Monitoring Liver Tumor Embolization in VX2 Rabbits: Four-Dimensional Transcatheter Intraarterial Perfusion (TRIP) MR Imaging

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Introduction: Transcatheter arterial embolization (TAE) and chemoembolization (TACE) preferentially deliver embolic agents to liver tumors via catheters positioned within the hepatic arteries. **TR**anscatheter **I**ntraarterial **P**erfusion (TRIP)-MRI is an intra-procedural technique to monitor liver tumor perfusion changes during TAE [1] and TACE [2]. Using targeted intraarterial (IA) delivery of small contrast doses, TRIP-MRI permits iterative tumor perfusion measurements during therapy. However, previously developed 2D TRIP-MRI approach provided only limited spatial coverage and limited capacity for accurate perfusion quantification. In this study, we present a quantitative four-dimensional TRIP-MRI technique (serial iterative 3D volumetric perfusion imaging) with rigorous B_1^+ field calibration and dynamic tissue R_1 measurement for intra-procedural assessment of liver tumor perfusion reductions during TAE.

Methods: We surgically implanted VX2 carcinoma into the left liver lobe of 4 rabbits. After 2-4 weeks, via femoral access and angiographic guidance we positioned a 2-F catheter to super-selectively deliver 40-120 µm Embospheres (BioSphere Medical™) to each tumor. After transfer to a 1.5T clinical MRI scanner (Siemens Magnetom Sonata), an *in vivo* B_1^+ map was first generated using 3D multi-slab turbo spin echo (TSE) double-angle method [3] with respiratory navigator trigger. Prior to each TRIP-MRI measurement, a baseline 3D R_{10} map was acquired using variable flip-angle (FA) spoiled-GRE method. 4D TRIP-MRI was performed before and after TAE using 3D dynamic GRE sequence with volumetric coverage of the entire liver at 1.6s sampling rate for 100s after IA injection of 3.0 mL 2.5% Gd-DTPA contrast agent. Imaging parameters included: 220×124×40 mm^3 FOV, 128×80×8 matrix; **GRE**: TR/TE = 6/1.66 ms, 850Hz/pixel BW, 50% slice over sampling; baseline FA = 2°, 9°, 19°, 4 averages; dynamic FA = 9°. **TSE:** TR/TE = 6000/10 ms, 186 Hz/pixel BW, FA= 120°/60° excitation, 120° refocusing, multi-slab acquisition, 100% spacing, 100% slice over sampling. 8 Gd vials were placed next to each rabbit for calibration purposes. With B_1^+ field calibration and baseline R_{10} map, an R_1 map time series and further contrast concentration map series were derived from each TRIP-MR image series [4]. Perfusion maps were calculated using peak gradient method [5]: $F\rho(r) = G_t(r)/E$, where F is perfusion flow (mL/min/100g), ρ is the tissue density (g/mL), G_t is the peak tissue contrast concentration gradient and E is the maximum contrast concentration in the feeding vessel. Since the flow rate of the catheter injection surpassed that of the feeding vessel, this injection dominated the maximum vascular contrast concentration. Separate regions-of-interest were drawn on perfusion maps to measure tumor perfusion. Functional embolic endpoints were reported as the % reduction in tumor perfusion. Perfusion measurements before and after TAE were compared using paired t-tests with α=0.05.

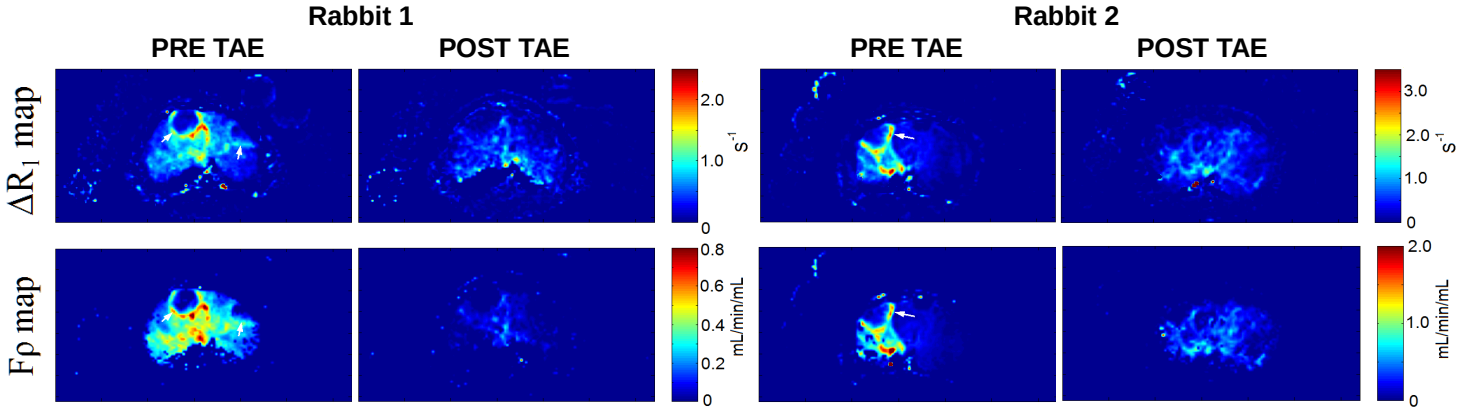

Figure 1. Representative TRIP-MR peak ΔR_1 and perfusion Fρ images in two VX2 liver tumor rabbits before and after TAE. Both pre-embolization ΔR_1 and perfusion Fρ maps demonstrate characteristic peripheral rim for each VX2 tumor (arrows).

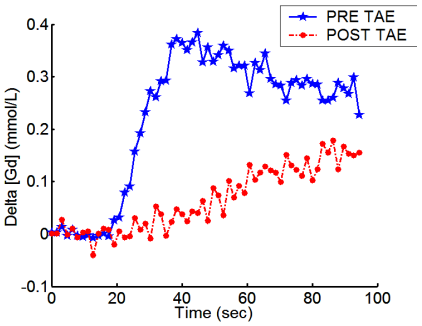

Figure 2. Representative $\Delta[Gd](t)$ curves for a single voxel of a VX2 liver tumor rabbit before and after TAE. The $\Delta[Gd](t)$ curve altered in both shape and amplitude after TAE. Relaxivity of Gd-DTPA: 3.9$Ls^{-1}mmol^{-1}$ at 37°C

Results: TRIP-MRI perfusion measurements were performed in 6 liver tumors during TAE. Representative peak ΔR_1 and perfusion maps in two VX2 liver tumor rabbits before and after TAE are shown in **Fig. 1**. The $\Delta[Gd](t)$ curves for a single voxel of a representative rabbit are shown in **Fig.** 2. The tumor perfusion Fρ reduction was 81.31% (95% CI: 75.86%-86.77%). Fρ decreased significantly from 0.633 (95% CI: 0.775-0.491) before TAE to 0.140 (95% CI: 0.200-0.079) (mL/min/mL, p<0.001) after TAE.

Conclusions: With intra-procedural B_1^+ field calibration and dynamic tissue R_1 measurement, quantitative 4D TRIP-MRI can monitor reductions in liver tumor perfusion during TAE. This technique offers the ability to measure serial objective changes in perfusion during therapy. TRIP-MRI measurements offer the potential to target optimal embolic endpoint for TAE and TACE.

References: [1] Wang et al., Radiology 2007 245:130-139 [2] Larson et al., Radiology 2007 *In press* [3] Stollberger et al., Magn Reson Med 1996 35:246–251 [4] Wang et al., ISMRM 2007 #1792 [5] Bader et al., Radiology 1998 209:129-134