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Seminar article

Clinical application of a 3D ultrasound-guided prostate biopsy system

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Abstract

Objectives: Prostate biopsy (Bx) has for 3 decades been performed in a systematic, but blind fashion using 2D ultrasound (US). Herein is described the initial clinical evaluation of a 3D Bx tracking and targeting device (Artemis; Eigen, Grass Valley, CA). Our main objective was to test accuracy of the new 3D method in men undergoing first and follow-up Bx to rule out prostate cancer (CaP).

Materials and methods: Patients in the study were men ages 35–87 years (66.1 ± 9.9), scheduled for Bx to rule out CaP, who entered into an IRB-approved protocol. A total of 218 subjects underwent conventional trans-rectal US (TRUS); the tracking system was then attached to the US probe; the prostate was scanned and a 3D reconstruction was created. All Bx sites were visualized in 3D and tracked electronically. In 11 men, a pilot study was conducted to test ability of the device to return a Bx to an original site. In 47 men, multi-parametric 3 Tesla MRI, incorporating T2-weighted images, dynamic contrast enhancement, and diffusion-weighted imaging, was performed in advance of the TRUS, allowing the stored MRI images to be fused with real-time US during biopsy. Lesions on MRI were delineated by a radiologist, assigned a grade of CaP suspicion, and fused into TRUS for biopsy targeting.

Results: 3D Bx tracking was completed successfully in 180/218 patients, with a success rate approaching 95% among the last 50 men. Average time for Bx with the Artemis device was 15 minutes with an additional 5 minutes for MRI fusion and Bx targeting. In the tracking study, an ability to return to prior Bx sites ($n = 32$) within 1.2 ± 1.1 mm SD was demonstrated and was independent of prostate volume or location of Bx site. In the MRI fusion study, when suspicious lesions were targeted, a 33% Bx-positivity rate was found compared with a 7% positivity rate for systematic, nontargeted Bx (19/57 cores vs. 9/124 cores, $P = 0.03$).

Conclusion: Use of 3D tracking and image fusion has the potential to transform MRI into a clinical tool to aid biopsy and improve current methods for diagnosis and follow-up of CaP.

Keywords: Prostate; Cancer; Artemis; Biopsy; MRI; Diffusion weighted imaging

1. Introduction

"The discovery that would have the greatest impact on our field would be the development of accurate imaging of tumor within the prostate." —Patrick C. Walsh [1].

Imaging prostate cancer (CaP), while in a curable state, has proven elusive, despite a half-century of interest and effort. Virtually all major cancers can be easily imaged within the organ of origin, but not CaP. Thus, diagnosis of CaP is often fortuitous, materializing only when systematic biopsy, which is usually driven by an elevated PSA level, is positive [2]. However, recent developments in magnetic resonance imaging (MRI) technologies—3 Tesla magnets and a multi-parametric approach—have led to a promising advance in prostate cancer imaging. Moreover, fusion of ultrasound and MRI by a new technology appears capable of bringing those images to the patient for biopsy guidance.

Challenges to imaging cancer within the prostate include (1) histologic similarity of cancer and benign tissue in many cases, (2) heterogeneity of prostate tissue in aging men, (3)

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decreasing volumes of CaP found today as a result of early biopsy stimulated by PSA levels, and (4) limited resolving power of available imaging devices. Systematic biopsy often detects insignificant cancers [3], which cannot reliably be distinguished by available biomarkers [4], and treatment decisions based on biopsy alone may be problematic. Overtreatment of localized CaP has been increasingly recognized [5], and active surveillance is gaining traction as a first choice for many men judged to have 'low-risk' CaP [6,7]. In two groups especially—men undergoing active surveillance and those with elevated PSA levels but negative biopsies—the ability to image CaP within the prostate (or exclude it) could help clarify characteristics of the underlying pathology.

Recent advances in magnetic resonance imaging may soon alter the landscape of CaP diagnosis. As detailed below, MRI has evolved to yield images within the prostate that are approaching a considerable degree of diagnostic accuracy [8–11]. The increased accuracy is attributable to machines that employ powerful 3 Tesla magnets, diffusion weighted imaging, and dynamic contrast enhancement. However, direct prostate biopsy within MRI machines is largely restricted to research institutions [8]. We tested a new device (Artemis; Eigen, Grass Valley, CA), which allows biopsy site tracking in ultrasound and fusion of real-time ultrasound with MRI. FDA approval [510(k)] was granted to the manufacturer in May 2008, but testing to date has been entirely on phantoms. We became early adopters of this technology, hoping to increase accuracy of prostate tissue sampling by recording biopsy sites and incorporating multi-parametric MRI detail into the site selection process. Development of the new technology at UCLA has involved an integrated collaboration between urology, radiology, pathology, and biomedical engineering. The program goals are to improve accuracy of prostate biopsy, to develop a method for visual follow-up and tissue sampling of 'low risk' lesions and, potentially, to aid in focal therapy. Herein we present an initial experience with the device, based on studies in the first 218 men who underwent 3D systematic biopsy in 2009–2010, 47 of whom underwent MRI/TRUS fusion biopsy.

2. Magnetic resonance imaging of prostate cancer

Magnetic resonance imaging has been used to evaluate the prostate and surrounding structures for nearly a quarter century [12]. Initially, investigators utilized the increased signal-to-noise ratio from the use of endorectal coils to study T1- and T2-weighted imaging (T2WI) and spectroscopic imaging for local staging [13–16]. Standard T2-weighted imaging provides excellent resolution, but does not discriminate cancer from other processes with acceptable accuracy [17,18].

Diffusion-weighted imaging (DWI) and dynamic contrast imaging (DCE), products of the past decade, appear likely to increase accuracy of prostate cancer detection. When added to T2-weighted imaging, these techniques constitute a form of "multi-parametric" MRI. The use of multiple MR sequences in the detection of localized CaP has shown to improve sensitivity over any single parameter [19–23]. Furthermore, the use of multiparametric imaging may also enhance overall accuracy in cancer diagnosis [24,25]. The use of multiple parameters also appears to improve biopsy yield, both MR- and US-guided [11,26–29]. Spectroscopy has also been evaluated in this context, but has not been shown to improve diagnostic accuracy when added to other imaging parameters [30–33]. Spectroscopy via endorectal coil is used for preoperative staging, but appears to add little in the diagnosis of intracapsular lesions [8,34,35].

Dynamic contrast enhanced (DCE) MRI allows for the visualization of blood perfusion, via a bolus injection of gadolinium contrast during rapidly repeated scanning with high temporal resolution. The use of DCE MRI for the detection of prostate cancer has been validated for over a decade [15,16]. DCE, modeled using pharmacokinetic parameters, is thought to be able to accurately image vascular pathophysiology, such as angiogenesis [20,36]. Furthermore, prior studies have suggested a correlation of such parameters with the histologic grade of disease [37,38]. Both simple and complex models of DCE have been shown useful for the detection of prostate cancer [17,21,24,39,40].

Diffusion weighted imaging (DWI) involves the quantification of free water motion, also known as "Brownian" motion, such that a lower apparent diffusion coefficient (ADC) corresponds to greater restriction in free water motion. Prostate cancer tissues restrict free water motion, likely on the basis of increased cellularity compared with normal prostate tissue [41–43]. The addition of diffusion-weighted imaging (DWI) to prostate MRI improves sensitivity and specificity for both peripheral and central gland disease [44–49] and has been shown useful for localization of biopsy targets in high risk patients who are initially biopsy-negative [26]. The degree of diffusion restriction also appears to correlate with Gleason score, perhaps reflecting cellular density [48,50]. Low ADC values are reported to correlate with unfavorable histology on repeat biopsy in men on active surveillance [51].

3. MR technique and interpretation

In our current work, we utilize multiparametric MRI (T2WI, DWI, and DCE) to prospectively assess likelihood of prostate cancer, and to improve CaP detection through biopsy. A transabdominal coil is used (1) to minimize patient discomfort and (2) because with multiparametric techniques, the endorectal approach does not appear necessary for detection and grade stratification [8,52]. Imaging is performed on a Siemens TrioTim Somatom 3T (Siemens Medical Solutions, Malvern, PA) magnet with high-performance gradients using a multi-channel external phased-