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Initial clinical experience with real-time transrectal ultrasonography-magnetic resonance imaging fusion-guided prostate biopsy

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Abstract

OBJECTIVE—To evaluate the feasibility and utility of registration and fusion of real-time transrectal ultrasonography (TRUS) and previously acquired magnetic resonance imaging (MRI) to guide prostate biopsies.

PATIENTS AND METHODS—Two National Cancer Institute trials allowed MRI-guided (with or without US fusion) prostate biopsies during placement of fiducial markers. Fiducial markers were used to guide patient set-up for daily external beam radiation therapy. The eligible patients had biopsy-confirmed prostate cancer that was visible on MRI. A high-field (3T) MRI was performed with an endorectal coil in place. After moving to an US suite, the patient then underwent TRUS to visualize the prostate. The US transducer was equipped with a commercial needle guide and custom modified with two embedded miniature orthogonal five-degrees of freedom sensors to enable spatial tracking and registration with MR images in six degrees of freedom. The MRI sequence of choice was registered manually to the US using custom software for real-time navigation and feedback. The interface displayed the actual and projected needle pathways superimposed upon the real-time US blended with the prior MR images, with position data updating in real time at 10 frames per second. The registered MRI information blended to the real-time US was available to the physician who performed targeted biopsies of highly suspicious areas.

RESULTS—Five patients underwent limited focal biopsy and fiducial marker placement with real-time TRUS-MRI fusion. The Gleason scores at the time of enrolment on study were 8, 7, 9, 9, and 6. Of the 11 targeted biopsies, eight showed prostate cancer. Positive biopsies were found in all patients. The entire TRUS procedure, with fusion, took ≈10 min.

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CONFLICT OF INTEREST

Jochen Kruecker and Sheng Xu are salaried employees of Philips Research North America. Philips has intellectual property in related fields. Neil Glossop is President and Founder of Traxtal, Inc. and has related intellectual property in the field.

CONCLUSION—The fusion of real-time TRUS and prior MR images of the prostate is feasible and enables MRI-guided interventions (like prostate biopsy) outside of the MRI suite. The technique allows for navigation within dynamic contrast-enhanced maps, or T2-weighted or MR spectroscopy images. This technique is a rapid way to facilitate MRI-guided prostate therapies such as external beam radiation therapy, brachytherapy, cryoablation, high-intensity focused ultrasound ablation, or direct injection of agents, without the cost, throughput, or equipment compatibility issues that might arise with MRI-guided interventions inside the MRI suite.

Keywords

magnetic resonance; ultrasound; prostate cancer; imaging; transrectal

INTRODUCTION

There are >200 000 new cases and nearly 30 000 deaths each year from prostate cancer [1]. PSA testing has allowed early detection of impalpable prostate cancer. In turn, early detection has lowered the incidence of advanced disease with extracapsular extension [2]. Progressively earlier detection appears to yield progressively improving survival [3].

Improving survival has sharpened the focus on reducing morbidity by minimizing damage to nearby normal tissue. Reducing the volume of normal tissue affected by therapy should minimize morbidity. Precise radiotherapy, e.g. intensity-modulated radiation therapy (IMRT), has allowed higher radiation doses to the prostate while minimizing toxicity by limiting the amount of normal tissue irradiated. Other focal therapies such as high-intensity focused ultrasound (HIFU) ablation [4-6], cryotherapy [7-9], and direct ethanol injection [10] have been studied.

For any highly focal therapy, reducing the treated normal tissue volume necessitates accurate delineation of cancer vs benign tissue. For differentiating benign from cancerous tissue, recent reports suggest that MRI is superior to TRUS [11-14]. A report using 3T MRI compared with whole mount specimens has reported significant correlation for prostate cancer delineation [15].

However, MRI is quite expensive and not widely available for image-guided procedures. Even simple prostate biopsies taken under direct MRI guidance can take hours and require highly specialized MRI-compatible equipment. Despite limited ability to delineate prostate cancer, US-guided prostate procedures have the virtues of speed, ease, cost, availability, and portability.

Procedures using US guidance with real-time overlay of prior MRI data combine the ability of MRI to delineate prostate cancer with the virtues of US. The purpose of this study was to evaluate a novel hardware and software combination and the feasibility and utility of real-time TRUS fused with previously acquired MRI to guide prostate biopsies.

PATIENTS AND METHODS

Eligible patients had biopsy-confirmed prostate cancer that was visible on MRI. Patients gave written informed consent to enroll on Investigational Review Board approved protocols for electromagnetic tracking and MRI-guided prostate biopsies (with or with no US fusion) during placement of fiducial markers. Prophylactic antibiotics were given to all patients. A mild oral sedative was given at the patient's request. Fiducial markers were used to guide patient set-up for daily external beam radiation therapy.

For MRI a Philips 3.0T Achieva scanner (Philips Medical Systems, Best, the Netherlands) with combined SENSE cardiac surface coil positioned over the pubic symphysis and endorectal coil (BPX-15, Medrad, Indianola, PA, USA) was used. After DRE, the endorectal coil was inserted and inflated with Fluorinert (3M, St Paul, MI, USA) to ≈ 60 mL. T2-weighted fast spin-echo images were obtained in three planes at a resolution of $0.46 \times 0.6 \times 3.0$ mm (field of view, FOV, 140 mm, matrix 234×304 , repetition time, TR/time to echo, TE 8852/120 ms). Dynamic-contrast enhanced (DCE) images were acquired during a single-dose injection of gadolinium-DTPA (Magnevist; Berlex Laboratories, Wayne, NJ, USA) at 3 mL/s with an injector (Spectrix MR Injection System; Medrad, Pittsburgh, PA, USA). The DCE acquisition consisted of a 10-slice three-dimensional (3D) gradient echo with a temporal resolution of 3.1 s with TR/TE of 5.5/2.1 ms, 15° flip angle, 26 cm FOV, number of signal averages two, SENSE factor of 4 and resolution of $0.86 \times 1.18 \times 6.0$ mm.

MRI was interpreted exclusively by one radiologist (P.C.). Suspicious areas were defined as hypo-intense regions on T2-weighted MRI and abnormally enhancing regions on DCE imaging using criteria similar to that defined by Futterer *et al.* [16]. Abnormalities were reported separately for the T2-weighted and DCE images according to standard sextant anatomy. Any suspicion of extracapsular extension or seminal vesicle invasion was recorded and laterality was noted in these cases.

Before the TRUS-MRI fusion-guided procedure, patients received a saline enema and a dose of lorazepam. Perioperative oral fluoroquinolones were also given. After their endorectal MRI, patients were brought to an US room outside of the MRI suite and underwent TRUS to visualize the prostate. An endorectal C9-5 transducer was used with an IU-22 or HDI-5000 US unit (Philips Medical Systems, Bothell, WA, USA). The US transducer was equipped with a commercial needle guide (Civco Inc., Kalona IA, USA) that was equipped with embedded miniature sensors (Traxtal Technologies Inc., Toronto, Canada) to enable spatial tracking and registration with MR images in six degrees of freedom.

Using the positional and orientation information from the tracking sensor attached to the US probe, the initial 2D-US data of the prostate was automatically reconstructed into a volumetric US image with an US sweep of the gland. Registration of the volumetric US with the prior MR images was done using manual visual methods at an adjacent workstation that was visible to the physician operating the TRUS. After registration, the real-time TRUS image was automatically fused with the same plane corresponding multiplanar reconstruction from the MRI on the same workstation at a frame rate of 10 frames/s.

The registration and fusion method and the registration error calculation have been previously described [17]. An US sweep of the entire prostate was obtained and reconstructed into a 3D-US image. Segmentations of the prostate in the MRI and the 3D-US were obtained by one radiologist for both registration and evaluation purposes. For registration, three orthogonal views of the 3D-US and MRI together with the MRI segmentation were visualized in custom software, which allowed manual mapping of the 3D-US onto the MRI (Figs 1,2). For evaluation, the same registration transformation that mapped the 3D-US onto the MRI was applied to the corresponding segmentations. Two measures of registration error were computed. The root mean square (RMS) distance was defined as the RMS of all distances between corresponding points on the registered segmentations. The maximum distance measure was defined as the maximum of all distances between corresponding points on the registered segmentations.

Based on all available imaging and pathology information with corresponding sextant location of previous positive biopsies, targeted biopsies of highly suspicious areas were obtained and sent to pathology.

Descriptive statistics (mean, median, range) were used to describe patient characteristics.

RESULTS

Five patients underwent biopsy and fiducial marker placement guided by real-time TRUS-MRI fusion. Of 11 targeted biopsies, eight showed prostate cancer (Table 1). In patient 2, one of targeted biopsy was highly suspicious but not diagnostic for cancer. This targeted biopsy was reported in the table as negative.

The TRUS procedure with fusion took ≈ 10 min. The mean (SD) registration error, computed as the RMS distance between the TRUS-based and MRI-based prostate segmentations, was 3.3 (0.4) mm. The mean (SD) maximum distance between the segmentations, typically found laterally near the rectal wall, was 12.7 (1.2) mm.

DISCUSSION

Real-time fusion of US and MRI images of the prostate is feasible and potentially able to identify regions of cancer for subsequent biopsy, which can be performed using MRI localization information without requiring the cost, difficulties or inconvenience of an MRI suite or MRI-compatible equipment.

Previous studies, using T2-weighted and/or MR spectroscopy, have investigated the cancer yield of MRI-guided prostate biopsy in a known or high-risk population [13,14,18,19]. Sensitivities and specificities for T2-weighted imaging with or with no spectroscopy in the aforementioned studies was 42.9–85%, and 22–97.9%, respectively, when considered on a core-by-core basis. These data are not inconsistent with the present findings where of the 11 targeted biopsies, eight were positive.

Due to the few samples, and perhaps more importantly due to the continuing development of our methodology, the present results must be interpreted with caution. In patient 1, a software problem prevented a durable real-time fusion of the US and MR images. In patient 4, the action of intercurrent hormone therapy (since the initial MRI) caused changes in the size of the prostate gland preventing reliable fusion. Nonetheless, with the available information from the location of previous positive biopsies and using the available imaging data, positive biopsies were obtained in both cases. Given positive results even with suboptimal fusion, inferences regarding the sensitivity and specificity of MRI-US fusion for detecting prostate cancer should not be drawn from the present data.

In fact, the degree of transducer insertion, the angle of insertion, the manual pressure upon the rectal wall and prostate, and resulting prostate deformation can lead to significant operator variability. Specifically, the largest discrepancy in segmentations was often noted at the posterior-lateral corner of the peripheral zone, which was geometrically deformed in different configurations by an endorectal balloon vs the smaller US transducer. This error does not preclude accurate axial target definition.

Current work includes methods to correct for prostate motion, organ deformation, and patient motion with dynamic compensation. US-based tissue tracking methodologies have been developed as well as deformable modelling for elastic or warped registration. Ultimately, any registration technique will be dependent upon the integrity of the underlying data (here, MRI). Thus, further validations of the sensitivity and specificity of MRI will be required to enable this registration approach to become a standard technique.

Regardless of the issues of MRI sensitivity for prostate cancer, biopsy with fiducial marker placement was the gold standard in the present study. The patients described here received

highly conformal IMRT. In the future, it might be possible to use this technique to guide other focal therapies, as the imaging guidance for such therapies develops and becomes more validated. We are currently in the process of planning canine studies of direct intraprostatic ethanol injection using this technique.

With continued development, MRI-US fusion might become a potentially rapid and cost-effective way to facilitate potential MRI-guided prostate therapies such as external beam radiation therapy, brachytherapy, cryotherapy, HIFU ablation, or direct injection of agents. In this way, multi-modality imaging with electromagnetic tracking of enabled devices can draw from the benefits of one method, while avoiding the limitations of another. Such a paradigm would preserve much of the utility of MRI (DEC MRI, MR spectroscopy), while avoiding many of the limitations of MRI-guided interventions (lack of access, time, cost) inherent to conventional MRI-guided techniques.

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Abbreviations

US, ultrasound; FOV, field of view; TR, repetition time; TE, time to echo; DCE, dynamic-contrast enhanced; IMRT, intensity-modulated radiation therapy; HIFU, high-intensity focused ultrasound; (2)3D, (two) three-dimensional; RMS, root mean square.

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FIG. 1.

Screenshot of the custom software used for registration and display of the fused MRI/TRUS data sets. The upper two and lower left panels show axial, coronal, and sagittal cross sections of the MRI volume using a grey-scale colour map. Superimposed with alpha blending using a blue-to-red colour map are multiplanar reconstructions (MPRs) of the reconstructed US volume. Also superimposed (green) is the segmentation border of the prostate in the MRI. Registration between the two volumes is achieved manually by manipulating the sliders on the left, which control the six parameters (three translational, three rotational) of the registration transformation. The volumetric registration is automatically converted into a registration between the real-time 2D-US image and the MRI volume. The lower right panel shows a live 2D-US image with a spatially corresponding MRI MPR in the background. Again, the MRI-based segmentation is superimposed in green. The subjectively adequate alignment between the MRI segmentation and the outline of the prostate in US suggests high registration accuracy.

FIG. 2.

After registration, the software renders MRI multiplanar reconstructions (left) that spatially correspond to the real-time TRUS image (right). Also rendered is the MRI-based prostate border segmentation (red). Again, note the subjectively adequate alignment of the MRI segmentation with the US image of the prostate. By blending the US image in and out of the display, a lesion can be identified in the MRI and then targeted using US guidance.

TABLE 1

Targeted and positive biopsies by patient

Patient number	Number of biopsies		Gleason score	
	Targeted	Positive	Initial	Targeted biopsy
1	2	2	9	9 (4 + 5)
2	4	2	6	6 (3 + 3)
3	1	1	9	9 (4 + 5)
4	1	1	7	7 (3 + 4)
5	3	2	8	8 (4 + 4) and 7 (4 + 3)