Quantitative Transcatheter Intraarterial Perfusion MRI to Predict Drug Delivery during Chemoembolization for Hepatocellular Carcinoma

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Introduction: Hepatocellular carcinoma (HCC) is the third most common cause of cancer death worldwide. Transarterial locoregional therapies (LRTs), such as transcatheter arterial chemoembolization (TACE) and yttrium-90 radioembolization, have promising roles in the management of HCC [1]. TACE in particular, is recognized as the standard of care for intermediate-stage unresectable HCC with demonstrated survival benefit [2]. However, conventional x-ray digital subtraction angiography (DSA) can not antecedently quantify biodistribution and spatial selectivity of subsequent drug delivery during LTRs. **T**ranscatheter **I**ntraarterial **P**erfusion (**TRIP**)-MRI, using catheter-directed intraarterial (IA) contrast injections, can measure selected arterial perfusion to the targeted tumor during transarterial LTRs in a combined clinical MR/DSA unit (termed MR-IR suite) [3, 4]. Because arterial tumor perfusion determines the degree of drug delivery to the targeted tumors [5], quantitative assessment of selected arterial tumor perfusion might be useful for guiding the spatial distribution of chemotherapeutic agent uptake during TACE. In this study, using post-TACE non-contrast CT as a reference standard, we tested the hypothesis that pre-TACE quantitative TRIP-MRI may be used to predict chemotherapy emulsion delivery to tumors during TACE.

Methods: In this prospective IRB-approved study, 20 patients with HCC underwent TACE procedures within a Siemens Miyabi MR-IR unit. Selective catheterization was performed under DSA guidance. Quantitative TRIP-MRI measurement was performed immediately before TACE in a 1.5T MAGNETOM Espree MR scanner. Quantitative TRIP-MRI [4] included baseline 3D variable flip angle R_{10} mapping, 3D targeted B_1 mapping (reduced FOV TSE catalyzed double-angle method), and dynamic 3D R_1 mapping using GRE sequence: TR/TE = 4.0/1.72 ms, flip angle = 15°, 192×128×24 matrix, 400~450 mm FOV, GRAPPA acceleration factor 2. The targeted liver volume was sampled for 33 sec after IA injection of 5 to 10 mL 20% Gd-DTPA contrast (Magnevist, Berlex). 2 hours after DSA-guided TACE, all patients underwent a non-contrast abdominal CT scan to verify the distribution of injected chemotherapy-lipiodol mixture. With B_1 calibrated R_1 maps, we converted dynamic TRIP-MR image series into contrast concentration map time series. Perfusion ($F\rho$) maps were produced using first-pass perfusion analysis for data acquired within the contrast bolus microvascular transit phase [4]. The mean whole tumor perfusion ($F\rho_{tumor}$), mean perfusion in the entire targeted region ($F\rho_{region}$), the whole tumor volume ($V_{tumor-MR}$), and the entire targeted volume ($V_{region-MR}$) were measured from perfusion maps. We subtracted the baseline signal intensity of normal liver parenchyma from all CT images. The mean whole tumor signal enhancement (ΔSI_{tumor}), mean signal enhancement in the entire targeted region (ΔSI_{region}), the whole tumor volume ($V_{tumor-CT}$), and the entire targeted volume ($V_{region-CT}$) were measured from CT images. We defined the selectivity of drug delivery to tumor as the proportion of drug delivered to the tumor over total drug delivered to the entire region. The selectivity factors from TRIP-MRI perfusion maps and CT images were calculated as $SF_{MR}= (F\rho_{tumor} \times V_{tumor-MR})/(F\rho_{region} \times V_{region-MR})$ and $SF_{CT}= (\Delta SI_{tumor} \times V_{tumor-CT})/(\Delta SI_{region} \times V_{region-CT})$, respectively. Volumes and selectivity factors from two modalities were compared using linear regression analysis (α=0.05).
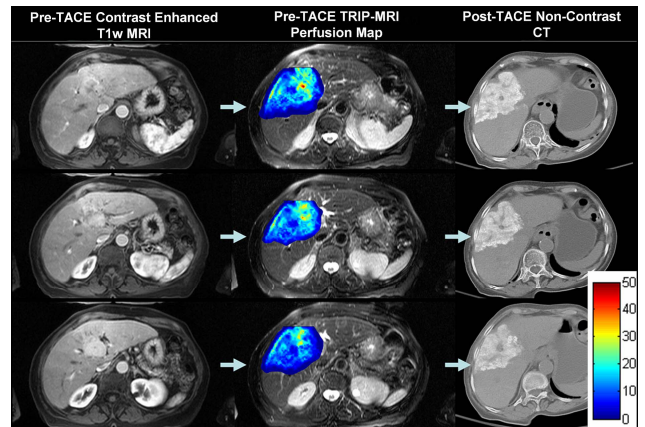

Fig 1. Pre-TACE TRIP-MRI perfusion maps and post-TACE CT images depict similar spatial patterns of contrast, whereas the pre-TACE contrast-enhanced T1-weighted images poorly resemble these spatial patterns. The perfusion unit is in mL/min/100mL.
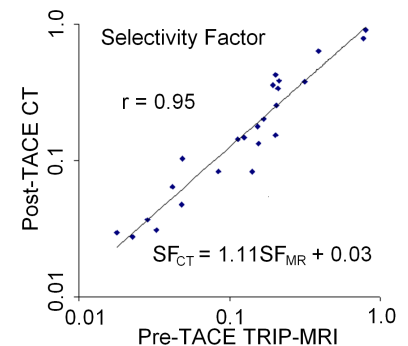
Results: Quantitative TRIP-MRI was performed immediately before TACE in all 20 patients. Analysis was conducted on 24 tumors in 18 patients with proper TRIP-MRI coverage. **Figure 1** shows representative pre-TACE contrast-enhanced T1-weighted MR images, corresponding perfusion maps fused with T2-weighted images, and corresponding post-TACE non-contrast CT images. Measured volumes and selectivity factors (mean ±SD) from pre-TACE TRIP-MRI and post-TACE CT images were closely matched: $V_{tumor-MR} = 22.7 \pm 21.5$ cm^3 versus $V_{tumor-CT} = 21.1 \pm 20.3$ cm^3; $V_{region-MR} = 233.7 \pm 127.7$ cm^3 versus $V_{region-CT} = 235.5 \pm 108.6$ cm^3; and $SF_{MR} = 0.20 \pm 0.21$ versus $SF_{CT} = 0.25 \pm 0.24$. Linear regression analyses revealed that the measured volumes and selectivity factors from TRIP-MRI and CT images were highly correlated and had strong linear relationships: $V_{tumor-CT} = 0.93V_{tumor-MR} - 0.12$ ($r = 0.99$), $V_{region-CT} = 0.79V_{region-MR} + 49.84$ ($r = 0.93$), and $SF_{CT} = 1.11SF_{MR} + 0.03$ ($r = 0.95$, **Figure 2**), with all $P < 0.001$.

Fig 2. Scatter plot of selectivity factors between two modalities with best linear fit line. Axes are in logarithmic scale.

Conclusion: Our study accessed the clinical utility of quantitative TRIP-MRI for predicting chemotherapy-lipiodol delivery during TACE. The volumes of drug distribution in the tumors and liver as well as the selectivity of chemotherapy emulsion delivery to the tumors obtained from pre-TACE TRIP-MRI highly correlated with corresponding parameters seen on CT scans after TACE. These findings suggest that quantitative TRIP-MRI may have the potential to provide important spatial biodistribution information of subsequent drug delivery during liver-directed transarterial LTRs with same catheter positioning.

References: [1] Riaz et al., J Clin Oncol 2009;27(34):5734-5742 [2] Llovet et al., Lancet 2002;359:1734-1739 [3] Larson et al., Radiology 2008;246(3): 964-971 [4] Wang et al., JMRI 2010;31:1106–1116 [5] Blasberg et al., Cancer Treat Rep 1981; 65(Suppl 2): 3-12