Published in final edited form as:

IEEE Trans Med Imaging. 2007 December ; 26(12): 1740–1746.

Progress in Multimodality Imaging: Truly Simultaneous Ultrasound and Magnetic Resonance Imaging

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Abstract

Multimodality medical imaging takes advantage of the strengths of different imaging modalities to provide a more complete picture of the anatomy under investigation. Many complementary modalities have been combined to form such systems and some are gaining use clinically. One combination that has not been developed, in large part due to technical difficulties, is a combined MR and ultrasound imaging system. Such a system offers the potential to combine the strengths of these modalities in a wide range of diagnostic and therapeutic applications. The goal of this study was to evaluate the feasibility of performing simultaneous multimodality ultrasound and MR imaging. An ultrasound imaging system capable of operation in a clinical MR imager was developed, and methods to perform simultaneous imaging were investigated. Simultaneous imaging was feasible without any mutual interference by either filtering the transmitted and received ultrasound signal, or by synchronizing data acquisition between the two imaging systems. Spatial registration between the two modalities was achieved by using a reference phantom with implanted glass beads in orthogonal planes. Excellent agreement was observed between spatial measurements of an object made with both modalities, and the feasibility of using this system in vivo was demonstrated in a rabbit model. Simultaneous ultrasound and MR imaging is achievable, and can provide complementary information about an object under investigation. This demonstration of technical feasibility and the development of a prototype system open up the potential to investigate the promising clinical applications of this combined technology.

I. Introduction

The combination of imaging information from multiple modalities is not new, but has traditionally been accomplished with separate acquisitions at different times (even different days) and subsequent image registration to align the data sets [1,2]. This can be an especially challenging problem in the presence of large organ deformation or in situations where patient positioning and involuntary movements can not be completely controlled. In addition, the related sequential combination of imaging modalities adds both time and cost making it less desirable and rarely available for routine clinical practice. The advantage of acquiring imaging information simultaneously with multiple modalities is that the images can be inherently spatially and temporally registered. In addition, the integration of multiple imaging modalities into a single system opens up the possibility of combining the images from each modality in a synergistic fashion to enhance the overall diagnostic information available.

These benefits have led to a concerted effort to develop hybrid multimodality imaging systems using various complementary technologies [3]. These systems are usually designed to combine the advantages of each independent imaging modality. For example, ultrasound imaging has been combined with near infrared tomography (NIR) [4,5] to enhance tissue discrimination with NIR while achieving good spatial resolution with ultrasound. The

combination of CT and positron emission tomography (PET) is gaining use clinically as a means to characterize a tumor with respect to geometry and function for improved radiation therapy planning [6,7]. MRI has been combined with a number of modalities including X-Ray [8], PET [9,10] and near infrared tomography (NIR) [11,12].

Two technologies that have not been integrated into a single hybrid system are ultrasound and MR imaging. MRI is used widely for both diagnostic and therapeutic planning applications because of its multi-planar imaging capability, high signal to noise ratio, and sensitivity to subtle changes in soft tissue morphology and function. Ultrasound imaging, on the other hand, has important advantages including high temporal resolution, high sensitivity to acoustic scatterers such as calcifications and gas bubbles, excellent visualization and measurement of blood flow, low cost, and portability. The strengths of these modalities are complementary, and the two are combined regularly (though separately) in clinical practice. The benefits of combining these modalities through image registration have been shown for intra-operative neurosurgical applications [13] and breast biopsy guidance [14]. By performing imaging with both modalities simultaneously a number of issues such as spatial and temporal registration between data sets can be simplified or resolved. In addition, measurements of unique physiological parameters can be made with each modality to fully characterize the organ or tissue under evaluation. Finally, a complete clinical exam requiring both modalities could be made more efficient with minimal added cost to an MRI by performing both studies simultaneously. In addition to these clinical benefits, an integrated MR and ultrasound system could offer novel insights into a number of research questions related to the biology and function of normal and diseased tissue as a research tool [3,15].

Some work has been reported concerning the integration of US and MR imaging systems. A method of synchronizing data acquisition with each modality was proposed in order to perform Doppler measurements during MR imaging [16]. Ultrasound imaging was not performed in this study, and no MRI compatible system was ever developed. The use of an electrically shielded commercial ultrasound transducer in a clinical 1.5T MR imager has also been attempted [17–19]. Shielding reduced electrical interference between the two modalities but was not completely successful, and the transducers were not specifically MRI-compatible. The main goal of these studies was not to perform simultaneous imaging with both modalities, but rather to track movement with ultrasound and to use this information to perform motion compensation during MR imaging. No integrated systems capable of simultaneous imaging have been developed to date.

The goal of this study was to explore the feasibility of performing simultaneous MR and ultrasound imaging. An MRI compatible ultrasound imaging system was developed and the capability to acquire ultrasound images during MR imaging was investigated. Methods for eliminating interference and achieving good spatial registration between the two modalities are also discussed.

II. Materials and Methods

A. Integrated US & MR Imaging System

The ultrasound imaging system designed in this study incorporated a mechanically scanned spherically focused transducer. Linear scanning was accomplished with a custom-designed MRI compatible motion system incorporating piezo-ceramic motors (HR4, Nanomotion, Inc, Yokneam, Israel) and encoders (LIA20, Numerik Jena, Jena, Germany). The system allowed positioning of the transducer with a step size of 0.2- μ m and a maximum velocity of 75 mm/s. The total range of motion was 50 mm with the linear stage. An MRI-compatible, custom manufactured single circular element US transducer (PZT 5, 1-3 piezocomposite) was used for the imaging (Imasonic, Besançon, France). The US transducer has a central

frequency of 5 MHz, a focal length of 50 mm, a 20-mm diameter and a bandwidth of 50% (at -3 dB in power). The housing, cabling and shielding of the transducer were designed to avoid magnetic materials thus ensuring the MR compatibility. A pulser/receiver (5072PR, Panametrics) furnished the excitation to the transducer, received and conditioned the echo signal. An oscilloscope (TDS2012, Tektronix) was used to digitize and record the RF signal at each location. The linear motion, transducer excitation and signal acquisition were controlled by a PC in these experiments. In order to produce an ultrasound image, individual A-lines were recorded as the transducer was scanned linearly across a total distance of 50 mm, with a step size of either 0.2 or 1 mm. No signal averaging, filtering or dynamic compression of the ultrasound RF signals was performed for these experiments. The RF signal from the pulser/receiver was directly digitized by the oscilloscope that had an 8-bit dynamic range and it was then numerically processed to obtain the image. The US RF signals of each line data were acquired at fixed (0.2 or 1 mm) intervals with no translation during the RF acquisitions. The RF signal processing after acquisition consisted in: elimination of the DC component, computation of echo signal envelopes and threshold rejection of low-level echoes under -60 dB. Apart from the transducer and linear stage, all of the electronics controlling the motors, encoders and the transducer were kept outside the magnet room. Cables containing RF signals for ultrasound imaging, and the motor and encoder signals passed through a filtered penetration panel prior to entering the MRI.

A closed-bore clinical 1.5T MR imager (Signa, GE Healthcare, Milwaukee, USA) was used to perform MR imaging in this study. Images were acquired using either a standard body coil, or an integrated single channel surface coil (depending on the experiment). The dynamic range for the MR images was determined by the 12-bit resolution used by the imager. An output signal proportional to the gradient waveform was used to gate ultrasound imaging during simultaneous operation. No other modifications were made to the scanner. Fig. 1 shows a schematic of the integrated simultaneous US-MR imaging system.

B. Simultaneous Imaging

Prior to acquiring images with both modalities, the spatial registration between the two imaging planes was established. This was accomplished by either geometrical considerations, or by using a reference gelatin phantom with embedded glass beads. In the first case, the MR imaging slice was prescribed such that it intersected the transducer (which was visible in the images) and was along the direction of the ultrasound beam. In the second case, a reference phantom with beads arranged in a triangular fashion in two orthogonal planes was imaged with both modalities. The position of each image was adjusted until all three beads were visible in both orientations, ensuring spatial registration of the imaging planes.

Two different test phantoms were used as imaging targets. The first phantom was made of multiple nylon strings at different spacing (2–12 mm) and diameters (0.2, 0.4mm) submerged in the water tank. Strings were arranged such that multiple targets were located in the lateral and axial directions of the ultrasound image. This phantom was used to test the resolution of the two imaging systems. The second phantom was a block of agar gel (4%) cut to produce 6 steps of approximately 5mm height each. This phantom was used to compare the distances measured in the MR and US images.

An initial test was performed to evaluate the influence of the ultrasound on the MR imaging acquisition. MR images were acquired with the ultrasound system in various configurations: 1) completely off, 2) ultrasound system on but not acquiring data, 3) transducer moving but not transmitting ultrasound, 4) transducer moving and transmitting ultrasound. Next, the influence of the MRI on the US imaging acquisition was investigated. The RF signals generated by the ultrasound transducer as a response to the echoes received were acquired

with the MR imager on and off, and the frequency spectrum of the received ultrasound echo was studied for interference. US images were also acquired while MR imaging was performed to observe the effect of MR-induced noise.

Two approaches were investigated to perform simultaneous imaging with both modalities. The first approach was to filter the transmitted and received RF signal to the ultrasound transducer with a low-pass filter (BLP10.7, BLP15, Mini-Circuits, Brooklyn, NY, USA). The purpose of the filter was to remove any harmonics in the transmitted pulse that might interfere with the MR imaging, and to remove any of the MR signals that might appear in the received echo. The center frequency of the ultrasound burst was nominally 5 MHz and the frequency of the MRI RF pulses 64 MHz thus, allowing clear frequency separation. The second approach was to synchronize the two systems such that ultrasound imaging was only performed during the time between the frequency encoding gradient and the subsequent RF pulse for the MR imaging. A clearer picture of the synchronization scheme is depicted in Fig. 2. The total US acquisition time for an image when the synchronization was used depended on the MR pulse repetition time and the pulse repetition rate. Multiple RF lines could be acquired between each MR pulse as the TR was in the order of milliseconds while the used PRF was 3 kHz. The whole US image was therefore completed when the final MR image was obtained. The MRI-compatibility of the scanning system enabled movement of the transducer at any point in the imaging process without causing significant interference.

In order to compare the different acquisition schemes, and to evaluate the interference between modalities the Signal-to-Noise ratio (SNR) was measured for both imaging modalities. For the MR images the mean signal S was measured within a region of interest (ROI) defined inside the object in the image; a second ROI was defined in the background of the image, in an area free of artifacts, and the standard deviation was measured (σ). The SNR was defined as S/σ . For each MR image, the SNR was obtained using 10 different ROI for the signal S , and finally the average and standard deviation of these SNR values were calculated. For the ultrasound images the SNR was defined as the root mean square (RMS) of the RF signal voltage (where echoes were present) divided by the RMS of the noise voltage (reference RF line where no echoes were observed). For each US image, the SNR value was obtained by averaging every RF signal with echoes present, and finally the average and standard deviation of these SNR values were calculated.

C. In vivo images

Simultaneous images were acquired of a rabbit kidney in vivo to demonstrate the feasibility of this system. A New Zealand White rabbit (female, 3.5kg) was anesthetized using a mixture of ketamine and xylazine, shaved and depilated in the abdomen. This experiment received approval from the local Animal Care Committee at Sunnybrook Health Sciences Centre. The rabbit was subsequently laid on a platform in the lateral decubitus position such that its kidney was over an acoustic window, and in contact with a water bath. The ultrasound transducer was scanned from below the animal to acquire a 2D image of the kidney. The ultrasound image was processed as described in section A with additional attenuation compensation and applying a 3×3 median filter. MR imaging was performed using an integrated surface coil embedded in the acoustic window. MR images were acquired using a fast spin echo image with the following parameters: 512×512 , TE/TR=15.00/180, FOV=16cm, Slice=3mm, ETL=1. The ultrasound images were acquired with a step size of 0.2 mm and 32 averages per A-line. Attenuation compensation and median filtering (3×3) were performed for the in vivo ultrasound images.

III. Results

A. Imaging alignment and interference elimination

Fig. 3 shows the ultrasound (left) and MR (right) images of the alignment phantom used to achieve accurate spatial registration between the two modalities. Three glass beads were arranged in each of the two perpendicular planes (L/R and S/I). The alignment of the MR and ultrasound imaging planes was performed before subsequent image acquisition. Excellent alignment was achieved with this simple method. MR images were acquired using a body coil with a gradient echo sequence (256×256, TE/TR=1.61/5, FOV=16cm, Slice=3mm, ETL=1, 1NEX).

The MRI compatibility of the transducers and linear scanning system was excellent and no significant artifacts were produced in the MR images due to the either of these components. In addition, the motors could operate during imaging with no influence on the MR imaging acquisition. Fig. 4 shows a series of MR images acquired while the transducer was being translated relative to a string phantom by the scanning system. The MR images were acquired using a body coil with a gradient echo sequence (256×256, TE/TR=25.00/110, FOV=17cm, Slice=5mm, ETL=1, 1NEX). This imaging sequence is sensitive to magnetic field inhomogeneities that might be caused by the movement of the transducer. As is evident in the images in Fig. 4, there was no significant degradation in the MR images while the transducer was moving.

Table 1 shows the average and standard deviation of the SNR measured in the MR and US baseline images as well as for the different acquisition and operation schemes. The MR image baseline was obtained with the ultrasound system turned on but without any US pulsing or motor movement and the obtained SNR was 22 ± 7 . The US image baseline was obtained without any filtering in the transmit/receive line and no MR pulsing and the SNR was 22 ± 9 . In order to account for noise in the baseline images, an MR image was obtained with the ultrasound system completely off and the measured SNR was 23 ± 7 . This SNR value showed that ultrasound imaging system electronics introduced some noise in the MR images even without any ultrasound pulsing. As well, an US image with the 10.7 MHz low-pass filter in the transmit/receive line was performed inside the magnet without MR pulsing and the measured SNR was 27 ± 15 . The filter improved the ultrasound SNR showing that the MR imager introduces some noise in the ultrasound imaging even without MR pulsing. The SNR measured in MR images during movement (21 ± 7) shows that no significant signal loss was caused by the motor function (Table 1). For reference, the nylon string phantom was also imaged outside the MR using a commercial ultrasound scanner (Philips EnVisor, Carotid linear array probe, focused at 50 mm, Philips Medical Systems, Netherlands) and an SNR value of 39 ± 8 was obtained using the method described for the MR images.

Fig. 5 shows ultrasound (left) and MR images (right) generated with the different acquisition schemes. The MR images were acquired using a body coil with a gradient echo sequence (256×256, TE/TR=3.14/51, FOV=20cm, Slice=10mm, 5NEX). The images in Fig. 5A were acquired with no synchronization or filtering, and electrical interference can be seen in both images. When analyzing the frequency spectrum in the acquired US signal, the MR RF pulse at 64MHz was clearly seen, showing that the noise observed in the US images came mainly from this pulse. Artifacts were seen in the ultrasound image as continuous lines, while the interference was observed in the MR image as regularly spaced horizontal lines. The MR images were very noisy and the SNR was very low (7 ± 7) as expected. The MR pulsing noise had less of an effect on the US images and this was reflected in the SNR (21 ± 8).

The images shown in Fig. 5B were acquired with a 10.7 MHz low pass filter (BLP10.7) in the transmit/receive line for the ultrasound imaging system. This filter was able to remove the interference in both images successfully, and enabled continuous operation of both systems. A low-pass filter with a higher cutoff frequency (BLP15) was substituted, but resulted in some noise appearing in the MR images. The SNR when the filter was present was high for the MR images (22 ± 7) as well as for the US images (26 ± 13).

The images acquired with synchronization of the two systems are shown in Fig. 5C. The synchronization was accomplished by gating the US acquisition between the end of the readout gradient and the subsequent RF pulse (Fig. 2). The SNR measured in the MR images was 21 ± 7 , which was close to the value obtained for the baseline and the filter.

Fig. 6 shows the US and MR image of the agar step phantom and a plot of the measured position of each step following the scanning and the depth directions. The measured parameter was the leading edge of each step following the scanning direction and the centre of the plateau for the depth direction. The measurements made in both directions (the scanning direction and the US propagation direction) were both highly correlated. The lateral resolution of the ultrasound images was lower than the axial resolution due to the fact that the images were acquired with a single-element focused transducer with gradually increasing beam diameter away from the focal zone. The focus of the US transducer was at 50 mm (centered at the fourth step), therefore explaining the slight discrepancy in the measurements of the width between the closest and the furthest steps. The MR images were acquired using a body coil with a fast spin echo sequence (256×256 , TE/TR=50.00/100, FOV=20cm, Slice=6mm, ETL=1, 5NEX).

B. In vivo Imaging

MR and ultrasound images acquired simultaneously in the rabbit kidney are shown in Fig. 7. The ultrasound image was processed with attenuation compensation (0.5 dB/cm/MHz) and applying a 3×3 median filter. The complementary nature of the two images is apparent. The skin interfaces are clearly shown by both modalities and the correspondence between the images can be observed. Some hyperechogenic zones can be appreciated in the US image, while they are not apparent in the MR image. The feasibility and the complementary nature of both modalities could be appreciated.

IV. Discussion

Simultaneous imaging with both ultrasound and MRI could provide complementary diagnostic information in a naturally co-registered fashion, opening up a number of clinical applications ranging from cardiology to oncology. To date, the challenges in integrating these technologies has been the lack of MRI-compatible equipment for ultrasound imaging, but recent developments in piezocomposite materials [20] as well as non-magnetic motors has made this integration feasible. This study demonstrated the capability to perform ultrasound imaging in a clinical MR imager with a mechanically scanned transducer during MR image acquisition. A prototype system was developed and tested in a clinical 1.5T MRI. The scanning system used to translate the transducer was completely MRI-compatible and exhibited no magnetic or electrical interference, enabling continuous operation during MR imaging.

Electrical interference between the two imaging systems was seen, and two acquisition schemes were proposed to eliminate it. The first approach incorporating a low-pass filter was a very simple solution that reduced the interference to an acceptable level. This approach enabled simultaneous operation of both systems without any timing considerations. The main drawback of this approach however, was the reduced bandwidth

available to the ultrasound imaging system that could impede future applications of this imaging technique. The synchronized acquisition was also successful at isolating the two imaging systems from each other. This approach required that there was sufficient time between the completion of the readout gradient and the subsequent excitation pulse in the MR imaging sequence to acquire an ultrasound echo. Ultimately, this approach lowers the total imaging time (or duty cycle) available to each modality, which could limit applications where high speed continuous imaging is required. However, the main advantage of this approach is that any MRI-compatible ultrasound system with a more complicated pulsing sequence could be integrated with the MR imager since the data acquisition of both systems is independent. In fact, this approach is applicable to performing any method of imaging or data acquisition in conjunction with MRI.

The string phantom images demonstrated the complementary nature of both modalities. The strings were easily observed in the US images due to the large difference in acoustic impedance, while the MR images depicted the surrounding water with clarity. The strings were only visible in MR when a very long imaging sequence with multiple averages was implemented, and still the smallest strings were not visible (Fig. 8). This is a simple example, but it clearly illustrates the fact that both imaging modalities are sensitive to different features in an object. The strings in this phantom could represent calcifications in tissue, which are seen regularly in clinical ultrasound [21]. Superimposing the calcifications for example to an MRI of a breast could provide additional diagnostic value.

The images of the step agar phantoms demonstrated the natural co-registration of the imaging modalities. The correlation between the measured dimensions of the steps between the two modalities was very high. The slight reduction in the correlation in the scanning direction was related to the beam shape of the transducer, and the 1-mm step size used to make the ultrasound images. With a smaller step size and dynamic focusing one would expect the same level of correlation in this dimension as well.

Finally, in the *in vivo* image, the correspondence between the images can be confirmed by observing the curvature of the skin and the appearance of similar structures in both images. The hyperechogenic zones that can be observed at the center of the US image correspond to the dark zone clearly perceived in the MRI. In addition, the two vessels feeding the kidney could be seen in both images. This experiment validated the feasibility of *in vivo* simultaneous MR and ultrasound imaging with this system and the complementary information provided by this technology.

The main benefits of using these modalities simultaneously include the ability to co-register imaging information without tissue distortion, reduced exam times, and the ability to capitalize on the strengths of each modality in a truly simultaneous fashion. These benefits could have broad number of applications in medicine. For example, tumor biopsy could be improved by using the real-time capability of ultrasound to guide needles to soft tissue targets visualized on MRI. In addition, the power to measure flow and motion simply with Doppler ultrasound could be used to gate and trigger cardiac MR imaging exams based on real-time motion compensation instead of ECGs. Finally, in the area of contrast enhancement, simultaneous imaging of both ultrasound and MR contrast agents could add another dimension to the information obtained in a diagnostic exam for tumor classification. The development of this technology will enable further study of these exciting areas.

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Fig. 1.
Experimental setup used to perform US imaging in a clinical MRI

Fig. 2.
Timing diagram for the acquisition of ultrasound images during a typical MR imaging pulse sequence.

Fig. 3.

Spatial alignment between US (left) and MR (right) images is achieved by imaging a gelatin phantom with glass beads implanted in two orthogonal planes. The US transducer was positioned at the bottom of the image facing up (at 0 mm). The observed shadow behind the farthest glass beads is caused by the reflection of the energy. The bright spot at the top of the image was explained by an incorrect matching between the back of the phantom and the absorbent.

Fig. 4. MR images of a gelatin phantom acquired while the ultrasound transducer was moving. The arrow represents the direction of motion.

Fig. 5. Simultaneous ultrasound (US) and Magnetic Resonance (MR) images of a string phantom. (a) Simultaneous imaging without any filtering or synchronization. (b) Simultaneous imaging using a 10.7 MHz low-pass filter in the US signal. (c) Synchronized ultrasound and MR imaging. Both the filtered and synchronized acquisitions were able to eliminate the interference between the two modalities.

Fig. 6. Simultaneous MR and US images of a step agar phantom. The plot shows the measured position of each step following the scanning and the depth directions. The measured parameter was the leading edge for the scanning direction and the centre of the plateau for the depth direction. Excellent agreement between the two modalities is shown in both directions.

Fig. 7.
Simultaneous MR and US acquired of a rabbit kidney *in vivo*.

Fig. 8. Simultaneous MR and US images of the string phantom with a high resolution MR image. Although the larger strings (0.4mm) can be resolved on the MR images, the ultrasound image was much more sensitive to them. This highlights the complementary information available with both modalities.

Table 1

Signal-to-Noise Ratio (SNR) for MR and US images with and without US RF signal filtering and synchronization

	MR pulsing	US pulsing	Motor Movement	Filter	Synchronization	MR image SNR	US image SNR
MRI Baseline (US off)	Yes	No	No	No	No	23 ± 7	–
MRI Baseline	Yes	No	No	No	No	22 ± 7	–
US Baseline & Filter	No	Yes	Yes	Yes	No	–	27 ± 15
US Baseline	No	Yes	Yes	No	No	–	22 ± 9
Motor	Yes	No	Yes	No	No	21 ± 7	–
No synchronization, No Filter	Yes	Yes	Yes	No	No	7 ± 7	21 ± 8
Filtering	Yes	Yes	Yes	Yes	No	22 ± 7	26 ± 13
Synchronization	Yes	Yes	Yes	No	Yes	21 ± 7	21 ± 9
Synchronization & Filter	Yes	Yes	Yes	Yes	Yes	22 ± 7	26 ± 14