Quantitative Perfusion Analysis for Transcatheter Intraarterial Perfusion MR Imaging

D. Wang[1], J. Chung[2], R. Lewandowski[2], R. Tang[2], R. Klein[2], R. Omary[1,3], and A. Larson[1,3]

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

Introduction: Transcatheter arterial embolization (TAE) and chemoembolization (TACE) are established treatment methods for unresectable liver tumor. **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]. However, previous developed TRIP-MRI approaches either used semi-quantitative perfusion analyses which have poorly-defined links to blood flow, or used a peak gradient method [3] which can oversimplify the description of contrast tracer kinetics, to calculate blood flow. In this study, we presented a potentially superior quantitative TRIP-MRI perfusion analysis approach, and evaluated its efficacy in a gel perfusion phantom and in rabbits with VX2 liver tumors during TAE.

Methods: All experiments were performed using a 1.5T clinical MRI scanner (Siemens Magnetom Espree). In phantom studies, we used a chromatography column packed with Sephadex gel as a perfusion phantom. The phantom flow rate was adjusted from 24 mL/min to 2 mL/min at a 2 mL/min interval, and TRIP-MRI measurement was performed at each flow rate. In animal studies, we surgically implanted VX2 carcinoma into the left liver lobe of 12 rabbits. 3 weeks after implantation, we catheterized each rabbit under angiographic guidance to super-selectively deliver 40-120 μm embolic microspheres to liver tumors. After raabits were transfer to MRI scanner, TRIP-MRI measurements were performed before and after TAE. A quantitative TRIP-MRI measurement involved 3D B_1 mapping using catalyzed double-angle method (60°/120°) [4], baseline 3D R_{10} mapping using GRE variable flip angle method (2°, 9°, 15°,19°), and dynamic 3D R_1 mapping using dynamic GRE sequence at 15° flip angle after intraarterial injection of Gd-DTPA contrast agent. Other dynamic imaging parameters included: phantom studies: TR/TE = 5/1.62 ms, 320×160×40 mm^3 FOV, 1.2 sec sampling rate; animal studies: TR/TE = 6/1.62 ms, 200×113×40 mm^3 FOV, 1.6 sec sampling rate. With B_1 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 [3]. We applied the commonly used modified Kety model to describe contrast tracer pharmacokinetics [5] (**Eq. 1**). Given that the super-selective transcatheter bolus injection temporarily suppress antegrade blood flow and control the maximum vascular contrast agent concentration at the catheter tip immediately proximal to the tumor tissues, we estimated $C_p(t)$ using prior information about the bolus injection parameters (**Eq. 2**).

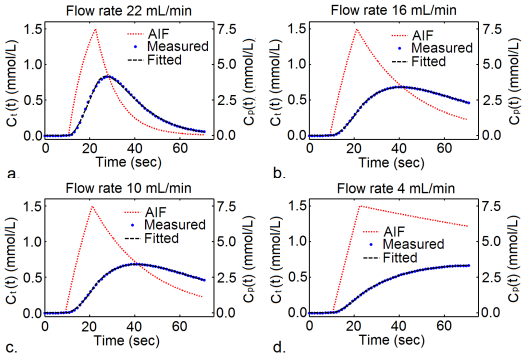

Fig 1. Representative TRIP-MRI phantom concentration time curves and model curve fittings at different flow rates.

$$C_t(t) = v_p C_p(t) + K^{trans} \int_0^t C_p(\tau) \exp\left(-k_{ep}(t-\tau)\right) d\tau \quad (1)$$

$$C_p(t) = C_{inject} \int_0^t C_c(\tau) \exp\left(-\beta(t-\tau)\right) d\tau \Big/ \max\left(\int_0^t C_c(\tau) \exp\left(-\beta(t-\tau)\right) d\tau\right) \quad (2)$$

where $C_c(t) = \begin{cases} 0 & t < T_{start} \| t > T_{end} \\ 1 & T_{start} \le t \le T_{end} \end{cases}$ is a normalized boxcar function, with 0 meaning no contrast solution being injected, 1 meaning contrast solution being injected, and T_{start} and T_{end} representing the beginning and ending times for the transcatheter injection of the contrast solution. Perfusion maps were generated by fitting combined Eqs. 1 and 2. As K^{trans} is primarily representative of blood flow under flow-limited conditions expected in extra-cranial tumor microvasculature, we therefore chose K^{trans} as the kinetic parameter to reflect liver tumor perfusion alterations during TAE. Whole tumor regions-of-interest were drawn on K^{trans} maps to measure intra-procedural tumor K^{trans} values. K^{trans} values before and after TAE were compared using paired t-tests with α=0.05.

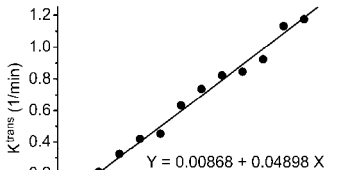

Fig 2. Regression plot demonstrates a strong linear relationship between measured K^{trans} and flow rate in the perfusion phantom.

Results: The phantom $C_t(t)$ curves, estimated $C_p(t)$ curves, and associated model curve fittings for different flow rates are shown in **Fig. 1**. The measured K^{trans} demonstrated a strong linear correlation to flow rate during our perfusion phantom studies (R^2 = 0.9876, P < .0001, **Fig. 2**). In animal studies, TAE and quantitative TRIP-MRI were successfully performed in 12 rabbits with 19 liver tumors. **Fig. 3** shows representative voxel-wise tumor $C_t(t)$ curves, estimated $C_p(t)$ curves, and associated model curve fittings from two representative rabbits. **Fig. 4** shows T2-weighted image, TRIP-MRI peak enhanced image, and corresponding K^{trans} maps before and after TAE from one representative rabbit. The tumor K^{trans} decreased significantly from 0.468 (95% CI: 0.328-0.607) pre-TAE to 0.093 (95% CI: 0.061-0.126) post-TAE (1/min, P < .0001), with a mean percentage reduction of 77.8% (95% CI: 70.3%-85.3%).

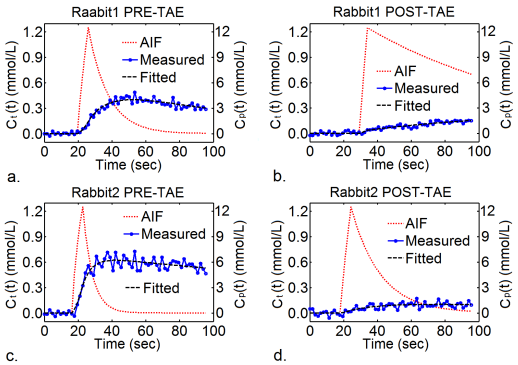

Fig 3. Representative TRIP-MRI voxel-wise tumor concentration time curves and the model curve fittings before and after TAE.

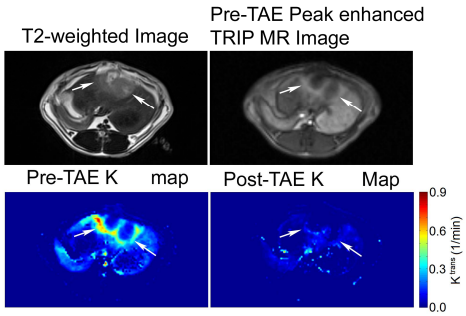

Fig 4. Images from one representative rabbit. T2-weighted image, TRIP-MRI peak enhanced image depict tumor positions (arrows). Corresponding K^{trans} maps demonstrate clear perfusion reductions after TAE.

Conclusions: Our study successfully evaluated the efficacy of the proposed perfusion analysis method for TRIP-MRI datasets in a perfusion phantom, and demonstrated the use of quantitative TRIP-MRI to monitor reductions in liver tumor perfusion during TAE. Quantitative TRIP-MRI measurements offer the potential to target optimal embolic endpoint for TAE and TACE, which maximizes tumor response and minimizes toxicity to normal liver tissues.

References: [1] Wang et al., Radiology 2007;245:130-139 [2] Larson et al., Radiology 2008;246:964-971 [3] Wang et al., Mag Reson Med 2008;60:970-975 [4] Wang et al., NMR Biomed 2009;22:882-890 [5] Roberts et al., JMRI 2006;23:554-563.

Acknowledgements: The authors wish to acknowledge grant support from NIH R01 CA126809-01A2 and R01 CA134719-01; the SIR Foundation; and the Rosenberg Family Cancer Research Fund.