Technology's Gift: Improved Diagnosis and Treatment

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The past 20 years brought a significant drop in the average age of prostate cancer (PCa) diagnosis. The demographics changed but the predominant standard of care was still traditional: whole-gland (radical) treatment by surgery or radiation. Despite introducing robotic-assisted prostatectomy, and more precise radiation such as proton beam, side effects risks remained. For younger patients this has been particularly disappointing; while older men may already have urinary, sexual and bowel problems at the time of diagnosis, younger men typically have normal baseline function in all areas. In other words, they have more to lose.

Statistics on treatment side effects are difficult to pin down. Studies rarely line up "apples to apples". However, a 2009 study[1] of over 400 cases of whole gland (radical) treatment is particularly noteworthy. Patients reported information on their pretreatment, or baseline, levels of urinary, sexual and bowl function. After treatment, they were tracked for 36 months. The authors then compared their initial baselines with their function three years later. Patients fell into four different treatment categories: nerve sparing radical prostatectomy (NSRP), non-nerve paring radical prostatectomy (NNSRP), external beam (EB) or brachytherapy (BT). Table 1 shows the 3-year dysfunction rates as reported by the patients themselves:

TABLE 1	NSRP	NNSRP	EB	BT
Urinary dysfunction	57%	43%	83%	83%
Sexual dysfunction	92%	94%	74%	54%
Bowel dysfunction	25%	25%	66%	66%

On balance, the authors found that those with **normal** function before treatment experienced the **greatest loss** of function afterward. It's no wonder that younger patients seek better diagnostics and less damaging treatments!

Technologic improvements in diagnosis

Traditionally, men suspected of having PCa underwent a systematic biopsy called the Transrectal Ultrasound guided (TRUS) biopsy. In its earliest form, it involved taking three needle samples from each side of the gland for a total of six, so it was called a sextant biopsy, from the Latin meaning "sixth part." While the outline of the prostate can be clearly seen on ultrasound, TRUS is considered blind because ultrasound does not differentiate tissue within the gland; a doctor does not know what he or she is aiming at.

When it became clear that sextant biopsies were missing cancer in the outer zones, the method was improved in the mid-1990s by aiming needles more laterally, but many

[1] Chen R, Clark J, Talcott J. Individualizing Quality-of-Life Outcomes Reporting: How Localized Prostate Cancer Treatments Affect Patients With Different Levels of Baseline Urinary, Bowel, and Sexual Function. J Clin Oncol 2009 Aug;27(24):3916-22.

cancers were missed anyway (false negatives). The next advance in TRUS biopsies consisted of new planning schemes using more needles. By 2005, it was routine to take anywhere from 10-14 needles. Not surprisingly, the cancer diagnosis rate increased. However, false negatives still occurred up to 30% of the time. For men with continually elevated PSA's, this led to either repeat biopsies, or undergoing saturation biopsies with far more needles. TRUS biopsies are considered generally safe and well-tolerated, but associated risks include infection, complications including erectile dysfunction, and pain. This brings us to the present.

Today's newest biopsy technologies are generating better results for patients, young and old alike. Two key breakthroughs are MRI (Magnetic Resonance Imaging) and fusion:

- High resolution, software-enhanced **MRI (Magnetic Resonance Imaging)** prostate scans provide detailed images of suspicious areas or masses within the prostate. MRI imaging is done in a radiology center and interpreted by a radiologist who is expert at reading the images. A report is sent to the urologist.
- **Fusion** is the merging of MRI images from a CD with real-time ultrasound in a urologist's office. It is also called co-registration, because the MRI and ultrasound images are precisely lined up to merge the two into one. It requires special software available to urologists; the computer generates a virtual 3D image of the gland showing the suspicious area within. This makes it easy for a urologist to interpret the image, and advise the patient as to whether a biopsy is necessary or not.

Due to these advances, **targeted** biopsies offer new benefits.

a) When the doctor can "see" suspicious areas using fusion, he/she can guide needles directly into the core of the suspected tumor and confirm the placement of the needles on real-time ultrasound. Thus, the biopsy process is no longer random or blind.
b) Capturing cells from the core gives the most accurate diagnosis of aggression. Tumors tend to harbor the most dangerous cells at the center. Thus, if low-risk cells are found, the doctor and patient can consider a less aggressive treatment, perhaps deciding on Active Surveillance or a minimalist focal treatment. On the other hand, if aggressive cells are found, a more aggressive treatment may prove beneficial.

Technologic improvements in treatment

To paraphrase an old saying, if all you have is a "blind" biopsy (and you believe prostate cancer is multifocal), then finding even a small amount of prostate cancer, regardless of aggression level, implies the necessity to remove or radiate the entire gland. But Table 1 shows the potential for lingering side effects.

Patient demand is spurring the development of effective treatments with better quality of life. Just as new imaging is improving biopsy procedures, so too it is transforming treatment. Image guidance allows minimal-to-non invasive ablation (destruction) of the entire gland. Imaging can also be used to confirm the ablated site soon after it's over, and to follow treatment results over time. Ablation of tissue within the body is done without

surgery or radiation by applying extreme heat or cold (thermal destruction), which immediately destroys cancer cells and their blood supply. Finally, for properly qualified patients, image-guided treatment can be directed for focal (targeted) ablation.

NOTE: Radiation is not considered true ablation because its affects are not immediate. It damages DNA gradually, such that cancer cells can't reproduce. After radiation, a patient's PSA may not reach its lowest point for up to two years, and may "bounce" after brachytherapy. After ablation, success is confirmed by a PSA test a few months later. Another difference between ablation and radiation lies in the ability to confirm tumor destruction almost immediately after treatment via imaging—with ablation, this is possible, but with radiation it is not.

HIFU: High Intensity Focused Ultrasound brings a treatment breakthrough

Ultrasound is the use of sound waves at a frequency unable to be heard for medical purposes. The frequency can be varied for different purposes. For example, imaging ultrasound is absolutely harmless and is routinely used to monitor fetal development within the womb. However, by changing the ultrasound frequency, intense heat can be created at a desired endpoint.

High Intensity Focused Ultrasound (HIFU) for localized prostate cancer is a way to deliver heat energy to targeted tissue within the body. To treat prostate cancer, sonic energy at a different frequency from imaging is focused *precisely* into targeted tissue. The waves pass harmlessly through all other tissue in their path, so they only destroy what's intended. Real time imaging identifies the neurovascular bundles in order to preserve them, and software for Tissue Change Monitoring assures the optimum amount of energy is delivered where it is needed so unwanted destruction does not occur. Thus, treatment can be customized for each patient's unique anatomy and disease.

The advantages of HIFU include:

- Outpatient procedure
- Noninvasive (no puncturing of skin)
- Real time imaging and tissue change monitoring assure both accurate destruction and protection of healthy tissue
- 92% of men successfully treated[2]
- Low risk of side effects (0ver 99% continence and 70% potency[2)]
- Can be done as a focal treatment
- Can be done as a salvage treatment for localized radiation recurrence
- Rapid recovery and return to normal activities

As an alternative to prostatectomy and radiation, HIFU has been used internationally for over a decade in over 30 developed nations to successfully treat prostate cancer. The next article examines clinical breakthroughs that make ablation treatments like HIFU increasingly appealing.

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[2] Ahmed, HU. High-intensity-focused ultrasound in the treatment of primary prostate cancer: the first UK series. BJC 2009;101:19-26.