

# Intra-procedural Transcatheter Intraarterial Perfusion MRI as a Predictor of Tumor Response to Chemoembolization for Hepatocellular Carcinoma

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**Introduction:** Hepatocellular carcinoma (HCC) is the third most common cause of cancer mortality worldwide. With established survival benefits, transcatheter arterial chemoembolization (TACE) is widely accepted as the first-line therapy for intermediate-stage unresectable HCC [1]. Early knowledge of tumor response to TACE is crucial for evaluating treatment efficacy, timing of repeat treatment, and patient prognosis. However, conventionally HCC response is available one to three months after TACE using MRI or CT based upon size and necrosis criteria. Few studies have investigated intro-procedural imaging biomarkers that may objectively predict future tumor response during TACE procedure. Furthermore, due to the incapability of conventional x-ray digital subtraction angiography (DSA) TACE monitoring for objective and reproducible blood flow assessment [2], the relationship between TACE-induced perfusion changes and tumor response remains 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 in a combined clinical MR/DSA unit (termed MR-IR suite) [3, 4]. In this study, we tested the hypothesis that TRIP-MRI monitored intra-procedural changes in tumor perfusion during TACE may predict future tumor response.

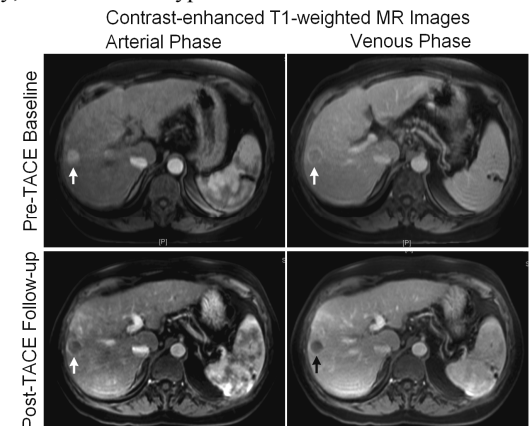
**Methods:** In this prospective IRB-approved study, 28 patients with 29 HCCs underwent TACE procedures within a Siemens Miyabi MR-IR suite. Each patient was catheterized under DSA guidance and transferred to a 1.5T MAGNETOM Espree MR scanner for pre-TACE TRIP-MRI measurements. After moving back to DSA unit, patients underwent DSA-guided TACE. Patients were then returned to MRI for repeat TRIP-MRI. 3D or 4D TRIP-MRI were performed using 2D saturation-recovery spoiled-gradient-echo (GRE) sequence (TR/TE/TI = 2.4/1.2/90 ms, 10-14 slices, 8mm thickness), or 3D GRE sequence (TR/TE = 4.0/1.7 ms, 24-28 slices, 5mm thickness), respectively. Other common parameters included: 15° flip angle, 192×128 matrix, 380-450 mm FOV, 670 Hz/pixel BW, and GRAPPA acceleration factor 2. Dynamic images were acquired for 35 sec after IA injection of 5 or 10 mL 20% Gd-DTPA contrast (Magnevist, Berlex). Imaging parameters were chosen to provide a relatively linear relationship between signal intensity and tissue contrast agent concentration. Tumor regions-of-interest in the central slice of each tumor were drawn on TRIP-MRI image series to generate time-signal enhancement curve. Area-under-the-curve (AUC) was measured as semi-quantitative perfusion parameter and percentage tumor perfusion change was calculated [3]. Tumor AUC perfusions pre- and post-TACE were compared using paired t-test ( $\alpha=0.05$ ). Imaging follow-up was performed one to three months after TACE. European Association for the Study of the Liver (EASL) criteria was used to access tumor response [5]. We used scatter plot to illustrate the relationship between intro-procedural perfusion reductions and tumor response. We subsequently categorized HCC samples based upon percentage AUC reduction quartiles and compared the tumor response rates. Univariate analysis using Fisher's exact test and multivariate analysis using multivariate logistic regression were further conducted to investigate factors associated with tumor response ( $\alpha=0.05$ ).

**Results:** TRIP-MRI monitored TACE was successfully performed in all cases. Intro-procedural tumor AUC decreased significantly after TACE (342.1 versus 158.6 a.u.,  $P < 0.001$ ). 27 HCCs ( $n = 27$ ) in 26 patients had follow-up imaging at mean 39 days (range 20-78 days) post-TACE. Representative pre-TACE baseline and post-TACE follow-up contrast-enhanced T1-weighted MR images are shown in **Figure 1**. Favorable response, defined as complete response or partial response, was present in 67% of treated tumors according to EASL criteria. Scatter plot demonstrates an inverted U-shaped relationship between intro-procedural perfusion reductions and EASL tumor response. The tumor groups with 25-50% and 50-75% perfusion reductions had the highest response rate (**Figure 2**). 15/16 (94%) tumors with 25-75% perfusion reductions, compared to only 3/11 (27%) tumors with perfusion reductions outside the above range, showed EASL response. The univariate analysis indicated intro-procedural tumor perfusion reduction ( $P = 0.001$ ) and Child-Pugh class ( $P = 0.004$ ) were significantly related to tumor response. The multivariate analysis confirmed both categorical variables were independent factors associated significantly with tumor response (**Table 1**).

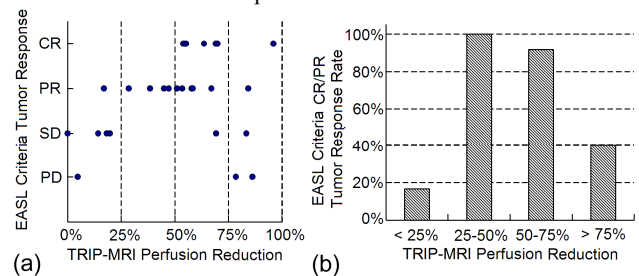
**Conclusion:** Our study demonstrated that intermediate level of tumor perfusion reduction was associated with improved EASL tumor response. TRIP-MRI, performed within an integrated MR-IR unit, offers the ability to monitor intro-procedural changes in tumor perfusion during TACE, and may potentially serve as an objective predictor of future tumor response at the time of TACE procedure.

**References:** [1] Lewandowski, Radiology 2010 [2] Lewandowski, JVIR 2007 [3] Larson, Radiology 2008 [4] Wang, JMIR 2010 [5] Bruix, J Hepatol. 2001

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**Fig 1.** Diagnostic and follow-up contrast-enhanced T1-weighted MR images in a 65-year-old patient. Complete EASL response was achieved with 69.1% AUC perfusion reduction after TACE.



**Fig 2.** (a) Scatter plot between perfusion reductions and tumor response demonstrates an inverted "U" shape relationship. (b) Bar graph indicates greater tumor response rate can be achieved with 25-75% than < 25% or > 75% perfusion reductions.

**Table 1** Factors Associated with Tumor Response

Variable	EASL Response		P-Value	
	Response (n=18, 67%)	Nonresponse (n=9, 23%)	Univariate Analysis*	Multivariate Analysis#
<b>Perfusion Reduction</b>				
25-75%	15 (94%)	1 (6%)	<b>0.001</b>	<b>0.012</b>
< 25 or > 75%	3 (27%)	8 (73%)		
<b>Child-Pugh Class</b>				
A	13 (93%)	1 (7%)	<b>0.004</b>	<b>0.047</b>
B	5 (38%)	8 (62%)		

\* Fisher's Exact Test; # Multivariate Logistic Regression