# Pilot: MRI Differences Associated with Dutasteride and Finasteride Treatments in Patients with Low Risk Prostate Cancer

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**Target audience:** Urologists, radiologists and researchers studying prostate cancer.

**Purpose:** Deregulation of the androgen receptor (AR) pathway plays an important role in prostate cancer progression. 5α-reductase enzymes convert testosterone to dihydrotestosterone (DHT). DHT has a higher affinity for AR than testosterone. One approach in regulating the AR pathway is to block DHT synthesis. Dutasteride and finasteride are drugs commonly used to irreversibly inhibit 5α-reductase. Multiparametric MRI (mpMRI) is a noninvasive technique used for staging and progression assessment in patients undergoing active surveillance. The purpose of this study was to determine if 5-ARI impacts the ability of mpMR imaging to discriminate between benign and low-grade prostate cancer tissues.

**Methods:** Fourteen men with biopsy proven G3+3 prostate cancers who underwent 3T mpMRI with an endorectal coil were studied. Seven patients were receiving 5-ARI treatment for at least a year at the time of the scan. Seven patients with untreated prostate cancers and comparable prostate volume, PSA density, and Gleason score were matched to the individuals in the treated group. For each subject, two regions representing cancerous and benign tissues were manually drawn on T2-weighted images, following areas of mpMRI concordance. MR apparent diffusion coefficient (ADC), signal intensity on high-b value (b=1350sec/mm$^2$) diffusion weighted images (DWI), coil-corrected[2], T2-weighted image intensity, and DCE MRI parameters: maximal enhancement slope, peak enhancement, and washout slope were calculated. Pharmacokinetically modeled parameters were determined from fits to an extended Tofts-Kermode ($K^{trans}$, $v_{ees}$)[3] and to a Luminal water model ($K^{trans}$, $v_{ees}$, $v_L$), which assumes Gd-DTPA cannot reach the luminal space, $v_L$[4]. Levels of prostate metabolites: citrate and choline detected during the $^1$H-MR spectroscopic imaging (MRSI) were also assessed.

**Results:** Figure 1 shows choline levels for treated and untreated patients in benign and cancerous regions. This figure is representative of the overall patterns we observe for the majority of imaging modalities: 1) better separation of benign and cancerous tissues in individuals treated with 5-ARI than for those untreated, 2) reduction in the coefficient of variation (COV) in both the benign and cancerous tissues for the treated group. COV was lower in the treated group compared to the untreated group for all parameters but T2w, $K^{trans}$, and $V_{ees}$. As shown in Table1, a logistic regression analysis yielded greater AUC values for the majority of imaging parameters (AUC was lower for T2w intensity values and citrate levels) in treated subjects when distinguishing between benign and cancerous regions.

| Modality | ROC-AUC Untreated | ROC-AUC Treated |
|---|---|---|
| T2w | 0.775 | 0.722 |
| High-b | 0.898 | 1 |
| ADC | 1 | 1 |
| Max Enh. Slope | 0.98 | 1 |
| Washout Slope | 1 | 1 |
| Max Peak Enh. | 0.837 | 0.944 |
| $K^{trans}$ | 0.796 | 1 |
| $V_{ees}$ | 0.571 | 0.674 |
| $V_L$ | 0.694 | 0.837 |
| $V_{cell}$ | 0.612 | 0.878 |
| Choline | 0.694 | 0.816 |
| Citrate | 0.694 | 0.49 |

Table 1: ROC-AUC for treated and untreated men when discriminating benign vs malignant tissues.

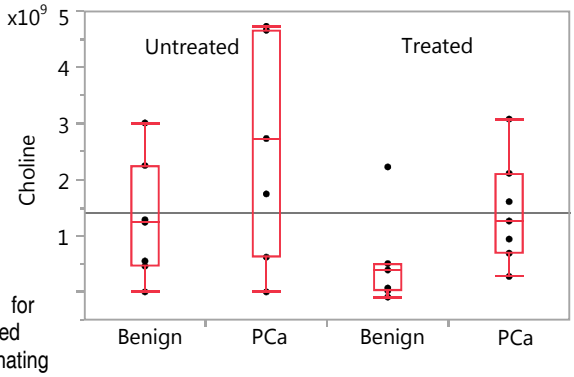


Figure 1: Box-plots comparing cholone levels in benign and cancerous (PCa) prostatic tissues for untreated individuals and those treated with 5α-reductase inhibitors.

**Discussion:** 5α-reductase inhibitors can have a profound effect on prostate tissues and associated imaging. When exposed to anti-androgen therapy, androgen sensitive glandular normal and BPH tissues quickly atrophy, decreasing the contribution of these tissues to MR measurements. The overall anti-androgen treatment effect is a decrease in the heterogeneity of the prostate tissues and a reduction in variability in MR measures, which allows cancer to become more apparent, potentially increasing diagnostic accuracy. The limitations of this study include small sample size, biopsy based Gleason grading of cancerous regions, and potentially unaccounted for differences between treated and untreated groups.

**Conclusion:** We report a clinically important finding that the majority of imaging parameters acquired during a routine prostate mpMRI scan demonstrate a better separation between low-grade cancerous and benign regions for prostate tissues exposed to 5-ARI. Pretreatment with 5-ARI may facilitate a better detection of low-grade prostate cancer and requires further exploration.

**References:** 1-Nacusi et al. Nat Rev Urol. 2011. 8(7):378-384. 2-Noworolski et al. JMRI 2010: 32(3): 652-62. 3-Tofts JMRI 1997;91-101. 4-Noworolski et al. ISMRM (2011).

**Acknowledgements**: NIH R01CA148708.