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2019 American Thoracic Society BEAR Cage Winning Proposal: Lung Imaging Using High-Performance Low-Field Magnetic Resonance Imaging

Clinical imaging of the lung is dominated by computed tomography (CT) and X-ray for the assessment of tissue morphology, and by nuclear imaging for the assessment of metabolism and lung function. Magnetic resonance imaging (MRI) allows evaluation of anatomy, function, and physiology during a single exam that is free of ionizing radiation. Significant efforts have resulted in progress toward clinical lung MRI (1, 2), including the development of ultrashort-echo-time imaging for improved depiction of lung structure (3, 4), as well as regional $\dot{V}/Q$ imaging using hyperpolarized gas, oxygen-enhanced imaging, and Fourier decomposition of dynamic lung imaging (5–9). However, proton MRI has suffered from inherent challenges associated with MRI in the lung, and hyperpolarized gas imaging has been hindered by the need for costly specialized equipment and technical expertise. Consequently, lung MRI has not been routinely adopted.

Clinical MRI systems operate with a magnetic field strength of 1.5 T or 3 T, and for many years there has been an impetus to develop systems with higher magnetic field strengths. MRI engineering and imaging methods have improved dramatically in the past several decades, and computational power has become readily available. In light of these advancements, the author's group recently developed a high-performance low-field MRI system that integrates modern technology at 0.55 T and provides superior imaging quality in the lung (10).

This high-performance low-field MRI system configuration, paired with optimal imaging approaches, improves visualization of lung parenchyma, thereby enabling an abundance of new lung imaging applications. This new lung imaging technology, along with its proposed clinical application, received the 2019 American Thoracic Society (ATS) Building Education to Advance Research (BEAR) Cage Innovation Award.

What Does High-Performance Low-Field MRI Offer to Clinical Lung Imaging?

Compared with other imaging modalities, MRI offers the advantage of flexible image contrast. For example, an MRI exam can include assessment of anatomical structure and tissue dynamics, quantification of blood flow, characterization of tissue edema/fibrosis/iron/perfusion/viability, quantification of fat and water, and evaluation of microarchitecture (11, 12). However, in the context of pulmonary diseases, these capabilities been hampered by poor image quality, and comprehensive lung MRI exams have been unattainable.

In the lung, MRI image quality suffers from low water density limiting the available MRI signal, and from air–tissue interfaces causing local magnetic susceptibility gradients (13). High-performance low-field MRI technology can mitigate some of these challenges for the following reasons:

1. A contemporary magnet design operating at lower field produces a more uniform magnetic field, such that the magnetic susceptibility gradients caused by air–tissue interfaces are diminished. The field homogeneity results in reduced image distortion and improves parenchymal visualization.
2. Oxygen performs better as a contrast agent at low field by virtue of increased T1 relaxivity (10, 14). Oxygen-enhanced MRI has been successfully applied on conventional MRI systems for regional ventilation measurements (15, 16), but the signal enhancement will be greater at lower fields, resulting in improved sensitivity.
3. Lower-field MRI technology offers workflow advantages compared with conventional MRI, including reduced acoustic noise and vestibular upset, resulting in improved patient comfort; improved physiological monitoring (e.g., with less

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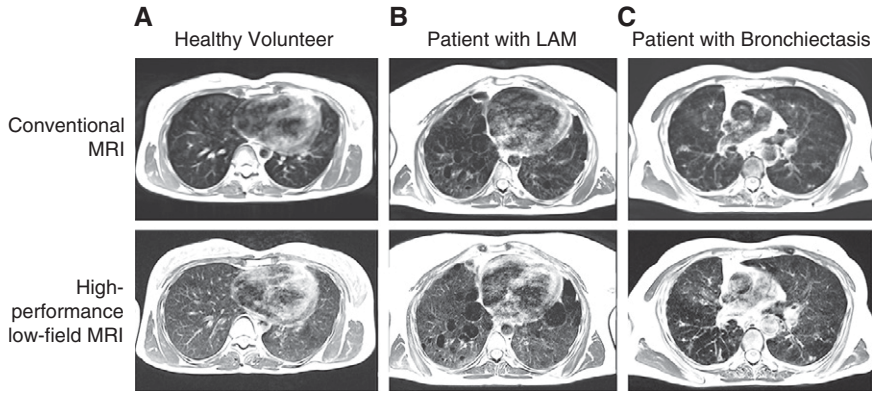

Figure 1. (*A–C*) Example T2-weighted magnetic resonance imaging (MRI) images obtained with a conventional MRI system (1.5-T MAGNETOM Aera; Siemens Healthcare) and the new high-performance low-field MRI system (prototype 0.55-T MAGNETOM Aera; Siemens Healthcare) from a healthy volunteer (*A*), a patient with lymphangioleiomyomatosis (LAM) (*B*), and a patient with bronchiectasis (*C*). The visibility of lung tissue using high-performance low-field MRI enables assessments of regional function and tissue characterization.

ECG distortion); and reduced costs for system manufacturing and installation, which may increase accessibility.

Figure 1 shows images obtained with conventional 1.5-T MRI and the high-performance 0.55-T MRI configuration, illustrating the clear improvement in parenchymal imaging.

A Comprehensive Functional Lung Imaging Exam

For the BEAR Cage Innovation award, the author proposed a comprehensive lung imaging exam that leverages the improved parenchymal visualization of high-performance low-field MRI (Figure 2). This exam is free of ionizing radiation, unlike CT, and it is less expensive and more accessible than conventional MRI. Moreover, it uses inhaled oxygen, which is more readily available than hyperpolarized gas, as a contrast agent. The proposed comprehensive lung MRI exam includes the following:

- Three-dimensional assessment of anatomy.
- Three-dimensional oxygen-enhanced ventilation mapping for regional assessment of lung function (6) (this method exploits the improved oxygen contrast at low field).
- Three-dimensional quantitative perfusion mapping for $\dot{V}/\dot{Q}$ mismatch assessment (17).
- Characterization of lung tissue using the flexible contrast of MRI (e.g., T1 contrast, T2 contrast, and diffusion imaging) for assessment of tissue characteristics, including edema, fibrosis, and microarchitecture.
- Assessment of blood oxygenation at rest and during exercise (18).

Implications of High-Performance Low-Field MRI in the Lung

High-performance low-field MRI systems will enable sophisticated diagnostic exams that have previously been difficult to perform. This new technology has important implications for the diagnosis and monitoring of pulmonary diseases, as well as our understanding of these diseases. Because MRI is free of ionizing radiation, the ability to obtain high-quality MR images of the lung could be particularly important for pediatric lung imaging.

Functional lung MRI will offer new clinical data to augment standard exams consisting of CT, spirometry, and exercise testing. For example, MRI measurements of regional $\dot{V}/\dot{Q}$ mismatch would offer an improvement over nuclear imaging methods that provide

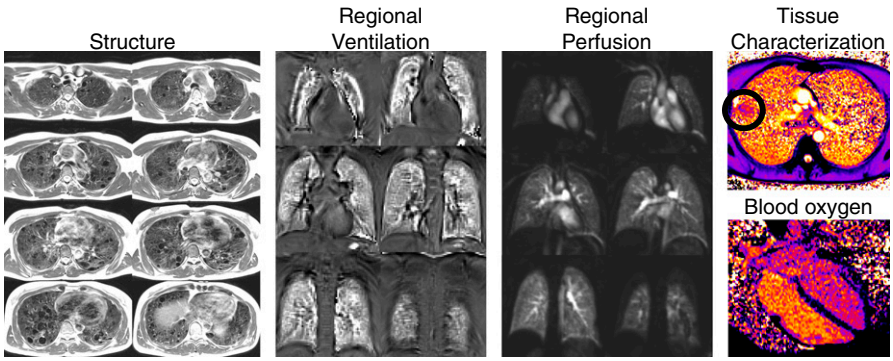

Figure 2. A comprehensive three-dimensional lung exam provided by high-performance low-field magnetic resonance imaging, including three-dimensional structural imaging, regional oxygen distribution mapping, regional perfusion mapping, tissue characterization from flexible magnetic resonance imaging contrast (T1 mapping shown here), and noninvasive assessment of blood oxygenation. This can be achieved in a single exam that is free of ionizing radiation. Adapted from Reference 23.

low resolution and are often inaccessible. Oxygen is an attractive contrast agent because it is less expensive, less demanding, and more available than hyperpolarized gas. Functional assessments of regional $\dot{V}/\dot{Q}$ will be valuable in a number of pulmonary diseases, including cystic fibrosis, chronic obstructive pulmonary disease, asthma, pulmonary embolism, and chronic thromboembolic pulmonary hypertension.

The ability to characterize the composition of lung pathology is also promising. For example, researchers have long sought to classify lung nodules as benign or malignant using other imaging modalities or radiomics (19, 20). MRI tissue characterization offers increased specificity and reduced radiation exposure compared with a contemporary clinical workflow in which patients are monitored over prolonged periods with CT imaging. Up to now, tissue characterization by MRI has not been successful, owing to the inadequate image quality obtained with conventional MRI. In the long term, such characterizations could reduce unnecessary lung biopsies, analogously to the reduction in prostate biopsies enabled by MRI screening technologies (21). Tissue characterization could also play an important role in imaging fibrosis, ischemia, and inflammation.

Ongoing Work toward Clinical Translation

Although these new imaging technologies are promising for improved clinical imaging of pulmonary diseases, significant technical development is required to implement optimal imaging methods for these new applications. Additional validation is required for oxygen-enhanced ventilation imaging and perfusion imaging at this field strength (22). Moreover, the evaluation of numerous individual pathologies is essential to understand the clinical significance of these new imaging markers. It is also possible to combine high-performance low-field MRI with hyperpolarized gas imaging, which may be desirable for some structure–function applications and could be explored in the future.

For our work, we adapted an existing MRI system (MAGNETOM Aera; Siemens Healthcare) to operate at a lower magnetic field strength (0.55 T) in collaboration with Siemens Healthcare. Whole-body, low-field MRI scanners with high-performance hardware suitable for lung imaging are not currently commercially available.

The ATS BEAR Cage Innovation Award

The BEAR Cage Innovation Award provides an opportunity for early career investigators to present their research proposals to both industry and academic representatives. The ATS Drug/Device Discovery and Development Committee sponsors this award to encourage innovation in translational research through the development of new technology. Three finalists among the early career applicants make an oral presentation at the ATS annual meeting, with questioning from the panel and the ATS conference attendees. The feedback received from this process is valuable to refine the research proposal and identify new salient avenues of investigation. The panel's selection of this MRI proposal indicates the clinical potential of this technology for lung imaging. ■

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