APPENDIX A

Publications (copyright permission obtained for reprint)**:**

Gregson, R. K., Stocks, J., Petley, G. W., Shannon, H., Warner, J. O., Jagannathan, R., & Main, E. 2007, "Simultaneous measurement of force and respiratory profiles during chest physiotherapy in ventilated children", *Physiol Meas.*, vol. 28, no. 9, pp. 1017-1028.
Electronic version with multimedia enhancements *http://stacks.iop.org/0967-3334/28/1017*

Gregson, R. K., Shannon, H., Main, E., & Stocks, J. 2007, "Factors influencing change in peak expiratory flow during chest physiotherapy in mechanically ventilated children", *Thorax*, vol. 62, no. Suppl_3, p. A78.

Gregson, R., Shannon, H., Main, E., Dunne, C., Warner, J., Goldman, A., & Stocks, J. 2007, "The relationship between age and forces applied during chest physiotherapy in mechanically ventilated children", *Physiotherapy*, vol. 93, no. Supplement 1, p. S517.

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.

Shannon, H., Gregson, R., Stocks, J., Cole, T. J., & Main, E. 2009, "Repeatability of physiotherapy chest wall vibrations applied to spontaneously breathing adults", *Physiotherapy*, vol. 95, no. 1, pp. 36-42.

Copies of **Publicity and Media Coverage** (2003-2008) included articles in:

- Portex Newsletter, UCL, Institute of Child Health, Autumn 2008, Issue 1, p5 'Cardio-Respiratory Physiotherapy'
- UCL, Institute of Child Health's Annual Research Review 2007, highlighting physiotherapy research at GOSH/ICH and the SPARKS project entitled 'Respiratory physiotherapy for children on ventilators'
- SPARKS News, 2006 no.1 'Baby sensing mat that may help ease breathing problems'
- www.londonpress.info STM_09184 13.02.2004
http://www.londonpress.info/lps/article.asp?uniqueID=3127&category=science
- University of Southampton bulletin, 01.09.2003
- http://news.bbc.co.uk/1/hi/england/hampshire/dorset/3185353.stm 23.08.2003
- http://www.innovations-report.com/html/berichte/medizin_gesundheit/bericht-20922.html 28.08.2003
- http://www5.medica.de/cipp/md_medica/custom/pub/content,lang,2/ticket,g_a_s_ 28.08.2003
- http://www.therapyweekly.co.uk 04.09.2003

APPENDIX B

Confirmation of Ethics' Committee Approval, information leaflet and consent form for the clinical study and repeatability studies at Great Ormond Street Hospital for Children NHS Trust (04AR10) and for the pilot studies in healthy children and in the paediatric ICU at Southampton University Hospitals NHS

APPENDIX C Data collection and analysis

(in **section 3.3.4**)

An example of the treatment data sheets and analysis databases used to explore individual children and group data. Child C's study code was 5029; the first treatment was video recorded (502901), a second treatment being monitored for the study later the same day (502902).

APPENDIX D PEF calculations

D.1 Calculations of the factors influencing PEF during CWV, alternatively using maximum (Fmax) and mean force (Fmean).

D.2 Full calculation details for exploration of the PEF model in a 1 and 10 year old

D.3 Quantification of treatment effects within individual children. Full calculation details for:
A & B) Validation of the PEF models using data from child C and child B

C) Analysis using the *complete data sets* for child C and child B

(Child C's study code = 502901; complete data records in Appendix C)

D.1 Calculations of the factors influencing PEF during CWV, alternatively using maximum (Fmax) and mean force (Fmean); in **section 3.4.6.2.2**

Equation 3.2 Factors influencing peak expiratory flow during chest wall vibrations; calculations involving maximum force

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

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

Equation D.1 Factors influencing peak expiratory flow during chest wall vibrations; calculations involving mean force

$\mathbf{PEF_{CP}}$ l/min/kg = **1.04** (0.87, 1.21) **constant** + **0.053** (0.036, 0.069) **VI** (ml/kg) + **-0.086** (-0.108, -0.064) **Age** (y) + **0.001** (0.005, 0.015) **Fmean** (N) ($R^2 = 0.49$)

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

D.2 Full calculation details for exploration of the PEF model in a 1 and 10 year old (in **section 3.4.6.2.4**)

The analysis models were verified using examples of a 1 and 10 year old child, comparing the calculated results with data recorded during the study. Estimates of PEF were derived after substituting the average observed values of VI and force into **Equations 3.1** and **3.2** (copied below).

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

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

Equation 3.2 Factors influencing peak expiratory flow during chest wall vibrations

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

Evaluation of the age-effect and '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** (copied below). Inflation volume during CWV was assumed to be 14.6 ml/kg, VI was assumed to be 7.2 ml/kg during baseline mechanical ventilation, rising to 8.8 ml/kg during manual inflations and 14.6 ml/kg in the breaths immediately prior to application of CWV, equal to the average group value in **Table 3.4**.

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	0.85
3) PEF_{Minf} at 14.6 ml/kg VI[a]	1.50	1.16
4) PEF_{CP} at 14.6 ml/kg VI & 60 N CWV	2.10	1.36
5) 'Added value' of 60 N CWV on PEF	*54%*	*27%*

[a] 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 3.4.6.2.1**

PEF_{Minf} - PEF during manual inflations; PEF_{CP} - PEF during chest physiotherapy (CWV & manual inflations)

A) Calculation details in a 1 year old.

1) PEF during baseline mechanical ventilation (using equation 3.1)
= 0.79 + (0.052 x 7.2 ml/kg) + (-0.042 x 1)
= **1.12 l/min/kg**

2) PEF during manual inflations, PEF_{Minf} (using equation 3.1)
PEF_{Minf} = 0.79 + (0.052 x 8.8 ml/kg) + (-0.042 x 1)
= **1.20 l/min/kg**

3) PEF due to increased VI during CWV, PEF_{Minf} (using equation 3.1)
PEF_{Minf} = 0.79 + (0.052 x 14.6 ml/kg) + (-0.042 x 1)
= **1.50 l/min/kg**
(a theoretical value, as this flow cannot be recorded due to the effects of the accompanying CWV).

4) Application of 60N during CWV (using equation 3.2)

PEF_{CP} = 1.04 + (0.054 x 14.6 ml/kg) + (-0.086 x 1 y) + (0.006 x 60 N)
= 2.10 l/min/kg

5) 'Added value' of CWV on PEF = 100 x ((2.1 - 1.50) / 1.12) = **54%**

B) Calculation details in a 10 year old.

1) PEF during baseline mechanical ventilation (using equation 3.1)

= 0.79 + (0.052 x 7.2 ml/kg) + (-0.042 x 10)
= **0.74 l/min/kg**

2) PEF during manual inflations, PEF_{Minf} (using equation 3.1)

PEF_{Minf} = 0.79 + (0.052 x 8.8 ml/kg) + (-0.042 x 10)
= **0.83 l/min/kg**

3) PEF due to increased VI during CWV, PEF_{Minf} (using equation 3.1)

PEF_{Minf} = 0.79 + (0.052 x 14.6 ml/kg) + (-0.042 x 10)
= **1.13 l/min/kg**

(a theoretical value, as this flow cannot be recorded due to the effects of the accompanying CWV).

4) Application of 60N during CWV (using equation 3.2)

PEF_{CP} = 1.04 + (0.054 x 14.6 ml/kg) + (-0.086 x 10 y) + (0.006 x 60 N)
= 1.33 l/min/kg

5) **'Added value' of CWV on PEF =** 100 x ((1.33 - 1.13) / 0.74) = **27%**

6) Application of 100N during CWV

PEF_{CP} = 1.04 + (0.054 x 14.6 ml/kg) + (-0.086 x 10 y) + (0.006 x 100 N)
= 1.57 l/min/kg

7) 'Added value' of CWV on PEF = 100 x ((1.57 - 1.13) / 0.74) = **59%**

D.3 Quantification of treatment effects within individual children (in **section 3.4.9.3**)

The analysis models were additionally verified with data recorded during the study. Estimates of PEF were derived for individual children (child C and child B) after substituting observed values of VI, age and force into the analysis detailed in **Equations 3.1** and **3.2**.

A) Validation of the model using data from child C: an 8 month (0.67y) 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 41N).

The observed changes in PEF, together with those predicted when applying the equations under the various measurement conditions are summarised in **Table 3.10**, **section 3.4.9.3.1**.

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

	PEF (l/min)	
	Observed	**Predicted**
1) PEF at 7ml/kg baseline VI	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 & 41 N CWV	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

Calculation details in child C.

1) PEF during baseline mechanical ventilation
= 0.79 + (0.052 x 7ml/kg) + (-0.042 x 0.67y)
= **1.12 l/min/kg or 11 l/min**

2) PEF during manual inflations (PEF_{Minf})
PEF_{Minf} = 0.79 + (0.052 x 10 ml/kg) + (-0.042 x 0.67y)
= **1.28 l/min/kg, or 13 l/min**

3) PEF due to increased VI during CWV (PEF_{Minf})
PEF_{Minf} = 0.79 + (0.052 x 17 ml/kg) + (-0.042 x 0.67y)
= **1.65 l/min/kg or 17 l/min**
(a theoretical value, as this flow cannot be recorded due to the effects of the accompanying CWV)

4) Application of 41N during CWV
PEF_{CP} = 1.04 + (0.054 x 17 ml/kg) + (-0.086 x 0.67 y) + (0.006 x 41 N)
= 2.11 l/min/kg, or 21 l/min

5) 'Added value' of CWV on PEF = 100 x ((27 - 17) / 9) = **111%**

B) Validation of the model using data from child B: in 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 79N).

The observed changes in PEF, together with those predicted when applying the equations under the various measurement conditions are summarised below as in **Table 3.11 (section 3.4.9.3.2**).

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

	PEF (l/min)	
	Observed	**Predicted**
1) PEF at 5.4 ml/kg baseline VI	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

Calculation details in child B.

1) PEF during baseline mechanical ventilation
= 0.79 + (0.052 x 5.4 ml/kg) + (-0.042 x 1y)
= **1.03 l/min/kg or 9.3 l/min**

2) PEF during manual inflations (PEF_{Minf})
PEF_{Minf} = 0.79 + (0.052 x 4.8 ml/kg) + (-0.042 x 1y)
= **1.00 l/min/kg or 9.0 l/min**

3) PEF due to increased VI during CWV (PEF_{Minf})
PEF_{Minf} = 0.79 + (0.052 x 5.7 ml/kg) + (-0.042 x 1y)
= **1.05 l/min/kg or 9.5 l/min**
(a theoretical value, as this flow cannot be recorded due to the effects of the accompanying CWV)

4) Application of 62N during CWV
PEF_{CP} = 1.04 + (0.054 x 5.7 ml/kg) + (-0.086 x 1y) + (0.006 x 79 N)
= 1.74 l/min/kg, or 15.6 l/min

5) 'Added value' of CWV on PEF = 100 x ((9.9 – 9.5) / 9.4) = **4%**

C. Analysis using the *complete data sets* for child C and child B (in section 3.4.9.3.2, **Tables 3.12** and **3.13**).

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

	PEF (l/min)	
	Observed	**Predicted**
1) PEF at 70 ml baseline VI	9	11
2) PEF_{Minf} at 100 ml VI	15	14
3) PEF_{Minf} at 170 ml VI	NA[1]	19
4) PEF_{CP} at 170 ml VI & 41 N CWV	27	27
5) 'Added value' of 41 N CWV on PEF	***89%***	

[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

Child C: VI was 70 ml during baseline mechanical ventilation, rising to 100 ml during manual inflations and 170 ml in the breaths immediately prior to application of CWV (Fmax 41N).

Equation D.2 Factors influencing peak expiratory flow, in the *absence* of force in child C

PEF l/min = 5.86 (constant [95% CI: 4.16, 7.55]) + (VI ml x 0.077 [95% CI: 0.060, 0.095]), ($R^2 = 0.45, p < 0.001$)

1) PEF l/min during baseline ventilation
= 5.86 (constant) + (70 ml x 0.077)
= 11.3 l/min

2) PEF_{Minf} l/min
= 5.86 (constant) + (100 ml x 0.077)
= 13.6 l/min

3) PEF_{Minf} l/min (*hypothetical value, as in Table D.3*)
= 5.86 (constant) + (170 ml x 0.077)
= 19 l/min

Equation D.3 Factors influencing peak expiratory flow during chest wall vibrations in child C

PEF_{CP} l/min = 6.69 (constant [95% CI: 5.13, 8.25])) + (VI ml x 0.069 [95% CI: 0.053, 0.084]) + (Fmax N x 0.21 [95% CI: 0.15, 0.26]) ($R^2 = 0.73, p < 0.001$)

4) PEF_{CP} l/min
= 6.69 (constant) + (170 ml x 0.069) + (41 N x 0.21)
= **27 l/min**

5) 'Added value' of CWV on PEF = 100 x ((27 – 19) / 9) = **89%**

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

	PEF (l/min)	
	Observed	**Predicted**
1) PEF at 49 ml baseline VI	9.4	8.8
2) PEF_{Minf} at 43 ml VI	7.1	8.5
3) PEF_{Minf} at 49 ml VI	NA[1]	8.8
4) PEF_{CP} at 49 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

Child B: median VI was 49 ml during baseline mechanical ventilation, falling to 43 ml during manual inflations, and 49 ml in the breaths immediately prior to application of CWV (Fmax 79 N).

Equation D.4 Factors influencing peak expiratory flow, in the *absence* of force in child B
PEF l/min = 6.08 (constant [95% CI: 5.29, 6.88]) + (VI ml x 0.055 [95% CI: 0.039, 0.071]),
$R^2 = 0.23, p < 0.001$

1) PEF l/min during baseline ventilation
= 6.08 (constant) + (49 ml x 0.055)
= 8.8 l/min

2) PEF_{Minf} l/min
= 6.08 (constant) + (43 ml x 0.055)
= 8.5 l/min

3) PEF_{Minf} l/min (*hypothetical value, as in Table D.3*)
= 6.08 (constant) + (49 ml x 0.055)
= 8.8 l/min

4) CWV force did not contribute significantly to PEF (p = 0.81)

APPENDIX E Commercial production of training aids

(**section 4.5**)

Marketable products and commercial competition

As a result of the research and development described in Chapter 2 (technique development and repeatability study), there appeared to be a need and market opportunity for the production of commercial chest physiotherapy training aids:

1. a realistic manikin as a patient substitute
2. a portable mat system to train and monitor treatment of patients

Such systems would have wide potential application in the teaching and training of both health professionals and family members giving chest physiotherapy at home to children or adults with chronic chest disorders. The repeatability studies (**section 2.3**) have additionally highlighted a role for a realistic manikin with a consistent respiratory pattern to be used in such studies. These training aids would additionally help address the issues of clinical governance, and the need for structured learning of treatment skills (Scally & Donaldson 1998). The manikin would have wider application in terms of training in manual lung inflation techniques and in cardio-pulmonary resuscitation (CPR) as discussed below.

No such manikin was available commercially. The current resuscitation manikins did not feel lifelike, simulate the physical properties of the chest wall nor have a realistic chest motion (**Figure E.1**). To create a route to market, discussions were initiated and progressed with appropriate commercial companies. Trucorp Ltd specialises in the creation of manikins for intubation purposes whilst novel$_{gmbh}$ has expertise in dynamic pressure and force characterisation. Commercial and legal guidance was provided by Liz Fletcher, Life Science Business Manager, Centre for Enterprise and Innovation, University of Southampton, and Emma Pendleton, Research and Development Office Manager, UCL, Institute of Child Health.

Aims and specifications

1. Development of a **realistic 'respiring' manikin** incorporating the pressure/force sensing technology into the 'skin' as a training aid for health professionals and families of children with chronic lung disease.
2. The **manikin** should have additional application in the field of cardiopulmonary resuscitation.
3. Development of a **pressure / force mat system**, for use with patients requiring chest physiotherapy. The mats will be 'simplified', using larger and fewer sensors than in the current prototypes.

Bio-feedback displays will be incorporated to indicate key force and respiratory variables.

Table E.1 provides descriptions of the commercial products proposed, summarising the status of the development and detailing the proposed markets. As a precursor to the manikin with sensors within the 'skin', an interim phase was included (product 2), whereby realistic chest physiotherapy manikins were created, and are currently being trialled at Great Ormond Street Hospital for Children, in combination with the existing prototype sensing mats.

Table E1

This phase hastened development of the manikin and allowed optimisation of the specifications required of both the sensing mats and manikin.

The requirements of the manikin measuring system are that it must:

- Be available in three models, the adult manikin version being created first:
  a) adult (for children above 10 years)
  b) paediatric (3 months – approximately 10 years, ie. 6-40 kg)
  c) infant (less than 5kg, approximately 3 months)
- The manikin will incorporate variable compliance of both the chest wall and the 'lungs'/bellows. Similarly, resistance to inspiratory and expiratory airflow will be variable, airflow and pressure being measured at the airway opening.
- Have a chest that feels lifelike, with a realistic chest composition that moves in an anatomically true way.
- Incorporate the pressure / force sensors into the manikin's 'skin'
- Incorporate analysis software to overlay and process the chest physiotherapy force and respiratory data
- Be affordable, transportable, with a carrying case, and be simple enough for carers to operate

Summary of progress to date

The processes completed to date are summarised below. Details of the future plans agreed to date are then provided.

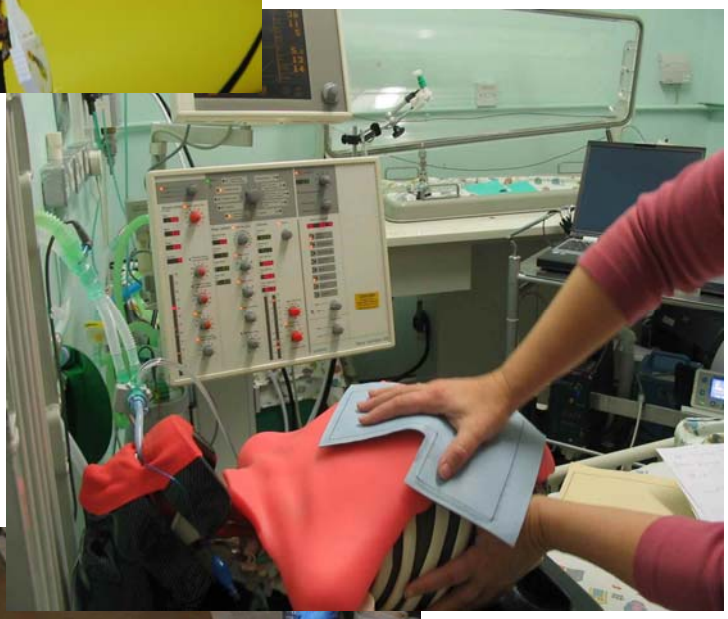
Processes completed

All the relevant stake-holders, including the charitable funding bodies involved, have been identified, and the percentage contribution of each party has been formalised and agreed. All commercial parties involved in the production of the training aids have signed Non-Disclosure Agreements. A summary of the planned commercial products and the timescales involved, has been tabulated (**Table E.1**), and the proposed markets have been identified. Market research has been undertaken by the commercial companies and the Centre for Enterprise and Innovation to confirm suggestions that a viable market opportunity exists. The steps required by the various parties to progress the products to market have been agreed. Reciprocal input from the various parties has been formalised. For example, a Research Evaluation Agreement has been drawn up between UCL, Institute of Child Health / Great Ormond Street Hospital for Children, London and the manikin company. This agreement formalises an arrangement whereby a 'physiotherapy manikin' is supplied free of charge to Great Ormond Street, London, in exchange for trial data about the performance of the manikin in the proposed new application. Preliminary evaluation of the initial prototype 'physiotherapy manikin' (**Figure E.1**) has been undertaken, and feedback provided on such areas as the composites used to create the 'chest and skin', and the characteristics of the inflatable 'lungs'. A subsequent prototype manikin (**Figure E.2)** is currently being trialled by physiotherapists at Great Ormond Street Hospital for Children.

Figure E.1 Commercially available rigid resuscitation manikin (a) and phase 1 prototype flexible manikin (b & c)

Top skin covering (red) reveals the rib structure underneath, which would normally be concealed beneath the skin. The manikin is intubated to allow 'lung' inflation, with the force-sensing mat in situ

(a)



(b)

(c)

Agreed processes

A series of trials commenced in January 2008 and have resulted in modifications to the initial prototype manikin, as shown in Figures E.1 and E.2. The manikin will also be trialled to explore its expanded capabilities as a training aid in cardiopulmonary resuscitation. Applications for technology grants will be prepared for early in 2009, to fund the production of a commercial training manikin which incorporates force / pressure sensors within the 'skin' of the manikin. The 'sensitive skin' will be subdivided for activation of discrete areas; for example i) covering the left lung, right lung for physiotherapy training ii) over the heart for cardio-pulmonary resuscitation training.

Figure E.2 Phase 2 prototype flexible manikin