In Vivo Size Error Measurements Of Potential Liver Lesions Detected On MRI

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Citation

Abstract
Background: With the increasing use of MR to evaluate liver lesions the ability to accurately characterize individual liver lesions becomes critical if diagnostic certainty regarding malignant versus benign etiology is to supplant biopsy in many of these lesions. Our aims were to establish the error margin for lesion size characterization in vivo so that it becomes possible to ascertain when there has been a true interval size change in a lesion detected on MRI of the liver.

Methods: A phantom study using 8mm chambers filled with water attached onto the abdomen of 2 volunteers during each undergoing 4 abdominal T2W MR exams using typical clinical parameters were measured twice each by 2 blinded observers and the size measurements (320 total) were analyzed for size consistency and variation.

Results: The mean measurement was 8.5 mm with a standard deviation of 0.5mm. Indicating that at least 1mm size change (on the computer monitor) must be detected prior to concluding a true change in a lesion detected on abdominal MRI. (P<0.05).

Conclusion: We recommend that at least a 1 mm change in size be used as a criteria to diagnose true lesion growth or regression when measured on T2W abdominal MRI.

INTRODUCTION
Liver lesion characterization has relied on the tendency for malignant lesions to be less bright on sequential echoes than cysts or hemangiomas with morphology and enhancement patterns used as adjuncts due to lack of certainty and consistency in lesion brightness characterization. Quantitative analysis has implemented dual echo T2 MR imaging with quantitation of T2 relaxation time showing an accuracy of 97% with consistent performance [1]. Unfortunately, prior work has demonstrated significant overlap of benign and malignant lesions [2] which makes use of T2 relaxation a weak predictor of lesion malignancy when in the range of 90-120msec.

It is our hypothesis that measurements of serial lesion size for equivocal liver lesions detected on T2W MRI may be the only means of ascertaining if a lesion is malignant based on interval growth. Our aims were to establish the error margin for lesion size characterization in-vivo to ascertain when there has been a true interval size change in a lesion detected on MRI of the liver. Though phantom studies in isolation can establish the reliability and repeatability of measurements on MRI, in-vivo liver lesion evaluation suffer from respiratory and patient body motion, phase encoding artifact and signal to noise effects due to body habitus. It was the purpose of this project to simulate these phenomena by placing a phantom onto the abdominal wall of volunteers adjacent to the liver so that in-vivo error measurements could be quantitated with a known ‘lesion size’.

MATERIALS AND METHODS
A phantom study using 8mm chambers filled with water attached onto the abdomen of 2 volunteers (males ages 25 [55Kg] and 32 [80Kg]) each imaged twice with a 30 day period between studies for a total of 4 abdominal T2W MR sequences during each examination. The phantom size was measured by 2 different observers on the computer monitor and on the film generated and the size measurements were analyzed for size consistency and variation.

MR IMAGING
All MR images were acquired on a superconducting 1.5-T MR imager (Gyrosan ACS NT; Philips Medical Systems, Best, The Netherlands) using conventional spin-echo
sequences, and Fast spin-echo sequences. On the conventional spin echo (SE) sequences to obtain both moderately and heavily T2-weighted images the following standard scan parameters were used; a repetition time (TR) of 3600 msec, a first echo time (TE) of 50 msec and a second TE of 160 msec (3600/50, 160) with two excitations. The matrix size was 256 x 128, with a field of view of 32 to 37cm, yielding an effective in-plane resolution of 1.25 to 1.44mm by 2.5 to 2.9mm. A body coil was used for both transmission and reception. Section thickness was 8mm with a 1mm gap. Respiratory and flow compensation was used routinely. The average imaging time for double-echo T2 weighted sequences was 15 minutes and 30 seconds. Images were obtained in the axial and sagittal planes with phase encode direction anterior to posterior.

On the Fast spin echo (FSE) sequences to obtain both moderately and heavily T2-weighted images the following standard scan parameters were used; a repetition time (TR) of 3000 msec, a first echo time (TE) of 40 msec and a second TE of 110 msec (3000/40, 110) with two excitations, and a turbo factor of 16. The matrix size was 256 x 256, with a field of view of 32 to 37cm, yielding an effective in-plane resolution of 1.25 to 1.44mm. A body coil was used for both transmission and reception. Section thickness was 8mm with a 1mm gap. Respiratory and flow compensation was used routinely. The average imaging time for double-echo FSE T2 weighted sequences was 5 minutes. Images were obtained in the axial and sagittal planes. Images were obtained with phase encoding in both the right to left and anterior to posterior directions on the axial plane and in the anterior to posterior direction in the sagittal plane. Table 1 summarizes all sequences examined.

**Figure 1**

Table 1: Dual echo T2 weighted sequences examined in each subject.

<table>
<thead>
<tr>
<th>Technique</th>
<th>Plane</th>
<th>Phase encode direction</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE</td>
<td>axial</td>
<td>Anterior to posterior</td>
</tr>
<tr>
<td>SE</td>
<td>sagittal</td>
<td>Anterior to posterior</td>
</tr>
<tr>
<td>FSE</td>
<td>axial</td>
<td>Anterior to posterior</td>
</tr>
<tr>
<td>FSE</td>
<td>sagittal</td>
<td>Left to right</td>
</tr>
</tbody>
</table>

**IMAGE ANALYSIS**

The phantom size was measured by 2 different observers on the computer monitor and on film blinded to each others results and at a date 3 months later these measure were repeated and the size measurements were analyzed for size consistency and variation. The phantom used consisted of a single width Lego block (Lego, Denmark) filled with distilled water and taped to the abdomen over the liver of each subject (figure 1). The depth (AP direction) on each image was measured by two blinded observers. The largest possible line located within the confines of the ‘lesion’ was selected. These measurements were recorded for each image from the computer monitor and the film hard copy on both moderately and heavily T2-weighted images on all cross-sections. Two measurements were recorded of the phantom at the short and long echo times and mean values and standard deviation were calculated and entered into a computer database (Microsoft Excel version 4.0, Microsoft, Bothel, WA). A total of 2 measures at 2 echo times for 5 sequences (SE in 2 planes and FSE in 2 planes and alternate phase encode direction) in 2 subjects imaged 2 times was done by 2 observers on 2 media (film and computer) yielding a total of 320 measures of the phantom were obtained. Table 2 shows the measures for the later echo of all the sequences with phase encoding in the anterior to posterior direction.

**Figure 2**

Table 2: Measurements of 8mm phantom on later echo from dual echo T2 weighted MR scans in two subjects by two observers on film and computer monitor and with repeat studies obtained in 30 days.

<table>
<thead>
<tr>
<th>Subject</th>
<th>Technique</th>
<th>Phase</th>
<th>Observer 1</th>
<th>Observer 2</th>
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<tr>
<td></td>
<td>SE</td>
<td>axial</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>film 1</td>
<td>film 2</td>
</tr>
<tr>
<td></td>
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<td></td>
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</tr>
<tr>
<td>repeat study</td>
<td>SE</td>
<td>axial</td>
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</tbody>
</table>

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Figure 3
Figure 1: Axial long T2W (FSE) second echo image of the abdomen of 1 volunteer with phantom taped over the abdomen demonstrating linear measurement at 8.3mm on monitor (not shown) between arrow heads.

STATISTICAL ANALYSIS
All measurements were collected and analyzed for inter and intra reader variation, and variation between sequences, imaging planes, and between the phase encoding directions with paired t-test analysis [3]. Analysis was performed between; observers, media, time, imaging plane, sequence type, echo time, phase encode direction and subject.

RESULTS
Analysis of variation between readers demonstrated no significant difference in size measurements based on film or monitor measurements, between sequences, or imaging planes. The mean measurement for phantom size was 8.5 mm with a standard deviation of 0.5mm. Measurements were reproducible in that there was no statistically significant difference between values calculated on two separate occasions with a standard error of the mean of less than 0.1mm. Paired t-test analysis demonstrated no significant difference between; observers, media, time, imaging plane, sequence type, echo time, phase encode direction and subject (p>0.05). Results are summarized in table 3. Note that low p values were noted between observers on the film measures on sagital SE and axial TSE sequences-suggesting a meaningful difference or bias on film measures, or a spurious statistical phenomena.

DISCUSSION
It is well recognized that the combined use of moderately and heavily T2-weighted MR images (double-echo T2-weighted images) is valuable for liver lesion characterization [4,5]. Compared with hemangiomas and cysts, malignant hepatic tumors retain less signal intensity on heavily T2-weighted images than on moderately T2-weighted MR images. The use of double-echo T2-weighted MR images for lesion characterization has been described, not only with conventional spin-echo imaging, but with breathing averaged and breath-hold fast spin echo sequences, half-fourier single-shot turbo spin-echo (HASTE) sequences and echo-planar imaging [10,11,12,13].

Visual analyses of MR signal characteristics are inherently subjective, and are prone to uncertainty and inconsistency as recent work has documented [2]. Lesion characterization using calculated T2 relaxation times derived from double-echo T2-weighted sequences has been shown to be more accurate than other quantitative methods (lesion-to-liver contrast-to-noise ratios, lesion-liver, lesion-fat, lesion-muscle signal-intensity ratios) at 1.5-T field strengths [1,15]. Furthermore, such measurements have been shown to be superior to subjective evaluations of both lesion brightness and morphology [1,2,16].

When attempting to differentiate benign from malignant liver lesions on MR imaging, observers combine a visual assessment of many variables including lesion brightness, lesion morphology, and patterns of contrast enhancement. The value of quantitative measures of T2 are that they provide objective evidence of lesion type and help reduce the uncertainty and inconsistency associated with visual inspection. In equivocal cases with T2 values between 90 and 130 msec serial studies may be needed to more accurately classify a given liver lesion. Until the accuracy of lesion size change is obtained certainty about tumor growth can be limited, hence the motivation for this study.

Table 3: Mean measures of phantom

<table>
<thead>
<tr>
<th>technique</th>
<th>plane</th>
<th>phase encode</th>
<th>measure 1 (mm)</th>
<th>measure 2 (mm)</th>
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<tbody>
<tr>
<td>monitor</td>
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<td>7.75</td>
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<td></td>
<td>SE</td>
<td>sagittal</td>
<td>8.00</td>
<td>7.99</td>
<td>0.58</td>
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<tr>
<td></td>
<td>FSE</td>
<td>axial</td>
<td>7.95</td>
<td>7.99</td>
<td>0.85</td>
</tr>
<tr>
<td></td>
<td>FSE</td>
<td>sagittal</td>
<td>7.95</td>
<td>8.23</td>
<td>0.21</td>
</tr>
<tr>
<td></td>
<td>FSE</td>
<td>axial</td>
<td>8.25</td>
<td>8.25</td>
<td>0.93</td>
</tr>
<tr>
<td>film</td>
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<td>axial</td>
<td>9.25</td>
<td>8.45</td>
<td>0.08</td>
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<tr>
<td></td>
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<td>8.55</td>
<td>8.10</td>
<td>0.001</td>
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<tr>
<td></td>
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<td>axial</td>
<td>8.80</td>
<td>8.35</td>
<td>0.02</td>
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<tr>
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<td>axial</td>
<td>8.56</td>
<td>8.35</td>
<td>0.59</td>
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</table>
It is in this void that we attempt to establish measurement error so that certainty about lesion growth is improved for liver lesions identified on MRI. In this study, double-echo T2-weighted images were acquired using SE and FSE sequences alone and lesion size variation was measured. In summary we recommend that at least 1 mm change (that is 2 standard deviations) in size be used as a criteria to diagnose lesion growth or regression when measured on T2W abdominal MRI. It is worthy to note that low p values between observers on the film measures on sagittal SE and axial TSE sequences may imply an element of bias on film measures, consequently lesion measures are more reproducible and reliable when done on the computer monitor.

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