Increasing Role of Functional MRI as Decision Making Tool in Management of Prostate Cancer Patients on Active Surveillance

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Purpose: Prostate cancer is often over-treated, as many men will not become symptomatic or die from their disease. Active surveillance (AS) is an attractive alternative to primary therapy with total prostatectomy or radiotherapy, buying time to determine if the disease needs to be treated and preserving function in many patients for over 5 years.[1] Active surveillance (AS) has been recommended as a "licensed therapeutic option" for this disease by both the American Urological Association and the European Urological Association. Patients on AS undergo periodic Transrectal ultrasound (TRUS)-guided biopsies for assessment of disease progression. TRUS, however, cannot reliably visualize cancer foci, with up to 40% of tumors being isoechoic. Furthermore, the regional distribution of biopsies, and hence the attribution to tumor location in the prostate relies on the expertise and somewhat subjective designations by the physician performing the procedure, and does not provide a 3D representation of tumor location. Functional MRI, including T2weighted, T1 non-contrast, T1 dynamic contrast-enhanced MRI (DCE-MRI), MR proton spectroscopy (MRS), and diffusion-weighted MRI (DWI) sequences have been shown to improve the sensitivity and specificity of tumor localization. In this study we utilize functional MRI to target suspicious regions in the prostate for AS patients using MRI-guided real time ultrasound (**MRIus**) image fusion in Artemis™ system (Eigen, CA).

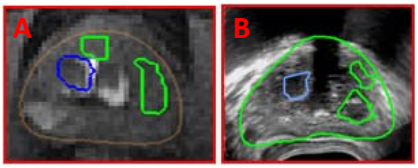

Figure 1. MRI–real time Ultrasound registration: (A) Contour of a cyst (blue) drawn on T2-weighted MRI (B) Contour coincide with the cyst, visible on real-time ultrasound after MRI/Ultrasound fusion.

Methods: Patients with Gleason score ≤6 with ≤ 2 cores positive and <50% of a single core, PSA ≤ 15ng/mL, age ≥35 and ≤75 were considered for active surveillance**.** Functional MRI datasets were acquired on GE Discovery MR750 3T MRI unit using standard clinical protocols. Images are loaded in ProFuse, a software application also from Eigen and regions of interest are annotated. **MRIus** image fusion in Artemis™ is part of the planning process during the biopsy procedure.[2] The MRI data, together with prostate and target contours are loaded on Artemis™. A 3-D TRUS is acquired just prior to biopsy by reconstructing sweeps of 2-D to 3-D. Both these volumes are subject to a semiautomatic segmentation that involves the specification of four or more points along the gland boundary. The triangulated gland surfaces from both modalities are registered using an adaptive focus deformable model followed by elastically interpolating the entire MRI volume to align with TRUS. During biopsy, as the operator visualizes the real time ultrasound volume on screen, motion correction runs automatically every few hundred milliseconds to compensate for any movement of the prostate after the acquisition of the 3-D volume. For better correlation of the prostate biopsy location with imaging, the inner tip of the biopsy is stained with ink. **Figure1** illustrates the precise coregistration of MRI and real time ultrasound.

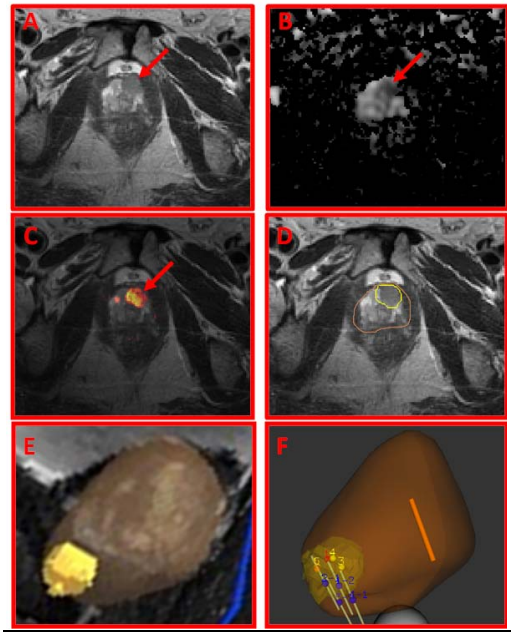

Figure 2. (A-B) T2-weighted MRI and Apparent Diffusion Coefficients (ADC) map, with arrow indicating tumor area; C) DCE-MRI, the brightest part representing the areas of rapid contrast wash-in and gradual washout; D) Contour (yellow) of suspicious area on T2 weighted MRI delineated by DCE-MRI and DWI. The prostate is also contoured (brown) and both volumes are transferred to Artemis™; (E-F) 3D representation of the prostate and tumor on ProFuse and Artemis, respectively, illustrating the extreme apical location of the tumor. The lines in F represent the biopsy locations.

Results: Since the FDA approval of the **MRIus** software two months ago, five AS patients underwent **MRIus** biopsies. Progression is defined if more than two cores are positive, and/or >50% involvement of any core and/or Gleason Score ≥ 7. Progression of disease was determined in one patient. The images from this patient are shown in **Figure 2**. **MRIus** biopsies determined Gleason 7 disease in the extreme apex of the prostate. The patient is a 67-year-old man who presented for evaluation of recently diagnosed cT1cN0M0 prostate cancer. After many years of stable PSAs in the low 4ng/ml range, he had a slightly higher PSA of 4.7ng/ml in September, 2011. Subsequent traditional TRUS was negative for malignancy, but showed a focus of high grade prostatic intraepithelial neoplasia in the left lateral base. A repeat TRUS-guided biopsy was performed on six months later, which showed Gleason 3+3 prostatic adenocarcinoma involving less than 10% of the core in the left lateral base and left apex. DRE revealed a large, smooth prostate with no discrete nodularity, mass, or induration. At this time he was a candidate for either active surveillance or primary radiotherapy treatment. The **MRIus** biopsy revealed Gleason 3+4 disease and the patient converted to treatment. The patient subsequently received radiotherapy.

Conclusions: The postponement of treatment and preservation of quality of life is of primary importance, particularly for men in their 50s and 60s. Since men in these age ranges most often have a long life expectancy, it is imperative that the window of opportunity for cure be preserved. Death due to prostate cancer occurs late, but is significantly greater in men observed versus those treated primarily. The key is to determine early those who are not good candidates for active surveillance. Recent reports show a 20-30% rate of conversion to treatment by 3 years. The men who require early conversion are probably those who have been understaged and/or undergraded by conventional assessments. **MRIus** fused biopsy is a more accurate way to target those lesions that might warrant conversion to treatment. If we can precisely take samples of the most worrisome areas, we can avoid subjecting patients to multiple biopsies but still closely monitor them for disease progression.