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Diffusion kurtosis imaging (DKI) in characterization in indetermined solitary pulmonary nodules (SPNs): comparison with conventional DWI and quantitative

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Abstract

We contrasted traditional DWI with quantitative imaging to better understand the function of diffusion kurtosis imaging (DKI) in characterising solitary pulmonary nodules (SPNs).

Forty-seven consecutive patients with SPNs (30 males, 17 females, median age: 61 years; range: 29 to 86 years) were included in this paper between March 2018 and July 2020. Quantitative DCE-MRI and multi-b factor DWI (b values ranging from 0 to 2000 sec/mm2) were obtained. We compared the ADC, Kapp, Dapp, Ktrans, Kep, Ve, and iAUC values between the malignant and benign groups, as well as between the various LC subtypes. The purpose of the ROC curves was to evaluate the diagnostic value. Kapp, Ktrans, Ve and iAUC values were obviously higher for malignant SPNs compared to that of benign SPNs (P < 0.035). ADC was obviously higher in benignity compared to malignant SPNs (P = 0.001). There exist no obvious difference in Dapp and Kep between the two groups (P = 0.06). Kapp value has highest sensitivity (81.8%) and accuracy (75.7%), and ADC value has highest specificity (80.0%). Combination of ADC and iAUC enhanced the sensitivity to 81.8%, specificity to 86.7% and precision to 83.8%.

Keywords: Diffusion Weighted Imaging (DWI), Apparent Diffusion Coefficient (ADC), Malignant SPNs, Quantitative DCE-MRI (Dynamic Contrast-Enhanced MRI)

Introduction

The highest death rate and maximum morbidity are traits of lung cancer (LC). Since many patients are detected at an advanced stage, the 5-year survival rate is only 18% [1]. Pulmonary nodules (SPNs) are the typical presentation of lung cancer (LC). SPNs are commonly found during low-dose CT screening for lung cancer and during CT exams in clinical practice, which lowers the death rate from LC [2]. As a result, prejudice against SPNs has grown in significance for clinical management. The differentiation of SPNs is commonly achieved using CT and PET/CT, but it is still challenging to avoid
false positives [3,4] (active granulomas, hyper-vascular benign tumours, etc.) and false negatives [5,6] (various neuroendocrine tumours, highly differentiated adenocarcinomas, etc.). MRI technology is being utilised more and more in lung disorders [7, 8]. It is very helpful in determining the type of lung tumours and nodules. Dynamic contrast-enhanced MRI (DCE-MRI) and DWI are the primary methods used to diagnose SPNs.

Water molecules are assumed by conventional DWI techniques to follow Gaussian diffusion, which causes the DWI signal to drop mono-exponentially with increasing b values. However, because cellular features restrict the passage of water protons in bodily tissues, water diffusion is non-Gaussian. This results in overlaps in DWI signals between lung abscesses, tuberculomas, and lung cancer. Compared to traditional DWI, diffusion kurtosis imaging (DKI), which was initially described by Jensen et al. [10], offers a more accurate evaluation of tissue microstructure because it captures non-Gaussian diffusion features. Initially used for cerebral diseases [11,12], DKI has expanded to tissues such as liver, muscle, breast, and prostate, showing high correlation with tumor grade and higher specificity in cancer diagnosis [13,14].

By improving diagnostic specificity by quantitative study of SPN vasculature using pharmacokinetic models, DCE-MRI improves distinction between benign and malignant SPNs [15,16]. It is yet unknown, nevertheless, whether combination testing can increase diagnosis accuracy or not when it comes to differentiating lung malignancies (LCs) from benign SPNs. DKI outperforms standard DWI and DCE-MRI in this regard. The purpose of this study is to investigate the relationship between diffusion and perfusion parameters and to assess the diagnostic utility of DKI in comparison to conventional DWI and DCE-MRI for SPNs.

Materials and Methods

Patients

Informed consent was obtained from research subjects and authorised by our hospital’s ethics committee. Included were 66 individuals who visited our hospital between March 2018 and July 2020 but did not have a diagnosis of SPNs. Two expert chest radiologists with over 20 years of experience
diagnosing pulmonary nodules with CT imaging determined the SPNs indeterminacy. Enrollment criteria included the followings: (a) all nodules were measured on MSCT according to RECIST criteria (version 1.1)[17,18] and the longest axis diameter was 8mm-30mm; (b) all patients were pathologically confirmed; (c) nature of SPNs was determined by pathological diagnosis within 2 weeks after MRI; (d) no prior treatment before MRI. Among them, nineteen cases were excluded due to following causes: patients who had not undergone surgery or biopsy (n=16), poor imaging quality due to various reasons (n = 1), and contraindications of MR scan or contrast administration (n=2).

Finally, up to 47 subjects were included. 30 males and 17 females with a median age of 61 years (29 to 86 years). The median age for males and females was 62.55 years, respectively. The pathological results were obtained by lobectomy in 42 cases (89.4%) and CT-guided biopsy in 3 patients (6.4%). 2 cases (4.2%) were determined by CT follow up that showed absorbed lesions.

MR Imaging acquisition

MR scans were performed on a 3.0 Tesla (T) 16-channel MR scanner (Magnetom Skyra syngo, Siemens Healthcare, Germany). The MR plain scan included HASTE T2-weighted imaging ([TR]=1100 ms, echo time [TE]=87 ms, field of view [FOV]= 360 × 360 mm2, [TA] = 35 s, thickness = 6.0 mm), transverse VIBE T1 weighted imaging (TR/TE=4.42ms/2.46ms, FOV=360×360mm2, matrix=256×256, TA=16 sec, slice thickness=3.0 mm) and axial respiratory triggered fat-suppressed BLADE T2-weighted imaging (TR/TE=3000ms/83ms, FOV=360×360mm2, matrix=320×320, TA=1 min 50 sec, slice thickness=5.0 mm). Multi-b factor fat suppressed diffusion weighted imaging (DWI) acquisition of DWI and DKI data using the single-shot echo planer imaging (SS-EPI) technique was performed with 7 b-values (0, 50, 200-2000 s/mm2) in the respiratory-triggered mode (TR/TE=2000ms/66ms; FOV= 340 cm, GRAPPA 2; maximum NEX of 10 and 24 sections, 3 orthogonal directions of X,Y and Z).

The DCE-MRI protocol consists of fast dynamic MR acquisition and multi-flip angle T1 mapping. Same parameters (TR/TE, thickness, FOV, etc.) for both sequences. Multi-flip angle T1 mapping with three flip angles (TR/TE=2.63/1.02ms, FOV=320×320mm2, matrix=320×320, TA=11-19 sec, thickness=4 mm, no gap, flip angles 2°/9°/12°)[19,20]. Then a TWIST-VIBE sequence based dynamic contrast enhanced scan with 65 phases was employed (TA=5min 33sec, thickness=4mm, no gap, flip angles 6°, temporal resolution=3.0 s/phase). Patients were scanned during each breath-hold of 12sec for 4 phases, followed by a 6-sec free breath. Finally, gadobiamide (Omniscan; GE Healthcare,
WI was rapidly injected with dose of 0.1 mmol/kg body weight (2.5 mL/sec) followed by 20 mL of saline (2.5 mL/sec). Post-processing of MR data

All DKI data were processed by using prototype software(MR body diffusion Toolbox version 1.3, Siemens healthcare, Germany). The calculation of DKI parameters were derived from the five b-values (0, 400, 800, 1400, and 2000s/mm²) according to the formula: \( S(b) = S0 \cdot \exp(-b \cdot Dapp + \frac{1}{6} \cdot b^2 \cdot Dapp^2 \cdot Kapp) \), in which \( S(b) \) and \( S0 \) refer to the signal intensity. Apparent diffusion coefficient \( Dapp \) (unit: \( \times \)10-3mm²/s), corrected to simulate non-Gaussian behavior. Kapp (the apparent kurtosis coefficient), a dimensionless parameter (unitless), represented the apparent diffusional kurtosis which may highlight cellular microstructural properties by digitally simulating intracellular barriers and compartments [23].

To better clarify the role of diffusion kurtosis imaging (DKI) in determining the characterization of isolated pulmonary nodules (SPNs), we compared conventional DWI with quantitative imaging. In this paper, from March 2018 to July 2020, forty-seven consecutive patients (30 male, 17 female, median age: 61 years; range: 29 to 86 years) with SPNs were included. Multi-b factor DWI (with b values from 0 to 2000 sec/mm²) and quantitative DCE-MRI data were acquired. ADC, Kapp, Dapp, Ktrans, Kep, Ve, and iAUC values were compared between malignant and benign groups and among subtypes of LC. The ROC curves were established to assess the diagnostic value.

The ADC was calculated using the above software following the equation \( \text{ADC})S(b)=S0\exp(-b\cdot\text{ADC}) \) for five b values of 0, 50, 200, 400, and 800 s/mm². Two radiologists, blinded to the pathologic results, performed the data analysis and parameter measurements independently. The solid part of the nodule was traced on the ADC map, and a region of interest (ROI) was drawn around the solid part and copied to the Kapp and Dapp maps. This operation was performed five times to ensure greater accuracy and the average of the obtained results was calculated.

The DCE-MRI data were processed by software Tissue 4D (Siemens Healthcare, Erlangen, Germany). The software is set to automatic mode and motion correction is performed internally and registered for use. Adjust to Tofts model mode and enter data to calculate the relevant parameters for pharmacokinetics. It was then adjusted to Arterial Input Function (AIF) mode, with the type selected as "intermediate" and located in the descending aorta on the same layer of the nodules. Perfusion parameters for ROI were subsequently obtained, including Ktrans, iAUC, Kep, and Ve. ktrans
represents the transfer constant of the substance as it crosses the endothelium; iAUC refers to the area under the concentration curve within 1 minute of gadolinium concentration injection. kep refers to the transfer rate of the contrast agent and represents the shuttling ability of the contrast agent in the extracellular extravascular space (EES) or plasma;

Statistical Analysis

The statistical programme SPSS 19.0 was used to analyse the data. Mean ± standard deviation is the description given to the measurement data. The data's homogeneity and normalcy were examined. The nonparametric test was used to verify the variables that did not follow a normal distribution, and the t-test was used to compare groups of data that did follow a normal distribution. ROC curves were used, according to DeLong et al. [24], to assess the usefulness of a variable in distinguishing between benign and malignant SPNs. The AUC was used to express each parameter's diagnostic efficacy.

The interobserver agreement of the measurements was evaluated based on the interclass correlation coefficient (ICC). ICC > 0.75 was considered to be a high agreement [25]. The relationship between the parameters was checked based on Pearson correlation test and expressed as correlation coefficient (r). 0.75 < r < 1.00, high; 0.50 < r < 0.74, moderate; 0.25 < r < 0.49, low correlation; r < 0.49, no correlation [18]. P < 0.05 was considered significantly difference.

Results

Pathologic Findings

Of the 47 SPNs, 30(63.8%) were male (median age, 61 years; range, 29–86 years) and 17(36.2%) were female (median age, 55 years; range, 39–70 years), 28(59.5%) were malignant and 19(40.6%) were benign. The malignant SPNs included squamous cell carcinoma (n = 4), adenocarcinoma (n = 19), adenosquamous carcinoma (n = 2), small cell lung cancer (SCLC) (n = 1) and metastasis (n = 2). Benign SPNs included tuberculous granuloma (n = 9), chronic inflammatory granuloma (n = 4), organized pneumonia (n = 2), active infection (n = 2), chondroma (n = 1) and aspergilloma (n = 1).

Comparison of DWI, DKI and DCE-MRI metrics between two group SPNs

The mean Kapp, Ktrans, Ve and iAUC values were obviously higher in malignant SPNs compared to that in benign ones (P<0.05). The mean Kapp, Ktrans, Ve and iAUC values for malignant and benign SPNs were 0.83±0.200 Vs 0.69±0.108(P=0.018), 0.44±0.273 Vs 0.27±0.198(P=0.034), 0.38±0.252 Vs
0.25±0.119(P=0.034) and 20.11±13,278 Vs 10,02±6.258(P=0.006). The ADC values were significantly lower (1.27±0.216×10⁻³mm²/s) for LC than those for benign SPNs (1.60±0.357×10⁻³mm²/s). Dapp and Kep values were found to be have no obvious difference between the two group (P=0.908 and P=0.988, respectively). See Table 1 and Figure 1 for details.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Malignant</th>
<th>Benign</th>
<th>t/z</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC(×10⁻³mm²/s)</td>
<td>1.27±0.216</td>
<td>1.60±0.357</td>
<td>-3.482</td>
<td>0.001*</td>
</tr>
<tr>
<td>Kapp</td>
<td>0.83±0.200</td>
<td>0.69±0.108</td>
<td>2.478</td>
<td>0.018*</td>
</tr>
<tr>
<td>Dapp(×10⁻³mm²/s)</td>
<td>2.14±0.826</td>
<td>2.11±0.698</td>
<td>0.116</td>
<td>0.908</td>
</tr>
<tr>
<td>Ktrans(min⁻¹)</td>
<td>0.44±0.273</td>
<td>0.27±0.198</td>
<td>2.119</td>
<td>0.034*</td>
</tr>
<tr>
<td>Kep(min⁻¹)</td>
<td>2.12±2.108</td>
<td>1.79±1.380</td>
<td>0.015</td>
<td>0.988</td>
</tr>
<tr>
<td>Ve</td>
<td>0.38±0.252</td>
<td>0.25±0.119</td>
<td>2.206</td>
<td>0.034*</td>
</tr>
<tr>
<td>iAUC(mmol.kg⁻¹.s)</td>
<td>20.11±13.278</td>
<td>10.02±6.258</td>
<td>2.769</td>
<td>0.006*</td>
</tr>
</tbody>
</table>

Note.—in general, data are m±SD.

t/z represents statistics value.

* means obvious difference between two group.

P value represents the significance between the two group.

Figure 1 Multi parameters in malignant and benign SPNs group.(**means P <0.05,****means P <0.01)
All this parameters were also compared among subtypes of lung cancer and benign SPNs. Compared to benign SPN, the adenocarcinoma had higher Kapp values and lower ADC values. There were no differences in other parameters between the three methods. See Table 2.

Table 2 Comparison of benign SPNs and lung cancer subtypes using DWI, DKI, and DCE-MR parameters

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Squamous cell carcinoma</th>
<th>Adenocarcinoma</th>
<th>Benign</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC$(\times10^{-3}\text{mm}^2/\text{s})$</td>
<td>1.32±0.254</td>
<td>1.23±0.212a</td>
<td>1.60±0.357a</td>
<td>0.012a</td>
</tr>
<tr>
<td>$K_{\text{app}}$</td>
<td>0.81±0.157</td>
<td>0.87±0.199a</td>
<td>0.69±0.108a</td>
<td>0.016a</td>
</tr>
<tr>
<td>$D_{\text{app}}$(\times10^{-3}\text{mm}^2/\text{s})</td>
<td>2.15±0.662</td>
<td>2.02±0.645</td>
<td>2.11±0.698</td>
<td>0.416</td>
</tr>
<tr>
<td>$K_{\text{trans}}$(min$^{-1}$)</td>
<td>0.49±0.47</td>
<td>0.43±0.208</td>
<td>0.27±0.198</td>
<td>0.236</td>
</tr>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
<td>Group 3</td>
<td>Group 4</td>
</tr>
<tr>
<td>----------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
<td>--------------</td>
</tr>
<tr>
<td>Kep (min⁻¹)</td>
<td>3.44±3.478</td>
<td>1.74±1.508</td>
<td>1.79±1.380</td>
<td>0.314</td>
</tr>
<tr>
<td>Ve</td>
<td>0.30±0.240</td>
<td>0.40±0.209</td>
<td>0.25±0.119</td>
<td>0.136</td>
</tr>
<tr>
<td>iAUC (mmol.kg⁻¹.s)</td>
<td>18.26±22.963</td>
<td>21.67±9.984</td>
<td>10.02±6.258</td>
<td>0.052</td>
</tr>
</tbody>
</table>

Note.—in general, data are m ± SD.

a means significant difference between adenocarcinoma and benign group.

P value represents the significance between groups

Diagnosis performance of DWI, DKI and DCE-MRI metrics between malignant and benign SPNs

Kapp value has highest sensitivity (81.8%) and accuracy (75.7%), ADC value has highest specificity (80.0%) and equal accuracy as Kapp. Combination of ADC and iAUC enhanced the sensitivity to 81.8%, specificity to 86.7% and precision to 83.8%. See Figure 2. Representative example is shown in Figure 3-4.

Figure 2 ROC curves of multi parameters in diagnosis of SPNs.

![ROC curves of multi parameters in diagnosis of SPNs](image)

Figure 3 Representative case of a low to moderately differentiated adenocarcinoma (arrow) in the right upper lobe of lung of a 61-year-old male case. (a) Axi T2-weighted MR image shows the tumor (arrow) in the posterior segment of right upper lobe.(b-e) multi-b factor diffusion weighted imaging. b=400,800,1400 and 2000 s/mm². respectively. (f)Kapp map of the SPN, Kapp value=0.74. (g)Dapp map of the SPN, Dapp value=1.76 mm²/s. (h) DCE-MR imaging of one phase shows moderate homogenous enhancement of the nodule. (i) Ktrans map, Ktrans=0.506 min⁻¹. (j) iAUC map, iAUC=18.43 mmol.kg⁻¹.s.
Correlation analyses of parameters derived from diffusion imaging and quantitative
Figure 4 right lower lung nodule 4 years after surgery. Pathology: sclerosing hemangioma (a). CT plain scan lung window, the size of the right lower lung is about 16.8 mm × 17.3 mm solitary pulmonary nodule. (b). MR plain scan T1WI and T2WI axis bitmap. (c-e) Axis bitmap of 30s, 1min and 4min during DCE-MRI scanning. (f-h) b=400 800 2000 s/mm2 diffusion weighted diagram. (i) Kapp pseudo-color map, Kapp=0.83. (j) Dapp pseudo-color image, Dapp=2.32 mm2/s

DCE-MRI

No significant correlation was found between the parameters of quantitative DCE-MRI and diffusion imaging, can be seen from Table 3.

Table 3 Correlation of Parameters Derived From Diffusion Imaging and Quantitative DCE-MRI

<table>
<thead>
<tr>
<th></th>
<th>Ktrans</th>
<th>Kep</th>
<th>Ve</th>
<th>iAUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC (×10−3 mm2/s)</td>
<td>r</td>
<td>-0.060</td>
<td>-0.141</td>
<td>-0.299</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.726</td>
<td>0.405</td>
<td>0.072</td>
</tr>
<tr>
<td>Kapp</td>
<td>r</td>
<td>-0.126</td>
<td>-0.084</td>
<td>0.204</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.456</td>
<td>0.621</td>
<td>0.226</td>
</tr>
<tr>
<td>Dapp (×10−3 mm2/s)</td>
<td>r</td>
<td>0.042</td>
<td>0.193</td>
<td>-0.187</td>
</tr>
<tr>
<td></td>
<td>P</td>
<td>0.807</td>
<td>0.252</td>
<td>0.267</td>
</tr>
</tbody>
</table>

Discussion

The term "solitary pulmonary nodules" refers to isolated round or quasi-circular nodules in the
lung parenchyma that have a maximum diameter of 3 cm and are not associated with pneumonia, atelectasis, enlargement of the hilar and mediastinal lymph nodes, or any other illnesses. Currently, the primary technique for differentiating between solitary pulmonary nodules is high-resolution spiral CT. However, this method is limited to speculating on the pathological nature of the lesions based on an examination of the nodules' morphological features, such as their location, shape, size, number, density, edge, internal structure, and impact on surrounding structures. As a result, CT has some difficulties when it comes to distinguishing between different solitary pulmonary nodules. Currently, PET/CT is thought to be the most used imaging technique for assessing the metabolic state of tumours. However, the ability to differentiate between malignant tumours and inflammatory lesions can be challenging at times, and the high expense of the examination and its high cost restrict its widespread use. In addition to providing information about the shape of lesions, MRI can also reveal details about their function, physiology, pathophysiology, and molecular features. MRI gradually resolves issues with soft tissue-gas interface magnetically sensitive artefacts, respiratory motion artefacts, cardiac pulsation artefacts, long scanning times, and high field strengths based on advancements in computer science, medical electronics, physics, and other fields. With the increasing use of ultra-high field magnetic resonance scanners for chest imaging, the diagnostic process for solitary pulmonary nodules has advanced from basic morphological imaging to functional imaging.

The DWI, DKI, and DCE-MRI parameters of SPNs with various attributes were examined and estimated in this work. The differences in each parameter between LC subtypes and benign and malignant SPNs were also compared. The outcomes demonstrated the three approaches' significant clinical utility in determining the kind of SPNs. The performance of the three approaches in differentiating between benign and malignant SPNs is comparable. Furthermore, the DWI-derived ADC value and the DCE-MRI-derived iAUC values have exceptional sensitivity and specificity and excellent accuracy in differentiating between benign and malignant SPNs.

DWI has been reported to be a predictive parameter of tumor cell load and heterogeneity[21]. Previous study of DWI in lung lesion differentiation reported ambiguous conclusions, for instance, several clinical studies have shown that the ADC values of benign SPNs do not differ from those of lung cancer [22]. [23] showed that the ADC values of benign SPNs were larger compared to those of lung cancer and that the ADC had a high value in predicting the nature of SPNs (sensitivity, 83.3%; specificity, 74.1%). The accuracy of the measurement of ADC values is related to the number
of b-values incorporated. The accuracy increases with the number of incorporated b-values [24]. In this study, a serial of 5 b values (0, 50, 200, 400, and 800s/mm²) were used to calculate the ADC value to make the parameter more accurate. Also, excellent interobserver agreements were found in ADC value. It verified the ADC value is a stable and repeatable parameter in SPN differentiation. The benign group was found to have higher AD values than the lung cancer, similar to some previous studies[23,24], indicating the hypercellularity, packed cell nucleus and decreased extracellular space and hence restricted water molecule diffusion in tumor tissues.

It is highly sensitive to the irregular diffusion of water molecules and obtains more accurate diffusion information through multi-parameter quantitative analysis of the diffusion characteristics of the non-Gaussian distribution of water molecules in the organisation. This allows the diffusion information to more accurately reflect the complexity of the microstructure environment of the organisation. There aren't many clinical trials of DKI in the lung because of how unique the lung is.

According to a previous study, there are certain rules for setting the b-value of DKI. To obtain the best kurtosis imaging, one b-value is set higher than 1000s/mm² and the other b-value is lower than 1000s/mm², b-values do not exceed a maximum of 1500-2000s/mm², a condition to effectively observe non-Gaussian behavior, but avoid violation of assumptions of the DKI model. In addition, the minimum b value can be 0. Intravoxel incoherent motion (IVIM) often interferes with the results, and in this case we can set the minimum b value to ≥200s/mm² to eliminate its perfusion effect. High NEX (number of excitation) and relatively low spatial resolution were used to increase the SNR for high b value images, which led to the acquisition of more precise kurtosis values, given the significance of SNR for high b value diffusion images. Breathing triggering was employed in this investigation since holding one's breath interferes with the DWI's signal-to-noise ratio (SNR) and impacts the outcomes. DKI can be manipulated in several dimensions thanks to the diffusion tensor, as was shown in an earlier work. In the study of tumors, the number of b-values is limited, so only 3 directions of DKI operations are required. Take all the above consideration, multi b values (0, 400, 800, 1400, and 2000s/mm²) with the largest NEX of 10, 3 orthogonal directions were taken to analyze DKI data.

The results showed that the parameters of DWI and DKI were correlated with SUVmax, which was classified as ADCmono: R=-0.67, P<0.01; Kapp: R =0.72, P <0.05; All parameters are also correlated with SUVmean, respectively ADCmono: R=-0.66, P<0.01; Kapp: R =0.71, P<0.005. It proves the feasibility of DKI in lung research.
The Kapp and Dapp values of benign SPNs and lung cancer were examined in this study. While there was no discernible difference in Dapp values between the two groups, lung cancer patients had high Kapp levels. According to this research, benign SPNs often have a Gaussian distribution, whereas lung cancer diffusion is more likely to be non-Gaussian. It refracts the interactions of water in cells and tissues as well as reflecting the distribution of surfaces inside them in an indirect manner. In addition to having a higher cell burden and a higher nucleus-cytoplasm ratio, malignant SPNs may have higher Kapp values due to extracellular space distortion, immature tumour angiogenesis, and the destruction of normal cellular framework. Given the impact of non-Gaussian behaviour, theoretically a correction to Dapp is applied as a diffusion coefficient. The intensity decay is depicted in accordance with the diffusion signal variation when the value of b is balanced, with Dapp serving as the slope. Dapp is thought to be more accurate than traditional ADC values. Nonetheless, the current study's results differ from those of earlier research on breast lesions in that no discernible differences in Dapp values were observed between the two groups. The cause is difficult to understand and requires additional analysis with a bigger sample size for confirmation.

For quantitative DCE-MRI, from the modified TOFTs model, Ktrans is a parameter reflecting capillary perfusion and permeability. Ve is the fractional volume in the EES, Kep was calculated as Ktrans/Ve, so that Kep can be used as the transfer rate when the contrast agent is shuttled between EES and plasma, iAUC, a parameter independent of any kinetic model, is an accumulation of the contrast concentration in the tissue from the intravenous administration to present time and can depict tissue microcirculation characteristics. The current study demonstrated that compared to benign SPNs, lung cancer had greater iAUC, Ve, and Ktrans values. The outcome is somewhat in line with earlier research. Increased permeability and leakage of juvenile capillaries in tumour tissues were indicated by elevated Ktrans. The Still, kep values for lung cancer were marginally higher than those for benign SPNs, despite the fact that kep was not significantly greater in lung cancer than in benign SPNs. Adenocarcinoma made up a sizable share (68.2%) of the lung cancer group and may have contributed to the higher Ve in lung cancer. In contrast, inflammatory SPNs and TB comprised 80% of the benignity and were associated with lower EES.

The AUC of the parameters was not great (0.695-0.785), with the sensitivity ranging from 72.7% to 81.8%, the specificity from 66.7% to 80.0%, and the accuracy from 67.6% to 75.7%, despite the fact that DWI, DKI, and DCE-MRI were all possible in SPNs distinction. When it came to identifying the
kind of SPNs, Kapp had the highest value in terms of sensitivity and precision (81.8%, 75.7%). ADC values had the same accuracy as Kapp values, and their specificity (80%) was the best of all the markers. This suggests that for the diagnosis of SPNs, DKI has a high clinical application. It has higher accuracy and sensitivity for the diagnosis of SPNs than DCE-MRI and DWI. By combining ADC and iAUC's for testing, the diagnostic efficacy is significantly improved, this finding confirmed that DCE-MRI could complement diffusion MRI in differentiating indetermined SPNs.

There are a few more limitations to our study. First, the results were skewed due to the short sample size, and the benign group's illness spectrum was primarily composed of inflammatory granulomas and tuberculosis. Secondly, it was challenging to prevent the respiratory artefact and susceptibility artefact. Third, there is disagreement about earlier research on the dissemination directions of DKI. We only utilise three diffusion directions since more directions can yield more exact parameters and better suit the DKI model; however, the scanning time is too long, which may lead to less precise results.

Conclusion

In conclusion, a lot of new MRI technology has been applied in clinical practice to examine lung illnesses. We anticipate a more novel perspective of observation (imaging genomics, image genomics, artificial intelligence machine learning algorithm) to accelerate various semi-quantitative and quantitative data processing, thereby promoting the in-depth study of MRI in solitary pulmonary nodules. This is made possible by the ongoing advancement and development of MRI technology as well as the advancement of advanced software and hardware technology. In comparison with traditional DWI and quantitative DCE-MRI, DKI is a practical and safe method for the identification of indeterminate SPNs, which can improve confidence of distinction. DKI can offer a thorough understanding of the nature of SPNs and gives clinicians more information for SPN diagnosis. This technique can enhance SPNs' discriminating capabilities. Future studies of DKI in SPNs should make use of multi-center and large sample size studies.

Abbreviations

SPNs  Solitary pulmonary nodules
DKI  Diffusion kurtosis imaging
DWI  Diffusion weighted imaging
Data Availability

The experimental data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest

The authors declared that they have no conflicts of interest regarding this work.

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Author Contributions

Conceptualization: Wenhui Fan; Methodology: Zikai Li; Formal analysis and investigation: Wenhui Fan; Writing - original draft preparation: Zikai Li; Writing - review and editing: Yi Liang; Funding acquisition: Yi Liang; Resources: Hanlin Wang; Supervision: Yi Liang.

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All authors reviewed the results, approved the final version of the manuscript and agreed to publish it.

Ethics approval and consent to participate
The studies involving human participants were reviewed and approved by the Ethics Committee of Wuhan Brain Hospital. The patients/participants provided their written informed consent to participate in this study.

Reference


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**Declaration of interests**

☒ The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

☐ The authors declare the following financial interests/personal relationships which may be considered as potential competing interests: