Transcatheter Intraarterial First-Pass Perfusion (TRIP) - MRI Monitoring of Liver Tumor Embolization in VX2 Rabbits

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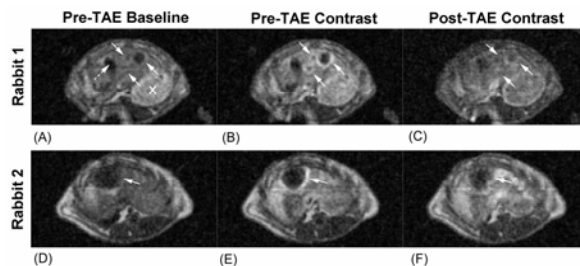
Introduction: Transcatheter arterial embolization (TAE) and chemoembolization (TACE) preferentially deliver embolic agents to hepatocellular carcinoma (HCC) via catheters positioned within the hepatic arteries. Iterative monitoring of liver tumor perfusion during TAE and TACE would facilitate selection of functional embolic endpoints. Dynamic contrast enhanced MRI permits hepatic perfusion measurements [1] and was previously used to evaluate alteration to HCC perfusion after TACE [2]. However, with intravenous contrast injection, the number of perfusion measurements is limited by cumulative dose and the requisite wash-out times between injections. Transcatheter intraarterial (IA) injections permit reductions in contrast dose while increasing liver tumor conspicuity and reducing wash-out times [3]. **TR**anscatheter **I**ntraarterial first-pass **P**erfusion (TRIP)-MRI may be ideal for the iterative perfusion assessment during TAE and TACE. In this study, we tested the hypothesis that iterative TRIP-MRI can detect serial reduction in rabbit liver tumor perfusion 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), serial TAE was performed with ~0.5 million Embospheres injected at each embolic stage (10min between stages). TRIP-MRI was performed at baseline and after each subsequent embolic stage using saturation-recovery spoiled-gradient-echo sequence (TR/TE/TI = 2.7/1.36/104 ms, 15° flip angle, 5 slices, 5mm thickness, 200×100 mm^2 FOV, 128×64 matrix, 500 Hz/pixel BW, 100 sec total scan time with 1 sec sample interval following IA injection of 3.0 mL 5% Gd contrast agent). Imaging parameters were optimized to maximize sensitivity while providing a relatively linear relationship between signal intensity and tissue R_1 over the expected range. Serial TAE and TRIP-MRI were repeated until suspected stasis (lack of tumor enhancement). Stasis was confirmed by follow-up angiography. Separate regions-of-interest were drawn to measure the first-pass time course of signal enhancement ΔSI[t] in both tumors and hepatic arteries. Tumor area-under-curve (AUC) and maximum upslope (MUS), each normalized by arterial input, were measured to assess iterative perfusion reduction. Perfusion measurements across TAE stages were compared using paired t-tests with α=0.05 and statistical power analysis at 95% confidence level. Linear regression was used to evaluate the correlation between corresponding AUC and MUS measurements and the relationship between embolic dose and perfusion response in those tumors with more than 4 embolic stages.
**Results:** TRIP-MRI semi-quantitative perfusion measurements were performed in 8 liver tumors during staged TAE. Representative MR images in two VX2 liver tumor rabbits before and after TAE are shown in **Fig. 1**. The ΔSI[t] curves for a single representative rabbit are shown in **Fig. 2**. AUC decreased from a pre-TAE baseline of 0.408±0.147 to 0.065±0.036 (mean±SD, p<0.0001, power>0.999) after completion of TAE. MUS decreased from a pre-TAE baseline of 0.151±0.057 to 0.027±0.009 (mean±SD, p<0.0001, power>0.999) after completion of TAE. Reductions to AUC and MUS after each embolic stage were statistically significant (p<0.006, power>0.918 for each group of paired comparisons, **Fig. 3**). AUC strongly correlated with MUS (r=0.966, p<0.0001, **Fig. 4**). AUC and MUS showed strong inverse relationships with embolic dose (all r<-0.933, p<0.021).

Conclusions: Iterative TRIP-MRI can detect serial reductions in liver tumor perfusion during TAE. Liver tumor perfusion monitoring during TAE and TACE should permit standardization of embolization end-points to optimize therapy while minimizing toxicity to normal liver tissues. Given that the TRIP-MRI technique offers the potential to determine functional endpoints of TAE and TACE, our results warrant early clinical translation using hybrid MR-IR suites [4].

Figure 1. Representative MR images in two VX2 liver tumor rabbits before and after TAE. Pre-embolization images acquired before contrast injection (**A** and **D**). Pre-embolization images acquired after IA injection at peak enhancement (**B** and **E**). Post-embolization images acquired after IA contrast injection (**C** and **F**).
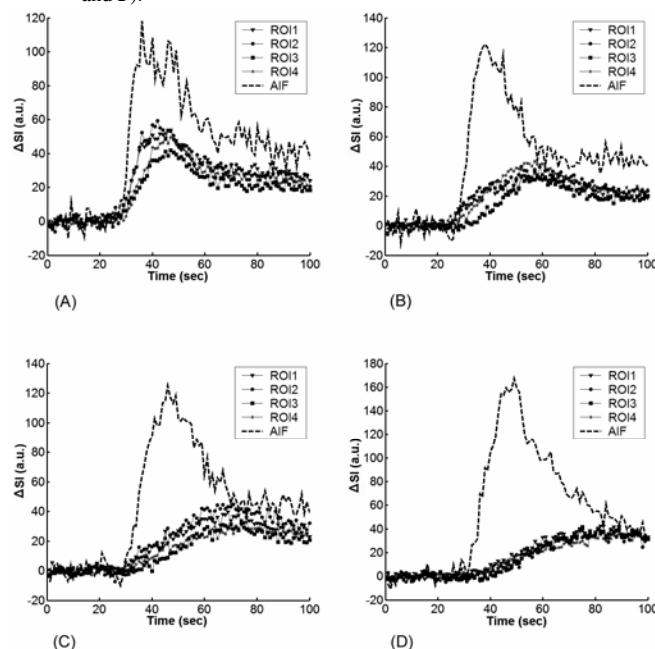
Figure 2. Representative iterative first-pass ΔSI[*t*] curves for a single VX2 liver tumor rabbit before (A) and during progressive TAE (B-D, separate measurement after each serial Embosphere® injection).

Figure 3. Box plots show that the reduction of both normalized AUC and MUS perfusion parameters after each embolic stage are statistically significant: (A) Normalized AUC, (B) Normalized MUS.

y = 0.01468 + 2.71277x
r = 0.966

Figure 4. Regression plot demonstrates a strong linear relationship between normalized AUC and MUS.
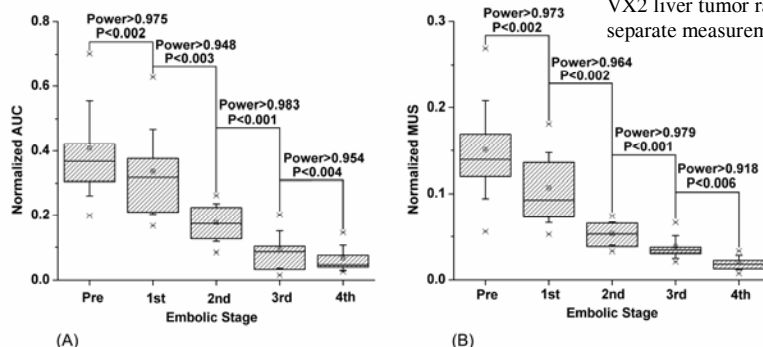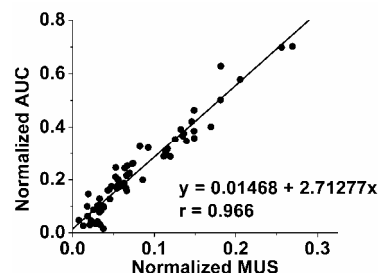
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