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Chapter 5

High-dose-rate Brachytherapy for Prostate

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5.1 Introduction

High-dose-rate (HDR) brachytherapy for prostate was introduced in 1976 (Martinez et al. 1985) as a boost to external-beam radiotherapy (EBRT) for locally advanced or recurrent prostate cancer. In the intervening 40 years, HDR prostate brachytherapy has proven to be a valuable and versatile part of the armamentarium for controlling prostate cancer. HDR brachytherapy as a boost is an established standard of care (Yamada et al. 2012; Hoskin et al. 2013), with level 1 evidence for its efficacy demonstrated via a randomized trial (Hoskin et al. 2012) as well as being supported by a large volume of clinical evidence (Morton and Hoskin 2013). There is also mounting evidence for using HDR brachytherapy as monotherapy, largely for low- and intermediate-risk patients, but in some cases for high-risk patients (Demanes and Ghilzean 2014; Yoshioka et al. 2013). More recently, HDR brachytherapy has been explored as a salvage therapy or to provide a focal boost to dominant intraprostatic lesions (Lee et al. 2007; Yamada et al. 2014; Chen et al. 2013; Crook et al. 2014; Banerjee et al. 2015).

5.1.1 Rationale for HDR BT for Prostate

There are manifold reasons that HDR brachytherapy is an attractive treatment option for prostate cancer, whether such cancers are low-, intermediate-, or high-risk disease. It permits a high biologically effective dose to the prostate (Yoshioka et al. 2014), with the greatest possible conformity, while exploiting the radiobiological advantage provided by prostate cancer cells having a lower α/β than the normal tissues that surround them (Morton 2014). By determining the treatment dosimetry prospectively, based on actual needle positions as placed in the prostate, HDR brachytherapy reduces operator dependence relative to low-doserate (LDR) brachytherapy and obviates concerns regarding inter- and intra-fraction motion that are associated with EBRT. HDR brachytherapy is a robust and successful treatment for prostate cancer as evidenced by the abundant clinical data generated over the past three decades supporting its use (Hoskin et al. 2013; Yoshioka et al. 2014; Morton 2014).

Conventional radiotherapy delivers doses of \leq 70 Gy to the target volume. In the case of prostate cancer, several randomized controlled trials have demonstrated that doses in excess of 78 Gy are required to provide durable local control (Kuban et al. 2008; Zietman et al. 2010; Beckendorf et al. 2011; Al-Mamgani et al. 2011). For prostate cancer, local control is directly related to improved outcomes, both in terms of biochemi-

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cal disease-free survival and the risk of distant metastasis (Zelefsky et al. 2012). Dose escalation has, therefore, become the standard of care for prostate cancer. EBRT doses of 76–80 Gy delivered with intensity modulated techniques in standard 2 Gy fractions have become routine (Pollack et al. 2013). Further dose escalation with EBRT is limited by the tolerance of surrounding normal organs (Pollack et al. 2013; Morton 2014). HDR brachytherapy provides a means of delivering significant dose escalation to the prostate and, as required, seminal vesicles, with a margin while maintaining low toxicity and providing a relatively easy means of boosting sub-volumes of the prostate. Yoshioka et al. found that, for monotherapy, HDR brachytherapy delivers EQD2 doses (i.e., doses biologically equivalent to 2 Gy fractions) ranging from 89 to 128 Gy with a median of 110 Gy (Yoshioka et al. 2014), while HDR brachytherapy boost fractionation schemes deliver 110 to 120 Gy in combination with EBRT.

Like permanent LDR brachytherapy, HDR brachytherapy delivers a higher dose more conformally than any EBRT technique (Skowronek 2013). Both LDR and HDR brachytherapy have been shown to provide a significantly better normal tissue sparing, including for the rectal and bladder walls, than any advanced external beam technique, including volumetric arc therapy, proton therapy, or carbon-ion therapy; HDR brachytherapy, however, provided the lowest overall normal tissue doses (Georg et al. 2014). In particular, HDR brachytherapy was shown to provide much better urethral sparing than LDR brachytherapy, with a mean EQD2 to the urethra of 62.9 ± 13.3 Gy for HDR brachytherapy and 106.6 ± 12.9 Gy for LDR brachytherapy. This is achieved by implanting needles within and around the prostate and using anatomybased inverse planning to optimize the dwell positions and dwell times within the needles, with the needles in their actual treatment positions (Lessard and Pouliot 2001). With the energy of the ¹⁹²Ir source typically used for HDR brachytherapy and the degrees of freedom permitted by greater than 100 source-dwell positions per implant, HDR brachytherapy for prostate typically produces planned distributions that are finely sculpted around the organs at risk. Due to the high dose-per-fraction nature of this treatment, however, meticulous attention to detail is required to ensure that the dose is delivered as planned.

Beyond increasing the therapeutic ratio through good dosimetric geometry, HDR brachytherapy also exploits the radiobiological advantage provided by the low α/β ratio of prostate tissue, which is in the range of 1.2–3.1 and most likely lower than that of the surrounding normal tissue (Brenner and Hall 1999; Yoshioka et al. 2013). Prostate cancer cells are, therefore, more susceptible to large per-fraction radiation doses than are adjacent normal tissue cells, making HDR brachytherapy a very efficient means of escalating dose.

These factors combine to create a treatment that, despite considerable heterogeneity in dose and fractionation, produces consistently high rates of 5-year biochemical control, with 85% to 100% reported for lowrisk disease, 83% to 98% for intermediate-risk disease, and 51% to 96% for high-risk disease (Yoshioka et al. 2014; Morton 2014; Yamada et al. 2012). These results are achieved with low rates of severe toxicity; late grade-3 rectal toxicity is rare, while reported rates of late grade-3 urinary toxicity are less than 15% (Morton 2014).

5.1.2 Review of Guidelines for HDR Brachytherapy for Prostate

Both the American Brachytherapy Society (ABS) and The Groupe Européen de Curiethérapie of the European Society for Radiotherapy & Oncology (GEC-ESTRO) have published consensus guidelines for HDR prostate brachytherapy (Yamada et al. 2012; Hoskin et al. 2013). These guidelines emphasize the need for an experienced multidisciplinary team to enable successful treatment of prostate cancer. The skill sets required of such teams (Hoskin et al. 2013; Thomadsen et al. 2014) include expertise in:

- a. transrectal ultrasound (TRUS) imaging,
- b. CT or MR interpretation,
- c. transperineal procedures,
- d. use of the treatment planning system (TPS),

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- e. use of the remote afterloader, and
- f. patient care throughout the procedure.

The team should consist of a radiation oncologist, medical physicist, radiation therapists, nurses, as well as possibly an imaging specialist and urologist.

For physicists, the most relevant aspect of the medical guidelines are those used to assess the feasibility of prostate brachytherapy, including prostate size (generally <50 cm³, although it is possible to successfully implant larger glands (Monroe et al. 2008; Vigneault et al. 2016), public arch interference, and prior radiation or surgery to the pelvis (for example, for colon cancer).

No particular dose and fractionation schedule is recommended given the heterogeneity of prescription doses reported in the literature, all of which are associated with excellent outcomes. HDR brachytherapy for prostate is typically delivered in 2 to 4 fractions of 4 to 11 Gy combined with EBRT delivering 40 to 50 Gy in 1.8 or 2 Gy fractions, although a single brachytherapy for prostate cancer is becoming more common (Morton et al. 2011). Monotherapy HDR brachytherapy for prostate cancer is currently typically delivered in 2 to 6 fractions with doses per fraction ranging from 6.5 to 13.5 Gy.

The insertion of the needles is generally performed under US guidance, although some centers perform this task under MR or CT guidance. Dosimetry involves the accurate identification of prostate, with contouring of the critical structures—urethra, rectum, and bladder—also necessary to properly evaluate the treatment plan. It is good practice for the physicist to be present throughout the procedure to ensure that needles are properly placed, that all imaging and treatment equipment is functioning properly, and that the treatment proceeds according to plan.

5.1.3 Approaches to HDR Brachytherapy for Prostate

Just as there are many dose and fractionation schedules for HDR prostate brachytherapy, there are diverse approaches to implantation and planning. All techniques involve placing the patient under general or spinal anesthetic and then inserting needles transperineally, usually using a template for guidance, although a free-hand technique has been described (Kim et al. 2004). Needles are placed throughout the target volume using TRUS guidance. Use of MRI to guide placement is also possible, but currently most clinical implementations incorporate TRUS for intra-operative positioning. Once the needles are in place, images are acquired, the target and organ at risk (OAR) volumes are contoured, and the needles are reconstructed. If available, multiparametric MRI can be used to better delineate the target or identify dominant intraprostatic lesions (DIL). Anatomy-based inverse planning is then used to determine the dwell times for each dwell position. Following quality assessments of the treatment plan and the patient setup, treatment is delivered and needles are removed. At all steps, great care must be applied to ensure that any needle displacement is recognized and compensated for. All techniques produce excellent clinical results, and the choice of technique is a matter of institutional resources, logistics, experience, and personal evaluation of each technique's strengths and weaknesses.

5.1.3.1 CT-based Planning

CT-based HDR prostate brachytherapy (Martin et al. 1999) starts with transperineal TRUS-guided insertion of the needles with the patient in the dorsal lithotomy position. Following recovery from anesthetic, the patient is transferred to a CT scanner. Images are obtained and adjustments made to the needle positions to compensate for the displacement between needle tip and prostate that occur when the patient's legs are low-ered (Holly et al. 2011). The physician then contours the target and OARs (bladder, rectum, urethra) before the physicist or dosimetrist identifies the needles and creates the treatment plan. The patient is then taken into the HDR brachytherapy treatment vault, needle positions are checked and corrected again, and treatment is

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delivered. It is not uncommon to deliver more than one fraction per implant. In these cases, the needle positions relative to both the prostate and the template should be confirmed before each fraction.

5.1.3.2 US-based Intraoperative Planning

First developed at Kiel University, US-based HDR prostate brachytherapy uses TRUS images to both guide needle insertion and plan the treatment (Bertermann and Brix 1990). Live 2D US images are used to ensure appropriate positioning of the needles and, once they are in place, a 3D US volume is acquired, in which the target and OARs are identified. Typically, only the urethra and anterior rectal wall are contoured. Needles are then reconstructed and a plan developed. Treatment is then delivered immediately, without moving the patient out of implant position. Following treatment, the needles are removed and the patient recovered from anesthetic. Significant changes in the relationship of the implant to the anatomy occur when the patient legs are lowered and the TRUS probe is removed (Seppenwoolde et al. 2008). These changes result in significant increases in urethral dose with a simultaneous decrease in PTV coverage. It is not, therefore, recommended to deliver more than one fraction per implant using a TRUS-based plan (Seppenwoolde et al. 2008).

5.1.3.3 MRI-based Intraoperative Planning

In MR-based planning, needle insertion and planning can both be performed under MR guidance (Menard et al. 2004). A rectal coil is placed, and a template is sutured to the perineum orthogonal to the coil, which is used to image the prostate. Needles are placed under MR guidance and, after all needles have been placed, a final MR image is taken to develop the treatment plan. Due to the excellent soft-tissue imaging, structures such as the penile bulb and neurovascular bundles can be contoured, along with the prostate, urethra, bladder, and rectum. If the patient is treated in the MR suite, pretreatment MR scans can be taken to ensure that the needles have not migrated during the planning process. If the patient is moved to the treatment room, imaging, such as orthogonal radiographs or CBCT, must be performed to ensure that the needles have not migrated during the patient transfer.

5.2 Equipment and Commissioning

Appropriate commissioning and staff training have been identified as key measures for the improvement of quality and safety in all forms of HDR brachytherapy (Thomadsen et al. 2014). A number of excellent guidance documents on the general practice of brachytherapy, and HDR for prostate specifically, are available to use as a basis for the development of commissioning standards (Erickson et al. 2011; Fraas et al. 1998; Kubo et al. 1998; Nath et al. 1997; Rivard et al. 2004; Thomadsen et al. 2014; Hoskin et al. 2013; Yamada et al. 2012; Perez-Calatayud et al. 2012). As with any commissioning process, the purpose is both to ensure functionality of the equipment and process while providing baseline data for ongoing quality assurance (QA). Care should always be taken to develop institutional-specific commissioning tests as warranted.

5.2.1 General

Regardless of imaging modality, all HDR prostate brachytherapy procedures involve an HDR brachytherapy afterloader, a TPS, needles, and guide tubes. A substantial majority of clinical work flows also involve a template, stepper, an US unit, and a trans-rectal probe.

5.2.1.1 Template, Stepper, and Ultrasound System

Geometric and volumetric fidelity of the US system should be checked with an appropriate phantom. Accuracy of the stepper motion should be confirmed. Registration between the template displayed on the US unit

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and the physical template mounted on the stepper should be assessed using a water bath or phantom as described in the AAPM TG-128 report (Pfeiffer et al. 2008).

5.2.1.2 Treatment Planning System

Specifically for prostate TPSs, care should be taken to ensure that images from US, CT, or other imaging modalities can be transferred into the TPS. Geometric and volumetric accuracy of the patient images should be validated by scanning phantoms of known dimensions (Pfeiffer et al. 2008). Phantom elements are then contoured and the dimensions and volume measured using tools in the TPS. The results are compared to actual measurements and volumes. Additionally, the geometric accuracy of the digital representations of the applicators—both needles and templates (if necessary)—and the source positions should be checked. Many planning systems come with source registry data already installed and commissioned; this data should be verified via source registry sites (e.g., the joint AAPM/IROC Houston QA Center Brachytherapy Source Registry at http://rpc.mdanderson.org/rpc/BrachySeeds/Source_Registry.htm). The correct brachytherapy dosimetry parameters can also be verified against published values. As described elsewhere, care should be taken to ensure the correct formalism is used (line vs point). Hand calculations should be performed to compute dose over an array of selected points or checked with a third party calculation system (Figure 5–1)

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Treatment Time (s	sec.) per frac	tion:	407			
Desc	X(mm)	Y(mm)	Z(mm)	TPS Dose(cGy) 1 fraction(s)	BC Dose(cGy) 1 fraction(s)	PCT Diff
urethra midpt	-14.562	2.211	-144.569	861.80	861.090	-0.080
Ant rec wall pt	-14.562	27.948	-141.160	614.60	614.550	-0.010
prostate ant 1	-15.931	0.240	-114.886	872.43	871.200	-0.140
prostate leftiat	9.038	0.240	-136.942	956.06	955.840	-0.020
prostate rtlat	-40.066	0.240	-136.109	769.62	769.160	-0.060
					Points < 5 %:	5
				Points >	= 5 % & < 10%:	0
					Points >= 10%:	0
				Total Num	ber of Catheters:	24
				Total N	umber of Dwells:	202
		<u> </u>	10			
		Calculate	ea By:			

Figure 5–1 Secondary calculation performed for HDR prostate brachytherapy. The program independently performs a TG-43 calculation based on the DICOM coordinates of the dwell positions and times of the sources and calculation points.

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Figure 5–2 Reusable needles are mounted in a phantom and a test plan is delivered to radiochomic film to verify that each needle delivers dose to the intended position along its length.

(Nathet al. 2016). The integrity of data transferred to the afterloader should be tested as well. These tests should be performed during initial implementation as well as whenever a TPS upgrade is performed (Kubo et al. 1998).

5.2.1.3 Needles and Guide Tubes

The mechanical integrity of the guide tubes should be confirmed via visual inspection to ensure they are free of cracks or breaks. The connector mechanism should also be tested for functionality, and the overall length of the guide tubes should be measured (Brown et al. 2016). Reusable needles should be visually inspected and their lengths and connections tested before being put into clinical use. Additionally, each new reusable needle should have its dosimetric length tested by running a test plan and creating an autoradiograph (Figure 5–2). For disposable needles, a set of needles should undergo these tests, and individual needles should be visually inspected before use. It is important to note that metal needles usually have a solid tip distal to the end of the source channel, resulting in some dead space at the tip of the needle. Manufacturers specify the position of the first dwell position relative to the physical tip, but this should be verified via autoradiography before use.

5.2.2 CT-based Planning

Needle identification in CT imaging is straightforward. Nevertheless, commissioning in a phantom should quantify the accuracy of the needle tip identification for each institution's CT imaging system to avoid geographical inaccuracies. Furthermore, individual institutions must carefully examine their clinical work flow to identify potential causes of needle displacement (e.g., patient transfers, changes in patient position, excessive elapsed time) and develop appropriate, yet clinically feasible, means of reducing, evaluating, and remedying needle migration. Prior to clinical implementation, devices to immobilize the patient or minimize the need for transfers should be investigated (Peddada et al. 2015). A robust technique for imaging the needle tips relative to a surrogate for the prostate base should be developed and tested, with attention paid to when the tip positions should be assessed (before imaging for planning and each treatment) and how to maintain the patient position consistently.

5.2.3 US-based Intraoperative Treatment Planning

Commissioning tasks specific to US-based intraoperative planning involve scrutiny of the reconstruction of the 3D US images to ensure the greatest degree of geometric accuracy possible. This will include validation

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of the encoded stepper used to determine where in physical space each individual US image was acquired. The imaging of string or bead phantoms can aid in assessing any distortions present in the images (Tong et al. 1996; Tong et al. 1998). Additionally, when using a biplane TRUS probe, the physical correlation between transversal and longitudinal imaging planes should be verified. It should also be noted that changing the frequency of the US transducer will change the scaling of the images. If the images are transferred via a video cable, the TPS scaling will need to be adapted manually.

Needle appearance in US images must be carefully examined in a phantom to fully understand the appearance of the needles before use in a patient (see Section 5.4.4). All commercial US-based TPSs incorporate some means of using a measure of the length of needle protruding from the template to increase needle tip identification accuracy (see Section 5.4.3). This process should be validated using phantoms, and users should expect to localize the tips within 1 mm (Siebert et al. 2009; Schmid et al. 2013; Batchelar et al. 2014). Accuracy of both image reconstruction and needle identification can be tested simultaneously by fusing US images with high-resolution CT scans of implanted phantoms (Figure 5–3) (Schmid et al. 2013).

5.2.4 MRI-based Planning

Use of MRI-based planning requires all equipment be MR compatible, including template, needles, and any ancillary equipment that is needed for the procedure (Murgic et al. 2016). Additional equipment needed includes a transrectal coil used to image the prostate and immobilization devices used for patient positioning on the MR couch. To properly use an MR for treatment planning, the distortions of patient anatomy must be measured. This requires the use of a specialized MR phantom to measure geometric distortion (Citrin et al. 2005).



Figure 5–3 Fused CT-US images of a prostate phantom illustrating the relationship between the needle lumen on CT (dark circles) and the bright flash of the needle in US. It can be seen in both of these images that the flash from these needles is generated largely by echoes from the posterior surface of the needles. (A) Acquired using the sagittal TRUS crystals by rotating the TRUS probe, contains an US-reconstruction error, leading to the flash being located lateral to the actual needle locations for peripheral needles. (B) Acquired using the axial TRUS crystals by translating the probe and does not contain this error.

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5.2.5 Technique Commissioning

Beyond commissioning of technical equipment, the implementation of any new brachytherapy technique must include the development of robust policies and procedures designed to address not only standard operating processes, but also to provide guidance in instances where the standard procedure cannot be followed (Brown et al. 2016). It has been found that the majority of errors in HDR brachytherapy arise from processrelated issues (Richardson 2012). To decrease the likelihood of these occurring, it is valuable for facilities developing a new program to collaborate with an institution experienced in the delivery of prostate HDR brachytherapy to aid in formulating an effective treatment process. Each institution will need to account for local variations in infrastructure, human resources, and work flow, among other factors, as they develop and commission an effective treatment process. This should, as often as possible, be done collaboratively by a multi-disciplinary implementation team.

HDR brachytherapy for prostate involves all standard radiation therapy professions (radiation oncologists, medical physicists, radiation therapists, and medical dosimetrists) as well as surgical professionals (anesthetists and nurses) and potentially MRI technologists. The roles, responsibilities, and qualifications for each profession have been laid out for brachytherapy, in general, in an ASTRO white paper (Thomadsen et al. 2014). It is not possible to assign specific roles within HDR prostate brachytherapy procedures, as it will depend on local factors as to whether, for instance, a physicist or dosimetrist creates the treatment plans. What should be true for all institutions is that each profession's role should be clearly defined and documented.

Once a comprehensive policy and procedure document has been developed, representatives from all professional groups involved should review it and agree that the process is robust and complete from their point of view. The implementation team should develop a series of safety checks (e.g., time outs, independent checks, checklists, etc.) throughout the procedure (Huq et al. 2016). Effort should be made to have the completed procedure document peer reviewed by an institution with active experience in HDR brachytherapy for prostate (Brown et al. 2016).

Before any treatments are undertaken, an end-to-end test run with all staff involved should be performed. That is, the entire procedure should be performed with a phantom standing in for the patient. All decisions regarding equipment (including which surgical drapes are required, etc.) should be finalized before treatments commence. It should be a goal that all personnel involved in the procedure partake in the procedure test run. In practice, this can be challenging to realize. It should at least be ensured that a representative staff member from each profession be present for both the test run and the initial procedure, for example, if only one scrub nurse can attend the test run, that nurse should be present for the initial procedure.

It is encouraged that staff responsible for needle insertion and subsequent needle identification perform additional phantom implants in advance of clinical implementation. This allows the team to better understand what is required of them by other members of the team, helps establish communication channels between the disciplines, and increases familiarity with the imaging equipment and planning software. This is of particular importance for US- and MRI-based planning, where needle identification in planning images is not as straightforward as in CT-based planning (Schmid et al. 2013).

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Figure 5-4 An overview of the CT-based procedure. (Courtesy G. Morton, University of Toronto.)

5.3 CT-based HDR Brachytherapy for Prostate

5.3.1 Process Overview

The work flow for CT-based prostate HDR brachytherapy is shown in Figure 5–4. The procedure consists of: 1) placing needles within the target volume under image guidance; 2) CT imaging with the needles in place; 3) contouring the relevant anatomical structures; 4) reconstructing the needles in the planning system; 5) optimizing the dwell times to achieve the dosimetric constraints; 6) performing pretreatment quality assurance, including verification and adjustment of needle positions to compensate for any shifts that occurred during planning; and 7) treatment delivery. If no subsequent fractions are to be delivered, the needles are then removed. This process typically takes 5–6 hours in total (Batchelar et al. 2016), although this time may be reduced if in-room CT is used to guide or plan the treatment.

5.3.2 Implant

Needles are typically inserted in an operating room (OR) with the patient under spinal or general anesthetic. Generating a list of equipment required in the OR (Figure 5–5) will ensure that the implant goes smoothly. This is particularly important if the OR used for implants is not in the radiation therapy department. The patient is positioned in dorsal lithotomy, and a Foley catheter is used to drain the bladder during the treatment procedure. Frequently, fiducial markers are inserted into the base and apex at the beginning of the implant. This aids both in judging the depth of needle tips and in delineating the prostate on CT images. Needle insertion is most commonly template-based and performed using TRUS image guidance, potentially augmented by fluoroscopy or C-arm CT imaging (Yamada et al. 2012; Hoskin et al. 2013; Morton 2014). Placement of the needles may be chosen individually for each patient, or a standard insertion pattern may be chosen as a starting point. In general, all needles are inserted to the base of the prostate.

When the implant is finished, the template should be sutured to the perineum and the legs lowered from lithotomy. As the change in leg position can alter the relative position of the prostate and needles, it is recommended that the depth of the tips be assessed before leaving the OR. This can be accomplished either via cystoscopy—in which an endoscope allows direct visualization of the needles tenting the bladder wall as they are advanced—or using C-arm fluoroscopy to visualize the needles relative to contrast in the bladder or the fiducial markers in the prostate base. Numbers may be assigned to the needles at this point; it is advisable to use the same numbering system for every implant (e.g., always increase numbering from bottom to top, left to right). Once the tips are satisfactorily positioned, the needles should be fixed to the template. This may be done using a template with a sliding plate (Figure 5–14), which locks all needles simultaneously, or by individually locking each needle using putty (Figure 5–6), locking collets (Figure 5–15), glue (Figure 5–35), or any other means devised by an individual institution. After fixation, the needles should be marked to make it

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easy to assess changes in the needle position relative to the template. These marks may be a simple line marking the point at which the needle exits the template or may be a series of marks at regular intervals as seen in Figure 5–6. Additionally, the template locations used should be mapped on a form, such as in figures 5–8 and 5–18, and photographs taken. It is also advisable to acquire radiographs recording the intended posi-

			Effective date: 9/12/
	HDR Prostate Sup	ply Pre	ep Checklist
<u>We B</u>	ring to OR:		
Bi	rachy Prostate Pack		
🗆 Pr	rostate Cart		
🗆 Pr	rolene Sutures x2		
G	old Seed Markers/Acculocs	OF	will Supply:
	Check for prior placement	<u>.</u>	win suppry.
	S manipulating arm		Sterile gloves for Dr.
	S arm base		Sterile instrument pack
U U	S unit(w/prostate probe)		Scissors
🗆 Er	ndocavity water standoff kit:		Needle driver
	Tape for water channel		Pickups
	lcohol Gauze Jar		Towel clamps
□ 1€	6 ISI Sterile Leur lock Catheter needles		Sterile H2O/ Saline for probe cover
□ 4	pillows		OR table
	ental putty in separate containers:		OR Fluoro (If needed)
	 1 scoop putty base 		Foley Catheter
	 1 scoop putty activator 		Contrast
🗆 Pa	aint pen		Cystoscope w/ 180 degree rotation
🗆 St	terile marker & ruler		, , , , ,
🗆 Re	ed catheter numbers		
	quaplast grids (3 x 4.5cm aprox.)		
□ St	triker stretcher ordered for OR by 4pm the		
da	ay before.		
🗆 Pa	, atient's chart		
	 Copy of brachy consent 		
	 Copy of procedure consent 		
	HDR Prostate yellow Rx sheet		
	Radiation Oncology Admission		
	History		Urologist:
	Pathology		
	Volume Study Notes		Number:
	Prior Acculocs?		
🗆 St	terilized friction cuffs.		Date of Marker
	opy of Updated Procedure		Discoment:
🗆 Ca	amera		
🗆 Ca	atheter cutter/extra blades		Prior external radiation: V or N
🗆 St	tepper Drape		
🗆 Sy	ringe and saline		
□ Zi	p sealed bag for patient supplies		
🗆 Pi	ink styrofoam		
	overmat w/ pump		
🗆 Be	etadine paint brush		
D'	VI cable		
herapis	st #1 Initials: Date:	:	
ooranic	st #2 Initials: Date:		

Figure 5–5 Generating an equipment list for the OR is useful. Lists for US- and MRI-based planning would be similar. (Courtesy of J Zoberi, Washington University.)

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Figure 5–6 An implant using a Syed-type template illustrating the needle fixation and marking.

tion of the needle tips at the end of implant (Figure 5–7). The patient is then transferred to a stretcher for recovery from anesthetic.

5.3.3 CT Localization

Following recovery, the patient is transferred to obtain CT scans for treatment planning, and again the marks are checked to verify that the needles have not moved within the template. As the needle tips will shift caudally within the prostate even if they have not shifted relative to the template (Holly at al. 2011), it is imperative that the positions of the tips be adjusted before the planning CT scan is obtained. Needle displacement can be assessed relative to any fiducial markers placed at the prostate base (Figure 5-7), but most commonly the tip positions are judged relative to the bladder based on radiopaque contrast infused into the bladder. To avoid CT artifact and masking of anatomy and needles, the contrast-to-saline ratio (mixed by volume) should not exceed 10%. It is important to train the CT staff and



Figure 5–7 Maintaining the intended position of the needle tips with respect to the prostate base is challenging in any HDR brachytherapy work flow where the patient is moved or there is a significant period between insertion, planning, and treatment. An AP radiograph obtained at the end of the implant records the intended position of the needle tips relative to both contrast in the bladder and fiducial markers in the base and apex (circled in red).

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document this protocol. Antero-posterior (AP) and lateral scout views of the pelvis are first obtained to verify needle location. If flexible plastic needles are used, metal stylets or CT markers should be used for the scout images to judge the tip positions. Any needle displacement observed should be adjusted and the scouts repeated until the needle positions are satisfactory. If necessary, needles should be re-affixed to the template, re-marked, and new photographs taken.

If used, metal stylets are then removed from the plastic needles and CT images are obtained from a level superior to the base to several centimeters inferior to the apex. The CT protocol should use slices of no more than 3 mm overlapping intervals (Hoskin et al. 2013). Smaller slice thicknesses will, however, reduce uncertainty when localizing the crainial-caudal position of the needle tips during CT-based HDR brachytherapy planning. In general, whatever imaging modality is used, the slice thickness should be minimized as much as is practical without degrading image quality (Kirisits et al. 2014).

The use of a CT simulation checklist, as shown in Figure 5-8, will help control the implant quality.



BJH/WUSM/SCC HDR Prostate Medical Physics Consultation

Figure 5–8 An example of a CT-Sim checklist used for prostate HDR brachytherapy physics consults. (Courtesy of J Zoberi, Washington University.)

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Figure 5–9 The appearance of plastic A) and steel B) needles in CT. In image B, the applicator reconstructed in the planning system is displayed showing that the tip of the applicator is offset from the tip of the needle as visualized in the images. This is to account for the solid, beveled needle tip, which is not part of the source channel.

5.3.4 Needle Reconstruction

In general, needle reconstruction based on CT images is very straightforward. If plastic needles are used, they will appear as air-filled holes within the gland (Figure 5–9). Steel needles may also be used; little obscuring artifact is generated by these thin-walled needles. In this case, the physical tip of the needle is easily located, but the dead space at the tip of the needle must be appropriately accounted for when reconstructing the needles (Figure 5–9). Digitally reconstructed radiographs from the planning system can be compared to CT scout images and radiographs taken in the OR to validate the reconstructed needles. If the needles were numbered at the time of implant, the reconstructed applicators in the planning system should be numbered identically. The map of the template locations used should be the guide for placing and numbering the applicators to match the implanted needle pattern and numbering. It is also possible to number the needles as they are reconstructed in the planning system. In this case, it should be ensured that the physical needles are assigned the same numbers.

5.3.5 Pretreatment Needle-positioning QA

Beyond the pretreatment QA discussed in Section 5.7, needle displacement is the most important element to scrutinize prior to treatment in CT-based prostate HDR brachytherapy. It is important to understand that there

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Figure 5–10 An illustration of the caudal shift of the needles relative to the prostate base that occurs between insertion and first fraction of treatment. Both images are AP radiographs of the same patient. Visible are the CT markers (dark vertical lines with a 1-cm, radio-transparent gap before a marker indicating the first dwell position) placed in plastic needles and four fiducial markers (circled in red), two at the base and two at the apex of the prostate. It is easily seen that significant caudal shift occurs, which must be corrected before delivery if the delivered dose is to match the planned dose.

are two components to this displacement (Hoskin et al. 2003). The first is that there may be movement of the needles within the template. This is easily detected by looking at the marks made on the needles themselves or by checking the length of needle protruding from the template. More challenging to assess and correct is ensuring that the needle tips are correctly placed relative to the prostate base. It is well known that such assessment should occur for subsequent fractions delivered with a single implant (Kim et al. 2007). It is, however, necessary even for the first, or only, fraction delivered with an implant. It has been demonstrated (Holly et al. 2011) that, even for a single-fraction delivery scheme, there is a mean caudal shift of the needle tips away from the prostate base of 1.1 ± 0.8 cm (Figure 5–10), without any increase in the protruding length of the needle beyond the template. Left uncorrected, this shift can reduce the prostate V_{100} by 20% and the D_{90} by 37%. Fluoroscopy or cone-beam CT can aid in repositioning the needle tips relative to fiducial markers or with respect to contrast in the bladder. The use of specially designed patient positioning devices and transferring the patient with these devices can reduce the magnitude of observed needle shift (Peddada et al. 2015).

5.3.6 Tips and Tricks

- Many centers purposefully implant a needle between the urethra and the rectum, in the central row of the template, to provide more control over the dose in this region between OARs.
- All HDR brachytherapy units can be operated inside the CT room if the shielding requirements have been met. Thus, the patient can be treated after planning without being moved if the HDR afterloader shares a room with the CT scanner there. This is referred to as an in-room CT work flow, which saves time and reduces the chance of needle displacement. It is also possible to have both the CT scanner and the HDR afterloader in the brachytherapy procedure room. In either case, it is still necessary to assess the relative positions of the base and the needle tips after the legs have been lowered for imaging.
- Patient movement should be minimized while the needles are implanted. Procedures should be developed to make patient transfers between the OR bed, CT couch, and stretcher easy. This will reduce the possibility of needle displacement, and the number of such transfers should be reduced as much as possi-

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Figure 5–11 A patient trolley with MR/CT compatible transfer top that would permit the patient to be implanted, imaged, and treated without being transferred off the transfer top. Prototype is a work in progress at the time of this writing from Qfix (Avondale, PA).

ble. Commercial devices to reduce or eliminate the need to transfer patients, regardless of department work flow, have been developed (Figure 5–11). All procedures and equipment should be thoroughly validated to assess their impact on needle position.

5.4 US-based Intraoperative HDR Brachytherapy for Prostate

5.4.1 Process Overview

US-based intraoperative HDR brachytherapy is a one-step process that uses TRUS imaging to both guide the implantation of the needles and for treatment planning. Needles are implanted using real-time 2D US imaging, and then a 3D US image is acquired for needle reconstruction and contouring of the relevant anatomy. Dwell positions and dwell times are then determined using this image. Once the plan is complete, the patient is treated and the needles are removed. This is all accomplished with the patient under anesthetic and in the same position as for implant, providing no opportunities for the needles to shift. The work flow for US-based intraoperative prostate HDR brachytherapy, shown in Figure 5–12, takes between 1.5–2.0 hours to complete.



Figure 5–12 An overview of the US-based procedure. (Courtesy G. Morton, University of Toronto.)

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5.4.2 Implant

As with CT-based planning, patients undergoing HDR brachytherapy using intraoperative TRUS-based planning have needles placed in an OR while under anesthetic and in the dorsal lithotomy position. It is preferable, when medically possible, to perform the procedure using general anesthetic as this provides a greater degree of patient immobilization than spinal anesthesia. A Foley catheter is inserted to drain the bladder and to aid in visualizing the urethra. This may be further enhanced by filling the catheter with aerated gel. The whole procedure is conducted using a bi-plane TRUS transducer mounted to a stepper equipped with an encoder for tracking the translational and rotational position of the transducer crystals. Three-dimensional US images are acquired either sagitally, by rotating the probe, or longitudinally, by translating it. Images are acquired at narrow intervals, and a 3D image set is reconstructed based on the encoded position the probe for each image (Tong et al. 1996). Needles are inserted using a template that is mounted to the stepper.

Commercial systems available for US-based planning incorporate acquisition of an initial image volume before needles are inserted. The intention is that the prostate and OAR would be contoured on this image set. These contours could either be used for inverse planning of needle positions or to aid in delineating the target following needle implantation. In practice, the current iteration of commercial optimizers for determining needle placement do not tend produce intuitive or robust needle arrangements. Since one of the strengths of using HDR brachytherapy is that you can prospectively determine the dose based on implanted needle positions, it currently makes more sense to manually develop a needle arrangement. This may be based on individual anatomy, or institutions may develop a standard pattern to use as a starting point (Batchelar et al. 2016). In the absence of optimization, a robust standard pattern (Figure 5–13) streamlines the implantation



Figure 5–13 The standard pattern used at the BC Cancer Agency, derived from G Morton's pattern at the Odette Cancer Centre (Morton 2015). This pattern can be used as a starting point for any planning modality.

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Figure 5–14 A sandwich style template. Templates of this style can be used with any imaging modality. This is a reusable template that fixes the cranial-caudal position of the needle by adjusting a sliding plate A) between the two main plates of the template. This quickly and simply locks all needles at the same time B). Care must be taken, however, because not all needles are fixed to the same degree. The needles are held in place by pressure applied by the sliding plate. The greatest pressure is applied in line with the adjustment screw in the center of the template, and it is possible to manually shift individual needles in the periphery, even when "locked" C) (Batchelar et al. 2014). Needles can be repositioned as intended, relative to the template, by marking on the needles the point at which they exit the face plate of the template and ensuring they have not shifted before acquiring a TRUS data set for planning and before treatment.



Figure 5–15 A prostate template with needles locked individually via collets. A) Collets are placed over the needles before implantation. B) As each needle is advanced to the prostate base, the collet is threaded into the template hole and tightened around the needle using a wrench designed to fit over the needle protruding from the template. No needle shift relative to the template is possible with this type of template. If equipped with the means of being stitched to the perineum, this template could be used with any imaging modality.

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procedure by removing the need to start from scratch for each patient. It is not required by current clinical systems that these initial images or contours be used. Due to changes in the prostate position and volume induced by the insertion of needles, it is preferable to use the 3D US data acquired after implanting the needles for contouring and dose planning.

Another important factor to keep in mind is that posterior needles may shadow more anterior needles, obscuring them in the final image. It is helpful to insert all needles to mid-gland and ensure that all are visible before advancing them to their final depth. If any needles do fall within a shadow, retracting and reinserting either needle shifted by a small amount (~ 2 mm) usually brings them into clear view. Figure 5–13 shows the standard pattern of 16 needles used at the British Columbia Cancer Agency. This pattern generally prevents shadowing needles by other needles and leaves enough flexibility that needles can easily be shifted to improve visibility or to accommodate a wide range of prostate volumes. Needles may be added or removed (± 2) to accommodate individual anatomical requirements. It should be noted that not all needles are necessarily inserted to the same depth in the patient. In particular, the anterior needles are often not as deep as the posterior ones. This can be verified in the longitudinal US view.

Once the needles are satisfactorily implanted, they are usually fixed to the template (Hoskin et al. 2013), either via a sliding plate within the template (Figure 5–14) or using individual locking collets (Figure 5–15). Marks may be made on the needles to easily monitor their cranial-caudal position. The template remains mounted to the stepper for TRUS-based HDR brachytherapy.

5.4.3 US Localization

Because the patient and applicators have already been positioned for treatment, simulation for TRUS-based HDR prostate planning consists of acquiring a final 3D US image and measuring the length of the needles protruding from the template. The planning image is acquired exactly as for the initial image. Care should be taken to ensure that all needle tips are included in the image. Visualization of the urethra is simplified by instilling a small volume of aerated gel in the Foley catheter (Figure 5–16).



Figure 5–16 A) Using live sagittal TRUS imaging, a small volume of aerated gel is instilled in the Foley catheter just until the gel can be seen in the Foley balloon. B) This allows easy delineation of the urethra for planning without obscuring any anterior needles.

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Figure 5–17 Measuring the protrusion length of a needle that has been implanted to the base of the prostate.

It is a recognized limitation of US-based planning that identifying needle tips based solely on the 3D TRUS images is challenging (Siebert et al. 2009; Schmid et al. 2013). This can be ameliorated by using the measured lengths of the needles that protrude from the implant template to adjust the cranial-caudal position of the needle tip. The ability to use the protrusion lengths for this purpose is incorporated into currently available commercial software, making needle tip localization in US as accurate as CT (Batchelar et al. 2014). Thus, the protrusion length of each needle should be measured (Figure 5–17), entered in the planning system as required, and independently recorded before planning. This independent record is useful in case of software issues; if anything happens to the digital record of the protrusion lengths, they can quickly be reconstructed without remeasuring. It is also good practice to independently record the template positions for each needle for QA purposes. These two records can be combined into a single, easily visualized check sheet (Figure 5–18).

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Figure 5–18 Needle position and protrusion length tracking document used at the BC Cancer Agency. As needles are inserted, their template positions can be marked in the correct locations on the sheet. When the protrusion length is measured, it can be entered in the corresponding square on the sheet.

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5.4.4 Needle Reconstruction

Once the second 3D TRUS image set is acquired, the target and OARs are contoured (see sections 5.6.2 and 5.6.3). The needles are then reconstructed using tools integrated in the planning system. For TRUS-based planning, it is imperative that the appearance of the needles in US images is fully understood (Figure 5–19) to ensure correct interpretation of the clinical images. Moreover, the intended relationship between the physical and virtual needles must be understood to be able to judge that the lumen of the needle and the center of the first dwell position are correctly positioned relative to the flash of the needles in the TRUS images (Figure 5–20) (Schmid et al. 2013). Some TPSs offer the possibility to perform needle reconstruction in the live US image. The benefit of this method is that needle visualization can be increased due to moving interactions with the needles (e.g., by rotating or tipping the needles). Also, tipping or rotating the implanted needles can help to identify them in the reconstruction step. The resulting needle positions identified in the live images are then transferred automatically to the previously acquired 3D US image. If this feature is not available, it is still possible to use information from the live image to inform needle reconstruction in the static image set. The needle under consideration can be rotated, and by scrolling through the live image and looking at the position of the flash relative to the template grid, the position of the needle in the acquired image set can be elucidated.



Figure 5–19 Images of two different needles in TRUS images: A is a reusable steel needle and B is a disposable plastic needle.



Figure 5–20 A correctly aligned virtual needle. The vertical line indicates the end of the active needle channel, the leftmost point of the horizontal line is the physical tip of the needle, and the green dot is the center of the first dwell position.

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5.4.5 Pretreatment QA

All general pretreatment QA outlined in Section 5.7 applies for TRUS-based planned cases. As for any brachytherapy procedure, a crucial part of ensuring safe and accurate treatment is confirming that the applicators have been reconstructed appropriately. For most multi-needle interstitial procedures, it is challenging to perform this at the end of treatment planning and, therefore, beneficial to have a real-time independent check as the needles are identified by the planner. In TRUS-based HDR prostate brachytherapy, this is essential. Identifying the tips and trajectories of the needles depends too closely on information only available and verifiable during the implant for the needles to be reviewed at the end of planning.

It should be ensured that the US probe is inserted as it was for imaging to maintain the planned relationship between the rectum and the prostate. The cranial-caudal position of the needles should be checked after the guide tubes are connected.

As treatment proceeds immediately after planning, with no change in patient position, it is not necessary to verify needle positions with respect to the prostate.

5.4.6 Tips and Tricks

- As this is a real-time technique, it is helpful to have a brief procedure checklist available for easy reference (Figure 5–21) to keep the process on track.
- Having the most posterior needles implanted 3–5 mm within the prostate capsule gives the best result with respect to rectal dose.
- Do not use a needle in the central row of the template, particularly posterior to the urethra. This will cause shadowing and obscure the urethra.
- The prostate will shift cranially as the needles are inserted. Make sure the probe can be inserted up to 3 cm farther than the initial position of the base. Also, the position of the anteriormost needles may need to be adjusted at the end of the implant.

HDR PROCEDURE CHECKLIST

BEFORE NEEDLES ARE INSERTED:

Confirm: Date=Today; Unit=HDRLake; Sk=40700; Prescription&isodoses match Set stepper angle to zero and Zero stepper angle readout Ensure that needle number assignment is correct (Screen L to R, bottom to top) Set the probe to 2-3 cm SUP of base and record stepper position (stepper > 20)	
Acquire a 3D US image set AS NEEDLES ARE INSERTED TO MID-GLAND:	
Turn on the embedded US overlay Drag needle representation to US flash Ensure can see all needles - not shadowed by other needles Ensure needles have been assigned to correct template hole	
AS NEEDLES ARE ADVANCED TO THE BASE:	_
Maunally align virtual needle one of the posterior needles Enter measured protrusion length and set needle as reference Enter each protrustion length in cm and click 'adjust' Ensure that at least one other needle tip is clearly visualized Lock all needles Ensure that green reference line has not been moved RO may review some of the needles and readjust depth	
BEFORE ACQUIRING FINAL IMAGE SET	_
Ensure urethra is visible - aerated gel Turn off the embedded US overlay Set stepper to original position and begin acquire, step back above needle tips	
AFTER IMAGE ACQUISITION	
WARNING - DO NOT SAVE WHEN IN ACQUISITION TAB Check that virtual needles align with the live and the acquired image set Switch to contouring and select brush tool	
AFTER CONTOURING	_
Print channel connection diagram for hook up Check:StepSize=0.3cm;DeadSpace=0.4cm;Offset=0cm;NeedleDiam=1.47mm Finalize the needle paths Check 3D view to make sure everythign looks reasonable	
AFTER NEEDLE TRACKING	
Check that dwell position range for peripheral needles is reasonable Load appropriate planning constraints Manually adjust to meet planning goals	
AFTER PLANNING	
Ensure at least 1 dwell position in each needle; Check for dwell times < 0.3s Planning Approve (RO) and Treatment Approve (MP) Probe IN for treatment	

Figure 5–21 Procedure checklist used at the BC Cancer Agency. The goal of this list is to ensure that no crucial steps are missed that would require repeating a portion of the procedure. It is not intended for plan checking.

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- Rotation of the prostate during needle insertion can be minimized by having the first two needles inserted on the left and right of the prostate. It is particularly helpful to insert the central needles (e.g., those in columns C and E in Figure 5–13) first.
- If the prostate is too wide to be covered by template, an experienced operator can implant the needles "free-hand." Care should be taken in the labeling of the needles because no template coordinates can be used for identification of the needles.

5.5 MRI-based HDR Brachytherapy for Prostate

5.5.1 Process

MRI can be incorporated into HDR prostate brachytherapy in three main ways. Pretreatment multi-parametric MR images can be fused to planning images, whether CT, US, or MR (Crook et al. 2014; Hosni et al. 2016), to define a sub-prostatic volume for focal dose escalation. MRI can also replace CT as the postimplant imaging modality used for treatment planning in a process analogous to that shown in Figure 5-4 (Buus et al. 2016). If the MR scanner is in the brachytherapy suite, the number of patient transfers are reduced or eliminated. Finally, MRI can be used both to guide needle insertion and for planning (Murgic et al. 2016), analogous to the TRUS-based process seen in Figure 5–12. Especially during the learning phase for the team, the entire procedure can take much longer than in CT- or US-based work flows (Buus et al. 2016; Murgic et al. 2016), with initial procedure time reported >7 hours, even with MRI in suite. This makes it imperative that the entire process should be simulated prior to implementation of an MR-based work flow in order to anticipate areas of difficulty that may be encountered (Buus et al. 2016). A detailed study of all of the steps required for MR-based treatment planning for HDR prostate brachytherapy has been published. (Buus et al. 2016). This study has several steps that are required if needle placement is performed under US guidance, but with MR-based planning. The US steps can be replaced with similar tasks if only MR is used for needle insertion. There are additional complicating factors for the process of using MR-based insertion of needles that require careful consideration and planning: a) all equipment that is used must be MR compatible, b) there is often limited workspace for placement of the needles due to the size of the MR bore, c) the needle insertion may be in a different position than is normally encountered within the clinic, and d) the patient most likely would need to be moved to the treatment area without the implanted needles being affected.

5.5.2 Implant

When MRI replaces CT or US only as the planning modality, needles are implanted under TRUS guidance as described in Section 5.4.2, with the caveat that MRI-compatible needles must be used. For MRI used also for needle-insertion guidance, the patient must be immobilized for the implant, either in lithotomy, decubitus position (Menard et al. 2004; Laloksi et al. 2011), or in a frog-leg position (Murgic et al. 2016). For implantation in the decubitus position, Aquaplast[®] sheets can be used over the patient's pelvis in order to immobilize the patient in the MR unit (Lakosi et al. 2011). Needles should be placed under MR guidance, either with the patient within the MR field or with the MR table withdrawn from the bore and then moved back into the bore for imaging. As experience is gained by the operative team, several needles can be placed at a time, with imaging after placement of each group of needles. Final imaging is performed after all treatment needles have been placed.

For patients treated in a lithotomy position, the needle insertion procedure can be expedited. The first needle can be placed via manual guidance, in which a finger in the rectum guides a needle into place between the rectum and the urethra. The position of this needle is verified by MR, and it then serves as a reference for

This concludes the first half of Chapter 5 of *Clinical Brachytherapy Physics*.

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