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Lung nodule detection in a high-risk population: Comparison of magnetic resonance imaging and low-dose computed tomography

Gregor Sommer[a,b,c,*], Jan Tremper[a,b,1], Marcel Koenigkam-Santos[b,d,e,2], Stefan Delorme[a,b,3], Nikolaus Becker[f,4], Jürgen Biederer[b,g,5], Hans-Ulrich Kauczor[b,g,5], Claus Peter Heussel[b,d,6], Heinz-Peter Schlemmer[a,b,7], Michael Puderbach[b,d,8]

[a] Department of Radiology (E010), German Cancer Research Center (DKFZ), Im Neuenheimer Feld 280, 69120 Heidelberg, Germany
[b] Translational Lung Research Center Heidelberg (TLRC-H), Member of the German Center for Lung Research, Heidelberg, Germany
[c] Clinic of Radiology and Nuclear Medicine, University of Basel Hospital, Basel, Switzerland
[d] Department of Diagnostic and Interventional Radiology with Nuclear Medicine, Thoraxklinik Heidelberg gGmbH, Amalienstr. 5, 69126 Heidelberg, Germany
[e] Department of Radiology, University Hospital of the School of Medicine of Ribeirao Preto – University of Sao Paulo, Av. Bandeirantes 3900, Campus Universitario Monte Alegre, 14048 900 Ribeirao Preto, SP, Brazil
[f] Division of Cancer Epidemiology (C020), German Cancer Research Center (DKFZ), Im Neuenheimer Feld 581, 69120 Heidelberg, Germany
[g] Department of Diagnostic and Interventional Radiology, University Hospital Heidelberg, Im Neuenheimer Feld 110, 69120 Heidelberg, Germany

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ABSTRACT

Objective: To investigate the potential of MRI for lung nodule detection in a high-risk population in comparison to low-dose CT.
Methods: 49 participants (31 men, 18 women, 51–71 years) of the German Lung Cancer Screening and Intervention Trial (LUSI) with a cancer-suspicious lung lesion in CT were examined with non-contrast-enhanced MRI of the lung at 1.5 T. Data were pseudonymized and presented at random order together with 30 datasets (23 in men, 7 in women, 18–64 years) from healthy volunteers. Two radiologists read the data for the presence of nodules. Sensitivity and specificity were calculated. Gold standard was either histology or long-term follow-up. Contrast-to-Noise-Ratio (CNR) was measured for all detected lesions in all MRI sequences.
Results: Average maximum diameter of the lesions was 15 mm. Overall sensitivity and specificity of MRI were 48% (26/54) and 88% (29/33) compared to low-dose CT. Sensitivity of MRI was significantly higher for malignant nodules (78% (12.5/16)) than for benign ones (36% (13.5/38); $P = 0.007$). There was no statistically significant difference in sensitivity between nodules (benign and malignant) larger or smaller than 10 mm ($P = 0.7$). Inter observer agreement was 84% ($\kappa = 0.65$). Lesion-to-background CNR of T2-weighted single-shot turbo-spin-echo was significantly higher for malignant nodules (89 ± 27) than for benign ones (56 ± 23; $P = 0.002$).
Conclusion: The sensitivity of MRI for detection of malignant pulmonary nodules in a high-risk population is 78%. Due to its inherent soft tissue contrast, MRI is more sensitive to malignant nodules than to benign ones. MRI may therefore represent a useful test for early detection of lung cancer.
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* Corresponding author at: Clinic of Radiology and Nuclear Medicine, University of Basel Hospital, Petersgraben 4, 4031 Basel, Switzerland. Tel.: +41 61 328 63 44.
E-mail addresses: gregor.sommer@usb.ch (G. Sommer), j.tremper@dkfz.de (J. Tremper), marcelk46@yahoo.com.br (M. Koenigkam-Santos), s.delorme@dkfz.de (S. Delorme), n.becker@dkfz.de (N. Becker), juergen.biederer@uni-heidelberg.de (J. Biederer), hu.kauczor@med.uni-heidelberg.de (H.-U. Kauczor), heussel@uni-heidelberg.de (C.P. Heussel), h.schlemmer@dkfz.de (H.-P. Schlemmer), m.puderbach@gmail.com (M. Puderbach).
[1] Tel.: +49 6221 42 2603.
[2] Tel.: +55 16 36022640.
[3] Tel.: +49 6221 42 2461.
[4] Tel.: +49 6221 42 4220.
[5] Tel.: +49 6221 56 6410.
[6] Tel.: +49 6221 396 1500.
[7] Tel.: +49 6221 42 2563.
[8] Tel.: +49 6221 396 1500.

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1. Introduction

The National Lung Screening Trial (NLST) [1] has demonstrated the benefit of lung cancer screening with multi-slice computed tomography (CT) in a high-risk population. Among a number of lung cancer screening programs in different countries, this was the first study that achieved a relative reduction of lung-cancer-specific mortality of up to 20% by using low-dose CT screening instead of radiography. However, as ionizing radiation associated with CT increases the individual risk to develop cancer depending on the participants' age [2,3], repetitive application of CT in long-term screening programs with accumulating doses is problematic. The additional risk of individual participants to develop cancer caused by annual low-dose CT for screening purposes in a population of current and former smokers aged 50–75 years is estimated to be 0.5–5.5% [4]. This may seriously counteract the positive effects of screening on cancer-specific mortality.

Magnetic resonance imaging (MRI), which is not associated with ionizing radiation, is applied increasingly in various pulmonary diseases including lung cancer [5,6] and may be discussed as a potential alternative to low-dose CT for detection of pulmonary nodules [7]. Previous studies dedicated to lung nodule detection with MRI have demonstrated its technical feasibility [8] and investigated its diagnostic performance in various pulmonary malignancies [9–11]. Furthermore, experience in large numbers of healthy subjects has been reported [12]. However, to the best of our knowledge, there is no data available elucidating the diagnostic potential of MRI for early detection of lung nodules in subjects at risk. The objective of this study was therefore to investigate the potential of MRI for early detection of cancer-suspicious lung lesions in a high-risk population in comparison to low-dose CT.

2. Materials and methods

2.1. Study participants

The study population consisted of 49 prospectively included individuals with unclear lung nodules and a control group of 30 datasets from healthy volunteers. The 49 individuals (31 men, 18 women, mean age 61 years, age range 51–71 years) were recruited consecutively between January 2009 and July 2012 among the participants of the ongoing German Lung Cancer Screening and Intervention trial (LUSI), which investigates the effects of CT-based lung cancer screening intervention in more than 4000 individuals with history of heavy smoking. Study concept and detailed inclusion criteria for LUSI are given in [13]. For the current study, we prospectively included those LUSI participants who were classified for immediate recall by prior CT according to the LUSI protocol and had no contraindications for MRI. Criteria for immediate recall were either presence of a pulmonary lesion larger than 10 mm or a lesion with calculated volume doubling time (VDT) less than 400 days at follow-up. All participants classified for immediate recall were recommended to attend an office-based pulmonologist for individual assessment. One patient did not follow this recommendation after initial CT, but attended the next screening round, where he was again classified for immediate recall due to nodule growth. Consequently, this patient received two CT and MRI exams in consecutive screening rounds, which were both included in this evaluation. All procedures were in accordance with the declaration of Helsinki. Informed consent was obtained from all participants. The requirements of the institutional review board were fulfilled.

2.2. CT examinations

CT scans were performed as an integral part of LUSI using a 16-row system (Aquilion 16, Toshiba Medical Systems, Neuss, Germany) and, from 2010 on, a 128-row system (Somatom Definition Flash, Siemens Healthcare, Forchheim, Germany). Both systems were operated in low-dose mode with maximum effective doses of 1.6–2 mSv per scan. Slice thickness was 1 mm with reconstruction intervals of 0.8 mm and 0.7 mm, respectively. Specially trained radiologists evaluated the CT data following the algorithm described in [13]. Initial CT scans were evaluated with 2D image viewing. Subsequent evaluation at follow-up was done with additional 3D presentation using computer-aided detection (CAD) software (MEDIAN Technologies, Valbonne, France).

2.3. MRI examinations

MRI exams for LUSI participants were arranged during a patient consultation after the corresponding CT and scheduled as shortly as possible thereafter. The mean time difference between MRI and prior CT was 45 days (standard deviation (SD) 21 days, range 15–140 days, median 37 days). All MRI exams were performed on a clinical 1.5 T whole-body scanner (Magnetom Avanto, Siemens Healthcare, Erlangen, Germany) with multi-channel phased-array receiver coils. The MRI protocol consisted of T2-weighted half-Fourier-acquired single-shot turbo-spin-echo (HASTE) and balanced steady-state free precession (b-SSFP) sequences in coronal and transversal orientation and T1-weighted 3D gradient-recalled-echo volume-interpolated breath-hold examination (VIBE) in transversal orientation. Sequence parameters referred to published standards [5,14] and are given in Table 1. No contrast agent was applied. Total in-room time was 15 min.

2.4. Definition of negative controls

Thirty MRI datasets (23 in men, 7 in women, mean age 33 years, age range 18–64 years) were retrospectively selected as negative controls from our institutional database after finalization of the study. This control group consisted of healthy volunteers who received MRI of the chest in different scientific contexts, but with identical sequences as used for the LUSI participants. Control subjects did not undergo CT or any other diagnostic workup. Informed consent was obtained from all volunteers and included consent both to the MRI examination itself and to the use of the acquired data for statistical evaluation at later times.

2.5. Image reading

The 50 MRI datasets from the 49 LUSI participants and the 30 volunteer datasets were pseudonymized and presented at random order. All information that was considered a potential bias for the readers (dates of birth, gender, study time, etc.) was removed from the Digital Imaging and Communications in Medicine (DICOM) file headers. Then two board-certified radiologists with 7 (M.K.S., Reader 1) and 13 years (M.P., Reader 2) experience in body MRI performed blinded readings of the resulting 80 MRI datasets for suspicious pulmonary lesions. Readers were asked to indicate the presence of suspicious lesions (yes/no) and their level of diagnostic confidence (high/medium/low) on a dedicated reporting sheet. In case of positive findings, readers also had to provide size and position (series, image number) of the detected lesion and indicate the sequence that was most useful for diagnosis. Additionally, signal intensity values from the lesions and the normal lung parenchyma were measured by regions-of-interest (ROI) in the transversal datasets. ROIs for lesions were oval shaped and defined to have the maximum possible size within the lesion. ROIs

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