Magnetic resonance imaging of pulmonary nodules: accuracy in a granulomatous disease-endemic region

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Aims and objectives

To estimate the diagnostic accuracy of signal intensity of the lesion-to-spinal cord ratio (LSR) and apparent diffusion coefficient (ADC) in diffusion-weighted (DW) magnetic resonance imaging of pulmonary nodules suspicious for lung cancer in granulomatous lung disease-endemic regions.
Methods and materials

Patients

This study received institutional review board approval, and all patients provided written informed consent. Patients with pulmonary nodules detected by chest CT between October 2010 and February 2015 from a single center from an endemic region of granulomatous disease were included. The inclusion criteria were: indeterminate solitary pulmonary nodule visible on CT, solid nodule, nodule diameter > 8mm, and histopathologic confirmation obtained or planned by surgical resection or transbronchial or transthoracic biopsy. All patients with inconclusive biopsy results were followed for 2 years. Lesions were considered to be benign (a) with histopathologic confirmation, (b) when the lesion subsequently disappeared or decreased in size, or (c) when the lesion appeared stable on follow-up (#24 months) CT. Identification of organisms in culture was also considered to be a benign finding.

MRI

MRI was performed using a 1.5-T scanner (Magnetom AERA; Siemens, Erlangen, Germany). For signal reception, a dedicated 08-element integrated matrix coil system that covered the whole thorax was used. This system consisted of one anterior and one posterior flexible phased-array coil, each containing a set of six receiver elements. A half-Fourier single-shot turbo spin-echo sequence was used, and the field of view (FOV) was patient adapted. The sequence was performed using respiratory gating, with a navigator signal that monitored the diaphragm position. The following sequence parameters were used: repetition time (TR)/echo time (TE)/flip angle, infinite/92 ms/150°; parallel acquisition factor, 2; slice thickness, 5 mm; distance factor, 20%; transversal (matrix, 380 × 256) and coronal (matrix, 400 × 320) orientations; and acquisition time, approximately 90 s. A volumetric interpolated breath-hold examination (VIBE) sequence was chosen for fast T1-weighted MRI. Imaging parameters for the VIBE sequence were: TR/TE, 5.12/2.51 ms; flip angle, 10°; partition thickness, 5 mm with no interslice gap; and matrix size, 256 × 116 with a three-dimensional breath-hold imaging technique. A T2-weighted fat-saturated BLADE (proprietary name for periodically rotated overlapping parallel lines with enhanced reconstruction in MR systems from Siemens Healthcare) sequence was also used, with the following imaging parameters: TR/TE, 4670/113 ms; and partition thickness, 5 mm with no interslice gap. DWI was performed using a single-shot echo-planar technique with a slice thickness of 5 mm under spectral attenuated inversion recovery, with respiratory-triggered scanning. The DWI parameters were: TR/TE/flip angle, 3000-4500ms/65ms/90°; diffusion gradient encoding in three orthogonal directions; $b = 0$ and 800 s/mm$^2$; field of view, 350 mm; and matrix size, 128 × 128.
The overall time spent in the MRI room was approximately 15 min. No patient required sedation. Contrast medium was not used.

**Image analysis**

Mean signal intensity on DWI was analysed semiquantitatively by focusing the region of interest (ROI) on the lesion with two gradient factors ($b_h$ and $b_l$), as well as on the spinal cord at the same level. When a lesion seemed to be heterogeneous, the ROI was placed at the location of highest signal intensity. Two radiologists with 24 and 12 years of experience, respectively, in chest MRI defined DWI section locations.

The ADC was estimated from the ratio of the two image signal intensities, according to the following equation: $\text{ADC} = \frac{\ln \left( \frac{SI_h}{SI_l} \right)}{b_h - b_l}$, where $SI_h$ and $SI_l$ are the signal intensities in the lesion of interest obtained with two mean pressure gradients ($b_h$ and $b_l$, respectively). In this study, $b_h$ was 800 s/mm$^2$ and $b_l$ was 0 s/mm$^2$.

The LSR of signal intensity was measured on the same DW image with a diffusion gradient of $b_h = 800$ s/mm$^2$. An ROI of the same size as that placed on the spinal cord was positioned on the lesion. The ROIs placed on the thoracic spinal cord were 50-80 mm$^2$, which was equivalent to 14-22 pixels. We used DW images with averaged multiple signal intensities obtained during quiet breathing, instead of performing no averaging of signal intensity obtained during breath holding. Accordingly, the signal-to-noise ratio was reasonably good and the LSRs obtained were reproducible.

Signal intensity on T1 and T2 images was measured in an ROI of 30-40mm$^2$ in the inner space of the nodule. The same ROI was used to measured T1 and T2 signal intensity in the longissimus dorsi muscle. The nodule:muscle ratios of T1 and T2 signal intensity were calculated for comparison.

No problematic motion artifact that resulted in poor image quality or instance of image distortion due to susceptibility occurred in this series.

**Statistical analysis**

Statistical analysis was performed with SPSS software (version 15.0 for Windows; SPSS Inc., Chicago, IL, USA). To compare ADCs and LSRs between lung cancer and benign lesions, the Mann-Whitney $U$ test was used. Receiver operating characteristic (ROC) curve analysis was used to evaluate the diagnostic capabilities of ADC and LSR in the differentiation of benign lesions and lung cancer. Cut-off values were calculated using the JMP IN statistical programme (version 5.1.1 for Windows; SAS Institute, Cary, NC, USA).
The accuracy of the two parameters was compared statistically using the McNemar test. 
*P* values <0.05 were considered to be significant in all analyses.
Results

Forty-nine patients (20 men; mean age 65.4 ± 14.2 years) with solitary pulmonary nodules were included in the study. The mean nodule size was 1.2 (range, 0.8-2.9) cm. Pathologic confirmation was obtained by surgical resection in 30 patients and by transbronchial or transthoracic biopsy in 19 patients. Biopsy demonstrated the inconclusive presence of inflammatory tissue in 10 patients, who were followed for 24 months. Lesion regression was demonstrated in seven of these patients (Figure 1). The sample comprised 31 cases of lung cancer (adenocarcinoma, n = 21; squamous cell carcinoma, n = 9; small cell carcinoma, n = 1) and 18 benign lesions (inconclusive inflammatory lesions, n = 7; fungal infection, n = 7; tuberculous mycobacterial infection, n = 3; cryptogenic organizing pneumonia, n = 1).

Table 1: Diagnostic capability of T2, ADC and LSR.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Cutoff Value</th>
<th>Sensitivity</th>
<th>Specificity</th>
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PPV: positive predictive value, NPV: negative predictive value, ADC is measured as x10[-3] mm²/sec.

*ADC vs. LSR (p=0.688); T2 vs ADC or LSR (p<0.005).

References: Bruno Hochhegger
Fig. 1: Images from a 59-year-old asymptomatic male smoker. (a) CT demonstrated the presence of a spiculated solid pulmonary nodule with a diameter of 2.4 cm in the right upper lobe. (b) A T2-weighted sequence showed hypointense signal in the nodule. (c) A T1-weighted sequences showed hyperintense signal in the nodule. (d) A diffusion-weighted sequence showed no restriction. CT-guided biopsy evidenced a nonspecific inflammatory process and follow-up CT (e) indicated reduction of lesion size. (ADC: 1.56 x 10^{-3} mm^2/sec; LSR: 0.85; T1 index 0.87; T2 index 0.67)

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ADCs

ADCs were obtained for all patients. The calculated mean ADCs ± standard deviations for lung cancer and benign lesions were 0.9 ± 0.2 and 1.3 ± 0.2 x 10^{-3} mm^2/s, respectively (P<0.001).

LSRs

LSRs were obtained for all patients. The mean LSRs for lung cancer and benign lesions were 1.4 ± 0.3 and 1 ± 0.1, respectively (P<0.001).
T1 and T2 ratios

The overall mean T2 signal intensity ratio was 1.1 ± 0.4. This ratio differed significantly between benign and malignant lesions (0.8 ± 0.2 vs. 1.6 ± 0.2; *P* < 0.05). The T1 signal intensity ratio did not differ according to lesion type (overall, 0.9 ± 0.2; malignant, 1 ± 0.2; benign, 0.9 ± 0.2).

ROC findings

ROC curves for ADCs, LSRs and T2 signal are shown in Figure 2. The area under the ROC curve was 0.9 (95% confidence interval, 0.8-1) for LSR and 0.9 (95% confidence interval, 0.8 -1) for ADC; this difference was not significant. Table 1 shows results for the diagnostic capability of ADC and LSR. With a cut-off value of $1.08 \times 10^{-3}$ mm$^2$/s, the ADC had a positive predictive value of 88.2%, a negative predictive value of 90.6%, and an accuracy of 89.8% in the detection of lung cancer. With a cut-off value of $1.20 \times 10^{-3}$ mm$^2$/s, the LSR had a positive predictive value of 94.1%, a negative predictive value of 93.8%, and an accuracy of 93.9% for the detection of lung cancer.
Fig. 2: Results of receiver operating characteristic analysis for the ADC, LSR and T2 signal. ADC, apparent diffusion coefficient; LSR, lesion-to-spinal cord ratio; AUC, area under the curve.

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*ADC vs. LSR (P=0.688); T2 vs ADC or LSR (p<0.005).

Table 1: Table 1. Diagnostic capability of the ADC and LSRs

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**Fig. 1:** Images from a 59-year-old asymptomatic male smoker. (a) CT demonstrated the presence of a spiculated solid pulmonary nodule with a diameter of 2.4cm in the right upper lobe. (b) A T2-weighted sequence showed hypointense signal in the nodule. (c) A T1-weighted sequence showed hyperintense signal in the nodule. (d) A diffusion-weighted sequence showed no restriction. CT-guided biopsy evidenced a nonspecific
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**Fig. 2:** Results of receiver operating characteristic analysis for the ADC, LSR and T2 signal. ADC, apparent diffusion coefficient; LSR, lesion-to-spinal cord ratio; AUC, area under the curve.

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Conclusion

In conclusion, DWI can help to differentiate malignant from benign lesions on the basis of tissue cellularity according to the ADC and the LSR, with a accuracy of at least 93.9%. In addition, the T2 signal intensity ratio differed significantly between benign and malignant lesions, with malignant lesions having larger T2 signal ratios than to benign lesions.
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