

IMAGE-GUIDED MINIMALLY INVASIVE THERAPY

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<1>INTRODUCTION</1>

The field of image-guided minimally invasive procedures has undergone a revolutionary change in the past decade. We have seen the development of advanced image-guided therapies for treatment of many different diseases, ranging from brain tumor resection and treatment to magnetic resonance (MR)-guided prostate brachytherapy and MR-monitored thermal therapies, such as cryotherapy. In the field of urologic oncology, today there are many image-guided procedures for obtaining diagnoses and guiding and delivering treatment. These range from simple biopsies to image-guided tumor ablations.

Minimally invasive therapy is used to treat the disease by operating through natural body openings or small incisions, thereby reducing the cosmetic or loco-regional tissue damage and the potential complications of open surgery. By reducing the need for invasive surgery, hospitalization is shortened, with fewer complications and faster recovery. These procedures have been allowed by the development of improved surgical techniques and, perhaps more importantly, improved imaging techniques. Because direct visualization without surgical intervention is not possible, the ability to combine multiple imaging modalities to plan and execute the surgery has permitted the full use of the new surgical techniques. This combination of imaging and therapy is known as image-guided therapy (IGT).

The purpose of IGT is to integrate the anatomic and physiologic information acquired before treatment with the therapy methods and allow the control and guidance of the treatment while it is being performed to improve the accuracy of treatment delivery. Not only can image-guidance improve targeting of cancer tissue during therapy, but it can also spare adjacent tissues and organs from being damaged during treatment. IGT is a multidisciplinary field in which surgeons, radiologists, oncologists, and computer experts combine efforts to integrate imaging systems with therapy systems.

Image-guided minimally invasive therapy is experiencing rapid growth driven by the introduction of new imaging modalities and significant improvement of existing ones as well as improving computer performance. The most important advancements of this field include integrating preprocedure and intraprocedure imaging, further improving image quality, and testing the usability of the techniques in clinical settings.

<1>HISTORY</1>

IGT evolved over the years with major advances in image-guided neurosurgery spreading to other disciplines including urologic oncology. In many cases, brain tumors may visually resemble healthy tissue to the naked eye or the extent of tumor invasion may be obscured by overlaying healthy tissue. Before image guidance the procedures were performed without proper visualization of the extent of the tumor or its specific geometry.

In the past decade or so, MR imaging (MRI) and computed tomography (CT) techniques have improved enormously. We have seen rapid MR scanners with high field strengths become standard clinical tools in many radiology departments around the world. New multidetector CT scanners allow rapid acquisition of high-resolution CT data sets that can now be reconstructed in coronal or sagittal planes. As the technology has advanced, the impact of the image data has expanded. Now imaging alone diagnoses nearly all renal cell carcinomas. Imaging alone stages the extent of vascular invasion by a renal cell tumor and plans the surgical approach. three-dimensional (3D) reconstructions allow the surgeon to determine the feasibility of a partial nephrectomy.

The imaging of solid organs, both to identify pathology and to accurately locate critical structures has become the province of x-ray CT and MRI. CT has been used primarily for guiding biopsies, although the advent of “CT fluoroscopy” has stimulated use in guiding interventional procedures, such as radiofrequency (RF) ablation.

Intraoperative ultrasound (US) has been used with increasing success for many decades, particularly in the imaging of solid organs, which can be directly contacted by the probe, giving both excellent images and explicit orientation of the image. US is particularly useful in observing vascular structures, which are both important landmarks and vital structures to be avoided during the resection of solid organs. Laparoscopic US shares the imaging advantages of intraoperative use, but due to the small size of the imaging head and the offset required for endoscopic insertion, it can be more difficult to interpret the content and orientation of the images.

The penetration of real-time CT and MRI into the broad range of surgical procedures has been slow, due to the complexity and cost of their implementation and difficult access to the patient. In the case of MRI, additional obstacles have been the incompatibility of surgical tools, devices and operating room equipment with the

magnetic field environment and the challenge of interpreting the MR image, which may require extensive training and/or expert consultation.

The attractiveness of MRI for guiding simple procedures, such as biopsies, was recognized as early as the mid-1980s. Many of the initial obstacles of real-time MRI guidance were overcome when an open MR scanner was introduced to guide neurosurgical procedures in Brigham and Women's Hospital, Boston, MA in December 1993. This new revolutionary method was envisioned by Dr. Ferenc Jolesz—radiologist and neurosurgeon—in 1987 when he began to put together a team of collaborators to create the “operating room of the future”.¹ The 0.5 T intraoperative MR scanner was designed by GE Medical Systems (Signa SP) and installed in a designated MR therapy (MRT) suite.² The scanner has a vertical gap that allows the physician to enter between the two magnets and makes it easy to access the patient to perform treatment (Figure 7-1). Images are generated using fast sequences resulting in near real-time imaging without disruption of the procedure. Initially, the scanner was used to guide percutaneous or transcranial biopsies but currently is utilized in a variety of procedures from neurosurgery to prostate brachytherapy and biopsy.

Since then many other open configuration magnets have been introduced including 0.2 T vertical type magnets (Picker, Siemens) and shorter bore (Philips, Picker) magnets. Conventional 1.5 T magnets are also used for guiding various procedures. The main disadvantage of those scanners is difficult access to the patient during the procedure, while the advantage is higher field strength and therefore better image quality.

In the field of urology IGTs advanced significantly from lithotripsy – shockwave removal of kidney stones under US or fluoroscopy guidance – to MR-guided procedures. While fluoroscopy remains a very popular method of image guidance in urology, it bears the risk of radiation exposure to both patient and physician. The advances in CT imaging made it possible to perform CT-fluoroscopy in real time. These advances, including 3D reconstruction, play a large role in the guidance of urologic procedures including CT-guided tumor ablations and CT-guided prostate brachytherapy and biopsy. Ultrasound guidance still remains very popular in clinical urology mainly because of its lower cost, portability, possibility of real-time imaging and safety to both patient and urologist. Currently many centers successfully use transrectal US (TRUS) for guiding prostate biopsies and brachytherapy. While US is the main imaging modality used in guiding focused ultrasound surgery (FUS)

procedures, current research is increasing the potential for MR-guidance of FUS. Finally, advances in MR imaging including image reconstruction in multiple planes, a higher signal to noise ratio that allows excellent differentiation between tissues, and new contrast agents make feasible MR-guided diagnostic techniques such as MR-angiography and MR- spectroscopy. The creation of open interventional MR made MR-guidance possible for several urologic procedures including prostate brachytherapy and biopsy.³

<1>OVERVIEW OF CURRENT MR-GUIDED IMAGE-GUIDED APPLICATIONS </1>

The field of MR imaging is attracting considerable research attention. MRI is superior to any other method in brain tumor localization and assessment and therefore is an excellent method for surgical guidance. Tumor margins and extent can be well defined, which in turn can help guide tumor eradication with minimal damage to healthy brain tissue. MR-guidance for neurosurgery provides substantial help in performing brain tumor surgery.⁴ The use of computerized navigation and 3D modeling further enhances precise tumor resection.

These improvements in MR-guided neurosurgery techniques, including 3D modeling, have provided a framework for an MR-guided prostate intervention program guiding prostate cancer therapy with interstitial brachytherapy—the permanent placement of radioactive sources (commonly I-125) directly into the prostate. Prostate MRI, especially with combined endorectal and phase array coils, provides images of even higher resolution and is used in prostate cancer staging as well as in determination of extraprostatic disease with up to 82% accuracy.^{5,6} The T1 and T2-weighted images are helpful in the differentiation between post-biopsy hemorrhage and prostate cancer, which presents as a low T1 and low T2 lesion, while hemorrhage presents as a high T1 and low T2 lesion. Contrast enhanced images and prostate spectroscopy are of great importance in distinguishing between normal and cancerous tissues. Perfusion of bladder and prostate cancers may be increased relative to normal tissue which thus is detected as signal enhancement following intravenous injection of MR contrast agents, such as Gadolinium-DTPA, with relative peak enhancement, time-to-peak and wash-out being of great importance in distinguishing and characterizing cancer.^{7,8,9} Added value comes from spectroscopy where metabolic differences can distinguish between cancer and healthy tissues. Normal prostate

metabolism is characterized by high citrate and low choline/creatinine levels, while these ratios are reversed in cancerous tissue.¹⁰ Prostate multivoxel spectra conveying metabolic information are superimposed on endorectal coil/phase array MR anatomic images allowing for precise localization of the tumor. Prostate imaging is now moving towards using higher field 3 T scanners, which provide higher signal to noise ratio images which allows for better visualization of prostatic substructures and increased MR-spectroscopy resolution.

The development of an interventional MR therapy (MRT) system made it possible to perform prostate brachytherapy under MR guidance. Even at lower field strength than routinely used for prostate cancer imaging (0.5 T versus 1.5 T) MRI provides images of good quality for target visualization, as well as identification of the urethra and rectum (see Figure 7-2 for comparison of 1.5 T and 0.5 T images). Computer software has been developed to provide dosimetry analysis used for both treatment planning and monitoring based on intraoperative MR images.¹¹ Image processing methods adapted from brain surgery are available to further facilitate precise radiation delivery to the prostate gland while sparing surrounding tissues. Currently, treatment delivery with a robot assist system is being developed and tested to improve radioactive seed placement.

After installation of the first interventional magnet at Brigham and Women's hospital in 1993 several other centers were created at teaching hospitals around the country including Stanford University, the University of Mississippi and Allegheny General Hospital in Pittsburgh. Since then the number of centers is growing and now includes many more sites in the US and overseas.

The great strength of MRI lies in its sensitivity to temperature changes.¹²⁻¹⁴ This sensitivity allows for monitoring the delivery of several thermal energy treatments, including RF and laser therapy for brain tumors, and cryotherapy and high-intensity focused US surgery (FUS) for breast, prostate, liver, and uterine lesions. Currently, MRI is a very useful guidance method for cryotherapy—tumor ablation by use of freezing—because it allows monitoring of the size of the ice ball in multiple dimensions.⁴ Intraoperative MR images are used to depict the slow expansion of the ice ball as well as tissue damage caused by the freezing process.

MR-guided FUS is a very promising method for noninvasive cancer treatment. While other minimally invasive therapies require direct insertion of special probes to reach the tumor, this method uses a high-intensity US beam focused on the target

lesion (as seen on the MR image) without disruption of skin and other tissues. FUS is based on the use of acoustic energy and its secondary thermal effect, which causes thermal coagulation of the target tissue. As early as 1955 it was clinically shown that FUS was capable of destroying mammalian tissues.¹⁵ Broad use of this treatment method has been hindered by lack of appropriate image guidance techniques for the tumor targeting and most importantly real-time monitoring of temperature changes. The introduction of MR-guidance provided an excellent method for monitoring treatment planning and delivery with direct temperature mapping (using MR phase-contrast techniques), as well as posttreatment confirmation of necrotic tissue changes.⁶ Using the MR images the physician can identify the target lesions, and temperature change during treatment delivery is monitored using MR temperature maps. A special transducer moves from one spot to another according to a pretreatment plan until the entire volume is treated. To date this method has been successfully used in the treatment of breast fibroadenomas, cancers and uterine leiomyomas.¹⁶⁻¹⁸ Application of this treatment in prostate cancer, liver lesions and brain tumors is currently under investigation.

<1>IMAGE-GUIDED THERAPY: ROLE OF IMAGE PROCESSING/1>

The key to IGT is the *integration* of a coordinated image process with the therapy process. Early problems with IGT were lack of integration of the imaging with therapy instruments, as well as difficulties with image display and processing especially when using MR imaging. As the image processing technology improved, feedback from imaging to the therapy became possible and the role of imaging became more prominent, using MRI for intraoperative guidance. As the processing improved, imaging became almost instantaneous or “real-time,” allowing for tight integration of imaging and therapy.

There are several components critical to all image-guided therapies; these are: planning, targeting, navigation, control, and monitoring. Pretreatment planning allows for the assessment of the approach that will provide the most effective eradication of the tumor and at the same time the least damage to the surrounding vital organs. For example, when delivering radiation therapy, pretreatment dosimetry planning determines the volume of the target and the placement of radiation sources. Targeting during IGT refers to precise pretreatment localization of all tumor targets that need to be treated and is essential for precise navigation of equipment during treatment

delivery. Navigation refers to the guidance of surgical equipment during procedures to target the tumors precisely and spare healthy tissue. Current research efforts in the field of navigation are directed towards automatization of the procedure and increasing the use of surgical robots.^{19,20} Real-time controlling and monitoring of the treatment delivery by means of intraoperative imaging allows for necessary adjustments of the therapy to reflect movement of the tissues and permits alterations of the plan in response to initial therapy.

Many different image postprocessing techniques have been developed to allow use of anatomic and functional information to improve tumor detection and treatment planning. These techniques include image segmentation, fusion, and registration. The purpose of image segmentation is to distinguish organs or structures of interest (e.g., prostate or its peripheral zone [PZ]) from the surrounding organs and tissue in order to perform volumetric and shape analyses, as well as treatment planning (see Figure 7-2). This is currently done by either manual outlining of the structure of interest or by semiautomated methods.²¹ The future of medical image segmentation is to automate the process and replace manual segmentation.^{22,23} Registration is a technique used to match images taken using different modalities, the same modality at different time points, or different imaging sequences (see Figure 7-2). The process involves mapping one image into the coordinate system of another image. Fusion is the merging of the anatomic and functional information provided by different imaging modalities into a single volume in order to provide better information of the underlying anatomy and tissue characteristics (Figure 7-3). Applications for fused images include not only IGT but also minimally invasive diagnosis and treatment planning.

<1>IMAGE-GUIDED MINIMALLY INVASIVE PROCEDURES IN UROLOGY </1>

Many of the image-guided minimally invasive procedures in urologic oncology are directed towards diagnosis and treatment of prostate cancer. In prostate procedures, IGT and diagnosis can be guided by different image modalities; transrectal US (TRUS) is the most widely used method. TRUS provides good delineation of the prostate margin, simplicity of imaging, relatively low cost compared to other modalities, and availability. TRUS is a widely used technique for guidance of both prostate biopsies and brachytherapy. However, the positive predictive value of this method remains quite low (17% to 57% for hypoechoic lesions as summarized by

Boges et al.²⁴). Currently research focuses on improving the accuracy of TRUS in detection and staging of prostate cancer including power and color Doppler, 3D imaging and elastography.

CT-guidance was used primarily for prostate biopsies but has also been used in prostate cancer therapy guidance.²⁵ CT provides clear visualization of prostate boundaries with high spatial resolution and contrast among different organs. Additional placement of a Foley catheter in the bladder allows for good visualization of the urethra that helps avoid urethral damage during treatment delivery.

MR-guidance of prostate procedures grew in importance after the development of the interventional MR scanner described above. Compared to US and CT imaging, MR provides superior visualization of the prostate and its zonal anatomy, tumor location, as well as depiction of surrounding vital organs like the rectum, neurovascular bundles (NVBs), and urethra.

Minimally invasive image-guided procedures for treatment of early stage organ-confined prostate cancer include cryotherapy; CT-guided brachytherapy (CTBT); 2D transrectal US-guided brachytherapy (USBT)—both with and without external beam radiation therapy, with and without neo-adjuvant hormonal therapy; MR-guided brachytherapy (MRBT), with and without external beam radiation therapy; FUS; and US- and MR-guided biopsy.

In general, the group of patients that may benefit from IGT as monotherapy for prostate cancer is comprised of men with organ-confined disease. Lieberfarb et al.²⁶ showed that in low risk patients with the following: clinical stage = T2a (according to the American Joint Commission on Cancer Staging—AJCC system), PSA = 10 ng/ml, and = 50% positive biopsies, the likelihood of extracapsular extension (ECE) with or without positive margins was 18%, and seminal vesicle involvement was 2%. For an overview of prostate therapy outcomes see Jani and Hellman (2003)²⁷ and Peschel and Colberg (2003).²⁸

<2>THERAPY</2>

<13>Cryotherapy</3>

Cryotherapy refers to the application of low temperatures to necrotize the tumor. In addition to its use as a primary treatment for prostate cancer it has also been used as a salvage therapy after failure of radiation therapy.²⁹⁻³¹ Cryosurgery was first proposed as a treatment for prostate disease in 1966.³⁰ In the following years, several open

transperineal procedures were performed under visual control. Because of many serious posttherapy complications, including urethro-cutaneous and urethro-rectal fistulas, cryosurgery was not commonly used until its revival with US guidance in 1993.³³

<4>Procedure</4>

Cryotherapy is usually performed with the patient placed in the lithotomy position and placed under general anesthesia. The specific technique and the number of freezing cycles vary slightly between centers, with 2 cycles used most commonly. After positioning of the TRUS probe, multiple suprapubic cryoprobes are placed using US guidance. To prevent damage to the urethra, a warming urethral catheter is placed. Thermal sensors are placed around the periphery of the gland to allow good temperature control in critical locations. At the end of the procedure, the cryoprobes are thawed and removed.

A newer approach to the use of cryotherapy in image-guided interventions is MR-guided cryotherapy, which has the major advantage of allowing clear visualization of the “ice ball” induced in the tissue, as it occurs. This allows for direct thermal monitoring of the treatment effect (Figure 7-4).

<4>Outcomes</4>

Because of the fairly recent revival of cryotherapy due to image guidance improvements, the long-term treatment results are still being investigated. Several groups reported their preliminary results following TRUS-guided cryotherapy. At 5 years, the progression-free rate defined as undetectable PSA (< 0.3 ng/ml) ranged from 48% to 77%, depending on patients' risk factors.^{34,35}

Complications of the treatment included incontinence, urethral sloughing, rectal fistula, and perirectal abscess.³⁴⁻³⁶ Patient self-reporting erectile dysfunction (ED) following cryosurgery was quite high compared to other minimally invasive prostate cancer treatments, ranging from 53% to 87%.³⁴⁻³⁷ A recent study showed pilot results on a new “nerve sparing” cryosurgery with the preservation of potency in 7 of 9 treated men at a median follow-up of 36 months (range from 6 to 72 months).³⁸

<3>Brachytherapy</3>

Interstitial brachytherapy refers to the permanent placement of small radioactive sources directly into the prostate. These are typically iodine or palladium sources contained within a titanium-jacket and measure about 4 mm in length. Similar to

cryosurgery, interstitial brachytherapy can be used as a primary treatment or as a salvage therapy after external beam radiation or initial implant failure.³⁹⁻⁴¹ Interstitial brachytherapy for prostate cancer was introduced in the 1960s by Scardino and Carton.⁴² The placement of radioactive seeds was performed using a freehand technique that did not provide homogenous seed distribution and resulted in both underdosing of tumors and overdosing of vital structures (rectum, urethra, NVBs). This resulted in many posttreatment complications, and the procedure was discontinued until its revival with US image guidance in 1983 by Holm and colleagues.⁴³ Further improvements in imaging techniques and technology resulted in the first MR-guided implant being performed in 1997 in Brigham and Women's Hospital in Boston.⁴⁴

<4>US-Guided Brachytherapy</4>

<5>Procedure</5>

A patient is placed in the lithotomy position, a Foley catheter is inserted, and general or spinal anesthesia is administered. The TRUS probe and probe stabilizer are positioned and the probe stepper is attached to the stabilizer. US images are obtained every 5 mm from the apex to the base. Some centers use designated treatment planning software for preplanning of the procedure.⁴⁵ The images are transferred to a computer connected to the US equipment. A 3D reconstruction of the prostate, urethra, and rectum is produced, and the dose of radiation to those structures is visualized. Dose-volume histograms and the number of radioactive seeds per needle are then calculated. The template for needle guidance is placed against the patient's perineum. After insertion of each needle a sagittal mode of the US acquisition is used to determine the depth of the needle insertion. Some centers use fluoroscopy to visualize seeds placement.⁴⁵

<5>Outcomes</5>

Although investigators used slightly different definitions of biochemical failure, the overall results of similar studies are quite consistent. At present, there are only a few studies presenting 10-years outcome data for prostate USBT. Biochemical disease-free survival rates after 10 years following treatment ranged from 70% to 87%.⁴⁶⁻⁴⁸ At 5 years, relapse-free survival rates reached 85% to 94% for the low-risk group, 77% to 82% for the intermediate-risk group, and 62% to 65% for the high-risk group.⁴⁹⁻⁵¹

Reported complications following USBT included urinary incontinence, urethral strictures, cystitis, urinary retention, prostatitis, proctitis, rectal ulceration, and rectal fistulas. Transient irritation and obstruction of the urinary tract 2 to 6 months after treatment was common, and about 10% of patients showed symptoms of acute urinary retention (AUR).⁵² Preservation of potency ranged from 64% to 79% at 3 years to 39% at 6 years. Pretreatment ED and a higher implant dose caused greater impotency.⁵³⁻⁵⁵

<4>CT-Guided Brachytherapy</4>

<5>Procedure</5>

The prostate gland immobilization before the procedure is similar to US-guided therapy. A Foley catheter, with radio-opaque wire to fluoroscopically localize the urethra, is placed, and general anesthesia is administered. Preoperative CT images collected using 5 mm slices are used to outline the prostate gland for treatment planning. Posteroanterior and lateral fluoroscopic images are used to determine needle position before seeds are deposited. The seeds are placed under fluoroscopic control.

Recently, CT-guided transischiorectal stereotactic brachytherapy has been introduced and tested.⁵⁶⁻⁵⁸ This approach can be used in patients with larger prostates. Axial CT images acquired every 5 mm are used for pretreatment planning. The patient is placed in the prone position, a Foley catheter is inserted, and spinal or epidural anesthesia is administered. A 3D stereotactic template used to guide needle placement is attached to the CT table and tilted at the same angle as the gantry. Electronic grids are superimposed on every second CT image to determine needle depth. CT images are used for needle visualization, placement corrections are introduced if necessary, and radioactive seeds are deposited.

<5>Outcomes</5>

Biochemical disease-free survival rates reached 99% for low, 96% for intermediate, and 90% for the high-risk group at a median follow-up of 4.5 years (2 to 8 years).⁵⁹ Treatment complications included urinary retention, incontinence, and rectal symptoms.

<4>MR-Guided Brachytherapy</4>

<5>Patient Selection</5>

The patient selection criteria for this program in our institution are: clinical stage T1cNXM0 (according to AJCC), PSA less than 10 ng/ml, biopsy Gleason score not more than 3 + 4, low cancer volume, and endorectal MRI demonstrating organ confined disease. Patients with prior transurethral resection of the prostate (TURP) are excluded. We do not exclude men with larger volume prostates, as pubic arch interference can be avoided in this approach. All patients undergo endorectal coil MRI for prostate cancer staging prior to the treatment visit (Figures 7-5 and 7-6). An MR radiologist assesses prostate gland volume, tumor location and volume, the presence or absence of extraglandular disease, seminal vesicle invasion (SVI), and possible spread to pelvic lymph nodes or bones.

<5>Procedure</5>

This multidisciplinary procedure uses many different computer, imaging, and technical skills and therefore requires the cooperation of specialists from various medical and nonmedical fields, including radiation oncologists, medical physicists, radiologists, anesthesiologists, urologists, nurses, radiology technologists, and computer scientists.

For the procedure the patient is placed in an open configuration 0.5 T Signa SP MR scanner in the lithotomy position. The patient is positioned on the table between two magnets with vertically oriented open space for easier access to the patient during the treatment (see Figure 7-1). A Foley catheter is inserted, skin prepared, the template for needle guidance placed against the patient's perineum and secured, and a rectal obturator is inserted (Figure 7-7). T2-weighted MR images are acquired in axial, coronal, and sagittal planes. The radiologist uses the T2-weighted images (see Figure 7-2, *right*) to identify the peripheral zone (PZ), urethra, and anterior rectal wall on each axial MR slice. These are then outlined using the 3D Slicer surgical simulation software designed and operated by members of the Surgical Planning Laboratory (SPL) at Brigham and Women's Hospital in Boston (Figure 7-8). The 3D Slicer is free, open-source software for two- and three-dimensional display, registration, and segmentation of medical images (see www.slicer.org for more information on 3D Slicer). Pretreatment planning, as well as calculation of the MRI-based peripheral zone as a clinical target volume (CTV), is then performed by the medical physicists using designated planning software.¹¹ The number of I-125 seeds per catheter and the depth of catheter insertion are calculated. The physicians then insert each preloaded catheter in the prostate gland. After every catheter insertion,

axial gradient-echo MR images are obtained in real-time and compared to the catheter's expected location according to the plan. Dose volume histograms (DVH) for the CTV, anterior rectal wall, and urethra are recalculated, adjustment of the catheter placement is performed when necessary, and seeds are deposited.

Approximately 6 weeks after the procedure, MRI and CT imaging of the prostate is performed to identify the location of radioactive seeds and calculate final DVHs. Since seeds can be well visualized on CT images, and the underlying anatomy is better depicted on MR images, MR-CT fused images are used to calculate dose distribution to the surrounding tissues (Figure 7-9).

<5>Outcomes</5>

Long term biochemical outcomes were compared for similar patients over similar time frame between MR-guided brachytherapy and radical prostatectomy by D'Amico et al.⁶⁰ At 5-years PSA control was 95% for brachytherapy and 93% for RP patients (median follow-up was 3.95 years and 4.2 years for brachytherapy and RP patients, respectively). The percentage of positive prostate biopsies was found to be a significant predictor of the time to post-brachytherapy PSA failure.

Short-term toxicity following MR-guided brachytherapy was rare, and no patient reported gastrointestinal or sexual dysfunction during the first month after treatment.⁶¹ Acute Urinary Retention (AUR) was observed in 12% of men within 24 hours of removal of the Foley catheter and was self-limiting within 1 to 3 weeks. MR-determined prostate volume, transitional zone (TZ) volume, and total number of seeds were found to be significant predictors of AUR on univariable analysis. The TZ volume was the only significant predictor of AUR on multivariable logistic regression analysis. The authors concluded that benign prostatic hyperplasia (BPH) that results in larger TZ volume, is the most important predictor of AUR. No urinary incontinence was seen at a median follow-up of 14 months (from 9 months to 2 years).⁶²

MR-guided brachytherapy is a very new approach thus there is only one report to date summarizing long-term toxicity.⁶³ Albert et al.⁶³ found low incidence of rectal bleeding (8%) and no urethral strictures at a median follow-up of 2.8 years (0.5 to 5 years). While ED reached 82%, two-thirds of the patients reported good erectile function after sildenafil (Viagra). No radiation cystitis was estimated at 4 years after MRBT.

Quality of life (QoL) outcomes collected using a previously validated questionnaire⁶⁴ are currently being assessed, and early reports indicate that MR-

guided prostate brachytherapy has better symptomatic outcomes than the conventional US-guided approach (J. Talcott, personal communication).

Current research projects will study further the radiation dose distribution to vital organs and its impact on the side effects. Image segmentation techniques are used to identify those important organs on endorectal coil MR images. Radiation dose to the organs can then be correlated with changes in patient-reported QoL.

<3> Focused Ultrasound Surgery</3>

<4>US-Guided High-Intensity Focused Ultrasound for Prostate Cancer</4>

This approach uses a high-intensity US beam that is focused on the target lesion which then undergoes thermal coagulation. In 1996, Galet et al.⁶⁵ were the first to evaluate clinical application of FUS for treatment of organ-confined prostate cancer.

<5>Procedure</5>

For the treatment the patient is placed in the lateral position and anesthetized. A suprapubic catheter is placed to assure urinary drainage, and an imaging and treatment probe is inserted into the rectum. The probe is surrounded with a balloon filled with cooling fluid to avoid overheating of the rectal wall. Target areas are identified using biplanar US imaging and the treatment is planned. Therapy is performed using a 2.25 to 3-MHz transducer.

<5>Outcomes</5>

Early results showed 56% to 100% therapy response rates when using Ablatherm probes, however the criteria of PSA failure after FUS are still under debate.⁶⁶⁻⁷² Blana et al.⁷³ reported outcomes following FUS for localized prostate cancer at the median follow-up of 22.5 months (4 to 62 months). After follow-up for 22 months 87% of patients had a PSA level below 1ng/mL, and 93.4 % had negative control biopsies. Reported treatment adverse effects included urinary tract infection, stress incontinence, rectal burn, rectourethral fistulas, urethral stricture, and impotence. MR-guided FUS for treatment of prostate disease is currently under investigation with initial animal tests appearing very promising. FUS treatment can be monitored by thermal maps and contrast enhanced MR (Figure 7-10).

<2>DIAGNOSIS</2>

<3 > US-guided Prostate Biopsy</3>

Currently, diagnosis of prostate cancer is aided using TRUS to guide the biopsy and is a widely used and accepted procedure.⁷⁴⁻⁷⁶ However, the sensitivity and positive predictive value of sextant biopsy remain quite low, 60% and 25%, respectively.⁷⁷⁻⁷⁹ The first transperineal prostate biopsies under US control were performed in the mid 1980s and a few years later TRUS become the primary modality for biopsy guidance.⁸⁰ Initially the sextant biopsy technique recommended the collection of six samples from the base, midgland and apex on both sides. Subsequent literature, however, showed the advantages of increasing the number of samples to 10, 11 or even 12 to detect cancer with up to a 96% success rate. Also it was recommended that the number of core biopsies increase with the prostate volume since bigger gland sizes introduced high sampling error and therefore required more sampling.⁸¹⁻⁸⁵ However the ideal number of cores is still not clear.

<4>Procedure</4>

Prior to the insertion of the endorectal probe the patient undergoes a digital rectal exam (DRE). The patient is positioned on the table in either lithotomy or lateral decubitus position. The ultrasound probe is inserted and stabilized and the prostate volume is calculated using transverse and sagittal imaging. If the procedure is performed in lithotomy position, the template for needle guidance is placed against the patient's perineum. The positions of needles are identified by grid coordinates on the template and the depth by the probe stepper attached to the probe stabilizer. These coordinates are used to guide biopsy under real-time US imaging. Biopsy is performed using an 18-gauge biopsy gun.

<3>MR-Guided Prostate Biopsy</3>

In addition to being an excellent method for guiding prostate cancer therapy, MR imaging also appears to be useful for guiding diagnostic biopsy.⁸⁶ Similar to its use in therapy, metabolic information from spectroscopy and dynamic contrast MR data can be combined with routine MR images to allow precise tumor targeting.

Our group has adapted the interventional MR system to perform MR-guided prostate biopsy.^{86,87} This transperineal technique does not use endorectal devices and provides an excellent diagnostic alternative for patients who have undergone rectal surgeries and in whom US-guided procedure is impossible to perform. An additional group of men who can benefit from MR-guided procedure are those with persistently rising PSA values and have had prior negative US-guided biopsies. Preliminary

feasibility results of this method in facilitating prostate cancer diagnosis are promising.⁸⁷ One of the unique aspects of this approach is the interactive imaging provided by using the 3D Slicer, as reported by Hata et al.⁸⁶, which facilitates T2 imaging in “near-real time.” D’Amico et al.⁸⁸ reported results of the procedure from two MRI-targeted lesions in a patient who could not undergo US-guided procedure because of previous rectal surgery. Several transurethral biopsies yielded negative results in this patient. Following MR-guided biopsy, cancer was confirmed in 15% and 25% of the 2 cores.

<4>Procedure</4>

Prior to the procedure, each patient undergoes endorectal coil MRI using a 1.5 T imaging system. The T1 and T2-weighted and contrast-enhanced images are collected, and multivoxel spectroscopy is performed. Using this information the radiologist identifies biopsy targets. Patient positioning for the procedure and initial preparation is similar to MRBT except that an endorectal obturator may not be used in some cases with previous rectal surgery. Subsequently, T2-weighted images are collected at 3.5 mm intervals in a 0.5 T interventional magnet. The information from preprocedure and intraprocedure images are correlated, and target lesions are identified. Computer software is used to calculate appropriate coordinates on the perineal template for transperineal needle insertion, as well as needle insertion depth. Additionally, 0.5 T T2-weighted images and intraprocedure fast gradient-echo images are loaded into the 3D Slicer software and displayed in an alternating fashion to provide real-time image guidance during biopsy. All target locations along with sextant biopsies of the PZ from the right and left apex, mid-gland and base are sampled using MR-compatible 18 gauge biopsy guns. **Figure 7-11** of the needle tip artifact in PZ after needle insertion and just before biopsy. This procedure is currently under general anesthesia as a day surgical procedure. It is well tolerated and offers a second line biopsy approach in selected patients.

<1>SUMMARY</1>

The areas covered in this chapter serve to illustrate the significant advances that have occurred in image-guided procedures and therapy for both diagnosis and treatment of prostate cancer. These are only some of the many new IGT applications available today. As the imaging techniques continue to improve and as surgical

approaches become even less invasive or completely noninvasive (as with FUS), the future looks very exciting for both urology patients and their doctors.

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FIGURE 7-1. Open 0.5 T MR system for performing image-guided procedures.

FIGURE 7-2. Prostate gland segmentation and registration. Segmentation identifies PZ (green) and central gland (red) in pretherapy endorectal coil MR (1.5 T, left) and MR-guided therapy images (0.5 T, right). Registration matches the segmented areas in the different images.

FIGURE 7-3. MR-CT image fusion of prostate gland. Registration allows fusion of MR image (left) with CT image to yield fused image (right). Black arrows indicate radioactive seeds.

FIGURE 7-4. Axial MR image showing a percutaneous cryotherapy probe in the lateral aspect of the left kidney, during an MR-guided cryoablation of a small renal cell carcinoma. The “black” ice-ball is clearly seen, note the close proximity of the left colon.

FIGURE 7-5. Endorectal coilMRI of prostate. Axial (left) and coronal (right) T2-weighted images provide superior visualization of the prostate and its zonal anatomy. White arrows indicate PZ.

FIGURE 7-6. Prostate cancer. Axial T2-weighted endorectal coilMR image shows low signal lesion located in PZ of the left side of prostate gland (white arrow).

FIGURE 7-7. Close up view of a patient in the open 0.5 T *Signa SP* magnet, during MR-guided prostate brachytherapy. The patient is in the lithotomy position and the perineal template used for catheter guidance is seen in the center.

FIGURE 7-8. Image segmentation using 3D Slicer surgical navigation software. PZ (green), rectal wall (red), and urethra (blue) are identified on T2-weighted image acquired in a 0.5 T scanner for MRBT planning.

FIGURE 7-9. MR-CT fusion of post-MRBT images. Posttherapy MR image (left) and CT image (middle) are fused resulting in MR-CT image (right) to allow better visualization of individual seeds and facilitate dose distribution calculation. Black arrows indicate radioactive seeds.

FIGURE 7-10. MR-guided focused US surgery of uterine fibroid. *A*, Coronal T2-weighted FSE image (4000/90) used for treatment planning. The sonication locations and sizes (green lines) were determined by the planning software from this prescription (and the tissue depth) and displayed on top of the treatment plan. During the treatment, the accumulated thermal dose (yellow region) was displayed on top of the treatment planning images. A dose threshold of 240 equivalent minimum{AU: **Change okay?**} at 43° C is displayed. *B*, Sagittal T2-weighted image (2500/98)

showing the treatment plan and the area that achieved the threshold thermal dose. *C–D*, Temperature sensitive phase-difference FSPGR images (39.9/19.7) acquired at peak temperature rise during two sonications, one imaged perpendicular to the direction of the US beam (Coronal, *C*), and one imaged parallel to the direction of the beam (sagittal, *D*). These images were used to estimate the thermal dose (blue line) for each sonication. *E–F*, Result of the treatment. *E*, Sagittal contrast-enhanced gradient-echo image (245/1.8) acquired 2 days after US therapy. The nonenhancing area (white arrow) is clearly seen. *F*, Gross pathologic cut specimen showing the central area of hemorrhagic necrosis.

FIGURE 7-11. Biopsy needle artifact. Real-time axial (A), coronal (B) view of prostate gland on pre- (left) and intra-MR-guided biopsy images (middle and right). The black arrow indicates the tip of the biopsy needle.

FIGURE 7-12. Biopsy needle artifact. Real-time 3 D view of prostate gland on intra MR-guided biopsy images.