

## Introduction

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# Seeing is believing

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For many of our patients, “seeing is believing.” In fact, some of the most tangible discussions about cancer are centered on an X-ray image. The X-ray image, brightly lit from behind, historically has given a physical quality to the relatively nebulous term “cancer.” Imaging studies in many solid organ cancers have improved to the point that we consider their presence on film to be vital part of the diagnosis and treatment paradigms.

Prostate cancer is the number one non-cutaneous malignancy and number two cancer killer in men. In fact, one in six men will be diagnosed with the disease in his lifetime [1]. This fact coupled with the poor sensitivity and specificity of the screening tests, i.e., digital rectal exam and prostate specific antigen (PSA), means that only about one in four men sent to the urologist in a referral population actually will be diagnosed with the disease [2]. In essence, a vast number of men are affected by our inability to actually image the cancer. However, this is just the beginning. Imagine yourself or a loved one undergoes a transrectal ultrasound guided prostate needle biopsy (against the advice of the American Academy of Family Physicians [3], but squarely in line with the American Cancer Society [4], and the test is negative. You may think this is fantastic news. Unfortunately, your happiness may be short lived because your urologist should tell you that the diagnostic false negative rate of prostate needle biopsy is approximately 30% [5]. This means that if your PSA goes up or your DRE changes you will need to repeat the uncomfortable process again. After subsequent blood tests show an increasing PSA level, your prostate needle biopsy is repeated; however, this time cancer is found. Unfor-

unately, no X-ray image or equivalent is available to gather your family and your thoughts around. Similarly, the treating physician has no reliable image information to help plan treatment. Furthermore, the PSA, DRE and biopsy Gleason grade [6] only predict “true” pathologic stage and grade with approximately 75% accuracy [7–9], and these tests can only predict freedom from cancer after treatment at 76% accuracy [10].

To make matters worse, your urologist almost certainly will inform you that some cancers, especially “good risk cancers” [11], may not need to be treated at all [12,13]. And that in many cases men will often die of another cause, particularly those with good risk cancers [14]. So if you have a good-risk cancer, you may be encouraged to simply place your cancer under surveillance. The bug-a-boo is that the same tests that were so unreliable for diagnosing your cancer will be used to follow it while it remains under surveillance.

This is not a small problem. Prostate cancer kills over 30,000 men a year in the US [15]. As the “baby-boomer generation” ages, these numbers will grow. This situation poses serious disease-management problems, particularly when we have only poor diagnostic tests and when some of these cancers will not be treated in favor of surveillance. A well informed public, cognizant of the morbidity associated with definitive prostate cancer treatment [16], will demand better diagnostic and therapeutic based imaging. If we could accurately image the prostate cancer, then screening and diagnosis in men would be easy, early detection would be the norm, and urologists and radiation therapists would have a road map of the disease for setting their sights and for

use as an effective means of planning and monitoring treatment as well as performing surveillance.

The urologic oncologist and radiation therapist now have no such road map. This makes careful observation of the disease more difficult. Active Surveillance protocols in Canada have started to mature [17], and more are planned in the US and Europe [18]. If these trials confirm the data retrospectively reported by the Connecticut Tumor Registry Data [14], then the growing population of “at risk” men will begin to ask the inevitable question of whether their disease could be treated “in situ.” This has already been done in an ad-hoc fashion using prostate biopsy based mapping studies [19]. Currently no clinical trials exist to validate this approach. Nevertheless the logic is clear: “If active surveillance is good enough for good risk disease, then perhaps focal ‘in situ’ based therapy of the disease is better.”

A reliable, minimally invasive imaging method is essential in order to provide accurate, early diagnosis and therapy options for men at risk for prostate cancer. We must have high quality images of prostate cancer to provide a tangible, objective means of planning, executing, and monitoring therapy. In the 21st Century, as physicians and scientists responsible for the care of men at risk for this common disease, we cannot allow prostate cancer to remain a nebulous entity.

## References

- [1] D.F. Penson, J.M. Chan and the Urologic Diseases of America Project: Prostate Cancer, *J Urol* **177** (2007), 2020–2029.
- [2] I.M. Thompson, D.P. Ankerst, C. Chi, P.T. Goodman, C.M. Tangen, M.S. Lucia, Z. Feng, H.L. Parnes and C.A. Coltman Jr, Assessing prostate cancer risk: Results from the Prostate Cancer Prevention Trial, *J Natl Canc Inst* **98**(8) (2006), 529–534.
- [3] AAFP. Summary of recommendations for periodic health examination. American Academy of Family Physicians, 2005.
- [4] R. Smith, V. Cokkinides and H. Eyre, American Cancer Society guidelines for the early detection of cancer, *CA Cancer J Clin* **53** (2003), 27.
- [5] N.E. Fleshner et al., Prevalence and predictors of a positive repeat transrectal ultrasound guided needle biopsy of the prostate, *J Urol* **158** (2007), 505–509.
- [6] A. Lopez-Beltran, G. Mikuz, R.J. Luque, R. Mazzucchelli and R. Montironi, Current practice of Gleason grading of prostate carcinoma, *Virch Arch* **448**(2) (2006), 111–118.
- [7] D.V. Makarov, B.J. Trock, E.B. Humphreys, L.A. Mangold, P.C. Walsh, J.I. Epstein and A.W. Partin, Updated nomogram to predict pathologic stage of prostate cancer given prostate specific antigen level, clinical stage, and biopsy Gleason score (Partin Tables) based on cases from 2000 to 2005, *Urology* **69** (2007), 1095–1101.
- [8] M.L. Blute, E.J. Bergstralh, A.W. Partin, P.C. Walsh, W.M. Kattan, P.T. Scardino, J.E. Montie, J.D. Pearson, J.M. Slezak and H. Zincke, Validation of Partin Tables for predicting pathological stage of clinically localized prostate cancer, *J Urol* **164** (2000), 1591–1595.
- [9] H. Augustin, T. Eggert, S. Wenske, P.I. Karakiewicz, J. Palisaar, F. Daghofer, H. Huland and M. Graefen, Comparison of accuracy between the Partin Tables of 1997 and 2001 to predict final pathological stage in clinically localized prostate cancer, *J Urol* **171** (2004), 177–181.
- [10] A.J. Stephenson, P.T. Scardino, J.A. Eastham, F.J. Bianco Jr, Z.A. Dotan, C.J. DiBlasio, A. Reuther, E.A. Klein and M.W. Kattan, Postoperative nomogram predicting the 10-year probability of prostate cancer recurrence after radical prostatectomy, *J Clin Oncol* **23**(28) (2005), 7005–7012.
- [11] A.V. D’Amico, M. Hui-Chen, A.A. Renshaw, B. Sussman, K.A. Roehl and W.J. Catalona, Identifying men diagnosed with clinically localized prostate cancer who are at high risk for death from prostate cancer, *J Urol* **176** (2006), S11–S15.
- [12] L.H. Klotz and R.K. Nam, Active surveillance with selective delayed intervention for favorable risk prostate cancer: Clinical experience and ‘number needed to treat’ analysis, *Can J Urol* **13**(Suppl 1) (2006), 48–55.
- [13] L.H. Klotz, Active surveillance for good risk prostate cancer: Rationale, method, and results, *Can J Urol* **12**(Suppl 2) (2005), 21–24.
- [14] P.C. Albertsen, J.A. Hanley and J. Fine, Twenty-year outcomes following conservative management of clinically localized prostate cancer, *JAMA* **293**(17) (2005), 2095–2101.
- [15] A. Jemal, R. Siegel, E. Ward, T. Murray, J. Xu and M.J. Thun, Cancer statistics, 2007, *CA Cancer J Clin* **57** (2007), 43–66.
- [16] D.C. Miller, M.G. Sanda, R.L. Dunn, J.E. Montie, H. Pimentel, H.M. Sandler, W.P. McLaughlin and J.T. Wei, Long-term outcomes among localized prostate cancer survivors: Health-related quality-of-life changes after radical prostatectomy, external radiation, and brachytherapy, *J Clin Oncol* **23**(12) (2005), 2772–2780.
- [17] L.H. Klotz, Active surveillance for favorable risk prostate cancer, *J Natl Compr Canc Netw* **5**(7) (2007), 693–698.
- [18] R.C. van der Bergh, S. Roemeling, M.J. Roobol, W. Roobol, F.H. Schroder and C.H. Bangma, Prospective validation of active surveillance in prostate cancer: The PRIAS study, *Eur Urol* (2007).
- [19] W.E. Barzell, R.I. Carey and M.R. Melamed, The utility of transperineal 3-dimensional pathological mapping in counseling patients seeking expectant management for low-volume prostate cancer. Abstract: Society of Urologic Oncology, 2006.