Utility of lung ultrasound scanning in neonatology

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ABSTRACT
The utility of point-of-care lung ultrasound in neonatology is rapidly expanding. This review summarises current evidence of a diagnostic, procedural and observational tool valuable in the management of newborns requiring intensive care. Approaching a patient, probe in-hand with focused clinical question is essential, and barriers to implication together with important research questions are explored.

INTRODUCTION
Point-of-care lung ultrasound (LUS) has a widely established role in adult and paediatric critical care, emergency and prehospital medicine for the evaluation of patients with respiratory and cardiovascular compromise.1 2 Its use within neonatology is not new,3–5 yet despite international consensus evidence-based recommendations,6 why is it yet to be widely adopted?

Why it is an attractive diagnostic tool almost goes without saying: rapid, simple to perform, non-invasive, radiation free and providing dynamic, real-time information without a radiological time lag using ultrasound equipment already in situ in neonatal intensive care unit (NICU) for clinician-performed cardiac, cranial and abdominal assessments. Equal if not superior validity to conventional radiology has been reported in most clinical settings in neonatal patients.4 6–8 Consistent validity has been reported of a mean time of <5 min to perform and high reliability in interobserver agreement across the range of experienced to novice.6–10

So, why sceptical? One could argue a lack of international conformity in scanning techniques, variation in ultrasound equipment and settings (there is no one agreed neonatal lung preset) and confusion in nomenclature have made things challenging. Research declaring rapid summation of artefact interpretation into specific diagnostic statements and simplistic algorithms or lacking essential methodology warrant interpretation with caution. Even the term ‘Lung Ultrasound’ is not exactly correct; we are rarely ever observing actual lung parenchyma, just the interpretation based purely on artefact generation.1

THE PHYSICS
Multiple resources eloquently translate the principles of physics and artefact generation that we observe in LUS scanning1–3 (online supplementary video S1a–f) Artefacts are generated from the behaviour of ultrasound beams as they encounter variation in acoustic impedance between air/liquid/tissue interfaces and represented by a combination of processes including shadowing, reverberation, mirroring, comet tail and ring down artefacts. There is literally an LUS alphabet of prescribed nomenclature1 starting with A lines (horizontal reverberation artefacts of the pleural tissue/air interface), B lines (discrete laser-like vertical reverberations originating from the pleural line moving synchronously with sliding) and C lines (fractal comet-tails radiating from an irregular air/tissue interface of consolidated lung), and although a few letters are missing, it does go up to and include Z lines. However, it is the interpretation of artefact generation at the pleural surface that we strictly correlate with clinical, radiological and biological data.

THE VERY FIRST BREATH
To fully conceptualise the value of information gained from performing LUS, it is helpful to start from the moment of birth with initiation of breathing, clearance of lung fluid and transition to extrauterine life. Blank et al11 characterised such ultrasound appearances in 63 healthy term and late preterm infants assigning a simple yet eloquent grading system type 0–3 (figure 1). Establishment of the pleural line was demonstrated within the first few breaths (median 4 breaths4–6) consistent with aeration of distal lung units and substantial liquid clearance within 10–20 min in all infants.11

DOES LABOUR MATTER?
Studies comparing rate of fluid clearance in infants born via vaginal delivery, caesarean section (after labour) and elective caesarean section (without labour) have reported faster clearance within the
WHAT HAPPENS WHEN IT GOES WRONG?
What are the sonographic observations when an infant fails to transition with delayed fluid clearance from alveoli and interstitium or born preterm with respiratory distress syndrome (RDS) secondary to surfactant deficiency and atelectasis? Copetti and Cattarossi described their observation of ‘Double Lung Point’ (DLP) in 32/60 infants within the first hour of birth demonstrating sharp transition of near normal in appearance (thin regular pleural line, A Line profile and few intermittent B lines) in superior regions versus a bright, coarse, irregular pleural line with densely compact B lines in inferior/lateral lung fields. Authors acknowledged an ambitious sensitivity and specificity of 100% of DLP for the diagnosis of transient tachypnoea of the newborn (TTN), not observed in healthy newborns or those of 28–36 weeks’ gestation, including 40 controls (15 preterm 28–36 weeks’ gestation, without reported lung disease).

First 20 min in those born in presence of labour, irrespective of mode of delivery, but near complete clearance typically achieved within the first 4 hours in all healthy infants. One study of smaller sample size reported early differences observed in the rate of B line clearance between infants born via vaginal versus caesarean section resolved by 24 hours.

PREDICTING PATIENT TRAJECTORIES: HOW USEFUL IS EARLY LUS IN REGARDS TO DIAGNOSTIC ACCURACY AND PREDICTION OF NICU ADMISSION, RESPIRATORY SUPPORT AND REQUIREMENT FOR SURFACTANT?
The functional application and predictive value of point-of-care LUS in neonatology is where it gets exciting. LUS scoring systems have been validated worldwide with minor modifications according to clinical context to evaluate these questions.
Both were required in all 14 babies with type 1 (‘white lung’) LUS appearance (4 ventilation and surfactant; 10 CPAP and oxygen). While 4/46 (8%) exhibiting type 2 (moderate B profile) required CPAP/oxygen, in contrast to none exhibiting a type 3 (A line profile). One caveat was lack of discriminatory power between milder and more severe conditions of RDS requiring mechanical ventilation. Signs of pulmonary adaptation were reported with serial ultrasounds demonstrating observation of an A line profile in 98% of infants at 36 hours, correlating with clinical improvement.22

Blinded analysis of LUS has been shown to reliably predict and outperform conventional radiographs for the failure of non-invasive ventilation after a 2-hour period of stabilisation and the need for intubation and surfactant administration within 24 hours.5 One acknowledged limitation was non-escalation of CPAP beyond 5 cm H2O prior to intubation, differing from most adopted clinical practice.

A strong correlation between bedside LUS reaeration scores and peep-induced lung recruitment (measured via pressure volume curves) in adult patients with ARDS is promising.23 However, authors report inability to accurately assess lung hyperinflation, which differs from our personal observations of a near perfect A line profile with reduced amplitude of pleural sliding, considered ‘too good’ in the context of respiratory distress in infants on positive pressure support (online supplementary video S3a,b).

Martelius et al24 reported no significant correlation between changes in static lung compliance (a measure of lung elasticity in mL/KPa/kg correlating with epithelial sodium transport and lung fluid resorption shown to increase significantly during postnatal adaptation25) and abundance of B lines on LUS during transitioning in healthy term infants. Observations in 130 term and preterm NICU infants with respiratory distress in the first hours of age demonstrated good correlation with oxygenation status irrespective of respiratory condition and good reliability to predict surfactant need in those <34 gestation receiving CPAP up to 6 cm H2O (AUC 0.93; 95% CI 0.86 to 0.99).10 Recent research has further demonstrated the value of LUS score to predict the need for a first surfactant dose (area under curve (AUC) 0.94; 95% CI 0.90 to 0.98; p<0.0001) in extremely preterm neonates with RDS, independent of gestational age.26 Major strengths of these studies include a comprehensive examination taking <5 min, standardised criteria for surfactant administration (European consensus 201327) and application of a modified scoring system28 inclusive of consolidation.

**RAPID DETECTION OF AIR LEAK**

Animal studies demonstrate precision in determining pneumothorax in the preterm lamb model using postmortem examination as the gold standard.28 A very clear diagnostic pathway is illustrated in the 2012 international consensus recommendations8 and well accepted as a reliable and accurate tool in comparison to conventional radiography in adult critical care.1,2

In its simplest form, an indication of air leak comes from the observation of ‘standstill’ and lack of artefact generation from visceral pleural contact and movement on parietal. If you can observe horizontal pleural sliding, your question stops there; even the presence of one B line or transmission of lung pulse is enough to confirm direct pleural apposition at that point. Lung point is pathognomonic representing the limit of pleural separation8 (figure 3 and online supplementary video S3c).

Differentiating true absence of observed pleural sliding from appearance of a vertical bounce and other ‘parasitic’ artefacts
generated from chest wall excursion with marked recession or inadvertent movement of the probe can be challenging in neonates (online supplementary video S4a,b). Lichtenstein1 provides expert guidance on scrutinising artefact generation that is unchanged as it transcends the pleural line in M-mode in the presence of air leak generating an uninterrupted pattern from tissue recession that continues below the pleural line with abolished lung sliding (Avicenne sign, chapter 14, page 93–94 figure 14.3).

Cattarossi et al7 compared the performance of conventional chest radiographs, transillumination and LUS for the diagnosis of pneumothorax in 49 babies with respiratory distress. LUS outperformed both modalities, consistently diagnosing pneumothorax in all 23 babies with a sensitivity and specificity of 1, compared with 0.96 and 1 for chest x-ray and 0.87 and 0.96 for transillumination.7 Raimondi et al29 demonstrated high diagnostic accuracy in detection of pneumothorax in the critically ill neonate outperforming clinical evaluation and reducing time to imaging diagnosis and drainage (mean time 5.3±5.6 min vs 19±11.7 min). Point-of-care ultrasound is thus extremely valuable in clinical environments with foreseeable delay in obtaining and interpreting radiology. Successful ultrasound-guided emergency needle thoracocentesis of extremely preterm infants on respiratory support has been reported10 enables accurate delineation of the limit of pleural separation, without blind aspiration at a prescribed conventional landmark.

Surveillance of pleural recontact postprocedure necessitating further intervention or later facilitating timing of catheter removal is consistent with our experience in pneumothoraces in extremely preterm babies receiving high-frequency jet ventilation (figure 4A–D and online supplementary video S4c).

Pitfalls encountered with the detection of air leak are subtle transition in appearance to lung point in infants with hyperinflation A line profile and reduced amplitude of sliding, in comparison with stark contrast with adjacent coalescent B line profile. Search for lung point may be unrewarding in an infant with massive tension pneumothorax separating visceral from parietal pleural as far as one can apply the probe. Differentiating small pneumothoraces in perihilar regions from pneumomediastinum may also be challenging but largely facilitated by lack of visualisation of expected anatomical structures at that position, for example, thymus and cardiac vessels.2

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**Figure 3** Lung point illustrating sharp transition of a thin, regular pleural line with lack of sliding, absence of B lines or lung pulse in the superior lung field where pleura are separated by air leak, adjacent to region showing a bright, coarse, irregular pleural line with sliding, multiple B line artefacts, indicative of visceral and parietal pleural apposition.

**Figure 4** (A) Right anterior longitudinal view of pneumothorax in the inferior region in a 27-week gestation preterm infant supported on high-frequency jet oscillation showing a thin regular pleural line and mirror image artefact but lacking of horizontal sliding, B lines or lung pulse. Lung point identified in adjacent superior region with pleural apposition and associated artefacts generated (horizontal sliding of a coarse pleural line with synchronous movement of B lines). (B) Superior region using M-mode demonstrating a seashore sign (confirming pleural apposition and movement). (C) Inferior region using M-mode demonstrating the vastly different appearance of a stratosphere sign in presence of air leak. (D) anterior-posterior (AP) chest x-ray confirming persistent air leak in the right anterior lung regions despite an intercostal catheter in situ.
PLEURAL EFFUSIONS

Point-of-care ultrasound literally outshines conventional radiographs when it comes to the diagnosis, assessment, procedural guidance and serial observation of pleural effusions. Pleural effusions are largely visualised as an anechoic space between the parietal pleura and the now non-apposed visceral pleural (lung line). Fluid collection is beautifully depicted in contrast to adjacent structures with dynamic visualisation of diaphragmatic activity and artefacts representing the lung line beneath during respiration. (figure 5 and online supplementary video S5) The clinical application of LUS has enormous potential from delivery room management of fetal hydrops enabling safe anatomical demarcation of diaphragm movement, guiding positioning and depth of percentesis. Serial three-dimensional (3D) assessment of the function of in situ intercostal catheters (complications of blockage or displacement) or guidance on timing of removal with clinical resolution that would otherwise mandate (yet another) static, two-dimensional CXR and unwelcome patient handling.

Can ultrasound reliably distinguish between transudate, exudate and haemorrhage? Probably not, but neither can a chest radiograph. Internal echo signals and fibrin deposition may be observed more frequently in exudative effusions, (figure 6 and online supplementary video S6), but diagnostic analysis of fluid would provide such answers.

CONSOLIDATION AND ATELECTASIS

The sonographic appearance of lung is well described with loss of acoustic reverberations of aerated lung and hence disruption of the pleural line, hypoechoic areas exhibiting a tissue-like appearance (‘Hepatization’), often with irregular margins or wedge-shaped boarders (figure 7 and online supplementary video S7). This appearance may represent a range of pathology including infectious exudate, meconium aspiration, pulmonary haemorrhage to name but a few. Contention arises where authors attribute a specific pathology to a sonographic appearance observed that may lack specificity in diagnosis, for example, a diagnostic flow diagram illustrating consolidation with dynamic air/fluid bronchograms equals pneumonia.

In adult and paediatric critical care, the presence of dynamic or static air bronchograms and regularity of the margin of hypoechoogenicity have been useful in differentiating consolidation from atelectasis. Dynamic air bronchograms are hyperchoic, linear elements representing air in the bronchioles that appear within an hypoechoic region (with irregular margins) observed mostly in the context of consolidated lung (figure 6 and online supplementary video S6). Dynamic describes a centrifugal movement in relation to respiration, while in static bronchograms, this is not observed and boarders are more regularly defined, suggestive of atelectasis.

However, in the neonate, small hepatised regions moving in and out of ultrasound plane in the context of rapid tachypnoea can make accurate differentiation challenging. In a recent paper reporting 100% sensitivity and specificity of large regions of consolidation with irregular margins for the diagnosis of neonatal pneumonia, dynamic air bronchograms were only observed in 52% of confirmed cases.

Lung pulse is the transmission of cardiac activity on adjacent lung parenchyma and visceral pleura, replacing horizontal pleural sliding with a more vertical ‘bounce-like’ motion, which may be readily observed in both consolidated and atelectatic
lung.\(^1\,^2\) In neonatal patients, it is not uncommon to observe a wide impact of cardiac pulsation over a large surface of the lungs given the relative size and relations of the organs within the small chest. A limitation of LUS is inability to identify deep regions of consolidation that do not reach the pleural surface.\(^6\)

LUS has been valuable in the serial imaging and assessment of newborns with severe meconium aspiration, observing dynamic and heterogeneous patterns of B line coalescence, subpleural consolidations, atelectasis and bronchograms.\(^5\,^3\,^3\) In paediatric patients, it has an establishing role in the diagnosis and management of bronchiolitis and community-acquired pneumonia.\(^2\,^6\,^5\,^7\)

A holistic approach is to perform LUS with a focused clinical question. In the case of an extremely preterm ventilated baby with raised inflammatory markers, increasing oxygen requirements and worsening ventilation, there would be value in performing a systematic and comprehensive ultrasound assessment, to provide dynamic, real-time information to assist 3D visualisation of the global status of lung aeration, presence of consolidations, effusions, air leak or potential iatrogenic pathology (eg, from endotracheal tube migration into the right main bronchus causing atelectasis of the right upper lobe). Only with appropriate correlation with clinical, biological and radiographical information is one in a position to narrow differential diagnoses of reabsorptive atelectasis, infection, aspiration, pulmonary haemorrhage, air leak syndromes to optimise patient and respiratory management.

### PREDICTING DEVELOPMENT OF BRONCHOPULMONARY DYSPLAGIA (BPD)

Three studies have specifically investigated the predictive value of LUS in the evolution of BPD in preterm babies with RDS.\(^3\,^8\,^4\,^0\) Each focused on the appearance of the lung bases using transabdominal windows, reporting either the earliest day at which persistence of retrodiaphragmatic hyperechogenicity (that otherwise resolved in unaffected infants) or transition to a non-homogenous BPD pattern of variable hyperechogenicity, with contiguous regions of sparing and pleural line anomalies (thickening, irregularity and subpleural consolidations) lent the greatest predictive value for development of BPD. Results vary between day 9\(^3\,^9\) and day 18\(^3\,^8\) for persistence of retrodiaphragmatic hyperechogenicity and given the majority of patients within each study did not develop BPD, authors highlight the NPV of this finding close to 95%. Ahuja \(\text{et al}\)\(^4\,^0\) reported presence of an abnormal pattern on day 14 had the greatest predictive value (94% accuracy) for development of clinical BPD (defined as oxygen dependency at 28 days) in infants <32 weeks’ gestation. Although impressive, conclusions are drawn from 6/33 babies for persistence of RDS.\(^3\,^8\,^4\,^0\) Each focused on the appearance of the lung bases using transabdominal windows, reporting either the earliest day at which persistence of retrodiaphragmatic hyperechogenicity (that otherwise resolved in unaffected infants) or transition to a non-homogenous BPD pattern of variable hyperechogenicity, with contiguous regions of sparing and pleural line anomalies (thickening, irregularity and subpleural consolidations) lent the greatest predictive value for development of BPD. Results vary between day 9\(^3\,^9\) and day 18\(^3\,^8\) for persistence of retrodiaphragmatic hyperechogenicity and given the majority of patients within each study did not develop BPD, authors highlight the NPV of this finding close to 95%. Ahuja \(\text{et al}\)\(^4\,^0\) reported presence of an abnormal pattern on day 14 had the greatest predictive value (94% accuracy) for development of clinical BPD (defined as oxygen dependency at 28 days) in infants <32 weeks’ gestation. Although impressive, conclusions are drawn from 6/33 babies demonstrating conversion from an hyaline membrane disease (HMD) to a persistent BPD pattern and clinical diagnoses of BPD. Of interest, three babies also demonstrating a conversion (HMD) to a persistent BPD pattern and clinical diagnoses of reabsorptive atelectasis, infection, aspiration, pulmonary haemorrhage, air leak syndromes to optimise patient and respiratory management.

The concept of spared areas is contentious; BPD is described as a non-homogenous disease of the lung periphery, but are we really observing ‘normal’ patches? It is feasible that artefacts generated are heavily dependent on the relative angle of insonation to the pleural surface, when at precisely 90° at a given moment may act as a reflector, generating an A line profile, usually observed within a single intercostal space and interpreted as ‘sparing’. Practically, scanning the preterm infant with an uneven chest curvature, marked recession, tachypnoea and comparatively large size ratio of linear probe can make image acquisition entirely free of parasitic movement challenging.

### WIDER APPLICATIONS

The potential utility of LUS in neonatology is exciting and evolving rapidly. A high diagnostic accuracy in assessing pulmonary overflow via abundance of B lines during the first days of life of infants with congenital heart disease has been reported, correlating well with echocardiography.\(^3\,^2\) Bedside imaging opportunities exist for infants with congenital malformations (congenital cystic adenomatoid malformation (CCAM), pulmonary sequestration and diaphragmatic hernia) and correlation with CT/MRI findings. Is LUS going to change our approach from counting anterior ribs on a static chest radiograph to a dynamic assessment of optimal targeted volume or mean airway pressure? Can we correlate LUS appearance with early successful extubation in the extreme preterm? Can we reliably inform bed and nursing resource planning in NICU in regards to predicted patient trajectories? Or avoid mother–infant separation in long-distance retrieval to tertiary NICU from remote clinical environments in cases predicted to require minimal respiratory support?

I doubt very much our radiographer colleagues are at imminent risk of redundancy, but there is opportunity in using LUS as a value-adding tool and reduce X-ray exposure with the appropriately focused clinical question.\(^4\,^3\)

### WHERE NEXT?

Technological advances in image acquisition and quantitative texture analysis may dominate our future directions.\(^4\,\,^4\) The need for appropriately powered, prospective multicentred studies with sound correlation with clinical data has been recognised,\(^4\,\,\) together with standardisation and validation of point-of-care LUS techniques, evidence-based training programmes and accreditation standards. These may only be achieved with international collaboration, robust discussion and consensus.\(^4\,\,\,^6\) The NeoLUS\(^5\) international expert group inaugural congress in Lung Ultrasound in Neonates and Children scheduled in Paris, 2019 (https://www.mcscientificevents.eu/firstlaunch) and the Australasian Society of Ultrasound Medicine certification in clinician-performed ultrasound Certificate in Clinician Performed Ultrasound (CCPU) in neonatal lung are exciting developments as part of this journey ahead.

### Contributors

PW is the sole author of this article and responsible for performing all original ultrasound studies presented herein. The author wishes to acknowledge Associate Professor Andrew Gill for his peer support and contribution to the implementation and teaching point-of-care neonatal lung ultrasound in neonatology at King Edward Memorial Hospital in Perth and as faculty of the Australasian Society...
of Ultrasound Medicine. Mr Malcolm Bruce is also acknowledged for his assistance with medical illustrations.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Competing interests** PLW is a co-author of the online learning package hosted by ASUM. Lung Ultrasound In Neonatology with reference to illustrations provided in online supplementary video files S1a–f.

**Patient consent** Not required.

**Provenance and peer review** Commissioned; externally peer reviewed.

**REFERENCES**


