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Distribution of tidal ventilation during volume-targeted ventilation is variable and influenced by age in the preterm lung

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Abstract *Purpose:* Synchronised volume-targeted ventilation (SIPPV + VTV) attempts to reduce lung injury by standardising volume delivery to the preterm lung. The aim of this study is to describe the regional distribution and variability of ventilation within the preterm lung during SIPPV + VTV. *Methods:* Twenty-seven stable, supine, preterm infants with <32 weeks gestation receiving SIPPV + VTV were studied. From each infant, the anterior-to-posterior impedance change due to tidal ventilation (ΔZ_{VT}; countless units) was determined during every breath from three, 30-s, electrical impedance tomography recordings. ΔZ_{VT} within the anterior, middle and posterior thirds of the chest were compared using area under the curve analysis. The coefficient of variation (CV) of ΔZ_{VT} in the anterior and posterior hemithoraces, inflation pressure and, where available, V_T at airway opening were compared. Infants were sub-grouped by age ($\leq$7 and >7 days), supplemental oxygen requirement and set tidal volume. *Results:* In all sub-groups, the middle third of the chest accounted for the greatest ΔZ_{VT} [$p < 0.0001$, repeated-measures analysis of variance (ANOVA)]. The middle third of the chest constituted a greater relative ΔZ_{VT} in infants aged >7 days compared with $\leq$7 days ($p < 0.0001$, repeated-measures ANOVA). Set tidal volume and oxygen requirement did not significantly influence the regional distribution of ΔZ_{VT}. The mean (standard deviation, SD) CV of ΔZ_{VTANT} and ΔZ_{VTPOST} were 30.6% (14.0%) and 31.9% (12.7%). ΔZ_{VTANT} and ΔZ_{VTPOST} expressed greater breath-to-breath variability than the variation in inflation pressure and V_T at airway opening ($p = 0.012$ and $p < 0.0001$, respectively, paired *t*-tests). *Conclusion:* During SIPPV + VTV the preterm infant exhibits marked breath-to-breath variability in regional ventilation which is influenced by age.

Keywords Ventilation · Mechanical · Infant · Premature · Tidal volume · Electrical impedance tomography

Abbreviations

ΔZ	Relative impedance change
ΔZ_{VT}	Relative impedance change with tidal ventilation
ΔP	Pressure amplitude
CI	Confidence interval
CV	Coefficient of variation
EIT	Electrical impedance tomography
FiO_2	Fraction of inspired oxygen
IQR	Inter-quartile range
PEEP	Positive end-expiratory pressure

PIP	Positive inspiratory pressure	SIPPV	Synchronised intermittent positive pressure ventilation
RDS	Respiratory distress syndrome	VTV	Volume-targeted ventilation
SD	Standard deviation	V_T	Tidal volume

Introduction

Preterm lungs are particularly susceptible to ventilator-induced lung injury (VILI) [1, 2], a major contributor to chronic lung disease. VILI is multi-factorial and includes barotrauma, volutrauma, atelectotrauma and biotrauma, all processes exacerbated by ventilation inhomogeneity [3, 4]. Lung-protective ventilation strategies aim to reduce exposure to these factors [5, 6]. Recently, time-cycled, pressure-limited ventilation modes using volume-targeted ventilation (VTV) and synchronised with spontaneous inspiratory effort (SIPPV) have been advocated as a method of reducing volutrauma [7, 8].

During SIPPV + VTV, positive inspiratory pressure (PIP) is automatically adjusted after each inflation to achieve a constant, operator-determined tidal volume, generally derived from measurement of expiratory flow at the airway opening [9]. This method adapts to rapid compliance change but assumes the lung behaves as a single compartment with uniform mechanics [1]. In animal studies, the diseased lung exhibits regional variations in compliance [3, 4, 10, 11]. The resultant pattern of ventilation inhomogeneity can alter on a breath-by-breath basis, leading to regional asynchrony of tidal inflations [12, 13] such that delivered PIP may not be optimal for all regions. This may partly explain the relatively small reductions in morbidity when using SIPPV + VTV in preterm lung disease [7].

Electrical impedance tomography (EIT) is a technique that may overcome some of the practical difficulties of measuring regional lung mechanics at the bedside [14–17]. EIT is simple to use, non-invasive and independent of flow and has been validated against computed tomography, scintigraphy and gas wash-out techniques as a method for determining the relative distribution of ventilation [18–22]. EIT exploits differences in electrical impedance generated by changes in lung tissue conductivity due to tidal variations of gas volume during respiration [15, 18, 21, 23, 24] and has previously been used to describe regional ventilation characteristics in spontaneously breathing [16, 25] and mechanically ventilated infants [22]. Understanding the distribution of ventilation in the preterm lung may improve SIPPV + VTV, thereby reducing respiratory morbidity.

This study aims to describe the gravity-dependent regional distribution and variability of ventilation within the preterm lung during SIPPV + VTV.

Methods

A detailed description can be found in the Electronic Supplementary Material.

Study population

This study was performed in the Neonatal Unit, The Royal Women's Hospital, Melbourne and was approved by the institution's Ethics Committee. Informed parental consent was obtained for each infant.

Stable infants with <32 weeks completed gestation at birth, between 24 h and 10 weeks old and receiving SIPPV + VTV (Dräger Babylog 8000+; Drägerwerk, Lübeck, Germany) were eligible for inclusion. Ventilator settings, including the set tidal volume, were determined by the treating clinician and not altered during the study. Infants who were unstable during handling, with fragile skin, fractional inspired oxygen concentration (FiO_2) >0.9, refractory hypotension, active air leak syndrome, evolving abdominal pathology, congenital cardiac disease or chromosomal anomaly were excluded.

Measurements and method

Relative impedance change (ΔZ) during tidal inflations was measured in supine position using EIT (GeoMFII EIT system; Cardinal Health, Hoechberg, Germany) sampling at 44 Hz [26, 27]. This involved placing 16 pre-trimmed EIT electrodes equidistant around the thorax at nipple level. During a period of quiet rest, and at least 20 min since electrode application, three 2-min recordings, separated by at least 2-min intervals, were taken. The sequence was repeated 20 min later. Airway pressure was simultaneously recorded from the ventilator by the EIT unit. Tidal volume (V_T) at the airway opening was integrated from the flow signal acquired from the ventilator at 200 Hz using separate software. During each recording the infant's chest was video-recorded to detect movement artefact.

Data analysis

The six unfiltered EIT recordings were reviewed in reverse order (accounting for improved electrode conductance with time) using a custom-built program (MatLAB

Mathworks Inc., Natick, MA, USA). The first three, 30-s, artefact-free periods were selected, each from separate recordings. To determine ΔZ due to ventilation (ΔZ_{VT}), a low-pass filter was applied to the impedance signal at 10 breaths/min above the respiratory rate to eliminate signal noise and cardiac-associated impedance changes [15, 16, 22, 23].

Distribution of tidal ventilation

A functional EIT (fEIT) image was generated from each 30-s recording using the standard deviation of the impedance time course of each individual pixel within the 32 × 32 matrix [26, 28, 29]. The relative ΔZ_{VT} within each of the 32 anterior-to-posterior (gravity-dependent) chest slices was determined by summing all the pixel values within each slice [25, 30]. To simplify interpretation, the area under the curve (AUC) for the slices occupying the anterior, middle and posterior thirds of the chest, and the geometric centre of ventilation within the chest, was calculated [15, 25].

Regional variability of tidal ventilation

In each 30-s period, the PEEP to PIP amplitude (ΔP) for all inflations, and the corresponding ΔZ_{VT} amplitude in the anterior (ΔZ_{VTANT}) and posterior (ΔZ_{VTPOST}) hemithoraces, were determined. To compare the variability of ΔP, ΔZ_{VTANT} and ΔZ_{VTPOST}, the coefficient of variation (CV) in each recording was calculated. The CV of V_T at the airway opening within each 30-s recording was also determined if synchrony of the EIT and flow sensor signals could be confirmed for all inflations.

The study population was analysed overall and by the following subgroups: postnatal age (≤7 versus >7 days to delineate differences from pathological or maturational factors), inspired oxygen concentration (FiO_2; air versus FiO_2 >0.21) and by set VTV (≤3.0 versus >3.0 mL, 3 mL being the median value). A convenience sample of 30 infants was chosen, as differences in ΔZ_{VT} are not known. Data were analysed with *t*-test or repeated-measures ANOVA with Tukey post-test as appropriate using GraphPad Prism version 4.02 (Graphpad Software, San Diego, CA, USA).

Results

Demographics

During the study period 325 infants with <32 weeks completed gestation were admitted to our unit. Sixty-three were eligible for study. Twenty-three infants were not approached to participate for the following reasons: investigators unavailable (15), language/social barriers (5), death of a twin (2), severe intracranial pathology (1). Ten families declined consent. One infant died unexpectedly prior to being studied, and equipment failure rendered data unsuitable in a further two instances. Study protocol was completed for 27 clinically stable infants. From the resultant 81 complete sets of EIT data, 3,410 inflations were available for analysis. Artefact rendered 71 inflations unsuitable for analysis within the posterior hemithorax (total 3,339 inflations).

Table 1 Demographics and ventilation characteristics

	Total study population	Age	
		≤7 days	>7 days
n	27	16	11
Gestational age (weeks)	26 (2)	27 (2)	25 (2)
Age at study (days)	10 (10)	4 (1.5)	18 (12)
Birthweight (g)	851 (295)	905 (350)	773 (176)
Weight at study (g)	904 (316)	890 (356)	909 (252)
FiO_2	0.28 (0.13)	0.23 (0.03)	0.35 (0.17)
PEEP (cmH_2O)	5.6 (0.7)	5.5 (0.8)	5.7 (0.6)
V_T (mL)	3.6 (1.4)	3.4 (1.4)	4.0 (1.5)
V_T (mL/kg)	3.9 (0.6)	3.7 (0.4)	4.3 (0.8)*
SpO_2(%)	91.9 (5.7)	91.8 (6.5)	92.0 (4.1)
Heart rate	154 (13)	150 (12)	160 (12)
Respiratory rate	61 (13)	63 (14)	57 (9)

There was no difference in demographic characteristics within the inspired oxygen and VTV subgroups apart from the parameter that defined the group. All data mean (SD)

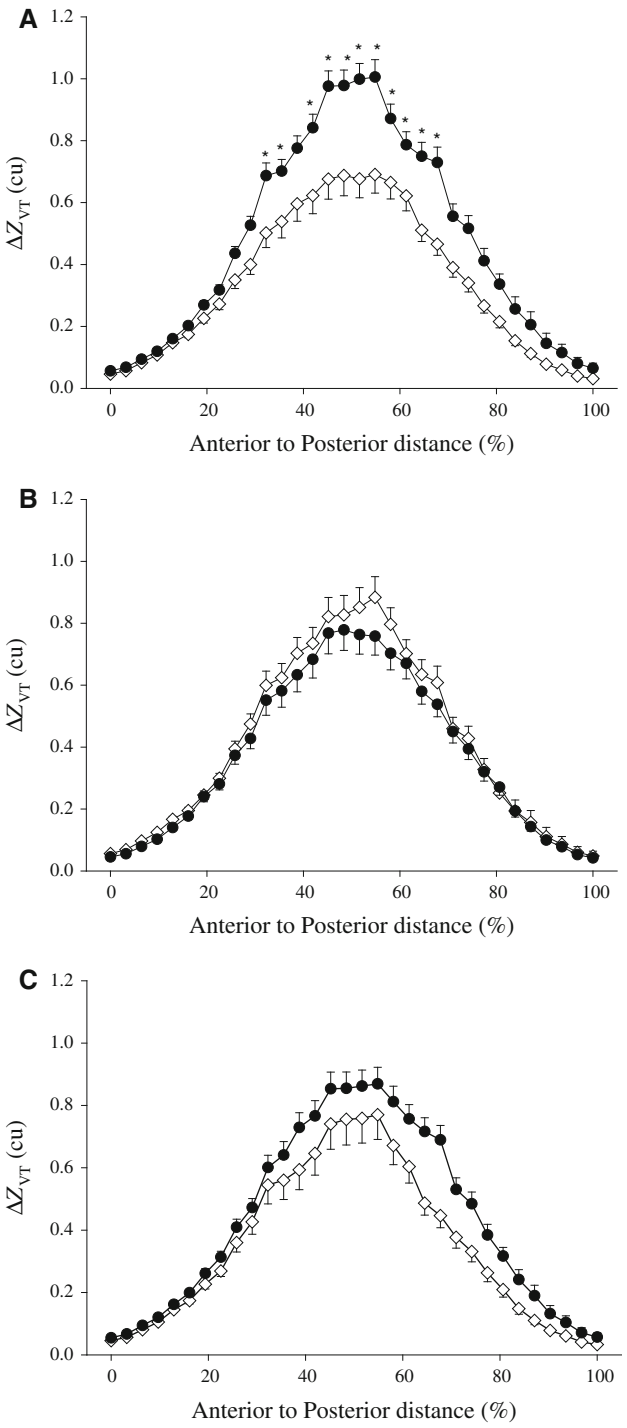
g grams, *FiO_2* fraction of inspired oxygen, *PEEP* positive end-expiratory pressure, V_T set tidal volume

* $p < 0.05$, *t*-test

Demographics and ventilation characteristics of the study population are summarised in Table 1. There were 16 infants aged ≤7 days, 15 requiring supplemental oxygen [mean (SD) FiO_2 0.36 (0.15)] and 12 whose set VTV was ≤3.0 mL. Fifteen had a PDA considered significant by the attending clinicians. This did not influence the results. No infants had an active air leak, although this had previously occurred in two infants. The mean (SD) endotracheal tube leak was 5.7% (11.6%), with a leak of >10% (maximum 45%) recorded in six infants. The mean set VTV was 2.6 (0.3) mL in the low-V_T group and 4.4 (1.5) mL in the high-V_T group ($p = 0.0005$, *t*-test). There was no significant difference in set VTV by age or need for supplemental oxygen.

Regional distribution of ventilation

Figure 1 illustrates the relative distribution of ventilation in the 32 anterior-to-posterior regions of the chest. In all subgroups the pattern of distribution was similar, with the middle third of the chest accounting for the greatest



◀ **Fig. 1** Relative distribution of tidal ventilation (ΔZ_{VT} in countless units; cu) within 32 anterior-to-posterior slices through the thorax (expressed as percentage distance from the most anterior aspect, the sternum). **a** Data for those infants aged ≤7 days (*open diamonds*) and >7 days (*closed circles*) at the time of study. Relative prominence of ΔZ_{VT} in the middle third of the chest was significantly greater in those infants aged >7 days; $*p < 0.001$, repeated-measures ANOVA with Tukey post-test. There was no difference in ΔZ_{VT} within the anterior and posterior thirds of the chest. **b** By need for supplemental oxygen (*closed circles*) and air (*open diamonds*). **c** By set V_T ≤3.0 mL (*open diamonds*) and >3.0 mL (*closed circles*). For oxygen requirement and set V_T the pattern of regional distribution of ΔZ_{VT} did not differ between each group. In all sub-groups, ΔZ_{VT} was greatest in the middle third, with no difference in the anterior and posterior thirds; all $p < 0.0001$, repeated-measure ANOVA post-test analysis. All data mean and standard error of mean (SEM)

proportion of tidal ventilation (Table 2). Overall, the mean (SD) AUC of ΔZ_{VT} within the middle third of the chest was 21.3 (10.3) cu compared with 7.3 (2.9) cu and 7.6 (5.0) cu within the anterior and posterior thirds ($p < 0.0001$, repeated-measures ANOVA). Within each sub-group there was no difference in ΔZ_{VT} within the anterior and posterior thirds of the chest (ANOVA with Tukey post-test).

Between sub-groups, only age altered the regional distribution pattern of ΔZ_{VT}. There was a relatively greater weighting of ΔZ_{VT} within the middle third of the chest in those infants aged >7 days compared with those ≤7 days; mean [95% CI] difference in ΔZ_{VT} AUC within the middle third was 7.3 [3.1, 11.5] cu (ANOVA with Tukey post-test). These results were not altered by limiting analysis to an equal number of outer pixels in each third of the chest, accounting for the greater inherent pixel weighting in the middle third of the chest and the influence of the large airways in the central regions.

The mean (SD) geometric centre of ventilation was located slightly more anterior in those infants aged ≤7 days at mean (SD) of 49.1% (2.8%) of the distance

Table 2 Distribution of tidal ventilation within the anterior, middle and posterior thirds of the chest expressed as the area under the curve (AUC) of the fEIT ΔZ_{VT} (cu) within each region. In each group the middle third accounted for the greatest AUC, and thus regional V_T

	Total	Anterior	Middle	Posterior
Total population	40.0 (17.9)	7.3 (2.9)	21.3 (10.3)*	7.6 (5.0)
Age				
≤7 days	34.4 (18.7)	6.7 (3.2)	13.4 (11.1)*	6.1 (3.6)
>7 days	48.3 (13.1)	8.3 (2.2)	25.7 (7.1)*,†	9.7 (5.9)
FiO_2				
0.21	41.9 (16.1)	7.7 (2.5)	22.4 (9.2)*	7.6 (5.7)
>0.21	38.5 (19.3)	7.0 (3.2)	20.5 (11.1)*	7.4 (4.4)
V_T				
≤3.0 mL	35.8 (19.6)	6.9 (3.0)	19.6 (11.9)*	6.0 (3.7)
>3.0 mL	43.5 (15.9)	7.7 (2.9)	22.8 (8.6)*	8.8 (5.5)

All data mean (SD) in countless EIT units (cu)
FiO_2 Fraction of inspired oxygen, V_T tidal volume
* $p < 0.0001$ compared with anterior and posterior regions (repeated-measures ANOVA with Tukey post-test)
† $p < 0.001$ compared with middle region within the other sub-group (ANOVA with Tukey post-test)

between the anterior and posterior chest walls compared with 50.6% (3.5%) in those infants aged >7 days with mean [95% CI] difference −1.5% [−2.9%, 0.0%] ($p = 0.043$, *t*-test). The geometric centre of ventilation was located a mean [95% CI] 1.7% [0.3%, 3.0%] (*t*-test) more anterior in the low-set-VTV group compared with high: mean (SD) 48.8% (2.6%) and 50.5% (3.5%), respectively. There was no difference in the geometric centre of ventilation for those infants requiring air or supplemental oxygen: 49.3% (3.4%) and 49.9% (3.0%), respectively.

Breath-to-breath variability of regional tidal ventilation

There was considerable breath-to-breath variability in ΔZ_{VT} in both hemithoraces. The mean (SD) ΔZ_{VTANT} and ΔZ_{VTPOST} CV was 30.6% (14.0%) and 31.9% (12.7%). There was no difference in the CV in each hemithorax ($p = 0.302$, paired *t*-test). The corresponding mean (SD) ΔP CV of 23.3% (21.4%) was significantly less than ΔZ_{VTANT} ($p = 0.012$) and ΔZ_{VTPOST} ($p = 0.003$), suggesting regional variations in breath-to-breath compliance. Age, inspired oxygen concentration and VTV did not influence the CV of ΔZ_{VTANT} and ΔZ_{VTPOST}.

In 15 infants a complete set of synchronised breath-to-breath ΔZ_{VTANT} and ΔZ_{VTPOST}, V_T and ΔP data could be collected. In these infants, the variability of V_T at the airway opening was less than ΔP, ΔZ_{VTANT} and ΔZ_{VTPOST} (Fig. 2). The mean (SD) CV for V_T was 17.0% (8.4%), compared with 23.7% (18.7%) for ΔP ($p < 0.0001$), 35.3% (15.6%) and 35.2% (14.0%) for ΔZ_{VTANT} and ΔZ_{VTPOST} ($p < 0.0001$, all paired *t*-tests). Similar to the entire data set, the variability of ΔZ_{VTANT} and ΔZ_{VTPOST} was not different but both exhibited significantly more breath-to-breath variability than ΔP ($p < 0.0001$, paired *t*-tests).

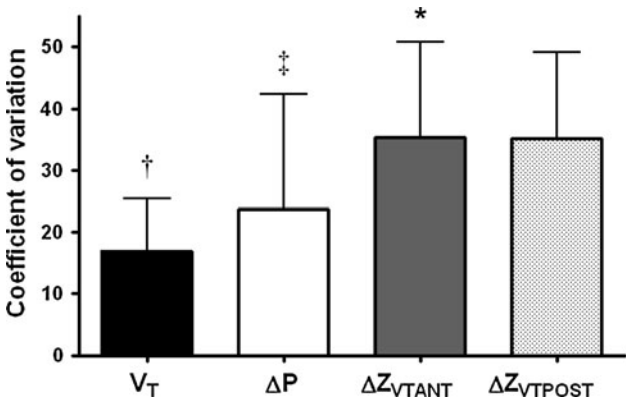


Fig. 2 Breath-to-breath variability in tidal ventilation within the anterior (ΔZ_{VTANT}; *grey bar*) and posterior (ΔZ_{VTPOST}; *dotted bar*) hemithoraces, as measured by EIT, compared with tidal volume at the airway opening (V_T; *black bar*) and pressure amplitude (ΔP; *white bar*). Variability of each parameter expressed as the coefficient of variation within each 30-s recording ($n = 45$). $^{\dagger}p = 0.0069$ ΔP compared with V_T; $^{\ddagger}p < 0.0001$ ΔZ_{VTANT} and ΔZ_{VTPOST}; $^{*}p < 0.0001$ V_T compared with ΔZ_{VTANT} and ΔZ_{VTPOST} (all paired *t*-tests). All *bars* mean and SD

Discussion

This study found that describing regional ventilation using EIT was possible in the stable, mechanically ventilated, extremely preterm infant receiving SIPPV + VTV. Ventilation was greatest in the middle third of the chest, with only a slight preference for distribution of ventilation towards the non-dependent lung. We also identified marked breath-to-breath variability in the regional behaviour of tidal ventilation. These findings suggest a complexity in the regional volumetric behaviour of the preterm lung that may not be adequately described by measures of global lung mechanics. Investigating regional variations in ventilation may help in better understanding the mechanics of respiration in the vulnerable extremely preterm lung.

Management of respiratory disease in preterm infants remains challenging. Despite advances in ventilatory techniques, a universally accepted method for optimising ventilation whilst reducing the risk of VILI proves elusive. In part, this is due to difficulties at the bedside in describing the regional interaction between heterogeneous, diseased lung and the mechanical ventilator, which uses algorithms based upon a single compartment, or homogeneous, lung model. EIT is a relatively novel technique, validated against computed tomography and inert gas wash-out methods, for describing regional lung volume in animals and adults [18–21]. It has been used to describe regional ventilation in small cohorts of spontaneously breathing [16, 25] and ventilated infants [30–32]. We have shown that EIT is both feasible and practical for individual assessment of regional ventilation in ventilated extremely preterm infants.

There was marked regional variability in breath-to-breath ΔZ_{VT} in all infants despite using a ventilation modality that aims to adapt to rapid compliance changes and achieve a standardised V_T delivery at the airway opening. This was greater than the variability in measured V_T at the airway opening and the 5.5 ± 1.5% error of the pneumotachograph [33]. Whether these findings represent rapid regional compliance changes within the lung, inconsistent respiratory effort, untriggered spontaneous inflations or the inherent limitation of the ventilator in correctly predicting an inflation pressure based on a previous breath's V_T measurement [33, 34] cannot be determined from this study. The observation that, in some infants, inflation pressure varied considerably whilst in others it did not, despite regional changes in ΔZ_{VT}, suggests that a combination of all is occurring. Future studies

should attempt to assess the infant's individual breath-by-breath contribution to trans-pulmonary pressures using oesophageal pressure manometry. The regional variability in ΔZ_{VT} has important clinical implications as the preterm lung is particularly vulnerable to VILI from atelectasis, volutrauma and shear forces [35, 36]. Animal studies have shown that rapid changes in regional ventilation and volume state are particularly injurious [3, 4]. Our study suggests that lung mechanics within the mechanically ventilated preterm lung are more complex than described by global measures of expiratory flow at the airway opening [10, 37–40]. In part, this may explain the relatively small reduction in short-term morbidity using SIPPV + VTV [7] and highlights the importance of delivering ventilation targeted to the individual regional mechanical properties present at that point in time.

Regional ventilation has previously been shown to be preferentially distributed to the non-dependent (uppermost) lung in infants and children with abnormal lungs [41] and in animal models of neonatal lung disease [10]. Our study found that most of the ΔZ_{VT} occurred in the middle third of the anterior-posterior axis, with little difference between the most anterior and posterior regions. This was unexpected but may be explained by limitations of EIT. Firstly, EIT is unable to differentiate between the ΔZ_{VT} within alveoli and the large airways. Secondly, EIT creates a single-slice cross-sectional grid of the chest of equally sized pixels, a technique that has been validated against volumetric magnetic resonance imaging (MRI) recordings in an adult [42]. Whether our findings hold true at other levels throughout the preterm thorax cannot be determined by this study. By virtue of the circular chest shape, the middle third contains more pixels than the anterior and posterior thirds and therefore carries a greater weighting of ΔZ_{VT}. Accounting for these limitations did not alter patterns of distribution. Additionally, the geometric centre of ventilation was located near 50% in all subgroups, with the statistical differences identified unlikely to be of clinical significance. The infants in our study had considerably less lung disease than in animal [10, 43] and adult studies [39, 40, 44] that have previously described a gravity-dependent distribution of ventilation and benefits of alveolar recruitment manoeuvres. This may explain our distribution findings but, as illustrated by the high breath-to-breath variability in regional ΔZ_{VT} identified in many infants, does not exclude gravity-dependent ventilation during many of the individual breaths documented. In this observational study, the PEEP was held constant and, in some cases, may have been inadequate for maintenance of alveolar recruitment. Currently, clinicians have few tools to guide optimal PEEP delivery. EIT may assist in determining whether, and when, an infant may benefit from additional PEEP or alveolar recruitment manoeuvres.

The relative increase in the weighting of ΔZ_{VT} observed within the middle third of the chest in the infants aged >7 days suggests differing lung mechanics from those ≤7 days, as evident by the higher set V_T in this older cohort. The age-related medial prominence in the distribution of ΔZ_{VT} is interesting. Whether this represents age-related effects of prolonged ventilation, such as distension of major airways, a more heterogeneous parenchymal lung injury or a combination of many factors, cannot be determined from this study. An increase in set V_T with age was noted in a retrospective study of extremely preterm infants requiring SIPPV + VTV [45]. An increase in airway calibre and alveolar dead-space with age was postulated as the explanation. Our findings are consistent with this hypothesis. In newborn animal models, maturational differences in airway development and lung perfusion are known to occur [46]. It was surprising that we did not observe differences in the distribution of ΔZ_{VT} between the air and oxygen cohorts. Oxygen requirement is an accepted proxy for severity of lung disease [47], and in adults and animal models the degree of lung disease has been shown to alter the distribution of lung volume [10, 11, 44]. Our limited sample size precluded more detailed sub-group analysis, but our results suggest that future research in this population should consider the potential for maturational changes in tidal ventilation as well as degree of lung disease.

Previous clinical studies of the infant lung have been limited to healthy, spontaneously breathing infants [16, 25] or small cohorts of infants ventilated using various strategies [32]. Applying the regional ventilation findings of these studies to the ventilated preterm infant may not be appropriate. Our study involved preterm infants who were physiologically stable, recovering from their hyaline membrane disease, ventilated for recurrent apnoea or weaning. Many had minimal lung disease, and much of the potential for severe VILI was likely to have already occurred. Equally, it should not be assumed that our findings readily translate to the early phase of hyaline membrane disease. Rather, our findings should be considered as a description of the behaviour of the 'normal' ventilated preterm lung and serve as a reference for future EIT studies during the initial phases of acute preterm lung disease.

This study has several other limitations not previously mentioned. As the absolute regional tidal volumes during each EIT recording are unknown, interpretation of the functional EIT data between subjects should be limited to comparison of the pattern of relative distribution of ventilation within the chest. The EIT unit used was limited to a single analogue input channel, precluding our ability to record ΔZ_{VT}, pressure and flow simultaneously. Due to the small thoracic circumference, ensuring precise, equidistant lead placement around the preterm infant's chest can be difficult and result in less precise spatial interpretation of the regions of interest. EIT is also extremely sensitive to movement. We attempted to limit the effect of movement artefact by using video, though it is still

possible that small movements have not been excluded. All our infants were studied in supine position to standardise any gravitational effects on ventilation. Our results may have been different if these infants had been studied in other positions. Prone positioning is known to improve regional ventilation in adults [48]. In ventilated preterm infants, turning of the head results in left-to-right regional differences in ventilation [32]. Study of the effects of posture on regional ventilation in ventilated preterm infants is warranted.

Conclusions

There appears to be a maturational change in the regional distribution of ventilation, likely due to large airway changes. More importantly, regional lung mechanics in the ventilated preterm lung are complex and often vary significantly between breaths, even with the use of ventilation modalities which attempt to standardise lung mechanics. This variability was not identified by monitoring at the airway opening. Regional lung mechanics should be considered in the development of future lung-protective ventilation strategies.

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Conflict of interest The authors declare that they have no competing interests.

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