MR Imaging of the Abdomen

Pancreatic Cancer: Correlation of MR Findings, Clinical Features, and Tumor Grade
Jorge Elias, Jr., M.D., Ph.D., Richard C. Semelka, M.D., Ersan Altun, M.D., Masakatsu Tsurusaki, M.D., Ertan Pamuklar, M.D., Mauricio Zapparoli, M.D., Vasileios Voultsinos, M.D., Diane M. Armao, M.D., and Tara Rubinas, M.D.

Whole-Body Diffusion-Weighted Imaging: Technical Improvement and Preliminary Results
Shuo Li, M.D., Fei Sun, M.S., Zheng-yu Jin, M.D., Hua-dan Xue, M.D., and Ming-li Li, M.D.

Multinodular Focal Fatty Infiltration of the Liver: Atypical Imaging Findings on Delayed T1-Weighted Gd-BOPTA-Enhanced Liver-Specific MR Images
Daniele Marin, M.D., Riccardo Iannaccone, M.D., Carlo Catalano, M.D., and Roberto Passariello, M.D.

Gadobenate Dimeglumine–Enhanced Magnetic Resonance Imaging of Primary Leiomyoma of the Liver
Daniele Marin, M.D., Carlo Catalano, M.D., Massimo Rossi, M.D., Antonino Guerrisi, M.D., Michele Di Martino, M.D., Pasquale Berloco, M.D., and Roberto Passariello, M.D.

Evaluation of Optimized Inversion-Recovery Fat-Suppression Techniques for T2-Weighted Abdominal MR Imaging
Thomas C. Lauenstein, M.D., Puneet Sharma, Ph.D., Timothy Hughes, Ph.D., Keith Heberlein, Ph.D., Dana Tudorascu, M.S., and Diego R. Martin, M.D., Ph.D.
Invivo is proud to sponsor SMRT educational seminars and toasts the extraordinary dedication of radiology technologists around the world, as they continue their education towards a higher standard of patient care.
We are pleased to present the SMRT Educational Seminars, Volume 11, Number 4: “MRI of the Abdomen.” This is the forty-second home study developed by the SMRT, exclusively for the SMRT members.

In selecting articles for this home study as well as others including our new electronic home studies, I am constantly asking myself (and others, driving them to distraction) “What do technologists and radiographers need to know?” Possibly of greater importance. “What do technologists and radiographers want to know?” I am sure there are many things that we need to know but without the desire to learn, it is practically impossible to absorb the information and to retain it for later utilization. With that in mind, I am once again requesting all SMRT members to send me an email and tell me what topics you would like to see in these home studies, paper and/or electronic (amsawyer@stanford.edu).

I recently attended an ISMRM educational course on Practical Body MRI: Impact of New Technology in Berkeley, California, USA. I was honored to act as a co-organizer of the meeting that included Nancy Talbot, M.App. Sc., M.R.T.(R)(MR) from Toronto, Ontario, Canada, and Bill Faulkner, B.S., R.T.(R)(MR) from Chattanooga, Tennessee, USA as faculty. I was impressed to see the number of clinical MR facilities embracing so many new technologies including Diffusion-Weighted Imaging and Double Contrast Enhanced Imaging in the abdomen both as a means to improve early detection and specificity.

Pancreatic cancer is reported to be the fourth (or fifth, dependent upon the publication) leading cause of death from cancer in the United States. Worldwide, pancreatic cancer ranks thirteenth in incidence but eighth as a cause of cancer death. As with all cancers, early detection is critical. The ability to characterize, to differentiate between malignant and benign or slow growing cancers, is becoming more important as therapies are being developed that target specific diseases. Our first article presents a carefully organized and conducted study of MR imaging of pancreatic cancer.

Whole-body diffusion-weighted imaging is a quickly growing technique for MR of the abdomen. This provides an additional tool to assist in the characterization of disease, assessment of response to therapy and tumor staging. The scans are quick as we have come to expect from diffusion-weighted imaging, and as seen in this second article, a free-breathing technique that is reported as being “without slice misregistration, fat contamination, significant distortion or nonuniformity.”

Contrast media continues to be developed to address special needs in imaging. Applications continue to evolve after the contrast is approved for use and experience is shared through word-of-mouth and peer-reviewed publications. Our third article reports on atypical findings in the use of delayed T1-weighted imaging using contrast enhancement to look at multinodular focal fatty infiltration of the liver. Our fourth article evaluates contrast-enhanced MRI of primary leiomyoma of the liver.

Our fifth and final article evaluates “Inversion-Recovery Fat-Suppression Techniques for T2-weighted Abdominal MR Imaging.” A spectral-attenuated inversion recovery (SPAIR) fat-suppression technique is compared to conventional inversion recovery fat-suppression in clinical abdominal MRI.

We would like to express our grateful appreciation to Chesanie Beam (Lincolnton, North Carolina, USA) and Gina Greenwood (Madison, Wisconsin, USA) for writing the questions that compose the quiz required to obtain Category A continuing education credits.

Special thanks goes to Lewis Shin, M.D., Assistant Professor, Department of Radiology, Stanford University, Stanford, California, USA for acting as our expert reviewer.

Thanks also to Paul McElvogue, SMRT Publications Chair and in the Berkeley, California, USA office of the ISMRM/SMRT. Jennifer Olson, Associate Executive Director, Mary Keydash, Publications Director, and the staff for their insight and long hours supporting these educational symposia.

Finally, we would like to thank John Wilkie and all of the terrific people at Invivo Corporation who support our home studies program, the SMRT Educational Seminars. Their continuing support to advance technologist and radiographer knowledge brings quality continuing education to the SMRT membership worldwide.
Pancreatic Cancer: Correlation of MR Findings, Clinical Features, and Tumor Grade
- Review current status of medical imaging of pancreatic carcinoma.
- Discuss the MRI scan parameters selected and their value.
- Review the analysis of the images that was conducted.
- Compare the different cancer groups including tumor size, borders, localization, extension, invasion, distant metastases and lymph node involvement.

Whole-Body Diffusion-Weighted Imaging: Technical Improvement and Preliminary Results
- Review basic physics of diffusion-weighted imaging.
- Explain the MRI scan parameters and RF coil selection.
- Compare results of PET and MRI scans in patients.

Multinodal Focal Fatty Infiltration of the Liver: Atypical Imaging Findings on Delayed T1-Weighted Gd-BOPTA-Enhanced Liver-Specific MR Images
- Discuss current medical imaging and characterization of multinodal focal fatty infiltration.
- Review the selection of MRI scan parameters and gadolinium contrast media.
- Compare the appearance and results of contrast-enhanced CT and MRI scans.

Gadobenate Dimeglumine-Enhanced Magnetic Resonance Imaging of Primary Leiomyoma of the Liver
- Review the morphology and current medical imaging methods of primary leiomyoma of the liver.
- Discuss the scan parameters and contrast enhancement utilized for CT and MRI imaging to detect and characterize lesions in the liver.
- Compare the appearance of liver lesions on post-contrast images using liver specific MR gadolinium contrast agents.

Evaluation of Optimized Inversion-Recovery Fat-Suppression Techniques for T2-Weighted Abdominal MR Imaging
- Explain the current methods for MRI of the abdomen including the advantages and disadvantages of each.
- Review the selection of scan parameters for the MR imaging protocol.
- Discuss the physics for each of the MR imaging sequences and the effect upon tissue contrast.
- Explain the method of T1 optimization being used.
- Review the image analysis and statistical analysis conducted.

Educational Objectives

Quiz Authors:

Chesanie Beam, B.S., R.T.(R)(MR)
Lincolnton, North Carolina, USA

Gina Greenwood, B.S., R.T.(R)(MR)
Madison, Wisconsin, USA

Expert Reviewer:

Lewis K. Shin, M.D.
Assistant Professor
Department of Diagnostic Radiology
Veterans Affairs Palo Alto Health Care System
Stanford University
Stanford, California, USA
Pancreatic Cancer: Correlation of MR Findings, Clinical Features, and Tumor Grade

Jorge Elias, Jr., M.D., Ph.D., Richard C. Semelka, M.D., Ersan Altun, M.D., Masakatsu Tsurusaki, M.D., Ertan Pamuklar, M.D., Mauricio Zapparoli, M.D., Vasileios Voultsinos, M.D., Diane M. Armoo, M.D., and Tara Rubinas, M.D.


Purpose: To assess the frequency of occurrence of poorly-marginated and focally-defined pancreatic ductal adenocarcinoma by MRI and to determine whether these appearances correlate with clinical features and histopathological grade.

Materials and Methods: Institutional review board with waiver of informed consent was obtained for this HIPAA compliant study. A total of 33 patients (16 female, 17 male, mean age = 63.5 ± 12.8, ranging from 41 to 80 years) with histopathologically-proven pancreatic ductal adenocarcinoma who underwent MR examination between August 2000 and February 2005 were retrospectively evaluated. Clinical data and histopathological tumoral grade were obtained from clinical charts; nine of 33 patients were excluded of the histopathological evaluation since their diagnosis was performed by fine needle aspiration biopsy and it was not possible to obtain the histopathological grade. Two radiologists reviewed all cases independently to identify whether cancers were poorly-marginated or focally-defined. Agreement between radiologists was assessed using the kappa coefficient. The overall correlation between imaging findings, clinical features, and histopathological grade was assessed with contingency tables using the Fisher’s exact test.

Results: Of the 33 patients, nine (27.2%) were classified as poorly-marginated and 24 (72.8%) as focally-defined. Agreement between the two reviewers was excellent (k = 0.92, 95% confidence interval [CI] = 0.78–1.0). Poorly-marginated cancers exhibited well- to moderately-differentiated histopathology in 71.4% of cases, while focally-defined cancers had well- to moderately-differentiated histopathology in 17.6% of cases, P = 0.02.

Conclusion: A poorly-marginated appearance of pancreatic ductal carcinoma on MRI is not uncommon. These cancers exhibited statistically significant moderate- to well-differentiated histopathology compared to focally-defined cancers.

Key Words: MRI; pancreatic cancer; histopathology; gadolinium-enhanced MR technique; tumor grade

THE TYPICAL MRI FINDINGS of pancreatic carcinoma have been well described (1–4). Most cases present as a focal low-signal-intensity mass that is best visualized and characterized on immediate postgadolinium T1-weighted images (1–3.5). This occurs primarily due to the scirrhus nature of the tumor, which has dense fibrotic tissue associated with the neoplastic cells. The tumor, therefore, appears distinctly hypointense relative to the pancreatic parenchyma during the arterial phase of dynamic contrast enhancement, when the pancreas is maximally enhanced (6).

Pancreatic cancer may occasionally be ill-defined in morphology with poorly-defined margins (1.7). In this setting, tumors will be difficult to visualize on all MR sequences. Secondary findings such as pancreatic or biliary ductal dilatation, regional and distant metastases, and vascular invasion can help to establish the diagnosis. Poorly-marginated and/or isoattenuating pancreatic cancer has been previously described in computed tomography (CT) series, occurring in 4% to 32% of patients (8–10). In one of these studies, isolated biductal dilatation (i.e., no associated tumor mass seen by CT) was seen in 2.8% of patients (8). Another study showed 11% of patients had isoattenuating pancreatic adenocarcinoma on contrast-enhanced biphasic multidetector row helical CT (9). Only one of these previous reports correlated histopathologic and imaging findings: primarily, tumor CT enhancement with tumor histopathologic grade and vessel count (10). They observed a correlation between degree of malignancy and tumor enhancement, in which more poorly-differentiated cancer exhibited lesser enhancement (10). To our knowledge, the appearance of poorly-marginated pancreatic ductal adenocarcinoma is infrequent and rare.
carcinoma has not been previously described on MR studies.

Hence, the purpose of our study was to determine the frequency of occurrence of poorly-marginated and focally-defined pancreatic ductal adenocarcinoma by MRI, and to determine whether these appearances correlate to clinical features, tumor staging, and histopathological grade.

MATERIALS AND METHODS

Patients

Institutional review board approval, with waiver of informed consent was obtained for this Health Insurance Portability and Accountability Act (HIPAA)-compliant study. We retrospectively reviewed our institutional Pathology registry database from August 2000 to February 2005 to identify all patients with histopathologically-proven pancreatic ductal adenocarcinoma. We correlated this with imaging data obtained from our clinical information system to identify all patients with histopathologically-proven pancreatic ductal adenocarcinoma who underwent at least one MR exam prior to treatment.

A total of 81 patients were identified with pancreatic ductal adenocarcinoma. A total of 48 patients were excluded because they were studied by CT exam only (N = 32) or their MR exam was done elsewhere (N = 16). A total of 33 patients (16 female, 17 male, mean age = 63.5 ± 12.8 years; age range = 41–80 years) were included in the study (Fig. 1). Histopathological diagnosis of pancreatic ductal adenocarcinoma was performed by excised mass histopathologic evaluation (N = 15), intraoperative biopsy (N = 9), or fine needle aspiration (N = 9).

The interval between onset of disease and tumor diagnosis was 71.5 ± 55.2 days (mean ± SD) (range = 7–180 days, median = 60 days). Of the 33 patients, 15 (45.5%) underwent partial pancreatectomy, 10 (30.3%) were treated with chemotherapy and/or radiation therapy, and eight (24.2%) had no cancer treatment.

Two of the 33 patients had been followed until the end of this review, both for more than three years, without signs of recurrent disease. A total of 25 of the 33 patients had died with a mean survival time of 190.8 ± 118.7 days (range = 30–480 days; median = 180 days). The remaining six patients were followed elsewhere.

MRI

All MRI studies of the abdomen were performed on a 1.5T MRI (Vision, Sonata, or Avanto; Siemens Medical Solutions, Malvern, PA, USA) using a phased-array torso coil. All MR examinations were performed using a set protocol including: precontrast T1-weighted images with and without fat suppression acquired as breath-hold spoiled gradient echo (SGE) (TR = 120–170 msec, TE = 4.0–4.5 msec, flip angle = 80–90°, section thickness = 8 mm, matrix size = 128 × 256, and phase frequency encoding) and T2-weighted half-Fourier acquisition single-shot turbo spin echo (HASTE) sequence with and without fat-suppression (TR = infinite, effective TE = 90 msec, flip angle = 180°, section thick-
ness = 8 mm, matrix size = 192 × 256). Gadolinium was administered by power-injector (Medrad, Pittsburgh, PA, USA) as a bolus of 0.1 mmol/kg of gadolinium chelate (Omniscan; Nycomed, Princeton, NJ, USA) at 2 mL/second in all patients. Two variations of the protocol were used for the postcontrast MR sequences in this series due to software upgrade and availability of improved sequences. A total of 11 of 33 patients were included in this analysis, in which the histopathologic diagnosis was performed by fine needle aspiration biopsy and it was not possible to obtain the histopathological grade by this method. Therefore, 24 patients were included in this analysis, in which the histopathological grade was grouped as: Group I = well-differentiated, well- to moderately-differentiated, and point scale was used, which ranged from 1 = definitely focally-defined (obvious low signal intensity on postgadolinium T1-weighted images, indisputable clear border definition between mass and pancreas, observation of a mass); 2 = most probably focal (lower signal intensity on postgadolinium T1-weighted images than the pancreatic parenchyma, lesser border definition between mass and pancreas than in 1, presence of a mass); 3 = possibly focal (signal intensity on postgadolinium T1-weighted images slightly lower than the pancreatic parenchyma, lesser border definition between mass and pancreas than in 2, presence or absence of a mass); 4 = probably poorly-marginated (minimal signal intensity difference with pancreas parenchyma on postgadolinium T1-weighted images, poor definition of margins, and negligible presence of a mass); and 5 = definitely poorly-marginated (isointensity with pancreas parenchyma on postgadolinium T1-weighted images, no definition of margins, no evidence of tumor mass lesion, with indirect signs of pancreas tumor).

The presence or absence of pancreatic and biliary ductal dilatation and pancreatic atrophy were evaluated. Also evaluated were tumor stage, including: local tumor extension beyond the pancreas with or without invasion of adjacent structures, vascular invasion, distant metastases, and lymph node involvement.

After independent MRI evaluations, the frequency of these findings was determined by the reviewers in a consensus reading.

Lesion sizes were measured in the consensus reading session by two reviewers together. Lesion size was difficult to determine for poorly-marginated cancer, and size was estimated on ancillary features such as length of high-grade ductal narrowing and length of subtly expanded pancreatic margins.

**Histopathological Grade Analysis**

The histopathologic tumor grade was based on the criteria described by the World Health Organization (11). Archived hematoxylin and eosin–stained slides and gross descriptions of the corresponding surgical cases were reviewed by one experienced pathologist (TR) who confirmed the histologic findings. Well-differentiated pancreatic adenocarcinomas are characterized by the presence of infiltrative well-formed glands with minimal to mild cytologic atypia. Poorly-differentiated pancreatic adenocarcinoma lack well-formed glands and infiltrate as either single cells or sheets of cells. The tumor cells in poorly-differentiated lesions display increased cytologic atypia. The histologic findings of moderately-differentiated pancreatic adenocarcinoma are intermediate between the well- and poorly-differentiated morphologies.

In the determination of the association between poorly-marginated MRI features and histopathological grade, nine of 33 patients were excluded because the histopathologic diagnosis was performed by fine needle aspiration biopsy and it was not possible to obtain the histopathological grade by this method. Therefore, 24 patients were included in this analysis, in which the histopathological grade was grouped as: Group I = well-differentiated, well- to moderately-differentiated, and

---

**MRI Analysis**

All MRI examinations were retrospectively and independently reviewed by two radiologists experienced in MRI interpretation (JEJ and EA), both with more than five years of experience in body MRI. Patient clinical history and the original MR interpretation were withheld from the reviewing radiologists, but they were aware that pancreatic tumor was present.

Pancreatic cancer was identified as a mass lesion or a region with lower enhancement compared to background pancreas on postgadolinium T1-weighted sequences, with loss of marbled pancreatic texture, and presence of high-grade biliary and/or pancreatic ductal obstruction with abrupt or irregular transition. The reviewers were asked, in each MR study evaluation, which was the best sequence to evaluate for the pancreatic lesion.

The differentiation between poorly-marginated and focally-defined cancer was evaluated qualitatively based on predetermined findings as follows: signal intensity, definition of a mass, and definition of lesion border with adjacent pancreas on postgadolinium T1-weighted sequences, including the presence or absence of a border with greater enhancing pancreatic tissue. A lesion that appeared as a mass, with definable margins and lower signal intensity than pancreatic parenchyma on postgadolinium T1-weighted sequences was considered a focally-defined cancer, with the ancillary features of adjacent rim of greater enhancing pancreatic tissue. An ill-demarcated lesion without clear margination with adjacent pancreas and little or no definition of a mass was considered a poorly-marginated cancer. Due to intrinsic subjectivity of data evaluation, a five-
moderately-differentiated (8/24); and Group II = moderately- to poorly-differentiated and poorly-differentiated (16/24) (Fig. 1).

**Statistical Analysis**

In the analysis of patient characteristics, data are expressed as mean ± SD. Differences in proportions between groups were analyzed using the chi-squared test. Parametric data were compared using the Student’s t-test, and nonparametric data were compared using the Mann-Whitney U-test. Correlations were analyzed using the Spearman coefficient (rs) between the reviewers’ evaluations for type of tumor morphology on MRI, between the tumor sizes obtained from pathological reports and measured on MRI, and between type of tumor morphology on MRI and histopathological grade.

The overall correlations between tumor morphology on MR, and location of tumor, ductal dilatation, pancreas atrophy, determinants of tumor staging, and histopathological grade were assessed with contingency tables using the Fisher’s exact test.

All P values were derived from two-tailed tests, and a level of less than 0.05 was accepted as statistically significant.

Agreement between the two reviewers was assessed for all independent evaluations using kappa statistic with associated 95% confidence intervals (CIs). The level of agreement was defined by kappa values as follows: <0 = no agreement; 0–0.40 = poor agreement; 0.41–0.75 = good agreement; and 0.76–1.0 = excellent agreement. To determine the agreement between the reviewers for the evaluation of tumor morphology, cancer groups were classified by the five-point scale as focally-defined (1 to 3 points) and poorly-marginated (4 and 5 points).

**RESULTS**

Of the 33 patients, nine (27.2%) were classified as poorly-marginated and 24 (72.8%) as focally-defined.

There was only one discordant case (classified by reviewer 1 as 5 and by reviewer 2 as 2), which was resolved by consensus reclassification as 2 (focally-defined cancer).

The best sequence chosen to evaluate for the pancreatic lesion was the immediate postcontrast T1-weighted sequence, in 27 out of 33 patients (81.8%), comprising all patients studied by the 2D technique and 16 out of 22 of patients (72.7%) studied by the 3D technique. In the remaining six of 33 patients, the reviewers chose the precontrast fat-suppressed T1-weighted sequence in four of 33 patients (12.1%), and the 45 and 90 seconds postcontrast T1-weighted sequences in one patient each (3%). There was no case in which a T2-weighted sequence was chosen as the best. There was an excellent agreement between the reviewers for the selection of best sequence (kappa = 0.96, 95% CI = 0.89–1.0). There was no significant difference (P = 0.65) between poorly-marginated and focally-defined cancer groups regarding the best sequence chosen to evaluate the pancreatic lesion, as immediate postcontrast T1-weighted sequence was chosen in eight of nine poorly-marginated cancer patients and in 19 of 24 focally-defined cancer patients.

The time interval between onset of symptoms and diagnosis was 76.3 ± 57 days (mean ± SD), ranging from seven to 180 days, and median of 60 days for focally-defined cancer patients and 55.8 ± 50 days (mean ± SD), ranging from 14 to 150 days, and median of 45 days, for poorly-marginated cancer patients (Table 1).

There was no significant overall difference between the poorly-marginated and focally-defined cancer groups regarding age, gender, time interval between onset of disease and cancer diagnosis, and survival time (Table 1).

The mean tumor size was 1.4 × 2.0 cm (range = 1.0–3.6 cm) for the poorly-marginated cancer group and 2.7 × 3.6 cm (range = 1.0–9.9 cm) for the focally-defined cancer group. There was a significant difference of the mean tumor size by MRI between both cancer groups (P < 0.001) (Table 1).

Only 15 of 33 patients had tumor size evaluation described at pathologic report (mean tumor size = 2.5 × 2.8 cm; range = 1.1–6.6 cm). There was good correla-

<table>
<thead>
<tr>
<th>Comparison of Clinical Data and Tumor Size With Respect to Poorly-Marginated and Focally-Defined Pancreatic Cancer Groups</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pancreatic cancer groups</strong></td>
</tr>
<tr>
<td><strong>Focally-defined</strong></td>
</tr>
<tr>
<td><strong>P</strong></td>
</tr>
<tr>
<td>Age (mean ± SD)</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Mean time interval between onset of symptoms and diagnosis (mean ± SD)</td>
</tr>
<tr>
<td>Mean survival time* (mean ± SD)</td>
</tr>
<tr>
<td>Tumor size by MRI (mean)</td>
</tr>
</tbody>
</table>

*The survival time was obtained from 20 of 24 patients with focally-defined cancer and from seven of nine patients with poorly-marginated cancer; the remaining patients have been followed elsewhere.
tion between tumor measurements obtained by pathological and MRI evaluations \((r_s = 0.53; 95\% \text{ CI} = 0.01447–0.8274; P = 0.03)\). A total of 18 of 33 patients had no tumor size evaluation at pathology studies because their diagnosis was done by intraoperative biopsy \((N = 9)\) or fine needle aspiration \((N = 9)\).

There was no significant difference between poorly-differentiated and focally-defined pancreatic cancers regarding pancreatic and biliary ductal dilatation or pancreatic atrophy, although poorly-marginated cancers showed a tendency toward more frequent ductal dilatation \((P = 0.05)\) (Table 2). There was no significant difference between the two groups regarding local extension of tumor beyond the pancreas with or without invasion of adjacent structures, vascular invasion, distant metastases, and lymph node involvement (Table 3). However, focally-defined cancers showed a tendency toward more frequent distal metastases compared to poorly-marginated cancers \((P = 0.06)\) because the frequency of distant metastases detected in focally-defined cancers was substantially more than that in poorly-marginated cancers. All poorly-marginated tumors were located in the pancreatic head, which showed a trend toward difference, although with no statistical significance. The lesions were located in the head of the pancreas in 27 (81.8%) of 33 patients, in the body in three (9.1%) patients, and in the tail in three patients (9.1%).

Poorly-marginated cancers (Fig. 2) possessed well- to moderately-differentiated histopathology in five of seven patients (71.4%) while focally-defined cancers (Fig. 3) possessed moderately- to poorly-differentiated histopathology in 14 of 17 patients (82.4%). The difference was statistically significant \((P = 0.02)\) between poorly-marginated and focally-defined pancreatic cancer groups in terms of histopathologic grade (Table 4). While moderately-, moderately- to well-, and well-differentiated pancreatic cancers were significantly correlated with poorly-marginated cancers on MRI; poorly-to moderately- and poorly-differentiated pancreatic cancers were significantly correlated with focally-defined cancers on MRI \((r_s = 0.51; 95\% \text{ CI} = 0.14–0.76; P = 0.01)\).

### DISCUSSION

While most of the patients (72.8%) in our study possessed a definable focal mass, poorly-marginated cancer occurred in 27.2% of patients. The percentage of poorly-marginated cancer is higher in our series than has been reported in some CT studies, in which it ranged from 6% to 11% of patients (8,9), although it is lower than a more recent report that showed a frequency of 32% (10). This can be explained by different imaging criteria as well as different imaging modalities. As with focally-defined cancer, the most useful se-

### Table 2

<table>
<thead>
<tr>
<th>Pancreatic cancer groups</th>
<th>Biliary ductal dilatation</th>
<th>Pancreatic ductal dilatation</th>
<th>Pancreatic and/or biliary ductal dilatation</th>
<th>Pancreatic atrophy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(+)</td>
<td>(-)</td>
<td>(+)</td>
<td>(-)</td>
</tr>
<tr>
<td>Poorly-marginated</td>
<td>6</td>
<td>3</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Focally-defined</td>
<td>14</td>
<td>10</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Total</td>
<td>20</td>
<td>13</td>
<td>21</td>
<td>12</td>
</tr>
<tr>
<td>(P)</td>
<td>0.28</td>
<td>0.19</td>
<td>0.05</td>
<td>0.22</td>
</tr>
</tbody>
</table>

\(^{a,b,c} \text{There was perfect agreement between the reviewers for these analyses (kappa = 1.00).}\)

\(^{a,b} \text{There was no significant association between those groups by Fisher’s Exact Test.}\)

\(^{c} \text{There was excellent agreement between the reviewers (kappa = 0.92, 95% confidence interval, 0.78–1.00).}\)

\(^{d,e} \text{There was a good agreement between the reviewers (kappa = 0.74, 95% confidence interval, 0.51–0.97).}\)

\(^{e} \text{There was excellent agreement between the reviewers (kappa = 0.92, 95% confidence interval, 0.78–1.00).}\)
quencetodefinethelesionwastheimmediatepostga-
dolinium T1-weighted sequence, as previously shown
(1–5, 12). Thepopulationwestudiedshowedasimilardistribu-
tion of pancreatic carcinoma for age, gender, interval
betweenonsetofsymptomsanddiagnosis,andsurvival
time with the actuarial published data for this entity
(13–15). The localization within the pancreas of the
ductal adenocarcinoma concurred with prior studies,
and in our series most of the tumors occurred in the
head(81.8%),followedbythebodyandtailofthepan-
creas (9.1% and 9.1%, respectively). Although no sig-
nificant difference was observed between poorly-mar-
ginated and focally-defined cancers for the location
withinn the pancreas, the importance of the observation
that all poorly-marginated tumors were localized in the
head is the most common location for pancreatic ductal adenocarcinoma in general.

Although no significant difference was observed be-
tween poorly-marginated and focally-defined cancer regar-
ding the presence or absence of biliary or pancreatic
ductal dilatation, poorly-marginated cancers showed a
tendency toward more frequent ductal dilatation ($P = 0.05$). However, this is most likely related to the location
of the tumor and caused by the fact that all poorly-
marginated cancers were localized in the head and
caus ed ductal dilatation whereas six of 24 focally-de-

Figure 2. A 43-year-old woman with poorly-marginated pancreatic cancer at MRI; well-differentiated at histopathology. Axial fat-suppressed T2-weighted (a) and fat-suppressed T1-weighted (b) images; and immediate (c), and late (d) postgadolinium images show an ill-defined region in the head of the pancreas (arrows in a–d) that is difficult to visualize on all sequences. The histopathologic sections (hematoxylin-eosin stain), with magnification of $\times 2$ (e) and $\times 4$ (f), show hyper-
chromatic glands infiltrated in a haphazard fashion (white circle, e–f). Nonneoplastic tissue with features of chronic pancreatitis occupies the lower half of the image. Note that the background stroma in each area is similar, consisting of fibro-
sis and scattered inflammation. The main microscopic feature that favors the diagnosis of adenocarcinoma includes the pres-
ence of infiltrative glands with loss of normal lobular arrange-
ment of duct and surrounding acini as demonstrated here
(arrowheads, e–f). This lesion was also difficult to identify at gross pathology evaluation.

Table 4

<table>
<thead>
<tr>
<th>Pancreatic cancer</th>
<th>$A^*$</th>
<th>$B^*$</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poorly-margined</td>
<td>5</td>
<td>2</td>
<td>7</td>
</tr>
<tr>
<td>Focally-defined</td>
<td>3</td>
<td>14</td>
<td>17</td>
</tr>
<tr>
<td>Total</td>
<td>8</td>
<td>16</td>
<td>24</td>
</tr>
</tbody>
</table>

$^*$Fisher’s Exact Test, $P = 0.02$; 95% confidence interval = 1.07–158.4.

$^a$A comprises well-differentiated, well- to moderately-differentiated,
and moderately-differentiated ductal adenocarcinomas.

$^b$B comprises moderately- to poorly- and poorly-differentiated ductal adenocarcinomas.
fined cancers were localized in the body or tail and only one of these tumors caused ductal dilatation. It is useful to note that an important diagnostic feature in poorly-marginated cancers was the presence of high-grade obstruction despite the lack of clear evidence of a definable mass. This may prove to be an important observation for detection of poorly-marginated pancreatic cancer.

No significant difference was observed between poorly-marginated and focally-defined cancers regarding the findings of tumor staging. This may again reflect the small number of patients in our study group. However, focally-defined cancers showed a greater tendency for the occurrence of distant metastases compared to poorly-marginated cancers. This tendency may be explained by the fact that focally-defined cancers were significantly correlated with poorly-differentiated histopathological grade.

At the inception of the study, our expectation was that poorly-marginated cancers would more commonly exhibit poorly-differentiated histology, as is generally the case with cancers from many other sites, for example, hepatocellular carcinoma (16,17). However, we believe that our findings show that the MRI characteristics of poorly-marginated pancreatic cancers reflect the more comparable histological architecture of well-differentiated carcinoma to background pancreas compared to poorly-differentiated carcinoma. This hypothesis is borne out in the pathology literature, as well-to-moderately-differentiated pancreatic adenocarcinomas are characterized by well-developed glandular and ductal structures with mucin production (Fig. 2), reminiscent of normal exocrine pancreatic parenchyma (11,18,19). Unlike well-differentiated lesions, the cells of poorly-differentiated adenocarcinoma do not histologically resemble their nonneoplastic pancreatic cell counterparts (11,18,19). In poorly-differentiated lesions, the prominent cytologic atypia and architectural disorder are a stark contrast to the adjacent nonneoplastic pancreatic parenchyma (Fig. 3).

A previous study showed that the degree of malignancy of pancreatic carcinoma was inversely proportional to its extent of CT enhancement (10). In that study, 75% (12/16) of patients with well-differentiated pancreatic adenocarcinoma showed the mass to be iso-dense on postcontrast CT (10). To express our data in those terms, 62.5% (5/8) of patients with well-differentiated tumors were poorly-marginated, showing concurrence of our data with theirs.

Poor definition of pancreatic cancer may reflect one or a combination of multiple characteristics: extensive replacement of pancreatic parenchyma by diffusely infiltrative pancreatic cancer, similar cell architectural and vessel count to background pancreas, and limitations of the modality. In our study, we did not observe any examples of extensive infiltration of the pancreas with cancer. In a large series on pancreatic cancer published based on CT discovery, approximately 11% of cancers are considered to be diffusely infiltrative (9). It does not appear to be feasible to retrospectively analyze these studies to determine what the underlying histology was. The second category of similar histopathology features (cell architecture and vessel count) we believe forms the basis of the category of patients with poorly-marginated tumors in our study. It is our opinion that although there is overlap with tumor size, i.e., small tumors may have well-differentiated histology, this is not an exclusive association. In previous studies, and in our clinical experience, high-quality, capillary-phase dynamic gadolinium-enhanced T1-weighted gradient-echo images are able to detect pancreatic tumors in the range of 1 cm (12). Based on this current study, we believe that this may be highly influenced by the underlying histopathology, where poorly-differentiated cancers may be intrinsically more conspicuous than well-differentiated tumors, at this small size. Limitations of the imaging modality, the third above-described cause for poor definition of cancers, may contribute to this finding; however, in general MRI is reported to have very high conspicuity for pancreatic cancer (5).

A recent study, based on a refined WHO grading system for pancreatic adenocarcinoma, demonstrated that histopathologic grade serves as a highly significant independent prognostic indicator. Additionally, individual criteria, including glandular differentiation and mucin production, each proved to be significant independent parameters in their contribution to the grade (20). The more frequent occurrence of distant metastases in focally-defined cancers compared to poorly-marginated cancers in our study group may be suggestive of the prognostic importance of poorly-differentiated histopathology. Although, no difference was observed between poorly-marginated and focally-defined cancers for survival time in our study, we believe that this can be explained in part by other factors like heterogeneity of applied therapy and the small sample number. Thus, we still believe that the clinical impact of MRI findings in relation to poorly-marginated vs. focally-defined pancreatic cancers remains to be determined.

Limitations of this study include the retrospective design and relatively small number of patients. We believe that further prospective studies using quantitative histopathologic analysis will contribute to the understanding of factors that contribute to definition of tumor margination at MRI and histopathological tumor grade. It would also be of future interest to determine if poorly-marginated tumors, as observed on MR images, are associated with better patient outcome.

In conclusion, poorly-marginated pancreatic cancer was not uncommon, and was observed in 27.2% of patients. Poorly-marginated cancer had a significant association with moderate- to well-differentiated histopathology in comparison to focally-defined cancers.

**ACKNOWLEDGMENT**

J.E., Jr. is supported by CNPq-Brasilia/Brazil.

**REFERENCES**

Whole-Body Diffusion-Weighted Imaging:
Technical Improvement and Preliminary Results

Shuo Li, M.D., Fei Sun, M.S., Zheng-yu Jin, M.D., Hua-dan Xue, M.D., and Ming-li Li, M.D.


**Purpose:** To optimize the free-breathing whole-body diffusion-weighted imaging (WB-DWI) protocol by using the short T1 inversion-recovery diffusion-weighted echo-planar imaging (STIR-DWEPI) sequence and the built-in body coil. Additionally, to evaluate the feasibility of tumor screening using high-resolution three-dimensional (3D) maximum intensity projection (MIP) images.

**Materials and Methods:** The prescan procedure of STIR-DWEPI was modified using the data from 30 volunteers. During each exam, an optimized center frequency (CF) was used to minimize the slice offsets in consecutive scan stations. Prescan time was reduced from 50 seconds to 20 seconds with improved station profile. Total scan time was 30 minutes for five stations and 1.2 m coverage. A total of 30 patients with histologically-proven malignant disease were scanned under the final protocol using a built-in body coil. The image quality and the degree of background body signal suppression were assessed.

**Results:** Free-breathing WB-DWI was 100% successfully performed in all patients, without slice misregistration, fat contamination, significant distortion, or nonuniformity. The reconstructed 3D-MIP images were adequate to depict malignant lesions in all 30 patients. The results of WB-DWI were found to be comparable to those of single-photon emission computed tomography (SPECT) and positron emission tomography (PET).

**Conclusion:** Stable and high-resolution WB-DWI is feasible using the technical improvements described in this study. WB-DWI might have important clinical value for the detection of primary and metastatic malignancies within the whole body. The potential for diagnosis and therapeutic assessment of tumors should be further assessed in a larger patient cohort.

**Key Words:** diffusion magnetic resonance imaging; whole-body imaging; STIR; tumor imaging


---

1Department of Radiology, Peking Union Medical College Hospital, Chinese Academy of Medical Sciences & Peking Union Medical College, Beijing, China.

2MR Modality: GE Healthcare (China), Beijing, China.

*Address reprint requests to: Z-Y.J., Peking Union Medical College Hospital, 1 Shuaifuyuan, Dongcheng District, Beijing 100730, China. E-mail: zhengyu-jin@tom.com

Received December 4, 2006; Accepted June 1, 2007.

DOI 10.1002/jmri.21074
Published online in Wiley InterScience (www.interscience.wiley.com).

**MAGNETIC RESONANCE IMAGING (MRI)—**with its excellent tissue contrast, high spatial resolution, and detailed morphological information—appears promising for tumor screening. Previously, MRI has been employed for the assessment of focal pathologies in restricted anatomical regions or organ systems. The development of fast imaging sequences such as echo-planar imaging (EPI) and parallel imaging techniques have accelerated the use of MRI as a potential tool for screening.

Initial experiences have demonstrated that whole-body (WB) MRI using standard T1-weighted (T1w), T2-weighted (T2w), and short T1 inversion-recovery (STIR) sequences is feasible within one single examination (1–3). Different studies have shown advantages for MRI in the detection of parenchymal and bone marrow lesions compared with bone scintigraphy (4–6). Coronal T1, T2, and STIR sequences have high spatial resolution, but there is too much information within the images and it is difficult for radiologists to screen the whole patient without missing one tiny lesion. Although most lesions can be found in retrospective studies, these images do not have significant lesion contrast. The need for repeated coil positioning and long sequence times have further limited the routine clinical application of these techniques.

Diffusion-weighted imaging (DWI) is based on water proton free motion. Most tumor lesions are associated with architectural malformations and water diffusivity changes. Heavy diffusion-weighting and inversion-recovery methods can suppress most healthy tissue, which are composed mainly of free water and fat (7). Thus, superior disease contrast with background body signal suppression can be achieved using the STIR-diffusion-weighted echo-planar imaging (STIR-DWEPI) sequence, which will be beneficial for patient screening or treatment monitoring. Here, we present our work in optimizing the WB-DWI protocol and evaluate its feasibility in tumor imaging.

**MATERIALS AND METHODS**

All images were obtained on a 1.5 Tesla MRI system (gradient strength = 40 mT/m, slew rate = 150 T/m/second; GE Healthcare, HDMR, Milwaukee, WI, USA). The imaging study protocol was approved by the local institutional review board and informed consent was obtained from all patients and volunteers.
Parameter Optimization

The EPI sequence is sensitive to the center frequency (CF) of the radar frequency (RF). The imaged object will have an offset in the phase-encoding direction if there is a frequency difference between the excited RF and intrinsic CF. The offset distance is

\[ \delta y = \delta f \times \text{esp} \times \text{FOV}/(2\pi). \]  

(1)

Here, \( \delta y \) is the offset distance in the phase-encoding direction, \( \delta f \) is the frequency difference between excited RF and the induced CF by \( B_0 + B_1 \), esp is the echo spacing time, and FOV is the field of view. The WB diffusion acquisition is separated into several stations covering 1170 mm, from head to thigh. In order to cover the interesting region (normally five stations), the diffusion acquisition is separated into several stations with a spacing time, and FOV is the field of view. The WB diffusion will result in different CFs. The junction slices will become uniform 3D reformatted image, we also needed to fix both the analog and digital receiver gains (R1 and R2 in GE scanner) for different stations. By combining the fixed receiver gains (R1 = R2 = 13) and the fixed CFs, we were able to optimize the prescan procedure of the STIR-DWEPI sequence. The original prescan included a "low resolution CF,” “transmission gain calculation,” “gradient shimming,” “high resolution CF,” and “receiving gain calculation.” In our protocol, only “transmission gain” and “gradient shimming” were necessary for each station after determining the CF from full prescan procedure of Loc3 and Loc1. After this modification, the prescan time was reduced from 50 seconds to 20 seconds.

Feasibility of WB-DWI of Patients by Using the Built-In Body Coil

At the beginning of this study, no reference could be found with regard to experience gained using body coils for WB-DWI with a field strength of 1.5 T. Therefore, before starting patient examinations, some explorative tests on phantoms and volunteers were made to find stable sequences and compare the image quality of WB-DWI between using the peripheral vascular (PV) coil and body coil (not presented here).

A total of 30 patients (mean age, 48 years; range, 13–77 years; 12 females/18 males) with histologically-proven malignant disease were included in this initial study.

Table 1

<table>
<thead>
<tr>
<th>Loc1</th>
<th>Loc2</th>
<th>Loc3</th>
<th>Loc4</th>
<th>Loc5</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diffavg (Hz)</td>
<td>27.95</td>
<td>42.90</td>
<td>22.16</td>
<td>28.94</td>
</tr>
<tr>
<td>Position pair</td>
<td>(Loc1 + Loc5)/2</td>
<td>(Loc1 + Loc4)/2</td>
<td>(Loc1 + Loc3)/2</td>
<td>(Loc1 + Loc2)/2</td>
</tr>
<tr>
<td>Diffavg (Hz)</td>
<td>18.92</td>
<td>20.08</td>
<td>13.20</td>
<td>18.69</td>
</tr>
<tr>
<td>Position pair</td>
<td>(Loc2 + Loc4)/2</td>
<td>(Loc2 + Loc3)/2</td>
<td>(Loc3 + Loc5)/2</td>
<td>(Loc3 + Loc4)/2</td>
</tr>
<tr>
<td>Diffavg (Hz)</td>
<td>16.80</td>
<td>20.80</td>
<td>18.92</td>
<td>20.67</td>
</tr>
</tbody>
</table>

*Diffavg = the difference in CF of each position (eg. Loc1) or position pair (eg. (Loc1 + Loc5)/2) to the average CF of all five locations, averaged from 30 volunteers scan.

Loc1 = head part, Loc2 = neck and upper chest part, Loc 3 = lower chest and upper abdomen part, Loc4 = lower abdomen and upper pelvis part, Loc5 = lower pelvis and upper thigh part (in volunteers of 1.75 m height).
Infiltration by lymphoma. The ADC value of bone marrow is markedly and diffusely increased, consistent with marrow DWI. The signal from bone marrow in the axial skeleton is the ribs are unsuppressed signals from liver and spleen. considered the lymphoma infiltration. The shaded areas below the ribs are unsuppressed signals from liver and spleen.

The categories of malignancy included: non-Hodgkin lymphoma (N = 13), Hodgkin lymphoma (N = 2), chronic lymphatic leukemia (N = 1), acute myeloblastic leukemia (N = 1), breast cancer (N = 1), sarcoma (N = 1), multiple bone metastases from lung cancer (N = 9), recurrent bladder cancer (N = 1), and pancreatic cancer (N = 1). In two patients, one with acute myeloblastic leukemia and the other with multiple bone metastases from lung cancer, two examinations were performed before and after chemotherapy with an interval of three months. In four patients, three with non-Hodgkin lymphoma and one with multiple bone metastases from lung cancer, WB-DWI was compared with PET scans within seven-day intervals.

WB diffusion studies were performed using the built-in quadrature body coil and a five-station STIR-DWEPI sequence with coverage from the head to the thigh (1170-mm coverage). Each station was composed of 39 axial slices with thickness = 7 mm and slice gap = −1 mm. Imaging parameters were: TR = 4500 msec, TE = 62.4 msec, TI = 160 msec, number of excitations (NEX) = 6, matrix 128 × 128, and FOV = 36–40 cm. The diffusion gradients were applied in three orthogonal directions with b = 0 and b = 800 seconds/mm². High-resolution 3D-MIP images and black-white inverse grey scale was used in all cases. The acquisition time for each diffusion station was five minutes and 33 seconds and the total scan time was less than 30 minutes. In the regions of the lesions, conventional T2-w fast spin-echo (FSE) images (TR/TE = 3100 msec/85

**RESULTS**

WB-DWI was successfully performed using the STIR-DWEPI sequence and the built-in body coil in 100% of patients. The reconstructed 3D-MIP images showed uniform, continuous sagittal or coronal views for all 30 patients without fat contamination. The uniformity and station consistency can be best demonstrated in the case of small B-cell lymphoma (Fig. 2). Uniformly increased diffusion signal is observed within bone marrow associated with histological evidence of marrow infiltration by lymphoma in the routine iliac crest biopsy. Fat and normal tissue suppression is demonstrated in Fig. 3, in a patient with plasmacytic lymphoma. The primary lesion and the metastatic lesions are displayed with excellent CNR. An example of DWI for therapeutic monitoring is presented in Fig. 4 from a 65-year-old female patient with multiple metastases from lung cancer, demonstrating the protocol’s stability and potential in treatment monitoring. The 3D-MIP image shown in Fig. 4a was obtained prior to chemotherapy. A large lung mass and multiple metastases to the liver, bones, and lymph nodes are clearly visualized. Three months after chemotherapy (Fig. 4b), all of the lesions have evidently diminished and the improvements that underwent both WB-DWI and PET within seven-day intervals, WB-DWI precisely identified all of the sites of primary tumors, regional lymph nodes, and distant metastases. WB-DWI was very consistent with PET. In one case of non-Hodgkin lymphoma (Fig. 5), severe swelling and fusion of lymph nodes in both-sided neck and supraclavicular, lung hilum, mesenteric, and retroperitoneal portions were demonstrated clearly on WB-DWI. PET confirmed fluorodeoxyglucose (FDG) uptake in the same regions. But due to no higher standard uptake value (SUV) comparing with the spine, a metastatic lymph node of the right lung hilum was not reported by PET (Fig. 5g). The presence of this lymph node was confirmed using the axial DWI image (Fig. 5f) and T2w image (Fig. 5h). The lymph nodes of right-sided neck were even not found on the PET image (Fig. 5d).

**DISCUSSION**

Tumors generally have increased nuclear-to-cytoplasmic ratio and hypercellularity, which reduces the extracellular matrix and the diffusion space of water molecules in both extracellular and intracellular dimensions. This results in a decreased ADC. DWI has great potential for tumor imaging. Several studies have already reported its feasibility and importance in various malignancies, such as hepatic cancer (8), breast cancer (9,10), and soft tissue tumors (11). Yet malignancies do not always locate at focal lesion and have the characteristic of invasion and extension. Accurate tumor detection is of vital importance for effective therapeutic management and precise follow-up. During the past decade, 18F-FDG
PET imaging has become an essential tool for diagnosing and staging a wide variety of malignancies. However, glucose metabolism is not significantly increased in some tumor types, such as prostate carcinoma. Infection, inflammation, granulomatous diseases, and many other physiologic or pathologic conditions also show high $^{18}$F-FDG uptake (12). PET is also expensive, involving ionizing radiation and requiring large facilities such as a cyclotron. All of these drawbacks limit the utility of PET in oncology. Routine tumor-staging procedures clinically involve thoracic and abdominal contrast-enhanced computed tomography (CT) scan, ultrasound, and sometimes aspiration and biopsy. However, CT is limited by the radiation exposure, ultrasound is limited by the low spatial resolution, and biopsy is limited by the invasive nature. Besides, all of these methods do not have enough coverage and sensitivity.

Improvements in MR technology—both hardware and pulse sequences—have permitted the acquisition of DW-EPI images in a fast and stable way and probably overcome all the shortcomings listed above. The present protocol is designed to generate uniform and continuous WB diffusion images using our current hardware configuration. If there are surface coils that can seamlessly cover the WB without too much weight and will not cause significant respiratory artifact, the overall scan time will be reduced and image quality will be improved.

We used the built-in body coil instead of the PV coil mainly because it is more comfortable for patients. It requires less weight to be placed onto patients and its coverage is large. Although the signal-to-noise ratio (SNR) and contrast-to-noise ratio (CNR) of the body coil are inferior to those of the PV coil, its image quality is clear enough for detecting diseased lesions. The signal loss of the body coil between junction slices is smaller than that of the PV coil. There was no statistical difference between the apparent diffusion coefficient (ADC) value calculated using the body coil and the PV coil (data not shown).

During the acquisition, breathing was not controlled but remarkably little motion artifact was noticed. This
permitted scans with broader coverage and also higher SNR due to multiple excitations. One possible explanation is that the acquisition time of a single-shot EPI train is only 100 msec. The movement of organs caused by respiratory motion is limited during this short acquisition time. Signal averaging is performed in the image domain, which prevents destructive phase artifacts. Muro et al (13) also proved that the ADC value does not change significantly when it is acquired during motion.

The STIR-EPI-DWI sequence was used in the present study to obtain uniform background body signal suppression. Compared with the normal DWI sequence, STIR-DWI efficiently suppresses the signal of vessels, muscle and fat, and it is not affected by B1 inhomogeneity (7). The most prevalent remaining signals arise from brain, bone marrow, kidneys, prostate, and testes. Shinmoto et al (14) verified that the remaining signal of spleen was due to the T2 shinethrough effect. In the present study, a compromised b value of 800 seconds/mm² was chosen to balance the scan time, SNR, and T2 effect.

The results of our feasibility study indicate that WB-DWI might have important clinical value in the detection of primary and metastatic lesions in tumor screening. It is also an effective method for evaluating the involvement of bone marrow by disease. There is high concordance between the detection of WB-DWI and bone marrow biopsy. The potential in diagnosis and therapeutic assessment of tumors has to be further assessed in a larger patient cohort.

Despite the excellent sensitivity of this technique, there are some limitations that must be taken into account. Because of T2 contrast, remaining hyperintense signals arise from the spleen, brain, kidneys, prostate, testes, and a few sinuses. These signals will interfere detection and interpretation of the diseased lesions. Since there are only a few articles that have reported the application of WB-DWI in tumor imaging, there are no well-developed criteria for differentiation between benign and malignant tumors. Last, DWI images alone are not sufficient to screen for all types of tumors, such as sclerotic metastases that do not have increased diffusion and will be missed in DWI. It should be combined with routine MR sequences for a protocol with high sensitivity and specificity, such as using WB-DWI first to screen the WB for suspect lesion, then localized T1, STIR, T2, and contrast-enhanced T1 for a better specificity.

In conclusion, WB-DWI is a promising technique that can help with tumor staging, differentiation of malignant from benign lesions, and assessment of therapeutic response. By optimizing the prescan procedure and scan parameters of the STIR-DW-EPI sequence, fast, stable, and sensitive diffusion images can be obtained. Future work may include monitoring of radiation therapy of animal lymphoma model by ADC value and analysis of the relationship between bone signal and red bone marrow concentration.

REFERENCES

Figure 5. A 41-year-old male with non-Hodgkin lymphoma. a: Coronal MIP image of WB-DWI. b: Coronal image of PET. severe swelling and fusion of lymph nodes in both-sided neck and supraclavicular, lung hilum, mesenteric, and retroperitoneal portions are demonstrated clearly on WB-DWI. PET confirms FDG uptake in the same regions. But the lymph nodes of right-sided neck (d) and lung hilum (g) were not reported by PET. The presence of lymph nodes were confirmed using the axial DWI image (c,f) and T2w image (e,h).
Multinodular Focal Fatty Infiltration of the Liver: Atypical Imaging Findings on Delayed T1-Weighted Gd-BOPTA-Enhanced Liver-Specific MR Images

Daniele Marin, M.D., Riccardo Iannaccone, M.D., Carlo Catalano, M.D., and Roberto Passariello, M.D.

We report a case of pathologically confirmed multinodular focal fatty infiltration. MRI was performed after bolus injection of gadobenate dimeglumine (Gd-BOPTA, MultiHance®; Bracco, Milan, Italy), a liver-specific paramagnetic, gadolinium (Gd)-based MR contrast agent that concomitantly enables the acquisition of a standard dynamic phase with timing strategies similar to those used for other extracellular fluid contrast agents, followed by a delayed T1-weighted liver-specific phase (the so-called hepatobiliary phase). In the present case, multiple rounded areas of fatty infiltration, although confidently diagnosed using chemical shift sequences due to a significant signal intensity reduction on out-of-phase images, were unexpectedly hypointense during the delayed liver-specific phase of Gd-BOPTA. Reduced Gd-BOPTA concentration during the liver-specific phase is generally correlated with liver malignancy. Since such lesions can be prospectively mistaken for metastatic disease, we performed a hepatic biopsy to establish a definitive diagnosis. Our empirical observations suggest that Gd-BOPTA uptake may be impaired in fatty infiltrated liver tissue. Because at present there is no report evaluating the kinetics of Gd-BOPTA in fatty liver, further studies are needed to specifically investigate this issue.

Key Words: liver, MR; liver, contrast agents; liver, steatosis


CASE REPORT

A 40-year-old man was referred to our hospital because a surveillance ultrasonographic (US) examination of the abdominal area revealed multiple small echogenic foci within the liver.

The patient had a history of chronic hepatitis C virus (HCV) infection. At admission, the physical examination was unremarkable, as were vital signs and laboratory examination tests (i.e., complete blood count, serum levels of glucose, electrolytes, albumin, globulin, and bilirubin). The results of renal-function and coagulation tests also were within normal limits. The level of alanine aminotransferase was 110 U/liter, and that of...
aspartate aminotransferase was 65 U/liter. The level of carcinoembryonic antigen was 2 ng/mL (normal levels: <2.5 ng/mL), and the alpha-fetoprotein level was 8 ng/mL (normal levels: <10 ng/mL). A chest radiograph showed probable pulmonary emphysema, but no infiltrates, masses, effusions, or lymphadenopathy were seen.

A multidetector row CT scan (Somatom Plus 4 Volume Zoom; Siemens, Forchheim, Germany) was performed before and after dynamic injection of 130 mL of an iodinated contrast medium (iomeprol, Iomeron® 350; Bracco, Milan, Italy) by using a power injector (flow rate = 4 mL/second). Nonenhanced CT images confirmed the presence of multiple (more than 20) well-defined, low-attenuating lesions (Fig. 1a) scattered throughout the liver. The mean attenuation values of the liver lesions and the normal hepatic parenchyma were 25 (attenuation range = 10–30) and 50 (attenuation range = 40–60), respectively, as determined by user-defined regions of interest (ROIs) on CT images. In all cases, lesion-attenuation was at least 10 HU less than that of splenic tissue (11). On contrast-enhanced CT images acquired during the hepatic arterial phase (HAP, 35 seconds after contrast material injection), the portal venous phase (PVP, 70 seconds), and the equilibrium phase (EP, 180 seconds), lesion-enhancement was comparable to that of surrounding liver showing progressive isoattenuation (Fig. 1b–d).

Overall, based on the radiographic appearance and absence of any significant mass effect (i.e., neither displacement of contiguous vascular structures nor bulge of the liver contour by peripheral lesions), a diagnosis of multinodular focal fatty infiltration was suspected. Multifocal hepatocellular carcinoma (HCC) was ruled out due to the absence of both hypervasularity on HAP (12), and washout on EP (13) of liver lesions.

However, to increase diagnostic confidence, Gd-BOPTA-enhanced MRI was performed using a 1.5-T magnet (Magnetom Vision; Siemens Medical System, Forchheim, Germany) with a torso phased-array surface coil. The following MR sequences were used: transverse T2-weighted half-Fourier rapid acquisition with relaxation enhancement (HASTE; repetition time (TR)/echo time (TE) = $\infty$/74 msec, flip angle = 180°; echo train length = 104), transverse T1-weighted in-phase fast low angle shot (FLASH) spoiled GRE (TR/TE = 160/4.5 msec, flip angle = 80°), and transverse out-of-phase FLASH spoiled GRE (TR/TE = 160/2.2 msec, flip angle = 80°). Following intravenous injection (flow rate = 2 mL/second) of 20 mL Gd-BOPTA (gadobenate dimeglumine, MultiHance®; Bracco, Milan, Italy), serial

**Figure 1.** Multinodular focal fatty infiltration in a 40-year-old man with chronic HCV infection. a: Transverse nonenhanced CT scan shows multiple well-defined, nodular-shaped, low-attenuating lesions within the liver. Note the lower density of lesions relative to the spleen. b: Transverse contrast-enhanced CT scan obtained during the hepatic arterial phase after bolus injection of contrast material. Both the liver lesions and hepatic parenchyma show mild contrast enhancement. The lesions remain slightly hypoattenuated relative to the surrounding liver. c,d: Transverse contrast-enhanced CT scan obtained during the portal venous and equilibrium phases demonstrates homogeneous enhancement of liver lesions that have become isoattenuated compared to hepatic parenchyma. No displacement of adjacent vascular structures or bulge of the liver contour can be observed.
contrast material-enhanced T1-weighted fat saturated FLASH images (TR/TE = 160/4.8 msec; flip angle = 80°) were acquired during HAP (25 seconds, after contrast medium injection), PVP (60 seconds), and EP (180 seconds).

Moreover, additional T1-weighted fat saturated FLASH images during the hepatobiliary phase (at 120 minutes from the start of contrast medium injection) were also acquired (9).

All MR sequences imaged the whole liver in the transaxial plane during a single breath-hold. A rectangular field of view (FOV) was used to improve spatial resolution, and presaturation bands were positioned above and below the imaging volume for T1-weighted GRE sequences to minimize flow-related artifacts.

On the T2-weighted images the lesions showed slight hyperintensity (Fig. 2a). On nonenhanced in-phase T1-weighted images, they were not detectable because of signal isointensity to the hepatic parenchyma (Fig. 2b). In contrast, on out-of-phase T1-weighted images, the lesions showed marked signal loss and appeared as hypointense areas (Fig. 2c) relative to the adjacent hepatic parenchyma, a finding that is highly consistent with a fatty component within the lesions (13). On contrast-enhanced MR images, lesions enhanced to a lesser degree relative to hepatic parenchyma and were slightly hypointense during different vascular phases (i.e., HAP, PVP, and EP; Fig. 2d–f). Moreover, during the delayed hepatobiliary phase images (the so-called hepatospecific phase), lesions were still recognizable as

Figure 2. a: Transverse noncontrast T2-weighted HASTE sequence (TR/TE = ∞/90 msec, 180° flip angle) shows multiple, faintly hyperintense liver lesions. b: On the transverse nonenhanced in-phase T1-weighted image (TR/TE = 160/4.7 msec, 80° flip angle), the lesions are isointense compared to normal hepatic parenchyma. c: Corresponding nonenhanced out-of-phase T1-weighted image (TR/TE = 160/2.6 msec, 80° flip angle). The lesions show significant signal loss relative to the surrounding liver and appear as multiple hypointense foci. d–f: Transverse Gd-BOPTA-enhanced fat-saturated T1-weighted images (TR/TE = 160/4.7 msec, 80° flip angle) acquired during the hepatic arterial, portal venous, and equilibrium phases. The lesions enhance to a lesser degree compared to hepatic parenchyma and are slightly hypointense. g: Delayed fat-saturated T1-weighted image acquired during the hepatobiliary phase (120 minutes after Gd-BOPTA infusion). The lesions are detectable as multiple well-defined, nodular-shaped foci of signal hypointensity. This finding may be related to insufficient contrast medium concentration from normal hepatocytes within the lesions. This poses problems in the differential diagnosis with malignant liver disease, such as metastases. Note the high signal intensity of background liver and common bile duct (arrowhead) due to the hepatobiliary excretion of Gd-BOPTA.
well-defined, hypointense foci on the background of adjacent liver that showed high signal intensity due to normal uptake of Gd-BOPTA (Fig. 2g).

Since hepatic metastases may also lack contrast material concentration, and thus appear as hypointense lesions on Gd-BOPTA-enhanced MR images acquired during the hepatospecific phase, the patient underwent US-guided percutaneous fine-needle biopsy of the dominant lesion and one smaller lesion to establish a definitive diagnosis. Specimens were prepared with methods that included hematoxylin-eosin staining for routine histologic analysis and quantification of fat content, reticulin staining for identification of hemosiderin deposition and hepatocyte regeneration, and Masson trichrome staining for detection of fibrous tissue. Histologic analysis demonstrated normal hepatic parenchyma with macrovesicular steatosis and scattered inflammatory infiltrates. No fibrosis or scarring was present in the sample specimens.

A contrast-enhanced CT study was performed six months later and showed lesion stability.

The patient currently undergoes periodic medical surveillance at our institution for his HCV infection.

DISCUSSION

Multinodular focal fatty infiltration is considered an uncommon and atypical manifestation of focal fatty liver. Because of its spherical shape and multifocal distribution, multinodular focal fatty infiltration does not meet the conventional imaging criteria generally used for the diagnosis of focal fatty liver (7). Therefore, this multinodular variety of focal fatty infiltration has frequently been mistaken for metastatic disease (2–6,14).

Although CT generally provides nonspecific imaging clues, such as the absence of mass effect and low attenuation value of liver lesions, MRI currently represents the most specific imaging modality for the diagnosis of fatty liver. Specifically, due to fundamental differences between the magnetic properties of water and triglyceride protons, their phases oppose each other on out-of-phase GRE sequences and thus interfere destructively (2,3,8). As a result, signal loss occurs in voxels where both lipid and water signals are represented, such as fatty infiltrated liver tissue.

Gd-BOPTA (MultiHance®; Bracco, Milan, Italy) is a paramagnetic, Gd-based contrast agent that, due to a lipophilic moiety, is partially taken up by functioning hepatocytes (3–5% of injected dose) and excreted without biotransformation through the biliary route by means of an adenosine triphosphate-dependent transporter, Mrp2 (10). In addition, compared to conventional Gd-based agents, Gd-BOPTA has a twofold greater T1 relaxivity in human plasma. In the first minutes after bolus injection of Gd-BOPTA, a standard dynamic study is routinely performed with timing strategies similar to those used for other extracellular fluid contrast agents. Afterwards, because of the marked, long-lasting enhancement of MR signal intensity in normal liver parenchyma, delayed liver-specific T1-weighted images are also acquired, in the so-called hepatobiliary phase (10). Thus, Gd-BOPTA-enhanced MRI simultaneously provides both morphological and functional information.

Previous studies demonstrated that the liver-specific distribution phase substantially improves the detection and characterization of liver lesions that lack functioning hepatocytes (i.e., lesions that do not retain the contrast agent, such as metastases, cysts, hemangiomas, and hepatocellular carcinomas) (15–17). In contrast, benign liver lesions of hepatocellular origin usually exhibit homogeneous and prolonged contrast medium retention, and appear at least isointense to the normal liver parenchyma on delayed liver-specific MR images (16,17).

We present a case of multinodular focal fatty infiltration, in which Gd-BOPTA-enhanced MRI was performed to rule out metastatic disease. We speculated that MRI, in addition to the well-known usefulness of chemical shift sequences, might provide an additional benefit during the delayed liver-specific phase of Gd-BOPTA by discriminating normally enhancing fatty liver tissue, which contains functioning hepatocytes, from nonenhancing liver metastases.

However, although the lesions showed marked signal loss on out-of-phase T1-weighted images, they unexpectedly lacked any contrast material accumulation on the delayed liver-specific phase, and thus appeared as well defined, hypointense foci on the background of the high signal intensity of the surrounding liver.

Since reduced contrast medium concentration during the delayed liver-specific phase is generally considered a typical finding of malignancy, we performed a hepatic biopsy to rule out metastatic disease. However, histology showed normal hepatic parenchyma with fatty metamorphosis.

Although it has been demonstrated that biliary excretion of Gd-BOPTA is largely unaffected by the presence of impaired liver function (18), there is evidence of a correlation between Gd-BOPTA kinetics and bilirubin metabolism. The results of experimental studies that evaluated Gd-BOPTA administration in animals with either congenital (19) or iatrogenic (20) elevated bilirubin levels indicated a blockage of the contrast medium excretion through the biliary route associated with increased clearance through the renal pathway. In addition, Graziole et al (21) recently showed that Gd-BOPTA is insufficiently concentrated in hepatic adenomas, benign liver lesions that are of hepatocellular origin but completely lack biliary ductules.

To our knowledge, no previous reports have specifically evaluated the kinetics of Gd-BOPTA in fatty liver or in liver lesions with fatty metaplasia. On the basis of our clinical observation, we can speculate that Gd-BOPTA uptake may be impaired in the presence of fatty infiltrated hepatic parenchyma.

Further studies are needed to confirm this hypothesis and investigate the possible underlying pharmacokinetic mechanisms.

REFERENCES


Gadobenate Dimeglumine–Enhanced Magnetic Resonance Imaging of Primary Leiomyoma of the Liver

Daniele Marin, M.D., Carlo Catalano, M.D., Massimo Rossi, M.D., Antonino Guerrisi, M.D., Michele Di Martino, M.D., Pasquale Berloco, M.D., and Roberto Passariello, M.D.

We report a case of histologically proven primary leiomyoma of the liver that was evaluated with multiphasic 64-section computed tomography (CT) and gadobenate dimeglumine–enhanced magnetic resonance (MR) imaging. This lesion showed vivid enhancement during the arterial phase with sustained enhancement during the hepatic venous and equilibrium phases. During the liver-specific MR imaging phase (150 minutes after contrast injection), the same lesion demonstrated lack of contrast retention, thus appearing hypointense compared with the background liver. Because of this latter finding, the patient underwent partial resection of the liver. In primary hepatic leiomyoma, the absence of contrast uptake during the liver-specific phase of gadobenate dimeglumine–enhanced MR imaging may be inappropriately interpreted as a sign of malignancy, thus leading to unnecessary, aggressive management of such lesions.

Key Words: liver, MR; liver, MR contrast agents; benign liver tumors


LEIOMYOMA is a benign tumor composed of interlacing bundles of smooth muscle fibers (1). Although this type of lesion is frequently found in the genitourinary and gastrointestinal tracts, a few cases of primary leiomyoma of the liver have been reported (2–9). Clinical presentation can range from small, incidentally discovered asymptomatic lesions to large, palpable upper abdominal masses (up to 15 cm in maximum diameter) often accompanied by abdominal pain. Although primary leiomyoma of the liver rarely degenerates into a malignancy, liver resection is often required to yield a definite diagnosis. Therefore, a noninvasive diagnostic technique could avoid unnecessary, aggressive management of these lesions.

Due to nonspecific imaging findings at both computed tomography (CT) and magnetic resonance (MR) imaging, making a differential diagnosis, which includes other liver lesions, either benign or malignant, is a challenging task (4). Recently, liver-specific MR contrast agents have been shown to be useful for improving detection and characterization of hepatic lesions, by simultaneously providing specific morphologic and functional information about the liver, including focal lesions (10,11).

We present a case of pathologically confirmed primary leiomyoma of the liver that was evaluated with liver-specific contrast-enhanced MR imaging in addition to multiphasic 64-section CT. To the best of our knowledge, this is the first report describing imaging findings of leiomyoma after administration of a hepatobiliary MR contrast agent.

CASE REPORT

A 64-year-old woman was referred to our hospital because of an incidentally discovered liver mass in the right hepatic lobe at a surveillance ultrasonographic examination of the upper abdomen. The patient had a history of pathologically confirmed primary biliary cirrhosis, which was diagnosed several years earlier. Upon admission, physical examination was unremarkable as were vital signs and laboratory examination tests, which included complete blood count, serum levels of glucose, electrolytes, albumin, globulin, and bilirubin. The results of renal function and coagulation tests were also within normal limits. The level of alanine aminotransferase was 55 U/liter and aspartate aminotransferase was 49 U/liter (normal ranges, 10–60 and 10–42 U/liter, respectively). Carcinoembryonic antigen was 2.1 ng/mL (normal level, <2.5 ng/mL), and α-fetoprotein level was 3.4 ng/mL (normal, <10 ng/mL).

The patient underwent multiphasic CT of the abdomen using a 64-section CT scanner (Somatom Sensation 64; Siemens Medical Solutions, Erlangen, Germany) with the following parameters: collimation, 0.6 × 64 mm; effective section thickness, 3.0 mm; recon-
struction interval, 3.0 mm; pitch, 1; effective mAs, 250; and kVp, 120. The patient received 120 mL (1.3 mL/kg body weight) of intravenous, nonionic contrast medium containing a high concentration of iodine (Iomeprol, 400 mg I/kg) (Iomeron 400; Bracco Imaging SpA, Milan, Italy). Contrast medium was administered with a power injector (Stellant D CT; Medrad, Indianola, PA, USA) at 5 mL/sec through an 18-gauge intravenous catheter inserted into an arm vein. CT was performed immediately before contrast medium administration and during the hepatic arterial, hepatic venous, and equilibrium phases at 35, 70, and 180 sec, respectively, after the start of contrast injection. Pre-contrast CT (Fig. 1a) confirmed the presence of a well-defined, low-attenuating lesion (3.0 cm in maximum diameter) in the right hepatic lobe. During the arterial phase (Fig. 1b), the lesion showed markedly increased enhancement compared with the surrounding liver, with the exception of a small central area, which resembled a scar. During the hepatic venous (Fig. 1c) and equilibrium (not shown) phases, the lesion showed sustained and homogeneous enhancement compared with the adjacent hepatic parenchyma. Because imaging findings were nonspecific, atypical focal nodular hyperplasia or, alternatively, flash filling hemangioma was regarded as the most likely diagnosis. Due to the lesion’s arterial enhancement and the patient’s underlying chronic liver disease, hepatocellular carcinoma was also included in the differential diagnosis.

The patient underwent gadobenate dimeglumine–enhanced (MultiHance; Bracco Imaging) MR imaging of the abdomen using a 1.5-Tesla scanner (Magnetom Avanto; Siemens Medical Systems) equipped with a high-performance gradient system (45 mT/m). Gadobenate dimeglumine is a liver-specific, gadolinium-based MR contrast agent with a vascular-interstitial distribution in the first minutes after bolus injection, followed by delayed hepatobiliary excretion (12). The MR imaging protocol comprised: (1) pre-contrast T2-weighted turbo spin-echo images [repetition time (in msec)/echo time (in msec), 5000/103; refocusing flip angle (FA) 150°]; (2) pre-contrast T1-weighted spoiled dual gradient-echo in-phase and out-of-phase MR images (100/2.1 and 4.2, 90° FA); and (3) T1-weighted three-dimensional spoiled gradient-echo and volumetric interpolated breath-hold examination (VIBE) sequences (5.7/2.8, 10° FA). The patient was imaged before contrast administration and during the hepatic arterial, hepatic venous, and equilibrium phases (25, 60, and 150 sec after contrast administration, respectively), and the delayed hepatobiliary phase (150 minutes after administration).

On pre-contrast T2- (Fig. 2a) and T1-weighted (Fig. 2b) images, the lesion showed isointensity and marked hypointensity to the surrounding liver, respectively. As with the previous CT examination, the lesion showed intense enhancement on T1-weighted VIBE images acquired during the arterial phase (Fig. 2c), followed by persistent and homogeneous enhancement during the hepatic venous and equilibrium phases (Fig. 2d and e, respectively). During the delayed hepatobiliary phase (Fig. 2f), the lesion showed lack of contrast retention and, thus, was identified as a well-defined, hypointense focus against the highly enhanced background liver. Because MR imaging findings were not indicative of either hepatic hemangioma (i.e., lack of high signal intensity on T2-weighted images) (13) or focal nodular hyperplasia (i.e., absence of contrast retention on T1-weighted images during the delayed hepatobiliary phase) (14), the patient underwent partial resection of the liver. At gross inspection of the resected specimen, a white, well-demarcated, firm tumor nodule was confirmed. Histopathologic analysis of the lesion revealed multiple interlacing bundles of uniform spindle cells, without evidence of active mitoses (Fig. 3). Immunohistochemical examination demonstrated positive staining of tumor cells to α-smooth muscle actin (Fig. 4), but lack of expression of CD34. Based on these findings, the final diagnosis of hepatic leiomyoma was established.

The patient underwent contrast-enhanced CT follow-up at 6 and 12 months without tumor recurrence within the liver.

Figure 1. A 64-year-old woman with primary biliary cirrhosis and incidentally discovered hepatic leiomyoma undergoing (a–c) multiphasic CT imaging. (a) Transverse pre-contrast CT scan demonstrates a well-defined, low-attenuating lesion (arrows) in the right hepatic lobe. (b) On the corresponding image, during the arterial phase, the lesion shows intense enhancement (straight arrows), with the exception of a tiny central area (curved arrow). The corresponding image acquired during (c) the hepatic venous phase shows sustained and homogeneous enhancement of the lesion compared to the adjacent hepatic parenchyma.
DISCUSSION

Primary leiomyoma of the liver is an extremely rare, benign tumor that affects both children and adults, with increased frequency in patients with acquired immunodeficiency syndrome (AIDS) or immunosuppressed state after organ transplantation. Besides typical histologic findings, such as demonstration of spindle cells that express α-smooth muscle actin at immunohistochemical analysis (1), the presence of a mesenchymal tumor at other primary sites must be excluded to establish a definite diagnosis (9). Results of previous imaging studies (2–8) have shown marked arterial enhancement to be a common occurrence with this lesion, although specific imaging findings have not been determined. Further hindering definitive diagno-

Figure 2. The same patient undergoing (a–f) gadobenate dimeglumine–enhanced MR imaging. On corresponding (a) T2-weighted, respiratory-triggered turbo spin-echo [repetition time (in msec)/echo time (in msec), 5000/103] and (b) T1-weighted in-phase gradient-echo (100/4.2) MR images, the lesion (arrows) shows isointensity and hypointensity, respectively, compared with the surrounding liver. T1-weighted three-dimensional spoiled gradient-echo and volumetric interpolated breath-hold examination (VIBE) sequences (5.7/2.8) demonstrate intense peripheral enhancement of the lesion during (c) the arterial phase, followed by persistent and homogeneous enhancement during the (d) hepatic venous and (e) equilibrium phases. (f) On the corresponding image, during the delayed hepatobiliary phase (150 minutes after contrast administration), the lesion shows marked hypointensity compared with the highly enhanced background liver due to the absence of contrast retention by smooth muscle cells.

Figure 3. Photomicrograph (original magnification: ×100; hematoxylin–eosin stain) of a section through the mass shows multiple spindle cells with plump, oval nuclei. Mitoses are absent.

Figure 4. Immunohistochemical stain demonstrates expression of α-smooth muscle actin within the tumor cells (original magnification: ×200).
sis is the wide range of either benign (eg, hemangioma, focal nodular hyperplasia, and hepatic adenoma) or malignant (eg, hepatocellular carcinoma, hypervascular liver metastases) hypervascular hepatic lesions that should be included in any differential diagnosis.

With recent development of liver-specific MR contrast agents, which include reticuloendothelial system–specific contrast agents and hepatocyte-selective contrast agents, the detection and characterization of liver lesions can be improved by coupling both functional and morphologic information (10,11). Gadobenate dimeglumine is a paramagnetic, gadolinium-based contrast agent that is partially taken up by functioning hepatocytes (3–5% of injected dose) and excreted without biotransformation through the biliary route due to a lipophilic moiety (12). As with other nonspecific extracellular gadolinium chelates, gadobenate dimeglumine shows a vascular-interstitial distribution in the first minutes after bolus injection, thus enabling a standard dynamic study of the liver. In addition, normal liver and benign focal hepatic lesions show increased signal intensity on T1-weighted MR images during the delayed liver-specific phase (time range, 60–180 minutes) because of active contrast uptake by functioning hepatocytes. Accordingly, absence of contrast retention during the liver-specific phase has generally been regarded as a hallmark of malignant liver lesions because the lesion appears hypointense compared with the highly enhanced background liver (15).

In this case report, we have reported a case of primary leiomyoma of the liver, which was incidentally discovered in a patient with chronic liver disease. Based on the lesion’s marked arterial enhancement associated with an absence of contrast retention at gadobenate dimeglumine–enhanced MR imaging during the delayed liver-specific phase, the patient underwent hepatic resection to exclude liver cancer. Our observation is in accordance with the results of two previously published reports (9,10) that demonstrated an equivocal appearance of primary hepatic leiomyoma during the liver-specific phase after administration of a reticuloendothelial system–specific MR contrast agent. As in our case, this finding was erroneously interpreted as a sign of malignancy, thus leading to inappropriate surgical resection of the lesion. Although other benign, non–hepatocyte-containing liver lesions, such as biliary cysts, hemangioma, angiomylipoma, and peliosis hepatitis, may also lack contrast uptake during the liver-specific phase of gadobenate dimeglumine–enhanced MR imaging and, thus, simulate a malignant tumor, these lesions can be confidently diagnosed in the majority of cases with the combined interpretation of precontrast and dynamic contrast-enhanced MR imaging.

In conclusion, based on our empirical observation, as well as the results of previously reported cases, we suggest that liver-specific MR contrast agents may be misleading for the diagnosis of primary hepatic leiomyoma. In the absence of distinctive imaging findings during different vascular phases, the absence of contrast retention during the delayed liver-specific phase can be inappropriately interpreted as a sign of malignancy, thus leading to possibly unnecessary, invasive management of such lesions.

ACKNOWLEDGMENT

The authors thank Richard Youngblood, MA, Department of Radiology, Duke University Medical Center, for editorial assistance in the preparation of this manuscript.

REFERENCES

Evaluation of Optimized Inversion-Recovery Fat-Suppression Techniques for T2-Weighted Abdominal MR Imaging

Thomas C. Lauenstein, M.D., Puneet Sharma, Ph.D., Timothy Hughes, Ph.D., Keith Heberlein, Ph.D., Dana Tudorascu, M.S., and Diego R. Martin, M.D., Ph.D.


**Purpose:** To test the theoretical benefits of a spectral attenuated inversion-recovery (SPAIR) fat-suppression (FS) technique in clinical abdominal MRI by comparison to conventional inversion-recovery (IR) FS combined with T2-weighted (T2W) partial Fourier single shot fast spin echo (SSFSE).

**Materials and Methods:** 1.5T MRI studies of the abdomen were performed in 28 patients with liver lesions (hemangiomas n = 14; metastases n = 14). T2W sequences were acquired using IR and SPAIR SSFSE. Measurements included retroperitoneal and mesenteric fat signal-to-noise (SNR) to evaluate FS; liver lesion contrast-to-noise (CNR) to evaluate bulk water signal recovery effects; and bowel wall delineation to evaluate susceptibility and physiological motion effects.

**Results:** SPAIR-SSFSE images produce significantly improved FS and liver lesion CNR. The mean SNR of the retroperitoneal and mesenteric fat for SPAIR SSFSE was 20.5 ± 10.2 (±1 SD) and 12.7 ± 6.2, compared to 43.2 ± 24.1 (P = 0.000006) and 29.3 ± 16.8 (P = 0.000005) for IR-SSFSE. SPAIR-SSFSE images produced higher CNR for both hemangiomas CNR = 164 ± 88 vs. 126 ± 83 (P = 0.00005) and metastases CNR = 75 ± 27 vs. 53 ± 19 (P = 0.007). Bowel wall visualization was significantly improved using SPAIR-SSFSE (P = 0.002).

**Conclusion:** The theoretical benefits of SPAIR over conventional IR FS translate into significant multiple improvements that can be measured on clinical abdominal MRI scans.

**Key Words:** fat suppression; inversion recovery; abdominal MRI; retroperitoneum; bowel MRI

© 2008 Wiley-Liss, Inc.
as bowel wall contractions, will lead to imprecise localization of the IR prepulse and the subsequent excitation-readout SSFSE acquisition for that slice.

A less commonly implemented IR FS SSFSE method uses a nonspectral, spectral attenuated inversion-recovery (SPAIR) technique. SPAIR inversion pulses excite only the fat protons, based on the inherent frequency shift between fat and water (224 Hz at 1.5T). The theoretical benefits of SPAIR over conventional IR include preservation of bulk water signal due to selective fat inversion and diminished sensitivity to motion due to the use of nonslice-selective IR pulses.

The aim of our study was to evaluate these theoretical advantages of SPAIR, compared to conventional IR, using the following specific measures extracted from clinical abdominal images: 1) measuring retroperitoneal-mesenteric fat SNR to evaluate the degree of FS; 2) measuring liver lesion CNR to evaluate bulk water suppression effects; and 3) qualitatively evaluating bowel wall delineation to determine motion and susceptibility effects.

MATERIALS AND METHODS

Patients

Our study was approved by our Institutional Review Board and was HIPAA-compliant. Informed consent and permission for subsequent retrospective analysis of MRI data was obtained from all subjects. Our study group consisted of one healthy volunteer and 28 patients (17 female, 11 male; mean age: 62 years, range 31–80 years). In all, 14 patients with hepatic metastatic disease and 14 patients with hepatic hemangiomas were retrospectively identified using the electronic medical records of the hospital information system. The patients had undergone an abdominal MRI at our institution between January and April 2007.

Diagnosis of hepatic hemangiomas was supported by identifying characteristic image patterns on comprehensive MRI, including dynamic gadolinium-enhanced images, as described in the literature (9). All 14 oncology patients had multiple hepatic metastases with typical MRI features for metastatic carcinoma (9). All oncology patients had a tissue diagnosis of primary malignancy: breast cancer (n = 7); colorectal cancer (n = 5); lung cancer (n = 1); and testicular cancer (n = 1). Confirmation of MRI findings was made by biopsy (n = 5) and/or subsequent follow up imaging showing either growth or response to therapy over no less than a 6-month interval.

MR Imaging Protocol

All MR examinations were performed on a 1.5T scanner (Magnetom Avanto, Siemens Medical Solutions, Erlangen, Germany) using phased array surface coils. Each patient had a comprehensive clinically indicated contrast-enhanced abdominal MRI. The test sequences analyzed for our study were employed after completion of the scout images and prior to administration of contrast.

FS T2W SSFSE was performed in the axial plane using either IR or SPAIR. All primary imaging parameters were kept consistent between SPAIR and IR-SSFSE sequences. Acquisition parameters were as follows: 30 acquired slices with a slice thickness of 7 mm; echo time (TE) = 92 msec; slice repetition time (TR) = 1000 msec; excitation flip angle = 90°; matrix = 256 × 146; partial Fourier acquisition: 4/8; field of view = 350 mm; acquisition time = 30 seconds.

IR-SSFSE Technique

IR FS T2W SSFSE was performed using the commercially available sequence IR-HASTE (Half Fourier Acquisition Single Shot Turbo Spin Echo; Siemens Medical Systems). It consisted of a nonspectral slice-selective inversion pulse, timed relative to the SSFSE acquisition. This was achieved using an adiabatic hyperbolic secant inversion pulse (10), which is an amplitude- and frequency-modulated RF pulse with improved rectangular slice profiles and heightened B1 insensitivity compared to conventional sinc RF pulses. IR excitation was followed by a spoiler gradient to destroy residual transverse magnetization. The inversion time was set to null the signal from fat and was optimized using Eqs. [1] and [2], below, for T1 = 250 msec. This resulted in an inversion time of 170 msec for IR-SSFSE. The SSFSE readout module was interleaved in 2 or 3 packages to avoid slice crosstalk, while k-space was acquired linearly, which placed effective TE (TE-eff) near the middle of echo train.

SPAIR-SSFSE Technique

SPAIR is a fat suppression technique that applies a spectrally selective inversion pulse to invert the fat spins in the imaging volume. It consists of a nonspectral adiabatic inversion pulse tuned to the fat frequency such that only the fat spins are inverted. Following the IR pulse is a large spoiler gradient to destroy any transverse magnetization. The fat spins will subsequently decay according to the T1 relaxation and after a characteristic time (TI-null) the fat longitudinal magnetization will be zero and the SSFSE module commences. The required timing can be calculated for FSE type sequences by following the approach of Rydberg et al (10) who derive the following formula for the magnetization evolution:

\[ M_z(t) = M_0(1 - (1 - \cos \theta_{inv})e^{-t/T1} + e^{-(TR-TE_{rest})/T2}) \]  \[1\]

Where \( M_z(t) \) gives the evolution of the magnetization, \( t = 0 \) corresponds to the application of the SPAIR pulse, \( \theta_{inv} \) is the flip angle of the SPAIR pulse (in this case 180°), \( TE_{rest} \) is the last echo in the echo train, and T1 is the relaxation constant for fat. An expression for \( T1_{null} \) can be derived by solving Eq. [1] for “t” when \( M_z(t) = 0 \). For the particular case where the SPAIR pulse is 180° this gives:

\[ T1_{null} = T1 \cdot \left[ \ln 2 - \ln \left( 1 + e^{-(TR-TE_{rest})/T1} \right) \right] \]  \[2\]

For an SSFSE sequence, the repetition time for a given slice will be long (TR ∼ ∞); however, the repetition time
between SPAIR pulses is 1000 msec, making TI selection a nontrivial matter. A pulse diagram for both fat saturation methods is shown in Fig. 1.

**TI Optimization**

Three healthy subjects were examined using SPAIR in order to confirm the calculated optimized TI time to be used clinically and also to detail the dependence of TI delay times on image quality. The subjects were imaged in the axial plane using SPAIR SSFSE, with 320 × 280 mm field of view (FOV) (256 × 171 matrix), 35 slices of 7 mm thickness (1.4 mm gap), TR/TE = 1000 (TR effective = 98) / 224 msec, and frequency offset of 224 Hz. The TI was varied from 50 to 300 msec in 50-msec steps. Quantitative fat signal data was measured in the mesenteric and the retroperitoneal fat (described below) and analyzed for the different inversion times to extract the optimal value. The inversion time of 150 msec produced the optimum fat signal suppression in both the retroperitoneum and mesentery, with average SNR values of 7.5 ± 5.2 and 10.7 ± 3.1, respectively.

**Image Analysis**

Two radiologists with expertise of 12 and 5 years in abdominal MRI assessed the images in consensus. Readers were blinded to the fat suppression technique. All MR images were reviewed on a postprocessing workstation (Syngo, Siemens Medical Solutions). For each method of assessment the paired SPAIR and IR SSFSE T2W images were displayed simultaneously for each patient and matched for slice position. Qualitative analysis was performed to evaluate the delineation of bowel wall margins on SPAIR and IR SSFSE images. Conspicuity of the small bowel wall was rated on a 3-level scale (1 = poor, 2 = moderate, 3 = good delineation).

Quantitative analysis of residual intraabdominal fat signal to compare the fat-suppressed images was performed using operator-defined regions of interest (ROIs). Size and anatomical localization of ROIs were identical for comparative SPAIR and IR SSFSE images. The minimum ROI diameter was 1.0 cm. For all image sets the standard deviation (SD) of background noise (BN) was determined by placing a 2-cm diameter ROI outside the anterior abdominal wall. The signal of retroperitoneal fat was measured adjacent to the left kidney in the posterior retroperitoneal space (Fig. 1). Mesenteric fat signal was measured between small bowel loops (Fig. 2). Based on these signal intensity measurements, SNRs were calculated by a standard equation: SNR = Sfat/SDBN, with lower SNR indicating superior fat suppression.

Quantitative evaluation of liver lesions was performed to compare the CNRs generated on SPAIR versus IR SSFSE liver images. An ROI (minimum of 1 cm diameter) was placed over the selected liver lesion. The selection of the tumors was based on being no less than 2 cm to avoid volume averaging contamination of the ROI measurements. Selection of tumors no greater than 4 cm was decided as a method to avoid excessive heterogeneity, as is commonly seen in larger tumors. This is particularly true in metastases due to necrosis, but also may be seen in hemangiomas. Of 5 patients with more than one lesion meeting the selection criteria for size, the lesion most central within the liver and surrounded by the largest amount of adjacent liver parenchyma was selected to facilitate measurement of the CNR. This was done in consensus based on the T1W gradient echo images to avoid any bias from examining the T2W images first. Another ROI was placed on adjacent liver, avoiding intrahepatic blood vessels. The lesion CNR was calculated by a standard equation: CNR = (Slesion − Sliver)/SDBN.

**Statistical Analysis**

Statistical comparison of SPAIR and IR fat-suppressed quantitative analysis was performed applying a paired Student’s t-test. A nonparametric Wilcoxon Rank test was applied for the qualitative analysis of the bowel wall.

![Figure 1. Pulse diagram for SPAIR-SSFSE (a) and IR-SSFSE (b).](image-url)
We measured SNR of mesenteric and retroperitoneal fat to determine the degree of fat suppression. Improved fat suppression on SPAIR-SSFSE may be the result of using a nonselective adiabatic IR pulse, compared to a slice-selective adiabatic IR pulse, as used in many commercial IR SSFSE applications. Even though adiabatic pulses are recognized to provide optimal insensitivity to B1 inhomogeneity (11), slight motion and misregistration between IR and imaging slice may become apparent when slice-selective pulses are used.

A critical difference between SPAIR and conventional IR techniques is demonstrated by the significant improvement in CNR of the liver lesions. Finding improved liver lesion contrast on SPAIR-SSFSE images is in keeping with the predicted benefits of using a frequency-sensitive inversion pulse. By only inverting the fat spins, this leaves the maximum possible water signal intact. We examined two families of focal liver lesions in order to evaluate a practical range of image contrast between the lesions and liver, from relatively high (hemangiomas) to relatively low (metastases) CNR. The CNR was found significantly increased for both families of lesions, compared to IR SSFSE. An analysis inclusive of all the different types of benign and malignant liver delineation. A P-value less than 0.05 was considered significant.

RESULTS
In all 28 patients fat suppression in the retroperitoneum was significantly superior on the SPAIR images. Similarly, SNR of mesenteric fat was significantly lower in all patients on the SPAIR images. Comparative examples for fat suppression in the retroperitoneum and mesenteries are shown in Figs. 2 and 3. Table 1 summarizes the measured data.

Conspicuity of liver lesions was significantly superior on SPAIR images with demonstration of significantly increased CNR (Table 1). This was also determined separately for hemangiomas and metastatic lesions. Examples of liver hemangioma (Fig. 4) and liver metastases (Fig. 5) are shown for both the IR and SPAIR techniques. Bowel wall delineation was significantly superior on SPAIR SSFSE (Table 1). An example is shown in Fig. 6.

DISCUSSION
Our findings show that the theoretical benefits of SPAIR SSFSE can be measured on clinical abdominal images.

Figure 2. 51-year-old female patient with hepatic hemangiomas. Measurement of retroperitoneal fat signal adjacent to the left kidney (circle) on IR SSFSE images (a) was found to be lower (superior) using SPAIR SSFSE technique (b).

Figure 3. 58-year-old female patient with hepatic hemangioma (not shown). SNR of mesenteric fat (circle) was significantly higher (less well suppressed) on IR SSFSE (a) than on SPAIR images (b).
Conspicuity of bowel wall was shown to be markedly improved on SPAIR SSFSE. This improvement is likely due to at least two factors that differentiate SPAIR SSFSE: one factor is the relatively greater sensitivity to motion of standard IR SSFSE (see Introduction); another factor is that bowel wall visualization should benefit from the increased SNR of water-containing structures on SPAIR SSFSE.

Limitations of our study include the many factors affecting image quality that could not be tested directly. Susceptibility effects are ubiquitous and can be considerable in degree within the abdomen, due to bowel gas, surgical clips, and irregular body surface contours. Effects of motion from bowel wall contractions were also not tested specifically. Perhaps the use of a bowel paralytic agent could add further insight into explaining the mechanism for the benefits of SPAIR shown in our study. Direct comparison to other FS methodology was not performed. Chemical FS, using partial excitation-spoiler prepulses tuned for fat resonance, has also been used extensively for abdominal SSFSE applications. We chose to restrict our comparison to IR FS techniques to maintain similarity in design and implementation between the methods. The SPAIR pulse is also restricted in the extent of its excitation bandwidth, which ensures

<table>
<thead>
<tr>
<th></th>
<th>SPAIR</th>
<th>IR SSFSE</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>SNR (fat retroperitoneal)</td>
<td>10.5 ± 10.2</td>
<td>43.2 ± 24.1</td>
<td>0.000006</td>
</tr>
<tr>
<td>SNR (fat mesenteric)</td>
<td>12.7 ± 6.2</td>
<td>29.3 ± 16.8</td>
<td>0.000005</td>
</tr>
<tr>
<td>CNR (all liver lesions)</td>
<td>119.3 ± 78.1</td>
<td>89.3 ± 69.8</td>
<td>0.000001</td>
</tr>
<tr>
<td>CNR (liver metastases)</td>
<td>75.1 ± 27.4</td>
<td>53.0 ± 19.0</td>
<td>0.007</td>
</tr>
<tr>
<td>CNR (liver hemangiomas)</td>
<td>163.4 ± 87.7</td>
<td>125.6 ± 83.2</td>
<td>0.00005</td>
</tr>
<tr>
<td>Bowel wall delineation (index)</td>
<td>2.8 ± 0.5</td>
<td>1.9 ± 0.6</td>
<td>0.0002</td>
</tr>
</tbody>
</table>

**Figure 4.** 44-year-old male patient with hepatic hemangioma (arrow). CNR of the liver lesion was lower on the IR SSFSE (a) image, and significantly higher using the SPAIR technique (b).

**Figure 5.** 75-year-old female patient with colon cancer and liver metastasis in the right hepatic lobe (arrow). Compared to IR SSFSE (a), the lesion produces higher CNR and can be better delineated and on SPAIR images (b).
lipid sensitivity compared to water. However, sensitivity to B0 field inhomogeneities still exist, potentially causing lipid resonances outside the SPAIR frequency range to remain partially affected or unaffected by the IR pulse. This is a potential source of nonuniform fat suppression, especially in high susceptibility regions, regions furthest from the isocenter, and near the edge of the FOV. The T1 value of fat is also presumed to ensure efficacy of SPAIR fat suppression. Variability of fat constituents may alter the fat T1, and therefore fat suppression, necessitating minor TI adjustments.

The significance of continued improvements in SSFSE FS T2W techniques for abdominal imaging is supported by the existing literature. The overall observation is that FS T2W MRI can provide evaluation for edema associated with inflammatory intraabdominal processes. FS is imperative to distinguish the elevated signal from water associated with edema from the high signal of fat. Nitta et al (2) examined 37 consecutive patients with clinically suspected acute appendicitis using T2W FSE images. Signal intensity of periappendiceal tissue on these images correlated well with pathological severity of appendicitis. It is expected that SPAIR imaging may be superior for the evaluation of appendicitis due to significantly improved conspicuity of bowel wall and improved FS. Preservation of water signal on SPAIR should provide better detection of edema related to inflammation. This has been shown in the application of SPAIR SSFSE for detection of active inflammation related to Crohn’s disease of the small bowel (12). The use of MRI for evaluation of Crohn’s disease (4,5) and appendicitis is compelling considering that most patients are young and have a greater concern for ionizing radiation-induced malignancies from CT (13–16). Other intraabdominal inflammatory processes shown to be delineated by T2W FS imaging includes diverticulitis (1,17) pancreatitis (18,19), pyelonephritis (20), cholecystitis (21), and for evaluation of the acute abdomen (8,19,22).

There are overall benefits of SPAIR SSFSE that can be measured on clinical abdominal MR images regarding fat saturation, particularly in fat adjacent to bowel and for improving overall image contrast even between nonfatty soft tissues, such as can be demonstrated with liver masses. We expect that improvements in FS SSFSE, as we have shown is possible using the SPAIR technique, may have favorable diagnostic clinical impact on the evaluation of a broad range of inflammatory processes within the abdomen.

REFERENCES


Figure 6. 49-year-old female patient with liver metastases (not shown). The small bowel wall is difficult to delineate on the IR SSFSE image (a), but can be better visualized on the SPAIR images (b).
<table>
<thead>
<tr>
<th>Qty</th>
<th>Vol.</th>
<th>No.</th>
<th>Home Studies Title</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>1</td>
<td>Functional MRI: Capabilities and Limitations</td>
</tr>
<tr>
<td>1</td>
<td>2</td>
<td></td>
<td>Concepts in MR Physics</td>
</tr>
<tr>
<td>2</td>
<td>1</td>
<td></td>
<td>Considerations in Low Field MRI</td>
</tr>
<tr>
<td>2</td>
<td>2</td>
<td></td>
<td>Directions in Basic Cardiac Imaging</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td></td>
<td>Directions in Advanced Cardiac Imaging</td>
</tr>
<tr>
<td>2</td>
<td>4</td>
<td></td>
<td>The Basics of Magnetic Resonance Angiography</td>
</tr>
<tr>
<td>3</td>
<td>1</td>
<td></td>
<td>Introduction to Spectroscopy</td>
</tr>
<tr>
<td>3</td>
<td>2</td>
<td></td>
<td>Renal MR Imaging</td>
</tr>
<tr>
<td>3</td>
<td>3</td>
<td></td>
<td>A Primer on MR Pulse Sequences</td>
</tr>
<tr>
<td>3</td>
<td>4</td>
<td></td>
<td>Artifacts Encountered in Abdominal MRI</td>
</tr>
<tr>
<td>4</td>
<td>1</td>
<td></td>
<td>Safety Aspects in MRI</td>
</tr>
<tr>
<td>4</td>
<td>2</td>
<td></td>
<td>Directions in MRI of the Liver</td>
</tr>
<tr>
<td>4</td>
<td>3</td>
<td></td>
<td>MR Techniques in the Evaluation of the Uterus</td>
</tr>
<tr>
<td>4</td>
<td>4</td>
<td></td>
<td>Fundamental Principles for MR Imaging of the Brain</td>
</tr>
<tr>
<td>5</td>
<td>1</td>
<td></td>
<td>Atlas of Cranial Neuroanatomy</td>
</tr>
<tr>
<td>5</td>
<td>2</td>
<td></td>
<td>MRI of the Ankle &amp; Foot</td>
</tr>
<tr>
<td>5</td>
<td>3</td>
<td></td>
<td>MR Imaging of the Breast</td>
</tr>
<tr>
<td>5</td>
<td>4</td>
<td></td>
<td>Diffusion-Weighted Imaging of the Brain</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td></td>
<td>Directions in MRA of the Abdominal Aorta and Lower Extremities</td>
</tr>
<tr>
<td>6</td>
<td>2</td>
<td></td>
<td>Fundamental Principles of MR Imaging of the Head, Neck, and Spine</td>
</tr>
<tr>
<td>6</td>
<td>3</td>
<td></td>
<td>Advances in Interventional MRI</td>
</tr>
<tr>
<td>6</td>
<td>4</td>
<td></td>
<td>Diffusion-Weighted MR Imaging of the Pediatric Brain</td>
</tr>
<tr>
<td>7</td>
<td>1</td>
<td></td>
<td>The Role of Neuroimaging in the Diagnosis of Alzheimer’s Disease</td>
</tr>
<tr>
<td>7</td>
<td>2</td>
<td></td>
<td>Cardiovascular MRI: Update I</td>
</tr>
<tr>
<td>7</td>
<td>3</td>
<td></td>
<td>K-Space in the Clinic</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td></td>
<td>MR Imaging and Spectroscopy of the Prostate</td>
</tr>
<tr>
<td>8</td>
<td>1</td>
<td></td>
<td>Atlas of Knee Anatomy</td>
</tr>
<tr>
<td>8</td>
<td>2</td>
<td></td>
<td>Cardiovascular MRI: Update II</td>
</tr>
<tr>
<td>8</td>
<td>3</td>
<td></td>
<td>Update: Safety in MR Examinations</td>
</tr>
<tr>
<td>8</td>
<td>4</td>
<td></td>
<td>Parallel MR Imaging</td>
</tr>
<tr>
<td>9</td>
<td>1</td>
<td></td>
<td>MRI of Breast Cancer: Update I</td>
</tr>
<tr>
<td>9</td>
<td>2</td>
<td></td>
<td>MR Atlas of the Shoulder</td>
</tr>
<tr>
<td>9</td>
<td>3</td>
<td></td>
<td>Exploring Magnetic Field Strengths: Challenges and Opportunities</td>
</tr>
<tr>
<td>9</td>
<td>4</td>
<td></td>
<td>MRI of Breast Cancer: Update II</td>
</tr>
<tr>
<td>10</td>
<td>1</td>
<td></td>
<td>MR Imaging of Perfusion</td>
</tr>
<tr>
<td>10</td>
<td>2</td>
<td></td>
<td>MR Imaging Artifacts:Appearance, Cause &amp; Cure</td>
</tr>
<tr>
<td>10</td>
<td>3</td>
<td></td>
<td>Techniques in Cardiovascular MR Imaging</td>
</tr>
<tr>
<td>10</td>
<td>4</td>
<td></td>
<td>MRI of the Brain</td>
</tr>
<tr>
<td>11</td>
<td>1</td>
<td></td>
<td>Update: Musculoskeletal MRI</td>
</tr>
<tr>
<td>11</td>
<td>2</td>
<td></td>
<td>Contrast Media in MRI Examinations</td>
</tr>
<tr>
<td>11</td>
<td>3</td>
<td></td>
<td>Head and Neck MRI at 3.0T</td>
</tr>
</tbody>
</table>

**Back issues of SMRT educational seminars are for sale to SMRT members only!**

**Payment Methods**

**PAYMENT WITHIN U.S.A.:**
Personal checks, money orders, cashier’s checks and company checks are acceptable. Institutional purchase orders are acceptable and will be invoiced, but payment must still be received prior to shipment.

**PAYMENT FROM OUTSIDE U.S.A.:**
Checks: The check must be payable “to” (NOT “through”) a U.S. bank in U.S. Dollars. The check must be imprinted with the computer encoding and routing information authorized by the American Banking Association.
Traveler’s Checks: Traveler’s checks in U.S. dollars for the exact amount, properly counter-signed, are acceptable.
International Money Order: The money order must be in U.S. dollars and be imprinted with the computer encoding and routing information authorized by the American Banking Association. U.S. dollar International Postal Money Orders imprinted as stated above are acceptable.

**WIRE:** DO NOT PAY BY WIRE.

**SHIPPING:** We will contact you with the shipping cost before we process your order. No orders will be processed before you have confirmed the actual shipping cost.

**SMRT Member ID # (Required) __________________________**

Name __________________________
Address __________________________
City __________________________ State/Province __________________________
Postal Code/ZIP + 4 Country __________________________
Phone ( ______ ) Fax ( ______ )
E-mail __________________________

Please check to pay by credit card: [ ] VISA [ ] MasterCard [ ] AMEX
Card # __________________________
Expiration Date MM/YY Security Code ____________
Billing Address __________________________
Billing Postal Code/ZIP + 4 ____________ Payment Amount ____________
Cardholder Signature __________________________

Credit card orders may be faxed directly to the Society’s office at: +1 510 841 2340.

**Total quantity ordered** [ ]

**Quantity ordered** [ ]

x US$25.00 each [ ]

Subtotal* [ ]

*does not include shipping [ ]
MR Imaging of the Abdomen