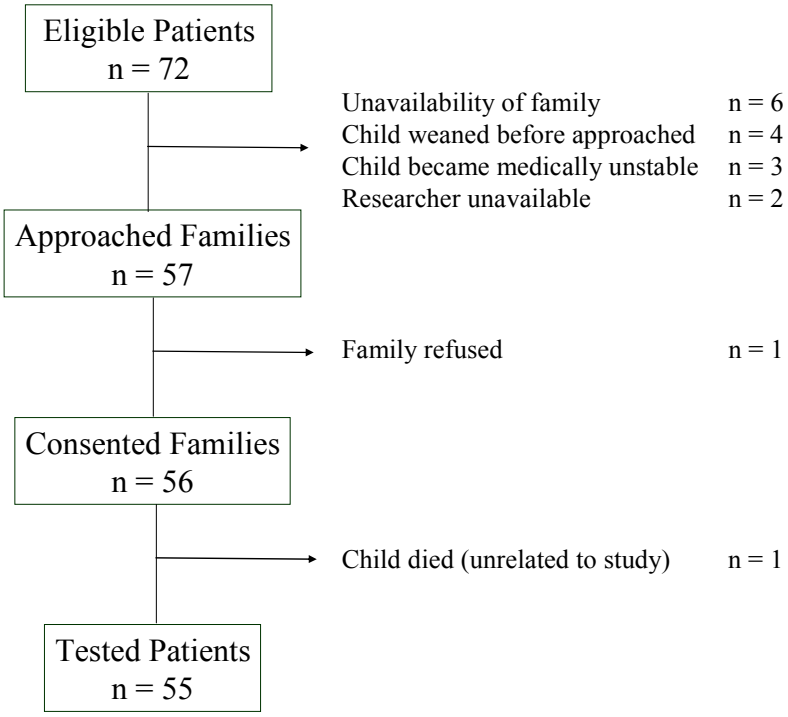
The data obtained in the first and second 15 minute intervals after treatment were compared as proposed by Bland and Altman, to explore whether measurements obtained at 15 minutes were representative of those recorded at 30 minutes (Bland & Altman 1986;Bland & Altman 1995).

3.4 Results

3.4.1 Study population

Of the 72 children who were eligible for the project between March 2005 and November 2006, 55 were studied (**Figure 3.4**). Recruitment failure was predominantly due to the unavailability of family members to give consent, children being weaned earlier than expected from the ventilator, or the child becoming too unstable to recruit. Only one family declined to participate in the study, as they did not wish to be involved in medical research of any sort.

Figure 3.4 Consort diagram of recruitment



3.4.1.1 Demographics of the study population

Fifty five children (30 males, median age 1.6 years [range, 1 week to 13.7 y], of whom 32 were < 2 years old) who had a range of clinical diagnoses were enrolled from the general paediatric and cardiac ICUs (**Table 3.1**). This table shows that the severity of illness was comparable between children in the two ICUs. Seven different forms of mechanical ventilation were employed across the 55 children, involving various combinations of

pressure and volume regulation and providing total ventilation or synchronised, intermittent ventilation.

Table 3.1 Indices of severity of illness and diagnostic categories for the 55 ventilated children

	CICU	PICU	Total
Number of Children	30	25	**55**
Days ventilated[1]	2 (1-14)	3 (1-7)	
PRISM Score (%)	12 (4-21)	15 (4-32)	
Oxygenation Index	7 (2-14)	4 (2-18)	

	CICU		PICU		
Diagnostic categories: Age:	**Cardiac**	**Upper Airways**	**Primary lung involvement**	**Secondary lung involvement**	**Total**
Under 2 years	15[2]	6	6	5	32
Over 2 years	9	-	6	8	23
Subtotal	24	6	12	13	
Total	**30**		**25**		**55**

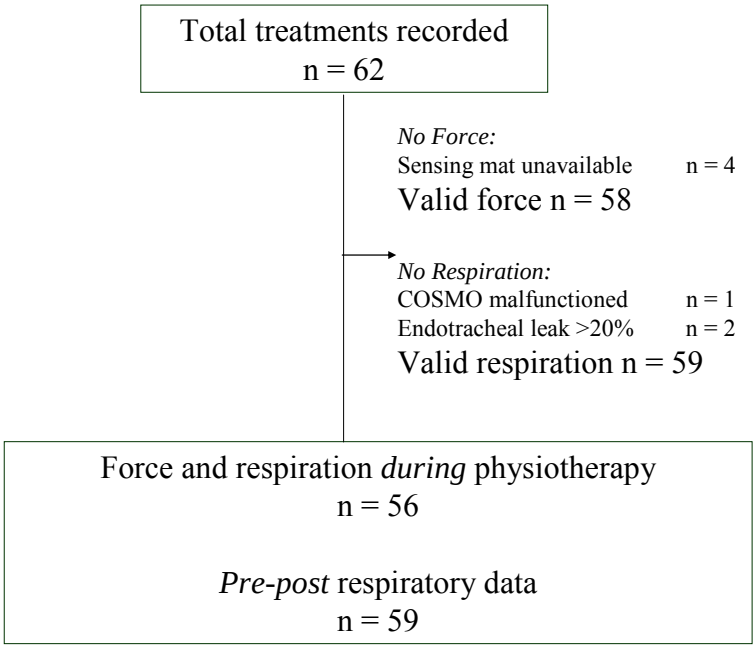
Data presented as median (range). Normal values for: Oxygenation Index < 10; see section 3.3.4
CICU = Cardiac Intensive Care Unit, PICU = Paediatric Intensive Care Unit.
[1]Days ventilated prior to measurement.
[2]2 cardiac children additionally had respiratory distress syndrome and 1 had asthma.

In the cardiac ICU, of the 15 children younger than 2 years, two children with cardiac disease also had respiratory distress syndrome and one had multiple medical problems including asthma. The six children with upper airways disease had undergone surgical correction of long stem tracheal stenosis. The population also included children who had received: a lung transplant (aged 5 years), a heart transplant which was showing signs of rejection (aged 13.7 years) and a cardiac bypass implant, the Berlin Heart (aged 8 months). The physiotherapy treatment of this last patient was randomly chosen to be video recorded, and is featured on the available CD (see **section 3.4.9**).

In the paediatric ICU, of the 12 children with primary lung involvement, five were asthmatic, four had respiratory distress syndrome, one had bronchiolitis, one had chronic lung disease and one had undergone repair of a diaphragmatic hernia. The population also included five children with severe head injuries, one of whom developed lung consolidation.

Data were successfully collected in all 55 children recruited. Seven children were measured during two treatments each, making a total of 62 treatment recordings, 32 of which occurred in children who were pharmacologically paralysed. Combined respiratory and force data during treatment were available during 56 physiotherapy treatments (in 53 children), as shown in **Figure 3.5**.

Figure 3.5 Summary of valid data recorded during and after physiotherapy



Arterial blood gases from indwelling lines were sampled before and after physiotherapy in 43 children, four of the children each receiving two treatments, making a total of 47 cases with arterial samples; venous blood analysis was performed on one child. The parents of six children declined blood sampling when consenting to the rest of the study, while a further six children did not have any post-treatment samples for logistical reasons including an absence of nursing staff.

3.4.1.2 Physiotherapist population

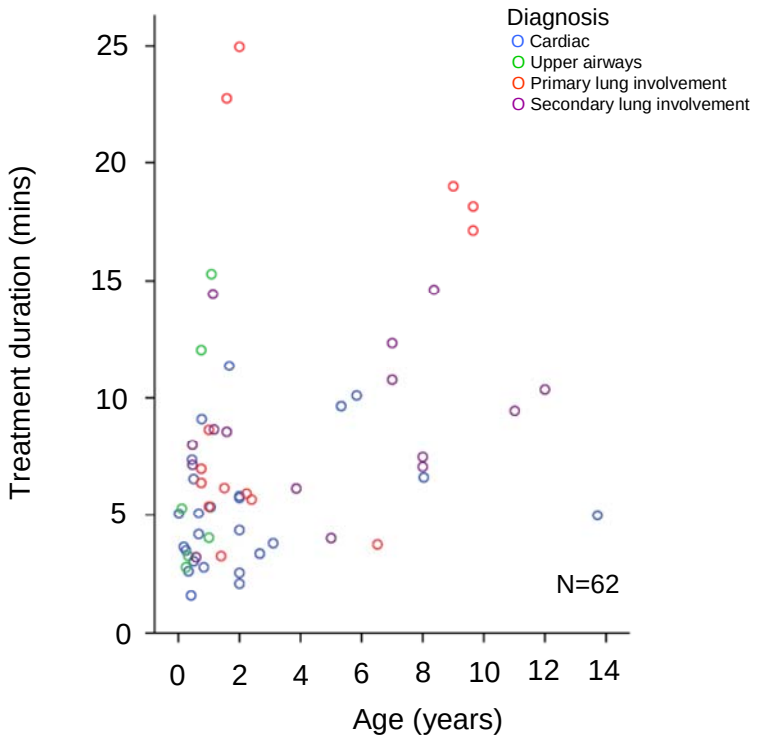
All twelve respiratory physiotherapists who delivered the children's treatments agreed to be monitored. In descending order of seniority, those who took part were: one clinical specialist, two senior grade I and nine senior grade II physiotherapists. A physiotherapy student assisted the clinical specialist during treatment of two children. The protocol proved

feasible and acceptable to the staff, despite the complexity of the conditions of the children recruited.

3.4.2 Treatment details and adverse events

Intersurgical® manual lung inflation circuits were used in both intensive care units, a 500 ml bag for children under 20 kg and a 2 litre bag for larger children. Saline was instilled into the endo-tracheal tube during 54 of the 62 treatments, (median volume [range] 0.3 ml/kg [0.04 - 2.1 ml/kg]).

Figure 3.6 Relationship of treatment length with the child's age and diagnosis



Treatment length ranged from 1.6 to 25 minutes (median 6 minutes), as shown in **Figure 3.6**; 77% of treatments lasted 10 minutes or less, half of which (22/62) were completed within 5 minutes. The majority (23 out of 33) of treatments in CICU lasted 5 minutes or less, including physiotherapy for the oldest and youngest patients; there was no relationship between treatment duration and the child's age. Although there was considerable overlap, many of the shortest treatments were for the young cardiac patients. The seniority of the staff delivering these treatments is discussed in **sections 3.4.9.7** and **4.4.4.1**. Children whose treatments lasted over 10 minutes generally had copious secretions. The two longest

treatments (lasting over 20 minutes) occurred in a 2 year old with asthma and a 19 month baby following repair of a diaphragmatic hernia, who required prolonged manual lung inflations to stabilise the children's transcutaneous oxygen saturation levels, as detailed in **Table 3.2**.

Table 3.2 Details of short-lived adverse events recorded during physiotherapy, and actions required to resolve the event

Patient's age & diagnosis	**Adverse event and *Action taken***
2y asthma	Acute oxygen desaturation to 80% during treatment from 89% pre-treatment *Manual lung inflations stabilised saturation*
19m diaphragmatic hernia	Acute oxygen desaturation to 89% during treatment from 93% pre-treatment *Manual lung inflations; returned to ventilator on increased FiO_2*
7y, head injury (see **section 3.4.9.4**)	Acute rise in ICP (doubled to 25 mmHg) during treatment and oxygen desaturation following physiotherapy *Fentanyl bolus and manual lung inflations; increased FiO_2*
2y, cardiac surgery	Pulmonary hypotensive crisis *Blood pressure stabilised spontaneously as treatment ceased*
9m, cardiac failure	Pulmonary hypertensive crisis *Blood pressure stabilised spontaneously as treatment ceased*

FiO_2 – Inspired oxygen concentration, ICP – intra-cranial pressure

3.4.3 Magnitude and Pattern of Force

Table 3.3 summarises the CWV forces recorded in this study, all of which fell within the measurement range of the force-sensing system. As can be seen from the table, there was a wide range of forces recorded, with marked differences in the maximum forces and oscillatory patterns, the oscillations varying both in frequency and amplitude. Chest wall vibrations were applied swiftly, as indicated by the rapid rise times (within 0.3s in all subjects and in 60% of cases within 0.1s).

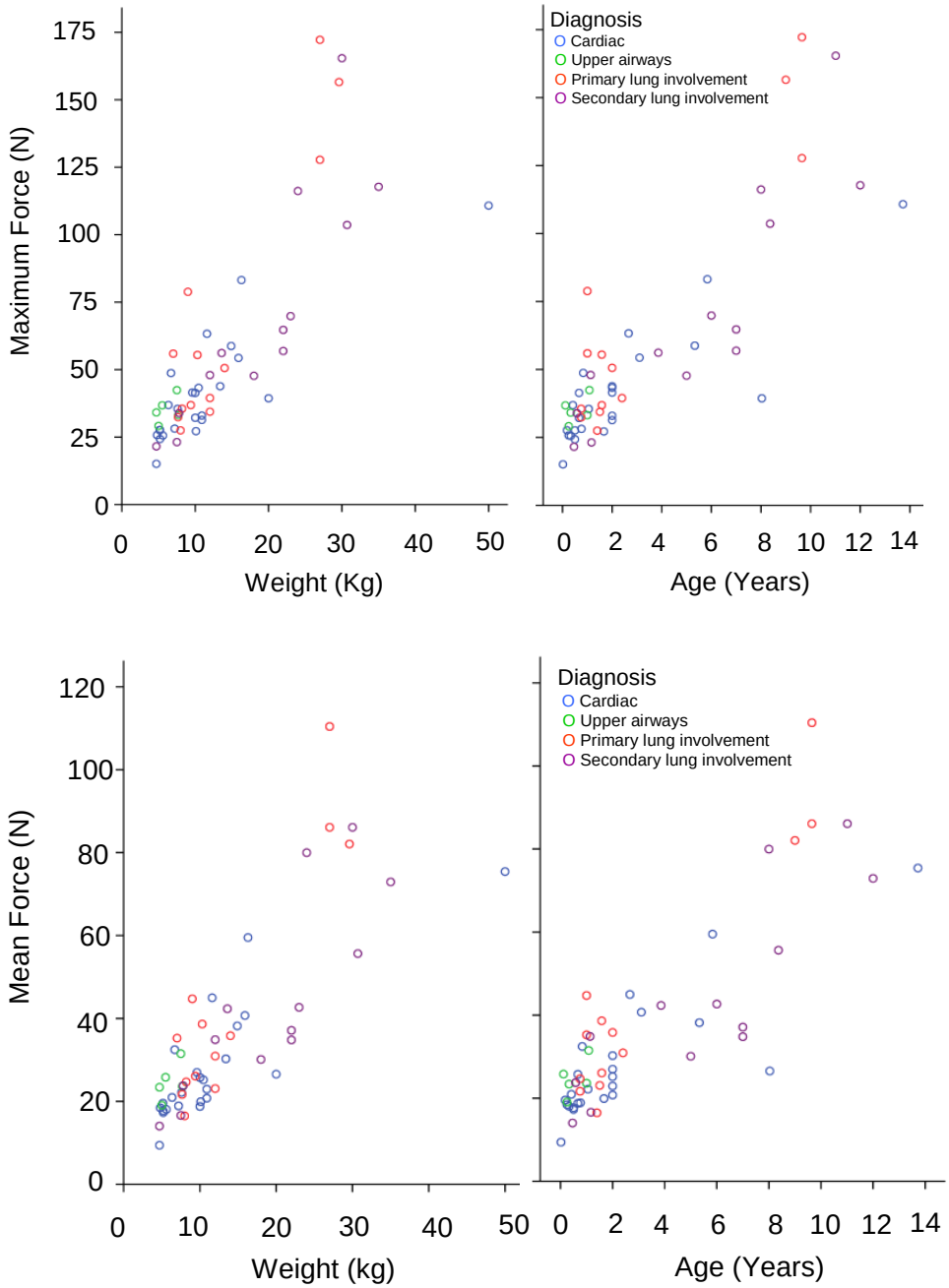
Table 3.3 Summary of chest wall force variables delivered during physiotherapy

Outcome measure	Median (range)
Maximum Force (N)	41 (15 – 172)
Mean Force (N)	27 (9 – 110)
Baseline Force (N)	3 (0 – 16)
Rise time (s)	0.1 (0.04 – 0.3)
No. of oscillations per CWV	3 (0 – 21)
Frequency of oscillation (Hz)	3 (0.4 – 11)
Amplitude of oscillation (N)	5 (1 – 56)
Duration of single vibration (s)	2 (0.8 – 4.6)
Number of vibrations per treatment (n)	10 (3 – 20)
Number of sessions of CWV per treatment (n)	3 (1 – 11)
Duration of entire treatment (min)	6 (1.6 – 25)

The magnitude of maximum force increased with the child's age (Spearman's correlation, $r = 0.76$) and weight ($r = 0.77$) $p < 0.001$, as shown in **Figure 3.7**. Forces greater than 85 N were only delivered to children over the age of 8, but there was marked variability within an age group, forces in those less than 2 years ranging from 15 – 79 N. Maximum forces

over 150 N were applied to two asthmatic children and a child with head injury and lung consolidation. By contrast, less force (110 N) was applied to the oldest child in the study, a 14 year old who was showing signs of rejection following a heart transplant.

Figure 3.7 Relationship between the forces applied during chest physiotherapy and age and weight

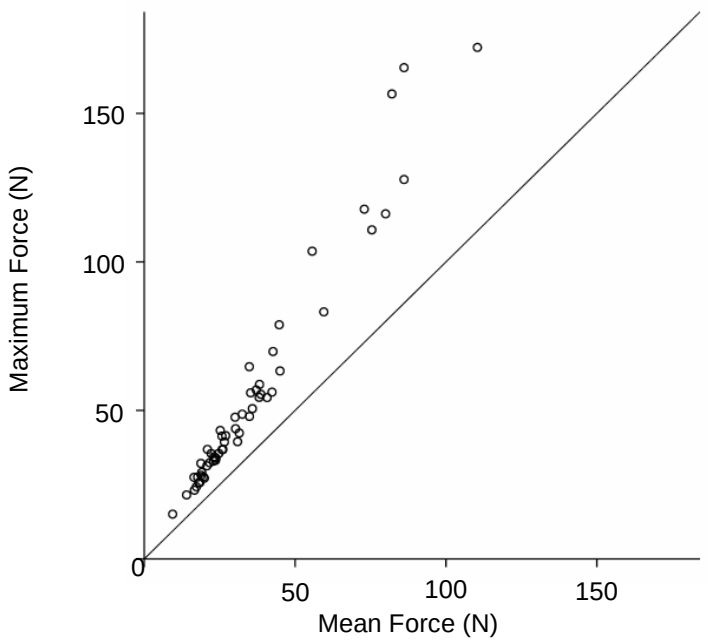


Similar correlations were obtained for mean force (Fmean with age r = 0.75, weight r = 0.76). The force-size relationships remaining unchanged when analysed according to the

children's diagnostic categories. No clear force patterns emerged between these subgroups.

Figure 3.8 shows the strong correlation between maximum and mean force (r = 0.98). The difference between the two measures was proportional to the absolute force with maximum force being on average 40% (SD 9%) higher than mean force (range 24 - 63%), depending on the pattern of force application.

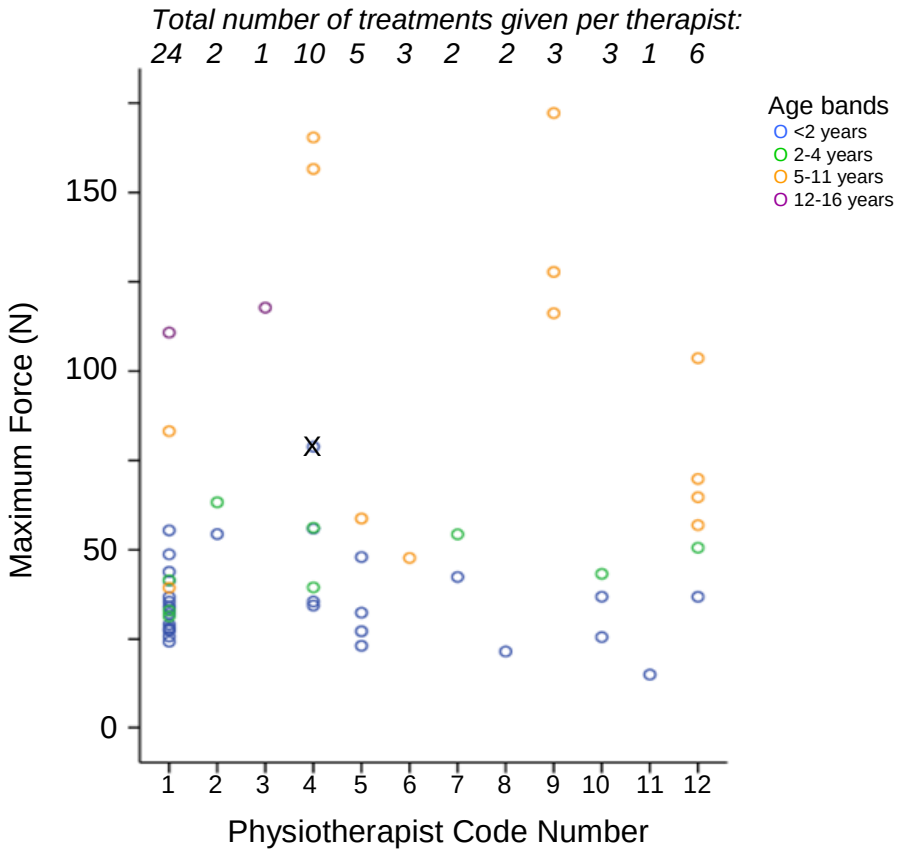
Figure 3.8 Comparison of within-subject maximum and mean applied force



Line of unity has been added for reference

Three physiotherapists treated more than five children each (**Figure 3.9**). Only the clinical specialist (physiotherapist 1) treated children across all four age categories; the majority (17) of the 24 children she treated were under 2 years of age. In this study the highest maximum forces were delivered by therapists who predominantly or only treated older children (physiotherapist 4 and 9). The force-age pattern generally held across the physiotherapists. The force profile of an exception, a child with bronchiolitis (child B) aged below 2 years, is shown in **Figure 3.10**.

Figure 3.9 Maximum force applied to children of different ages by individual physiotherapists

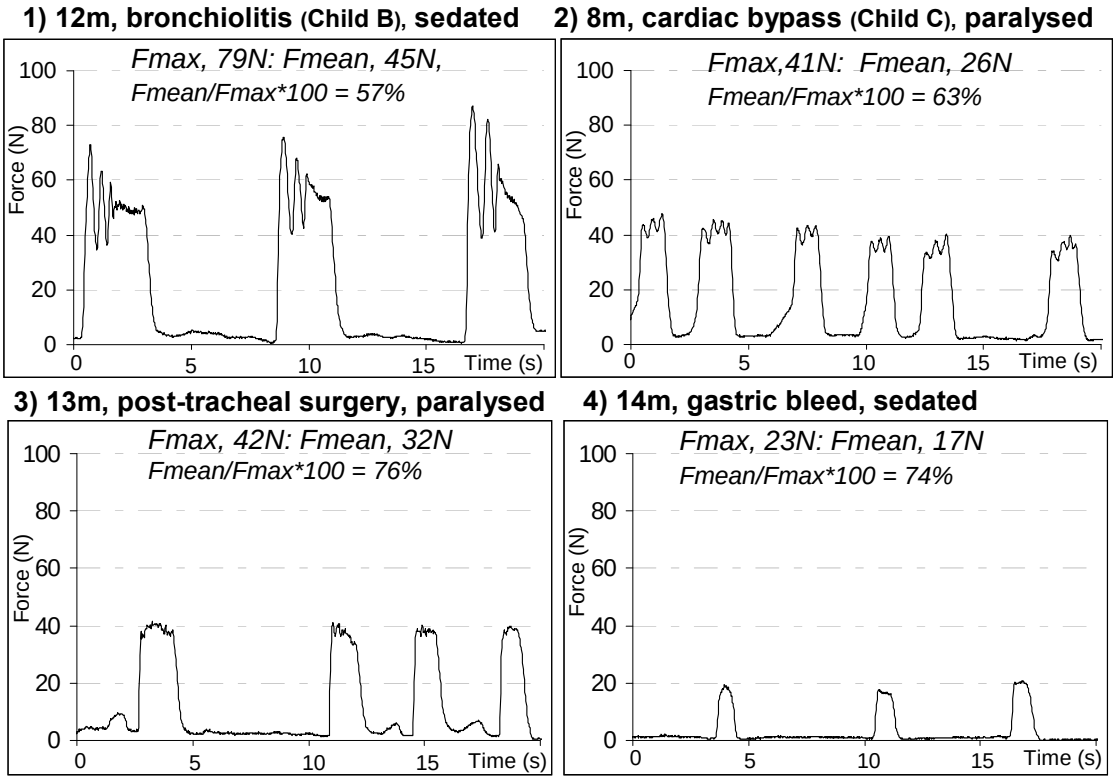


X – Outlier: Child with bronchiolitis, called child B (< 2y)

There were clear differences in the force-time profiles applied by individual physiotherapists with respect to the magnitude of applied force, frequency and magnitude of oscillations and the duration of each chest vibration. Each physiotherapist's force-time profile remained consistent within a treatment, the physiotherapists demonstrating a particular 'signature' profile (median [range] within-treatment CV being 11% [4.5-29%] for

Fmax and 12% [4.3-27%] for Fmean). A wide spectrum of profiles was recorded between the physiotherapists, examples of which are presented in **Figure 3.10**.

Figure 3.10 Variations in the oscillatory style of force profiles delivered to four infants aged below 15 months by four different physiotherapists



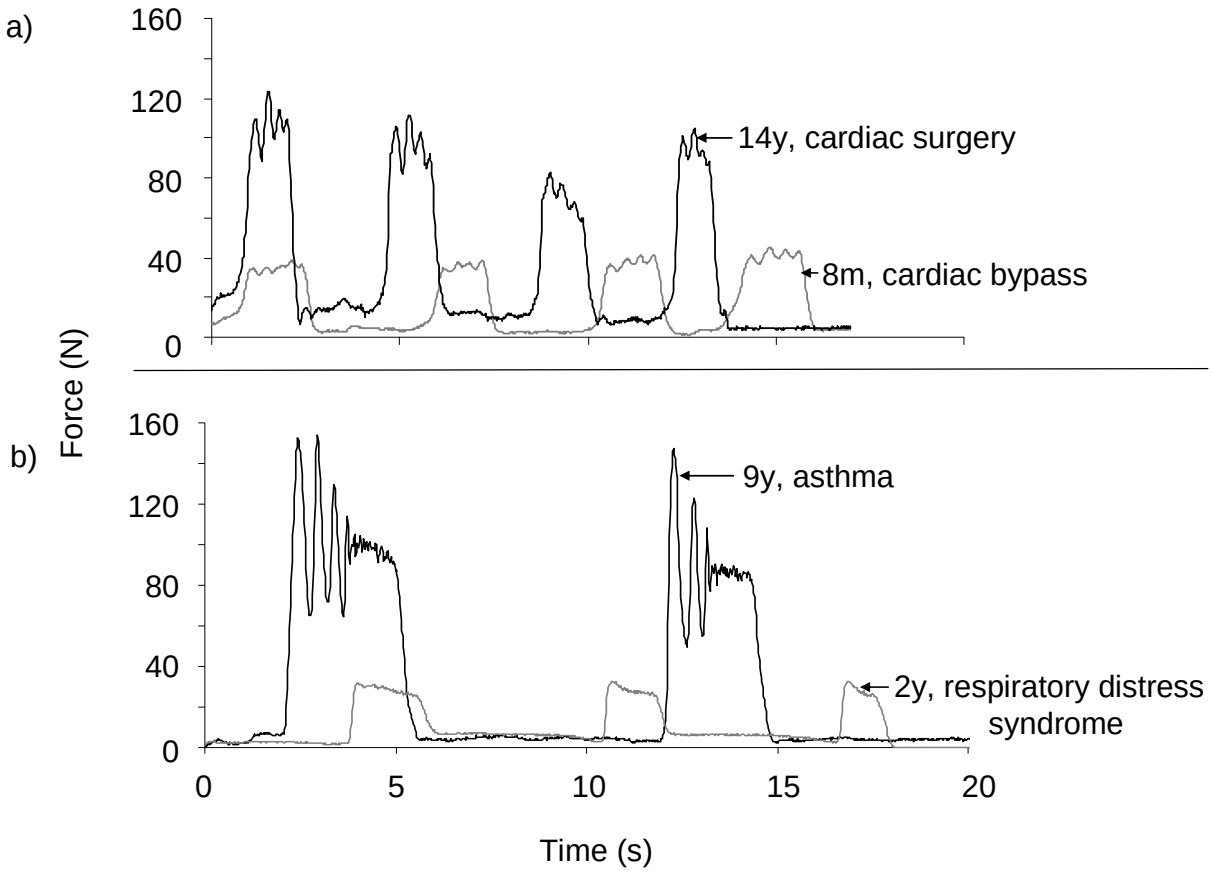
The contrasting treatments for child B and child C are discussed in detail in **section 3.4.9**

Maximum force in profile 1 was four times greater than that in profile 4, and double that seen in profiles 2 and 3. The profiles could be described according to their relative oscillatory and compressive patterns, which were reflected in the percentage relationship of Fmean to Fmax. Large amplitude oscillations resulted in a proportionately lower mean force relative to the inward compressive force, Fmax. An example of this is profile 1's treatment (child B), where a high initial chest compression (Fmax) was briefly applied, largely released then reapplied, the peak force lessening over time. Whilst a high maximum force was applied (**Figure 3.10**), this pattern significantly reduced the total force applied over one second, Fmean. The oscillatory pattern was variable in this child's treatment, the initially large amplitude oscillations (or 'shakes') being replaced by finer 'tremors' towards the end of the CWV. By contrast, profiles 3 and 4 were composed of these finer tremors

throughout, as reflected in their higher Fmean to Fmax percentages. Profile 2's oscillatory frequency of 3 Hz contrasts with the 8 Hz of profile 3.

The treatment style of the physiotherapists also appeared consistent when treating children of different ages, as shown in the physiotherapist's treatments featured in the panel (a) of **Figure 3.11**.

Figure 3.11 Examples of force profiles from two physiotherapists when treating children of different ages

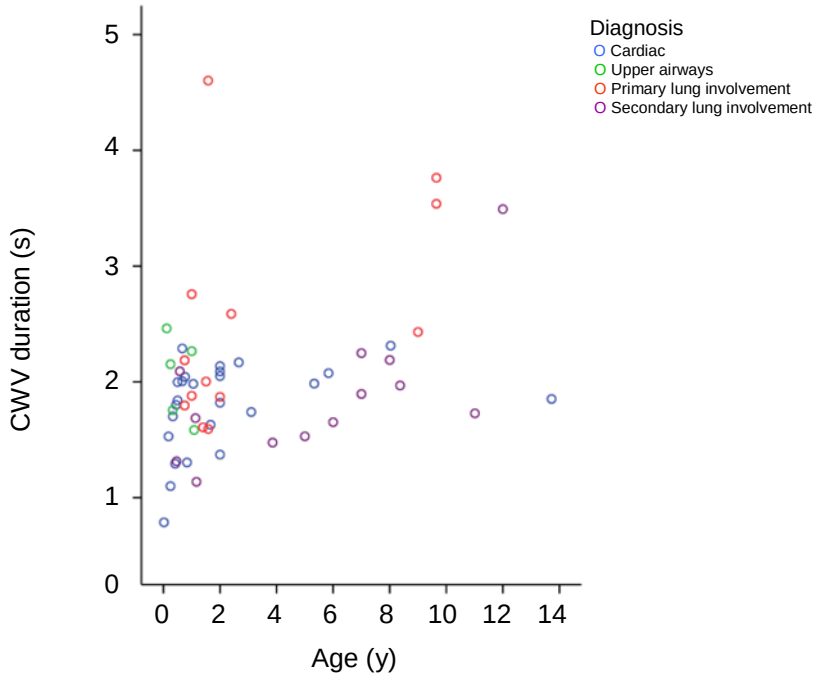


Note the proportionally similar pattern of applied force, and the similar frequency of CWV (approximately one every four seconds). An initial baseline force was applied in both instances, this value being higher (but proportionately similar) in the older child. The only exception to this consistency was shown by one physiotherapist, whose treatments are shown in panel (b) of **Figure 3.11**. The physiotherapist adopted one treatment style of minimal oscillation when treating children less than 5 years, but showed increased

amplitude of oscillation when treating older children. In addition to developmental differences between the two children (**section 4.4.3.2**) they also had different diseases which may further have influenced the physiotherapist's treatment style, as discussed in **section 4.4.3.4**. There were clear differences between the featured treatments of these two physiotherapists, not only in terms of the profile shapes but also regarding the time interval between successive CWV.

Vibration forces predominantly lasted less than 3s, as shown in **Figure 3.11** and **Figure 3.12**. The longest vibrations were given to older children (with larger lung volumes) and those with primary lung pathology and severe airway obstruction (predominantly asthma), resulting in a longer time constant. The cardiac children and those with lung involvement secondary to mechanical ventilation predominantly received CWV lasting less than 2s. These factors are discussed further in **sections 4.4.3.4** and **4.4.4.3**.

Figure 3.12 Relationship of the duration of a chest wall vibration with the child's age and diagnosis



3.4.4 Ventilatory Changes during Chest Physiotherapy

During baseline mechanical ventilation there was a strong relationship between inflation volume and body size, which was accompanied by marked increases in both PEF and PIF throughout childhood (**Figure 3.13**). The greater variability of PEF than PIF probably reflects differences in underlying lung pathology. Peak inflation pressure remained relatively constant throughout childhood.

Figure 3.13 Relationship between ventilatory parameters and weight during baseline mechanical ventilation

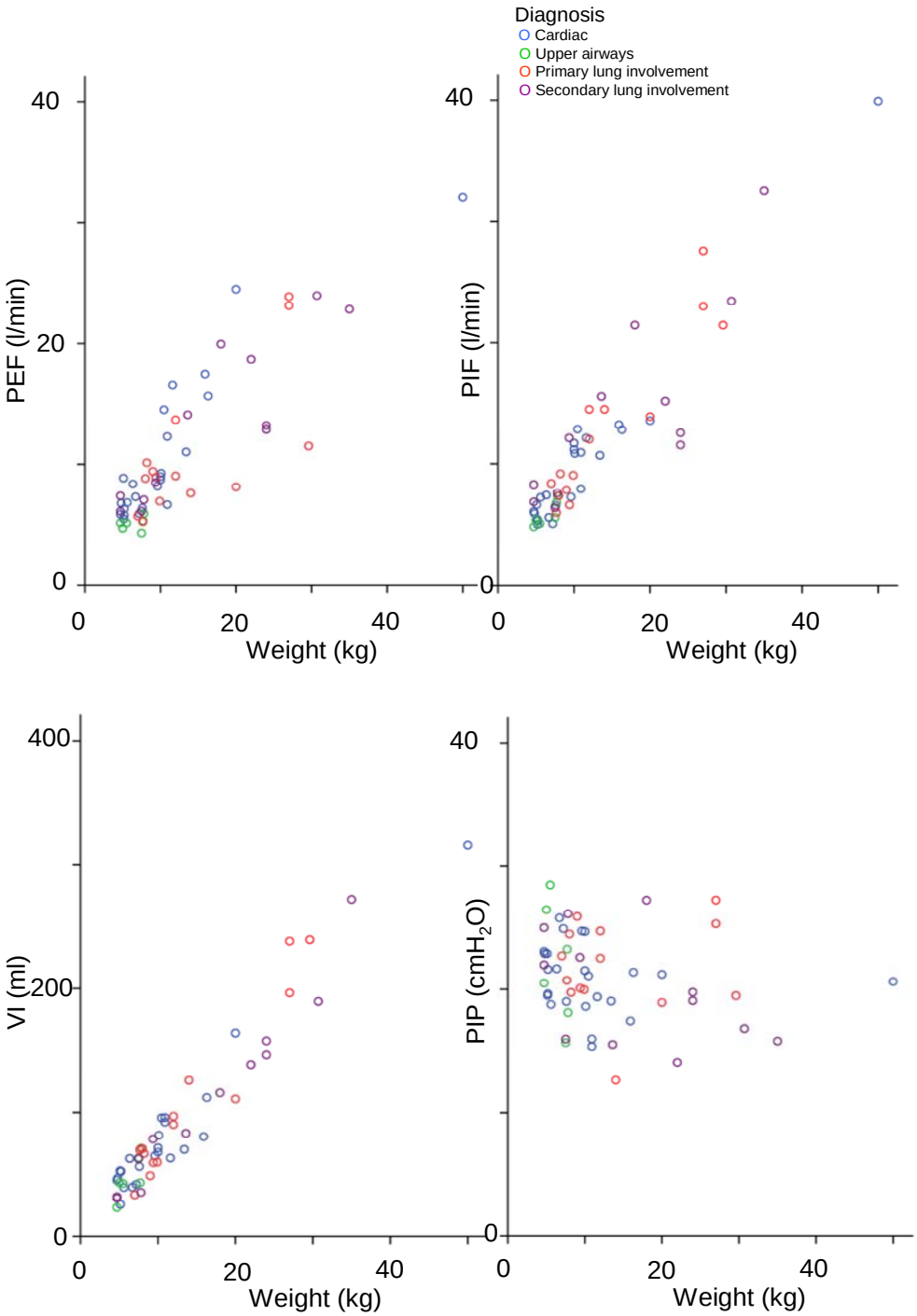


Table 3.4 details the ventilatory changes during physiotherapy, in relation to baseline mechanical ventilation. To allow comparison of relative changes across the wide age range studied (**Figure 3.7**), the flows and volumes were standardised by expressing them per kg body weight. As can be seen there was a wide range of individual responses in the variables assessed.

Table 3.4 Changes in ventilation during physiotherapy

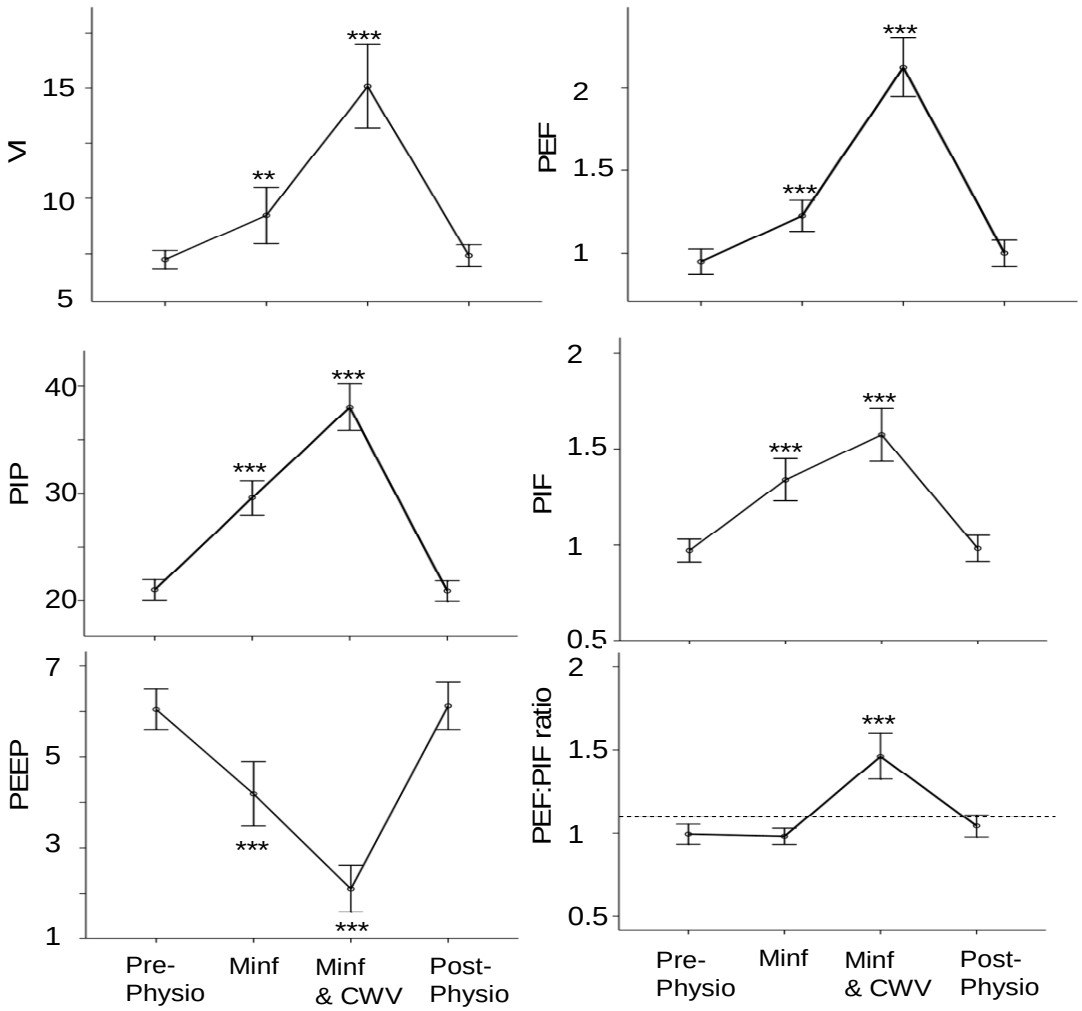
Variable	Ventilator Baseline	Minf	(Minf & CWV)	% Change Minf – Baseline	% Change (Minf & CWV) – Baseline
PEF (l/min/kg)	1.0 (0.3)	1.2 (0.3)***	2.1 (0.7)***	34 (19, 38)	118 (100, 136)
PIF (l/min/kg)	1.0 (0.2)	1.3 (0.4)***	1.6 (0.5)***	40 (27, 53)	66 (52, 80)
PEF:PIF ratio	1.0 (0.2)	1.0 (0.2)	1.5 (0.5)***	*0 (-8, 8)*	45 (28, 62)
VE (ml/kg)	7.2 (1.5)	8.0 (2.8)*	18.0 (5.7)***	14 (3, 25)	154 (134, 176)
VI (ml/kg)	7.2 (1.6)	8.8 (3.3)**	14.6 (5.3)***	23 (11, 36)	102 (80, 121)
PEEP (cmH_2O)	5.9 (1.4)	4.2 (2.7)***	2.1 (1.9)***	-26 (-40, -12)	-62 (-73, -50)
PIP (cmH_2O)	21.2 (3.9)	29.5 (6.0)***	37.9 (8.2)***	43 (33, 52)	82 (71, 93)
ΔP (cmH_2O)	15.3 (3.9)	25.4 (5.9)***	35.9 (8.0)***	75 (60, 91)	145 (125, 165)
tE (s)	1.7 (0.5)	1.1 (0.7)***	2.0 (1.0)*	-34 (-43, -24)	20 (4, 37)
tI (s)	0.9 (0.1)	0.8 (0.4)	1.3 (0.6)***	*-9 (-21, 4)*	50 (29, 70)
Respiratory rate (per min)	25 (7.7)	37 (15)***	33 (11.6)***	50 (35, 64)	36 (23, 49)
	Values expressed as mean (SD)			Values expressed as mean (95% CI)	

Comparison with pre-physiotherapy baseline values: $^{*}p < 0.05$, $^{**}p < 0.01$, $^{***}p < 0.001$
Minf – manual lung inflations, CWV – chest wall vibrations, **ΔP** - change in pressure (PIP – PEEP),

After adjusting for repeated measures in individual children, analysis of variance demonstrated that with the exception of PEF:PIF ratio and inflation time (tI) during manual inflations, there was a significant change in all variables during manual inflations both with and without CWV (as indicated by the 95% confidence intervals of the change, which did not encompass zero). During baseline mechanical ventilation, inflation volume (VI) was equal to expired volume (VE). During manual inflations, inflation volume exceeded expired volume, suggesting that despite the lack of leak at baseline, some pressure-

dependent leak developed at higher inflation pressures. Inflation volume doubled during CWV, which was achieved by an increase in both inspiratory time and pressure. In addition, expired volume exceeded inflation volume during CWV, as proportionately more air was forced out of the lungs during the longer expiratory time (tE). Regarding flows, during manual lung inflations both PEF and PIF increased from baseline by approximately 40%, reflected in the PEF:PIF ratio remaining at the mechanical ventilation value of 1.0. By contrast, during CWV the PEF:PIF ratio increased significantly due to the relatively greater increase in PEF, which doubled from baseline. Pressure monitoring during CWV showed that positive end-expiratory pressure (PEEP) dropped while peak inflation pressure (PIP) rose to a level which at times exceeded 35 cmH_2O. These changes are summarised in **Figure 3.14**.

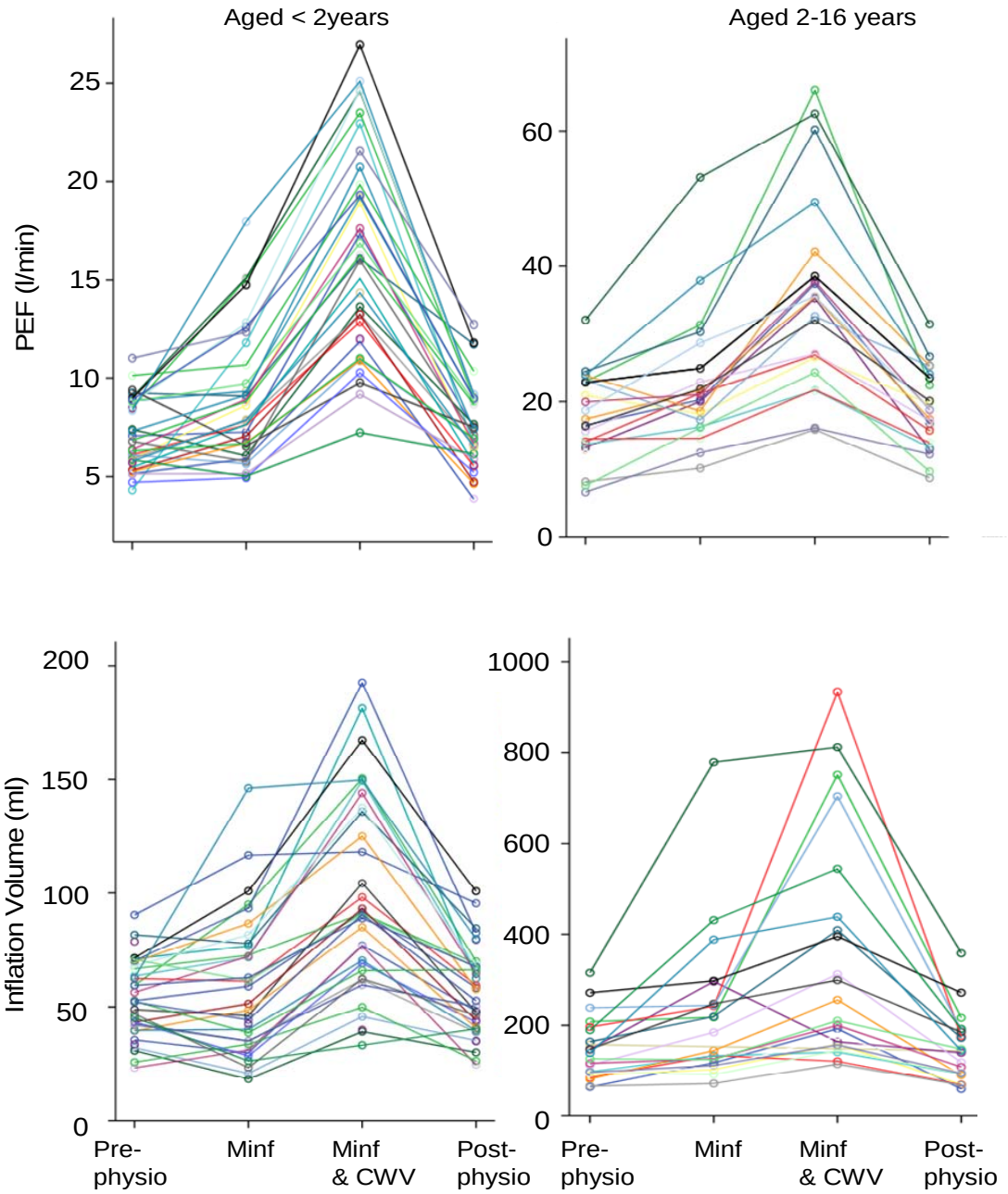
Figure 3.14 Comparison of respiratory variables during chest physiotherapy compared to those during mechanical ventilation before and after treatment



Comparison with pre-physiotherapy baseline values; $^{**}p < 0.01^{***}$, $p < 0.001$.
Units: Inflation volume (VI), ml/kg; Peak inflation pressure (PIP) & Positive end-expiratory pressure (PEEP), cmH_2O; Peak expiratory and inspiratory flows (PEF & PIF), l/min/kg. PEF:PIF broken line denotes the ratio of 1.1:1. Minf – manual inflations, CWV – chest wall vibrations, Physio – physiotherapy.

Figure 3.15 demonstrates a general increase from baseline values in PEF during manual lung inflations, with a further significant increase on the delivery of CWV ($p < 0.001$); there were rare instances where PEF dropped during manual inflations. The pattern of increase in PEF was mirrored by the changes in inflation volume, as shown in **Figure 3.15**.

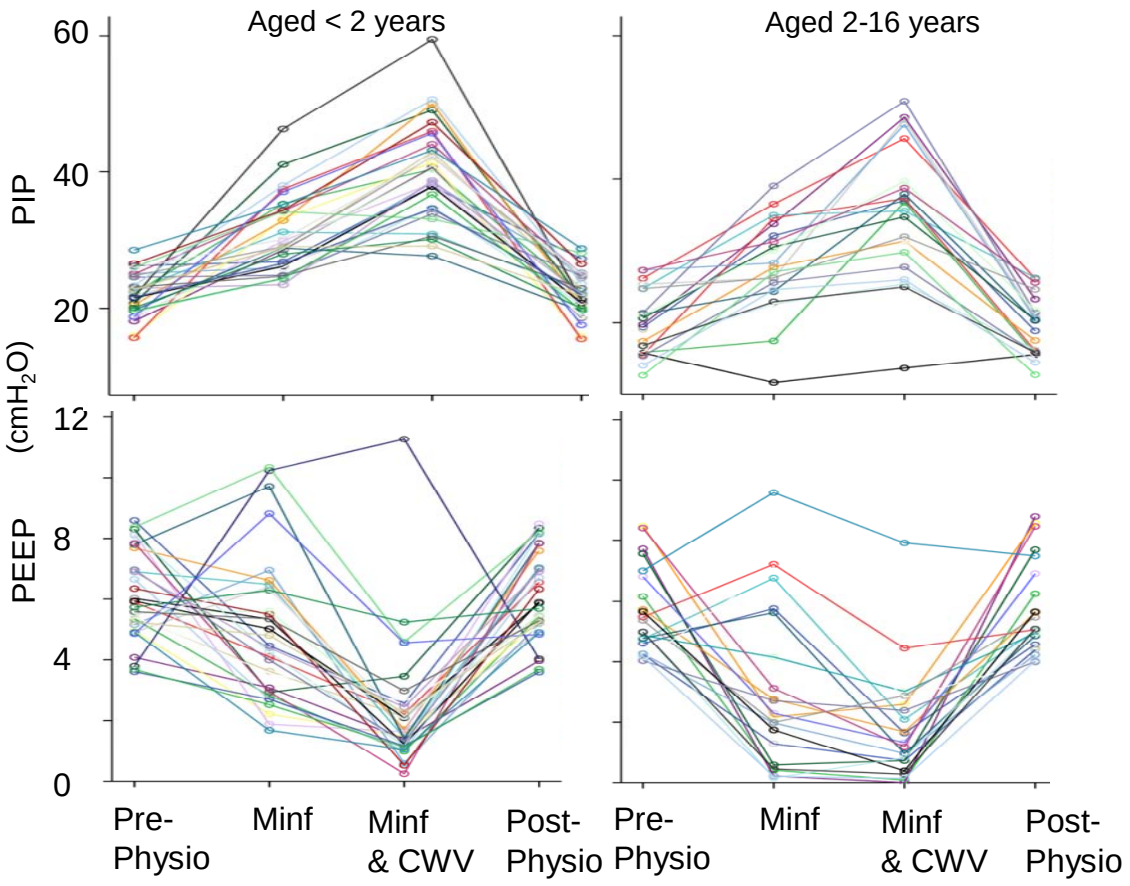
Figure 3.15 Peak expiratory flow and inflation volume during physiotherapy compared with values during mechanical ventilation



Minf – manual inflations, CWV – chest wall vibrations, Physio – physiotherapy.

Figure 3.16 demonstrates a general increase from baseline values in PIP during manual lung inflations, with a further significant increase on the delivery of CWV ($p<0.001$); again, there were rare instances where PIP dropped during treatment. There was more variability in the level of PEEP maintained during physiotherapy (**Figure 3.16**), which dropped significantly during manual inflations with a further decrease during CWV, as the chest compressions forced the air out of the lungs (**Table 3.4**). Since all therapists used the same lung inflation circuits, the range of pressure changes recorded is likely to relate both to the child's underlying diagnosis and to the patterns of lung inflations and CWV.

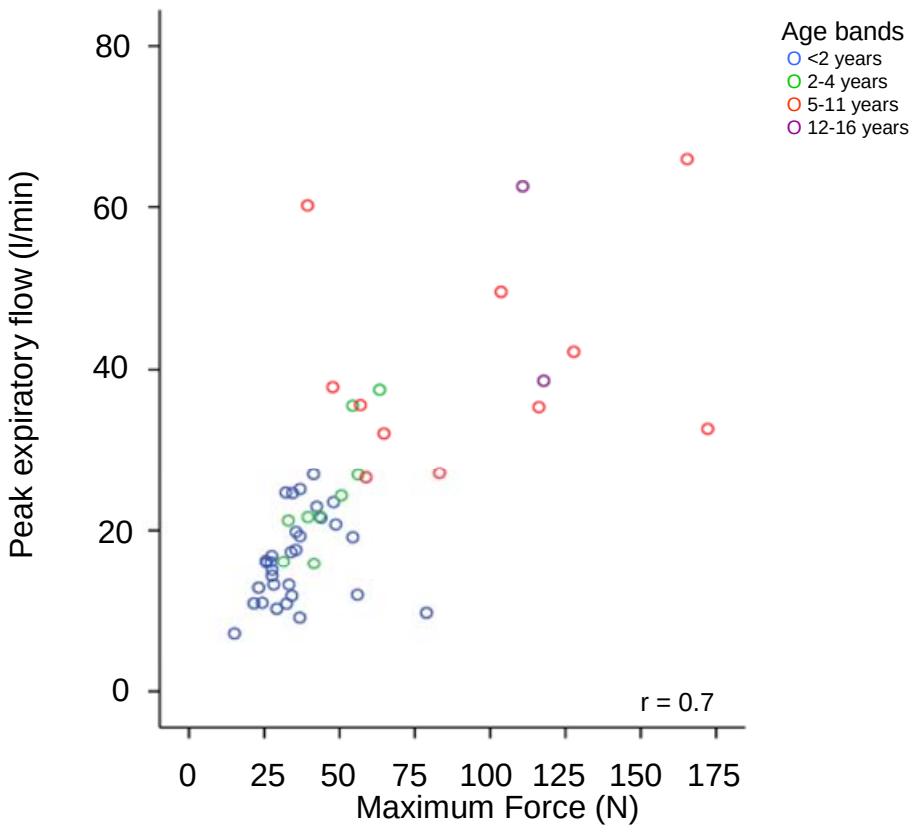
Figure 3.16 Peak inflation pressure and positive end-expiratory pressure during physiotherapy compared with values during mechanical ventilation



Minf – manual inflations, CWV – chest wall vibrations, Physio – Physiotherapy.

Figure 3.17 shows the relationship of PEF to maximum force during CWV for children in the different age bands. The relationship with mean force was similar. Despite a strong correlation (Spearman's $r = 0.7$, $p < 0.01$), the plots display clear outliers, where a relatively low force was associated with a relatively high PEF, and vice-versa. Furthermore, interpretation of this relationship requires simultaneous changes in inflation pressures and volumes to be accounted for, as discussed in **section 3.4.5**. Mean force is an averaged value which is strongly influenced by the amplitude of oscillation, as shown earlier in **Figure 3.10**, therefore it is more likely to relate to changes in mean expiratory flows. By contrast, the initial compressive force (Fmax) is related to the transient maximum increase in expiratory flow (PEF). Maximum force has therefore been used in all respiratory calculations of PEF in the remainder of the chapter.

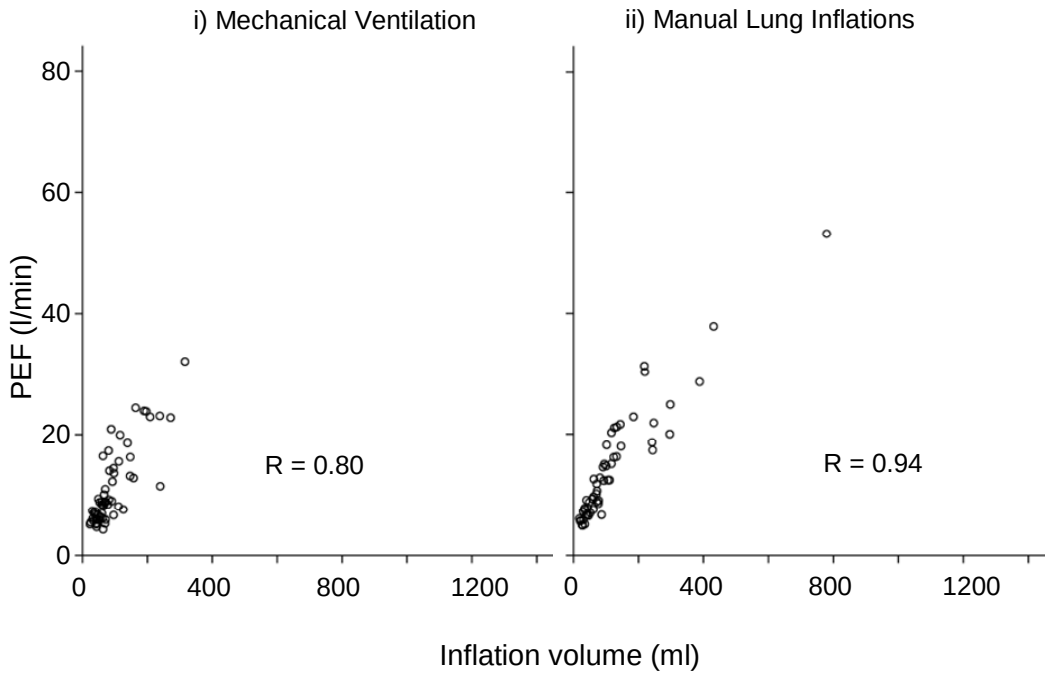
Figure 3.17 Relationship of peak expiratory flow with maximum force, according to age group

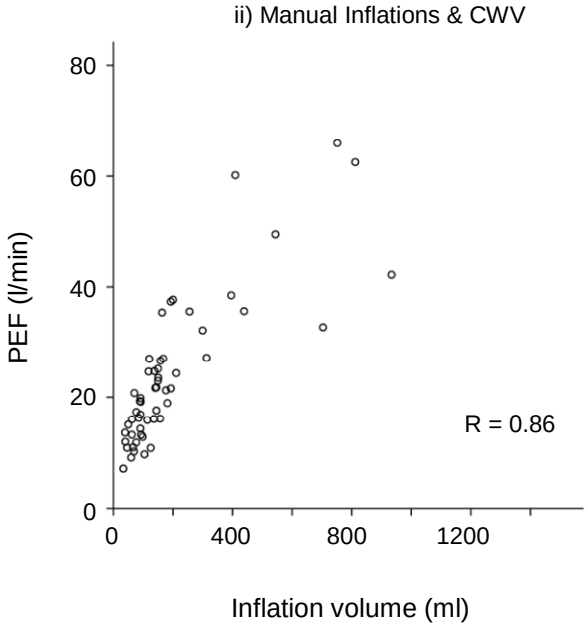


3.4.5 Factors influencing peak expiratory flow

Although these results clearly demonstrate that PEF was greater during CWV than during manual inflations or mechanical ventilation, the potential impact of associated changes in ventilatory pattern between different measurement conditions must be considered before the impact of CWV forces per se can be determined. There was a clear relationship between PEF and inflation volume during all measurement conditions, as shown by the high Spearman correlations ($p < 0.001$) in **Figure 3.18**.

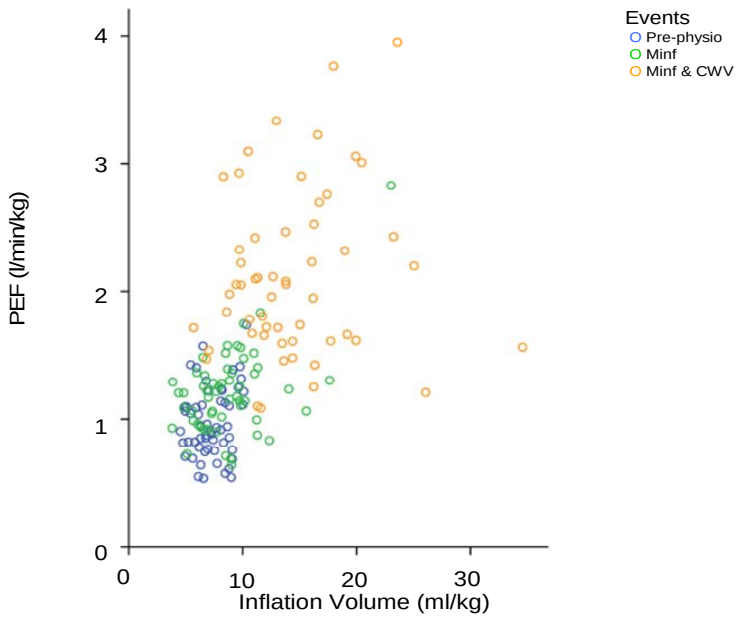
Figure 3.18 Relationship between peak expiratory flow and inflation volume, according to measurement condition





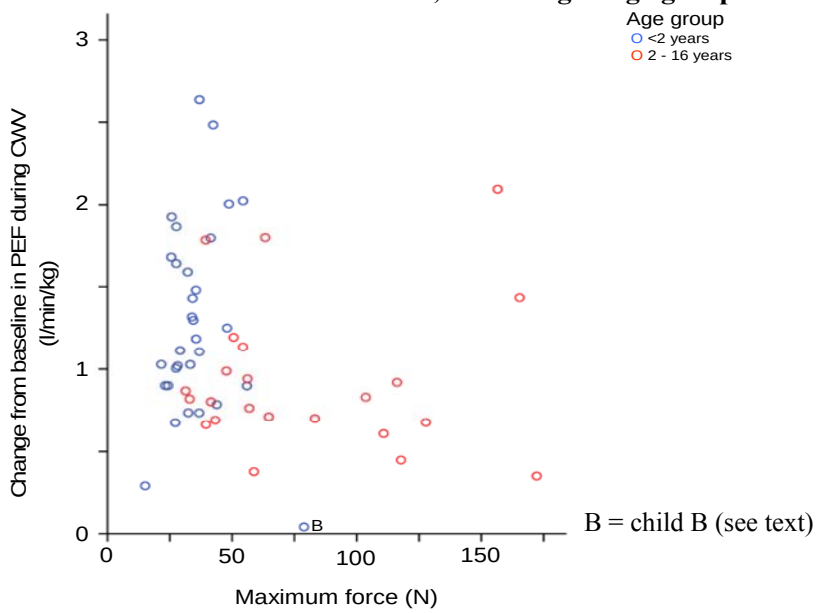
After correcting for body weight, PEF increased significantly from baseline during manual lung inflations (mean [95% CI] % change, 34% [19, 38%], $p < 0.001$), increasing further with application of CWV (118% [100, 136%], $p < 0.001$), as shown in **Figure 3.19** and **Figure 3.20**.

Figure 3.19 Relationship of standardised peak expiratory flow and inflation volume according to measurement condition



Despite lower forces being applied to the younger children (**Figure 3.7**), there was a relatively greater increase in PEF in those aged below 2 years ($p = 0.01$), as shown in **Figure 3.20**. This difference became highly significant ($p < 0.001$) when the problematic treatment of a 1 year old with bronchiolitis (child B, discussed in **section 3.4.9.2**) was excluded from analysis.

Figure 3.20 Relationship between change in peak expiratory flow and applied force during chest wall vibrations, according to age group



3.4.6 Development of a model to explain changes in peak expiratory flow

Having established that PEF increased during physiotherapy, analysis was then undertaken to determine the relative contribution of the force component in increasing PEF, over and above that resulting from the accompanying changes in ventilatory pattern. Since many of the respiratory variables were inter-related (for example, PIP and VI), multiple regression analysis was undertaken to determine the relative contribution of each variable. Initially, factors shown to be significant on univariable analysis were added into the model in a stepwise manner. Those which became non-significant in the multivariable model were then removed. Differences in body size were adjusted for in the calculations by using weight-corrected measures.

3.4.6.1 Univariable analysis

The effects of the individual determinants of PEF were calculated using a summary of each child's data (aggregate), using the data collected during both baseline ventilation and chest physiotherapy.

- Peak expiratory flow was significantly influenced by the child's age, inflation volume, positive end expiratory and inflation pressures, respiratory rate and maximum force, as summarised in **Table 3.5**.

Table 3.5 Factors significantly influencing peak expiratory flow (l/min/kg) during univariable analysis, based on data collected during both baseline ventilation and chest physiotherapy

Variable	Contribution (Beta)	Significance
PIP (cmH_2O)	0.689	<0.001
VI (ml/kg)	0.544	<0.001
Fmax (N)	0.456	<0.001
Resp.Rate (per min)	0.331	<0.001
PEEP (cmH_2O)	-0.326	<0.001
Age (y)	-0.238	0.002

3.4.6.2 Multivariable analysis

- After correcting for weight, the major determinants of PEF *in the absence of CWV* were VI and age ($R^2 = 0.38$, $p < 0.001$). The contribution of PIP was less than VI (PIP and age, $R^2 = 0.31$, $p < 0.001$). Once VI and age were accounted for the other factors had no or minimal significance.

A 4-step process detailed below determined i) the age-related effects of CWV on PEF, and ii) the extent to which increases in PEF during CWV could be attributed to the forces applied over and above that due to any accompanying increases in VI.

3.4.6.2.1 The effects of inflation volume and age on PEF

The relationship between PEF, VI and age *in the absence of CWV* (PEF_{Minf}) was calculated using the children's aggregated data which was collected during baseline mechanical ventilation and manual lung inflations (**Equation 3.1**).

Equation 3.1 Factors influencing peak expiratory flow, in the *absence* of force

$$\mathbf{PEF_{Minf}}\ \text{l/min/kg} = \mathbf{0.79}\ (0.66, 0.91)\ \mathbf{constant} + \mathbf{0.052}\ (0.038, 0.067)\ \mathbf{VI}\ \text{ml/kg} + \mathbf{-0.042}\ (-0.057, -0.027)\ \mathbf{Age}\ \text{y} \quad (R^2 = 0.4)$$

Brackets contain 95% CI; $p < 0.001$ for each variable

3.4.6.2.2 The effects of force, inflation volume and age on PEF

The relationship estimating the combined effect of VI, age and force on PEF *during CWV* was then calculated using all aggregates collected during baseline ventilation and chest physiotherapy, **Equation 3.2**. Force was entered as equal to zero during both baseline ventilation and manual inflations. PEF_{CP} (chest physiotherapy) denoted the flow generated by the manual inflation combined with the CWV force.

Equation 3.2 Factors influencing peak expiratory flow during chest wall vibrations

$$\mathbf{PEF_{CP}}\ \text{l/min/kg} = \mathbf{1.04}\ (0.87, 1.21)\ \mathbf{constant} + \mathbf{0.054}\ (0.037, 0.071)\ \mathbf{VI}\ \text{ml/kg} + \mathbf{-0.086}\ (-0.109, -0.064)\ \mathbf{Age}\ \text{y} + \mathbf{0.006}\ (0.002, 0.009)\ \mathbf{Force}\ \text{N} \quad (R^2 = 0.49)$$

Brackets contain 95% CI; $p < 0.001$ for each variable

- The increase in PEF was significantly related to the magnitude of the applied force and VI, and inversely related to age ($p < 0.001$ for all).

Although the decision was made in **section 3.4.4** to relate changes in PEF during treatment to maximum force applied, similar equations were obtained for mean force (**Appendix D.1**).

3.4.6.2.3 The 'added value' of CWV on PEF during chest physiotherapy

The *additional* increase in PEF due to the CWV, above that which could be accounted for by the increased inflation volumes during physiotherapy, was then estimated by relating the values derived from **Equation 3.1** in the absence of force to that derived at matched inflation volumes during CWV using **Equation 3.2**. Examples of these calculations are presented below.

3.4.6.2.4 Use of the model to explore age-related effects on PEF and the 'added value' of CWV

The model estimating PEF was explored for a 1 year old and a 10 year old child by analysing the relative effect of applying the same maximum force (60 N) and standardised inflation volume to both children, as shown in **Table 3.6** (using **Equation 3.2**). Inflation volume during CWV was assumed to be 14.6 ml/kg, equal to the average group value in **Table 3.4**. The results were compared with calculations using **Equation 3.1** to explore:

- the effects of baseline inflation volumes on PEF (calculation 1)
- manual lung inflations per se on PEF (calculation 2)
- the influence of the inflation volume delivered immediately prior to CWV (calculation 3), and
- the 'Added value' of CWV on PEF, over and above that due to the accompanying increase in VI (calculation 4)

This procedure was necessary in order to separate out the individual effects of increased inflation volume and CWV during physiotherapy. Full details of all the calculations are presented in **Appendix D.2**.

Table 3.6 Use of the model to estimate PEF during the different measurement conditions in children of different ages

	PEF (l/min/kg)	
	1 y	**10 y**
1) PEF at 7.2 ml/kg baseline VI	1.12	0.74
2) PEF_{Minf} at 8.8 ml/kg VI	1.20	0.83
3) PEF_{Minf} at 14.6 ml/kg VI[1]	1.50	1.13
4) PEF_{CP} at 14.6 ml/kg VI & CWV of 60 N	2.10	1.33
5) 'Added value' of 60 N CWV on PEF	*54%*	*27%*

[1]no breaths were observed with a VI of this magnitude in the absence of CWV, this value being included simply to match (and calculate the effect of) the VI delivered prior to CWV forces – see **section 3.4.6.2.3**

- **Table 3.6** illustrates the relatively higher weight-corrected PEF at any given lung inflation in the younger child, reflecting the significant inverse relationship of PEF with age indicated in **Equation 3.1.**

- The relative increase in PEF during chest physiotherapy when compared with baseline was similar in both age groups (88% for the 1 year old [i.e. 100 x (2.10-1.12)/1.12] and 80% for the 10 year old)

- The relative increase in PEF due to increased inflation volumes above baseline (i.e. 100 x [1.50 – 1.12]/1.12 in the 1 year old) was somewhat lower in the younger age range (34% versus 53% at 10 years).

- By contrast, the average increase in PEF that could be attributed solely to the CWV (e.g. 100 x [2.10 -1.50]/1.12 at 1 year of age) was somewhat higher in the younger child (54%) than in a 10 year old (27%). These calculations support the suggestion in **Figure 3.20** that force was more effective at increasing PEF in younger children.

In practice, higher forces tended to be used in older children (**Figure 3.7**). Application of a force of 100 N in a 10 year old would result, on average, in a 59% increase in PEF due to

CWV alone, similar to that observed in a 1 year old when 60 N were applied (see **Appendix D.2** for details).

The validity of these equations for predicting changes in PEF under a variety of measurement conditions were verified by comparing the calculated PEFs with recorded data presented in **Table 3.4** and **Figure 3.19**. Despite the marked between-subject variability, the calculated values concur with the average data recorded in the study. In this way modelling of the group data provided clear evidence of the significant additional impact of CWV on PEF, over and above that due to increased VI.

Estimates of PEF were also derived for individual children, substituting their age and observed values of VI and force into the analysis. The results are presented along with details of the children's treatments in **section 3.4.9.3**.

3.4.6.3 Summary of the model's value in explaining peak expiratory flow

This model allowed the added effect of CWV forces over and above that due to the increase in VI to be determined. While the extent to which the equations derived from the current population can be extrapolated to other populations of ventilated children or adults has yet to be determined, the underlying principles will be widely applicable. Once these relationships have been established, it is possible to estimate whether the increase in PEF during physiotherapy in any individual during any specific treatment occasion is greater, smaller or similar to that expected in relation to other patients within the population, as demonstrated in **section 3.4.9.3**. These processes have great potential in terms of gathering evidence-based data on the efficacy of different physiotherapy techniques, examples of which are discussed in **section 4.4.3.5**.

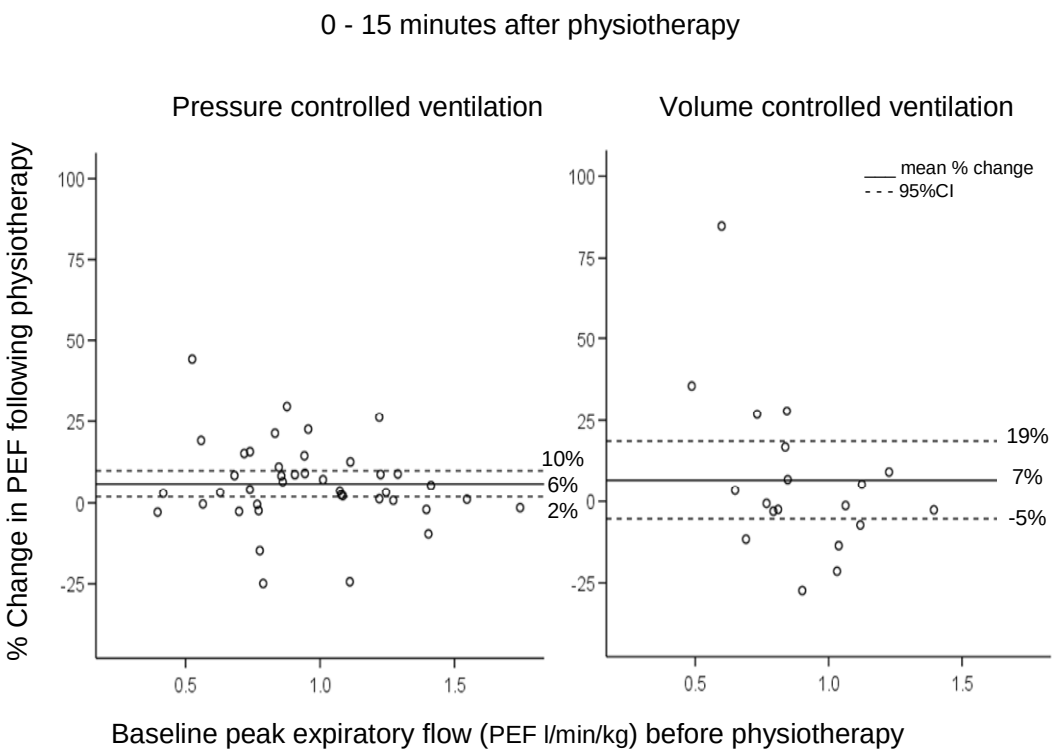
3.4.7 Short-term clinical changes following chest physiotherapy

Three of the 62 treatments monitored had no valid respiratory data before and after physiotherapy; in 2 tracheal leaks exceeded 20% and equipment failed in 1, as shown in **Figure 3.5**. In 45 of the remaining 59 sets monitoring continued for half an hour post-physiotherapy, resulting in data for analysis both at 15 and 30 minutes. Respiratory stability was assessed during baseline monitoring of mechanical ventilation. Peak expiratory flow, expired volume and peak inspiratory pressure were stable, variability reflecting the inclusion of children who were not pharmacologically paralysed (mean [SD] CV 3.1% [2.5%] for PEF, 2.4% [2.2%] for VE and 3.4% [2.3%] for PIP).

3.4.7.1 Peak Expiratory Flow

Figure 3.21 shows the change in PEF following treatment, ranging from an 85% increase to a 27% drop. However, when analysing results from all subjects, there was a significant overall increase within and between subjects following physiotherapy, with a mean increase of 7% (95% CI: 2%, 11%, $p < 0.01$) in the first 15 minutes after treatment, and 6% (95% CI: 1%, 11%, $p < 0.05$), half an hour after treatment. When analysed according to ventilation mode, changes in PEF were only significant in the group receiving pressure-controlled ventilation ($p < 0.05$), as shown in **Figure 3.21**.

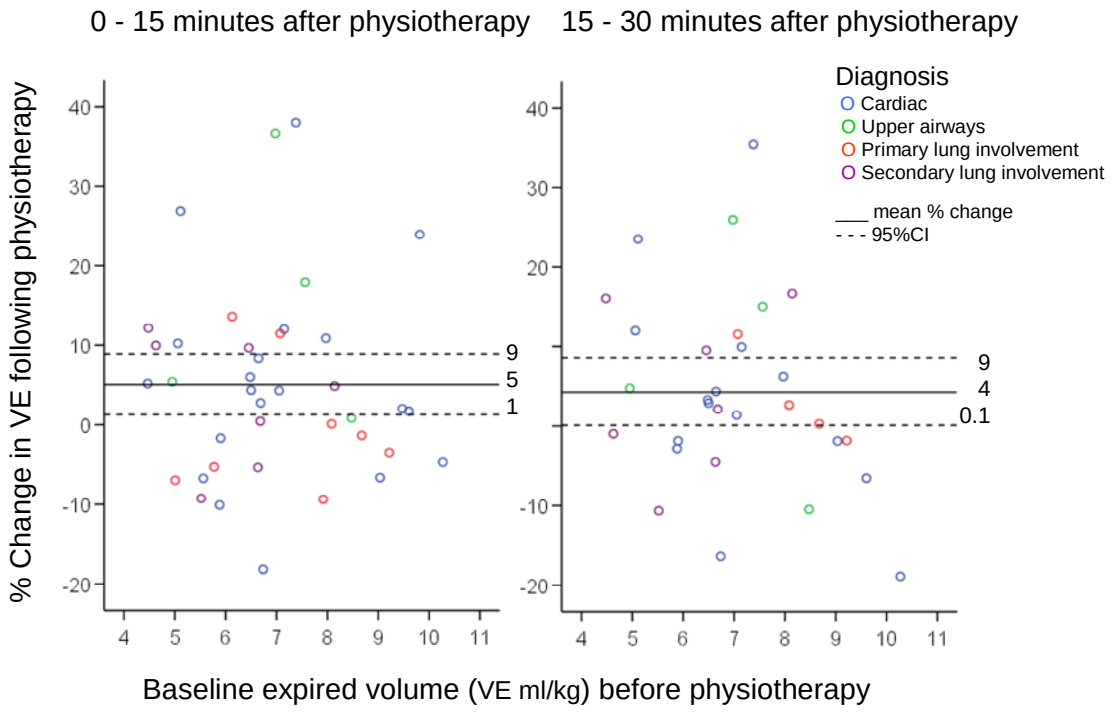
Figure 3.21 Percentage change in peak expiratory flow following physiotherapy compared to baseline ventilation, according to ventilation mode



3.4.7.2 Expired volume

The 17 children who were receiving volume controlled ventilation were not included when analysing the impact of physiotherapy on expired volume. In 32 of the 42 remaining treatments, monitoring continued for half an hour post-physiotherapy, the relevant data periods therefore being available for analyses both at 15 and 30 minutes. **Figure 3.22** shows the significant mean group increase of 5% (95% CI: 1%, 9%) in the first 15 minutes after treatment, and 4% (95% CI: 0.1%, 9%) $p < 0.05$, half an hour after treatment. Again, there was considerable variation in respiratory response, which ranged from -18% to 38% following physiotherapy, the two results at the extremes both being from children with cardiac disease.

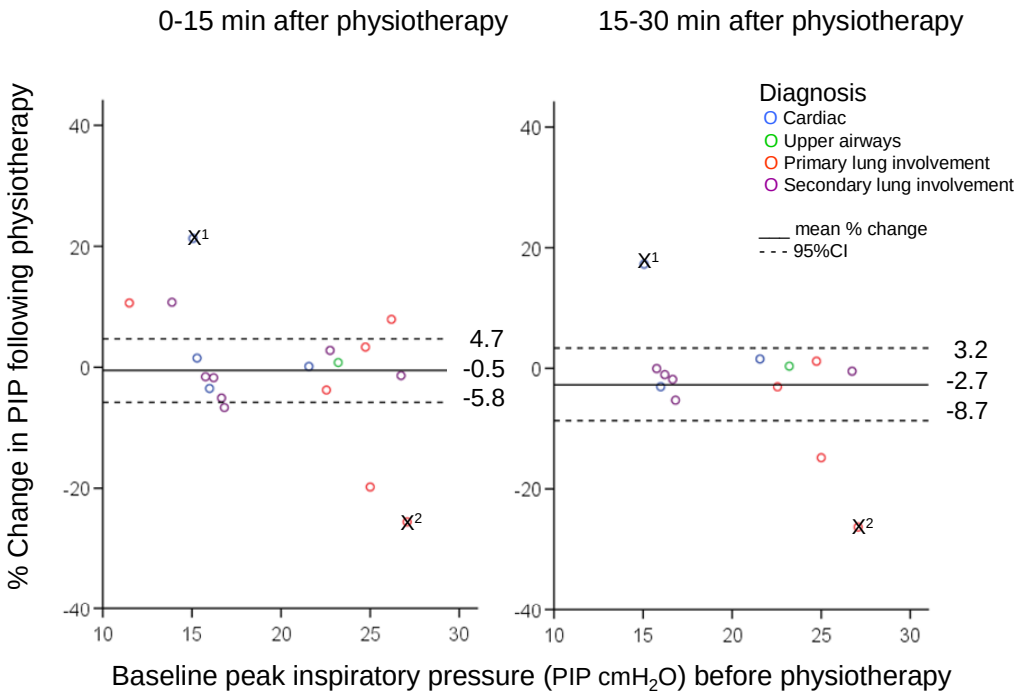
Figure 3.22 Percentage change in expired volume following physiotherapy compared to baseline ventilation, according to diagnosis



3.4.7.3 Peak inflation pressure

The 17 children on volume controlled ventilation demonstrated no overall change in peak inflation pressure during the first or second 15 minute periods of follow-up monitoring, as shown in **Figure 3.23**. The largest change was recorded in a child with asthma who showed an average decrease of 26% in peak inflation pressure during the first 15 minutes, which was maintained half an hour after treatment. By contrast, inflation pressure initially rose by 21% in the first 15 minutes, dropping to 17% in the second period in a child with cardiac failure and pulmonary hypertension.

Figure 3.23 Percentage change in peak inspiratory pressure following physiotherapy compared to baseline ventilation, according to diagnosis



X^1 –cardiac failure; X^2 –asthma

3.4.7.4 Arterial blood gases

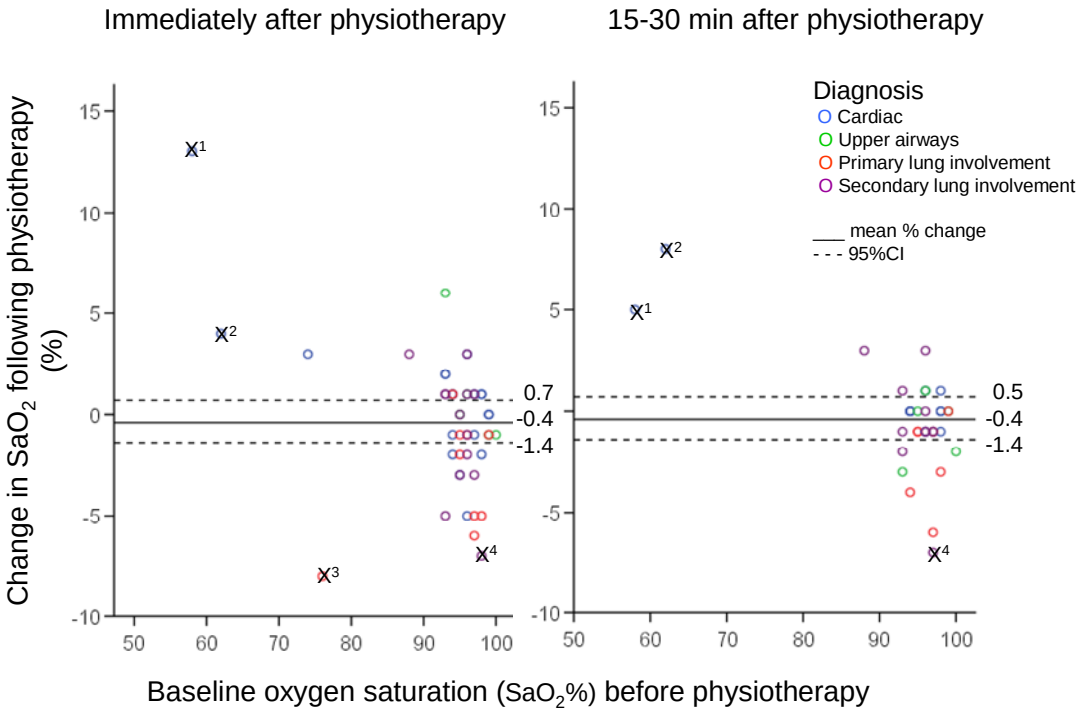
Repeated baseline sampling of arterial blood gases at 15 minute intervals was performed prior to 27 physiotherapy treatments in 25 ventilated children (median age 1.6 years [range 1 m to 13.7 y]). The mean [95% CI] changes in $PaCO_2$ (0.24 kPa [0.02, 0.46 kPa]) suggested a small general increase prior to treatment, which may have related to the

presence of the $CO_2SMO^{®}$ (which increased respiratory deadspace) in the ventilation circuit. No overall group change occurred in PaO_2 or oxygen saturation (0.36 kPa [-0.16, 0.88 kPa] for PaO_2 and -1.1% [-2.84%, 0.62%] for SaO_2). The first blood sample following treatment was taken within the first 5 minutes after physiotherapy ended, further samples being taken between 15 and 30 minutes later in 34 of the 47 treatments with blood samples.

3.4.7.4.1 Oxygen saturation

The majority of children (43 out of 47) had an oxygen saturation > 80% before physiotherapy, whereas the remaining four had extremely low baseline saturations, as shown in **Figure 3.24**.

Figure 3.24 Changes in arterial oxygen saturation following physiotherapy compared to baseline ventilation, according to diagnosis



X^1 – cardiac surgery; X^2 – cardiac disease; X^3 – diaphragmatic hernia; X^4 – head injury

Overall there were no significant changes in arterial oxygen saturation levels following treatment, but considerable variation in response. Both children who showed the largest improvements 15-30 minutes after treatment were cardiac children with initially low saturations. The child with the highest initial increase in oxygen saturation (13%) rose to 72% from a baseline of 58%, dropping 30 minutes later to 63%. The largest immediate

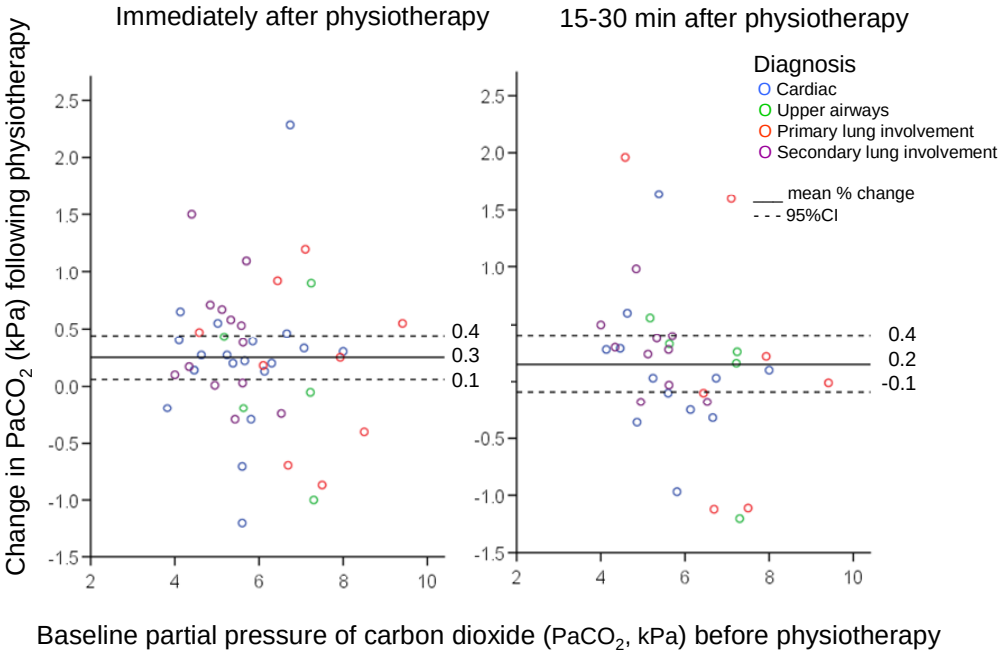
deterioration in oxygen saturation occurred in a child following repair of a diaphragmatic hernia in whom arterial saturation fell from 76% to 68%. Whilst the majority of children with head injuries improved or maintained their oxygen saturation, one child with head injury and secretion retention showed a drop of 7% to 90% immediately after treatment, which remained when sampled 15 minutes later.

The two treatments which resulted in the largest improvements and deteriorations in arterial saturation on final measurements after physiotherapy are presented and discussed in **section 3.4.9.4**.

3.4.7.4.2 Partial pressures of carbon dioxide

A wide range of values was observed both in the baseline partial pressures of oxygen and carbon dioxide and in the response following treatment (**Figure 3.25** and **Figure 3.26**). Group analysis of $PaCO_2$ showed an initial short-lived rise (mean [95% CI] rise 0.25 kPa [0.06, 0.43 kPa], $p < 0.05$) immediately after treatment, which resolved within 15 minutes (0.2 kPa [-0.1, 0.4 kPa]).

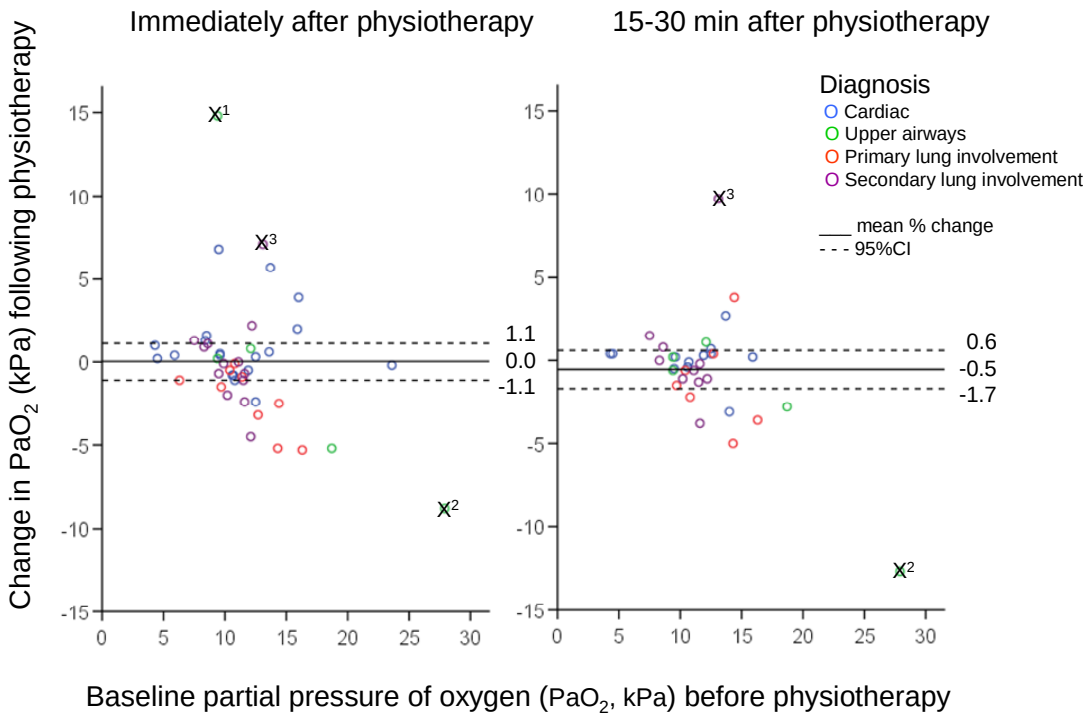
Figure 3.25 Changes in partial pressure of carbon dioxide following physiotherapy compared to baseline ventilation, according to diagnosis



3.4.7.4.3 Partial pressures of oxygen

Analysis of PaO_2 showed no significant group changes over the 30 minutes of sampling (**Figure 3.26**), but marked changes in some individuals. Again, children who had had repair of tracheal stenosis showed the largest changes in PaO_2 immediately after treatment, these changes occurring in both directions. As can be seen from the figure, the child with tracheal stenosis who showed the most marked deterioration had unusually high baseline partial pressures prior to treatment. A child with head injury and secondary lung involvement showed the greatest overall improvement.

Figure 3.26 Changes in partial pressure of oxygen following physiotherapy compared to baseline ventilation, according to diagnosis



X^1 – tracheal stenosis (in whom measurement ceased after 15 minutes). X^2 – tracheal stenosis; X^3 – head injury and secondary lung involvement;

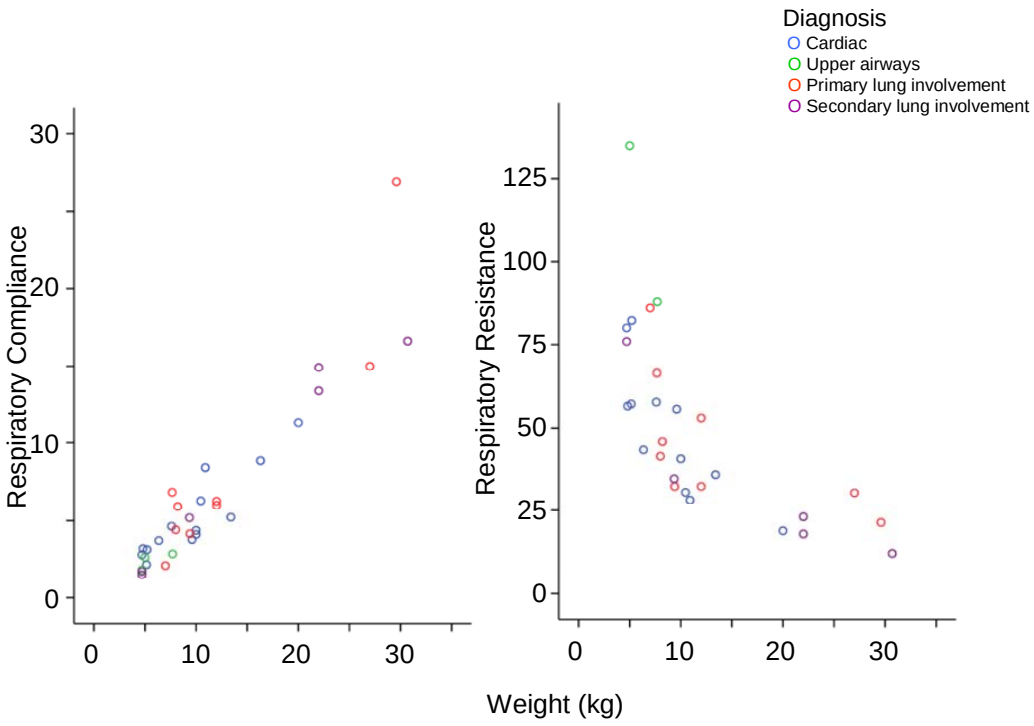
3.4.7.5 Respiratory mechanics

3.4.7.5.1 Baseline stability and the effect of growth changes on respiratory mechanics

Respiratory mechanics data were collected in 29 pharmacologically paralysed children (median age 18 months [range 1 week to 9 y]), 3 of whom received two treatments each, resulting in 32 data sets. Recordings of 15 minute epochs of respiratory variables in the paralysed, fully ventilated children were reproducible, with mean (SD) CV for respiratory compliance of 3.3 % (3%) and 2.9% (2.6%) for resistance.

Baseline mechanical ventilation data showed respiratory compliance was proportional to weight (Spearman's correlation coefficient, $r = 0.8$, $p < 0.001$), as shown in **Figure 3.27**. Respiratory compliance was therefore expressed per kg body weight to compare the relative magnitude of changes between children of different ages and underlying pathology. Weight-corrected compliance was highest in a 9 year old with asthma. This surprising result may have been due to an underestimation of alveolar pressure by the measurement of pressure at the airway opening, due to the child's long time constant and poor pressure equilibration (Gappa et al. 2001). Respiratory resistance showed an inverse curvilinear relationship weight ($r = - 0.8$, $p < 0.001$). Baseline resistance was highest in a 3 month baby following repair of tracheal stenosis.

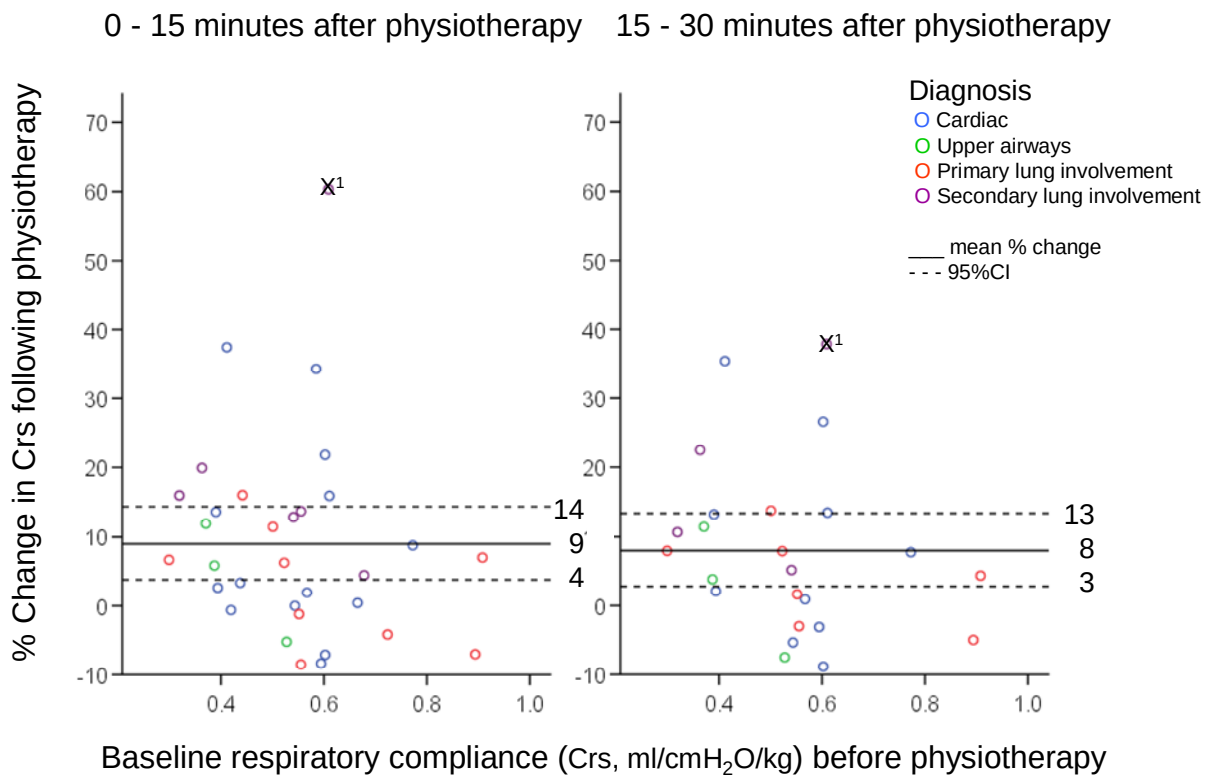
Figure 3.27 Relationship of respiratory compliance (ml/cmH_20) and resistance (cmH_20/l/s) to weight during baseline ventilation, according to the child's diagnosis



3.4.7.5.2 Respiratory compliance

Following physiotherapy, compliance increased significantly from baseline by an average of 9% (95% CI: 4%, 14%) in the first 15 minutes after treatment and 8% (95% CI: 3%, 13%) thereafter, as shown in **Figure 3.28** and confirmed with repeated measures ANOVA ($p < 0.01$). Although the mechanics data did not meet the assumptions for normality, after appropriate adjustments (Greenhouse-Geisser and Huyn-Feldt tests) the observed differences for compliance remained significant. The largest improvement (60% at 15 minutes, 38% at 30 minutes) was in a child with head injury, who had secretion retention. This child's treatment will be discussed in more detail in **section 3.4.9.4**. The other two children who demonstrated marked increases in respiratory compliance (> 30%) had had cardiac surgery; treatment effects were maintained during the short period of monitoring after treatment.

Figure 3.28 Percentage change in respiratory compliance following physiotherapy compared to baseline ventilation, according to diagnosis



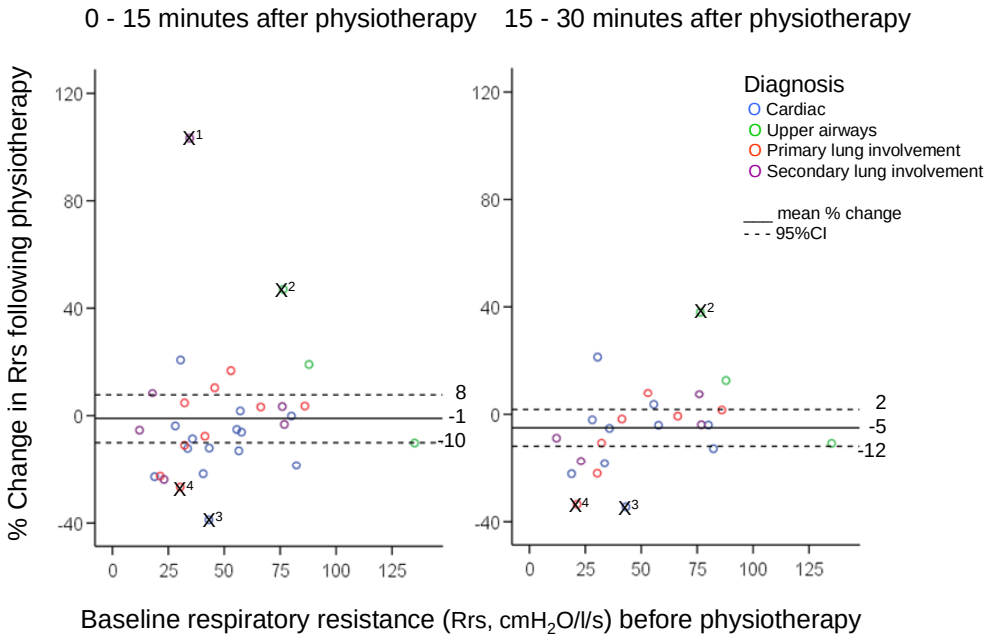
X^1 – head injury and secretion retention

Percentage change in compliance correlated with percentage change in PEF following physiotherapy ($r = 0.47$, $p < 0.01$).

3.4.7.5.3 Respiratory resistance

Overall, there was no significant difference in respiratory resistance in the half hour following treatment, as shown in **Figure 3.29**. However, within individual children, some potentially clinically significant changes occurred, including a 1.5 year old with fibromuscular hyperplasia and oesophageal resection in whom a doubling of resistance occurred immediately following treatment (103%). A rise of more than 40% occurred in a 1 year old who had had repair of tracheal stenosis (discussed in section **3.4.9.7**). By contrast, resistance dropped by 40% in a child post-cardiac surgery and in an asthmatic.

Figure 3.29 Percentage change in respiratory resistance following physiotherapy compared to baseline ventilation, according to diagnosis



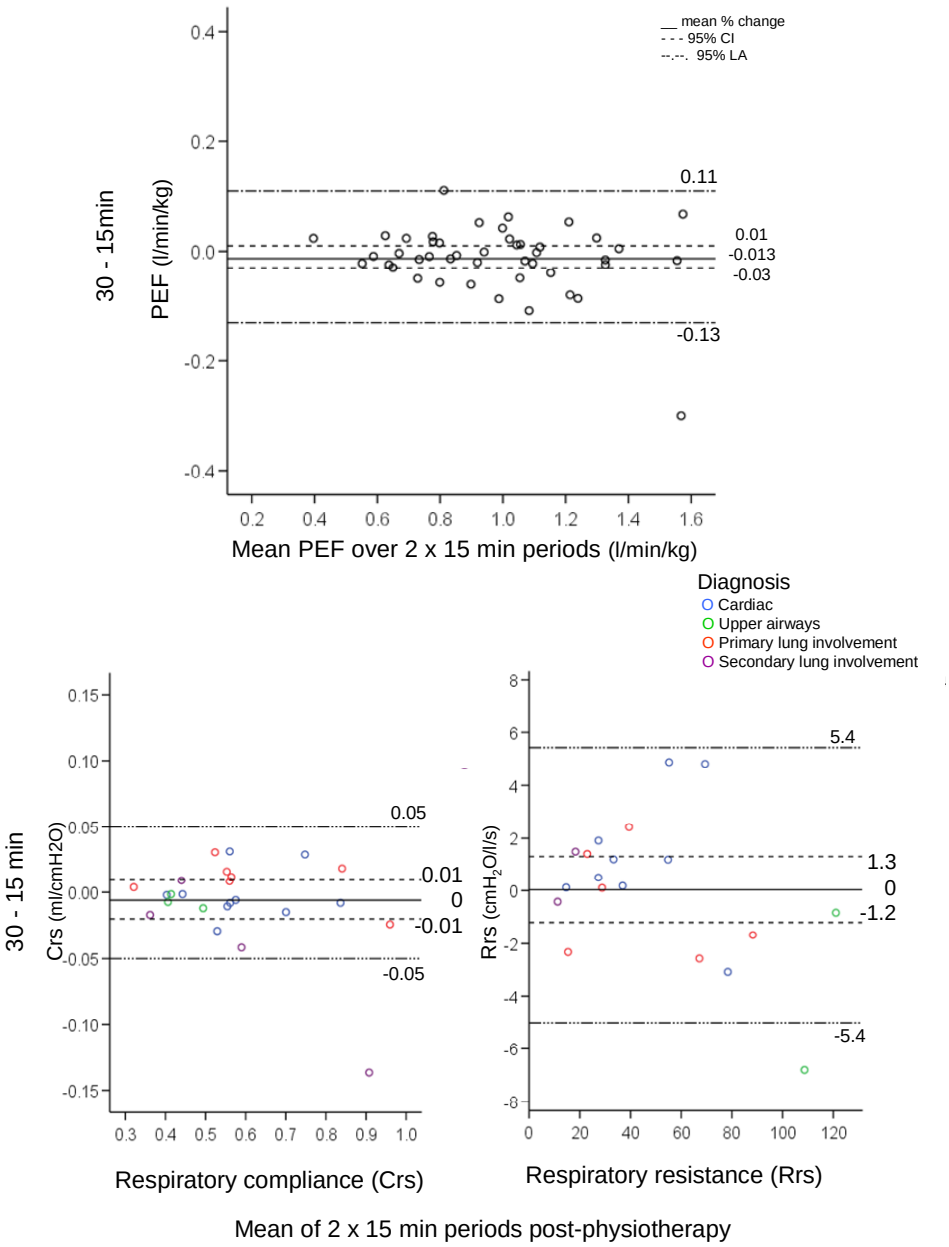
X^1 – fibromuscular hyperplasia and oesophageal resection; X^2 – tracheal stenosis; X^3 – cardiac surgery; X^4 – asthma

In summary, analysis of the group showed that there was a general improvement in respiratory compliance, expired volume and PEF following physiotherapy, with no overall deterioration in oxygen saturation but a transient hypercapnia immediately following treatment. There was no significant group change in respiratory resistance. The wide variation in results may be related to the child's underlying diagnosis or to the individual therapist's treatment style, as will be discussed in **section 3.4.9**.

3.4.7.6 Comparison of measurements recorded after treatment

The data obtained in the first and second 15 minute periods after treatment were compared, to discover whether changes recorded in the first 15 minutes were representative of the changes that occurred half an hour after physiotherapy. The graphs in **Figure 3.30** show the difference between data obtained over the two measurement periods (30 min – 15 min) plotted against the mean of the two values, for PEF, respiratory compliance and resistance. In the majority of cases, the changes recorded in the first 15 minutes were representative of the changes half an hour after treatment. Similar graphs were obtained for expired volume and peak inflation pressure.

Figure 3.30 Relationship between values recorded 15 and 30 minutes after physiotherapy, for PEF, respiratory compliance and resistance



3.4.8 Relationship of change in PEF during physiotherapy to short-term outcomes

Table 3.7 shows the relationship of change from baseline in PEF during physiotherapy and change in respiratory mechanics and PEF in the first fifteen minutes after treatment. Change in PEF during physiotherapy was poorly correlated with both change in PEF and respiratory resistance following treatment. There was no significant correlation between change in PEF during CWV and change in respiratory compliance after treatment, but there was between the change in PEF during manual inflations, as shown in **Figure 3.31**. Peak expiratory flow increased during CWV in all children who showed an increase in respiratory compliance following physiotherapy. However, there was a wide variation in response with, for example, a doubling of PEF during CWV being associated with changes in respiratory compliance that ranged from a decrease of 3% to an increase of 60%.

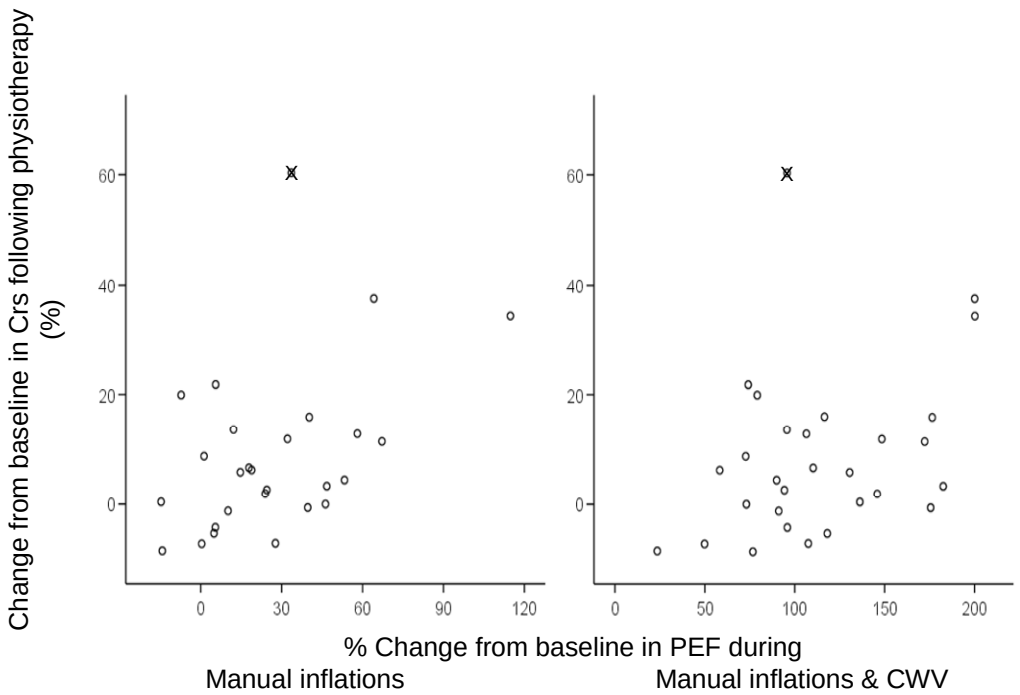
Table 3.7 Relationship of change in short-term outcomes following treatment with change in PEF during chest physiotherapy

% change following physiotherapy	Number of treatments	Correlation with % change from baseline in PEF during:	
		Minf	Minf & CWV
PEF	55	0.20	0.20
Crs	29	0.48**	0.32
Rrs	29	-0.03	-0.22

Minf – manual inflations ; CWV – chest wall vibrations

Spearman's correlation coefficient, r
** $p < 0.01$

Figure 3.31 Relationship of percentage change in PEF during physiotherapy to percentage change in respiratory compliance following treatment



X – child with head injury (child H.I. in **section 3.4.9.4**)

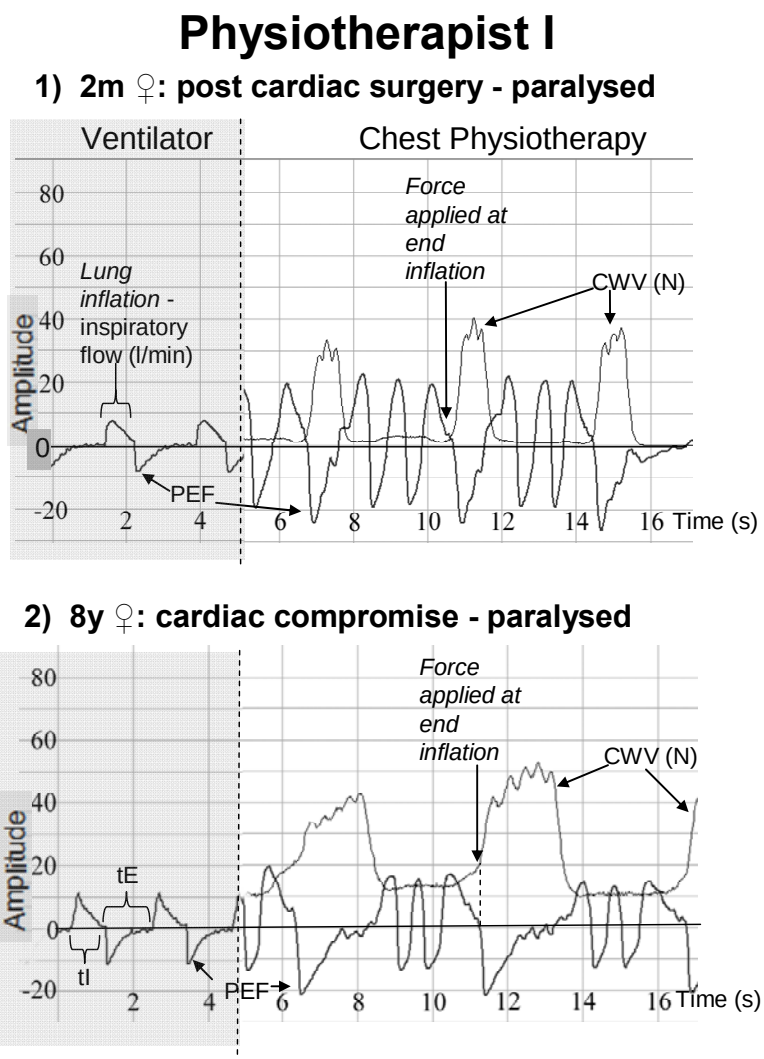
Figure 3.31 shows a clear outlier in whom a 60% increase in compliance was associated with only a moderate increase in PEF during manual inflations with and without CWV. The treatment of this child with head injury is discussed in detail in **section 3.4.9.4**. When the outlying value was excluded from analysis there was a higher correlation of change in compliance with change in PEF (Pearson's correlation $r = 0.59$, $p = 0.001$ during manual inflations and $r = 0.5$, $p < 0.01$ during CWV).

The general lack of a direct relationship between change in PEF during treatment and the outcome measures shown in **Table 3.7** may reflect the heterogeneity of the children's underlying pathophysiology and the combined influence of multiple physiotherapy treatment variables on outcome. This aspect is explored in the following section (**section 3.4.9**, containing individual treatment examples) and discussed in **section 4.4.4**.

3.4.9 Evaluation of physiotherapy treatments for individual children

Just as CWV profiles varied between physiotherapists and children, so did the resultant effects on PEF. **Figure 3.32** and **Figure 3.33** show CWV force profiles and corresponding respiratory flow traces obtained from 2 physiotherapists, each treating 2 children of varying ages and with different underlying pathology.

Figure 3.32 Profiles from physiotherapist I, treating two children of varying diagnoses and ages

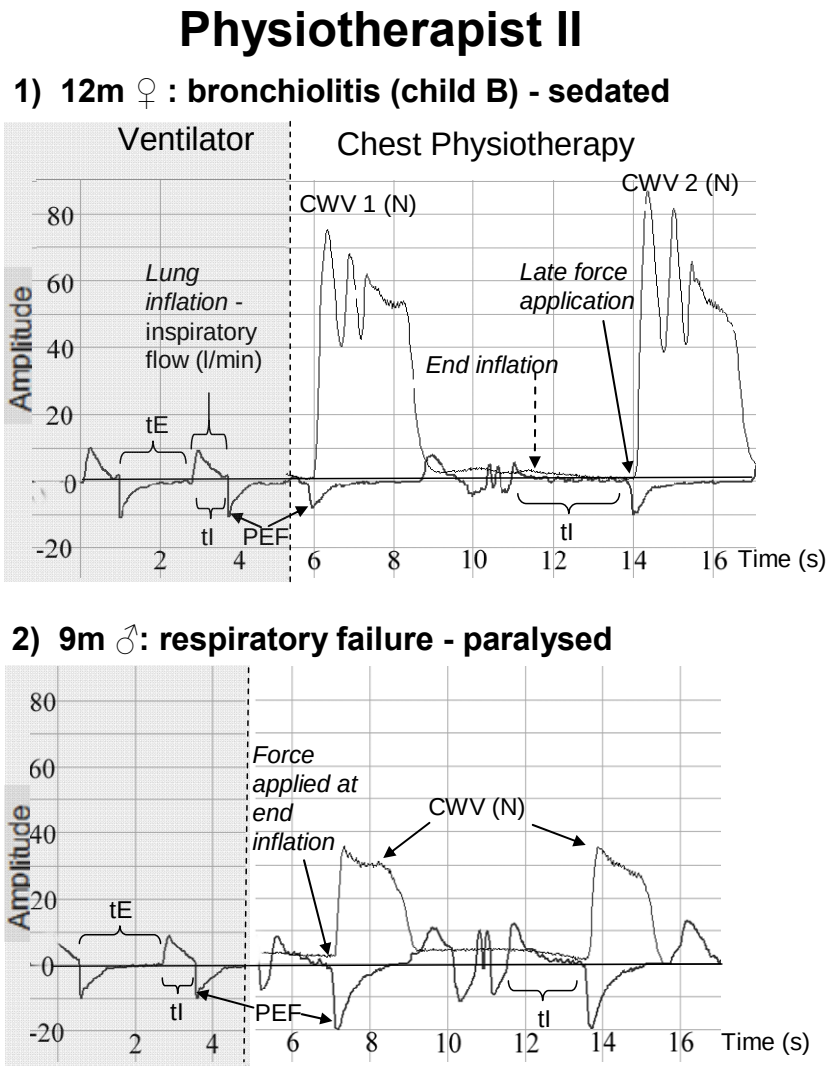


Physiotherapist 1 was the clinical specialist, whose treatments are discussed in **section 3.4.9.7**.
Please note: the chest physiotherapy data do not continue directly in time from the ventilator data.

With respect to the outline shape of the CWV profile, Physiotherapist I displayed a consistent pattern, within and between the children. The CWV forces were co-ordinated to begin at end inflation and in both children PEF was consistently increased from baseline

during CWV. A series of manual lung inflations (not shown) were consistently delivered at the end of this physiotherapist's treatments, prior to reconnecting the child to the mechanical ventilator.

Figure 3.33 Profiles from physiotherapist II, treating two children of varying diagnoses and ages



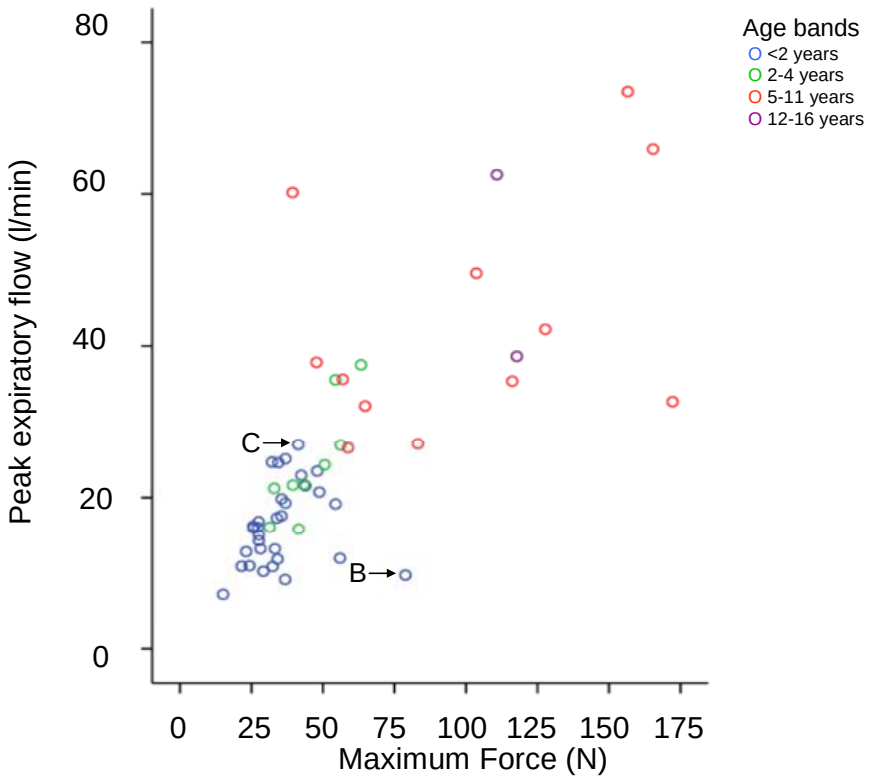
Please note: the chest physiotherapy data do not continue directly in time from the ventilator data.

Physiotherapist II delivered initial large amplitude oscillations in the 12 month baby with bronchiolitis (child B, profile 1) which were not observed during treatment of the 9 month baby (profile 2). In the latter treatment, there was an increase in PEF with delivery of CWV, despite a relatively small application of force. By contrast, the relatively large force applied by physiotherapist II to child B was not accompanied by any corresponding

increase in PEF. There appeared to be a problem with timing the second force application (labelled CWV 2) in child B. The force was applied after a prolonged inspiratory time (tI) during which minimal flow occurred. This overlaid force-flow profile suggests the child's treatment may have been more problematic than the other treatments shown, which may relate to this child's underlying diagnosis of bronchiolitis, widespread inflammation and right upper lobe collapse.

Individual treatments from children labelled C (cardiac bypass) and B (bronchiolitis) are presented to explore in more depth the relationship between force and flow. Changes in outcome following their treatments are then presented in **section 3.4.9.4**. The two children labelled C and B were aged below 2 years and were selected to provide examples of contrasting treatment effects (**Figure 3.34)**. In child C the force and respiratory data were representative of the general physiotherapy treatment trend and response. This child was additionally chosen because the treatment was recorded visually (random selection) to supplement the study descriptions contained in the thesis. Child B (shown in **Figure 3.33** and highlighted earlier in **Figure 3.20**) was treated with an unusually high force with little corresponding increase in PEF.

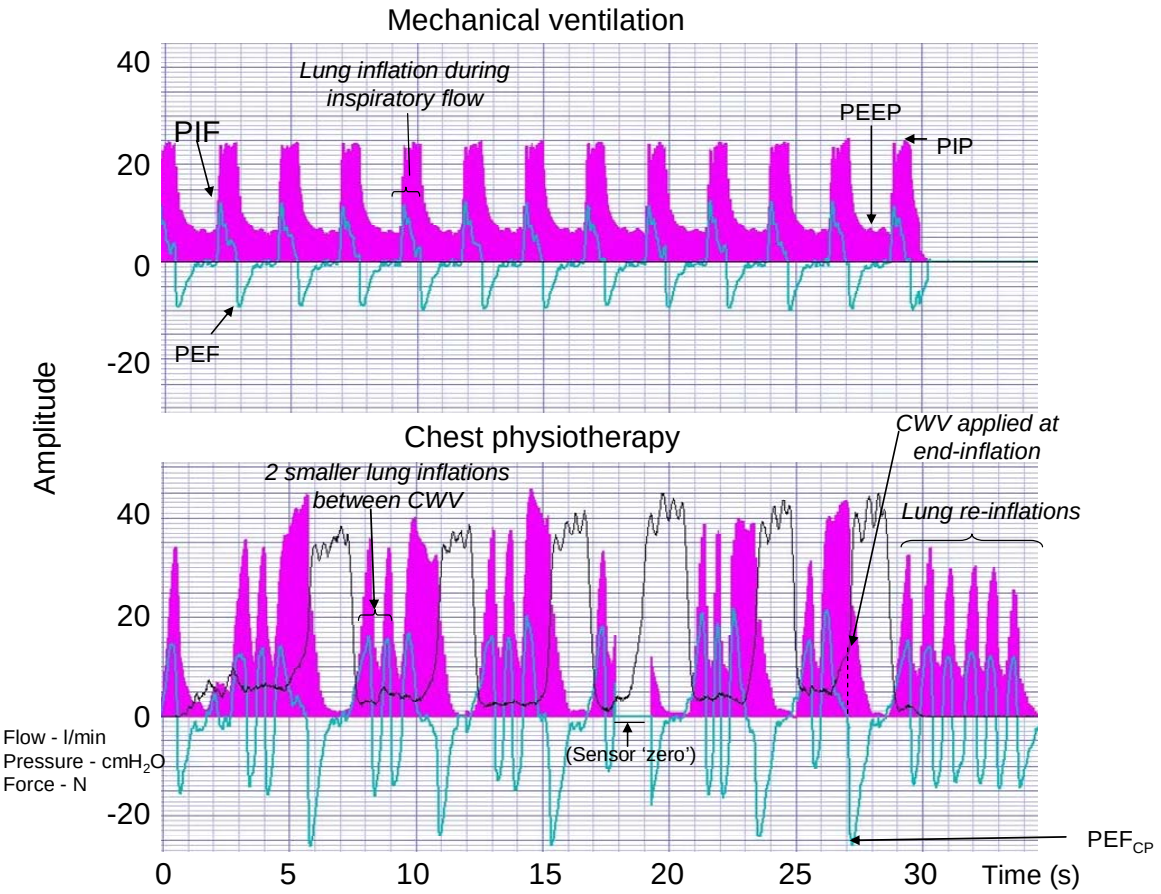
Figure 3.34 Examples of a representative treatment (child C) and an unusual pattern of force and PEF (child B), both aged under 2 years



3.4.9.1 Treatment of a paralysed baby on cardiac bypass

In child C, PEF increased 3-fold (i.e. 200%) to 27 l/min during the manual inflations with CWV compared to that during baseline mechanical ventilation, as shown in **Figure 3.35** and **Figure 3.36**. Peak inspiratory pressure increased from 25 cmH_2O during mechanical ventilation to in excess of 40 cmH_2O during CWV (**Figure 3.35** and **Table 3.8**). The smaller lung inflations interspersed between the inflations for CWV were delivered at least double the rate of mechanical ventilation, PEEP being maintained during these breaths (but not during the vibration forces), as shown in **Figure 3.35**. This figure also shows that CWV were followed by a series of lung inflations to re-recruit collapsed lung tissue. Other important treatment features included the co-ordinated application of force towards end-inspiration (**Figure 3.35**) and the delivery of a large inflation volume preceding the CWV (**Figure 3.36**).

Figure 3.35 Baseline ventilation and treatment of the paralysed child C, on cardiac bypass



PEF_{CP} – peak expiratory flow during chest physiotherapy (CWV & Minf)

Figure 3.36 Relationship of peak expiratory flow to inspired volumes and pressures before, during and after chest physiotherapy in child C

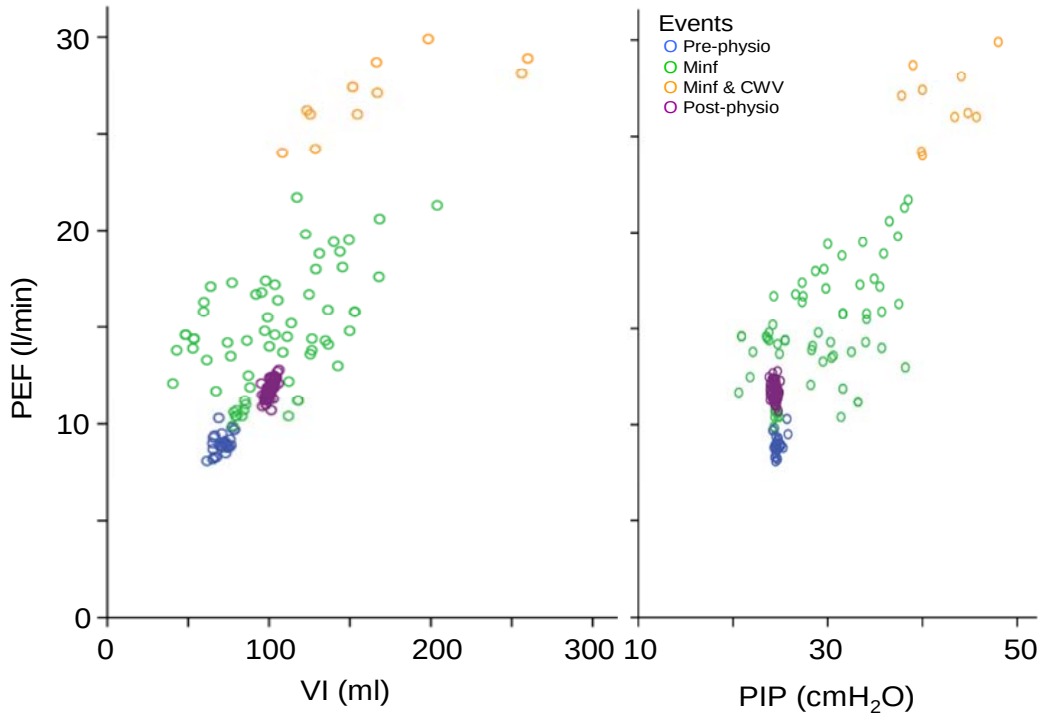


Table 3.8 Summary of child C's clinical details, ventilation and force application during mechanical ventilation and CWV

Child C: 8 m, paralysed, cardiomyopathy. 10 days on ECMO; 1 day post-op, on cardiac bypass (Berlin Heart): on pressure controlled ventilation **OI-2.75, PRISM-6**
Treatment duration : 5 min
Saline : 0.2ml/kg
1 chest compression during suction: Fmax 47 N, 2s

	VI ml/kg	PIP cmH_2O	PEEP cmH_2O	PEF l/min/kg	PIF l/min/kg	PEF:PIF	RR / min	Fmax N	Fmean N
Baseline	7.1	25	6	0.9	1.2	0.8	25	-	-
CWV	16.7	42	1.2	2.7	1.9	1.4	40	41	26
% change	135	71	-80	200	66	----[1]	60	-	-

Mean values presented. [1]Only absolute PEF:PIF ratio is relevant.
ECMO – extra-corporeal membrane oxygenation, OI - oxygenation index; PRISM - paediatric risk of mortality (see **section 3.4.1.1**)

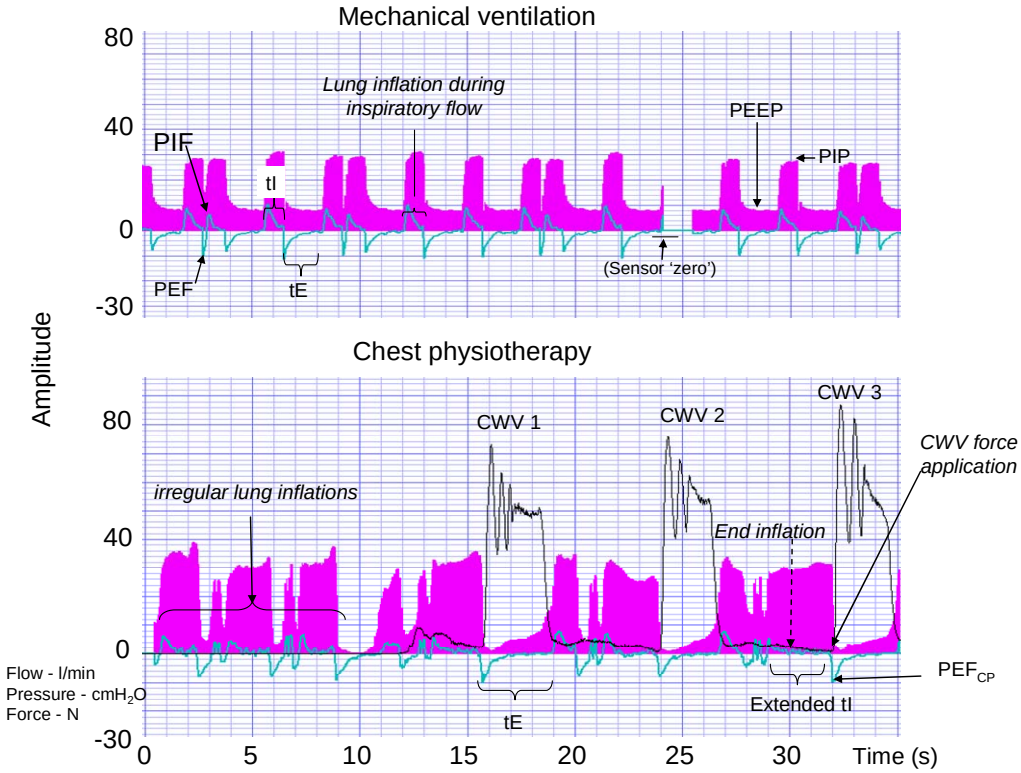
Figure 3.36 shows the increase in inflation volume immediately after treatment, suggesting recruitment of collapsed areas of the lung. This was further suggested by a 36% increase in respiratory compliance compared with pre-treatment levels, as discussed in **section 3.4.9.4**. This meant that a larger inflation volume could be delivered using the same PIP that was delivered prior to therapy. The resulting increased expired volume (36%) was accompanied by an increased PEF (19%). There was a parallel drop in respiratory resistance (-34%), the immediate improvements in respiratory mechanics

continuing during the 30 minute period of monitoring. Both PaO_2 and $PaCO_2$ were minimally changed (plus and minus 1%, respectively) from baseline 30 minutes after treatment. This is likely to be accounted for by the baby's high initial arterial saturation of 98%, which was maintained and rose briefly by 1% following treatment. It was noted that the PEF:PIF ratio during baseline mechanical ventilation was 0.8, creating an inspiratory bias of airflow which would potentially promote retrograde flow of mucus deeper into the lungs, as discussed in **section 1.6.2**.

3.4.9.2 Treatment of a sedated baby with bronchiolitis

By contrast, inspiratory and expiratory flows were reduced compared to mechanical ventilation levels during CWV in child B's treatment, as shown in **Figure 3.37** and **Table 3.9**. Lung inflations were erratic and although some large breaths were delivered to this baby during CWV the majority were small and insufficient time was given for expiration during lung inflations (**Figure 3.38)**.

Figure 3.37 Baseline ventilation and treatment of the sedated child B, with bronchiolitis



PEF_{CP} – peak expiratory flow during chest physiotherapy (CWV & Minf)

During CWV inspiratory time was frequently extended (median 1.5s, range 0.5 to 3s), but no additional air entered the lungs, suggesting the lungs were fully inflated early during the inspiratory phase. This was particularly apparent in the prolonged inspiratory breath before the final chest compression (CWV 3) in **Figure 3.37**, where inspiratory flow was virtually zero. In addition, expiratory flow had ceased during a large part of the expiratory time (tE) over the 3 second period while the forces were still being applied.

Figure 3.38 Relationship of peak expiratory flow to inspired volumes and pressures before, during and after chest physiotherapy in child B

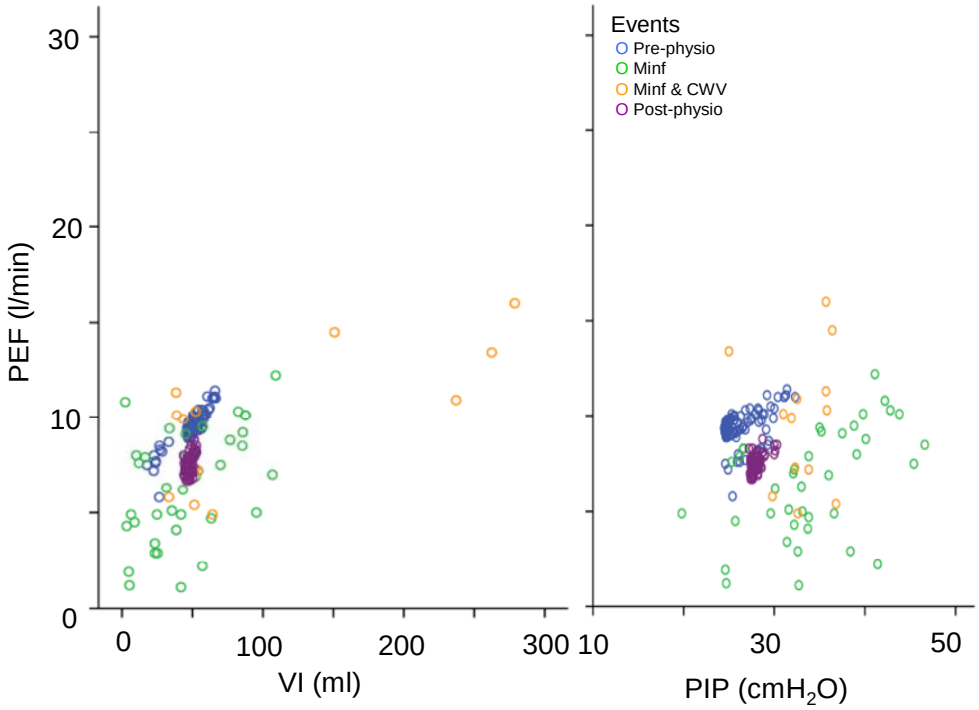


Table 3.9 Summary of child B's clinical details, ventilation and force application during mechanical ventilation and CWV

Child B: 12 m, sedated, bronchiolitis & right upper lobe collapse; 1 day since acute onset; volume controlled ventilation OI-13.6, PRISM-11
Treatment duration : 9 min
Saline : 0.4 ml/kg
4 chest compressions during suction (median Fmax 87 N; 3.9s), 4 decompressions (median Fmax 62 N; 6s)

	VI ml/kg	PIP cmH_2O	PEEP cmH_2O	PEF l/min/kg	PIF l/min/kg	PEF:PIF	RR / min	Fmax	Fmean N
Baseline	5.4	25	8	1.1	0.9	1.1	24	-	-
CWV	5.8	33	5	1.1	0.8	1.4	27	79	45
% change	7	32	-38	0	-11	----[1]	13	-	-

Median values presented. [1]Only absolute PEF:PIF ratio is relevant
OI - oxygenation index; PRISM - paediatric risk of mortality (see **section 3.4.1.1**)

Removing the child from the ventilator reduced the PEEP maintained during inflations with and without CWV. Whilst PIP showed an average increase of 32% above baseline levels during CWV, there was wide variation (**Figure 3.38**). Inflation volumes during CWV ranged from 33 to 278 ml, the median volume of 52 ml equating with that delivered during mechanical ventilation (49 ml). Despite the use of high CWV forces (80 N) there was minimal increase in PEF, contrasting sharply with child C's response to CWV, in whom far

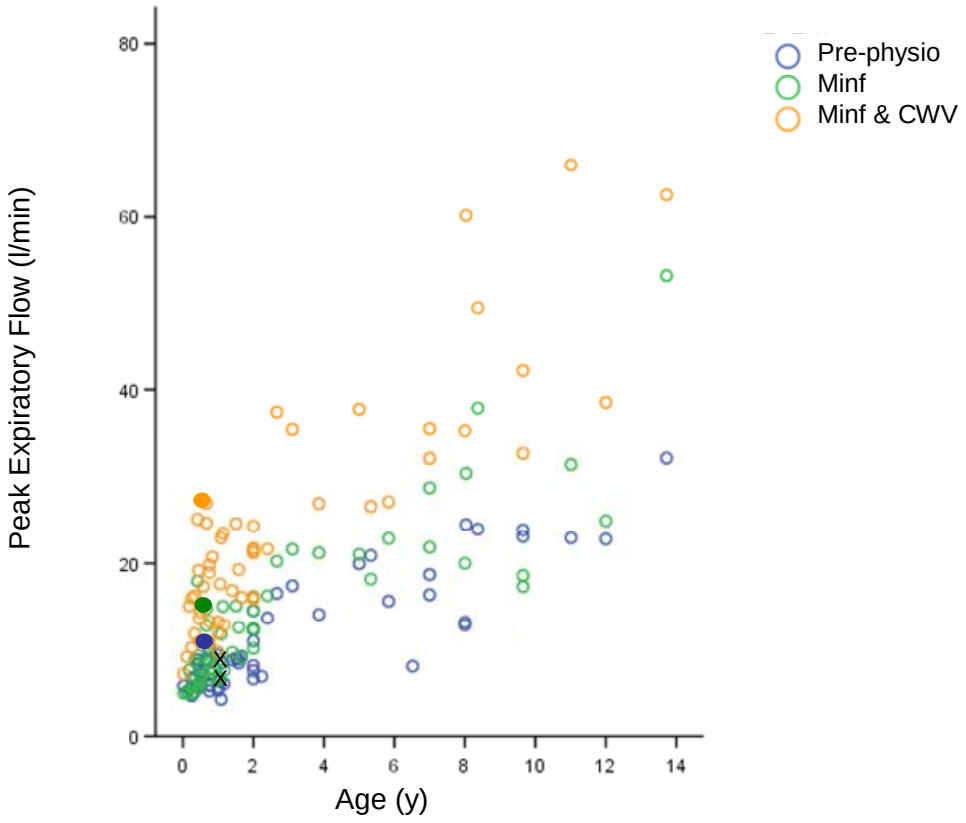
lower forces were applied. Child B also received chest compressions during suction and chest decompressions (**Table 3.9**), the longer, sustained decompression forces being used to reduce hyperinflation within the lungs.

These data are consistent with the presence of widespread airways obstruction and lung hyperinflation, as suggested by the overlaid force-respiratory profiles (**Figure 3.37**). Furthermore, there was a general fall in PEF following treatment despite a tendency for raised PIP in this infant. Although this child was on volume controlled ventilation, expired volume dropped by 5% following treatment (**Table 3.14**, section **3.4.9.4**). Arterial blood gases were unavailable on child B and respiratory mechanics data were invalid as the child was making spontaneous respiratory efforts. However, transcutaneous oxygen saturation dropped from 96% pre-treatment to 90% in the 15 minutes of monitoring following physiotherapy.

3.4.9.3 Quantification of treatment effects within individual children

Estimates of PEF were derived for these individuals. The data were analysed using the equations derived in section **3.4.6.2** to predict PEF according to age, inflation volume and CWV force. These values were compared with those observed during the treatment in **Figure 3.39**.

Figure 3.39 Peak expiratory flow before and during physiotherapy according to age



Markers: X – child B (bronchiolitis); solid circles - child C (cardiac), during the three measurement conditions. Only 2 crosses are visible for child B because the markers are overlaid for values recorded pre-physiotherapy and during manual inflations with CWV.

3.4.9.3.1 Analysis of PEF based on the child's aggregate data

Validation of the group equations using data from child C: an 8 month (0.67 y) infant weighing 10 kg, in whom VI was 7 ml/kg during baseline mechanical ventilation, rising to 10 ml/kg during manual inflations and 17 ml/kg in the breaths immediately prior to application of CWV (Fmax 41 N).

Full calculations for the values shown in **Table 3.10** are contained in **Appendix D.3**.

Table 3.10 Comparison of predicted PEF with observed values in child C

	PEF (l/min)	
	Observed	**Predicted**
10 Baseline ventilation at 7ml/kg	9	11
2) PEF_{Minf} at 10 ml/kg VI	15	13
3) PEF_{Minf} at 17 ml/kg VI	NA[1]	17
4) PEF_{CP} at 17 ml/kg VI & CWV 41 N	27	21
5) 'Added value' of 41 N CWV on PEF	*111%*	

[1] no breaths were observed with a VI of this magnitude in the absence of CWV, this value being included simply to match (and calculate the effect of) the VI delivered prior to CWV forces

- The predicted PEF during chest physiotherapy (21 l/min) was less than that recorded during the study, this child's response to treatment appearing to exceed the group average.

Validation of the group equations using data from child B: a 12 month (1 y) infant weighing 9 kg, in whom median VI was 5.4 ml/kg during baseline mechanical ventilation, falling to 4.8 ml/kg during manual inflations, and 5.7 ml/kg in the breaths immediately prior to application of CWV (Fmax 79 N).

Full calculations for the values shown in **Table 3.11** are contained in **Appendix D.3**.

Table 3.11 Comparison of predicted PEF with observed values in child B

	PEF (l/min)	
	Observed	**Predicted**
1) Baseline ventilation at 5.4 ml/kg	9.4	9.3
2) PEF_{Minf} at 4.8 ml/kg VI	7.1	9.0
3) PEF_{Minf} at 5.7 ml/kg VI	NA[1]	9.5
4) PEF_{CP} at 5.7 ml/kg VI & 79 N CWV	9.9	15.6
5) 'Added value' of 79 N CWV on PEF	*4%*	

[1] no breaths were observed with a VI of this magnitude in the absence of CWV, this value being included simply to match (and calculate the effect of) the VI delivered prior to CWV forces

- The calculations summarised in **Table 3.11** confirm that during physiotherapy PEF consistently fell below predicted values, the 79 N force having no additional impact over the flow expected from the inflation volume alone (9.5 l/min). The predicted values were themselves considerably lower than those calculated for child C (**Table 3.10**), due to the small inflation volumes delivered.

3.4.9.3.2 Analysis of PEF based on the child's complete data set

The *complete* data sets based on all individual breaths (rather than the aggregate values) from child C and child B were then independently analysed to determine the effects of physiotherapy on PEF within each child. Full details of the resulting equations and calculations are included in **Appendix D.3**. When analysing data within children to establish the relationship between PEF, VI, and force, age will be constant and can therefore be excluded from the model.

Table 3.12 Comparison of predicted PEF with observed values in child C, using the *complete* data set

	PEF (l/min)	
	Observed	**Predicted**
Baseline ventilation at 70ml	9	11
a) PEF_{Minf} at 100 ml VI	15	14
b) PEF_{Minf} at 170 ml VI	NA[1]	19
c) PEF_{CP} at 170 ml VI & 41 N CWV	27	27

[1] no breaths were observed with a VI of this magnitude in the absence of CWV, this value being included simply to match (and calculate the effect of) the VI delivered prior to CWV forces

- In child C, VI was significantly related to PEF during all measurement conditions ($p < 0.001$)
- In this child, there was a 200% increase in PEF during physiotherapy when compared to baseline (**Table 3.12**), of which 8 l/min (27-19) could be directly attributed to the effect of CWV after adjusting for the increase in VI (i.e. approximately 2 l/min for every 10 N CWV)
- The 'added value' of CWV in increasing PEF was thus 8 / 9 = 89% in this child

Table 3.13 Comparison of predicted PEF with observed values in child B, using the *complete* data set

	PEF (l/min)	
	Observed	**Predicted**
Baseline ventilation at 49 ml	9.4	8.8
a) PEF_{Minf} at 43 ml VI	7.1	8.5
b) PEF_{Minf} at 51 ml VI	NA[1]	8.9
c) PEF_{CP} at 51 ml VI & 79 N CWV	9.9	†

[1] no breaths were observed with a VI of this magnitude in the absence of CWV, this value being included simply to match (and calculate the effect of) the VI delivered prior to CWV forces.
† cannot be calculated as force did not contribute significantly to PEF

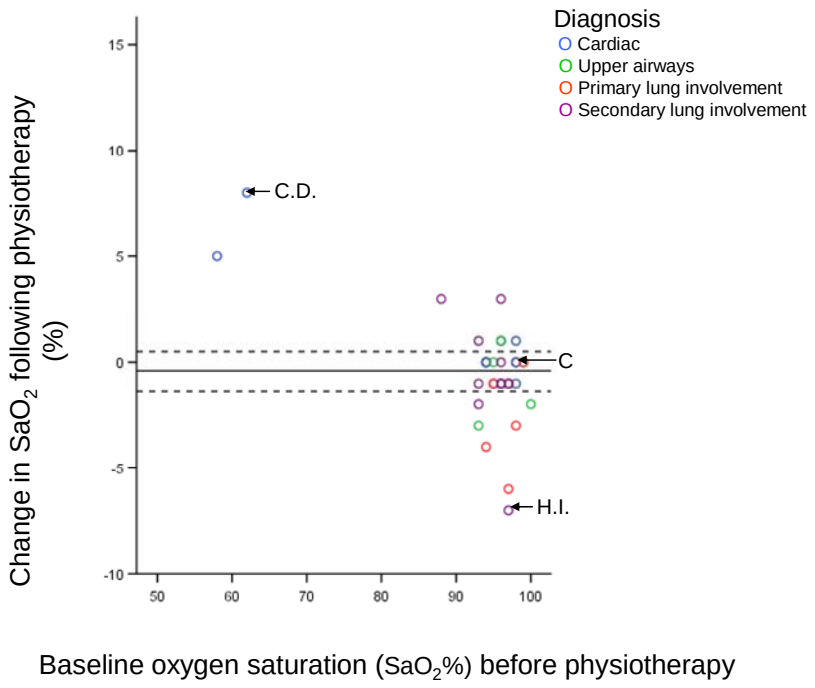
- **Table 3.13** shows that in contrast to child C, the derived equations for child B confirmed the observation from the time-based plot and graph of PEF versus VI (**Figure 3.37** and **Figure 3.38**) that CWV did not significantly increase PEF ($p = 0.81$). Indeed the 79 N CWV only succeeded in returning PEF to baseline ventilation levels.

In summary, the calculations based on the child's entire respiratory data set confirmed the considerable increase in PEF resulting from the CWV forces in the cardiac child C, over and above that accounted for by the accompanying increase in VI. By contrast, similar calculations in the child B with bronchiolitis confirmed the failure of CWV to increase PEF in this child.

3.4.9.4 Relationship of physiotherapy to short-term outcomes

The treatment profiles of the two children whose oxygen saturation levels showed the greatest change from baseline in either direction were selected to explore the relationship of their treatments to short-term clinical changes (**Figure 3.40**), along with those children whose data were previously highlighted (children B and C). The child with the greatest negative and positive saturation thirty minutes after physiotherapy will be termed C.D. (cardiac disease, who showed improved oxygen saturation) and child H.I. (head injured, who showed oxygen desaturation).

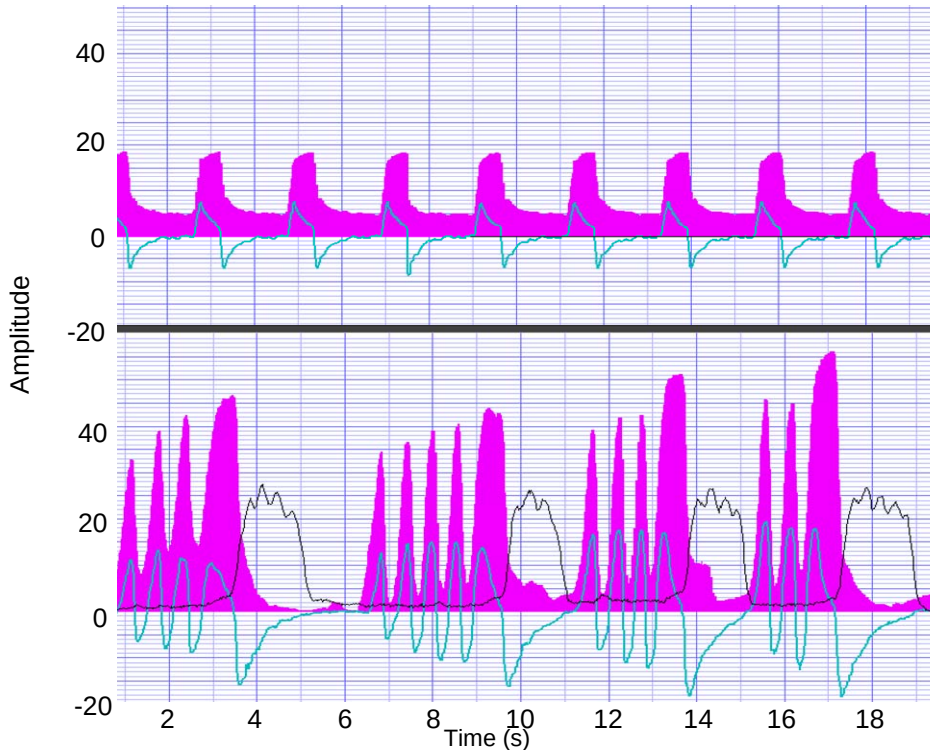
Figure 3.40 Identification of the children who showed the greatest changes in oxygen saturation following physiotherapy



Child C.D. (cardiac disease); child H.I. (head injury); child C (cardiac bypass); child B had no blood analysis

The children's treatment profiles and characteristics (including treatment duration, use of saline and chest compressions during suction), respiratory changes from baseline ventilation, respiratory trends and oxygen saturation before and after treatment are presented for each of the children (**Figure 3.41** and **Figure 3.42**).

Figure 3.41 Treatment profile, tabulation and graphs of respiratory variables during CWV in child C.D., who demonstrated the largest increase in oxygen saturation following physiotherapy



Child C.D.: 4 m, non-paralysed, cardiac disease & upper respiratory tract infection; on synchronised intermittent mandatory volume ventilation with pressure support. O.I.-8.3; PRISM-9;
Treatment duration : 2.6 minutes
Saline : 0.27 ml/kg
Suction compressions: none

	VI ml/kg	**PIP** cmH_2O	**PEEP** cmH_2O	**PEF** l/min/kg	**PIF** l/min/kg	**PEF:PIF**	**RR** / min	**Fmax** N	**Fmean** N
Baseline	7	19	4.9	1.2	1.3	0.95	28	-	-
CWV	15	46	4.5	2.9	2.5	1.2	48	26	18
% change	116	144	-6	138	97	-	71	-	-

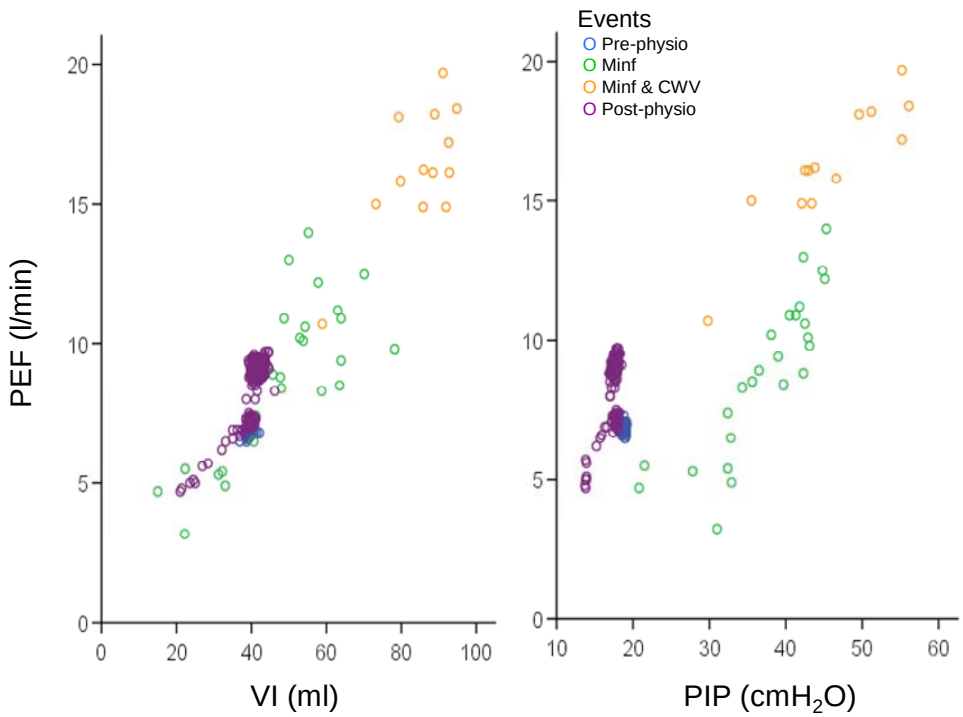
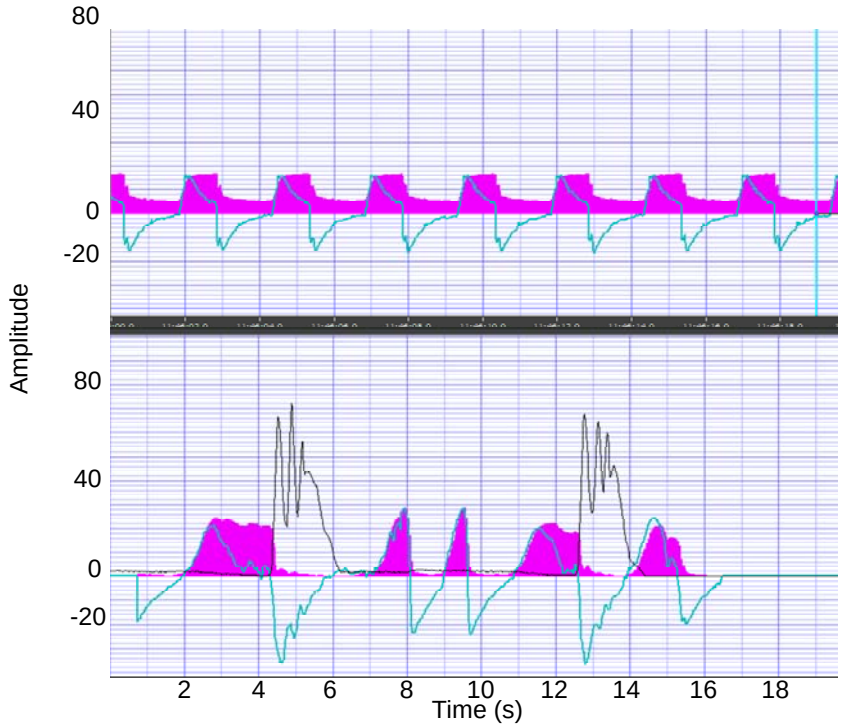
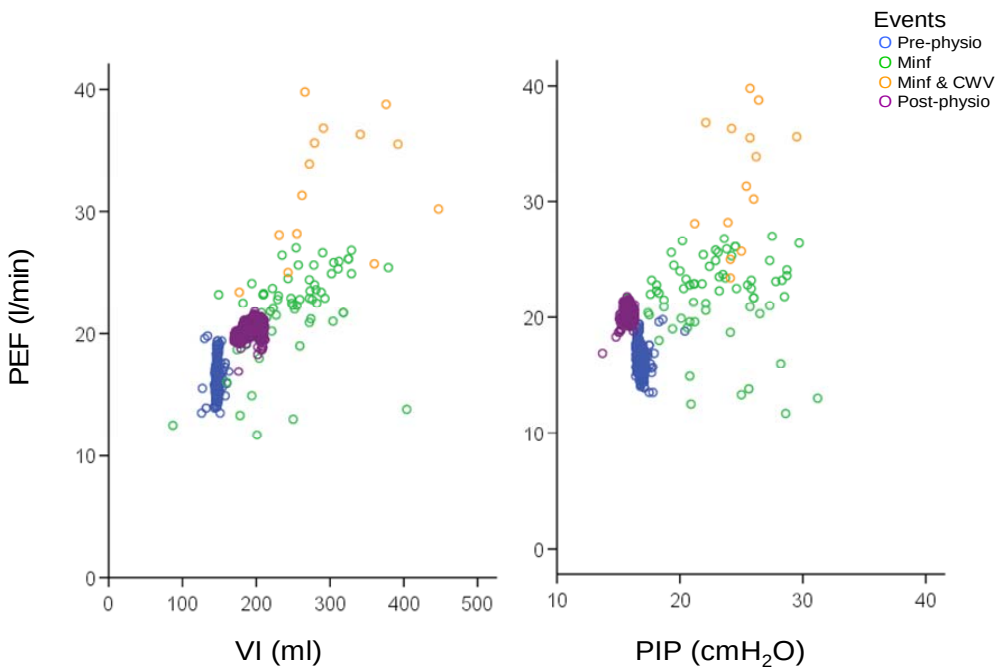


Figure 3.42 Treatment profile, tabulation and graphs of respiratory variables during CWV in child H.I., who demonstrated the largest decrease in oxygen saturation following physiotherapy



Child H.I.: 7 y, paralysed, head injury and secretion retention; diffuse consolidation; 2 days post-event; on pressure controlled ventilation O.I.-3.19; PRISM-14
Treatment duration : 12 minutes & 5 minutes manual lung inflations to reduce ICP (total 17 min)
Saline : 0.64 ml/kg
2 compressions during suction: mean Fmax 56 N; duration 6s

	VI ml/kg	PIP cmH_2O	PEEP cmH_2O	PEF l/min/kg	PIF l/min/kg	PEF:PIF	RR / min	Fmax N	Fmean N
Baseline	6.7	16.8	5	0.74	0.73	1.0	24	-	-
CWV	13.6	25	0.28	1.46	0.9	1.7	19	65	35
% change	103	49	-94	96	22	-	-21	-	-

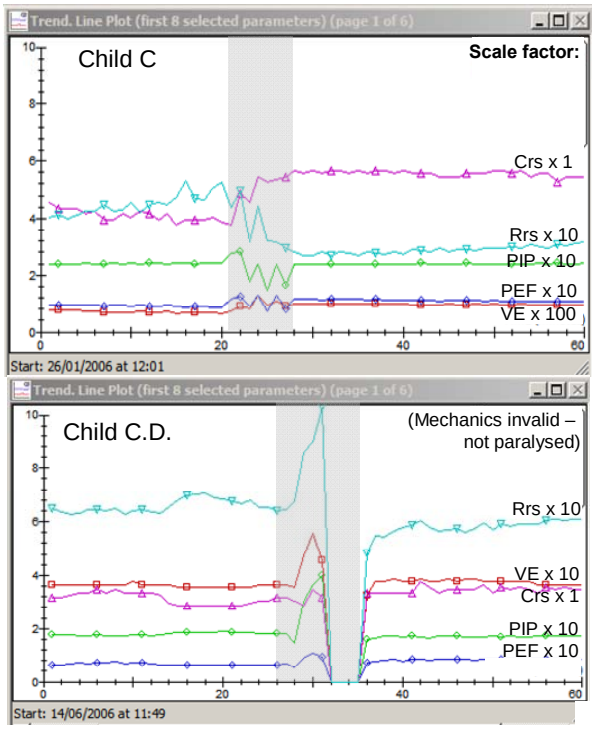


The respiratory trends before and after treatment in the 4 examples are presented in **Figure 3.43.** The data are presented according to whether the children improved or deteriorated in the short-term following treatment (**Table 3.14**). Child C and child C.D. received short treatment, which appearing to involve less respiratory 'disturbance' to the children.

Figure 3.43 Respiratory trend data over 1 hour, recorded before and after chest physiotherapy in the children who a) improved b) deteriorated

a)

Key:
VE red
PIP green
PEF blue
Crs purple
Rrs turquoise



b)

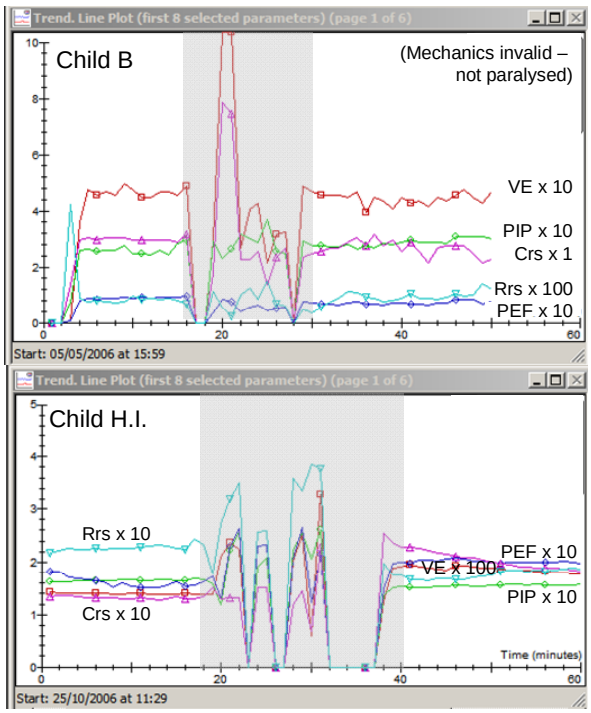


Table 3.14 summarises the treatment features in these children, and their respective changes in ventilation, respiratory mechanics and arterial oxygen saturation half an hour after chest physiotherapy. Potentially important treatment elements highlighted by the four examples additionally included the co-ordination between lung inflations and CWV, as discussed in **section 3.4.9.5**. Both children who were paralysed showed a drop in respiratory resistance following treatment. It is likely that child B would have had increased resistance following the physiotherapy, as suggested by the 21% decrease in PEF and 8% increase in PIP.

Table 3.14 Treatment features in the four examples, and their respective changes in ventilation and arterial oxygen saturation 30 minutes after chest physiotherapy

	C (cardiac bypass)	**C.D. (cardiac disease)**	**B (bronchiolitis)**	**H.I. (head injury)**
Treatment features	Representative treatment	SaO_2 ↑ 8%	Fmax 79 N; no ↑ in PEF	SaO_2 ↓ 7%: ICP ↑ to 26 mmHg
Paralysed / sedated	Paralysed	Sedated	Sedated	Paralysed
CWV & Minf co-ordinated?	Yes	Yes	No	Variable
Treatment duration (min)	5	3	9	11
PEF: % change during CWV	200	139	4	96
SaO_2: Pre , Post	98 , 98	62 , 70	96 , 90[1]	97, 90
% change post-physiotherapy				
Crs	36	NA	NA	38
Rrs	-34	NA	NA	-18
VE or (PIP)	36	(-8 PIP)	-5 (8 PIP)	28
PEF	19	32	-21	24

[1] Transcutaneous oxygen saturation values, as no arterial blood analysis performed; follow-up monitoring discontinued after 15 minutes.

3.4.9.4.1 Summary of treatments resulting in beneficial outcomes

Child C (**section 3.4.9.1**) and child C.D. (**Figure 3.41**) maintained or increased their oxygen saturations after physiotherapy. Respiratory mechanics additionally improved in child C (these measures were not valid in the non-paralysed child C.D.). The children were treated by different physiotherapists, each of whom delivered swift treatments (duration ≤ 5 minutes) and used less than 0.3 ml/kg saline during suction, the median volume recorded in this study (**section 3.4.2**). Peak expiratory flow increased during CWV, and the lung inflations and CWV were co-ordinated with end-inspiration. Peak inflation pressure rose by 71% in child C and by 144% in child C.D.. Positive end-expiratory pressure was maintained to a varying degree during CWV.

3.4.9.4.2 Summary of treatments resulting in detrimental outcomes

The difficulties encountered in the treatment of child B with bronchiolitis are detailed in **section 3.4.9.2**. Child H.I. (**Figure 3.42**) was haemodynamically unstable due to his head injury. The 12 minute treatment produced a rise in the child's level of ICP, from 12 mmHg during baseline measurements to 26 mmHg during treatment. This was resolved by the administration of Fentanyl and a period of manual hyperinflations from a more senior nurse practitioner (**Table 3.2**). The child's oxygen saturation dropped by 7% to 90% (**Table 3.14**), the most marked deterioration in oxygen saturation recorded 30 minutes after physiotherapy, despite increasing the inspired oxygen concentration. Partial pressure of carbon dioxide rose from 4.8 kPa to 5.9 kPa, whilst oxygen dropped from 11.6 kPa to 7.9 kPa. Potential factors contributing to this deterioration include an absence of PEEP during manual lung inflations (**Figure 3.42**) and the potentially detrimental effects of a sedation bolus, as discussed in section 4.4.4.1. In contrast to the other examples, the ventilatory rate during CWV was slower (by 21%) than during baseline ventilation, and PEEP was not maintained during the lung inflations. Chest compressions during suction were applied for 6s, three times longer than when force was applied during CWV. The volume of saline used during suction (0.64 ml/kg) was twice the median amount administered during study treatments. Inflation volume doubled during CWV (65 N), producing a doubling in PEF from baseline. Chest wall vibrations were applied after an end-inspiratory pause during which little or no inspiratory flow occurred and the 49% rise in PIP during CWV was less than that in child C and C.D. This child showed the largest recorded increase from baseline in respiratory compliance (60% at 15 minutes and 38% at 30 minutes after treatment, **Figure 3.28**). The unusually large increase in respiratory compliance in relation

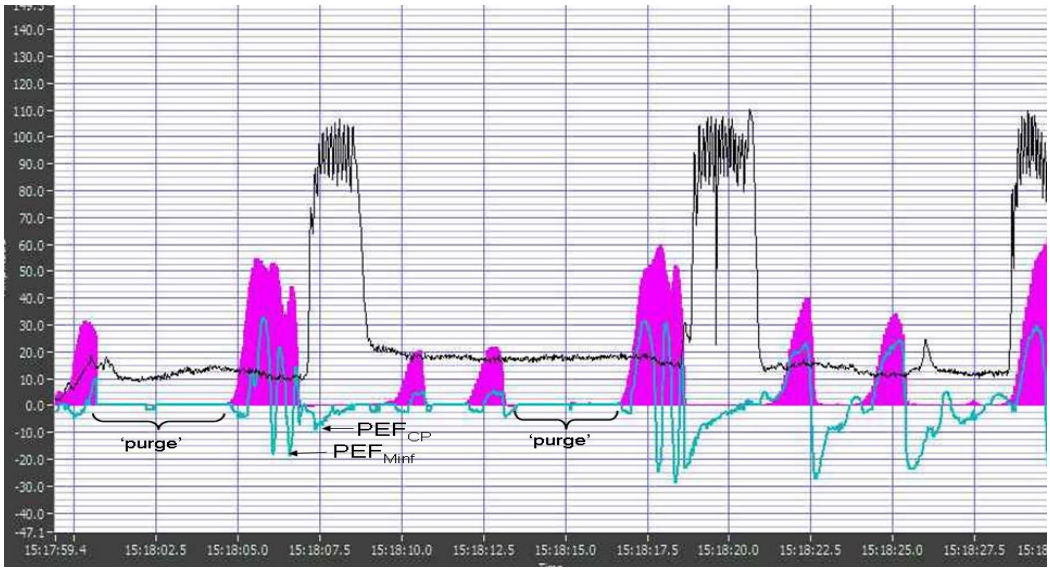
to PEF during treatment (**Figure 3.31**) may also have been influenced by the manual lung inflations delivered for 7 minutes following chest physiotherapy, to reduce the raised ICP. These lung inflations were not recorded with the CO_2SMO®. The significance of the child's treatment and short-term response is discussed in **section 4.4.4.1**.

The treatment patterns in the 4 examples and in the group as a whole suggested the importance of co-ordinating the CWV with the lung inflations to increase PEF during CWV, and that treatment duration might be another influential variable (**Figure 3.43**).

3.4.9.5 Co-ordination between lung inflations and CWV

Protocol refinements to align force and respiration continued during data collection in the first 24 children (**section 2.2.5.5**). In subsequent children with aligned force and respiratory data, CWV to augment PEF were generally applied towards end inspiration, as represented by child C's treatment profile (**Figure 3.35**). In others the co-ordination between the lung inflations and the CWV appeared to be reduced, as suggested in child B with bronchiolitis (**Figure 3.37**).

Figure 3.44 Lack of co-ordination between the lung inflations and force applications when these tasks were performed by separate physiotherapists, reducing the resulting PEF



PEF$_{Minf}$ – peak expiratory flow during manual inflations; PEF$_{CP}$ – peak expiratory flow during chest physiotherapy (CWV & Minf); 'purge' - sensor purge (**section 2.2.5.5**)

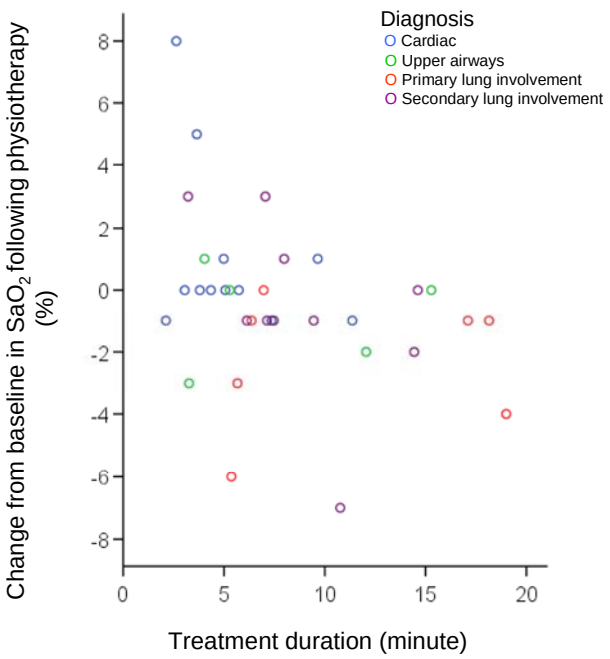
In **Figure 3.44**, two physiotherapists were involved in the treatment of an 8 year old with a head injury, one delivering the lung inflations while the other applied the CWV. In the

first CWV featured in **Figure 3.44**, the 100 N force was applied when only a small inflation breath had been delivered, PEF during CWV (10 l/min) being half that produced during lung inflations alone and similar to baseline ventilation (13 l/min). Difficulty in co-ordinating the lung inflations and CWV may have been related to the fact that these manoeuvres were conducted by separate individuals.

3.4.9.6 Treatment duration and outcome

The majority of treatments when oxygen saturation was maintained or improved took less than 10 minutes, as shown in **Figure 3.45**. However, decreases in oxygen saturation were observed even during physiotherapy lasting less than 5 minutes. This may have been due either to the treatment delivered or because of the child's predisposition to an adverse response to physiotherapy. As an example of the latter, after an initial rise in oxygen saturation a decrease from baseline of 3% in oxygen saturation was observed in a child following repair of tracheal stenosis and tracheo-malacia (diagnosis code 'upper airways'), who was treated for 3 minutes by the clinical specialist using her standard technique (**Figure 3.46**). This was the only child in whom the specialist's treatment produced such a decrease in oxygen saturation, as discussed in **section 3.4.9.7**.

Figure 3.45 Relationship of treatment duration and change in oxygen saturation following treatment, according to diagnosis



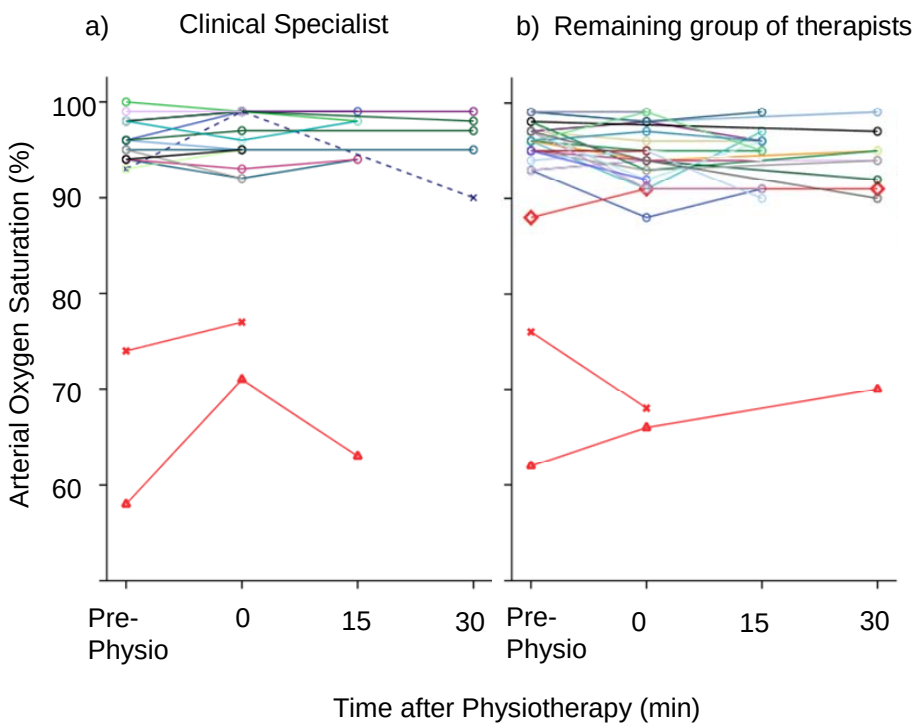
Although not predictive, there was a negative correlation between treatment duration and the change in oxygen saturation following treatment (Spearman's correlation $r = -0.4$, $p < 0.01$), which increased when analysis was restricted to those children who were not pharmacologically paralysed during physiotherapy ($r = -0.6$, $p < 0.01$, data not shown).

3.4.9.7 Post hoc analysis of a specific treatment style

While this study was not designed to make comparisons between individual therapists, *post-hoc* analysis of the clinical specialist's treatments was performed because this specialist delivered the highest proportion of recorded treatments (24 of the 62, **Figure 3.9**), all of which were given to patients on the cardiac ICU. She additionally demonstrated a distinct and consistent treatment pattern (**Figure 3.32**).

Analysis of the clinical specialist's data showed that, with the exception of the child mentioned in **section 3.4.9.6** (with repair of tracheal stenosis) oxygen saturation was maintained in those with baseline saturations above 90% before treatment (**Figure 3.46**). Oxygen saturation rose in both children in whom baseline saturations were below 80%.

Figure 3.46 Change from baseline in arterial oxygen saturation following treatments by the a) clinical specialist b) remaining group of therapists



Children marked in red had baseline oxygen saturation < 90%; broken line denotes a child who had undergone repair of tracheal stenosis (see text)

In contrast to the group changes (**section 3.4.7.4.2**), there was no transient rise in partial pressure of carbon dioxide following treatments by the clinical specialist. The significant improvements in ventilation (PEF and expired volume, $p < 0.01$) mirrored the group changes (**section 3.4.7**). Modelling of the data according to physiotherapist identified the same influencing variables (inflation volume, age and force, **section 3.4.6**) for the clinical specialist and for the remaining therapists.

These favourable results may have been due in part to the population of children treated (those with cardiac disease) and to the therapist's characteristic treatment style evident in child C's treatment. This involved:

- consistent maintenance of PEEP during manual lung inflations
- short treatments (median 4.4 minutes)
- minimal handling / changes in the child's position during treatment
- consistent, co-ordinated inflation patterns and CWV forces
- use of small volumes of saline (median 0.2 ml/kg) when required during suction
- use of lung hyperinflations following CWV and suction manoeuvres to re-inflate collapsed lung regions

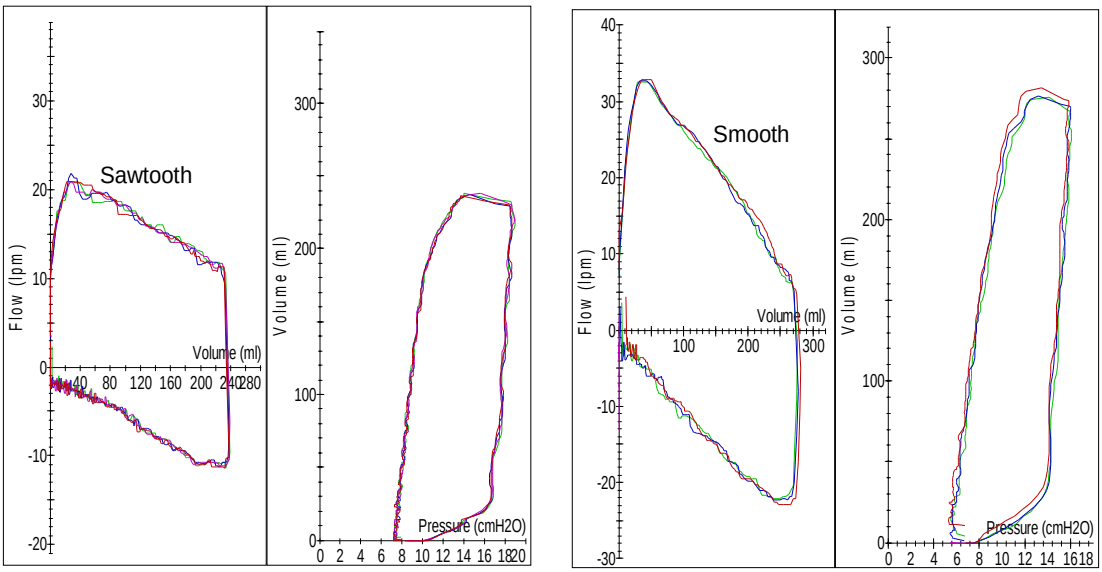
Any influence the clinical specialist's treatments may have had on the generalisability of the findings is discussed in **section 4.4.5**.

Although the numbers of children with a specific diagnosis and who were treated by the same physiotherapist were small, two of the six children who had undergone repair of tracheal stenosis responded adversely to treatment. The child with tracheal stenosis who was treated by the clinical specialist and demonstrated a decrease in arterial oxygen saturation also showed a 40% rise in airway resistance following physiotherapy (**Figure 3.29** and **Figure 3.46**). Another child (treated by one of the remaining group of therapists) demonstrated the greatest drop in PaO_2 (**section 3.4.7.4.3**). These results are discussed in **section 4.4.4.1**.

A 'sawtooth' pattern in the ventilator waveform was observed in children with marked secretion retention who were monitored for this study. **Figure 3.47** shows the contrasting $CO_2SMO^{®}$ flow-volume loops and accompanying pressure-volume traces recorded pre-treatment in a child with a) asthma and sawtooth expiration, and b) head injury and smooth

expiration. In future studies it may be useful to classify the pattern of expiratory flow during baseline monitoring in an attempt to provide evidence that a patient has problems of secretion retention and requires treatment. The waveform classification category could then be compared with the sputum volume suctioned during treatment (**section 4.4.3.4**).

Figure 3.47 Use of expiratory waveform pattern to detect secretions in ventilated children



4 overlaid ventilator breaths recorded pre-treatment

a) 9 y old with asthma

b) 12 y old with head injury

3.5 Summary of main findings

- A wide range of physiotherapy techniques have been identified, in terms of forces applied, lung inflation and treatment patterns.
- Maximum and mean forces applied during chest wall vibrations were directly related to the size and age of the child.
- Physiotherapists demonstrated consistency within a treatment session.
- Manual lung inflations resulted in an increase in peak expiratory flow above that observed during mechanical ventilation.
- Application of chest wall vibrations resulted in a further increase above that observed during manual inflations alone.
- Models to quantify the effect of lung inflations and the additional effect of the force were derived.
- The increase in peak expiratory flow during physiotherapy is influenced by inflation volume, magnitude of force applied and age of the child.
- Force was more effective at increasing PEF in the younger child.
- Respiratory monitoring before and after treatment has highlighted group changes, including significant short-term improvements in respiratory compliance, expired volume and PEF following treatment.
- Arterial oxygen saturation was maintained in the group, those with low initial saturation levels showing a general improvement following physiotherapy.
- Evidence has been provided suggesting the potential of different styles of chest physiotherapy to cause detrimental as well as beneficial short-term treatment effects. Important variables include the treatment duration, the magnitude and co-ordination of lung inflations with CWV, and suction procedures including the volume of saline used.

The final chapter discusses the strengths and limitations of the study, ways in which this research has extended the knowledge-base for chest physiotherapy, the clinical implications of the findings and plans for future research.

Chapter 4 Discussion

4.1 Overview of achievements

Extensive development and subsequent validation of both the force-sensing mats and the accompanying software have successfully enabled detailed characterisation of the forces applied during physiotherapy. This was the main focus of the work, the clinical study being undertaken to prove that the tools produced could be employed even in the most difficult environment of a paediatric ICU. For the first time, data have been provided which relate both the forces and manual lung inflations to changes in airflow during treatments of ventilated children. The results highlight the complexities of the previously masked interactions between the inflations and CWV, providing clear evidence of the variability between physiotherapists' treatment styles, not only in terms of the chest compressions and patterns of oscillation but also regarding the accompanying lung inflations. Whilst the aim of recording the outputs from the clinical study was predominantly to generate hypotheses for future research, these data have also enabled specific hypotheses to be tested. Factors influencing both the applied force and simultaneous changes in expired flow during CWV include the child's age and body size. A wide range of response was measured in the clinical outcomes following physiotherapy. It has additionally been possible to suggest key treatment features, including treatment duration and the co-ordination between lung inflations and CWV, and to relate these to changes in the patient's clinical outcomes following treatment.

Work undertaken for this thesis has successfully addressed the research hypotheses and the initial objectives detailed in **section 1.9**, and provided a valuable tool, analysis format and preliminary data with which to design future studies. Interpretation of the clinical implications of physiotherapy depends both on consideration of treatment factors influencing the short-term clinical changes recorded, and the relationship and significance of these short-term changes with the child's longer term well-being, which will be discussed in **section 4.4.4**.

4.2 Strengths and limitations of the research

4.2.1 Equipment & Methods

The weak evidence base for chest physiotherapy has largely resulted from having no means of quantifying either the input variables (CWV and manual lung inflations) or ventilatory changes regarding the effects of an intervention. Before one could begin to evaluate the efficacy of chest physiotherapy in general, or compare specific techniques, it was therefore important to devise an appropriate technology and methods of assessment, as detailed in Chapter 2.

4.2.1.1 Force-sensing technique

In this study, a mat was created to quantify the force applied directly through the physiotherapist's hand to the patient's chest during chest wall vibrations. No method of describing or summarising these vibrations was available as only one study had quantified physiotherapy forces, and these related to chest percussions in healthy adult subjects (Blazey et al. 1998), no data being found in children. The added complication existed of how to relate force to ventilatory changes during treatment.

Previously described measuring systems have used an instrumented treatment plinth to quantify force indirectly by measuring that transmitted to the force plate below the subject (Blazey et al. 1998;McCarren et al. 2006a). Whilst a plinth causes no interference at the patient/therapist interface, it is likely that the force transmitted to the plinth is considerably attenuated compared to that applied directly through the therapist's hands. Furthermore, force attenuation may be greater in younger children who have highly compliant chests. In contrast to previously described force measuring systems, the thin, pliable mats devised in this study can be wrapped around the patient's chest to measure the compressive forces applied directly through the therapist's hand. The current system therefore has a significant advantage and is eminently suitable for use in clinical situations including difficult environments such as intensive care, where a treatment plinth would be inappropriate. The software developed for the mat allowed detailed characterisation not only of the maximum and mean forces, but also the speed of compression, the amplitude and frequency of oscillations and the duration of each CWV. These variables will be discussed further in **section 4.4.3**.

The system proved to be ideally suited to quantify the most commonly used technique of CWV (van der Schans et al. 1999;Main et al. 2004;McCarren et al. 2006a). Additional work is required to adapt the technology to sample the lower forces delivered during chest percussions and the higher frequencies of mechanical CWV. Recent advances in the Novel pliance® data acquisition software have facilitated simultaneous data collection from two mats and from the CO_2SMO® using a single computer.

4.2.1.2 CO2SMO® respiratory monitor

At the start of this research no measures of respiration *during* CWV were available. The CO_2SMO® respiratory monitor was selected to measure flow and pressure at the airway opening because it provided real-time data to explore breath-by-breath ventilatory changes during treatment and had been successfully validated for use in intubated children (Main et al. 2001;Castle et al. 2002;Main et al. 2004).

Initial anxieties relating to flow signal distortion and sampling frequency during treatment proved to be unfounded and the flow data recorded during physiotherapy were within the range of the sensors' linearity. The paediatric/adult sensor used initially in the older children has the disadvantage that it 'purges' to remove condensation from the sensor, a process which results in a pause in data collection of several seconds (**section 2.2.5.5**). In addition, all the sensors demonstrated brief (< 1s) periods of zero data collection, which allowed the system to correct any signal drift. Both the sensors' 'purging' and data-zeroing processes had implications when synchronising force and respiration, as discussed in **section 4.2.1.3**. The system was primarily designed for tidal monitoring of steady-state ventilation. It is therefore unsurprising that spurious data were generated when the system was required to operate at the limits of its capacity during physiotherapy treatments involving frequent respiratory circuit disconnections and reconnections during physiotherapy, or during suction when the sensor was left attached to the mechanical ventilator's circuit but open to atmosphere distally (**section 2.2.5.5**). Nevertheless, following discussions with the manufacturers and suitable protocol modifications, valid data were obtained both during and after physiotherapy. In addition, the CO_2SMO® offers the facility to store continuously timed and electronically entered treatment notes to document the different treatment periods of manual lung inflations, CWV and suction. This information was important in facilitating data analysis and interpretation.

Monitoring the interplay of the patient's cough response to saline, the negative pressure generated from a suction catheter and hence the inspiratory/expiratory flow bias as a result of this interplay would have provided further useful information for exploring the impact of chest physiotherapy. However, since closed, in-line suction circuits were not used in the participating intensive care units there was a need to remove the CO_2SMO from the circuit during saline instillation and suctioning (as discussed in **sections 2.2.5.4** and **3.3.4**). This is a significant limitation of the technique which could perhaps be avoided in future studies by the use of in-line suction circuits or by allowing continuous measurement of flow by suctioning via a t-piece placed distal to the flow meter. However, the potential effects of such modifications on measured airway resistance and hence on airflow would require full in-vitro and in-vivo evaluation prior to future study protocol modifications. It should be emphasised that this limitation in no way lessens the value of this newly devised technique, which has provided novel respiratory data *during* CWV.

4.2.1.3 Alignment and analysis of force and respiration during chest physiotherapy

It was a challenge to overcome the difficulties of relating force and respiration during treatment because the two data streams began at different times, were collected at different sampling frequencies and spurious data were generated by the CO_2SMO®. These problems were largely overcome by the protocol modifications discussed in **section 2.2.5.5**. The software written in-house to integrate the force and respiratory data streams successfully aligned the two inputs using the registration signals which were repeatedly applied before, during and after the treatment to synchronise the data. By this method, it was possible to measure the direct breath-by-breath effects of applied force on airflow and pressure, and to compare these with baseline respiration. The respiratory-force overlay software allows pressure, flow and volume to be displayed. However, the volume data displayed in the exported '.csv' file does not directly represent the inflation and expiratory volume values produced by CO_2SMO®, its primary role being to detect and correct any baseline drift in the sensors. The actual inflation and expired volume values are derived from flow using algorithms within the CO_2SMO® analysis software. Since the study's hypotheses related to changes in PEF this was not a problem. However, although breath sizes within a trace can be compared (by comparing the area under the flow signal, volume = flow x time) the lack of a reliable visual volume trace remains a limitation when describing what is happening during the treatment.

Considerable thought was required on how to summarise data from the complex treatments as no reports of similar data analysis during chest physiotherapy in ventilated patients could be found in the literature. By analysing separately the manual inflations when CWV were applied from the remaining lung inflations, it has been possible to evaluate the 'added value' of CWV forces on peak expiratory flow, over and above that resulting from any accompanying increase in inflation volume. A useful additional analysis category might be to further subdivide the manual lung inflations without CWV into those delivered *between* the inflations for CWV ('maintenance inflations'), from any larger inflations *following* suction or CWV, to re-inflate collapsed lung areas prior to recommencing mechanical ventilation ('re-recruitment inflations'). This subdivision would quantify the flows and volumes used specifically in re-recruitment manoeuvres.

4.2.1.4 Integrated system

During this study, the integrated system used two computers (one for respiratory variables and one for recording force data), was bulky and expensive (Novel pliance® system currently exceeds £30,000) and data analysis was semi-automated. As previously stated, a single computer can now be used to collect both data streams. Analysis involved time-consuming processes to overlay the data streams, clean the data of invalid force or respiratory events, categorise each event appropriately into one of the four measurement conditions and aggregate the data accordingly. Nevertheless, other physiotherapists have now been successfully trained in the process of data collection and analysis, and have applied this technique to their research projects as discussed in **section 4.5**. Such detailed analysis has resulted in clear identification of the treatment components and has provided a transferable technique and technology, which is useful both in ventilated and spontaneously breathing subjects of all ages. Furthermore, this measurement approach may also be adapted to provide an integrated research and teaching aid in the future (**section 4.5**).

4.2.2 Study design and choice of measures to quantify treatment and outcome

4.2.2.1 Study design and protocol

In this study, the primary aim was to quantify current practice in two intensive care units, characterising the input variables *during* treatment and measuring the respiratory response. At the inception of this thesis no data were available on either the physiotherapy forces or

manual lung inflation techniques used to treat mechanically ventilated children, nor on the potential influence of developmental changes on the children's response. The decision was therefore made to monitor children of all ages and with a range of clinical diagnoses. The acceptance rate was high (only 1 family declined participation), measurement failure was low and all physiotherapists who were approached agreed to participate, thereby precluding selection bias. However, the study may have been biased towards collecting data in children with cardiac problems over those nursed in the general ICU, as a larger proportion of the cardiac children required mechanical ventilation. These children were predominantly in the youngest age group (below 2 years) and many of the treatments were provided by a single clinical specialist. Post hoc analysis was therefore undertaken to determine any influence of this therapist's treatment, as discussed in **section 3.4.9.7**.

Whilst this novel measurement technique allows comparison between changes during and after the physiotherapy in ventilated children, the period of follow-up monitoring in individuals was relatively short, generally up to half an hour. This is an inherent problem in the paediatric intensive care environment, where the children's condition can fluctuate rapidly, requiring multiple treatments or investigations and resulting in relatively short periods of non-intervention. Although not all children were monitored even for 30 minutes, the data gained in the first 15 minutes appeared to be representative of the immediate post-treatment effects (**section 3.4.7.6**)

4.2.2.2 Statistical Analysis

Previous research exploring changes in outcome measures following paediatric chest physiotherapy had demonstrated that it was feasible to recruit 30-40 ventilated children a year at Great Ormond Street Hospital for Children, with at least 80% success rate in obtaining complete measurements (Main & Stocks 2004;Main et al. 2004). While smaller numbers (< 30 children) would provide sufficient power to detect statistically significant group changes in respiratory measures in response to physiotherapy, we wished to characterise force profiles in children of different ages, and examine factors that may contribute to any variability, such as the ventilation pattern, clinical severity and diagnosis; hence the need for a larger population in order to undertake multivariable analyses. Optimal sample size depended on within and between subject variability of the force profiles, information that was to be collected during the first 6 months of the clinical study. *A priori* power of study calculations for assessment of force were therefore not feasible at

the outset of this research. Consequently, a decision was made to obtain measurements in similar numbers of children above and below 2 years, with at least 20 children in the lower age group. In reality, 32 of the 55 children were aged below 2 years.

Use of multivariable analysis allowed the complex relationships between the applied force, ventilatory pattern and the child's age and body weight to be examined in a way that would not be feasible from univariable analysis. By recording the impact of increased inflation volumes on PEF in the *absence* of CWV, it was possible to differentiate the effects of force *per se*.

4.2.2.3 Clinical relevance of respiratory input and outcome measures

The $CO_2SMO^{®}$ was selected for this research because it allowed both measurement of the respiratory changes during manual lung inflations, and quantification of resulting changes in PEF and expiratory flow bias [PEF:PIF ratio >1.1(King et al. 1985a;Kim et al. 1987)] during treatment – the significance of which is discussed in **section 4.2.2.3.1**. Furthermore, this equipment provided the opportunity to explore respiratory changes following treatment (expired volume, peak inflation pressure and PEF) which may at least partly reflect lung recruitment and airway clearance. These measures were supplemented by additional monitoring of respiratory mechanics in the paralysed subgroup of children, providing further indirect measures of lung recruitment and airway clearance. Arterial oxygen saturation and partial pressures of oxygen and carbon dioxide were available in the majority of children, providing direct measures of gaseous exchange.

4.2.2.3.1 Assessment of airway clearance

The clinical relevance of recording PEF during treatment is limited in that although it may provide a surrogate measure of airway clearance, it does not directly measure the volume of secretions cleared. However, such measures are simple, available and generalisable and were important to establish the direct effects of CWV on expiratory flow. Additional potential options included intra-thoracic measures such as oesophageal manometry, which would have provided information on the transmission of pressure to the lungs (Coates et al. 1996;McCarren et al. 2006b). However, this is a more invasive measure that is not widely applicable, making the results obtained less generalisable than with the measures selected.

Respiratory resistance is primarily influenced by airway calibre and patterns of airflow. It may therefore be considered a somewhat blunt tool because of the confounding impact of the endo-tracheal tube in ventilated children, as reflected by the absence of a group reduction in resistance in the current study. Respiratory compliance reflects both the elastic properties of the lungs and chest wall and the state of lung inflation, and can therefore be used as a measure of lung volume recruitment resulting from the physiotherapy. This was clearly demonstrated in child C, who showed an increased inflation volume and respiratory compliance when returned to pressure-controlled mechanical ventilation following treatment. There is a difficulty in selecting either expired volume or peak inflation pressure as outcome measures in children receiving different forms of mechanical ventilation in that many forms of ventilation involve a combination of pressure and volume regulation. By contrast, PEF offers the advantage of being applicable to children on all forms of ventilation, reflecting the pattern of mechanical ventilation (inflation volume and pressure) delivered to the child. Furthermore, there was a correlation in change in tidal PEF when related to change in compliance following physiotherapy, supporting the use of this marker as a surrogate marker of lung recruitment when it is not possible to record changes in respiratory compliance (i.e. in non-paralysed subjects).

Arterial oxygen saturation provided a direct measurement of the level of oxygen exchange occurring in the lungs, and is historically considered the 'gold standard' with which to define a child's clinical condition. Whilst the partial pressure of oxygen and carbon dioxide were also monitored serially, they may be of little use in exploring group changes in heterogeneous populations of patients because of the wide range of values recorded during baseline measurements. Serial measures within more homogenous patient groups are however likely to be of value.

In summary, the study design and measures used to quantify treatment and outcome were appropriate and successful for testing the research hypotheses and achieving the objectives established at the outset of this research. The choices reflect the study's primary aim of exploring the mechanisms of CWV, rather than proving efficacy. The clinical relevance of the selected variables used to characterise force and measure response will need to be assessed in future larger studies. Nevertheless, with the exception of rate of change of force, the selected variables fulfilled the original objective of being able to characterise

applied force in a clinical situation in a way that has never previously been achieved. Furthermore, the ability to record changes in flow *during* physiotherapy will greatly facilitate comparison of different physiotherapists' techniques in more homogenous populations in the future.

4.3 Comparison of the research with published literature

4.3.1 Treatment variability and CWV force characteristics

The current repeatability studies in healthy adults showed that while physiotherapists applied CWV consistently within a treatment session, there was wide variability in the forces used by different physiotherapists, concurring with results of a previous study in healthy adults (Jones et al. 2005). In the study by Jones, force was applied by four physiotherapists to 14 subjects and measured using a piezoelectric force plate beneath the subject. The study found a strong intra-class correlation coefficient (ICC) between trials performed by a single therapist (within-subject ICC 0.82), with substantial variations between physiotherapists (ICC 0.082), based upon three CWV performed on each subject. Unlike the current study, the magnitude of force delivered was not reported. The current research appears to be the first to explore the long-term variability in physiotherapy treatments following a 6 month interval. The significant variability detected *between* physiotherapists' treatment of the same subject suggested that clinical studies are required to evaluate the physiological effects of the different treatment profiles and to investigate the significance of the wide variation recorded.

This appears to be the first study to report the forces applied to mechanically ventilated children, and the age-related changes in such forces. The range of maximum forces encountered in the older children in this clinical study were comparable with those recently reported using an instrumented plinth to record CWV in healthy adults [(peak force 137 N (SD 66.7 N) (McCarren et al. 2006a)] and lower than the highest forces recorded in the repeatability studies in healthy adults (**section 2.3.2**). The unavailability of commercially available instrumented plinths means that at the current time it is not possible to compare between forces applied directly through the hand (measured with the sensing mat) and those forces transmitted to a plinth beneath the subject. However, such studies would be valuable in the future. The current research also clearly demonstrated the variability in

physiotherapists' oscillatory force patterns, contrasting with McCarren's previous research in which only one oscillatory profile was presented, despite the large variability reported. The oscillatory frequencies recorded in this study encompass the resonant frequency of the lungs and the respiratory cilia (Rutland & Cole 1981;Clary-Meinesz et al. 1997), and the oscillatory range believed to assist secretion removal (King et al. 1984). However, the range was slightly lower than 13Hz, the optimal frequency for animals quoted by several research groups (King et al. 1984;Chang 1984;Rubin et al. 1989).

4.3.2 Respiratory changes during CWV

At the inception of this study, no data were available on the patterns of ventilation in intubated children during physiotherapy and there were limited data on PEF generated during CWV. In the current study, the children demonstrated an average increase of 120% in PEF during lung inflations with CWV compared with that during baseline mechanical ventilation ($p < 0.001$). This compares with a mean increase in PEF of 34% found during lung inflations without CWV. Maclean reported an increase in PEF of 42% during manual ventilation with CWV when compared to manual ventilation with no CWV in 9 ventilated adults (Maclean et al. 1989). This increase is lower than that detected in the current study. No data were presented to allow comparison of the results with PEF during baseline ventilation, and no data on the accompanying lung inflations or CWV were produced. More recently, McCarren reported a similar increase to our own (150% increase from tidal breathing) during CWV in a spontaneously breathing healthy adult (McCarren et al. 2006a).

The average increase in inflation volume of 23% during manual lung inflations is considerably lower than the 113% increase previously reported during lung hyperinflations (with no CWV) in ventilated adults (Clarke et al. 1999). However, the 102% increase from baseline recorded during inflations for CWV concurs more closely with Clarke's hyperinflation volumes. The combined influence of inflation volume and CWV on PEF found in this study concurs with McCarren et al.'s recent research (McCarren et al. 2006a;McCarren et al. 2006b). However, their research explored the effects of increasing the driving pressure within the lungs in spontaneously breathing adults rather than in ventilated children.

4.3.3 Short-term effects of chest physiotherapy

The improvement in dynamic respiratory compliance reported in the paralysed subgroup of children in this study concurs with a recent paediatric study (Main et al. 2004) and earlier research in ventilated adults (Mackenzie et al. 1980). Although no significant group changes in these measures were detected, Main et al. reported a trend for respiratory compliance to increase and resistance to decrease in individual children following physiotherapy when compared with nursing procedures of suction and manual lung inflations. The study, a precursor to this current research, was conducted in the same clinical environments on a similar cohort, except that it was limited to paralysed children. An improvement in respiratory compliance and resistance has also recently been reported in 15 mechanically ventilated adults who were treated with manual lung hyperinflations and suction (Choi & Jones 2005). The absence of any change in respiratory resistance recorded in this study concurs with a study exploring the effects of endotracheal suction in 78 ventilated children (Morrow et al. 2006). Morrow also reported a fall in respiratory compliance and expired tidal volume in the 5 minutes of monitoring post-suction. However, the validity of these measures is questionable, since not all the patients were pharmacologically paralysed. In Morrow et al.'s study the patients were returned to the mechanical ventilator immediately following suction, with no lung re-inflations prior to the reconnection.

The increase in tidal volume recorded in this study concurs with results obtained following chest physiotherapy when compared with suction alone in 20 ventilated infants with bronchiolitis (Bernard-Narbonne et al. 2003). No treatment details regarding the physiotherapy were given in the latter study, except the comment that treatment "differed from that given by English colleagues". Previous studies in ventilated children do not appear to have measured changes in tidal PEF following physiotherapy. Whilst not directly comparable, an increase in tidal PEF has previously been reported in spontaneously breathing children with cystic fibrosis following physiotherapy (Desmond et al. 1983).

Arterial oxygen saturation levels were maintained in the group following physiotherapy, conflicting with earlier research both in neonates in which mechanical vibrations and lung inflations reduced arterial saturation (Fox et al. 1978) and with Main et al.'s more recent research in paralysed, ventilated children (Main et al. 2004). The general improvement noted in the current study in those with low initial saturations (> 80% SaO_2) concurs with

an increase in arterial oxygen saturation recently reported in a non-randomised study exploring expiratory flow increase techniques in 22 infants with acute obstructive respiratory failure (Almeida et al. 2005).

The significant advantage of the current research over all of these previous studies is the ability now provided to relate short-term clinical changes directly to the changes during treatment, the clinical implications of which are discussed below.

4.4 Clinical implications of the results

This study has revealed the complex interactions between the lung inflations and CWV, demonstrating that it is too simplistic to relate force applied to the expiratory flow generated and that many additional variables need to be considered. As hypothesised, the application of CWV increased PEF, over and above that due to any accompanying increase in inflation volume. The study has therefore shown that there is a physiological basis for using CWV, increases in PEF and expiratory flow bias to create PEF:PIF ratio > 1.1(King et al. 1985a;Kim et al. 1987;Benjamin et al. 1989) during treatment reflecting an increase in airway calibre or reduction in airway obstruction (and hence potentially surrogate for airway clearance). However, the data confirm that effective treatments relate to considerably more than an ability to increase PEF during CWV. Indeed, whilst the increases observed in PEF could be related to the force and inflation volumes used, short-term clinical deterioration was recorded in children exposed to extreme forms of treatment, with respect to duration, magnitude of applied force and / or lung inflations, as discussed in **section 4.4.4**.

4.4.1 Force characterisation

Results from this study showed a wide range of CWV profiles with respect to their magnitude, oscillatory patterns and duration of vibrations and treatments. The question of whether physiotherapists applied greater force to older children (with relatively stiffer, less compliant chests) was also addressed. Whether the pattern of applying increasing forces with age continues into adulthood or plateaus once growth ceases has yet to be determined.

The consistency of maximum force applied during single treatments was remarkably similar in both the repeatability studies involving 2 healthy subjects (CV 10%) and during the

children's treatments (CV 11%). Clinically, it is likely that some variability in CWV is intended, the therapist adapting and modifying the CWV in response to the feedback received. Physiotherapists may develop individual CWV patterns based on various factors including clinical expertise, training or personal preference, as well as in response to direct feedback from the patient, which will be discussed in **section 4.4.4.3**. Further work is required to establish the effects of the different oscillatory patterns on airway clearance, relating the varying frequencies and amplitudes to changes in the rheological properties of the mucus and exploring any direct effects on airway clearance (**section 4.5**). Implications of the inter-related force and ventilatory patterns during chest physiotherapy are discussed in **section 4.4.3**.

4.4.2 Changes in ventilatory support during physiotherapy

The magnitude of change in inflation volume and pressure that was observed in this study during manual lung inflations compared with baseline ventilation was unexpected.

4.4.2.1 Inflation volume and PEEP

During lung inflations preceding CWV, inflation volume doubled from mean (SD) baseline ventilation volumes of 7.2 (1.6) ml/kg to 14.6 (5.3) ml/kg. In parallel, PEEP fell to two thirds of baseline values, dropping to on average 2 cmH_2O. In previous studies of patients with acute lung injury and acute respiratory distress syndrome, it has been shown that mechanical ventilation with lower tidal volumes resulted in decreased mortality and increased the number of days without ventilator use (ARDSnet 2000). Recent studies have also suggested that the use of lower tidal volume and PEEP appear to prevent pulmonary inflammation and acute lung injury in mechanically ventilated patients without any pre-existing lung injury, when compared with traditional ventilation volumes and no PEEP (Choi et al. 2006;Wolthuis et al. 2008). Traditional and low ventilation volumes were respectively defined as 12 ml/kg and 6 ml/kg of ideal body weight; the level of PEEP used with low volume ventilation was 10 cmH_2O.

Clearly, the highest inflation volumes recorded during physiotherapy exceed the higher lung volumes believed to cause lung injury, PEEP simultaneously falling to one fifth of the level that has been suggested to help protect the lungs. However, in this study it was not possible to determine whether such short-term changes in ventilation could result in lung injury, as previous studies investigating the mechanisms of lung injury have been based on

alterations in the subjects' ventilatory pattern which were maintained between a minimum of 3 hours and several days (Dreyfuss et al. 1988;Choi et al. 2006;Halter et al. 2007;Wolthuis et al. 2008). Nevertheless, the available literature suggests that it would be wise to at least control and monitor inflation volumes and pressures and maintain end-expiratory pressures during physiotherapy treatments.

4.4.2.2 Peak inspiratory pressure

During cough, intra-thoracic and subglottic pressures in excess of 40 cmH_2O have been recorded (McCool 2006). Whilst these high pressures account for some of the adverse events related to cough (including cardiovascular and neurological events), such transient 'cough pressures' are not generally associated with lung injury. However, unlike cough manual inflation techniques involve positive lung inflations.

In this study, peak inspiratory pressure rose on average to 38 cmH_2O (SD 8 cmH_2O), exceeding the 35 cmH_2O recommended for safe mechanical ventilation (Dreyfuss et al. 1988). However, in the majority of treatments, these peak values occurred briefly, as seen in child C whose treatment was representative of the general trend. It may be that it is not only the absolute peak inflation pressure at the airway opening that is important, but the time for which the pressure is maintained (the product of inflation time and pressure) and the proportion that is transferred to the intra-thoracic airways.

The specific contribution of ventilatory changes during physiotherapy requires further investigation, both in terms of evaluating the beneficial effects of treatment and preventing any lung or cardiac compromise.

4.4.2.3 Implications of lung injury research on inflation techniques

Physiotherapy treatments should probably aim to balance ventilatory patterns to optimise secretion removal (by increasing expiratory flow and expiratory airflow bias), lung recruitment and prevention of atelectasis, with the need to avoid over-distension and repetitive stress due to opening and closing of small airways (Taskar et al. 1997). In this way treatment could be directed at ventilation of the lungs within a 'safe' zone. Regarding secretion retention in mechanically ventilated patients, it was observed that in some children baseline ventilation encouraged an *inspiratory* flow bias, as was the case in child

C (**section 3.4.9.1**). Such patterns of ventilation may encourage the migration of secretions deeper into the lungs (Volpe et al. 2008;Ntoumenopoulos 2008).

Manual lung inflation circuits vary in design and function (Maxwell & Ellis 2003;Savian et al. 2005;Maxwell & Ellis 2007;Hodgson et al. 2007). Clinically, circuits which offer the facility to pre-set a maximum pressure and / or inflation volume per kilogram body weight would help prevent the occurrence of extreme ventilatory patterns. The use of circuits with end-expiratory valves which maintain PEEP during the physiotherapy could protect the lungs from airway closure, diminishing any detrimental effect from CWV of excessive duration. However, the effects within the lung would need to be evaluated in the context of any cardiovascular changes produced. While further research is required to define 'best practice', both in terms of lung inflations and CWV, routine use of the CO_2SMO® (or equipment offering similar measurements of flow, pressure and volume at the airway opening on a real-time display with minimal time lag) would assist clinical physiotherapists in providing controlled, effective and safe inflation patterns, with and without CWV. Computer-based alerting systems could additionally control the ranges of treatment forces and ventilatory patterns used. An alternative approach would be to control the ventilatory pattern by using mechanical ventilators to deliver the hyperinflation breaths during physiotherapy (Berney & Denehy 2002;Savian et al. 2006).

4.4.2.4 Relationship of inflation pattern to the child's pathophysiology

The pattern of lung inflations required for treatment will be influenced by the child's pathophysiology with, for example, different patterns being required to aid lung recruitment depending on whether airway obstruction or decreased lung compliance is the dominant feature.

4.4.2.4.1 Airway obstruction

There is an increasing recognition of the heterogeneity of airway obstruction in ventilated subjects with airways disease. This can result in uneven ventilation and potential lung injury during mechanical ventilation from over-distension in the areas of least resistance and highest compliance, while other regions remain collapsed (Haake et al. 1987;Denehy 1999;Clarke et al. 1999;Verbanck et al. 2003;Tgavalekos et al. 2005;Venegas et al. 2005). In the presence of uneven distribution of ventilation due to varying degrees of airway obstruction and airway calibre, one can predict areas of lung collapse behind closed,

obstructed airways and severe over-inflation in the remaining lung areas (Calverley & Koulouris 2005). Such a pattern of ventilation almost certainly existed in the case of child B with bronchiolitis, where it is likely that the physiotherapy may have increased the degree of airway hyper-reactivity or spasm in this child, causing further respiratory compromise (**section 3.4.10.2**). These combined factors would account for the deterioration in the child's condition following treatment. Since the main cause of airway narrowing in bronchiolitis is airway wall inflammation rather than bronchospasm, pre-dosing with bronchodilator therapy may have a deleterious effect by increasing airway wall compliance (Zach et al. 1981;Maayan et al. 1989). Closing volume (and hence gas trapping) is directly proportional to airway wall compliance (Stocks & Hislop 2002). The higher the airway compliance the more likely it is to close when there is reduced calibre due to airway obstruction, and in instances of high transmural pressures including during forced expiration, cough or chest physiotherapy (**section 1.6.1**).

In the presence of uneven time constants, such as were likely to be present in child B, one might assume that lower inspiratory flows (longer inflation times for a fixed volume) would allow air to reach the more obstructed parts of the lung, thereby reducing the influence of airway resistance on the distribution of ventilation. The pattern of lung inflations required for children with airways obstruction, and for re-recruitment following CWV and suction, should therefore probably include low inspiratory flows with an end inspiratory pause to overcome the effects from uneven airway resistance or compliance. Such a pattern of lung inflations between the breaths for CWV, combined with application of PEEP and an increased expiratory time coupled with appropriate chest decompressions to reduce hyperinflation may have improved the patient's treatment outcome.

4.4.2.4.2 Low lung compliance and 'stiff lungs'

Child C (on cardiac bypass) showed a 36% improvement in respiratory compliance and a 34% decrease in resistance for at least half an hour after treatment, maintaining baseline oxygen saturations above 98%. Whilst the re-recruitment inflations delivered did not conform to the slow inflation pattern recommended above, these results suggest the cardiac child's overall treatment requirements may not have related primarily to relieving airway obstruction. Indeed the cardiac child was more likely to present with low lung compliance, as will be discussed.

During manual lung inflations, depending on the flow and respiratory mechanics, a shortening of expiratory time in relation to inspiratory time may contribute to dynamic elevation of lung volume within the lung, as less air is allowed to leave the lung before the next inspired volume is delivered. This will be especially effective in those with stiff lungs (low compliance), and in whom lung collapse may occur unless a degree of PEEP is applied. Children with cardiac problems with a large left to right shunt and resulting 'wet' lungs are likely to fall into this category. Indeed, this pattern of shortening expiratory time to maintain PEEP during the manual lung inflations was employed by both physiotherapists whose treatments exemplified effective physiotherapy in child C and child C.D. (**section 3.4.9.1**and **3.4.9.4**). Conversely, such a pattern may lead to an unacceptable degree of hyperinflation in those with airways obstruction.

4.4.3 Inter-relationship of force and ventilatory pattern on PEF during physiotherapy

Change in PEF during physiotherapy was selected as a surrogate marker of the effectiveness of CWV. However, during treatment many changes occur, including the discontinuation of mechanical ventilation which results in changes in inflation volume, pressure and PEEP, these in turn influencing PEF and respiratory function. These changes are compounded when CWV forces are applied. All such changes must be considered before the impact of CWV force can be considered. Indeed, had only univariable analysis been performed one might have assumed that force was the dominant factor influencing PEF (**Figure 3.17**).

4.4.3.1 Inflation volume and PEF

During manual inflations, the volume delivered will depend not only on the age and size of the child, the respiratory compliance and peak inflation pressure but also on inflation time. If inflation time is too short, expiration will occur before lung filling is complete, thereby reducing the elastic recoil that could potentially be achieved with a given inflation pressure, as will be discussed in **section 4.4.3.3**. Similarly, if inflation commences from a relatively high PEEP, inflation volume will be relatively small for any given inflation pressure. In this way, both inflation time and PEEP can reduce the inflation volume in relation to peak inflation pressure. However, in this study PEEP generally dropped during treatment and its inclusion in the general analysis model for PEF showed that it was not significant on multivariable analysis.

4.4.3.2 Influence of growth on PEF

This study has shown the independent and age-related effects of inflation volume and force on an increase in PEF during CWV. The increased efficiency of force application in younger subjects may reflect both the relatively large airways in relation to their lung volume and higher chest wall compliance found during early life (Stocks & Hislop 2002).

4.4.3.3 Timing and co-ordination between lung inflations and CWV

In this study, the co-ordination of the lung inflations and chest compressions appeared to be an important treatment feature in increasing PEF (**section 3.4.9.5**). Protocol refinements to align the force and respiratory data continued during the first half of the clinical study. It was therefore not possible to categorise all the children's treatments according to the point at which CWV were applied during the respiratory cycle. However, in 38 of the 62 data sets force and respiration were well aligned.

When chest compressions were applied towards end inspiration they combined with the increased driving pressure within the lungs to augment PEF. By contrast, the example treatment involving two physiotherapists, where CWV were applied prematurely when only a small volume of air had been delivered, resulted in a reduced PEF as elastic recoil was lower (**section 3.4.12.1**). Furthermore, if force is applied whilst the lung is actively being inflated towards total lung capacity there may be a danger not only of baro-trauma and excessive intra-pulmonary pressures but also the possibility of a pneumothorax. Because elastic recoil falls during expiration as lung volume declines from mid to low lung volume, late force application might similarly result in a reduced PEF. Physiologically, one would expect that rapidly applied and accurately timed CWV at end inspiration should be combined with the rapid release of the lung inflation reservoir, creating a large pressure gradient from the airways to atmosphere thereby maximising change in expiratory flow. This was indeed the pattern adopted in many of the treatments, as exemplified by child C's respiratory-force profile (**Figure 3.35**). Further work is underway using this technology to explore the effect of varying the co-ordination between the CWV and lung inflations (**section 4.5.3**). Future clinical studies will need to consider the effectiveness of treatment, exploring factors including the combined effects of the magnitude and inter-relationship of the lung inflations with CWV and the overall level of treatment 'expertise' (including the speed and appropriateness of the intervention), as will be discussed in **sections 4.4.4.3** and **4.5.2**.

4.4.3.4 Influence of the child's pathophysiology

In addition to considering the age-related changes during treatment and the timing of force application, a further consideration is the child's underlying pathophysiology. In this study, CWV were applied for longer in older children and those with airways obstruction. By contrast, shorter CWV were generally used in the young cardiac children with no airway obstruction, in whom lung emptying would be expected to be more rapid. It is possible that lower forces applied for longer might be more effective in older children and those with marked airway obstruction. Additional measures of improved airway function in response to such a protocol could include changes in mean airflow.

Studies have suggested that a 'sawtooth' expiratory airflow pattern demonstrated in **Figure 3.47** is a good indicator of retained secretions in mechanically ventilated patients, indicating the need for airway clearance manoeuvres (Leclerc et al. 1996;Guglielminotti et al. 2000). In future studies it may therefore act as a useful variable for bedside detection and categorisation of children with secretion retention.

4.4.3.5 Comparison of treatment effects within and between children

The model derived from multivariable analysis extends the value of this novel measurement technique as it is possible to compare the effects of physiotherapy treatments, both within and between treatment occasions. Furthermore, a particular treatment can be compared with 'expected' group changes. This approach could equally well be used to compare response to physiotherapy at different stages or severity of disease within a child, or to compare within–subject response to different physiotherapy techniques (or similar treatments by different physiotherapists) during periods of clinical stability. Analysis involving the complete data set has the advantage of highlighting any variability within a child's treatment, which cannot be investigated when single aggregates are used. Such analysis further illustrates the complex treatment interactions that need to be accounted for, and that may influence outcome.

This approach is proving to be valuable in a current study to compare the treatments given by the intensive care physiotherapists with those who cover the unit only on an 'on-call' basis in the evenings or at week-ends (**section 4.5.2**). The robustness of the current model needs to be established by applying it to populations of children with different underlying pathophysiology, as well as extending its application to adults.

4.4.4 Short-term impact of chest physiotherapy

This study has shown that there is a physiological basis to CWV, resulting in the general short-term maintenance of oxygen saturation, improvements in markers of ventilation (inflation volume and peak expiratory flow) and surrogate measures of lung recruitment (respiratory system compliance). However, no group changes were recorded in respiratory resistance, a surrogate marker of airway clearance. Given the variability of changes in respiratory resistance, which ranged from an increase of 103% to a decrease of 40% following physiotherapy, the current study was under-powered to detect significant changes in this variable (Main et al. 2004). This broad range of response may reflect the heterogeneity of both the population and the treatments applied. Although respiratory resistance is recognised as a somewhat blunt measure of airway clearance in intubated children (**section 4.2.2.3**), a marked increase in resistance (in the absence of leak) would be a useful measure to identify children at particular risk from chest physiotherapy or inappropriate treatments, as discussed below.

4.4.4.1 Factors influencing short-term improvement

Whilst an increase in PEF during treatment was moderately correlated with short-term improvements in respiratory compliance (**section 3.4.8**), the general lack of a direct relationship between change in PEF during treatment and the short-term outcome measures may reflect the heterogeneity of the children's underlying pathophysiology and the combined influence of multiple physiotherapy treatment variables on outcome. Successful treatment is likely to be related to more than simply the ability to produce an increase in PEF. Furthermore, there may be an optimal increase in PEF required to remove secretions, above which further increases in PEF are of no additional value. The contributions of the child's age and pathophysiology, the inflation volume and force have all been discussed. In this heterogeneous group of children some will have required removal of large quantities of sputum (for example those with asthma) whilst treatment in others may have been aimed more at prophylaxis and lung maintenance during mechanical ventilation (**section 4.4.4.2**). Further studies are required in more homogenous patient groups using standardised treatments in standardised treatment positions (**section 4.5**).

Other important variables influencing treatment outcome appears to include the speed of treatment, as shown by the generally beneficial oxygen saturations recorded following the shorter treatments (**section 3.4.9.6**). However, this relationship may be associative rather

than causal, sicker children taking longer to treat. Furthermore, this finding is potentially confounded by the fact that treatments delivered by the clinical specialist in the cardiac unit were consistently brief (**section 3.4.9.7**). Deleterious treatment outcome may be associated with a loss of PEEP resulting from disconnecting the patient from the ventilator to perform either manual lung inflations or open-circuit airway suctioning (Berney & Denehy 2002;Savian et al. 2006). The order in which interventions are given may also influence outcome. For example, since CWV and suction may cause alveolar collapse and reduced respiratory compliance, if these manoeuvres are not followed by compensatory lung re-inflations the overall treatment outcome is more likely to result in atelectasis (Brandstater & Muallem 1969;Zidulka et al. 1989;Unoki et al. 2003;Unoki et al. 2004;Unoki et al. 2005;Choi & Jones 2005;Morrow et al. 2006). Treatment duration, the co-ordination of CWV with lung inflations, the controlled use of suction (including suction brevity and minimal use of saline), the effects of repositioning the children, use of heat and moisture exchangers and the order of interventions are all factors which will require further investigation in future controlled trials.

In addition to analysing the group changes, use of this innovative technology and analysis format to characterise the treatment delivered has helped to explain short-term clinical changes in individual children. Examples of effective treatments and short-term improvements have been contrasted with occasions where more extreme treatment patterns were delivered, resulting in deleterious short-term outcomes. The results have additionally confirmed the importance of simultaneously considering changes in multiple outcome measures. For example, whilst treatment of a head injured child (child H.I., **section 3.4.9.4**) resulted in significant improvements in respiratory compliance after treatment (38% increase from baseline), these changes were accompanied by a drop of 7% from baseline arterial oxygen saturation levels, to 90% following treatment. Whilst this drop could be related to a ventilation/perfusion imbalance following chest physiotherapy (Main & Stocks 2004), it may also relate to a deleterious treatment effect in this child whose intra-cranial pressure rose significantly during treatment. It is known that patients with head injury are a vulnerable group, requiring particular care during chest physiotherapy (Prasad & Tasker 1990). The response to an increased oxygen demand during physiotherapy in critically ill children is influenced by their resting condition and their ability to use 'reserve capacity' to increase oxygen extraction (Weissman et al. 1994;Horiuchi et al. 1997). Increases in physiological activity related to physiotherapy are

believed to involve both exercise-like, muscular responses and sympathetic, stress-like responses which include blood pressure and cardiac changes (Horiuchi et al. 1997). Although the exercise-response can be abolished by inducing pharmacological paralysis (as in child H.I.), the sympathetic response is not abolished by this method. This child's adverse response may relate to the pattern of physiotherapy (inflations, CWV and treatment duration) and / or to the pattern of suction (duration, repetition and use of saline). Saline has previously been reported to reduce oxygen saturation for patients with head injury (Ackerman & Mick 1998), and this child received double the median volume of saline recorded in the study. Other potentially detrimental influences include the impact of bolus sedation on ventilation and oxygenation (Barr & Donner 1995;Angelini et al. 2001). In addition, vagal stimulation either as a direct result of suctioning or resulting from the enhanced movement of airway secretions more centrally may result in adverse changes in intracranial pressure and arterial saturations (Kerem et al. 1990;Shah et al. 1992;Gemma et al. 2002). The possibility of such an occurrence is suggested by the absence of improvement in arterial saturation merely on increasing the inspired oxygen concentration. Useful additional information on the cardiac effects of the physiotherapy could have been obtained with the NICO® respiratory monitor, which additionally provides a non-invasive measure of cardiac output (**section 4.5.1**). Simultaneous measurements of oxygen consumption, carbon dioxide production and cardiac output would have provided valuable insights into the patient's stress response to treatment. Further studies should explore these measures in combination with medium term outcome measures, co-relating the short and medium-term changes. Reassuringly, of the 5 children with head injury only child H.I. responded adversely to treatment.

Another high-risk group may be those children who have undergone repair of tracheal stenosis, a condition characterised in a subgroup of the children by tracheo-malacia distal to the site of repair. All six children who underwent surgery received similar physiotherapy treatments yet two showed worse outcomes than the others following physiotherapy. One of these children was treated by the clinical specialist, and was the only child treated by her to show a significant rise in airway resistance (40%) with a 3% drop in arterial saturation following physiotherapy (**section 3.4.9.7**). The deterioration following treatment in this child suggests that despite the physiotherapist's skill there may be occasions where treatment is particularly difficult, physiotherapy resulting in an adverse response. This new technique offers the opportunity to identify patient groups who may

have a heightened vulnerability to physiotherapy and to define appropriate treatment strategies to optimise patient care.

4.4.4.2 Treatments for prophylaxis and resolution of acute respiratory problems

Chest physiotherapy is used not only to resolve instances of acute secretion retention but also prophylactically, to prevent respiratory complications from ventilation. In such circumstances, one might not expect dramatic improvement in the respiratory and blood markers, as the treatment is aimed at maintaining the child's existing clinical status. Indeed, whilst child C showed significant improvement in short-term measures including lung compliance and resistance following the morning treatment recorded on video and presented in this thesis, the afternoon treatment resulted in less dramatic changes. This may reflect the child's improved pre-treatment baseline following the morning treatment. This observation emphasises the difficulty of conducting valid clinical repeatability studies because of frequent, rapid changes in the children's clinical status (**section 2.2**). Further studies are required to determine the role of prophylactic treatments and to explore the impact of chest physiotherapy (**section 4.5**). The clinical significance of short-term changes and their impact on medium term health indices such as length of time on a ventilator or length of stay in ICU remain unknown. Further studies should explore medium term outcome measures, relating these to the short-term changes.

4.4.4.3 Clinical expertise and the 'cost-benefit relationship' of treatment

It is known that chest physiotherapy and suction may result in adverse haemodynamic, metabolic, cardiovascular or cerebrovascular responses, and that children may be particularly susceptible (Zidulka et al. 1989;Horiuchi et al. 1997;Argent & Morrow 2004;Morrow et al. 2006). The 'cost' of treatment will depend not only on the treatment pattern given but also on the clinical stability and vulnerability of the child. Such factors are likely to influence the physiotherapy treatment, as suggested by the proportionately low force used to treat a 14 year old with a 'rejecting' heart transplant (**Figure 3.7**). In this research the child's severity of illness was quantified by measures including PRISM scores, oxygenation indices and the number of days since the onset of the current acute episode (Trachsel et al. 2005;Willson et al. 2005;Brady et al. 2006). Such measures give a global indication of the child's vulnerability. However, effective treatment may depend on less quantifiable aspects of treatment relating to factors including the physiotherapist's

clinical expertise. Physiotherapists rely upon a combination of feedback mechanisms including auditory, visual and tactile input, all of which will be influenced by level of clinical expertise. For example, an experienced physiotherapist may process considerable amounts of information regarding the child's clinical condition and general vulnerability to treatment during the initial assessment prior to commencing treatment. The therapist will additionally be ensuring the child has appropriate pre-treatment medication, including sedation, analgesia or bronchodilator therapy. Further information concerning the child's clinical condition, including the degree of chest wall compliance and airways obstruction, secretion retention and the child's response to treatment, would be gained throughout treatment, commencing during the first few breaths of lung inflations, the force and ventilatory patterns being modified according to the feedback received. For example, lower forces may be required to increase expiratory flow in more compliant chests (**section 4.4.3.2**) or a greater time may be required for expiration to prevent lung hyperinflation when airways obstruction is present. Visual displays of respiratory flows, pressures and volumes could greatly facilitate assessment of the child's response. The concept that physiotherapists modify their technique in response to feedback could be investigated in future clinical trials using this technique to explore whether treatment changes progressively over serial sessions given by the same physiotherapist to an individual patient.

In this study, arterial carbon dioxide rose significantly immediately physiotherapy ceased, but returned to pre-treatment levels within 15 minutes. This transitory change is perhaps surprising since one might have expected a drop in carbon dioxide levels following the lung hyperinflations. Explanations may include the fact that secretion removal from the more peripheral to more central airways compromised ventilation (especially in the paralysed patients). In addition, clearance of airways obstruction will initially increase deadspace, increasing the ventilation-perfusion mismatch, thereby influencing both oxygen saturation and carbon dioxide retention (Main & Stocks 2004). Subgroup analysis according to physiotherapist suggested that this rise in carbon dioxide may be related to physiotherapy techniques, since no increase was observed in the children treated by the clinical specialist (**section 3.4.9.7**). Further explanations include the fact that this therapist predominantly treated cardiac children. The patient's diagnosis, major airway stability, type of sedation/paralysis, cough response and clearance of secretions during intervention would all have been important variables in influencing outcome.

4.4.5 Generalisability of the results

The novel technique developed in this thesis to characterise chest physiotherapy is suitable for use in both paralysed and spontaneously breathing patients in hospitals and in the community, to monitor treatments in adults and in children. While it is not possible to define 'best practice' from the current thesis, this research has provided the technology and analysis format for use in future studies. Indeed the research group at the UCL, Institute of Child Health with Great Ormond Street Hospital for Children is currently expanding the studies incorporating this technology, as discussed in **section 4.5**.

The existence of a broad range of treatment patterns in current use raises the question as to what extent clinical practice should be standardised. Whilst a degree of flexibility will be required to accommodate the individual patient's response to treatment, there is a need to conduct studies to produce guidelines to optimise clinical practice and minimise adverse events. This study has demonstrated that such guidelines will be dependent on the age and clinical condition of the child. The heterogeneity of the children's clinical conditions monitored in this study has suggested individuals in whom treatment may be particularly difficult, including those with haemodynamic or cerebrovascular instability (head injury), following upper airway surgery (tracheal stenosis) and in those with bronchospasm and airways obstruction, including bronchiolitis.

Since the clinical specialist delivered 24 of the 62 treatments, analysis of the data was additionally performed separating the clinical specialist from the remaining physiotherapists (**section 3.4.9.7**). In general, similar results were produced for the specialist as for the remaining therapists, confirming the generalisability of these results. Furthermore, although the specialist predominantly treated children with cardiac disease, this should not have diminished generalisability of the findings, since treatment outcomes in those with and without cardiac disease overlapped (**section 3.4.7**).

4.4.6 When should CWV be used?

In this study the children were treated with CWV because of acute respiratory problems and secretion retention or because they were acutely vulnerable to respiratory compromise during mechanical ventilation, as discussed in **section 1.3**. Although CWV are used to replace the expiratory effort during the expulsive phase of cough, there is no isometric muscular contraction against a closed glottis, the compressive phase responsible for

generating the high initial intra-thoracic pressures and resultant high expiratory flows (McCool 2006). Furthermore, the effects of the CWV on PEF may be reduced by dissipation of the force during cephalad displacement of the abdominal contents (Maclean et al. 1989). Previous research has shown that whilst PEF generated during CWV increased by 150% in healthy adults compared to during normal tidal breathing, the value obtained during CWV was at least 80% lower than that generated by the same adult during a spontaneous cough (McCarren et al. 2006a). A similar discrepancy between CWV and cough was also found in young adults with cystic fibrosis (McCarren & Alison 2006). Although it is difficult to make direct comparisons between subjects of such differing body size and ages, the average increase during CWV compared with tidal breathing was similar to that observed in the ventilated children (130%). In this study no data were collected during cough, but it is likely that the PEF generated during CWV in intubated children will also be significantly lower than the maximum rates that would have resulted from cough. Further work is needed to compare expiratory flow during CWV and cough in intubated children. Based upon the current data and McCarren's research it would appear that CWV are unlikely to be appropriate in situations where secretions are easily mobilised and where the patient is able to produce an effective cough to clear secretions. By contrast, the demonstrable and age-related additional effect of CWV on PEF, over and above that due to inflation volume, may be beneficial in cases where secretions are tenacious (as in cystic fibrosis) or when the patient's own ability to clear secretions is compromised (for example in those with neuromuscular disease or during mechanical ventilation).

4.5 Future Directions

Future clinical studies can now be extended to explore treatments in adults and spontaneously breathing patients of all ages. The research should aim to define 'best practice' for patients of all ages by evaluating treatment response to standardised procedures. By studying patients with more homogenous lung conditions the significance of clinical changes may be more easily interpreted. Having established the validity of this technology and the data collection protocols, the value of changes in PEF during treatment as a surrogate for airway clearance could be further explored by direct comparisons with sputum clearance. Further work is required to model the effects of increased expiratory flows on mucus transport mathematically. Randomised placebo-controlled trials are required to explore the short and medium-term impact of 'best practice' chest physiotherapy.

The current research suggested there is a role for a realistic manikin and a modified, commercial version of this respiratory-force technology for research purposes, for monitoring clinical practice and as an objective training aid for professionals and carers within the clinical / academic environment and in the community. No such manikin was available commercially at the inception of this thesis. To this end commercial collaborations have been forged and realistic prototype manikins with inflatable 'lungs' have now been produced (**Appendix E**). Wider applications exist in the field of resuscitation training, in terms of both modifying the system for evaluating the forces applied during cardio-pulmonary resuscitation and monitoring lung recruitment techniques during manual lung inflations. Since these inflation techniques are widely used by medical and paramedical personnel, in-vivo research is also required to explore the impact of the resulting short-term ventilatory changes on lung injury.

Important questions that are currently being addressed using the new technique in this research group at UCL, Institute of Child Health include:

1. Characterisation of chest physiotherapy in mechanically ventilated adults
2. Quantification of characteristics differentiating specialist and 'on-call' physiotherapists' treatments
3. Manikin studies to explore the inter-relationship of CWV and lung inflations
4. Use of abdominal binders to augment PEF during CWV in ventilated patients
5. Modelling of the effects of airflow on mucus transport

4.5.1 Comparison of CWV forces in ventilated adults and children

Primary researcher H. Shannon, in collaboration with G. Ntoumenopoulos et al., Guys and St Thomas' NHS Foundation Trust

Data are being collected to explore whether the force-age relationship observed in children ceases in adulthood, once chest wall compliance has stabilised. Clinical data are also required to explore flows, pressures and volumes during chest physiotherapy in ventilated adults. The $CO_2SMO^{®}$ has recently been superseded by the company's upgraded respiratory monitor, the $NICO_2^{®}$; this is being evaluated to explore the extent to which the problems encountered with its predecessor have been resolved. As discussed in **section 4.4.4.1**, this monitor offers the additional advantage of providing non-invasive cardiac output measurements.

4.5.2 Quantification of characteristics differentiating specialist and 'on-call' physiotherapists' treatments in paediatric ICU

Primary researcher H. Shannon

A cross-over design study is currently underway to explore differences between the treatment characteristics of senior physiotherapists who have specialised in the treatment of mechanically ventilated children with those who only cover the intensive care units at night or during week-ends on an 'on-call' basis. The multivariable analysis approach developed in the current research will be used to compare changes in PEF within individual children when treated by an experienced and by an 'on-call' physiotherapist.

4.5.3 Manikin studies to explore the inter-relationship of CWV and lung inflations.

Primary researcher R. Stiger (née Dell)

Conference Presentations:

Shannon, H., Dell, R., Gregson, R.K., Main, E. (2008) *"Timing of chest wall vibrations within the breath cycle: Effects on peak flow and pressure in a ventilated lung model."* Chartered Society of Physiotherapy Congress, Manchester.

Stiger, R., Shannon, H., Main, E., (2008) *"Are chest wall vibrations in ventilated patients more effective with ventilator or manual hyperinflations?"* European Respiratory Society Congress, Berlin.

The use of the realistic manikin provides an opportunity to explore single CWV treatment features while controlling ventilatory variables, thereby producing a valid treatment model without compromising patient care. Current studies have explored the effect of varying the timing of CWV during lung inflations (Shannon et al. 2008 conference presentation). Such data will provide an opportunity to optimise techniques to augment flow and mobilise secretions. The lung model also allows comparison of the effects of manual and ventilator hyperinflation on peak expiratory flow, with and without chest wall vibrations (Stiger et al. 2008 conference presentation). Important additional questions to be addressed include exploration of within and between-operator variability of CWV when 'treating' a manikin ventilated with a standardised respiratory pattern.

4.5.4 Use of abdominal binders to augment PEF during CWV in ventilated patients

Primary researcher P Rajoo, in collaboration with G. Ntoumenopoulos et al., Guys and St Thomas' NHS Foundation Trust

It has been suggested that the use of 'abdominal binders' improves trans-pulmonary transmission of the force applied and increases PEF by reducing displacement of the abdominal contents during CWV (Maclean et al. 1989). The current technique is being used in a study of ventilated adults to explore the effect of abdominal binders on PEF during CWV. Use of such binders to augment PEF and promote secretion clearance may allow lower forces to be used during chest physiotherapy.

4.5.5 Modelling of the effects of airflow on mucus transport

Dissertations:

Setchi A,. (2007) *"Mathematical modelling of lung physiotherapy"*. Dissertation for the degree of Master of Science, University of Oxford.

Carter R., (2006) *"Mathematical modelling of lung mucus clearance during manual physiotherapy."* Report for the Royal Society, University of Oxford.

Collaborations have been forged with researchers at Oxford University to develop mathematical models explaining how the changes in airflow during chest physiotherapy affect mucus clearance from the lungs (lead collaborator, Dr T Roose). Data gained from the current study are being used to test two models to explore the interaction of airflow and mucus firstly in rigid upper airways and secondly in compliant small airways, relating airflow to the force applied.

Additional areas of research proposed for future studies include:

4.5.6 Randomised controlled trials to evaluate 'optimised' chest physiotherapy techniques

Randomised controlled trials exploring short and medium-term outcomes are required in more homogenous groups of patients (in terms of pathophysiology and age), comparing 'best practice' physiotherapy techniques with suction techniques performed as part of routine nursing care. Prior to such studies, use of the new manikins (**Appendix E**) could confirm whether the participating physiotherapists were able to deliver: i) consistent lung inflations, and ii) consistent CWV in conditions of standardised lung ventilation.

4.6 Summary & Conclusions

In addition to achieving all the specified aims, this multi-disciplinary research has provided a wealth of unique information regarding the patterns of CWV and the simultaneous respiratory changes, highlighting the importance of the accompanying manual lung inflations. Considerable new evidence has been provided with which to generate further hypotheses. The research has demonstrated that an increase in PEF during physiotherapy was related both to the magnitude of the manual lung inflations and forces applied. Moreover, the clinical data collected in these ventilated children have enabled models to be constructed to quantify the 'added value' of the CWV on PEF, over and above that resulting from the accompanying alterations in ventilatory pattern. The wide spectrum of physiotherapy practice observed in this study with respect to lung inflations and force profiles may reflect a number of factors including the age of the child and underlying pathophysiology. Such factors will need to be explored thoroughly in future clinical trials. Clinical studies incorporating this technique will allow physiotherapists to explore objectively why some treatments enhance respiratory function whilst others do not, providing an important tool with which to develop evidence-based practice.

The integrated system also has a potential application in teaching and training of both health professionals and family members giving chest physiotherapy at home; this could greatly facilitate the delivery of optimal treatment for patients in the future.

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