**Clinical Background and Significance**

PCa is the most common noncutaneous cancer among men in the United States. Approximately 1 in every 6 men will develop PCa during their lifetime, with the median age of diagnosis at 67. [1](#_ENREF_1)It is also the second leading cause of cancer related death, with 1 in 36 men dying from the disease. The National Cancer Institute estimates that 238,590 men will be diagnosed with PCa in 2013 and 29,720 will die from the disease.[1](#_ENREF_1)

PCa diagnosis usually begins by screening with PSA and DRE. Definitive diagnosis is made by random TRUS-guided biopsies, which are then used to provide the clinician with the proper Gleason score. The combination of these factors—as well as staging—determines the appropriate therapy and prognosis.

PCa screening has led to earlier diagnosis of smaller tumors and more localized disease. However, it is well known that the sensitivity and specificity of PSA and DRE are not optimal. In addition, DRE has a low predictive value at lower PSA ranges, and PSA yields many false positives.[2-4](#_ENREF_2) As such, a theoretical risk of over-diagnosis and treatment of low-grade—and possibly clinically insignificant—disease exists. Moreover, due to the random nature of biopsies, cancer located outside the routine sampling site can be missed and the extent of the cancer might be underestimated.[3](#_ENREF_3) [5](#_ENREF_5) For example, in a study by Mufarrij et al 45.9%-47.2% of patients who were candidates for active surveillance but underwent radical prostatectomy had a higher Gleason score on final histopathology than after TRUS biopsy.[6](#_ENREF_6) These inaccuracies may lead to inappropriate diagnosis, imprecise risk assessment and potentially avoidable morbidity.

**The Use of Magnetic Resonance Imaging in Prostate Diagnostics**

Early prostate MR techniques relied mostly on analysis of morphology via T1 and T2- weighted imaging. More recently, biologic and functional dynamic parameters have been added to MR analysis. Current prostate MR focuses on a multiparametric approach, where 2 or more imaging sequences—including anatomic and functional data—are used together to try to arrive to a diagnosis.[7](#_ENREF_7) As MR technology continues to evolve and improve, its role in PCA diagnosis, staging, treatment planning and follow-up has gained much attention.

*T2-Weighted Imaging and Prostate Anatomy*

T2WI sequences are crucial components of prostate MR imaging. T2WI is particularly useful in prostate analysis due to its excellent soft tissue contrast resolution, which can be maximized by using thin sections of 3-4mm and a small field of view of approximately 14cm.[3](#_ENREF_3),[8](#_ENREF_8) T2 sequences are the most helpful for tumor localization as they can clearly show overall prostate morphology, internal structures and prostatic margins.[3](#_ENREF_3)

The prostate can be divided into glandular and nonglandular components. The glandular components include the peripheral zone (PZ) and the central gland (CG), which are typically easily distinguishable on T2WI. The CG includes the central zone, transition zone and the periurethral glandular tissue.[9](#_ENREF_9) Other anatomical markers such as the urethra, verumontanum and ejaculatory are also often seen on T2WI.

Approximately 70% of the prostatic tissue is found in the PZ, which is high in water content and thus of higher signal intensity in T2WI.[9](#_ENREF_9) Seventy five percent of prostatic tumors are found in the PZ and normally show hypointense T2 signal when compared to the higher intensity PZ.[4](#_ENREF_4) [10](#_ENREF_10) However tumors can sometimes seem of similar intensity as the surrounding tissue and false positives can occur secondary to post biopsy changes/hemorrhage, hyperplasia or prostatitis, making diagnosis more challenging.[10](#_ENREF_10)

*Functional MR Sequences*

Even though T2WI is the mainstay of prostate MR, its overall performance in prostate cancer diagnosis is not optimal. The incorporation of two or more functional sequences in mpMRI has been shown to significantly improve the performance of MRI in cancer diagnosis.[11](#_ENREF_11) Functional sequences include diffusion-weighted imaging (DWI), dynamic contrast-enhanced (DCE) imaging and MR spectroscopic imaging (MRSI).

DWI is based on the free movement of water particles in tissue and measures the degree of motion restriction.[12](#_ENREF_12) Normal prostatic tissue is very glandular with plenty of water molecule movement. On the other hand, tumors have high cellular density and restricted water movement, which leads to decreased diffusion. Due to this restricted diffusion, tumors seem to be of higher intensity on DWI.[12](#_ENREF_12)

DCE-MRI provides a measure of tumor vascularity and takes advantage of tumor-induced angiogenesis in PCa. [13](#_ENREF_13)Increased vascularity in PCa results in earlier and higher peak contrast enhancement and a faster washout when compared to normal prostatic tissue. These known characteristics of PCa are helpful when trying to localize lesions.

Like DWI, MRSI can be helpful in lesion characterization as it provides information on the presence of certain metabolites in tissue. [7](#_ENREF_7) Choline and citrate are especially useful in the setting of PCa. Choline is critical in cell membrane synthesis and is thus usually elevated in cells with cancerous behavior.[3](#_ENREF_3) Healthy prostate epithelium synthesizes and secretes large quantities of citrate but levels are decreased in PCa.[14](#_ENREF_14),[15](#_ENREF_15) Therefore, an increase in the choline-to-citrate ratio on MRSI can be used as an indicator of malignancy.[8](#_ENREF_8)

**Acoustic Radiation Force Impulse Imaging**

ARFI imaging is an ultrasound technique that evaluates the mechanical properties of tissues. It generates short-duration acoustic radiation forces that result in tissue displacement. The response can then be measured for tissue characterization, with displacement being inversely proportional to stiffness.[16](#_ENREF_16) This characterization is of particular importance in prostate evaluation due to the gland’s complex and heterogeneous composition. Previous studies have shown that the central zone and PCA can be up to 3 times stiffer than PZ tissue.[17-19](#_ENREF_17) This finding can be explained by the PZ’s higher water content and is analogous to the higher signal intensity of the PZ on T2WI.

The potential of ARFI imaging to distinguish normal prostatic anatomy from pathologic tissue is promising in the future of PCa diagnosis and image guided therapies. B-mode US, which is currently used for real-time guidance in TRUS-guided biopsies, does not have the ability to clearly visualize PCa or to differentiate it from other normal structures or disease processes such as benign prostatic hyperplasia (BPH) or prostatitis.[17](#_ENREF_17) This has resulted in a systematic yet random approach to prostate core biopsies, with 6-12 cores routinely sampled from different anatomical regions.[20](#_ENREF_20) The ability to clearly distinguish PCa from other tissues could lead to targeted biopsies with increased sensitivity and resultant decreased morbidity. It could also aid in the development of targeted therapies for those with low burden of disease.

**1.** Howlader N, Noone AM, Krapcho M, Neyman N, Aminou R, Waldron W. SEER Cancer Statistics Review, 1975–2010, National Cancer Institute. Bethesda, MD, based on November 2012 SEER data submission, posted to the SEER web site, 2013. <http://seer.cancer.gov/csr/1975_2010> *(Accessed on June 08, 2013).* 2011.

**2.** Gosselaar C, Roobol MJ, Roemeling S, van der Kwast TH, Schröder FH. Screening for prostate cancer at low PSA range: the impact of digital rectal examination on tumor incidence and tumor characteristics. *The Prostate.* 2007;67(2):154-161 %@ 1097-0045.

**3.** Gupta RT, Kauffman CR, Polascik TJ, Taneja SS, Rosenkrantz AB. The state of prostate MRI in 2013. *Oncology.* Apr 2013;27(4):262-270.

**4.** Hricak H, Choyke PL, Eberhardt SC, Leibel SA, Scardino PT. Imaging prostate cancer: A multidisciplinary perspective1. *Radiology.* 2007;243(1):28-53 %@ 0033-8419.

**5.** Cornud F, Delongchamps NB, Mozer P, et al. Value of Multiparametric MRI in the Work-up of Prostate Cancer. *Current urology reports.* 2012;13(1):82-92 %@ 1527-2737.

**6.** Mufarrij P, Sankin A, Godoy G, Lepor H. Pathologic outcomes of candidates for active surveillance undergoing radical prostatectomy. *Urology.* 2010;76(3):689-692 %@ 0090-4295.

**7.** Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. *European radiology.* 2012;22(4):746-757 %@ 0938-7994.

**8.** Bonekamp D, Jacobs MA, El-Khouli R, Stoianovici D, Macura KJ. Advancements in MR imaging of the prostate: from diagnosis to interventions. *Radiographics.* 2011;31(3):677-703 %@ 0271-5333.

**9.** Jung AJ, Westphalen AC. Imaging Prostate Cancer. *Radiologic Clinics of North America.* 2012;50(6):1043-1059 %@ 0033-8389.

**10.** Hegde JV, Mulkern RV, Panych LP, et al. Multiparametric MRI of prostate cancer: An update on state‐of‐the‐art techniques and their performance in detecting and localizing prostate cancer. *Journal of Magnetic Resonance Imaging.* 2013;37(5):1035-1054 %@ 1522-2586.

**11.** Turkbey B, Choyke PL. Multiparametric MRI and prostate cancer diagnosis and risk stratification. *Current opinion in urology.* 2012;22(4):310-315 %@ 0963-0643.

**12.** Koh D-M, Collins DJ. Diffusion-weighted MRI in the body: applications and challenges in oncology. *American Journal of Roentgenology.* 2007;188(6):1622-1635 %@ 0361-1803X.

**13.** Noworolski SM, Henry RG, Vigneron DB, Kurhanewicz J. Dynamic contrast‐enhanced MRI in normal and abnormal prostate tissues as defined by biopsy, MRI, and 3D MRSI. *Magnetic resonance in medicine.* 2005;53(2):249-255 %@ 1522-2594.

**14.** Costello LC, Franklin RBa, Narayan P. Citrate in the diagnosis of prostate cancer. *The prostate.* 1999;38(3):237-245 %@ 1097-0045.

**15.** Kurhanewicz J, Swanson MG, Nelson SJ, Vigneron DB. Combined magnetic resonance imaging and spectroscopic imaging approach to molecular imaging of prostate cancer. *Journal of Magnetic Resonance Imaging.* 2002;16(4):451-463 %@ 1522-2586.

**16.** Nightingale K, Soo MS, Nightingale R, Trahey G. Acoustic radiation force impulse imaging: in vivo demonstration of clinical feasibility. *Ultrasound in medicine & biology.* 2002;28(2):227-235 %@ 0301-5629.

**17.** Zhai L, Madden J, Foo W-C, et al. Characterizing stiffness of human prostates using acoustic radiation force. *Ultrasonic imaging.* 2010;32(4):201-213 %@ 0161-7346.

**18.** Zhai L, Polascik TJ, Foo W-C, et al. Acoustic Radiation Force Impulse Imaging of Human Prostates: Initial< i> In Vivo</i> Demonstration. *Ultrasound in medicine & biology.* 2012;38(1):50-61 %@ 0301-5629.

**19.** Zhai L, Madden J, Foo W-C, et al. Acoustic Radiation Force Impulse Imaging of Human Prostates< i> Ex Vivo</i>. *Ultrasound in medicine & biology.* 2010;36(4):576-588 %@ 0301-5629.

**20.** Loch T, Eppelmann U, Lehmann J, Wullich B, Loch A, Stöckle M. Transrectal ultrasound guided biopsy of the prostate: random sextant versus biopsies of sono-morphologically suspicious lesions. *World journal of urology.* 2004;22(5):357-360 %@ 0724-4983.