Dynamic contrast-enhanced MRI versus \(^{18}\text{F}-\text{FDG}\) PET/CT: Which is better in differentiation between malignant and benign solitary pulmonary nodules?

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Abstract

**Objective:** To prospectively compare the discriminative capacity of dynamic contrast enhanced-magnetic resonance imaging (DCE-MRI) with that of \(^{18}\text{F}-\text{FDG}\) positron emission tomography/computed tomography (PET/CT) in the differentiation of malignant and benign solitary pulmonary nodules (SPNs).

**Methods:** Forty-nine patients with SPNs were included in this prospective study. Thirty-two of the patients had malignant SPNs, while the other 17 had benign SPNs. All these patients underwent DCE-MRI and \(^{18}\text{F}-\text{FDG}\) PET/CT examinations. The quantitative MRI pharmacokinetic parameters, including the trans-endothelial transfer constant (\(K_{\text{trans}}\)), redistribution rate constant (\(K_{\text{ep}}\)), and fractional volume (\(V_e\)), were calculated using the Extended-Tofts Linear two-compartment model. The \(^{18}\text{F}-\text{FDG}\) PET/CT parameter, maximum standardized uptake value (SUV\(_{\text{max}}\)), was also measured. Spearman’s correlations were calculated between the MRI pharmacokinetic parameters and the SUV\(_{\text{max}}\) of each SPN. These parameters were statistically compared between the malignant and benign nodules. Receiver operating characteristic (ROC) analyses were used to compare the diagnostic capability between the DCE-MRI and \(^{18}\text{F}-\text{FDG}\) PET/CT indexes.

**Results:** Positive correlations were found between \(K_{\text{trans}}\) and SUV\(_{\text{max}}\), and between \(K_{\text{ep}}\) and SUV\(_{\text{max}}\) (\(P<0.05\)). There were significant differences between the malignant and benign nodules in terms of the \(K_{\text{trans}}\), \(K_{\text{ep}}\) and SUV\(_{\text{max}}\) values (\(P<0.05\)). The areas under the ROC curve (AUC) of \(K_{\text{trans}}\), \(K_{\text{ep}}\) and SUV\(_{\text{max}}\) between the malignant and benign nodules were 0.909, 0.838 and 0.759, respectively. The sensitivity and specificity in differentiating malignant from benign SPNs were 90.6% and 82.4% for \(K_{\text{trans}}\), 87.5% and 76.5% for \(K_{\text{ep}}\), and 75.0% and 70.6% for SUV\(_{\text{max}}\), respectively. The sensitivity and specificity of \(K_{\text{trans}}\) and \(K_{\text{ep}}\) were higher than those of SUV\(_{\text{max}}\), but there was no significant difference between them (\(P>0.05\)).

**Conclusions:** DCE-MRI can be used to differentiate between benign and malignant SPNs and has the advantage of being radiation free.

**Keywords:** Solitary pulmonary nodule; dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI); positron emission tomography/computed tomography (PET/CT)

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Introduction

A solitary pulmonary nodule (SPN) is defined as a rounded lesion less than 3 cm in diameter that is completely surrounded by pulmonary parenchyma and without other pulmonary abnormalities (1). Ideally, the aims of diagnosis and management are to promptly perform surgery in all patients with operable malignant nodules and to avoid unnecessary treatment in those patients with benign lesions. For this reason, the accurate diagnosis of SPNs is very important. However, the differentiation of malignant from benign lung nodules is difficult in routine clinical practice. Initially, conventional computed tomography (CT) was used to obtain diagnostic information based on morphological images. As functional imaging has developed, some new methods, such as dynamic contrast-enhanced (DCE)-CT (2) and 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT), have been introduced to quantitatively evaluate pulmonary nodules (3,4). DCE-CT, 18F-FDG PET and integrated 18F-FDG PET/CT provide excellent diagnostic accuracies (2-4). However, these modalities subject patients to both ionizing radiation and its associated risks. Another disadvantage of an 18F-FDG PET/CT exam is its high price.

Magnetic resonance imaging (MRI) does not subject a patient to any ionizing radiation. While T1- and T2-weighted imaging, including in- and out-of-phase gradient echo T1-weighted images, can aid in distinguishing pulmonary hamartomas via macroscopic and microscopic fat from certain granulomas and pulmonary malignancy, DCE-MRI has been shown to add further diagnostic specificity (5). Several studies used DCE-MRI with semi-quantitative parameters for differentiating malignant nodules from benign nodules in both small and large patient populations, yielding a broad range of sensitivities (52%–100%), specificities (from 17%–100%), and accuracies (from 58%–96%) (6,7). Thus, the semi-quantitative assessments of DCE-MRI could help diagnose SPNs to a certain extent, though not reliably. More quantitative assessments can be made with the pharmacokinetic parameters of DCE-MRI, such as the trans-endothelial transfer constant (K_{trans}), the redistribution rate constant (K_{ep}), and the fractional volume (V_c) of the extravascular extracellular space (EES) (8). Several studies reported that quantitative DCE-MRI was able to differentiate malignant from benign brain, breast, and prostatic lesions with both high sensitivity and specificity (9-11). However, few studies have been performed using DCE-MRI for lung imaging because of the technical difficulties related to cardiorespiratory motion and its associated artifacts, which heavily influence the accuracy of the parameters (12,13). As registration methods have developed, so have non-rigid image registration procedures that are used to correct for motion artifacts during the dynamic data acquisition of MRI (14). This method is based on the restoration of the deconvolved joint statistics, which are forced to register between the images to estimate an initial spatial transformation (15). It can register not only the positional movement of organs but also their transformation. In Molinari et al.’s study of DCE-MRI of lungs, they used non-rigid registration to reduce motion artifacts, which effectively improved image quality (16). Therefore, the purpose of our study was to prospectively compare the capability of DCE-MRI using non-rigid registration with that of 18F-FDG PET/CT to distinguish malignant from benign SPNs.

Materials and methods

Patients

This prospective study was approved by the institutional review board of Nantong Tumor Hospital. The methods used in this study were carried out in accordance with the Declaration of Helsinki. Written informed consent was obtained from each subject prior the initiation of the study. From October 2013 to October 2016, a total of 54 consecutive patients, with newly detected SPNs via chest radiography or CT, needed further evaluation. The patients were enrolled in this study according to the following criteria: 1) the absence of calcification or definite fat attenuation of the nodule observed by CT; 2) a nodule diameter between 8–30 mm. Lesion size was calculated by using the maximum long-axis diameter of the lung window settings in the transverse plane; 3) the absence of recent history (within the prior month) of pneumonia or immunodeficiency; and 4) the ability to participate cooperatively in the procedures. Five of the 54 patients were excluded, 3 of whom had detected calcifications in the nodules and 2 of whom were uncooperative during the procedures. According to the inclusive and exclusive criteria, a total of 49 consecutive patients with SPNs were included (29 males; 20 females), with a mean age of 61.8 (range, 44–78) years.
**MRI protocol**

MR imaging was performed using a 1.5T system (Espree; Siemens Medical Solutions, Erlangen, Germany) with a 16-channel phased-array torso XL coil for signal reception. First, fat saturated T2-weighted fast spin-echo sagittal images were obtained with the following parameters: time of repetition/time of echo (TR/TE), 6,680 ms/109 ms; flip angle, 70°; image matrix, 256×186; field of view (FOV), 380 mm × 380 mm; thickness, 4.0 mm; and overlap, 0 mm. Both sequences encompassed the whole thorax. In reference to de Langen et al.’s method (17), all the DCE-MR images were acquired in transverse planes by using a breath-holding technique. For the DCE-MRI acquisition, first, volumetric interpolated breath-hold examination (VIBE) T1-weighted non-enhanced sequences with four different flip angles (3°, 6°, 9° and 12° respectively) were used to obtain a T1 map of the tissue (18). Then, we started the dynamic acquisition using a VIBE T1-weighted sequence (TR 5.57 ms, TE 2.38 ms, number of averages 1, FOV 380 mm × 380 mm, matrix 256×256, flip angle 12°, 20 slices, and slice thickness 4.2 mm). After three non-contrast acquisition phases were obtained as the baseline images, a volume (based on each individual’s body weight, 0.2 mmol/kg) of gadolinium (Omniscan, GE healthcare Ireland, Carrigtwohill, Ireland) was injected intravenously at a rate of 3 mL/s by a power injector. To minimize any artifacts caused by respiratory movement, a breath-hold scan was required during two phases (approximately 13 s) repeatedly throughout the acquisition. Finally, 40 phases were acquired, 3 of which were non-contrast phases (total data-acquisition time 5 min 27 s, with a temporal resolution of 6.4 s/phase).

**18F-FDG PET/CT examinations**

All the 18F-FDG PET/CT examinations were performed on a PET/CT scanner (Gemini TF, Philips Healthcare, Best, the Netherlands). The axes of the multidetector CT and PET systems were mechanically aligned so that one could move the patient from the multidetector CT scanner gantry to the PET scanner gantry by simply changing the position of the examination table. Seven to eight frames (3 min/frame) of emission PET data were acquired in the three-dimensional mode after obtaining a non-contrast CT scan from the base of the skull to the upper thigh (120 kV; 150 mA; section width, 3.75 mm). The emission 18F-FDG PET images were reconstructed using an iterative method (ordered-subsets expectation maximization with 2 iterations and 20 subsets, field of view, 600 mm, slice thickness, 3 mm) and were corrected by reference to the non-contrast CT image attenuation. All the patients were required to fast for at least 6 h before the PET/CT examination. Blood glucose measurements were obtained from all the patients before the administration of the 18F-FDG scanning, and glucose levels were required to be less than 140 mg/dL at the time of injection. Then, 18F-FDG was intravenously administered at a rate of 3.3 MBq per kilogram of body weight, and 18F-FDG PET/CT images were obtained from the skull to the middle region of the thigh 60 min after the completion of the injection.

**MR image and data analysis**

Morphologic evaluations and quantitative analysis of DCE images were performed by two radiologists with 7 and 10 years of experience in lung imaging and diagnosis, respectively. Both of them were blinded to the final diagnosis. The SPNs were analyzed concerning their size and margin (e.g., smooth, non-smooth). The MR images were reviewed independently by two observers who reached a decision by consensus. All of the DCE-MRI data were transferred into non-commercial software (OmniKinetics, GE Healthcare China, Beijing, China). A major problem in DCE-MRI of lungs is motion artifacts due to respiration; thus, motion correction is needed to improve the quantitative accuracy. Non-rigid registration with the OmniKinetics software uses free-form deformation and mutual information methods (18). The method adapts to not only the movements of rotation or translation but also local (elastic) deformations, such as in the lungs, liver or heart; the performance of this image processing step is necessary as it reduces the motion artifacts before the measurements of pharmacokinetic parameters (19). These transformations are capable of locally warping the last phase DCE-MR image to align with the first phase reference image (18). Thereafter, robust data were guaranteed. In our study, non-rigid registration was done before the measurements of the DCE-MRI parameters. The artery input function (AIF) was obtained by manually drawing a small, circular region of interest (ROI) in the thoracic aorta in the same plane as the maximal transverse diameter of the SPN. The enhancement kinetics from each pixel was measured throughout all the dynamic phases and was fitted by using a two-compartment extended Tofts model. The pharmacokinetic parameters Ktrans, Keq and Vc were...
derived, and a color map of each parameter was generated. A single slice of the axial DCE-MRI scans of the maximal area of each lesion was analyzed in order to assess pairs of the DCE-MRI images from almost identical parts of each nodule. A ROI was drawn manually to contour the border of each SPN at the level of the longest transverse diameter of the lesion based on post-contrast T1-weighted images (Figure 1A, 2A). Any visually identified vessels or necrotic areas were excluded.

**Measurement of ¹⁸F-FDG PET/CT parameters**

The ¹⁸F-FDG PET/CT images were visually evaluated on a dedicated workstation (Philips Advantage Workstation) by two nuclear medicine specialists with 5 years and 6 years of PET/CT experience. Both of them were blinded to the final diagnosis. The metabolic parameter, the maximum standardized uptake value (SUV\text{max}), was obtained using the Volume Viewer software (Shanghai Xingxiang Co. Ltd., China). ROI placement was performed using the same rules as those for DCE-MRI image ROI placement and was also drawn manually to contour the border of each SPN at the level of the longest transverse diameter of the lesion on the fusion ¹⁸F-FDG PET/CT images. Adjacent ¹⁸F-FDG-avid structures and areas exhibiting physiological uptake were avoided. The SUV\text{max} was calculated using the following formula: maximum pixel value multiplied by the decay-corrected ROI activity (MBq/mL)/[injected dose (MBq)/body weight (g)].

**Statistical analysis**

The numerical data are reported as \( \bar{x} \pm s \) of all three sets of measurements. The \( \chi^2 \) test, Fisher’s exact test and the Mann-Whitney U test were used to compare the clinical and MRI morphologic variables between the two groups. The intra-class correlation coefficient (ICC) and the coefficient of variation (CV) were calculated to evaluate both the intra- and inter-observer variability. A correlation coefficient of 0–0.5 was considered a poor correlation, 0.5–0.8 a moderate correlation and >0.8 a high correlation. The mean values of the three sets of data were used for the correlation analyses. Spearman’s rank correlation coefficients were calculated to measure the association between the ¹⁸F-FDG PET/CT and DCE-MRI parameters of the SPNs. The metabolic and perfusion parameters of benign and malignant lesions were compared using the Mann-Whitney U test. The sensitivity, specificity and accuracy for differentiating malignant from benign lung lesions were calculated for ¹⁸FDG-PET/CT and MRI.

![Figure 1](image_url) Transaxial images of an adenocarcinoma in the right lower lobe of a 67-year-old woman. (A) T1-weighted enhanced image showing a manually drawn region of interest (ROI) to contour the border of the lung lesion; (B, C, D) Transaxial perfusion map showing that the nodule (arrow) has high perfusion, with the trans-endothelial transfer constant (K\text{trans}), redistribution rate constant (K\text{ep}), and fractional volume (V\text{e}) determined to be 0.092 min\(^{-1}\), 0.417 min\(^{-1}\), and 0.221, respectively; (E) Transaxial fusion of the ¹⁸F-fluorodeoxyglucose (¹⁸F-FDG) positron emission tomography/computed tomography (PET/CT) image showing high uptake of FDG, with the maximum standardized uptake value (SUV\text{max}) of the lesion (arrow) determined to be 4.119; (F) Photomicrograph (original magnification, 20x; hematoxylin-eosin stain) demonstrating an adenocarcinoma.
parameters. A receiver operating characteristic (ROC) curve was used to find the optimal cut-off. In reference to DeLong et al.’s method (20), the area under the curve (AUC) of the DCE-MRI indexes and that of the SUV\textsubscript{max} were compared for distinguishing malignant from benign SPNs. All analyses were performed using SPSS 16.0 software (SPSS Inc., Chicago; IL, USA). For all tests, two-tailed \( P < 0.05 \) was considered statistically significant.

**Results**

**Final diagnosis**

Of the 49 patients, 33 underwent surgical resection, 14 underwent CT-guided needle biopsy, and two patients underwent a 6-month follow-up CT scan with lesion disappearance after initiation of antibacterial therapy; these latter two lesions were therefore considered clinically benign, solitary nodules. All nodules were classified into two groups on the basis of their final diagnosis. One group was composed of 32 patients with malignant nodules, of whom 23 had adenocarcinomas, 4 had squamous cell carcinomas, 1 had an adenosquamous carcinoma, 1 had a pleomorphic carcinoma, 1 had a lymphoepithelioma-like carcinoma, 1 had a small cell carcinoma, and 1 had a metastatic lung tumor from breast cancer. The other group was composed of 17 patients with benign nodules (of whom 11 had organized pneumonia lesions, 3 had tubercular granulomas, 1 had a hamartoma, and 2 had follow-up diagnoses of benign nodules).

**Clinical and imaging data**

*Table 1* summarizes both the clinical and imaging data. No significant differences were found in terms of age, sex, lesion size or margin of the SPNs between the two groups (\( P > 0.05 \)). Representative examples of the DCE-MRI and \(^{18}\text{F}-\text{FDG}\) PET/CT images are shown in *Figures 1* and *2*, illustrating the typical color changes in the respective parameter maps.

**Intra- and inter-observer reproducibility agreement**

The intra- and inter-observer reproducibility for the measurement of the DCE-MRI (\( K_{\text{trans}} \), \( K_{\text{ep}} \) and \( V_e \)) and \(^{18}\text{F}-\text{FDG}\) PET/CT parameters (SUV\textsubscript{max}) are presented in *Table 2*. Good intra- and inter-observer reproducibility were obtained for all DCE-MRI (\( K_{\text{trans}} \), \( K_{\text{ep}} \) and \( V_e \)) and \(^{18}\text{F}-\text{FDG}\) PET/CT (SUV\textsubscript{max}) parameters, with ICC values ranging from 0.942 to 0.999 and from 0.842 to 0.999, respectively. The intra-observer CV ranged from 2.165\% to 10.502\%, and the inter-observer CV ranged from 3.120\% to 16.840\%.

**Correlation analysis between \(^{18}\text{F}-\text{FDG}\) PET/CT and DCE-MRI parameters**

A correlation analyses of all perfusion parameters and SUV\textsubscript{max} revealed the following: \( K_{\text{trans}} \) had a positive correlation with SUV\textsubscript{max} (\( P = 0.006 \)), \( K_{\text{ep}} \) had a positive correlation with SUV\textsubscript{max} (\( P = 0.030 \)), and \( V_e \) did not correlate with SUV\textsubscript{max} (\( P = 0.661 \)).

**Comparison of \(^{18}\text{F}-\text{FDG}\) PET/CT and DCE-MRI parameters**

The comparisons of \(^{18}\text{F}-\text{FDG}\) PET/CT and DCE-MRI parameters are shown in *Table 1*. The mean \( K_{\text{trans}} \), \( K_{\text{ep}} \), \( V_e \) and SUV\textsubscript{max} of malignant nodules were 0.134±0.058 \text{min}^{-1}, 0.623±0.232 \text{min}^{-1}, 0.267±0.141, and 6.389±3.762, respectively.

**Table 1** Comparison of clinical and image data

<table>
<thead>
<tr>
<th>Variables</th>
<th>Benign nodules (n=17) (( \bar{x} \pm s ))</th>
<th>Malignant nodules (n=32) (( \bar{x} \pm s ))</th>
<th>( P )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>59.4±11.1</td>
<td>63.1±7.5</td>
<td>0.166</td>
</tr>
<tr>
<td>Male/Female</td>
<td>10/7</td>
<td>19/13</td>
<td>0.970</td>
</tr>
<tr>
<td>Lesion size (cm)</td>
<td>1.937±0.593</td>
<td>2.261±0.530</td>
<td>0.057</td>
</tr>
<tr>
<td>Smooth/Non-smooth*</td>
<td>5/12</td>
<td>4/28</td>
<td>0.244</td>
</tr>
<tr>
<td>( K_{\text{trans}} ) (\text{min}^{-1})</td>
<td>0.059±0.040</td>
<td>0.134±0.058</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( K_{\text{ep}} ) (\text{min}^{-1})</td>
<td>0.343±0.193</td>
<td>0.623±0.232</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>( V_e )</td>
<td>0.208±0.119</td>
<td>0.267±0.141</td>
<td>0.208</td>
</tr>
<tr>
<td>SUV\textsubscript{max}</td>
<td>3.401±2.084</td>
<td>6.389±3.762</td>
<td>0.003</td>
</tr>
</tbody>
</table>

*\( K_{\text{trans}} \), K_{\text{ep}}, V_e \), margin of solitary pulmonary nodules (SPNs) in MR images were assessed with smooth or non-smooth; \( K_{\text{trans}} \), trans-endothelial transfer constant; \( K_{\text{ep}} \), redistribution rate constant; \( V_e \), fractional volume; SUV\textsubscript{max}, maximum standardized uptake value.*
respectively; the mean $K^{\text{trans}}$, $K_{\text{ep}}$, $V_e$, and $\text{SUV}_{\text{max}}$ of benign nodules were 0.059±0.040 min$^{-1}$, 0.343±0.193 min$^{-1}$, 0.208±0.119, and 3.401±2.084, respectively. There were significant differences between malignant and benign nodules in $K^{\text{trans}}$ ($P<0.001$) and $K_{\text{ep}}$ ($P<0.001$). There was a significant difference between malignant and benign nodules in terms of $\text{SUV}_{\text{max}}$ ($P=0.003$). There was no significant difference between malignant and benign nodules in terms of $V_e$ ($P=0.208$).

The diagnostic capabilities of the DCE-MRI indexes and of $\text{SUV}_{\text{max}}$ are shown in Table 3. The AUC of $K^{\text{trans}}$, $K_{\text{ep}}$, and $\text{SUV}_{\text{max}}$ between malignant and benign nodules were 0.909, 0.838, and 0.759, respectively. The sensitivity and specificity in differentiating malignant from benign SPNs were 90.6% and 82.4%, respectively, for $K^{\text{trans}}$; 87.5% and 76.5%, respectively, for $K_{\text{ep}}$, and 75.0% and 70.6% for $\text{SUV}_{\text{max}}$, respectively ($\text{Figure 3}$). There was no significant difference in the AUC between $K^{\text{trans}}$ and $\text{SUV}_{\text{max}}$ ($P=0.080$) or between $K_{\text{ep}}$ and $\text{SUV}_{\text{max}}$ ($P=0.343$) in the diagnosis of SPNs.

**Discussion**

DCE-MRI is a promising technique that can be used to evaluate vascular permeability, which typically increases significantly in tumors secondary to tumor angiogenesis. Our study results show significant correlations between $\text{SUV}_{\text{max}}$ and $K^{\text{trans}}$ and between $\text{SUV}_{\text{max}}$ and $K_{\text{ep}}$ for all SPNs. In addition, the DCE-MRI parameters $K^{\text{trans}}$ and $K_{\text{ep}}$ have the capability to distinguish between benign and malignant SPNs and can offer the advantages of no ionizing radiation and high cost-effectiveness when
compared with 18F-FDG PET/CT. The evaluation of the reproducibility of the various 18F-FDG PET/CT and DCE-MRI parameters indicated that there was good to excellent concordance of each parameter in terms of the intra-observer and inter-observer measurements. Moreover, the reproducibility of all of the parameters evaluated in our study was consistent with those of indexes that were used in previously published studies (21,22). Regarding the reproducibility of DCE-MRI parameter measurements, Wang et al. recently reported good reproducibility (ICC>0.8) when measuring the perfusion parameters K\text{trans}, K\text{ep}, V_e in lung cancer patients (21). In a recent study, Ohno et al. also reported excellent reproducibility of SUV\text{max} as determined by 18F-FDG PET/CT in SPNs (22).

Positive correlations were observed between K\text{trans} and SUV\text{max} as well as between K\text{ep} and SUV\text{max}. 18F-FDG PET/CT and DCE-MRI reflect different aspects of physiological features and pathological changes of pulmonary nodules. A high SUV\text{max} is mainly associated with high cellular density, blood flow, hypoxia and tumor aggressiveness, while higher K\text{trans} and K\text{ep} are related to increased microvessel density and permeability (23,24). Therefore, it is not surprising that the higher metabolic activity is associated with increased perfusion and permeability. Our results are consistent with previous studies that reported good or excellent correlations among the perfusion parameters and SUV\text{max} of SPNs (19). Therefore, our results suggest that perfusion indexes of DCE-MRI can replace SUV\text{max} for functional assessment of pulmonary nodules to a certain extent.

Among the various parameters studied, our results demonstrate that the DCE-MRI parameters K\text{trans} and K\text{ep} were both significantly different for benign and malignant nodules. Nonspecific small molecular contrast media, as an in vivo tracing marker, can transfer in and out of microvessels and reach a steady state to maintain their intravascular and EES distribution. K\text{trans} is defined as the trans-endothelial transfer constant of the contrast media that reflects the perfusion and permeability status of the tissue microvasculature. Previous studies have demonstrated that a higher K\text{trans} is associated with more permeable vessels, which can result from tumor angiogenesis (12,13). K\text{ep} is defined as reflux from the EES to the plasma. As the EES pressure increases, the contrast media passes back into the vessel rapidly. Normally, a higher K\text{ep} indicates a higher cell density and vascular permeability of malignant tissue (25). The malignant SPN tissue has a higher microvascular density due to tumor angiogenesis and results in much more permeable capillaries (17,26). The amount of contrast media accumulates in the EES; that is why K\text{trans} and K\text{ep} are

![Graph illustrating the results of the receiver operating characteristic (ROC) analyses of quantitatively calculated dynamic perfusion magnetic resonance imaging (MRI) parameters [trans-endothelial transfer constant (K\text{trans}), redistribution rate constant (K\text{ep}),] and 18F-fluorodeoxyglucose (18F-FDG) positron emission tomography/computed tomography (PET/CT) maximum standardized uptake value (SUV\text{max}) as markers for distinguishing between malignant and benign nodules. The area under the curve (AUC) for K\text{trans} was the largest.](image)

**Table 3**

<table>
<thead>
<tr>
<th>Variables</th>
<th>AUC (95% CI)</th>
<th>Cut-off</th>
<th>Sensitivity (95% CI) (%)</th>
<th>Specificity (95% CI) (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>K\text{trans} \text{(min}^{-1})</td>
<td>0.909 (0.792–0.972)</td>
<td>0.082</td>
<td>90.6 (75.0–98.0)</td>
<td>82.4 (56.6–96.2)</td>
<td>87.8</td>
</tr>
<tr>
<td>K\text{ep} \text{(min}^{-1})</td>
<td>0.838 (0.705–0.928)</td>
<td>0.392</td>
<td>87.5 (71.0–91.6)</td>
<td>76.5 (50.1–93.2)</td>
<td>83.4</td>
</tr>
<tr>
<td>SUV\text{max}</td>
<td>0.759 (0.616–0.870)</td>
<td>3.807</td>
<td>75.0 (56.6–88.5)</td>
<td>70.6 (44.0–89.7)</td>
<td>73.5</td>
</tr>
</tbody>
</table>

K\text{trans}, trans-endothelial transfer constant; K\text{ep}, redistribution rate constant; SUV\text{max}, maximum standardized uptake value; SPN, solitary pulmonary nodule; AUC, area under the curve; 95% CI, 95% confidence interval.
markedly increased in malignant nodules compared with benign nodules. Consistent with our findings, Yuan et al. demonstrated higher $K_{\text{trans}}$ and $K_{ep}$ values in lung cancer than in benign lesions (13).

$^{18}$F-FDG PET/CT reflects the glucose metabolism of various tissues. Malignant nodules consist of metabolically active cells that have higher levels of glucose uptake due to overexpression of glucose transporter proteins (27,28). $^{18}$F-FDG becomes trapped and accumulates within these cells, as the radiolabeled glucose analogue is phosphorylated once but not metabolized further. $^{18}$F-FDG PET is reported to be an accurate non-invasive imaging test, with a meta-analysis reporting a pooled sensitivity of 96.8% and a specificity of 77.8% for malignant nodules (29).

In our study, the sensitivity and specificity of $K_{\text{trans}}$ and $K_{ep}$ in terms of their diagnostic performance in the differentiation of malignant from benign nodules were higher than those of SUV$_{\text{max}}$. There was no significant difference between $K_{\text{trans}}$ and SUV$_{\text{max}}$ or between $K_{ep}$ and SUV$_{\text{max}}$. Therefore, DCE-MRI can be considered at least as effective as $^{18}$F-FDG PET/CT. MRI has the following advantages over $^{18}$F-FDG PET/CT: 1) there is no radiation exposure; 2) less time is required for the examination (30 min in DCE-MRI versus 90 min in $^{18}$F-FDG PET/CT); and 3) the price of an $^{18}$F-FDG PET/CT exam is around 1,000 US dollars in China (official price in 2015), while the price of DCE-MRI per patient is around 200 US dollars in China (official price in 2015). Clearly, the cost of DCE-MRI is dramatically reduced. However, attention should be paid to gadolinium-induced nephropathy, which is still an issue even if it does not occur frequently (<2%) in patients without risk factors, such as impaired renal function, advanced age, and heart insufficiency (30).

There were several limitations of our study. First, this study was performed at a single center and the total number of patients was relatively small. The distribution of benign and malignant tumors, as well as the histopathologic subtypes, was not well-balanced. This has relevant implications for diagnostic specificity. Second, the study design did not aim to validate any acknowledged thresholds or to develop a classification model based on multivariate statistics or machine learning methods. These methods require large databases, which have not been established as of yet. Finally, the consistency and reproducibility of the DCE-MRI parameters in our study were good. However, our study was only performed on a Siemens MR Scanner and analyzed using non-commercial software from GE healthcare. As Heye et al. reported, there is substantial variability (>20% CV) in the calculated pharmacokinetic DCE-MRI parameters ($K_{\text{trans}}$, $K_{ep}$, $V_e$) across various commercially available DCE-MRI perfusion analysis solutions, severely limiting the comparability of our data (31). The consistency and reproducibility of pharmacokinetic parameter outputs across vendor platforms still need to be established.

**Conclusions**

We conclude that pharmacokinetic analysis by DCE-MRI can obtain an equivalent distinction of benign SPNs from malignant SPNs compared to $^{18}$F-FDG PET/CT and that DCE-MRI has the advantages of being ionizing radiation free and cost-effective.

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**Footnote**

**Conflicts of Interest:** The authors have no conflicts of interest to declare.

**References**


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