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Modern Pulmonary Imaging of Bronchopulmonary Dysplasia

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Abstract

Bronchopulmonary dysplasia (BPD) is a complex and serious cardiopulmonary morbidity in infants who are born preterm. Despite advances in clinical care, BPD remains a significant source of morbidity and mortality, due in large part to the increased survival of extremely preterm infants. There are few strong early prognostic indicators of BPD or its later outcomes, and evidence for the usage and timing of various interventions is minimal. As a result, clinical management is often imprecise. In this review, we highlight cutting-edge methods and findings from recent pulmonary imaging research that have high translational value. Further, we discuss the potential role that various radiological modalities may play in early risk stratification for development of BPD and in guiding treatment strategies of BPD when employed in varying severities and time-points throughout the neonatal disease course.

Introduction

Bronchopulmonary dysplasia (BPD), also referred to as chronic lung disease of prematurity (CLDP), is a serious and multifaceted cardiorespiratory morbidity in infants who are born preterm and/or at very low birth weight. Despite improvements in clinical care, including antenatal steroids and postnatal surfactant, the prevalence of BPD remains high, in large part due to the increased survival of infants who are born extremely premature (1). Cardiopulmonary functional limitations have been noted in a significant portion of children beyond the neonatal period and adults who were born preterm, demonstrating that BPD is a chronic condition with sequelae often persisting into later life (1–3).

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AUTHOR CONTRIBUTIONS

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CONFLICTS OF INTEREST

None

Several varying definitions of BPD severity have been proposed for use in the neonatal intensive care unit (NICU), most of which utilize clinical data to stratify disease. Commonly, BPD is defined by the requirement of supplemental oxygen for at least 28 days in infants born below 32 weeks gestation, with severity stratified by level of respiratory support required at a single time-point of 36 weeks post-menstrual age (PMA) (4). The objectivity of this definition is limited by the non-standardized administration of oxygen at different institutions (5). Most current definitions of BPD are insufficient in the prognosis of outcomes (6,7), particularly in the more severe cases, and generally do not account for the common central airway and cardiac comorbidities that can present with prematurity-related lung disease. There is a dearth of strong evidence for the usage and timing of various treatments and support modes (e.g., oxygen, bronchodilators, steroids, tracheostomy, diuretics), and clinical management using these focused therapies continues to be imprecise and arbitrary (8). As such, there is a need for objective and useful early life biomarkers in order to understand the severity and type of respiratory disease of prematurity, to build prognostic indicators of later outcomes, and further to guide treatment strategy in individual patients.

Radiological imaging has been an important tool in characterizing BPD since in 1967, when Northway and colleagues used chest x-ray radiographs (CXR) to describe distinct elements of small airway injury, inflammation, fibrosis, and hyperinflation in the lungs of preterm infants who had been exposed to mechanical ventilation and high oxygen concentrations (9). Current imaging practices in the NICU have not evolved significantly since the 1960s, with radiological inquiry of respiratory status in infants with BPD being largely limited to low-sensitivity CXR. Chest x-ray computed tomography (CT) has high 3D resolution and can sensitively detect structural changes in young BPD patients over time (10,11), but has historically been uncommon in neonates due to lingering concerns over exposure to ionizing radiation (12).

Modern developments in various radiological modalities – most notably in magnetic resonance imaging (MRI) – can provide novel, quantitative metrics of pulmonary structure and function in the presence of BPD, with strong clinical relevance. In this review, we will briefly highlight the well-documented utility of CXR and CT, with primary focus on numerous recent developments in MRI and ultrasound (US) that have potential for high translational value. Further, we discuss the potential role that radiological modalities may play in guiding treatment strategies of BPD in the NICU setting. In the near future, objective information from cutting-edge imaging may guide clinical management strategies in varying severities and time-points throughout a young pediatric disease course.

Pulmonary imaging toolkit

Chest x-ray radiography—Current standard of care for infants with BPD typically includes chest x-ray radiography (CXR) (Figure 1). Its frequent use in assessing acute lung morbidities of prematurity is due in large part to its accessibility and straightforward implementation in a critical care setting. In addition, CXR requires a very low amount of ionizing radiation and thus is generally considered to be safe for serial evaluation of neonates during disease progression (12). However, CXR provides only a 2D projection

of the chest (typically a coronal view), with limited structural resolution compared to tomographic modalities that provide high 3D resolution. Indeed, CXR has low sensitivity in identifying milder lung disease, since only the more severely abnormal structures are generally apparent.

Despite these limitations, CXR continues to be the first line of radiological inquiry in the neonatal setting and has been used safely for decades to detect gross abnormalities with clinical relevance, including hyperinflation, lobar emphysema, cysts, edema, and extensive fibrosis (13,14). Toce et al. demonstrated in 1984 that radiological scoring of BPD lung disease on CXR in early premature life has a strong correlation to growth rate, respiratory distress, and clinically-measured gas exchange at 21 days of life (13). More recently, Arai et al. found that a cystic/bubbly appearance on postnatal CXR was a potential risk factor of wheezing disorders in 3-year-old children who were born <28 weeks gestation and had a BPD diagnosis (14), and Luo et al. demonstrated that high Toce scores on CXR at 28 days of life were associated with poor pulmonary function and exercise performance at 4 years of age in very low birth weight infants (15). With high ease of implementation, relative safety, and modest clinical relevance, CXR is likely to remain the clinical standard for initial radiological evaluation of infants with lung disease in the foreseeable future.

Chest x-ray computed tomography—Chest x-ray computed tomography (CT) is a routine imaging modality with frequent use in adult respiratory disorders, including lung cancer screening and assessment of chronic obstructive pulmonary disease (COPD) (16), owing to its excellent tissue contrast and 3D anatomical resolution of lung parenchyma. However, application of chest CT in infants (Figure 1) has historically been limited primarily due to ionizing radiation exposure in children who may be radiosensitive during growth (12) and due to difficulties with transporting unstable infants. Chest CT of BPD is typically implemented in patients with more severe disease that require sensitive assessment.

Many studies have demonstrated the potential for high clinical value from chest CT of neonatal BPD. For instance, Ochiai et al. developed a CT-based scoring system with high reproducibility and objectivity, and with correlation between lung disease scores and duration of oxygen therapy (10). More recently, van Mastriigt et al. used a different CT scoring system (“PRAGMA-BPD”) to demonstrate that most infants with severe BPD have both tomographic structural abnormalities and impaired ventilatory function, as measured by polysomnography (17). In a cross-sectional study of children with BPD from 0–6 years old, the amount of opacities and lucencies evaluated on CT decreased with age (11), indicating that a BPD severity definition that incorporates assessments at several developmental time-points may be meaningful. Multi-volume CT is an appealing technique for capturing lung dynamics, specific gas volumes, and regional ventilation from inspiratory and expiratory views and has been used to identify regions of air trapping in emphysematous adults (18); application of this method in infants may be implemented to measure gas trapping and hyperinflation in BPD (19).

With a large body of evidence that correlates tomographic imaging with clinical outcomes, disease progression, and pulmonary function, chest CT will likely continue to be an important radiological tool in patients with more complex BPD. Encouragingly, pediatric

chest CT has increased its safety profile with recent development of low-dose CT protocols (20,21) and so may become more common for neonatal pulmonary imaging in the future. As such, standardization of CT acquisition protocol and post-processing analysis should remain an important goal across institutions, especially in noncompliant infant populations (22).

Ultrasound—Lung US (LUS) is a routine modality that provides non-invasive, non-ionizing, real-time evaluations that can be performed longitudinally at the bedside. This modality can be widely implemented for the assessment and management of critically ill neonates with a multitude of respiratory pathologies (23,24), including transient tachypnea of the newborn (TTN), respiratory distress syndrome (RDS), meconium aspiration syndrome, pneumonia, congenital malformation, and BPD (25–28).

The basic physics of US involves the transmission of mechanical sound waves from a transducer into a medium and the subsequent detection of reflected echoes (29,30). Typical probes for neonatal LUS are linear and microlinear, which are best for superficial objects and have high frequency, a small footprint (e.g., fit between rib spaces in premature neonates), and strong reliability between users with varying experience (31,32). However, high-frequency linear probes lose resolution with increased depth, which limits their ability to evaluate deep structures, including centrally-located respiratory pathologies.

There are two modes used in LUS: B-mode (“brightness”) which displays 2D gray-scale images, and M-mode (“motion”) which shows motion across a line of interest (33,34). In B-mode, a structure is considered anechoic (black, e.g. fluid) if no sound waves return to the transducer, hypoechoic (gray, e.g. tissue) when only a few sound waves return, and hyperechoic (white, e.g. air) when a large number of sound waves return.

LUS is based on interpretation of artifacts rather than direct visualization of lung parenchyma (28). Normal findings in B-mode include: pleural lines, A-lines, B-lines, acoustic shadowing, diaphragm, and lung sliding (Figure 2). A-lines represent reverberation artifacts from the pleural line and are displayed as horizontal, equidistant, hyperechoic lines. B-lines are vertical hyperechoic triangles that extend from the pleural line down toward the bottom of the image. B-lines represent reverberation artifacts from interstitial fluid. The presence of a few B-lines with A-lines are a normal finding after birth in the transitioning neonate. However, when B-lines are numerous and coalesce, this can be pathologic and represent significant pulmonary edema.

Acoustic shadowing is the anechoic shadow below the ribs in B-mode. Lung sliding, which refers to the normal sliding of the parietal and visceral pleural leaflets, is visualized as movement of the hyperechoic pleural line in B-mode. The absence of lung sliding is always pathologic and indicates disruption of the pleural leaflets (e.g., pneumothorax or pleural effusion). M-mode is utilized to further demonstrate normal lung sliding (“seashore sign”), and the absence of lung sliding is demonstrated by a stratosphere (“barcode”) sign. Visualizing the lung as a solid organ, called hepatization or consolidation, is pathologic as it indicates significant decreased aeration of the lung.

In recent years, LUS has been implemented in early neonatal life to characterize respiratory pathology after birth, including discerning between TTN and RDS (26,35,36), and to stratify risk of later disease course. Raimondi et al. demonstrated LUS follows a typical pattern after birth, with altered patterns correlating with respiratory distress and need for respiratory support (37). This group further demonstrated that LUS findings of a “white lung” (coalesced B-lines) was a better predictor of non-invasive ventilation failure than CXR findings in premature neonates (PPV 100% and NPV 94.7%, compared with 46.7% and 71.8%, respectively) (38). De Martino et al. then showed that LUS score at NICU admission predicted the need for surfactant administration in premature infants (26). Vardar et al. confirmed these findings in a prospective double-blind study, showing that a LUS score of 4 on the first day after birth predicted the need for surfactant (sensitivity 96% and specificity 100%) and need for mechanical ventilation (AUC 0.804) in premature infants with RDS, but did not predict development of BPD (36). Similarly, Gregorio-Hernandez et al. demonstrated, in a prospective study of infants <35 weeks gestation with RDS, that LUS scores (maximum of 3 points per lung zone) prior to 12 hours after birth predicted the need for surfactant administration (35).

Recent advances in LUS have prompted more study on the utility of LUS to aid in the early risk stratification and management of interventions for BPD. In a prospective observational study, Oulego-Eroz et al. found that scoring of lung aeration in 8 lung zones at one week after birth predicted severe BPD (AUC 0.94) (39). Avni et al. described that retrodiaphragmatic hyperechogenicity was found on LUS in all premature infants with RDS and, if present on day 18, could predict chronic lung disease (40); similar correlation to BPD was found by Pieper et al. when this hyperechogenicity persisted beyond the first week of life (41). Alonso-Ojembarrena et al. recently published a prospective trial further showing that LUS scores increased in the first week after birth and then decreased in infants who did not develop BPD, but that elevated scores in the second week predicted BPD (74% sensitivity, 100% specificity, AUC 0.93) (27). Gao et al. have described LUS findings in infants with the diagnosis of BPD, including an abnormal pleural line, pulmonary consolidations with irregular hyperechoic areas, and prominence of B-lines (42).

A major limitation of neonatal LUS is the lack of a standardized acquisition protocol, including a lack of universally accepted guidelines for training, performing, and interpreting LUS. Most groups recommend utilizing lung zones for consistent assessment; however, there is discrepancy on how to divide the lung zones and how to assign the score (26,42). De Martino et al. divides the lung into 6 zones (upper anterior, lower anterior, and lateral bilaterally) and then calculates a score of 0 to 3 based on aeration (26). Without standardization on how to determine and report lung zone findings, universal application of these studies’ findings will remain difficult. LUS also relies on the accurate interpretation of lung artifacts rather than direct visualization of the lung architecture, and is limited by losing resolution for deeper structures, which can lead to overlooked pathological areas. The ability of LUS to differentiate hyperechoic, irregular areas seen with BPD from those seen with pneumonia is also limited, making clinical correlation imperative.

LUS is well tolerated by neonates, easily reproduced, and can detect superficial pulmonary abnormalities that aid in distinguishing neonatal pathologies. While recent studies highlight

the growing utility of LUS as a primary imaging modality in the NICU, particularly as an early biomarker for BPD in preterm neonates, it is limited in comparison to other modalities such as CT and MRI that can delineate lung parenchyma, pulmonary vasculature, and lung function in infants with BPD. Even so, studies that evaluate its ability to predict long-term sequelae of BPD are merited.

Magnetic resonance imaging—As a non-ionizing modality, magnetic resonance imaging (MRI) is ideal for young pediatric imaging, particularly for preterm neonates in whom both routine and serial monitoring of evolving lung disease is advantageous. Infant MRI has become increasingly common for brain assessment in neonatal encephalopathy, seizures, and structural abnormalities (43). Historically, however, MRI of the lung has been limited due to technical challenges that are primarily posed by the inherently low density and numerous air-tissue interfaces of the parenchyma (44). These obstacles have largely been overcome in recent years by state-of-the-art developments in MR software acquisition strategies (45–50), and neonatal pulmonary MRI is now emerging as a technique that provides novel imaging-based biomarkers, has high translational value, and in the near future may be readily implemented to meet clinical needs in the NICU setting.

Ultrashort echo-time (UTE) MRI is the most common technique for imaging of pulmonary structure (45,51). Recent work has demonstrated that UTE MRI has diagnostic utility, yielding 3D submillimeter image resolution, tissue density visualization, and structural assessment comparable to that of CT (Figure 3) (50,52–54). Further, structural lung scoring of UTE MRI in infants with BPD has been shown to predict clinical outcomes at discharge (duration and level of respiratory support) (55) and at 2 years of age (initial hospitalization duration and readmission frequency) (56). Similar structural lung scoring may provide a clinically-useful tool for predicting whether an infant with BPD is likely to undergo later tracheostomy, which could help with usage and timing of this procedure (57). Future work will likely benefit from the ability of UTE MRI to quantify lung density (52,58), as demonstrated in a recent study from Adaikalam et al. on increased lung mass growth of the ipsilateral lung in infants with congenital diaphragmatic hernia (CDH) (59). Textural analysis has previously been performed with chest CT in various adult lung conditions, including idiopathic pulmonary fibrosis (IPF) (60) and lung cancer (61); with the diverse parenchymal abnormalities that present in extremely preterm lungs, textural analysis of structural patterns seen on UTE MRI is likely to be a promising technique in the near future for distinguishing subtypes of severe BPD.

While UTE MRI with CT-like visualization of lung structure is highly advantageous, an institution does not require cutting-edge UTE strategies to obtain useful biomarkers from chest MRI. Indeed, various studies have implemented product sequences that are available on all MRI systems (e.g., a gradient echo). Using these conventional techniques, Walkup et al. quantified elevated high-intensity lung tissue (putatively fibrosis, edema, and atelectasis) in preterm infants compared with control infants (62), and Schopper et al. combined fetal and neonatal chest MRI to demonstrate the potential for postnatal catch-up growth of lung volumes in infants with CDH (63).

In addition to structural metrics, UTE MRI can provide images of respiratory dynamics acquired while neonates are quietly tidal-breathing; this technique exploits the inherent radial acquisition scheme of UTE that is sensitive to respiratory motion modulations (64). Respiratory self-gated UTE MRI is somewhat akin to multi-volume chest CT, but without requiring sedation/anesthesia, intubation, or breath-hold maneuvers. This technique can provide straightforward measures of whole-lung and regional tidal volumes (64), as demonstrated by Yoder et al. in a study of hyperinflation and minute-ventilation at various BPD severity levels (65), and by Gouwens et al. in a study of cystic and non-cystic lung ventilation at varying support settings (66). Regional lung ventilatory function and temporal filling patterns have also been explored in a small cohort of patients with BPD and CDH, detecting abnormalities in ventilation efficiency and homogeneity compared with a control patient (67,68). Regional measurement of MR relaxation parameters (e.g. T_1 , T_2 , and T_2^*) is also feasible at various inflation states and may have promise in identifying patients with BPD-related lung disease (69,70).

Infants with BPD often have comorbid central airway abnormalities, including dynamic tracheal collapse (tracheomalacia). In addition to quantitative and regional evaluation of the lung parenchyma, assessment of neonatal central airway structure and dynamics can be simultaneously acquired “for free” during a chest UTE MRI acquisition. A non-invasive, non-sedated, non-ionizing method for quantifying regional dynamic airway collapse has recently been developed by Bates et al. (Figure 4) (71), with Hysinger et al. further validating this technique by comparing the quantitative degree of collapse on MRI with reader scoring of collapse severity on clinical bronchoscopy (72). This method has further been combined with computational fluid dynamics (CFD) techniques, demonstrating that neonates with tracheomalacia have significantly increased energy expenditure due to airway dynamic collapse, compared to infants without tracheomalacia (73). Future applications of respiratory CFD to measure work of breathing in preterm infants may have high value in understanding growth and nutrition in the context of elevated respiratory energy expenditure.

Hyperpolarized (HP) gas MRI is an established technique for pulmonary imaging that can measure functional and microstructural biomarkers which are not accessible through other imaging modalities. Briefly, this technique visualizes inhaled noble gases (^3He or ^{129}Xe) as an inert contrast agent to regionally assess gas distribution (“ventilation MRI”), microstructural airspace sizes (“diffusion MRI”), and gas exchange dynamics (“dissolved-phase MRI”). HP gas MRI has been applied in various adult and older pediatric conditions since the early 2000s, including COPD, interstitial lung disease (ILD), asthma, and cystic fibrosis (CF) (74–81), and has an extensive safety record (82–84). A small handful of recent studies have investigated older children and adults who are survivors of lung disease in infancy, including BPD and CDH (85–87), with findings that demonstrate ventilatory impairment and abnormally enlarged acinar airspaces that persist well after infancy.

Application of HP gas MRI in young pediatrics and infants has thus far been limited. One recent proof-of-concept study of HP gas ventilation in a small exploratory cohort of infants and young children demonstrated the feasibility of this imaging technique in a young population, noting clear ventilatory abnormalities in patients with CF, asthma, and BPD (Figure 5) (88). While this study represented a large step toward more widespread

application of this imaging technique in neonates, rigorous studies of neonatal ventilation MRI are required, and neonatal gas diffusion and dissolved-phase MRI have not yet been explored, but may in the future be able to quantify alveolar simplification, interstitial thickening, and impaired gas exchange. These HP gas MRI techniques offer rich potential for elucidating functional and microstructural pulmonary impairment on a regional basis in individual neonatal patients, with a level of quantitative information that has not been possible yet to obtain with existing in-vivo methods.

A small handful of logistical practicalities have limited the spread of MRI in the neonatal environment. The duration of an MRI exam is typically longer than that of other modalities, with individual scans that last up to several minutes and full cardiorespiratory exams that may be close to an hour. The feed-and-swaddle method has been used successfully to minimize image artifacts caused by bulk and respiratory motion, even without sedation or anesthesia (51,89). At present, neonatal MRI (and indeed, neonatal CT) at most hospitals would require transport of patients, support equipment, and clinical caregivers from the NICU to the radiology department. However, neonatal-specific MRI is becoming more commonplace, and MRI systems have been installed within the NICU at a small number of pioneering institutions, including Cincinnati Children's Hospital (United States) (90,91), Hammersmith Hospital (London, United Kingdom) (92), University of Sheffield (United Kingdom) (93), University of Texas Southwestern Medical Center (United States) (94), New York-Presbyterian (United States) (95), and likely others in the near future.

Modern developments in neonatal MRI may provide a comprehensive evaluation of the premature respiratory system with minimal risk, yielding novel information that is not possible through any other modality. These diverse MRI techniques can be applied in various other perinatal and pediatric conditions, such as CDH, respiratory distress syndrome (RDS), esophageal atresia/tracheoesophageal fistula (EA/TEF), and CF. Importantly, cutting-edge developments in neonatal pulmonary MRI acquisition and analysis strategies are broadly applicable throughout childhood and into adulthood. With mounting evidence that extremely preterm infants have impaired respiratory function and pulmonary hypertension in adulthood with little ability to "catch up" (2,96), it is likely that extremely preterm patients in NICUs today may in future years appear in adult pulmonary clinics with persistent sequelae of prematurity. MRI measurements in infancy may provide a strong baseline to better understand the disease trajectory and guide clinical decision-making in an individual patient.

Imaging-informed precision medicine in the neonatal intensive care unit

While the community of perinatal medicine ultimately aims to reduce the incidence of preterm birth, we must also engage with reducing the pulmonary impact of existing BPD. With recent developments in radiology, neonatal pulmonary imaging is now poised to tackle how preterm infants are treated in early life. The "arsenal" for neonatal pulmonary imaging now includes several modalities; the applications of CXR and chest CT are well established, and modern developments with MRI and US are promising. As such, there may be strong value in developing imaging-based clinical management strategies of preterm infants from birth through hospitalization course.

We have formulated guidelines for the potential role of specific imaging modalities at different stages of a preterm patient's NICU course, as shown in Figure 6. We envision that various imaging modalities may provide the highest utility in different disease severities and subtypes, and indeed at different institutions with varying radiological capabilities; no single technique will be most relevant in all situations but rather will depend on the specific questions being asked for a given patient. From the perinatal stage through ~34 weeks corrected gestational age (CGA), CXR may assess gross structural lung characteristics and rough disease severity, and LUS may be used to distinguish RDS from non-RDS conditions. LUS may also be useful as an early biomarker in the first several weeks after birth for risk stratification of which infants are most likely to develop moderate or severe BPD. Utilization of LUS could provide for earlier individualized management strategies prior to the development and diagnosis of BPD. As a patient nears term-equivalent age, there may be a different paradigm for clinical decision-making, depending on severity of disease. A patient that presents with mild clinical symptoms and doesn't struggle to wean will likely require only CXR and/or early US to monitor an uncomplicated trajectory. On the contrary, a patient with suspected moderate-to-severe lung disease would benefit from tomographic evaluation. Severe patients who continue to struggle with clinical symptoms and unsuccessful weaning should undergo a full cardiorespiratory evaluation via chest CT or MRI for lung assessment, bronchoscopy or airway MRI for central airway assessment, and echocardiography, catheterization, or cardiac MRI for cardiopulmonary assessment (97,98). This comprehensive set of imaging may then inform individualized patient care from a multidisciplinary team that includes neonatology, radiology, pulmonology, cardiology, respiratory therapy, nutrition, and physical therapy.

With strong preliminary evidence that pulmonary imaging can predict outcomes and need for specific respiratory support types, the comprehensive cardiorespiratory evaluation that is proposed here may help clinicians to differentiate various BPD phenotypes and thus delineate optimal treatment strategies. Indeed, such assessment may help clinicians decide whether an individual patient is likely to successfully wean, or whether the patient will benefit from additional interventions and at specific times (e.g. tracheostomy, steroids, bronchodilators, diuretics). Since MRI is tomographic and also has a strong safety profile, it is the most likely radiological candidate for serial assessment of interventional response and efficacy, and in determining *a priori* whether an individual patient is likely to respond to a specific treatment. For example, there has been limited and controversial evidence on the benefit and timing of postnatal corticosteroids for BPD (99); the potential for short-term and long-term adverse neurological effects is well accepted (100), and yet administration continues in many NICUs. The MRI-based techniques described here may serve as a four-dimensional evaluation of pulmonary disease to quantitatively and objectively assess structural and functional response to postnatal corticosteroids and other interventional treatments.

In summary, a myriad of pulmonary imaging modalities are clinically relevant in preterm infants with lung disease. The utility of pulmonary CXR and CT are well established, while state-of-the-art techniques in pulmonary MRI and US have thus far demonstrated great promise for providing early biomarkers for severe disease and novel metrics on lung

structure and function. In the near future, we envision that these modalities will play an important role in informing personalized clinical care and improving patient outcomes.

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ABBREVIATIONS

³He	helium-3
¹²⁹Xe	xenon-129
BPD	bronchopulmonary dysplasia
CF	cystic fibrosis
CGA	corrected gestational age
CFD	computational fluid dynamics
CLDP	chronic lung disease of prematurity
COPD	chronic obstructive pulmonary disease
CT	x-ray computed tomography
CXR	chest x-ray radiography
EA/TEF	esophageal atresia/tracheoesophageal fistula
HP	hyperpolarized
ILD	interstitial lung disease
LUS	lung ultrasound
MRI	magnetic resonance imaging
PMA	post-menstrual age
RDS	respiratory distress syndrome
TTN	transient tachypnea of the newborn
US	ultrasound
UTE	ultrashort echo-time

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Figure 1:

Clinical imaging of a patient with severe BPD and born extremely preterm (24 weeks gestation), acquired at ~41 weeks corrected gestational age. Left: Clinical chest x-ray radiograph (XR; coronal view). Right: x-ray computed tomography (CT; three axial views) of an extremely-preterm patient with BPD (24 weeks gestation at birth). XR and CT imaging occurred 4 days apart.

Figure 2:

Lung ultrasound in B-mode. Left: normal lung ultrasound in infant without respiratory symptoms; normal lung artifacts. Right: lung ultrasound in an infant with severe BPD who requires mechanical ventilation for respiratory support; abnormal pleural line, interstitial lung fluid, hyperechogenicity, disruption of normal lung artifacts.

Figure 3:
Comparison of slice-matched chest CT (left) and UTE MRI (right) in a neonatal patient with severe BPD. Despite the long interval between the two exams (77 days apart) and resulting progression of disease presentation, the image resolution and pulmonary tissue density are notably similar. Adapted from *Higano NS, et al. J Magn Reson Imaging. 2017 Oct;46(4):992–1000 (52).*

Figure 4:

Top: Axial views of 3D respiratory-gated ultrashort echo-time (UTE) MRI in a neonate with tracheomalacia. Images were acquired during tidal breathing. Bottom: 3D surface renderings obtained from airway segmentation of 3D UTE images (left, pink, end-expiration; right, green, end-inspiration). From *Bates AJ, et al. J Magn Reson Imaging. 2019 Mar;49(3):659–667(71).*

Figure 5:
Hyperpolarized ³He gas ventilation MRI in a 2-month-old preterm infant. Coronal image views are shown. Various regions of ventilatory impairment are evident; the arrow denotes one such large defect. From *Altes TA, et al. Clin Imaging. Sep-Oct 2017;45:105–110* (88).

Figure 6:

Potential role of pulmonary imaging for preterm infants during their NICU course. The inpatient course is represented by two periods (perinatal through ~34 weeks corrected gestational age [CGA], and ~34 weeks CGA through discharge), with a more mild course and more severe course delineated on top and bottom, respectively. Status and recommended imaging modalities are represented by grey boxes, evidence based on clinical factors is represented by rounded, white boxes (solid border), and evidence based on tomographic imaging is represented rounded, white boxes (dotted border). The value and practicality of each modality will vary depending on time-point in disease progression, severity and co-morbidities in each patient, and capabilities of individual institutions. Abbreviations: CXR, chest x-ray radiograph; US, ultrasound; MRI, magnetic resonance imaging; CT, x-ray computed tomography; bronch, bronchoscopy; echo, echocardiography; cath, catheterization.