

## Comparison of TRUS vs. MRI guided biopsy in MRI apparent prostate cancers: Preliminary Results

Adam J Jung<sup>1</sup>, Fergus V. Coakley<sup>2</sup>, Antonio C. Westphalen<sup>3</sup>, Daniel B. Vigneron<sup>3</sup>, and John Kurhanewicz<sup>4</sup>

<sup>1</sup>Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States, <sup>2</sup>Department of Radiology and Biomedical Imaging, University of California San Francisco, <sup>3</sup>Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA, United States, <sup>4</sup>University of California San Francisco

**INTRODUCTION:** Prostate cancer is the commonest non-cutaneous cancer, and second commonest cause of cancer death in men (1). The diagnosis, management, and prognosis of prostate cancer are largely dependent on histopathology obtained by transrectal ultrasound- (TRUS-) guided biopsy. TRUS-guided biopsy uses B-mode and Doppler imaging to localize the prostate and systematically obtain anywhere from 6 to over 40, 18-gauge biopsy cores. TRUS localizes the prostate, however often does not visualize the malignant focus because 37% to 50% of cancers may be isoechoic or only slightly hypoechoic (2). Accordingly, TRUS-guided biopsy demonstrates reported false negative rates of up to 30% (3). TRUS-guided biopsy Gleason scores are also often discordant with prostatectomy specimens and under-grade cancers in up to 38% of patients (4), indicating TRUS-guided biopsy results also misrepresent tumor aggressiveness. These data indicate TRUS-guided biopsy is prone to sampling error, resulting in pathology that does not accurately depict the degree of tumor presence or volume estimated by percentage of tumor in positive cores. Multiple risk stratification schemes including the commonly used Epstein and D'Amico criteria predict prognosis and dictate the decision to undergo active surveillance versus definitive treatment. These criteria rely heavily on the histopathologic findings of Gleason grade and percentage of tumor seen in the core biopsy specimen (5,6), which in turn are invariably dependent on the location of the needle tip and the region of the prostate sampled. It is clearly bad medicine and poor science for such critical decision-making algorithms to depend on flawed data regarding tumor extent and aggressiveness. Endorectal mMRI uses anatomic T1 and T2 weighted imaging, diffusion weighted imaging (DWI), MR spectroscopic imaging (MRSI), and perfusion based dynamic contrast imaging (DCE) imaging to localize and characterize prostate cancers. Previous studies have demonstrated that endorectal MRI and MRSI improve tumor localization, staging, and volume estimation to allow non-invasive identification of prostate cancer (7-9). Similarly, apparent diffusion coefficient maps correlated significantly better with Gleason grade versus TRUS-biopsy in prostatectomy specimens with Receiver Operating Characteristic (ROC) areas under the curve (AUC) of 0.82 and 0.46 respectively (10). Recent advances have allowed for direct MR imaging- (MRI-) guided biopsies of the prostate (11). The next logical step is to obtain focused tissue biopsies of clear-cut cancer foci visible on mMRI.

**METHODS:** The IRB compliant retrospective study evaluated 15 consecutive patients obtaining both TRUS- and MRI-guided biopsy from December of 2010 to October of 2011. Of these, we evaluated 12 patients who had clear-cut cancer foci visible on mMRI agreed upon by two experienced, blinded radiologists. mMRI was considered positive for cancer based on at least 2 abnormal parameters including T2-weighted signal abnormality, diffusion restriction, abnormal metabolic changes on MR spectroscopy, and/or abnormal enhancement on dynamic contrast enhanced imaging. These patients underwent MR Imaging-guided guided biopsy within 1 year of initial TRUS biopsy, with two to three 18-gauge cores obtained from each suspicious region of interest. A single experienced pathologist reviewed all repeat biopsy tissue samples. Histopathologic findings including Gleason grade and score, percentage of positive cores, and percentage of tumor seen in each positive core were evaluated. We also evaluated change in risk stratification and change in management from active surveillance to treatment based on D'Amico criteria following MR I-guided biopsies. Images demonstrating a T2-weighted and DWI apparent cancer focus that was not clearly visible on TRUS are demonstrated in Figure 1a. Subsequent MRI-guided biopsy image of the region is depicted in Figure 1b.

**RESULTS AND DISCUSSION:** 9 of 12 (75%) patients with clear-cut cancer foci seen on mMRI had positive MRI-guided biopsy pathology for prostate cancer. The remaining 3 patients demonstrated no cancer on the MRI and TRUS-guided biopsies. One of the negative biopsied samples was 3mm on mMRI and possibly missed due to its small size. The remaining two lesions were high-grade prostatic intraepithelial neoplasia and glandular benign prostatic hyperplasia changes respectively on histopathology. **Gleason Score:** Of the 9 patients with positive MRI-guided biopsies, 7 patients were subsequently upgraded in Gleason score relative to their initial TRUS-guided biopsy Gleason scores. 4 patients had negative prior TRUS-guided biopsy results and were given first-time Gleason scores of 7 (4+3), 7 (3+4), 6, and 8. The mean increase in Gleason score after MRI-guided biopsy was 1 (95% CI 2.25 to -0.24;  $p = 0.089$ ) in the remaining 5 patients with both TRUS- and MRI-guided positive findings. **Percentage of cancer in positive cores:** Total percentage of cores positive for cancer increased in 8 of 9 patients with positive MRI-guided biopsies. The mean maximum percentage of cancer in positive cores was higher post MRI-guided biopsies (41.8%) relative to TRUS-guided biopsies alone (14.7%), with a mean increase of 27.2% (95%CI 1.23-53%;  $p=0.0416$ ). **Percentage of positive cores obtained:** Total percentage of cores positive for cancer increased in 7 of 9 patients with positive MRI-guided biopsies. The mean percentage of positive cores in MRI-guided biopsies (50.7%) was higher than for TRUS-guided biopsies (14.9%), with a mean increase of 35.8% (95% CI = 9.7-61.9%;  $p= 0.012$ ). **Risk stratification and management:** MRI-guided biopsy obtained histopathology led to an upgrade in risk from favorable to intermediate in 8 of the 9 patients based on D'Amico criteria. Overall, 7 of 9 patients with positive MRI-guided biopsy findings were on active surveillance or "watchful-waiting" prior to MRI-guided biopsy; and, MRI-guided biopsy histopathology led to a change in management recommendation to active treatment in 5 of these 7 patients.

**CONCLUSIONS:** We demonstrated that MRI-guided biopsies significantly upgraded percentage of cancer within each positive core, and total number of positive cores when compared to TRUS-guided biopsies in a small sample of patients with highly suspicious cancer foci seen on mMRI. We upgraded Gleason score in 7 of 12 patients, however the mean upgrade in Gleason score was not significant between TRUS- and MRI-guided biopsies, likely secondary to the relatively small sample size. MRI-guided biopsies offers a new paradigm in diagnosing and characterizing prostate cancer, with the potential to upgrade disease and alter management from active surveillance to treatment in patients with clear-cut cancer foci visible on mMRI. Findings must be further substantiated in standardized prospective trials with larger patient cohorts.

**REFERENCES:** [1] ACS Facts and Figures, 2011. [2] Vo et al. Ultrasound quart. 2001;17(3):171-6 [3] Rabbani et al. J urol 1998;159(4):1247-50. [4] Kvale et al. BJU international. 2009;103(12):1647-54. [5] Epstein et al. JAMA 1994;271(5):368-74 [6] D'Amico et al. Urology 2000;55(4):572-7. [7] Scheidler et al. Radiology. 1999;213(2):473-80. [8] Yu et al. Radiology. 1999;213(2):481-8. [9] Coakley et al. Radiology. 2002;223(1):91-7. [10] Bittencourt et al. Eur radiology. 2011. Epub 2011/09/14. [11] Hamborack et al. Radiology. 2011;259(2):453-61. NIH R01 CA137207-01

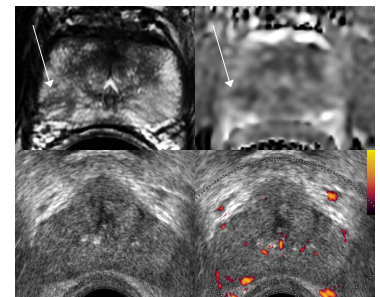


Figure 1a. T2-weighted (top left) and DWI (top right) visible cancer not seen on TRUS (below). Patient had negative 12-core TRUS-biopsy.

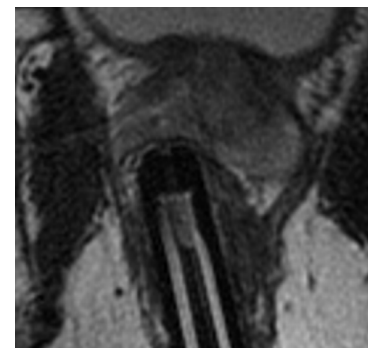


Figure 1b. Subsequent MRI-guided biopsy pathology: Gleason Score = 8, 60% of the core, 2/3 cores positive.