

SASCRO Prostate Brachytherapy Guidelines Task Group

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Introduction

These guidelines are a tool to assist medical practitioners in providing evidence based care for patients receiving prostate brachytherapy.

They are not implied to be the standard of care or to be inflexible rules and requirements of practice.

The sole purpose is to assist practitioners in delivering safe and effective medical care.

Variation in the approach toward prostate brachytherapy is common. The guidelines presented here are intended to aid practitioners in managing patients, not to rigidly define process or practice.

This guideline was revised collaboratively by a team of radiation oncologists, urologists, medical physicists and radiotherapists who have experience in the delivery of prostate brachytherapy, and endorsed by SASCRO (South African Society for Clinical and Radiation Oncologists).

The guidelines are based on the permanent prostate brachytherapy (PPB) and high-dose rate (HDR) brachytherapy guidelines published by ABS (1), ASTRO (2) and ESTRO (3).

Qualifications and Personnel

- Radiation Oncologist
- Urologist
- Medical Physicist
- Trained nurse in brachytherapy

As a licensed user of sealed radioactive sources, a radiation oncologist is essential in the treatment of patients undergoing prostate brachytherapy. Similarly, a qualified Medical Physicist is essential to the planning and quality assurance for brachytherapy.

The selection, workup and evaluation of patients for prostate brachytherapy is best done in a multi-disciplinary team comprising at minimum a radiation oncologist and urologist.

All of the above personnel should have formal training in prostate brachytherapy. If this training was not obtained during the approved undergraduate training course, then a post-graduate fellowship or mentorship program should be undertaken prior to independent practice.

Efforts to ensure the adequate quality of brachytherapy implants have led experienced brachytherapy centres to create programs which include a minimum case volume, submission of cases for peer review, and performance of continuous QA (38).

Brachytherapy Techniques

Prostate brachytherapy can be divided according to the technique, the clinical indication or the dose rate of the isotope used.

It can be delivered with permanent low-dose rate (LDR) seeds, commonly referred to as permanent prostate brachytherapy (PPB), or as a high-dose rate (HDR) temporary interstitial application.

PPB can either be preplanned prior to seed insertion (eg. Seattle Technique) or planned in real-time intra-operatively.

HDR is most commonly planned intra-operatively, but pre-planned and post-implant planning is possible.

PPB is typically given using the isotopes I-125 or Pa-103.

HDR brachytherapy is given using Ir-192 or Co-60.

Clinically it can be divided into monotherapy (given as the primary treatment in lower risk patients) or dose-escalated boost (DE-boost) when it is given as an adjunct to external beam radiotherapy in high-risk patients with or without ADT.

- **HDR**
 - Temporary
 - Remote afterloading
 - Commonly fractionated
 - Ir-192 or Co-60 isotope
 - Planned intra-operatively or post-implant
 - More commonly used as DE-boost although monotherapy is an option

- **LDR**
 - Permanent
 - Manual afterloading
 - Once off procedure
 - I-125 or Pa-103 isotopes
 - Preplanned or planned intra-operatively
 - More commonly used as monotherapy, although DE-boost is an option

The table 1 below lists the recommendations regarding HDR and LDR brachytherapy by ABS and ESTRO (33).

Table 1.

	<u>GEC ESTRO EUA</u>	<u>ABS</u>
<i>Monotherapy</i>		
HDR	Investigational	Standard
LDR	Standard	Standard
<i>Boost</i>		
HDR	Standard	Standard
LDR	Not stated	standard

Patient Selection

Patients with pathologically proven prostate cancer with no evidence of metastatic disease on workup for non-low risk presentations are candidates for prostate brachytherapy.

Minimum required elements of workup, absolute contra-indications as well as relative contra-indications have been published by the ABS and are tabled below (1).

Specific inclusion criteria for monotherapy and DE-boost are evolving and ongoing clinical trials will help better define patient selection for either treatment.

Prostate cancer has historically been divided into low, intermediate and high-risk groups (4).

Patients with low-risk disease are candidates for monotherapy. PPB combined with EBRT is unnecessary, as is ADT.

There is emerging data that patients with favourable risk, or low-tier intermediate risk prostate cancer, can be successfully treated with monotherapy alone (5).

The exact definition of low-tier intermediate risk is yet to be established but proposed definitions are:

- T1-T2c + GS 6 + PSA 10-15
- T1-T2c + GS 3+4 + PSA \leq 10 (6)
- Low volume disease, predominant pattern G1 3, only one intermediate risk feature (1)

Patients with high-risk disease are candidates for (dose-escalated) radiotherapy with or without androgen suppression. Dose-escalation can be achieved with DE-boost brachytherapy or external beam radiotherapy alone, however data suggests that patients have better biochemical control when DE-boost is used (39), and in a series by Stone et al (14), improved overall survival was shown if a greater biological effective dose was delivered.

ABS guidelines regard EBRT + ADT + DE boost using brachytherapy as a standard treatment option for high-risk disease (1).

Minimum required elements of workup for PPB (1).

- Positive biopsy indicating adenocarcinoma. Additional information regarding Gleason score and percent cancer is required.
- Pre-treatment PSA
- DRE – clinical T stage
- Negative metastatic screen (for high risk disease)
- TRUS directed prostate volume
- Determination of patient's ability to tolerate dorsal lithotomy
- Determination of suitability for anaesthesia

Absolute contra-indications for PPB (1)

- Limited life expectancy
- Unacceptable operative risk
- M1 disease
- Absence of rectum
- Large TURP defects
- Ataxia telangiectasia

Relative contra-indications for PPB (1)

(the factors alone do not preclude PPB, however they should be considered closely in selecting appropriate patients for PPB)

- IPSS>20
- Peak flow rate <10cc/sec or post void residual >100cc
- Previous pelvic radiotherapy
- TURP defects
 - Published results show that with accurate U/S identification, a TURP defect <25% the total prostate volume and at least 1cm margin around the defect, there is a low impact on urinary function post implant (41).
 - A TURP defect of >2cc has been correlated to increase urinary morbidity compared to patients with a defect <2cc (42).
 - If a TURP is needed, it is preferably done before brachytherapy with a 3month gap before implant.
- Large median lobes
- Prostate size > 60cc
 - Preimplant cytoreduction can be achieved with ADT +- 5 α -reductase inhibitor
- Inflammatory bowel disease

Procedure Specifications for PPB

Equipment

The key to achieving high quality implants is image guided source placement. This is best achieved with interactive trans-rectal ultrasound. The minimum requirements are:

1. Trans-rectal ultrasound (TRUS) with template software.
2. A stepping unit.
3. Seed planning software.

Although not essential, it can be helpful to have an image intensifier in the operating theatre and cystoscopy equipment (3).

In addition to the above equipment there is a need for stabilization and implant needles.

Facility

Brachytherapy has to be performed in a centre that is licensed to handle radioactive material. The radiation oncologist requires an Authority from Radiation Control Directorate to receive and use radioactive seeds . There should be access to anaesthesia and sterilization facilities.

All staff involved in the procedure should have adequate knowledge of radiation protection.

Ultrasound guidance

A transperineal approach under TRUS guidance is recommended. Full definition of the prostate in both longitudinal and transverse planes should be available. Typically a 5-12 MHz ultrasound probe is used for the TRUS. It is recommended to use a high-resolution biplanar ultrasound probe with dedicated prostate brachytherapy software.

Dose prescriptions

Monotherapy:	I-125:	140-160Gy
	Pa-103:	110-125Gy
DE-Boost:	I-125:	108-110Gy
	Pa-103:	90-100Gy

The prescribed dose is the minimum peripheral dose to the margin of the target volume specified according to the TG43 guidelines (19).

It is important to recognize that early literature on the use of I-125 used a prescription dose of 160 Gy, which after TG-43 became equivalent to a dose of 144 Gy (1).

In 2004, the American Association of Physicists in Medicine (AAPM) issued a report outlining I-125 and Pd-103 datasets for consistency in calculating brachytherapy dose distributions (19).

Based on the need for clinical constancy, the ABS recommended immediate implementation of the 2004 AAPM consensus brachytherapy dosimetry datasets.

They concluded that radiation oncologists should prescribe monotherapy doses of 145 Gy and 125 Gy for I-125 and Pd-103 respectively, and standard boost doses of 100-110 Gy and 90-100 Gy for I-125 and Pa-103 respectively (20).

Target Volumes

Despite numerous guidelines on prostate brachytherapy dosimetry and implantation, there has not been a consistent definition of clinical target volume (CTV), planning target volume (PTV) or defined boundaries for the organs at risk (OARs).

Based on an extensive review of the literature and informed by the GEC ESTRO European questionnaire results, recommendations were published by the GEC ESTRO working group to define the CTV, PTV and OARs (27).

Gross tumour volume

Whenever possible the GTV should be contoured on the pre-implantation ultrasound-acquired images. Where necessary, correlation with endorectal coil magnetic resonance and spectroscopy should be used.

Clinical target volume

For T1 – T2 prostate cancer the CTV corresponds to the visible contour of the prostate expanded with a three-dimensional volume margin of 3 mm.

This three-dimensional expansion can be constrained to the anterior rectal wall (posterior direction) and the bladder neck (cranial direction).

For T3 tumours, the CTV corresponds to the visible contour of the prostate including visible extension due to extracapsular growth which is then expanded with a three-dimensional margin of 3mm in each direction, with rectal and bladder constraints as above.

Planning target volume

Using online in vivo 3-D dosimetry and fluoroscopy in addition to TRUS to eliminate errors due to seed placement, there is no need for an expansion from the CTV to define the PTV, i.e. $PTV = CTV$.

Organs at risk

Different organs at risk can be defined in the pre-implantation setting.

- a. *Prostatic urethra*: common practice to obtain visualisation of the urethra is to use a urinary catheter. This should be a small gauge catheter, French gauge 10, to avoid distension of the urethra. The surface of the catheter is used to define the urethral surface from the prostatic base to apex. However in practice the urethra is not a circular structure and an alternative that may give a more accurate anatomical picture is to instill aerated gel into the urethra prior to obtaining the ultra- sound images.
- b. *Rectum*: using TRUS, visualisation of the anterior rectal wall is no problem but may introduce artifacts due to displacement and distension. Many simply outline the outer wall and this should be regarded as the minimum requirement; others define outer and inner walls to define a doughnut. In terms of the critical cells in the rectum for late damage the latter is probably more correct. For defining small volumes up to 5cc outlining the outer wall alone is therefore sufficient.
- c. *Penile bulb and/or neurovascular bundles*: currently this remains investigational.

Treatment Planning

Dosimetric planning should be performed in all patients prior to seed implantation. This can be achieved using the pre-planned technique or the intraoperative treatment planning (ITP) technique. TRUS, CT or MRI can be used (7).

Pre-planned

Pre-implant planning can be done either in a separate procedure or on the day in the operating room.

TRUS is considered the standard imaging modality, as it is the most reproducible (15), however MRI or CT is acceptable in experienced hands.

The treatment plan should indicate the needle locations according to the template, and the number, and strength of seeds in each needle using contiguous, transverse images of the prostate. A peripheral distribution of sources, frequently referred to as a “modified peripheral or modified uniform loading” is recommended so that the portion of the urethra receiving 150% dose (V_{150}) or greater can be limited (16).

A detailed description of the planning process is described by Sylvester et al (26).

Target volumes include the prostate plus a margin (as described above). The PTV is outlined on each individual TRUS transverse image. Margins are tighter posteriorly by the rectum and anteriorly at the dorsal venous plexus. Dosimetry involves creating a preplan that is simple and easy to reproduce in the theatre. The number of needles that contain only two seeds is limited to a minimum, and a plan that has peripheral needle(s) with only one seed/needle is not accepted. This reduces the number of needles used and thus is less traumatic than a plan that contains multiple needles with one or two seeds per needle. The plans are typically symmetrical mirror images, from the left side of the prostate to the right. Special loading with a reduced number of seeds in the few centrally placed needles helps avoid over dosage to the urethra.

There are several key factors that contribute to a consistent reproduction of a preplan in the theatre. The combination of planning on an undistorted TRUS, making a symmetrical plan that limits the number of needles with small numbers of seeds/needle, having a ~3-5 mm PTV margin (laterally), and using higher numbers of lower activity seeds.

Intraoperative Treatment Planning (ITP)

TRUS is performed in the OR, and the images are imported in real time into the treatment planning system. The target volume, rectum, and urethra are contoured on the treatment planning system either manually or automatically.

An optimized treatment plan is then formed, the dose–volume histogram (DVH) is generated, and the plan is evaluated.

To meet the dose parameters listed below, seeds may be added or deleted manually, and the new isodose distributions and DVH displays are regenerated. This can be achieved with interactive planning or dynamic dose calculation.

In *interactive planning*, the needles are placed into the prostate as per plan, and the computer planning system registers their position. Based on the needle positions, the treatment plan is then regenerated and the implant proceeds. The advantage here lies when the intraoperative treatment plan is found to be suboptimal as the implant proceeds, since individual needles can be adjusted and a new plan generated while in the operating room (18). It is critical that the dose calculation is updated based on seed positions derived from actual (imaged) needle positions (17).

Dynamic dose calculation relies on continuous deposited seed feedback. It needs specific technology with the potential to constantly update calculations of dose distribution (dynamic dose calculation) as the implant proceeds. It is essential that the exact seed position be known in three dimensions. Improvements in imaging are thus required, as TRUS image degradation with time is a major issue that impairs seed visualization. Imaging modalities available include TRUS-fluoroscopy, cone-beam CT and MRI. The advantage of dynamic dose calculation is its potential to adjust the

treatment plan to account for intra-prostatic seed migration as each seed is deposited and for the potential displacements of dropped seeds, caused by changes in the prostate position and volume during the implant procedure from edema or trauma (32).

Dose parameters

Various dose parameters are selected to help clinicians evaluate the dosimetric plan. These are aimed to ensure adequate coverage of the prostate, while minimizing the toxicity to the organs at risk.

Prostate

- D90: minimum dose received by the “hottest” 90% of the prostate volume, commonly described as the isodose enclosing 90% of the prostate. This is ideally kept >90% of the prescribed dose (>140Gy).
- V100: percentage of the target volume receiving 100% of the prescribed dose, ideally above 95%

Both of the above parameters have been shown to correlate to outcome. An acceptable dose range for post-implant D90 using I-125 may be between 130Gy-180Gy. D90<130Gy are associated with an increase in failure (21).

- V150: should be less than 50%
- If identified, the GTV should be covered by the 125-150% isodose line (27)

OAR

- Urethra:
 - UV5 <150%
 - UV30<125% (1)
 - D10 < 150% of the prescription dose
 - D30 < 130% of the prescription dose (27)
- Rectum:
 - RV100 is ideally kept below 1cc (1)
 - D2cc < prescription dose of 145 Gy
 - D0.1cc (Dmax) < 200 Gy (27)

Implant procedure

Pre-planned

At the preplanning session, the patient is placed in the lithotomy position identical to that to be used for the subsequent implant procedure. 5 mm ultrasound sections are taken of the prostate from base to apex using the stepping unit. The urethra should be positioned in the middle vertical row of the template and the posterior border at the rectal interface should lie as flat as possible along the first horizontal row of the template.

The planning ultrasound can be performed as an out patient procedure without anaesthetic but some centres have found that a short anaesthetic is more acceptable to patients and facilitates reproduction at the subsequent seed insertion.

If the volume is known accurately it is possible to combine the pre-plan with the implant during the same procedure (25).

After the planning ultrasound, a treatment plan (as described above) is generated.

The implant may be performed under general or spinal anaesthesia. The patient is placed in the lithotomy position with TRUS and template in same position as for the pre-planning session .

Contrast medium, or sterile water, can be inserted into the bladder to assist visualization on fluoroscopy and air-filled gel placed in the catheter to visualize the prostatic urethra on ultrasound. The position for implantation should correspond to the pre-plan.

The implant co-ordinates are defined from the template and the depth of insertion by a combination of ultrasound, fluoroscopy and measurement. Sources within the implant needles are inserted percutaneously under direct ultrasound control according to the pre-plan.

Because the prostate is very mobile it is helpful to stabilize prostate movement by two or three stabilizing needles that are positioned before the sources are inserted.

Intraoperative Treatment Planning (ITP)

ITP has some advantages over the two-step preplanned method. It avoids the need for two separate TRUS procedures and for the need for reproducing patient positioning and setup is obviated.

The patient positioning and setup is identical to that described above.

A common technique used has been described by Stock *et al.* (29) and Stone *et al.* (30). Using the VariSeed system, the implantation begins with insertion of needles, 1 cm apart, into the periphery of the gland using the largest TRUS transverse diameter cut as a guide. The position of the needles is determined on the acquired TRUS images by identifying the echo bright markings ("acroflash") of the implanted needles. The planning

system assumes that the needles run straight and do not deviate. Seventy-five percent of the seeds are then implanted through these peripheral needles using a Mick applicator.

The seed positions are marked on the planning system along the needle track, and isodoses are generated. The remaining 25% of the seeds are implanted using about 6 to 8 needles in the prostate interior such that they remain 0.5–1 cm from the urethra and cover the periphery of the base and apex. The needle positions in the interior are optimized to limit dose to normal structures (urethra, rectum) and minimize cold or hot areas within the prostate. Dose parameters as described above are used to adjust interior seed numbers and positions.

Other techniques, namely the MSKCC technique, the PIPER system and the Interplant System have been well described (18).

A comparison between preplanned and ITP is summarized in the table below (18).

	Preplanning	ITP
<i>Pre-procedure TRUS</i>	Full study and planning	Not done (or limited to volume measurement)
<i>Pubic arch assessment</i>	Usually done at pre-procedure TRUS	Not done
<i>Reproducing setup in theatre</i>	Essential	Not required
<i>Time and manpower</i>	Less	More
<i>Planning environment</i>	Low pressure, greater time	High pressure, time constraints
<i>Accounts for changes in prostate size during anaesthesia</i>	No	Yes
<i>Accounts for needle deviation</i>	No	Yes
<i>Accounts for seed movement after deposition</i>	No	No (interactive) Yes (dynamic)
<i>Account for post-implant oedema</i>	No	No

Seed Insertion

- There are several acceptable methods for seed insertion, these include;
 - 1) Preloaded needle technique: this is typically used for the preplanned technique
 - 2) Free seed technique: A Mick applicator (or similar device) is used to load seeds into the prostate.
- Seeds can be “stranded”, “linked” or “loose” within each needle. No difference in loss of seeds has been identified between the various options (9).
- Needles can be placed one at time, all at once, by row or based on peripheral and central locations.

Radionuclides

There are no recommendations regarding the choice of one radionuclide over another. There are no significant differences between the two isotopes I-125 and Pa-103 commonly used in PPB (8). Recently cesium-131 has been introduced in PPB monotherapy. Reference to current literature is advised.

Seed Activity

No consensus exists regarding optimal seed activity. Nomograms are available to calculate seed activity and number according to prostate size. In the RTOG clinical trials, seed activity has been specified at 0.23-0.43 mCi/seed for I-125, and 1.0-2.0 mCi/seed for 103Pd.

A randomized trial comparing low activity I-125 seeds (0.31 mCi), vs. high activity (0.60 mCi) found excellent dosimetry in both arms (22).

Sequencing of EBRT with Brachytherapy

Although EBRT is generally performed 0-8 weeks before PPB, no recommendations regarding the timing of PPB with respect to EBRT can be made because of lack of evidence. No studies have investigated either the sequencing of PPB and EBRT, or the time interval between the two.

Current practice and ongoing clinical trials favor delivering EBRT first

followed by PPB but there are rationales for either approach.

Supplemental EBRT

Target volume:

- Prostate and seminal vesicles with margin
- Prostate, seminal vesicles and pelvic lymph nodes for patients with a substantial risk of pelvic lymph node involvement

EBRT technique:

- 3DCRT
- IMRT
- IGRT

Rectal dose:

- For patients receiving 45 Gy of external beam radiation therapy, the D50 (the dose delivered to 50% of the rectum) should be kept as low as possible (28). The incidence of grade 2 rectal bleeding is significantly lower if the V30 is kept below 35% and the V35<25% (40).

Post implant procedures

Cystoscopy can be performed after the procedure if there is a concern for misplaced seeds or clot retention.

Patients should be advised that there is a risk of seed migration to lungs and other organs. Although ejaculation of a seed is uncommon, some practitioners advise patients to wear condoms for the first few encounters, or one month post therapy, whichever is first.

Urinary anaesthetics, antispasmodics, analgesics and stool softeners may be used for symptomatic patients.

Prophylactic use of alpha blockers can be used before and after the procedure (2).

Acute urinary retention is seen in 10-15% of patients and should be managed by intermittent or continuous bladder drainage.

The use of transurethral incision of prostate should be avoided in the first 6 months but if retention persists, transurethral incision of prostate or minimal

TURP may be considered, recognizing the risk of urinary incontinence after these procedures (23).

A patient undergoing a colonoscopy should communicate to the physician/surgeon beforehand that he has had prostate brachytherapy in case anything suspicious is noted in the rectal area.

Post implant Dosimetry for PPB

This is mandatory for each patient as actual dose delivered is calculated. Plain radiographs may be useful for seed counting, but are not adequate for dosimetric analysis.

CT or MRI is necessary to evaluate the seed position in relation to the prostate, urethra and rectum.

The optimal timing for post implant dosimetry is not known. It is often either done on day 0,1 or day 30.

Dosimetry obtained early (day 0 or 1) will underestimate prostate coverage (due to oedema) by approximately 10% compared with dosimetry obtained 30 days after implant (31).

ABS recommends CT based dosimetry is done within 60 days (1). Whichever is chosen, it is advised to be consistent with each practice.

There is no consensus on how to define target, rectal and urethral volumes.

The following parameters should be reported:

- The prescribed dose.
- The number of seeds and needles used.
- Prostate:
 - The D90, defined as the minimum dose received by 90% of the target volume.
 - V100, defined as the percentage of the target volume receiving 100% of the prescribed dose.
 - V150, percentage of target volume receiving 150% of the prescribed dose
- Rectum:
 - RV100, defined as the volume of rectum receiving 100% of the prescribed dose.
- Urethra;
 - UV5, the urethral volume in percent (approximates the urethral maximum dose)
 - UV30 (represents a clinically significant volume of urethra)

Radiation safety and QA

TRUS Imaging system

Physicists and physicians should pay attention to spatial resolution, gray scale contrast, geometric accuracy and distance measurement. The correspondence between the electric grid pattern on the ultrasound at the template grid pattern should be verified (10).

Brachytherapy source calibrations

The recommendations set forth by the AAPM TG-40, TG56 and TG64 reports and recommendations of AAPM Low energy Brachytherapy Source Calibration Working Group should be followed (11).

Implantation procedure

All staff involved in the procedure should have adequate training regarding radiation protection relating to sealed sources.

The total number of seeds implanted should be verified at the end of the implant procedure. At the completion of the implant, a radiation survey of the patient and the room shall be conducted with an appropriately calibrated survey instrument.

The empty needles and catheters (if removed in the OR) are also checked before they are discarded into the sharps waste containers.

Prior to the release of the patient, the medical physicist shall review the post-implantation survey results to confirm that all regulations regarding the release of patients with radioactive sources have been followed.

Post implant radiation safety considerations

Patients should be provided with written descriptions of the radiation protection guidelines, including, but not limited to, discussion of potential limitations of patient contact with minors and pregnant women. The radiation oncologist, the medical physicist, and the radiation safety officer should define the post implant radiation safety guidelines for patients treated with permanent seed implantation.

Procedure Specifications for HDR brachytherapy

HDR brachytherapy delivers radiation at a dose rate of ~12 Gy/h (12), and usually significantly higher. It requires remote afterloading of high-activity sources.

Patients have been treated heterogeneously, most commonly receiving an HDR boost with external beam radiation. The HDR boost schedules vary from 9-15 Gy in a single fraction to 26 Gy in four fractions, with numerous intermediary dose fractionation protocols.

In addition, HDR brachytherapy without external beam radiotherapy (monotherapy) has been used successfully introduced to treat early and intermediate-risk prostate cancer.

Equipment, Facility, Ultrasound

This is the same as for PPB.

In addition, it requires a remote afterloader with a stepping source, and an implantation room or brachytherapy suite with adequate shielding to perform the HDR treatment.

Fluoroscopy is advised to identify needle positions.

Many needle templates that are used incorporate a locking mechanism to aid placement, and fixation of catheters in position until treatment has been delivered.

Dose prescriptions

Given the heterogeneity of prescription doses described in the literature, no particular dose fractionation schedule can be recommended.

HDR brachytherapy has most frequently been used as a DE-boost given in one to six fractions in conjunction with external beam radiation, given to doses between 36 and 50 Gy.

In the setting of HDR monotherapy, treatment has been administered in three to six fractions. The trend over the past decade has been to deliver fewer fractions with a larger dose per fraction. This is especially true because the advent of ultrasound-based planning where one fraction per implant has now been introduced (34).

Published prescriptions from experienced brachytherapy centres are listed below:

Institution	DE-Boost	Monotherapy
<i>MSKCC</i>	7Gy x 3	9,5Gy x 4
<i>Toronto</i>	15Gy x 1	
<i>UCLA</i>	6Gy x 4	7.25Gy x 6
<i>UCSF</i>	15Gy x 1	10.5Gy x 3
<i>ABS</i>	10Gy x 2	10.5Gy x 3
<i>BCCA</i>	10Gy x 2	

Target volumes

Treatment planning is typically performed with TRUS, CT, or MRI-based imaging. Intraoperative planning uses TRUS imaging, while post-implant dosimetry typically uses CT images.

The prostate clinical target volume (CTV 1) is represented by the whole prostate gland visible on 5 mm separated TRUS images, often without safety margins (36).

Besides the prostate capsule (CTV 1) the peripheral zone can be delineated (CTV

2) and, if possible, regions infiltrated by macroscopic tumour (CTV 3) as these seem to be the most important boost target volumes inside the prostate.

There are different target and treatment philosophies in literature: for the whole gland (CTV 1) some groups apply a homogenous needle distribution using inter needle spacing of 10–15 and 5 mm space from the prostate circumference followed by planned hot-spots in visible tumour infiltration areas (tumor CTV 3), as well as well-placed low-dose areas according to critical structures (37).

In cases with advanced disease, there may be large volume disease near the edge of the clinical target volume. It is therefore especially important to review the biopsy and imaging data and know the precise location and extent of the tumor (extracapsular extension, seminal vesicle, etc.) at the time of the procedure to ensure the tumor volume is adequately covered. In such cases, HDR brachytherapy treatment planning is ideally suited to customize dosimetry to give the required dose to the tumor while sparing normal tissue.

Although the number and array of brachytherapy catheters depend on prostate shape, volume, and regional anatomy, generally a minimum of 14 catheters should be used to avoid unnecessary hot spots within the PTV (35).

Treatment planning

Images for treatment planning can be TRUS, CT, or MRI based. For CT-based planning, the images should be contiguous and no more than 3 mm thick in the axial plane. Imaging should extend at least 9 mm above and below the target volume, and should include the proximal tips of the implant catheters along with sufficient normal anatomy such as seminal vesicles, bladder, and bowel for meaningful normal tissue dosimetry. It is not necessary to include the patient's body contour for treatment planning purposes. Urethral identification is recommended using either a radio-opaque urinary catheter for CT or aerated gel for ultrasound.

After images are acquired, target volumes are determined by the radiation oncologist. The dose distribution is created, evaluated, and adjusted before the dose is delivered so as to reliably meet the requirements of the individual case.

Source dwell times at each stopping point are optimized to achieve target coverage while limiting dose to critical organs at risk. Post implant dose calculation performed before dose delivery allows for adjustments in the treatment plan to allow for individual patient anatomy and catheter positioning to optimize dose coverage of the target volume while minimizing high doses to adjacent normal tissues.

The prescribed dose will be the intended minimum dose delivered to the PTV. A computerized optimization program based on a geometric or inverse planning algorithm should be used, although manual optimization is also acceptable.

The planner must ensure that calculation parameters for the dose-volume histogram are set to obtain accurate values. The plan is optimized to meet the parameters listed below.

The dose plan is typically prepared by a dosimetrist or physicist. It is then reviewed and approved by the treating physician. An independent check should be performed and should include patient's identification, dates of treatment, total dwell time, prescription dose, catheter positions, dose coverage, and normal tissue doses.

Dose parameters

Prostate

The prescribed dose should not cover less than 90% of the target volume (V100 > 90%, with an expected V100 > 95%).

A range of isodose distributions of 50%, 100%, 110%, 120%, and 150% of the prescription dose relative to the PTV should be used for treatment plan evaluation.

OAR

Given the extreme heterogeneity in dose fractionation scheduled published in the literature, with corresponding excellent results, it is difficult to establish absolute dose guidelines for normal tissues.

Published dose constraints by experienced HDR centres are listed below (34):

Institution	Bladder	Urethra	Rectum
<i>MSKCC</i>		<120% prescribed dose (PD)	D2cc<70%
<i>Toronto</i>		D10<118% Max<125%	V80<0.5cc
<i>UCLA</i>		Max<120%	
<i>UCSF</i>	V75<1cc	V125<1cc V150<0cc	V75<1cc
<i>ABS</i>	V75<1cc	V125<1cc	V75<1cc

BCCA		Max<115%	1cc<7Gy
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Implant procedure

The setup and theatre preparations are the same as for PPB.

Transperineal catheter insertion is usually performed under general or spinal anesthesia, with TRUS guidance. Various catheter placement patterns have been described (34).

When more than one insertion is performed as part of the prescribed course of treatment, care should be taken to provide uniform treatment with each insertion. This can be best accomplished by reproducing the same patient positioning for each subsequent insertion, and using a similar catheter array, the same number of catheters and template to place brachytherapy catheters in the same position at each treatment.

It is not uncommon for the prostate to have varying volumes between brachytherapy procedures, and this must, of course, be taken into account on an individualized basis. However, the same procedures should be used to identify and contour targets and normal tissue structures with each insertion. However, each new insertion should be replanned instead of relying on the initial plan for subsequent fractions.

In cases where patients have HDR catheters in place and require hospital admission, appropriate pain management, such as oral, epidural, or intravenous patient-controlled analgesia is indicated. Routine precautions for deep venous thrombosis should be undertaken. If multiple HDR fractions are given using each implant, it is preferable to complete the sequence in less than 24 h to minimize risk of thrombosis, infection, and patient discomfort. It is better to repeat the implant rather than keep the patient in bed for multiple nights.

Radionuclides

Iridium 192 (¹⁹²Ir) is the most commonly used isotope for HDR. ¹⁹²Ir has an average energy of 380 KeV, a half-life of 73.8 days and a half value layer of 2.5 mm of lead.

¹⁹²Ir HDR brachytherapy uses a stepping source.

Sequencing and supplemental EBRT

As for PPB

Post implant Procedures

After removal of the HDR catheters, the bladder may need to be irrigated with a sterile solution to remove blood clots before removal of the urinary catheter. Perineal pressure after catheter removal will minimize the risks of hematoma formation. Antibiotics, steroid medications, and alpha-blockers can be prescribed as clinically needed.

Radiation Safety and QA

Before each HDR brachytherapy fraction, the patient's identification, date of treatment, source activity, total treatment (dwell) time, and dose prescription must be confirmed. Transfer tubes from the HDR afterloading apparatus must be correctly attached to each brachytherapy catheter and confirmed by the treating physician or physicist. Dose delivery should only begin after transfer tube and catheter patency, and linear dimension have been checked with a dummy source.

Treatment should be observed with real-time camera visualization of the patient, and preferably the afterloader also.

A medical physicist must be present at the treatment console throughout the entire fraction. A radiation oncologist must supervise the treatment in accordance with regulations.

The treatment room and the patient must be surveyed after the procedure to ensure that the source has properly retracted.

Follow up of Prostate Brachytherapy patients

Post-op follow up should consist of sufficient visits with the first 3 months to ensure patient safety and comfort. The frequency of subsequent visits may vary among the physicians involved with the patients care.

The best definition of biochemical failure has yet to be determined in brachytherapy patients. The ASTRO Phoenix definition is commonly used, although it has been argued that stricter criteria post brachytherapy should be applied (12).

Considerations should be given for PSA bounce in case of PSA rises 18-30 months after implant (13).

If a rising PSA occurs and prostate biopsy is undertaken, it should be recognized that the biopsy result may not be interpretable before 30 months after PPB, and a false call of failure may occur when actually a benign PSA bounce is likely (24).

Summary

Prostate brachytherapy is an effective modality for treating prostate cancer. Its safe and effective performance is a complex process that requires coordination between the radiation oncologist, urologist, medical physicist and other health professionals. Appropriate patient selection criteria and quality assurance procedures are important for a successful program.

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