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REVIEW

MRI of pulmonary nodules: technique and diagnostic value

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Abstract

Chest wall invasion by a tumour and mediastinal masses are known to benefit from the superior soft tissue contrast of magnetic resonance imaging (MRI). However, helical computed tomography (CT) (i.e. with multiple row detector systems) remains the modality of choice to detect and follow lesions of the lung parenchyma. Since minimizing radiation exposure plays a minor role in oncologic patients, there are only few routine indications for which MRI of lung parenchyma is preferred to CT. This includes whole body MR imaging for staging or scientific studies with frequent follow-up examinations. MR-based lung imaging in this context was always considered as a weak point. Depending on the sequence technique and imaging conditions (i.e. ability to hold breath) the threshold for lung nodule detection with MRI using 1.5 T systems was estimated to be above 3–4 mm. The feasibility of lung MRI at 0.3–0.5 T and 3.0 T systems has been demonstrated. The clinical value of time-resolved lung nodule perfusion analysis cannot yet be determined, although the combination of perfusion characteristics with morphologic criteria contributes to estimate the integrity of a solitary lesion.

Keywords: *Lung magnetic resonance imaging; pulmonary nodule.*

Introduction

Magnetic resonance imaging (MRI) of the lung is an evolving, powerful tool for research and specific clinical applications. Although computed tomography (CT) remains the workhorse and the gold standard for imaging lung patho-morphology in cancer patients, a number of applications warrant the use of MRI. The advantages of MRI over CT are not only limited to the lack of ionizing radiation, which is of particular interest for the assessment of lung disease in children (e.g. pneumonia, cystic fibrosis) or in patients who require frequent follow-up examinations (e.g. immunocompromised patients with fever of unknown origin). While CT provides optimum spatial resolution, it offers only limited soft tissue contrast. Therefore, MRI is the modality of choice for imaging chest wall invasion by tumours and mediastinal masses. For the study of respiratory mechanics, dynamic lung MRI with free breathing or after systematic instructions to the patients offers clear advantages beyond the scope of CT. In particular, for patients presenting with lung cancer, dynamic lung MRI is a quick and reliable method to estimate tumour motion and chest wall or mediastinal adhesion and invasion. This information can be useful for planning surgery as well as high precision radiotherapy to protect surrounding healthy lung tissue. In oncological patient care, MRI has been shown to be particularly sensitive for the detection of cerebral, abdominal and vertebral metastases. Therefore, comprehensive studies on whole-body MRI have been developed for screening and staging of metastatic cancer. Since MRI of the lung remained difficult for a long time, detection of either lung metastases or a primary malignancy of the lung such as lung cancer were considered the weakest point of this strategy. This was one among other motivations for the development of

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strategies for lung MRI on a routine basis. Another motivation was to evaluate the capabilities of MRI as a potential replacement for CT in lung cancer screening. The purpose of this overview is to outline the capabilities of MRI for the detection and characterization of lung nodules.

Lung nodule detection with MRI

Evaluation of the diagnostic accuracy of different magnetic resonance (MR) imaging sequences for the detection of small artificial pulmonary nodules inside porcine lungs was carried out as a basic experiment in the field[1]. Three-dimensional (3D) and two-dimensional (2D) gradient-echo (GRE) sequences reached a sensitivity of 88% for 4 mm nodules. T2-weighted fast spin-echo (T2-FSE), and T2-weighted half Fourier single-shot sequences (T2-HASTE) were slightly inferior. For lesions larger than 5 mm, the sensitivity, specificity as well as positive and negative predictive values of all sequences except T2-weighted HASTE came close to 100%. From this experiment, it was concluded that common MR imaging sequences such as 3D GRE have a high diagnostic accuracy in depicting small pulmonary nodules when artefacts from cardiac and respiratory motion can be compensated for.

These experimental results were consistent with published data from patient studies[2]. The sensitivity of T2-weighted half Fourier FSE imaging and T1-weighted gradient echo imaging for nodules larger than 4 mm were estimated to be close to 85% and 90%. Schroeder *et al*.[3] found sensitivity values for T2-HASTE of 73% for lesions less than 3 mm, 86.3% for lesions between 3 and 5 mm, 95.7% for lesions between 6 and 10 mm, and 100% for lesions larger than 10 mm. Bruegel *et al*.[4] reported on mean sensitivities for lesion detection with triggered short-tau inversion recovery (STIR), FSE, and STIR of 72.0%, 69.0%, and 63.4%, respectively. In this study, HASTE, IR-HASTE, and pre- and post-contrast volumetric interpolated 3D gradient-echo (VIBE) were inferior to conventional FSE sequences.

Overall, it appears realistic to assume a threshold size of 3–4 mm for lung nodule detection with MRI, given that conditions are optimal (i.e. patient can keep a breath hold for 20 s or perfect gating/triggering; for an example, see Fig. 1). For practical use, a probability of 0.9 that a 3 mm nodule will be detected with gradient echo sequences can be interpreted in a way that 90% of all patients with a single 3 mm nodule would be correctly diagnosed, if this method was used for screening. Another interpretation would be that 90% of all 3 mm nodules in one patient could be detected. Patients with a single nodule of 5 mm and more would be detected with a sensitivity of 100%. With this, MRI is clearly superior to plain chest X-ray, but still inferior to CT (in particular multiple row detector scanners) for the detection of small pulmonary nodules. It is important to note that this does not apply to grossly calcified nodules, which appear black on any sequence. Thus, lung MRI cannot be recommended for staging chondrosarcoma or other entities with calcified metastases.

Nevertheless, the required sensitivity of a lung imaging method with respect to the size of solid lesions detected strongly depends on the clinical context, as very small benign nodules are a common finding in healthy patients. The clinical importance of detecting a 3 mm nodule in a patient with malignant disease and the decisions for treatment depending on the absence of lung metastases differs from detecting a similar lesion in a healthy patient who takes part in a screening program. It is known from CT that the number of findings, e.g. small pulmonary nodules, increases with refined techniques, but the specificity and clinical relevance of these findings decrease at the same time. Even in high risk groups for lung cancer, more than 90% of the detected nodules smaller than 10 mm were found to be benign. The clinical relevance of detecting lesions below 3 mm in size remains unclear and subject to discussion. MRI may even be discussed for lung cancer screening. At present, a method which detects solid pulmonary lesions between 2 and 3 mm in diameter with reasonably high sensitivity (e.g. 80%) and all lesions above 3 mm seems to be fairly sufficient for screening. If limited to T2-half Fourier FSE (HASTE) and 3D-GRE, in-room times could be limited to less than 5 min, thus making the examination more economic. However, since to date the cost/value ratio of lung cancer screening cannot yet be finally defined for CT, discussion of the potential role of MRI remains academic.

Protocol suggestions for lung MRI at 1.5 T

Based on these experiences, detailed standard protocols for lung MRI have been suggested only recently[5].The necessary hardware is available in most state-of-the-art 1.5 T scanners. Partial parallel imaging helps to reduce examination times to breath-hold periods of 20 s and less, each allowing the complete chest to be covered with one acquisition. Following a GRE localizer (2D-FLASH), a coronal T2-weighted single-shot half-Fourier FSE (HASTE) sequence with a high sensitivity for infiltrates and a transverse T1-weighted 3D-GRE (VIBE) sequence with a high sensitivity for small lesions are acquired in a breath-hold. Afterwards a coronal steady-state free precession sequence (SS-GRE, TrueFISP) in free breathing is obtained. This sequence has a high sensitivity for central pulmonary embolism. Distinct cardiac dysfunctions as well as impairment of the breathing mechanics are visible. The last step of the basic protocol is a transverse T2-weighted STIR (T2-TIRM) in a multi breath-hold technique to visualize enlarged lymph nodes as well as skeletal lesions. Alternatively, T2-weighted STIR can be replaced by a

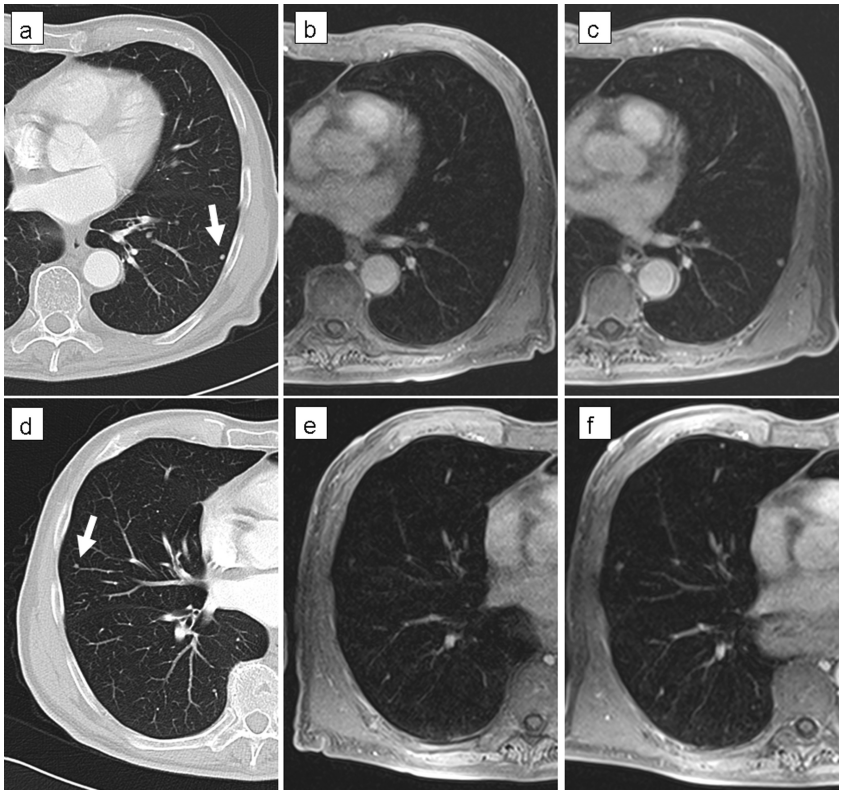

Figure 1 **An example demonstrating the limitations of MRI for the detection of small lung nodules: (a,d) Small pulmonary metastases of a malignant melanoma in a 62-year-old patient (5 mm slices of a standard helical CT scan). (b,e) MRI of the corresponding positions at the same time; (c,e) the follow-up MRI after 3 months (the contrast-enhanced transverse 3D-GRE (VIBE) images were obtained as part of a whole body study; TR/TE 3.15/1.38 ms, TA 20 s, +FA 8°, FOV 350×400 mm, slices 72/4 mm). The clearly visible 3 mm nodule in the left lower lobe ((a) and (b); marked with an arrow on (a)) grew to a diameter of 5 mm within 3 months (c). Another 3 mm nodule in the lateral right middle lobe (marked with an arrow on (d)) is hardly visible on the corresponding MRI due to cardiac pulsation, but becomes clearer in the follow up study after growing to 4–5 mm (f).**

fat saturated T2-weighted FSE with PROPELLER acquisition and reconstruction (T2 TSE BLADE). This navigator triggered approach does not reduce acquisition time but it significantly reduces motion artefacts even in patients with severe dyspnoea. For viewing 3D data obtained with breath-hold 3D-GRE (VIBE), a 3D viewer and reconstruction of 6–8 mm maximum intensity projection (MIP) reformations is recommended (Fig. 2).

Application of intravenous contrast material does not necessarily improve nodule detection. However, it improves the diagnostic yield of 3D-GRE sequences by the clearer depiction of vessels, hilar structures and pleural enhancement. Parenchymal disease and solid pathologies are also enhanced. Thus, contrast-enhanced series to exclude pulmonary malignancies, e.g. for staging purposes, preferably with a fat-saturated 3D-GRE sequence, may be useful. Contrast enhancement is also necessary in case of pleural processes (empyema, abscess, metastatic spread of carcinoma, mesothelioma) or for the further evaluation of solid masses as well as for functional imaging or angiography. This extension to the protocol with contrast-enhanced 3D-GRE sequences (VIBE) after contrast medium requires about 5 additional minutes for the procedure. Indications are tumorous lesions, unclear (malignant) pleural effusions and inflammatory diseases (vasculitis). This protocol can be further extended to a perfusion analysis using a 3D-GRE in a shared echo-technique (TREAT, TWIST) with high temporal resolution MR angiography (3D-FLASH) with high spatial resolution.

Further options to extend the standard protocol are T1- and T2-weighted SE or FSE-sequences with respiratory triggering (or gating). T2-weighted sequences contribute to the evaluation of lung parenchyma pathology and provide the same information about the chest wall and mediastinum and are thus preferred to T1-weighted SE. The value of this protocol extension for nodule detection is only minimal, but it contributes valuable information for separation of tumour from atelectasis and pleural effusion.

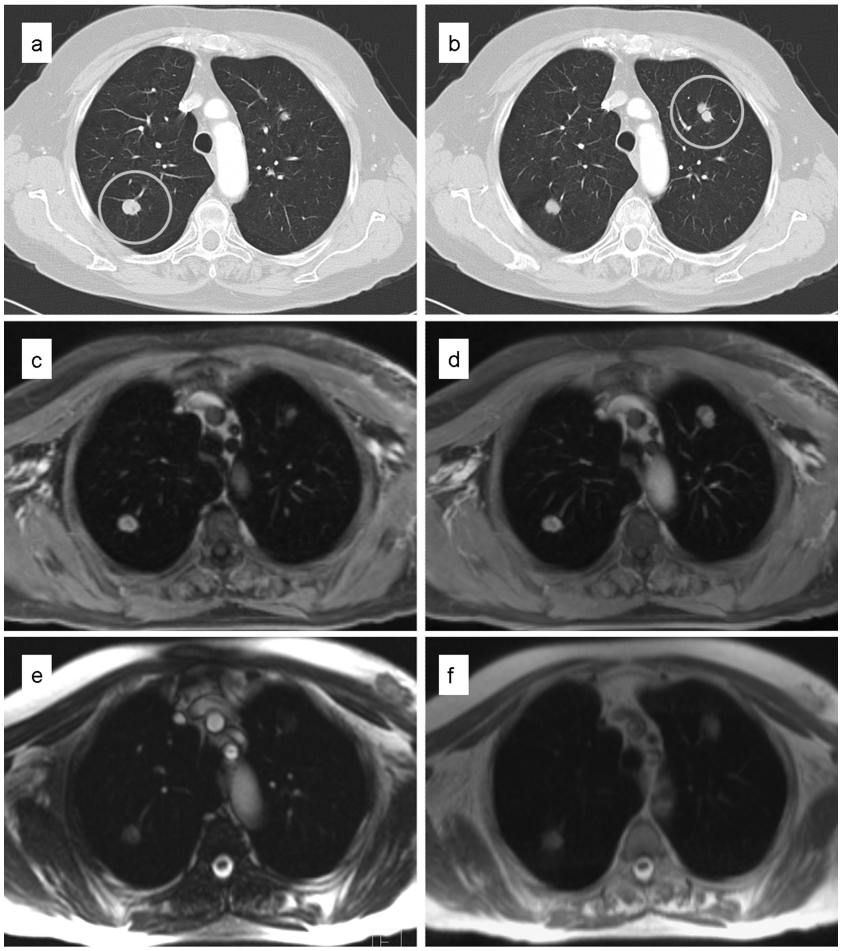

Figure 2 **A 67-year-old female patient with pulmonary metastases of a colorectal carcinoma. (a,b) Adjacent slices from a helical CT scan (Siemens Volume Zoom, 120 kVp, 70 mAs, 3 mm slice thickness). The images show a solid 1.4 cm nodule in the right upper lung lobe and two adjacent 0.7 and 0.9 cm nodules in the left upper lobe (lesions marked by circles on the CT images; histologic proof was obtained by wedge resection). (c,d) MR scans (Siemens Magnetom Avanto). Contrast-enhanced 3D-GRE (VIBE; on the left a single 4 mm slice, on the right an 8 mm MIP reconstruction; TR/TE 3.15/1.38 ms, TA 20 s, FA 8°, FOV 350 × 400 mm, slices 72/4 mm). (e) SS-GRE (TrueFISP; TR/TE 290.3/1.2 ms, TA 56 s, FA 80°, FOV 276 × 340 mm, slices 128/4 mm). (f) T2-weighted single-shot half-Fourier FSE (HASTE; TR/TE 550/30 ms, TA 16 s, FA 180°, FOV 309 × 450 mm, slices 35/6mm). All images were acquired using the breath-hold technique except for SS-GRE (free breathing); note the differences in chest wall configuration and nodule position.**

0.3, 1.5 or 3.0 T?

Within a few years, 3 T MRI has become widely available. The motivation to use a higher field strength is the almost linear increase of signal-to-noise ratios which allows increase in spatial resolution and thus should improve lesion detection. However, susceptibility artefacts also increase. They degrade the image quality and thus reduce the effectiveness of lung MRI in particular. Furthermore, ultra-high field systems increase the specific absorbed radiation (SAR) exposure of patients. This limits the use of fast breath-hold sequences which are already operating close to the SAR limits at 1.5 T. Therefore, to date only limited experience is available on lung MRI at 3 T. Dedicated sequences for this purpose have not been developed so far. Experimental studies and first reports on patients have shown that image quality using common pulse sequences developed for lung MRI at 1.5 T does not change substantially at 3 T[6,7]. Independently from field strength, T2-weighted FSE-MRI is favourable for the visualization of the mediastinum. Normal lung tissue can be visualized with good image quality using single-shot sequences (HASTE or TrueFISP). Lung nodules are ideally visualized with a volumetric interpolated 3D-GRE sequence (e.g. VIBE). HASTE-MRI is the preferred technique for the visualization of pneumonia at 1.5 T and 3 T, but also achieves good results for imaging lung nodules.

The particular problems of lung MRI imply that a lower field strength, e.g. 0.3–0.5 T should reduce

susceptibility to artefacts compared to 1.5 T in order to achieve a relative increase of lung signal intensity. However, practice shows that the gradient systems of the low field systems are usually weaker, so that the principle advantages at lower field strength have not been realized so far. Principally, low field MRI of the lung can be performed with T1-weighted GRE and T2-weighted FSE sequences. Steady-state gradient echo sequences with strong T1/T2 contrast producing high signals of solid and liquid pathology have also been found to be particularly useful. Also known as SS-FFE, TrueFISP or balanced steady-state acquisition with rewound gradient echo (BASG), they can be applied as 2D- or 3D-multislice acquisitions or as a single thick-slice technique. The studies conducted so far suggest a threshold nodule size of 6 mm for low field systems[8].

To conclude, at present no advantage can be seen in using ultra-high-field MR for scanning lungs; low-field scanners are economic and have the advantages of open systems regarding patient compliance, in particular with children.

Computer aided diagnosis (CAD)

Tools for automated lung nodule detection, known for some years for CT, have not yet been released for MRI. Only algorithms for lung nodule segmentation and volumetry as one component of these systems have been tested successfully so far[9]. If MRI should ever be discussed as a tool for lung cancer screening, reliable software for automated lung nodule detection would be a prerequisite.

Dynamic MRI for the characterization of pulmonary nodules

Dynamic contrast-enhanced MRI of solid lung lesions has been discussed as a non-invasive tool for evaluating the integrity of solitary pulmonary nodules, e.g. to replace biopsy. A first study used dynamic contrast-enhanced MRI on 51 patients with solitary pulmonary nodules to study kinetic and morphologic differences in vascularity and perfusion of malignant and benign lesions[10]. From this, a washout pattern appeared to be most specific for malignancy. When curve profiles and morphologic enhancement patterns were combined, sensitivity increased to 100%. So far, these results obtained in a small, selected patient group have not been confirmed by other authors and broader statistical evidence is required. Nevertheless, dynamic contrast-enhanced MRI can be considered a feasible, non-invasive method to study the perfusion kinetics of lung nodules. The potential of this method for monitoring chemotherapy (i.e. anti-angiogenetic agents) has not been investigated so far. As already concluded from similar studies based on CT perfusion, it can be assumed that absent or very low contrast uptake might have a high negative predictive value for the exclusion of malignancy of a lung nodule.

Conclusion

At the present time, the most advanced strategies for lung MRI have been adopted for 1.5 T scanners. Specific advantages of higher or lower field strengths may result in higher contrast to noise ratios, but are not yet defined. MRI has been proven to yield a higher sensitivity for lung nodules compared to plain chest X-ray, but it does not yet match CT. Specific advantages over CT are a higher soft tissue contrast, the capability of MRI to perform dynamic imaging of lesion displacement in relation to respiratory motion and the possibility of repeat studies due to the lack of radiation exposure. MRI may contribute to lesion characterization by evaluation of signal intensities and the dynamics of contrast uptake, but the criteria evaluated so far still need to be confirmed on a broad statistical basis. Experience from a number of comparative studies on CT and MRI of solid lung lesions is growing and will provide solid statistics in the very near future. For the time being, lung MRI has filled the gap within whole body MRI scanning in oncology and is ready to be used as a radiation free alternative to CT for screening purposes, given that numerous ongoing lung cancer screening trials should confirm the value of such programs. This would also open the way to develop dedicated scanners to perform studies with patients in an upright position to reduce in-room times for lung MRI on a routine basis.

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