# Dynamic 3D contrast-enhanced perfusion imaging of lung cancer with one-second temporal resolution

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**Introduction:** Perfusion imaging has proven to be capable of distinguishing malignant from benign pulmonary nodules [1]. However, application of kinetic models has not been possible to date, due to the low temporal resolution of conventional dynamic contrast enhanced (DCE-)MRI and the limited number of acquisitions available in CT due to radiation exposure. We describe a 3D DCE-MRI technique with very high spatial and temporal resolution, and show preliminary results of kinetic modeling.

**Methods:** Image acquisition and analysis techniques were optimized in 6 patients with pulmonary carcinomas of 1cm diameter or larger as determined by prior CT. All subjects provided informed consent under an approved IRB protocol. Studies were conducted on a 3T Siemens TIM Trio system using a body phased array coil.

DCE-MRI was performed during free breathing using a 3D spoiled gradient echo sequence. Up to 200 timepoints were collected in a single acquisition with a temporal resolution of 0.92 – 1.09 sec. The 3D imaging slab was prescribed in an oblique orientation, such that the excitation volume encompassed the tumor and passed through the aorta and pulmonary arteries. Bolus injection of Gd-DTPA was started 10 seconds into the data acquisition to ensure that baseline, uptake and washout phases of the contrast agent were all adequately captured. A low dose of Gd-DTPA (10cc Magnevist, administered i.v. at 5cc/sec followed by a 20cc saline flush) was used to avoid saturation of the signal in blood during the first pass. A variety of fast imaging techniques were combined to achieve high temporal and spatial resolution and good 3D coverage. Parallel imaging (GRAPPA) with an acceleration factor of 2 – 3 was applied in the phase-encoding direction, and partial Fourier sampling of 6/8 was used in both the slice- and phase-encoding directions. Sharing of high spatial-frequency data among adjacent timepoints was implemented in some patients using TWIST (pA = 25%, pB = 33%). The combination of these techniques enabled acquisition of 12 – 16 slice partitions (slice resolution and oversampling = 86% and 17% respectively) with an in-plane imaging matrix of 256 x 202 in 0.92 – 1.09 seconds. Other parameters were: TR/TE/FA = 2.05ms/0.72ms/10° and BW = 980Hz/px.

The imaging protocol also included pre- and post-contrast T1-mapping using a breath-hold TI-scout (segmented inversion-prepared SSFP sequence). This was to enable conversion of the signal on the perfusion images to ΔR1, which was used as a surrogate for Gd-DTPA concentration. A low FA of 10° was used to minimize the effect of readout excitations on the T1 decay. 40 images were acquired with inversion times of 0 – 4 sec. Other parameters were TR/TE = 2.9ms/1.2ms and BW = 930Hz/px.

The time of contrast arrival in the tumor was compared with that in the pulmonary and systemic arteries, and the signal timecourses were converted to ΔR1 values to study the tracer kinetics. The data were fitted using the adiabatic approximation to the tissue homogeneity (AATH) model [2], which incorporates contributions to the tumor enhancement from both the intravascular space and extravascular extracellular space (EES). The former provides information about the blood volume, mean transit time and flow, while the latter provides estimates of the volume transfer constant $K^{trans}$, the washout rate constant $k_{ep}$ and the fractional volume $v_e$ of the EES.

**Results:** Fig 1 shows images from a patient with a moderately to poorly differentiated adenocarcinoma of mixed cell type. A delay of 9 seconds elapsed between arrival of contrast in the pulmonary artery (PA) and aorta. Enhancement in the tumor coincided with that in the systemic arteries. The subclavian artery was used to estimate the arterial input function, since its signal exhibited less severe flow artifacts than the aorta, but it was large enough to avoid partial volume effects. Calibration of signal intensity against T1 was performed using pre-contrast rather than post-contrast values to avoid confounding effects of Gd-DTPA washout between the end of the perfusion acquisition and post-contrast T1 mapping. For the tumor, the pre-contrast T1 value was obtained from the baseline TI-scout. For blood, the accepted value of 1260ms was used. In this patient the tumor response (Fig 2) did not exhibit a distinct intravascular peak, so it was fitted initially to a 3-parameter model describing only the EES component, which gave values of $K^{trans}$ = 0.43/min, $k_{ep}$ = 1.4/min, and $v_e$ = 0.30. Fitting with a 5-parameter model, which included an intravascular contribution, did not significantly reduce the residual, and gave almost identical values for the previous parameters ($K^{trans}$ = 0.40/min, $k_{ep}$ = 1.4/min, and $v_e$ = 0.28). It also produced estimates for fractional blood volume, mean transit time and flow of $v_b$ = 0.03, MTT = 3 sec and Fρ = 0.8/min. Fig 3 shows images from 3 other patients.

**Discussion:** We have demonstrated dynamic 3D contrast enhanced perfusion imaging of lung tumors with very high spatial and temporal resolution. The 1-second acquisition time enables images of the tumor to be acquired during free breathing with minimal motion artifacts. Data can thus be collected continuously throughout the baseline, contrast uptake and washout periods. 3D coverage allows characterization of the entire tumor and ensures that the lesion remains within the imaging volume even as the patient breathes. It also provides coverage of pulmonary and systemic arteries for study of the tumor blood supply and measurement of an arterial input function. High temporal resolution throughout the uptake and washout phases permits application of kinetic models for quantitative determination of tumor vascularity and vessel permeability, which may provide information about angiogenesis. The accuracy of the models, however, relies on accurate conversion of signal intensity to ΔR1 values, and this remains a limitation. The TI-scout sequence is very quick to run, but is vulnerable to artifacts due to susceptibility differences between the tumor and surrounding lung. Also, the accuracy of the T1 calibration in blood is limited by the low signal-to-noise ratio of unenhanced blood on the baseline perfusion images. Further studies will be needed in a larger number of patients to optimize our acquisition and analysis techniques further and validate the results against pathology.

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**References:** [1] AJR 2007; 188: 26 [2] J Cereb Blood Flow Metab 1998; 18: 1365

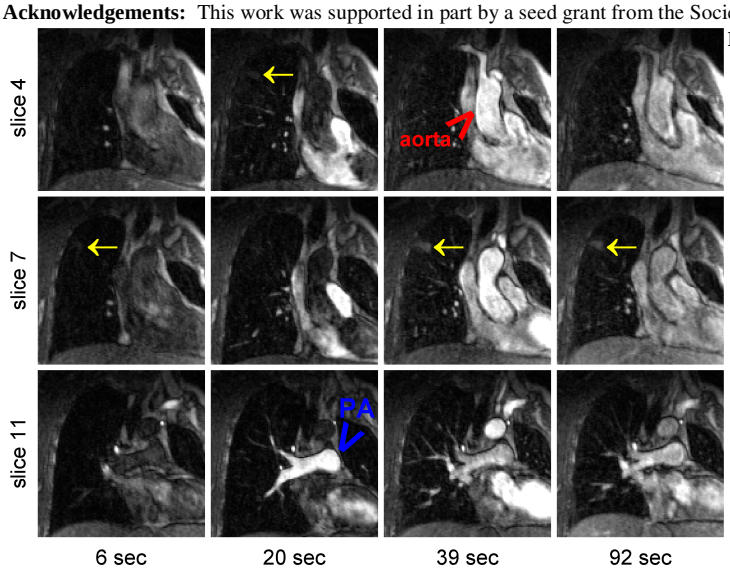


Figure 1. Images of 3 sections showing main PA (blue arrowhead), ascending aorta (red arrowhead) and tumor (yellow arrow) at 4 timepoints (baseline, PA phase, systemic arterial phase and washout). Nb. At the 20sec timepoint the patient inhales deeply, and the tumor moves anteriorly (to slice 4). Voxel size = 2.0 x 1.8 x 3.5 mm.

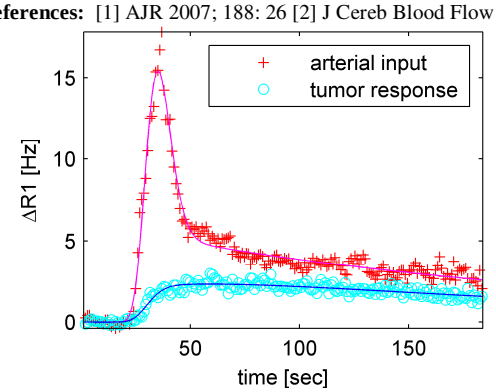


Figure 2. R1 changes in the tumor and the subclavian artery (used as the arterial input) from the same patient as in Figure 1. The blue line shows the best fit to the tumor data obtained with the AATH model.

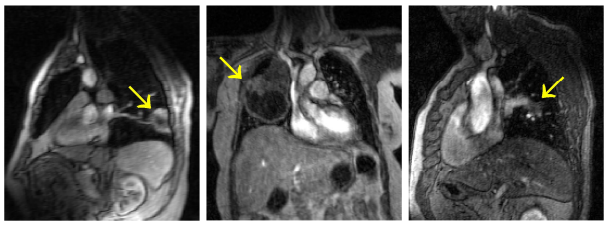

Figure 3. Images from 3 other patients. Arrows indicate the tumor.