Chemoembolization follow-up of hepatocellular carcinoma with MRI: utility of evaluating enhancement features on a 1 month follow-up in predicting residual disease after therapy

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Introduction
Hepatocellular carcinoma (HCC) is the 5th leading cause of death worldwide. Assessing response to chemoembolization is important for guiding patient management. Change in tumor size is a standard indicator of treatment response. However, size changes after therapy may require several months to manifest, and more sensitive, specific and rapid methods for measuring tumor response are desirable. Evaluating enhancement characteristics of treated tumor with MRI is expected to provide accurate, earlier diagnosis of residual disease. Focal HCC is a highly arterialized tumor and therapeutic response to chemotherapy is expected to manifest in a rapid decline in vascularity.

Purpose
To evaluate the sensitivity, specificity and accuracy of a contrast enhanced MRI performed 1 month after localized chemotherapy for the detection of viable HCC.

Methods
Patients: This trial was approved by our institutional review board and was HIPPA compliant. Inclusion criteria selected patients receiving chemoembolization for HCC between 12-2005 and 1-2008 who had contrast enhanced MRI within 1 month (mo) prior to treatment, in addition to post-procedure MRI at 1mo and 6 mo. Pathology was used as a surrogate for the 6 mo follow-up examination if the patient underwent transplantation between 1-6 mo post-therapy. The final study population consisted of 23 tumors (occurring within 21 patients) that fit into the imaging protocol. Chemoembolization: Performed with non-occlusive Doxorubicin-loaded LC beads in 21/23 tumors, TACE in 1/23, and Yi-90 in 1/23. MR Acquisition: Images obtained with our standard liver protocol, including 3 dimensional T1-weighted gradient echo sequences in the precontrast, bolus-triggered arterial, venous and delayed phases. Image analysis: All MRI data sets were evaluated separately by two radiologists at different times. Tumors were scored on both 1 and 6 mo follow-up as either showing complete loss of enhancement, or showing at least some partial or focal residual persistent tissue enhancement within the tumor bed. Additionally, changes in T1 and T2 signal (relative to adjacent liver parenchyma) and perilesional enhancement were tabulated and recorded by each reader. Size measurements: Lesion size was measured on pre-therapy, 1 mo and 6 mo exams by using 1-D measure of the longest dimension in keeping with RECIST criteria. An increase in tumor size from 1 to 6 mo of > 20% was used as confirmation of residual disease. In 5/23 tumors, interval explant was performed prior to the six-month follow-up exam, and review of the pathology served as the surrogate standard of reference for residual disease. Statistics: Sensitivity, specificity and accuracy of the 1 month follow-up MRI in predicting residual disease were computed along with 95% confidence intervals for each rater, using growth > 20% from 1 to 6 months (or pathologic analysis of the explant) as the standard of reference

Results
Table 1 demonstrates sensitivity, specificity and accuracy of the one-month follow-up MRI for predicting residual disease on the 6 month follow-up MRI or pathology. There was a high degree of agreement between the two readers for both the one month (kappa 0.88) and six month (identical findings) MRIs. Changes in tumor signal and perilesional enhancement were also documented. Figure 1 demonstrates a case of complete therapeutic response at 1 mo, while Figure 2 demonstrates a case of residual tumor identified at 1 mo.

Conclusions
This investigation demonstrates a high accuracy for predicting residual disease after chemoembolization of HCC on a one-month follow-up examination, demonstrating the utility of evaluating post therapy enhancement features in assessing tumor response.


Table 1: Statistics for detection of residual disease by 1 month follow-up MRI

<table>
<thead>
<tr>
<th>Reader</th>
<th>Sensitivity (%) [95% CI]</th>
<th>Specificity (%) [95% CI]</th>
<th>Accuracy (%) [95% CI]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Reader 1</td>
<td>85.7 [49.9]</td>
<td>100 [81-100]</td>
<td>95.7 [79.9]</td>
</tr>
<tr>
<td>Reader 2</td>
<td>71.4 [36.3]</td>
<td>100 [81-100]</td>
<td>91.3 [73.9]</td>
</tr>
</tbody>
</table>

Figure 1A Figure 1B Figure 2A Figure 2B