

Quantitative 4D Transcatheter Intraarterial Perfusion MRI for Monitoring Chemoembolization of Hepatocellular Carcinoma

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Introduction: Transcatheter arterial chemoembolization (TACE) is widely used for treatment of unresectable hepatocellular carcinoma (HCC). However, due to the high subjectivity and variability of conventional x-ray digital subtraction angiography (DSA) for monitoring angiographic TACE endpoints [1], optimal tumor perfusion reduction endpoints remain unknown. Transcatheter Intraarterial Perfusion (TRIP)-MRI, using catheter-directed intraarterial (IA) contrast injections, offers an objective method to monitor intra-procedural tumor perfusion changes during TACE. Prior semi-quantitative TRIP-MRI approaches were developed and validated in animal models and translated clinically for intra-procedural perfusion monitoring during TACE procedures in HCC patients [2]. A quantitative 4D TRIP-MRI technique (serial iterative 3D volumetric perfusion imaging), including rigorous B_1 calibrated dynamic tissue R_1 measurements [3] and further first-pass perfusion analyses for TRIP-MRI datasets, was recently developed. In this study, we test the hypothesis that quantitative 4D TRIP-MRI can be applied clinically to monitor intra-procedural liver tumor perfusion changes during TACE.

Methods: In this prospective IRB-approved study, 16 patients with HCC underwent TACE procedures within a Siemens Miyabi combined x-ray DSA-MRI unit. Each patient was selectively catheterized under DSA guidance and transferred to a 1.5T Espree MR scanner for pre-TACE 4D TRIP-MRI measurements. After moving back to DSA unit, patients underwent DSA-guided TACE. Patients were immediately returned to MRI for repeat 4D TRIP-MRI measurements. At the beginning of each 4D TRIP-MRI measurement, a baseline 3D R_{10} map was acquired using variable flip angle (FA) spoiled-GRE method, and an *in vivo* targeted B_1 map was generated using 3D reduced filed-of-view TSE catalyzed double-angle method [4]. 4D TRIP-MRI was performed using a 3D dynamic GRE sequence, with images covering the entire targeted liver segment(s) acquired at a 2.1 sec sampling rate for 33 sec after IA injection of 5.0 mL 20% Gd-DTPA contrast (Magnevist, Berlex). Imaging parameters included: **GRE:** TR/TE = 4.0/1.72 ms, baseline FA = 2°, 9°, 15°, 19°, 3 averages; dynamic FA = 15°, 192×128×24 matrix, 400–450 mm FOV, 670 Hz/Pixel bandwidth, GRAPPA acceleration factor 2; **TSE:** TR/TE = 400/12 ms, excitation/compensation FA = 60°/120° and 120°/60°, refocusing FA = 180°, catalyzation chain pulse FA = 90°, 3 catalyzation chain pulses, 128×28×16 matrix, ETL = 7, 660 Hz/pixel bandwidth. With B_1 calibrated R_1 mapping, we converted each dynamic TRIP-MR image series into contrast concentration map time series. Perfusion (Fp) maps were produced using first-pass perfusion analysis for data acquired within the contrast bolus microvascular transit phase [5]. Whole tumor regions-of-interest were drawn on perfusion maps to measure pre- and post-TACE tumor perfusion. Tumor perfusion values before and after TACE were compared using a paired t-tests ($\alpha=0.05$). Absolute and percentage reduction in tumor perfusion were reported.

Results: Quantitative 4D TRIP-MRI was successfully performed during 18 treatment sessions for 16 patients with HCC. Intra-procedural perfusion changes were measured in 22 separate tumors. Fig. 1 shows representative 4D TRIP-MRI voxel-wise tumor concentration time curves and the curve fittings using first-pass perfusion model from one HCC patient. Fig. 2 shows representative 4D TRIP-MRI peak enhancement images and corresponding perfusion maps before and after TACE in two HCC patients. Fig. 3 shows pre and post-TACE intra-procedural perfusion maps fused with T2-weighted anatomic images and a corresponding post-TACE non-contrast CT image from one HCC patient. Mean intra-procedural liver tumor perfusion Fp decreased from 16.33 (95% CI: 10.74-21.91) before TACE to 4.97 (95% CI: 3.45-6.50) (mL/min/100mL) after TACE. Intra-procedural tumor perfusion reductions were statistically significant ($P < 0.0005$), with a mean absolute perfusion change of 11.35 (95% CI: 5.63-17.08) (mL/min/100mL) and a mean percentage reduction of 60.96% (95% CI: 48.31%-73.62%).

Conclusions: Quantitative 4D TRIP-MRI can be performed successfully in a combined x-ray DSA-MRI unit to monitor intra-procedural reductions in liver tumor perfusion during TACE. This technique could potentially be used to target optimal embolic endpoint during TACE procedures to ensure complete treatment of the targeted tumor volume(s) while avoiding damage to adjacent liver tissues.

References: [1] Lewandowski et al., JVIR 2007;18:1249-1257 [2] Larson et al., Radiology 2008;246(3): 964-971 [3] Wang et al., Mag Reson Med 2008;60:970-975 [4] Wang et al., ISMRM 2009 #370 [5] St Lawrence et al., J Cereb Blood Flow Metab 1998;18:1365-1377.

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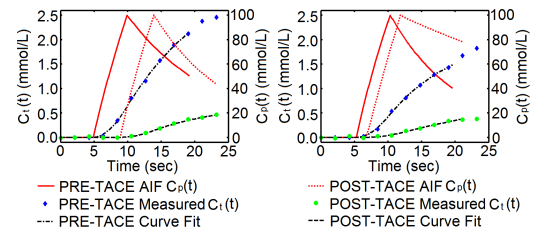


Fig 1. Representative 4D TRIP-MRI voxel-wise tumor concentration time curves and the first-pass perfusion model curve fittings before and after TACE.

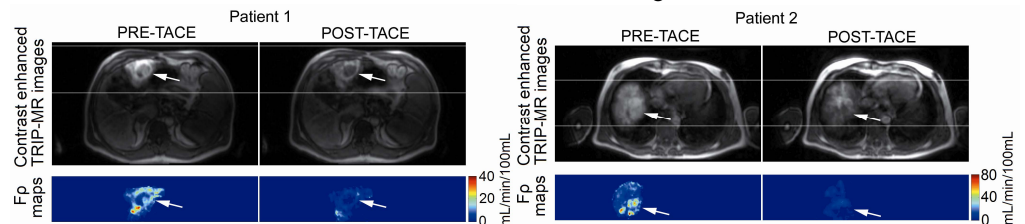


Fig 2. Representative TRIP-MRI monitored TACE images in two different patients with HCC. 4D TRIP-MRI peak enhancement images depict tumor position (arrows). Corresponding intraprocedural perfusion maps demonstrate clear perfusion reductions after TACE.

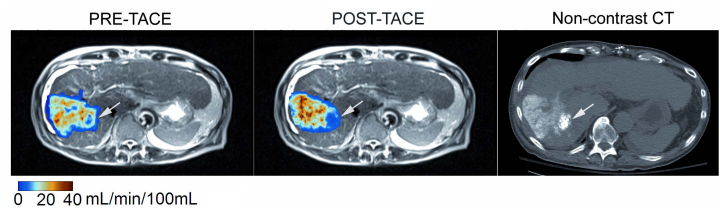


Fig 3. Intra-procedural perfusion maps fused with T2-weighted anatomic images reveal TACE-induced perfusion reductions in the targeted tumor (arrow). Post-TACE non-contrast CT image verifies chemotherapy emulsion distribution, showing ethiodized oil accumulation in the region of perfusion reduction in the targeted tumor (arrow).