

4D Transcatheter Intra-arterial Perfusion MR Imaging for Monitoring Uterine Artery Embolization in the Rabbit VX2 Tumor Model

J. C. Chung¹, R. K. Ryu¹, D. Wang², R. Tang¹, R. A. Omary^{2,3}, and A. C. Larson^{2,3}

¹Department of Radiology, Northwestern University, Chicago, IL, United States, ²Department of Radiology and Biomedical Engineering, Northwestern University, Chicago, IL, United States, ³Robert H. Lurie Comprehensive Cancer Center, Northwestern University, Chicago, IL, United States

Introduction: Uterine artery embolization (UAE) is frequently employed to treat symptomatic fibroids [1] and involves the minimally-invasive catheter-directed delivery of embolic particles to selectively block tumor blood supply. Currently, x-ray digital subtraction angiography (DSA) is used to guide UAE endpoint selection. However, this method of endpoint assessment is entirely subjective [2]. Consequently, variability of endpoint interpretation between operators could result in inadequate or excessive UAE, leading to ineffective treatment or considerable ischemic pain, respectively. As post-procedure pain is a major reason for longer hospital stays and recovery times after UAE [3], a more objective monitoring approach to determine an optimal UAE endpoint would be beneficial. Four-dimensional (4D) transcatheter intra-arterial perfusion (TRIP) MRI is one such monitoring technique that involves targeted intra-arterial (IA) injections of gadolinium (Gd) (<0.001 mmol/kg) to help quantify volumetric tissue-perfusion changes over time. This technique has previously been successful in the setting of liver-directed therapy [4]. Similar usage of radiofrequency (RF) B_1^+ calibration and dynamic R_1 measurements to improve accuracy of perfusion quantification could provide the necessary intra-procedural feedback required to refine current UAE practices. As a first pre-clinical step to improve clinical UAE endpoint determination, we tested the hypothesis that 4D TRIP MRI can objectively quantify perfusion changes during UAE in the rabbit VX2 uterine fibroid model.

Materials and Methods: Eight VX2 uterine tumors were grown in 6 rabbits. After selective DSA-guided catheterization of the uterine artery, rabbits were transferred to an adjacent 1.5-T clinical MRI system. Rabbits remained inside the scanner bore during both TRIP-MRI and UAE procedures in order to maintain image co-registration. UAE was performed with approximately 2 million (1 mL) 40-120- μ m gelatin microspheres.

Data Acquisition: We first depicted uterine anatomy with a 2D turbo-spin-echo (TSE) T2-weighted (T2W) sequence. A baseline 3D R_{10} map was then acquired using a variable flip-angle (FA) spoiled-GRE method. B_1^+ variation was corrected by using 3D TSE double-angle method to obtain *in vivo* B_1^+ maps co-registered to T2W axial images. A 3-mL intra-arterial injection of 2.5% gadolinium (Gd) was administered over 5 seconds at the beginning of each dynamic 3D spoiled-GRE sequence. The entire 8-partition volume of the uterus was continuously sampled at 1.44-second intervals for 86.4 seconds.

Imaging parameters: 128 \times 64 \times 8 matrix, 220 \times 100 \times 40 mm³ FOV; **GRE:** TR/TE = 6/1.62 ms, 660 Hz/pixel BW, 50% slice over sampling, baseline FA=2 $^\circ$, 9 $^\circ$, 15 $^\circ$, 19 $^\circ$, 4 averages; dynamic FA = 15 $^\circ$. **TSE:** TR/TE = 1500/10.4 ms, 660 Hz/pixel BW; FA= 120 $^\circ$ /60 $^\circ$ excitation, 180 $^\circ$ refocusing; multi-slab acquisition, 100% spacing, 100% slice over sampling.

MRI Data Analysis: We derived R_1 time-series and contrast-concentration maps from each TRIP-MR image series [5]. Perfusion maps were then generated using the peak gradient method [6]: $F_p(r) = G_p(r)/E$, where F is perfusion flow (mL/min/100mL), ρ is the tissue density (g/mL), G_p is the peak tissue-contrast concentration gradient, and E is the maximum contrast concentration in the feeding vessel. Because the rate of Gd injection was greater than the flow of the feeding vessel, the Gd concentration of the IA injection determined the maximum vascular Gd concentration. Perfusion maps were used to draw 2 separate regions-of-interest for each tumor. Pre and post-UAE mean perfusion values were compared with a paired t-test ($\alpha=0.05$). The overall embolic endpoint was reported as the mean percent reduction in fibroid tumor perfusion.

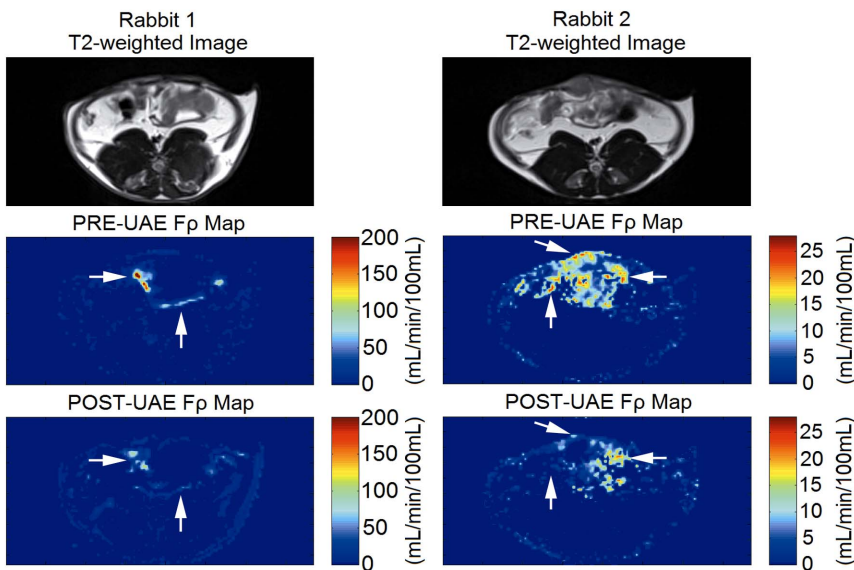


Figure 1. Representative T2W images and TRIP-MR absolute perfusion maps from 2 VX2 uterine tumor rabbits before and after UAE. Pre-UAE perfusion maps demonstrate the peripheral hypervascular rim characteristic of VX2 tumors (arrows). Post-UAE perfusion maps depict perfusion reductions in the targeted embolized regions for each VX2 tumor (arrows).

Results: Representative perfusion maps before and after UAE in 2 different rabbits are shown in **Fig. 1**. The Gd-concentration time-curves for a single voxel of another rabbit are shown in **Fig. 2**. Baseline VX2 uterine tumor perfusion exhibited a statistically significant decrease after UAE from 45.2 to 11.8 mL/min/100mL tissue ($p<0.0001$). Overall perfusion reduction was 73.8% (95% CI: 66.5-84.7%).

Conclusion: Quantitative 4D TRIP-MR imaging can be used to objectively monitor tumor perfusion changes after UAE in VX2 rabbits. The technique may have future clinical application in optimizing endpoints during UAE.

References: [1] Jacobson et al. Am J Obstet Gynecol 2007;196:601.e1-601.e6. [2] Lewandowski et al. J Vasc Interv Radiol 2007;18:1249-1257. [3] Pron et al. J Vasc Interv Radiol 2003;14:1243-1250. [4] Wang et al. MRM 2008;60:970-975. [5] Wang et al., ISMRM 2007 #1792. [6] Bader et al., Radiology 1998 209:129-134.

Acknowledgements: The authors wish to acknowledge grant support from NIH NCI grant R01 CA134719 and the SIR Foundation.

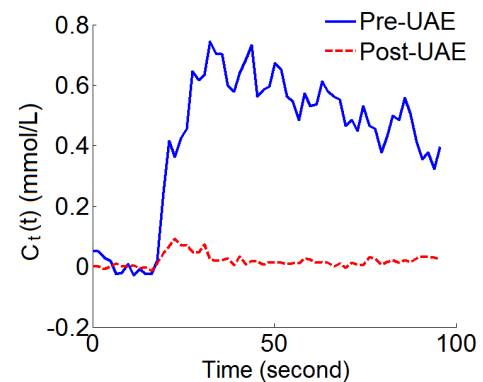


Figure 2. (Above) Representative $\Delta[Gd](t)$ curves for a single voxel of a VX2 uterine tumor pre and post UAE. The $\Delta[Gd](t)$ curve changed in shape and amplitude after UAE. Relaxivity of Gd-DTPA: 3.9 L/s/mmol at 37 $^\circ$ C