Real-Time Co-Registration Using Novel Ultrasound Technology: Ex Vivo Validation and In Vivo Applications

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Objective: The study objective was to evaluate whether a novel global position system (GPS)-like position-sensing technology will enable accurate co-registration of images between imaging modalities. Co-registration of images obtained by different imaging modalities will allow for comparison and fusion between imaging modalities, and therefore has significant clinical and research implications. We compared ultrasound (US) and magnetic resonance imaging (MRI) scans of carotid endarterectomy (CEA) specimens using a novel position-sensing technology that uses an electromagnetic (EM) transmitter and sensors mounted on a US transducer. We then evaluated in vivo US-US and US-MRI co-registration.

Methods: Thirteen CEA specimens underwent 3.0 Tesla MRI, after which images were uploaded to a LOGIQ E9 3D (GE Healthcare, Wauwatosa, WI) US system and registered by identifying two to three common points. A similar method was used to evaluate US-MRI co-registration in patients with carotid atherosclerosis. For carotid intima-media thickness (C-IMT) measurements, 10 volunteers underwent bilateral carotid US scans co-registered to three-dimensional US maps created on the initial visit, with a repeat scan 2 days later.

Results: For the CEA specimens, there was a mean of 20 (standard error [SE] 2.0) frames per MRI slice. The mean frame difference, over 33 registration markers, between MRI and US scans for readers 1 and 2 was -2.82 ± 19.32 and 2.09 ± 14.68 (mean $\pm$ 95% CI) frames, respectively. The US-MRI intraclass correlation coefficients (ICCs) for the first and second readers were 0.995 and 0.997, respectively. For patients with carotid atherosclerosis, the mean US frames per MRI slice (9 [SE 2.3]) was within range of that observed with CEA specimens. Inter-visit, intra-reader, and inter-reader reproducibility of C-IMT measurements were consistently high (side-averaged ICC >0.9).

Conclusion: Accurate co-registration between US and other modalities is feasible with a GPS-like technology, which has significant clinical and research applicability. (J Am Soc Echocardiogr 2011;24:720-8.)

Keywords: Carotid plaques, Co-registration, Magnetic resonance imaging, Plaque tissue, Ultrasound

All modalities used for imaging atherosclerosis have inherent advantages and disadvantages.[1] For example, magnetic resonance imaging (MRI) provides highly detailed, structural, and compositional information but suffers from relatively long study times and poor temporal resolution.[2,3] In contrast, ultrasonography provides real-time imaging with excellent temporal resolution, but image quality can be variable.

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Abbreviations

CCA = Common carotid artery

CEA = Carotid endarterectomy

C-IMT = Carotid intima-media thickness

CT = Computed tomography

DICOM = Digital Imaging and Communications in Medicine

ECG = Electrocardiography

EM = Electromagnetic

GPS = Global position system

ICC = Intraclass correlation coefficient

MRI = Magnetic resonance imaging

PDW = Proton-density weighted

SE = Standard error

US = Ultrasound

Combining imaging modalities could theoretically allow their strengths to complement each other and overcome their individual limitations. For example, the portability and immediate availability of real-time data from ultrasonography can be combined with highly detailed, anatomic information from MRI or computed tomography (CT) scans.

A key step for accurate comparisons between modalities involves co-registration, or matching anatomic features between imaging modalities.[4] A novel advance in ultrasound (US) technology, namely, real-time electromagnetic (EM) tracking of the US probe location and orientation, may now allow semiautomated registration between US and other imaging modalities. However, this technology has limited validation.[5-7]

Therefore, we pursued the validation of this novel real-time EM tracking feature now available in a vascular US system and compared the reliability of its co-registration system with manual registration. We first evaluated ex vivo co-registration between US and MRI using a set of carotid endarterectomy (CEA) surgical specimens and then, in pilot analyses, evaluated in vivo co-registration of US-US and US-MRI.

MATERIALS AND METHODS

All experiments were approved by the institutional review board.

Ex Vivo Co-Registration

Sample. Atherosclerotic plaques ($n = 13$) were obtained after CEA. Specimens were acquired 1 to 3 hours after surgical resection and preserved in phosphate-buffered saline/50% glycerol and stored at −20°C. This preservation method maintains the ultrastructural properties of the carotid plaque.[8]

Sample Preparation. Immediately before use, specimens were dialyzed for 24 hours against phosphate-buffered saline to remove the glycerol. Samples were then embedded in 3% [weight (grams)/volume (milliliters)] low-melting agarose gel (FMC Bioproducts, Philadelphia, PA). The agarose gel solution was created by adding distilled water to agarose gel powder and heating the mixture to 60°C. Before pouring the solution over tissue samples, vacuum suction was applied to the solution. We have found that application of vacuum suction to the solution after mixing minimizes the presence of air bubbles, which are hyperechogenic on US and interfere with US imaging. Once tissues were embedded, the solution was allowed to cool to room temperature before imaging.

Agarose gel was chosen as a support matrix for several reasons: (1) to minimize damage from tissue manipulation; (2) to preserve spatial arrangement of the morphologic features for comparisons between imaging modalities; (3) to minimize chemical interactions with biological tissue, which may interfere with MRI and US imaging; and (4) to provide a support medium necessary for US imaging. Plastic pipette tips were embedded near one end of the CEA sample to provide a non-anatomic reference point.

Magnetic Resonance Imaging

MRI scans were acquired after the CEA samples were embedded in 3% agarose gel in 15-mL culture tubes. These tubes were placed in a custom-built holder designed specifically for acquiring tissue MRI scans.[9] Specimens were imaged using a 6-cm phased array 4-channel carotid coil (Pathway Med Tech, Redmond, WA) on an Excite 3.0 Tesla MRI scanner (GE Healthcare, Wauwatosa, WI). Serial axial proton-density weighted (PDW), T1-weighted, and T2-weighted images were acquired (2-mm slice thickness, matrix 512 × 512, field of view 100 × 100 mm) using a fast-spin echo sequence providing 8–31 slices depending on tissue size with an in-plane resolution of ~0.195 mm. Correction algorithms adjusted for magnetic field strength gradients across the sample image.

Real-time Three-Dimensional US

After MRI, each of the 13 CEA tissue samples embedded in agarose was extruded intact with the agarose column from its culture tube. The column was then transferred to a plastic box (10.5 × 12.5 × 4.0 cm), and additional 3% molten agarose was added to form an agarose bed prepared as described under the sample preparation section. This procedure was performed to provide adequate surface contact for the US probe. Samples were imaged with a LOGIQ E9 US system (GE Healthcare) using a "free-hand 3-dimensional scanning with EM field sensors" approach. This approach used a mid-range DC magnetic transmitter to generate a weak magnetic field. Position sensors attached to a two-dimensional vascular US probe sensed this field and recorded the probe position through an in-built circuit system, which functioned similar to a global position system (GPS), thereby allowing the computer to know the position and orientation of the transducer and allow it to reconstruct three-dimensional volumes.[10]

Automated Co-Registration

The PDW sequences of the MRI of a given CEA sample were uploaded from a CD-ROM to the US system, and manual marking of two to three features was performed between the MRI and a real-time B-mode US scan. The PDW sequence was selected over T1- and T2-weighted sequences because the PDW sequences were found to have the best image quality (reduced noise, reduced motion artifacts, reduced blurring, and sharp edges). Common features used for initial marking included the plastic marker tip, calcifications, and, if present, the "bifurcation." After two to three common points between the MRI and the real-time US scans were marked, the US instrument ran an algorithm to create a transformation matrix, which mapped the two-dimensional probe position to a multiplanar reconstruction of MRI scans.[11] The real-time US scan was now registered to the MRI scans, such that movement of the US probe resulted in movement through reconstructed MRI scan planes, displayed next to the US scan.

Validation of US Co-Registration by Manual Methods

All image data were exported in Digital Imaging and Communications in Medicine (DICOM) format to CD-ROMs for off-line analysis. Image sets were loaded onto a free DICOM viewer. Each image in a set had three components: (1) a US image; (2) a US frame