Hepatocellular Carcinoma Lesion Characterization: Single-Institution Clinical Performance Review of Multiphase Gadolinium-enhanced MR Imaging—Comparison to Prior Same-Center Results after MR Systems Improvements

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Purpose: To measure diagnostic performance in the detection of hepatocellular carcinoma (HCC) by using the most recent technology and multiphase gadolinium-enhanced magnetic resonance (MR) imaging and to compare with earlier results at the same institution.

Materials and Methods: This retrospective study was institutional review board approved and HIPAA compliant. Informed consent was obtained. Between January 2008 and April 2010, 101 patients underwent liver transplantation and pretransplantation abdominal MR imaging within 90 days. Prospective image interpretations from the clinical record were reviewed for documentation of HCC, including size, number, and location. Liver explant histologic examination provided the reference standard for lesion analysis and was performed in axial gross slices in conjunction with the MR imaging report for direct comparison. Tumors were categorized according to size (≥2 cm or <2 cm), and MR imaging detection sensitivity, specificity, predictive values, and accuracy were calculated according to category. The Fisher exact test was used to compare results from this study against prior reported results.

Results: Thirty-five (34.7%) of 101 patients had HCC at explant analysis. Patient-based analysis of all lesions showed a sensitivity and specificity of 97.1% (34 of 35) and 100% (66 of 66), respectively. For lesions 2 cm or larger, MR imaging had a sensitivity and specificity of 100% (23 of 23) and 100% (78 of 78), respectively. For lesions smaller than 2 cm, MR imaging had a sensitivity and specificity of 82.6% (19 of 23) and 100% (78 of 78), respectively. Lesion-based sensitivity for all tumors was 91.4% (53 of 58) in the current study, compared with 77.8% in 2007 (P = .07). For lesions smaller than 2 cm, the sensitivity was 87.5% (28 of 32) in the current study, compared with 55.6% previously (P = .02).

Conclusion: MR imaging remains a highly accurate diagnostic method for the preoperative evaluation of HCC, and detection of small (<2 cm) tumors has been significantly improved compared with that of earlier studies.

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Hepatocellular carcinoma (HCC) is a common complication of chronic liver disease with increasing incidence worldwide (1,2). Liver transplantation remains the most validated curative intervention for HCC. In a seminal article from 1996, Mazzaferro et al (3) published survival data for liver transplantation in the setting of early HCC (Milan criteria), with a recurrence-free 4-year survival rate of 92%; patients with tumor burden beyond the Milan criteria had significantly increased mortality rates (3). Donor liver distribution in the United States is governed by the United Network for Organ Sharing, which uses the model for end-stage liver disease (MELD) for assessing recipient priority scores that are predictive of mortality risk. MELD continues to apply the Milan criteria for assessing priority scores in patients with HCC by recognizing that delays in transplantation may lead to HCC progression and by precluding further consideration for transplantation because of poor outcomes.

**Advances in Knowledge**

- Our institutional review data show that we have improved the sensitivity for detection of hepatocellular carcinoma (HCC) by using contrast material–enhanced multiphase MR imaging from 55.6% to 87.5% for tumors smaller than 2 cm during the past 2 years of clinical data collection ($P = .02$).
- The sensitivity for HCC detection for lesions 2 cm or larger remains high (96.2%), showing no significant change ($P = .59$).
- It is proposed that the diagnostic performance improvement noted with smaller HCC may result from technologic improvements implemented between study data collection periods, primarily from improvements in three-dimensional gradient-echo sequences and from uniform implementation of contrast-enhanced arterial phase timing by using a bolus-triggered technique.

**Implications for Patient Care**

- Improved detection of small (<2 cm) HCC lesions by using MR imaging will lead to earlier diagnosis and further minimize the role of biopsy in small lesions.
- Superior detection of small HCC will improve tumor surveillance in patients with chronic liver disease and contribute to more accurate liver transplantation preoperative staging and therapeutic treatment, particularly for patients with multifocal disease.
- Centers where MR imaging is performed with updated technology and techniques may yield substantial benefits in the detection of smaller HCC.

The United Network for Organ Sharing no longer requires biopsy confirmation and accepts magnetic resonance (MR) imaging as a foundation for staging disease in patients listed for liver transplantation (4). Numerous reports have compared MR imaging, computed tomography, and ultrasonography, with some of these reports showing superior sensitivity, specificity, and accuracy of MR imaging for depicting HCC (5–8) and for depicting focal liver lesions in general (9). It has been a general observation that MR imaging performs very well for HCC larger than 2 cm but has reduced lesion sensitivity for tumors smaller than 2 cm. For example, HCC detection sensitivity for tumors smaller than 2 cm has been reported to be as low as 15%–55% (10–12), while showing sensitivity of 95%–100% for detecting HCC larger than 2 cm (10,13).

Efforts to improve MR imaging technology are pursued with the expectation that this will yield benefits in diagnostic accuracy for disease, including HCC. The ongoing evaluation of transplant priority criteria necessitates an understanding of current and evolving diagnostic accuracy of imaging, and particularly MR imaging, given the growing use of this modality. We have previously published our center-based experience on the accuracy of MR imaging in the detection of HCC prior to liver transplantation (10). Since our prior report, we have implemented changes in our imaging technology and methods, with the expectation that these changes would improve the overall accuracy of HCC detection, especially for smaller tumors. The purpose of this study was to measure the sensitivity, specificity, and accuracy of multiphase gadolinium-enhanced MR imaging for HCC in pretransplantation patients by using current-generation technology and methods to determine if there was a measurable change from previous results.

**Materials and Methods**

**Patients**

This retrospective investigation was institutional review board approved and Health Insurance Portability and Accountability Act compliant. Informed consent was obtained. The study period was from January 2008 to April 2010 and was based on having had an updated stable set of MR imagers and methods during this interval. Selection criteria included having MR imaging performed within 90 days prior to liver transplantation and, for consistency, that the examination was performed at our...
center and reported by abdominal MR imaging experts (D.R.M. or B.K., with 14 and 5 years of experience, respectively). Patients outside these conditions were excluded (Fig 1).

**MR Image Acquisition**

Our MR imaging protocol has been updated from a previous report on HCC detection, and the major protocol changes are summarized in Table 1. Most notable are changes in the 3D T1-weighted GRE sequence parameters and the uniform application of a real-time bolus contrast material–enhanced timing technique for individually optimized acquisition of the arterial phase images (Fig 2). In detail, MR imaging examinations were performed by using current-generation 1.5-T MR imaging systems (Magnetom Avanto; Siemens Medical Solutions, Iselin, New Jersey). Our protocol consists of a combination of T2-weighted and dynamic contrast-enhanced T1-weighted multiphase imaging extending from the lung bases through the kidneys. T2-weighted images were acquired with a single-shot fast spin-echo sequence (350-mm² field of view, 256 × 198 matrix, partial Fou- rier acquisition of 4/8, 7-mm section thickness, 1500/83, flip angle of 180°, acceleration factor of two) in the coronal and axial plane without fat saturation and in the axial plane with fat saturation by using a spectral adiabatic inversion-recovery technique (14,15). A breath-hold (end inspiration) dual-echo spoiled GRE sequence was also performed for qualitative evaluation of tissue fat and iron. Three-dimensional T1-weighted GRE images were obtained during the precontrast phase (axial and coronal) and then subsequently during the arterial, venous, and delayed phases (axial) with the following parameters: 380-mm² field of view, 288 matrix (70% phase resolution), partial Fourier imaging, 3.8/2.0, flip angle of 10°, 96 sections at 3-mm section thickness, bandwidth at 380 Hz/pixel, and acceleration factor of two. Each patient’s weight was recorded, and gadobenate dimeglumine (MultiHance; Bracco Diagnostics, Princeton, NJ) was administered at a dose of 0.05 mmol/kg and a rate of 2 mL/sec, followed by a 30-mL saline flush at 2 mL/sec by using a dual-chamber power injector (Spectris; Medrad, Warrendale, Pa). This contrast enhancement protocol was adopted per institutional safety committee requirements in response to concerns about nephrogenic systemic fibrosis, with the objective of minimizing dose while preserving RI effects of a standard agent dose (16). Arterial phase images were acquired by using a real-time bolus-tracking method, with breath-hold instructions initiated when the contrast material bolus reached the diaphragm and the celiac trunk (trigger point), and imaging was initiated at an 8–10-second delay from the trigger point, as previously described (17). Acquisition time for 3D GRE imaging was 17–18 seconds, obtained in a single breath hold. Venous phase imaging was initiated at 70 seconds and delayed phase imaging at 180 seconds after the trigger point.

**MR Image Analysis**

All reports from patients meeting selection criteria (Fig 1) were reviewed for the description of HCC per standardized reporting protocol at our center and on the basis of United Network for Organ Sharing MR imaging reporting criteria (4). Prospective image interpretations were performed by one of the two interpreting radiologists (D.R.M. or B.K.); consensus readings were not used. The distribution of cases was based on the clinical duty schedule for MR imaging reporting without any preselection bias. No cases in this study were interpreted by any other radiologists. Only the clinical reports were used for this study, and they were prospectively interpreted and retrospectively collected from the electronic medical records. Available prior MR imaging and clinical information was reviewed during prospective interpretations per normal clinical routine, and images were interpreted on a workstation loaded with image review software (Ellim, version 3.0; Merge Healthcare, Chicago, Ill.). Reports indicated size (largest axial section diameter), number, and location of HCC lesions. Characterization of dysplastic nodules was similarly documented (13). Couinaud classification was used for anatomic reference to localize HCC. Criteria for the diagnosis of HCC at MR imaging included all of the following: (a) increased enhancement of the lesion compared with adjacent liver tissue in the contrast-enhanced arterial phase, (b) washout of the lesion (defined as becoming hypointense to adjacent liver tissue) during the later contrast-enhanced phases, and (c) development of a peripheral rim of enhancement, corresponding to pseudocapsule enhancement, on delayed phase images (Figs 3, 4). Alternatively, a diagnosis of HCC was attributed to a lesion showing only enhancement or only washout and capsule formation, if the lesion also demonstrated elevated signal intensity on T2-weighted single-shot fast spin-echo images. Lesions with focal hepatic arterial enhancement, but without washout, capsule enhancement, or abnormal increased T2 signal, were considered dysplastic nodules (if clearly a defined nodule) or nonspecific hypervascular lesions (if nonmarginated and subcapsular) (11). In every case, only the reported findings within the electronic medical patient records were used to populate the study database to evaluate
a retrospective second look of the MR images was performed (D.R.M. and B.K.) to examine the region of interest.

Table 1

|----------------------------------------|----------------------------|----------------------------|----------------------------------------------------------------------
| 3D GRE optimization                    |                            |                            |                                                                      
| Excitation radiofrequency pulse        | Fixed                      | Wider with section oversampling | Better homogeneity and contrast in outer sections                      
| Gradient spoiling                      | Fixed                      | Minimized for abdomen       | Better efficiency                                                     
| Echo asymmetry                         | None                       | Reversed (echo time closer to opposed phase) | Fat is suppressed more uniformly                                     
| Linear ascending partition reordering | None                       | Extended range              | Less edge ringing in the partition direction                           
| Contrast material administration      |                            |                            |                                                                      
| Agent                                  | Gadodiamide or gadopentetate dimeglumine | Gadobenate dimeglumine       | Reduced risk of nephrogenic systemic fibrosis (16)                     
| Dose                                   | 0.1 mmol per kilogram of body weight | 0.05 mmol/kg               | ...                                                                  
| Bolus timing                           | Heterogeneous—combination of fixed time delay and bolus tracking methods | Uniform use of semi-automated real-time bolus tracking methods | ...                                                                  
| T2-weighted single-shot fast           |                            |                            |                                                                      
| spin-echo optimization                 |                            |                            |                                                                      
| Fat suppression                        | Nonselective inversion recovery | Spectral adiabatic inversion recovery | Better contrast by preserving water signal and reduced motion effects | 
| Echo train                             | Standard single shot with partial Fourier transform | Echo train shortened with parallel processing | Improved image sharpness                                              |

Note.—GRE = gradient echo, 3D = three dimensional.

Figure 2

(a, b) Comparison of axial liver images of prior and current 3D GRE technique. Representative venous phase 3D GRE MR images obtained by using the technique common to (a) 2004–2006 and (b) 2008–2010 (refer to Table 1 for sequence differences). Sequence parameters for (a) included the following: repetition time msec/echo time msec, 3.6/1.4; flip angle, 12°; section thickness, 3 mm; matrix, 256 × 192; acceleration factor of two; bandwidth, 400 Hz/pixel. That for (b) was as follows: 3.8/2.0; flip angle, 10°; section thickness, 3 mm; matrix, 288 × 168 (70% phase); acceleration factor of two; bandwidth, 380 Hz/pixel. Fields of view were similarly adjusted to patient. When comparing image (b) with (a), there is improved fat suppression (arrow), reduced Gibbs artifact (arrowhead), and improved contrast and edge detail yielding better visualization of small enhancing structures such as peripheral vessels (ellipse).
as the reference standard. Subgroups were formed for HCC 2 cm or larger and HCC smaller than 2 cm. This size categorization was based on MELD criteria (19), in which importance is attributed to HCC tumors 2 cm or larger in diameter. The diagnostic accuracy for MR imaging was assessed with both a patient- and lesion-based analysis. Sensitivity, specificity, and accuracy were estimated for both analyses as proportions, and corresponding 95% confidence intervals were calculated according to the efficient-score method (corrected for continuity) (20). The Fisher exact test was used to compare current sensitivity, specificity, and accuracy of MR imaging between tumor size subgroups and with the values reported previously from our institution (10); a \( p \) value of .05 or less was considered to indicate a significant difference.

Results

Patients

Between January 2008 and April 2010, the number and selection pathway of the study patients is shown in Figure 1. The final study cohort consisted of 101 patients (average age, 52 years; age range, 18–73 years). There were 70 men (average age, 52 years; age range, 19–70 years) and 31 women (average age, 52 years; age range, 18–73 years). There was an average interval between MR imaging and liver transplantation of 43 days (range, 0–89 days). All patients had a clinical history of chronic liver disease, and the underlying cause of liver disease (some with more than one cause) included hepatitis C \((n = 37)\), hepatitis B \((n = 4)\), ethanol abuse \((n = 26)\), cryptogenic cirrhosis \((n = 9)\), primary sclerosing cholangitis \((n = 9)\), autoimmune hepatitis \((n = 6)\), primary biliary cirrhosis \((n = 3)\), \( \alpha_1 \)-antitrypsin deficiency \((n = 2)\), and other disease processes \((n = 10)\). Among the 101 patients in our study population, 20 (20%) underwent interval chemoembolization \((n = 19)\) or radiofrequency ablation \((n = 1)\) prior to explant. The average number of treatment interventions was 1.3 per patient (range, one to three), and

cysts were sampled for histologic examination, with particular attention paid to lesions reported at preoperative MR imaging. At microscopic examination, malignant nodules were characterized on the basis of histologic type, size, location, number, and stage (American Joint Committee on Cancer TNM staging system) (18). Lesion size and location were described in the manner used for the MR imaging evaluation. Any nonnodular cellular clusters with features of carcinoma that were incidentally detected at microscopy in the vicinity of or adjacent to a sampled region of interest that measured 4 mm or smaller in overall size were deemed microscopic disease of uncertain importance.

Statistical Analysis

Software (SAS, version 9.2; SAS Institute, Cary, NC) was used for all data analysis. The pathologic findings served to determine the possible cause for non-identical findings between MR imaging and pathologic examination.

Histopathologic Analysis

Explanted livers were serially sectioned into 5-mm contiguous slices in the axial plane to spatially correlate the explant with MR images. At gross examination, suspicious nodules were identified as those distinct from surrounding regenerative nodules in terms of size, texture, color, and degree of bulging beyond the cut surface of the liver. Localizations were subsequently confirmed by review of the MR images and the gross pathologic specimens by an expert pathologist (N.V.A. and A.B.F., 15 and 4 years of experience in hepatobiliary pathologic examination, respectively) in conjunction with the interpreting radiologists (D.R.M. and B.K.). All lesions other than regenerative nodules and benign

Figure 3: MR images show 2-cm HCC with characteristic features in 49-year-old man with hepatitis C viral disease. (a) Precontrast and (b) T1-weighted 3D GRE images show tumor that enhances in the arterial phase (arrow). (c) Delayed phase 3D GRE image shows washout and capsule enhancement (arrow). (d) T2-weighted single-shot image shows nearly imperceptible T2 differential signal intensity (arrow).
the average number of days from MR imaging to therapy was 34 (range, 12–69 days). In every case of prior therapy, microscopic evidence of HCC was made unequivocally at explant analysis, with a background of treatment changes, and therefore included in this study. Size of these lesions was reported only on the basis of the MR imaging.

**MR Imaging**

Review of pretransplantation clinical MR imaging reports demonstrated documentation of HCC in 34 of 101 patients with explanted liver and a total of 53 HCC tumors detected in the study population. Size characterization at MR imaging is described in Tables 2 and 3, with histopathologic findings representing the reference standard.

**Histopathologic Analysis**

Histopathologic analysis of the explants demonstrated the presence of HCC in 35 of 101 patients. Mean size for all tumors was 2.0 cm (range, 0.5–5.0 cm). Tumors 2 cm or larger were found in 23 of the 35 patients (mean size, 2.8 cm; range, 2.0–5.0 cm), while tumors measuring smaller than 2 cm were found in 23 patients (mean size, 1.4 cm; range, 0.5–1.9 cm). A total of 58 HCCs larger than 4 mm were found at histopathologic examination; 26 of these 58 lesions were 2 cm or larger, while 32 measured smaller than 2 cm. A single HCC was depicted in 17 patients, and 18 patients had more than one lesion (13 patients had two tumors and five patients had three tumors in their explanted liver). Incidental nonodule forming clusters of neoplastic cells were found at microscopy in three patients (measuring 3, 3, and 4 mm).

**Statistical Analysis**

The patient-based analysis results are displayed in Table 2. Concordant HCC diagnosis between MR imaging and pathologic examination was found in 34 of 35 patients, resulting in a patient-based sensitivity of 97.1%. The single discrepant patient had a 1.8-cm HCC that was diagnosed as a dysplastic nodule at MR imaging. The specificity of MR imaging was 100% (66 of 66). At patient-based analysis, all 23 patients with HCC 2 cm or larger and 19 (82.6%) of 23 patients with HCC smaller than 2 cm had diagnostic concordance between MR imaging and pathologic findings with regard to presence of tumor.

Lesion-based analysis of MR imaging for the detection of HCC is presented in Table 3. MR imaging–histopathologic lesion concordance was found in 25 (96.2%) of 26 HCCs 2 cm or larger and in 28 (87.5%) of 32 HCCs smaller than 2 cm. The overall detection sensitivity of MR imaging for both populations of HCC, either 2 cm or larger or smaller than 2 cm, compared favorably with previously reported findings (Table 4).

Of the 58 total HCC tumors detected at histopathologic examination, there were five tumors that represented false-negative findings at MR imaging. For two of these tumors, an HCC smaller than 2 cm at explant correlated with a reported finding of dysplastic nodule at MR imaging (Fig 5). In the additional three false-negative cases, no corresponding tumor of any type was reported at the MR imaging interpretation. All three of these lesions were 2 cm or smaller (sizes of 1.0, 1.5, and 2.0 cm) at explant pathologic examination. At retrospective second reexamination, MR imaging studies showed a corresponding lesion to the 2.0-cm tumor; this appeared as a washout lesion with elevated T2 signal but isointense at arterial phase imaging. The other two smaller lesions showed no corresponding findings at second-look MR imaging, and no image degradation or errors on the timed contrast-enhanced 3D GRE acquisitions were detected.

**Discussion**

Our results showed that there has been improvement in HCC diagnostic sensitivity...
Table 2

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Tumors (n = 35)</th>
<th>Tumors ≥2 cm (n = 23)</th>
<th>Tumors &lt;2 cm (n = 23)</th>
<th>P Value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>97.1 (34/35) [83.4, 99.9]</td>
<td>100 (23/23) [82.2, 100]</td>
<td>82.6 (19/23) [60.5, 94.3]</td>
<td>.05</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>100 (66/66) [93.1, 100]</td>
<td>100 (78/78) [94.2, 100]</td>
<td>100 (78/78) [94.2, 100]</td>
<td>&gt;.9</td>
</tr>
<tr>
<td><strong>Positive predictive value</strong></td>
<td>100 [87.4, 100]</td>
<td>100 [82.2, 100]</td>
<td>100 [79.1, 100]</td>
<td>&gt;.9</td>
</tr>
<tr>
<td><strong>Negative predictive value</strong></td>
<td>98.5 [90.9, 99.9]</td>
<td>100 [94.2, 100]</td>
<td>95.1 [87.3, 98.4]</td>
<td>.07</td>
</tr>
<tr>
<td><strong>Accuracy</strong></td>
<td>99.1 [93.8, 99.9]</td>
<td>100 [95.4, 100]</td>
<td>95.1896.0 [89.6, 98.7]</td>
<td>.06</td>
</tr>
</tbody>
</table>

Note.—Data are percentages, with numbers used to calculate the percentages in parentheses and 95% confidence intervals in brackets. Patients may be counted in both groups if they have HCCs both smaller than 2 cm and 2 cm or larger.

* P values were calculated by comparing tumors smaller than 2 cm with tumors ≥2 cm.

Table 3

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Tumors</th>
<th>Tumors ≥2 cm</th>
<th>Tumors &lt;2 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>No. detected at pathologic examination</strong></td>
<td>58</td>
<td>26</td>
<td>32</td>
</tr>
<tr>
<td><strong>No. confirmed at MR imaging</strong></td>
<td>53</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td><strong>No. missed at MR imaging</strong></td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td><strong>No. of false-positive findings at MR imaging</strong></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td><strong>Sensitivity (%)</strong></td>
<td>91.4 (53/58)</td>
<td>96.2 (25/26)</td>
<td>87.5 (28/32)</td>
</tr>
</tbody>
</table>

* P = .25 (calculated by comparing tumors <2 cm with tumors ≥2 cm).

Table 4

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All Tumors</th>
<th>Tumors ≥2 cm</th>
<th>Tumors &lt;2 cm</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>2004–2006</strong></td>
<td>77.8 (28/36)</td>
<td>100 (18/18)</td>
<td>55.6 (10/18)</td>
</tr>
<tr>
<td><strong>2008–2010</strong></td>
<td>91.4 (53/58)</td>
<td>96.2 (25/26)</td>
<td>87.5 (28/32)</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>.07</td>
<td>.59</td>
<td>.02</td>
</tr>
</tbody>
</table>

Note.—Data are percentages, with numbers used to calculate percentages in parentheses.

for smaller (<2 cm) tumors compared with earlier reported findings (10). We showed that the specificity and positive predictive values for HCC smaller than 2 cm is very high, while lesion-based sensitivity for these smaller HCC has been significantly improved compared with that of our prior institutional review (P = .02).

Prior reports showing reduced sensitivity for HCC smaller than 2 cm (ranging from 15% to 55%) (10–12) has led others to advocate diagnostic protocols involving combinations of imaging and biopsy to confirm the diagnosis of small lesions (21). However, the accuracy of needle biopsy is limited (22) and becomes increasingly challenging technically with smaller tumors. In addition, percutaneous biopsy of hepatic lesions introduces risks of bleeding, hepatic decompensation, tumor peritoneal seeding, and even death (23–27). More recent work by Choi et al (28), who assessed the accuracy of MR imaging for HCC detection in explanted livers and also utilized updated MR imaging systems, reports similar results to our current study for smaller (<2 cm) tumors. Major institutions that have oversight over tissue distribution now advocate to assess potential growth (31), which is generally a marker of malignancy or malignant transformation of a dysplastic nodule. Our current study helped to reexamine the relationship between the size of HCC and detection at MR imaging and further supports non-invasive diagnostic evaluation.

The reasons for the improvement in HCC detection sensitivity in our study may be multifactorial and include changes in sequence pulse programming of 3D GRE sequences, improved fat-suppression techniques, and more uniform application of improvements in reproducible timing of the arterial contrast-enhanced images (14,17,32–34). Every patient in this study was imaged with new MR imaging systems compared with those patients included in our prior report. The 3D GRE sequence has progressively changed on the MR imaging systems of all major manufacturers, with alterations including different...
The importance of tumors measuring less than 2 cm is not yet well understood. The Milan criteria remain the foundation for MELD scores and patient listing. Other criteria have been proposed, namely the University of California San Francisco criteria (35), which has shown that the Milan criteria may be too stringent and that patients outside the Milan criteria, with a solitary tumor up to 6.5 cm or two to three tumors not greater than 4.5 cm, have similar long-term disease-free intervals. With improving sensitivity for HCC smaller than 2 cm, the potential for finding the combination of a larger tumor (>3 cm with Milan or >4.5 cm with University of California San Francisco criteria) with smaller tumors increases, and therefore increases the potential for excluding patients from transplantation. Another potential concern is in patients who have more than three HCCs with one or more that are smaller than 2 cm. Milan criteria allow for up to three tumors, none larger than 3 cm in diameter. Patients with more than three lesions should be excluded from liver transplantation. Demonstrating improved accuracy of small HCC imaging at MR imaging, as in our current report, should be related to a reduced incidence of this type of incorrect staging of disease in patients. Given the excellent outcomes noted in studies of transplant patients with HCC, including Milan and University of California San Francisco criteria (3,35), we may hypothesize that the overall effect of missing lesions smaller than 2 cm may not have substantial adverse effects on transplant outcomes, but this specific question would benefit from further investigation.

Our study had a number of limitations. There were a number of differences between the current study design and the design of the previously reported institutional study. In particular, we used the clinically generated study reports in this study, while in our prior study we used retrospective review of the MR imaging acquisitions. While the current study used only cases interpreted by MR imaging experts, the retrospective review of the images, which also employed expert MR imaging readers, may be expected to increase the sensitivity for tumors (36,37), and yet we found that in our earlier study we achieved a lower sensitivity for smaller HCC. We also chose to exclude from statistical analysis nonnodule forming microscopic foci of malignancy that were incidentally detected at pathologic examination (three foci, all ≤4 mm). The clinical importance of these incidental microscopic clusters of malignant cells is unclear, and pretransplantation diagnosis of these foci by using any method (including biopsy) is not yet technically feasible. Furthermore, an average delay of 43 days between MR imaging and preparation acquisitions, k-space filling methods, echo spacing, fat-suppression methods, and alterations in postprocessing image construction. Throughout the course of this study, we used a semiautomated bolus trigger real-time liver examination technique (17) for improving timing of the arterial phase contrast-enhanced 3D GRE sequence. This is similar to conventional MR angiography and relies on a bolus trigger by using near real-time imaging to visualize the contrast material bolus. We are unable to analyze the specific role of each technical advance to the measured improvement in small HCC detection we observed.

Figure 5: MR images show small HCC without washout in 61-year-old woman with hepatitis C virus. (a) Precontrast and (b) arterial phase 3D GRE images show an 8-mm arterial enhancing focus (arrow). (c) Delayed phase 3D GRE image does not show washout (ie, becoming hypointense to adjacent hepatic parenchyma) or capsule enhancement (arrow). (d) T2-weighted fat-saturated single-shot image shows the lesion is inconspicuous (arrow). MR imaging features were reported as a dysplastic nodule, and short-term 3-month follow-up MR imaging was recommended to evaluate for a change in enhancement features or growth. However, this patient underwent transplantation after this study, and pathologic analysis corresponding to this location showed a 10-mm nodule with features of HCC.
transplantation may have resulted in situations where a tumor has developed or grown during this interval. This would then lead to an apparent underestimation of MR imaging sensitivity. Twenty percent (20 of 101) of patients in our study population underwent interval percutaneous treatment of tumor between MR imaging and explant, which may have improved detection rates of these necrotic lesions at explant pathologic examination. Other factors, such as improvements in liver specimen evaluation between the two studies, with thinner axial slicing and use of MR imaging reports to direct attention to regions of interest, may also yield higher pathologic sensitivities for small lesions. Any improvement in pathologic HCC sensitivity provides a better assessment of objective truth for the purposes of measuring MR imaging performance but changes in pathologic performance is not feasible in our study design. Another relative limitation was that we were only looking at lesion detection, while ultimately effect on patient selection and long-term outcomes will be the most important factors to consider when implementing diagnostic protocols. Given the time frame of this report, such investigation requires continued follow-up.

Our investigation demonstrated that MR imaging is a highly accurate diagnostic method for the preoperative evaluation of HCC and that there has been interval improvement in HCC detection sensitivity and characterization for smaller tumors compared with our earlier 2004–2006 study. This is likely a result of improvements in the hardware, sequence design of 3D GRE, and improvements in contrast-enhanced timing method.

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