Perfusion MRI of Solitary Pulmonary Nodules at 3T: Assessment of perfusion parameters and correlation with histology

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Background and purpose: Solitary pulmonary nodule (SPN) is one of the most common findings in chest imaging. In the most recent study, 50% of surgically resected SPNs were found to be benign (1). It is important to avoid unnecessary intervention for benign lesions, thereby lowering the associated mortality /morbidity. In this study, we applied perfusion MRI to evaluate perfusion characteristics of SPN and feasibility of perfusion MRI as a diagnostic tool to differentiate malignant from benign SPN. **Materials and Methods:** Thirty-four patients (9 males, 25 females, 26-87 years old, average 65 years old) with a SPN between15 to 30mm entered this study. The study was conducted under the guideline of the Internal Review Board and a written informed consent was obtained from all the participants. The initial diagnosis of SPN was made by CT and chest x-ray, and all patients underwent MRI study including T2-weighted axial half-Fourier acquisition single-shot turbo spin-echo (HASTE) images, pre and post contrast T1-weighed axial, sagittal, and coronal volumetric interpolated breath-hold examination (VIBE) images, and 2D turbo FLASH perfusion imaging. The perfusion study was performed with shallow free breathing. All MRI studies were performed on a 3T-superconducting magnet (Siemens Trio, TIM system, Erlangen, Germany) using a body array coil. After the imaging study, histological diagnoses were made in all SPNs except 4 cases. MRI parameters were as follows: T2-weighted HASTE (TR/TE=1200/100msec, FOV=400mm, 320x320, 1 excitation, BW=780kHz, FA=150, ETL=256, 5.5mm slice thickness/1.6mm inter slice gap, scan time=6min); T1-weighted VIBE (TR/TE=3.4/1.3msec, FOV=400mm, 260x320, 1 excitation, BW=505kHz, FA=10, 4mm slice thickness/0mm inter slice gap, scan time=1.7min); turbo FLASH (TR/TE=500/1.6msec, FOV=400mm, 192x180, 1 excitation, BW=360kHz, FA=10, 5mm slice thickness, oblique sagittal orientation, Temporal resolution=2sec, 124 frames, scan time=4min, Gd-DTPA iv. 0.1 mmol/kg). After obtaining perfusion images, time-intensity (TI) curves, mean transit time (MTT), time-to-peak (TTP), initial slope; {(peak intensity)-(base intensity)}/(TTPinitial), and maximum enhancemet (Emax) were calculated by gamma variant analysis. TI curves were classified into 4 patterns; Type A, B, C, and D. Type-A TI curve reaches to peak enhancement and started to washout before 3min. Type B shows a rise to the peak intensity within 3 min and starts to washout, but decrease of intensity is minimum during 4-min scan time. Type C shows slow continuous increase of intensity within the 4-minute scan time (enhancement continues up to 6.5min, estimated by gamma variant analysis, thus late washout was predicted). Type D shows no enhancement. Malignant or benign diagnosis was made based on the TI curves by 3 experienced radiologists. Perfusion parameters, Ktrans and ve, were calculated based on two-compartment model (2). After blinded data analyses, histology of the SPNs were correlated with each data. Sensitivity, specificity, accuracy, positive and negative predictive values were calculated for TI curve to diagnose a malignant or benign tumor. Scatter plot was created for Ktrans vs. ve. **Results:** Twenty-seven patients underwent surgical resection, and 3 patients underwent CT-guided needle biopsy. Four patients have not gone for any surgical procedure at this point. Histology included 17 adenocarcinomas, 5 squamous cell carcinomas, 3 carcinoid tumors, 1 fibrous tumor, 1 sclerosing hemangioma, 1 hamartoma, 1 reactive nodule, and 1 mycobacterial granuloma. Number of the cases in each type of TI curve is shown in Table 2. Sensitivity, specificity, accuracy, positive and negative predictive values for diagnosing malignant tumor based on TI curve are shown in Table 1. Mean MTT, TTP, Initial slope, and Emax for each TI curve type are shown in Table 2. Figure 1 shows a scattered plot for Ktrans vs. ve in patients, and Figure 2 shows the model fitting. **Discussion:** Malignant tumors in the lungs have higher microvascular density than benign tumors (3), which may fill contrast in early on and also start to washout early. Type-A TI curve may reflect such high vascularity of the tumor. In Type A, a shunt within tumor vessels could be suspected so that contrast washes out quickly decreasing about 15% of enhancement at the end of 4-minute scan, while Type B, C, and D do not decrease intensity as much within the same scan time. Two benign SPNs (fibrous tumor and sclerosing hemangioma) belonged to Type B along with 3 malignant. Both of these benign tumors are known to have relatively high vasculature. This may suggest relatively high vascularity in some benign tumors. Twenty-one out of 25 (84%) malignant SPNs (includes 2 carcinoid tumors) fell in to Type A and B curve patterns. Two observers categorized Type C to be potential malignancy and included these cases in malignant SPNs, and one observer to be relative benign including these cases in benign SPNs when blindly made diagnosis based on the curve types. As the histology result shows, 12% of malignant and 40% of benign SPNs showed Type C; it may suggest less tumor vascularity in either malignant or benign. One malignant SPN out of 2, mixed subtype adenocarcinoma showed Type D. This tumor was consisted with 40% bronchoalveolar, 40% acinar, 10% papillary, and 10% solid poorly differentiated tumor. It is reasonable that perfusion parameters reflected poor tumor vascularity with no obvious enhancement in the mostly bronchoalveolar/acinar-cell filled malignant tumor. The other Type-D SPN was a benign reactive nodule with necrotic debris, which did not have tumor vascularity. The distribution scatter plot of Ktrans vs. ve in a model fitting readily separated malignant from benign SPN (Fig. 2). However, in actual cases, Ktrans and ve values overlapped and did not clearly separate malignant from benign (Fig. 1). Only some SPNs that fit within the certain area of the scatter plot may be diagnosed correctly as malignant SPN by these parameters. This correlates with the result from the TI curve types. The SPNs that demonstrate Type A curve may be diagnosed as malignant with confidence, and the SPNs with other curve types could have possibility of either malignant or benign, even though majority of Type B SPNs were malignant and majority of Type C and D were benign. Also, sensitivity for diagnosing malignant SPN by TI curve was relatively high, while specificity was low. This is reasonable and fairly consistent with the results of other perfusion parameter analysis. From our results, perfusion parameters and the TI curve type may correctly diagnose about 28% of malignant SPNs, however, in order to diagnose rest of SPNs with confident, other additional information are still necessary. Determination of tumor perfusion characteristic alone would not clearly separate malignant from benign SPNs. **Conclusion:** Perfusion MRI parameters and TI curve have great potential to differentiate malignant vs. benign SPN, thus to avoid unnecessary surgical interventions.

Fig. 1: Ktrans vs. ve in patients.

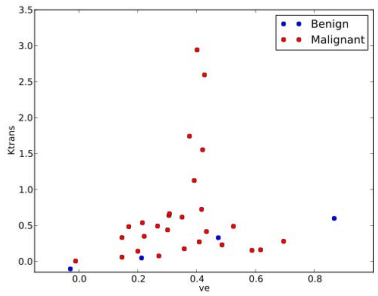

Fig. 2: Model fitting.

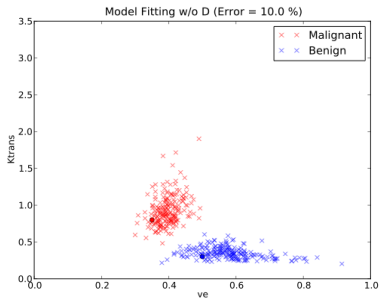

Table 1	Observer 1	Observer 2	Observer 3
Sensitivity (%)	**92**	**96**	**84**
Specificity (%)	**50**	**60**	**80**
Accuracy (%)	**83**	**90**	**83**
Positive predictive value	**92**	**92**	**96**
Negative predictive value	**50**	**75**	**50**

Table 2	Type A	Type B	Type C	Type D
Mean MTT (sec)	**301±80**	**386±58**	**452±64**	**-**
Mean TTP (sec)	**115±30**	**145±43**	**262±94**	**-**
Initial slope	**0.91**	**0.72**	**0.21**	**-**
Emax	**1.7±0.2**	**1.6±0.2**	**1.7±0.5**	**-**
# of malignant	**7**	**14**	**3**	**1**
# of benign	**0**	**2**	**2**	**1**

(1) Bernard A. *Ann Thorac Surg* 1996. (2) Tofts PS. JMRI 1997. (3) Schaefer JF et al. Lung Cancer 2006.

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