

CLINICAL INVESTIGATION

Prostate

AMERICAN BRACHYTHERAPY SOCIETY (ABS) RECOMMENDATIONS FOR
TRANSPERINEAL PERMANENT BRACHYTHERAPY OF PROSTATE CANCER

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Purpose/Objective: To develop and disseminate the American Brachytherapy Society (ABS) recommendations for the clinical quality assurance and guidelines of permanent transperineal prostate brachytherapy with ^{125}I or ^{103}Pd .

Methods and Materials: The ABS formed a committee of experts in prostate brachytherapy to develop consensus guidelines through a critical analysis of published data supplemented by their clinical experience. The recommendations of the panels were reviewed and approved by the Board of Directors of the ABS.

Results: Patients with high probability of organ-confined disease are appropriately treated with brachytherapy alone. Brachytherapy candidates with a significant risk of extraprostatic extension should be treated with supplemental external beam radiation therapy (EBRT). Patient selection guidelines were developed. Dosimetric planning of the implant should be carried out for all patients before seed insertion. A modified peripheral loading is preferred. The AAPM TG-43 recommendations requiring a change in prescription dose for ^{125}I sources should be universally implemented. The recommended prescription doses for monotherapy are 145 Gy for ^{125}I and 115–120 Gy for ^{103}Pd . The corresponding boost doses (after 40–50 Gy EBRT) are 100–110 Gy and 80–90 Gy, respectively. Clinical evidence to guide selection of radionuclide (^{103}Pd or ^{125}I) is lacking. Post implant dosimetry and evaluation must be performed on all patients. It is suggested that the dose that covers 90% (D_{90}) and 100% (D_{100}) of the prostate volume and the percentage of the prostate volume receiving the prescribed dose (V_{100}) be obtained from a dose-volume histogram (DVH) and reported.

Conclusion: Guidelines for appropriate patient selection, dose reporting, and improved quality of permanent prostate brachytherapy are presented. These broad recommendations are intended to be technical and advisory in nature, but the ultimate responsibility for the medical decisions rests with the treating physician. This is a constantly evolving field, and the recommendations are subject to modifications as new data becomes available.
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Prostate neoplasm, Brachytherapy, Ultrasound, ^{125}I , ^{103}Pd .

INTRODUCTION

Prostate cancer is the most common malignancy in men in the United States. The present treatment options include radical prostatectomy, external beam radiation therapy (EBRT), temporary and permanent brachytherapy, hormonal therapy, and watchful waiting. The relative efficacy of each method is controversial and is beyond the scope of this report (which specifically deals with the guidelines for brachytherapy). It has been noted that the proportion of patients treated by permanent brachytherapy is rapidly increasing, because brachytherapy offers several practical and

theoretical advantages over EBRT in selected patients. Firstly, due to the physics of radiation emanation from the implanted radioisotope, there is dose escalation within the prostate, with rapid dose fall in surrounding normal tissues. Target motion, set-up variation, and localization errors from day-to-day are not of major concern as they are with EBRT.

Brachytherapy is a simple, outpatient procedure that avoids hospitalization and allows the patient an early recovery and rapid return to normal activity. It has produced good 10-year outcome with relatively low morbidity. With widespread patient education of the available treatment options,

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its advantages have become more apparent to the general public. With the advent of the internet, there has been increased communication between patients, which has further increased the awareness of prostate brachytherapy as a treatment option.

It was estimated that of the 190,000 patients diagnosed with localized prostate cancer in 1996, only 8,000 (4.2%) were treated by brachytherapy (1). There has been an exponential growth in the use of brachytherapy and by 2006, it is expected that about half of patients will be treated by brachytherapy (1). The favorable results of permanent implant of the prostate that have been published by the major centers may not be reproducible by others if strict treatment guidelines are not followed (2–19). Recent surveys by the clinical research committee of the American Brachytherapy Society (ABS) and the Prostate Brachytherapy Quality Assurance Group (PBQAG) have shown that the indications, techniques, treatment regimens, and dosimetry being used for brachytherapy of prostate cancer vary widely (20–23). Several areas of controversy were identified in these reports:

- Selection of patients for brachytherapy as monotherapy;
- Selection of patients for brachytherapy combined therapy with EBRT;
- Role of combined hormonal blockade;
- Pre-implant treatment planning;
- The choice of radionuclide: ^{125}I versus ^{103}Pd ;
- Post-implant dosimetry evaluation.

The PBQAG as a subcommittee of the Clinical Research Committee of the ABS was entrusted by the ABS Board of Directors to establish the standards of care for permanent brachytherapy. This committee met to identify areas of consensus and controversy and to issue clinical and dosimetric guidelines for transperineal prostate permanent brachytherapy. Results of these deliberations and recommendations of the panel are presented to guide ongoing clinical practice and future investigations. It should be noted that these broad recommendations are intended to be technical and advisory in nature; however, the responsibility for the medical decisions ultimately rests with the treating physician. This is a constantly evolving field and the recommendations are subject to modifications as new data becomes available.

METHODS

The members of the committee after combining their clinical experience with an extensive review of literature, identified the clinical rationale, indications, techniques, and results of permanent ^{125}I and ^{103}Pd transperineal prostate brachytherapy. Specific recommendations for clinical therapy and directions for future investigations were made when there was a consensus. There were some areas where major controversy or lack of evidence did not allow the ABS to make specific recommendations. These were so noted. This report was reviewed and approved by the Board of Directors of the ABS.

RESULTS

Selection criteria

Previous surveys of prostate brachytherapists have shown a wide variation in patient selection criteria (21, 22). Pre-operatively, medical, technical, and clinical factors need to be met to insure a satisfactory result. If the patient meets these criteria, the next step is to assess whether prostate seed implantation alone or this in combination with EBRT is appropriate therapy. The patient selection and exclusion criteria are summarized in Table 1. Patients suitable for permanent prostate brachytherapy should have a reasonable life expectancy of 5 years or more. Patients who, for clinical reasons, are poor candidates for outpatient surgery, those with large trans-urethral resection of prostate (TURP) defects, and those with distant metastasis, are not candidates for brachytherapy. Greater risk of complications has not been reported in elderly patients. The present literature does

Table 1. Selection criteria for permanent brachytherapy of the prostate

Clinical Exclusion Criteria:

Life expectancy < 5 years
 Large or poorly healed TURP defect
 Unacceptable operative risks
 Distant metastases

Relative Contraindications for Brachytherapy:

These patients are not ideal candidates for brachytherapy, but have nevertheless been successfully implanted. Beginners should not implant these patients.

Patients at increased risk of developing complications

Large median lobes
 Previous pelvic irradiation
 High AUA score
 History of multiple pelvic surgeries
 Severe diabetes with healing problems

Technical difficulties which may result in inadequate dose coverage

Previous transurethral resection of prostate (TURP)
 Gland size > 60 cc at time of implantation
 Prominent median lobe
 Positive seminal vesicles

Brachytherapy as Monotherapy:

Stage T1 to T2a and
 Grade Gleason sum 2–6 and
 PSA < 10 ng/ml

Brachytherapy as a Boost to EBRT:

Stage Clinical T2b, T2c *or*
 Grade: Gleason sum 8–10 *or*
 PSA > 20 ng/ml

Other possible indications for Brachytherapy as a Boost to EBRT:

Perineural invasion
 Multiple positive biopsies
 Bilateral positive biopsies
 MRI positive for capsular penetration

Brachytherapy (including Boosting EBRT) in Conjunction with Androgen Deprivation:

Patients with initially large prostate (> 60 cc) that have downsized sufficiently

not address the effects of other preexisting medical conditions.

There are patients who are not ideal candidates for brachytherapy, but have nevertheless been successfully implanted. Beginners should not implant these patients. These include patients at increased risk of developing complications and those for whom technical difficulties may result in inadequate dose coverage. For example, large prostate size (> 60 cc), prominent median lobes, and prior TURP are associated with increased technical difficulties. Patients with previous multiple pelvic surgeries, severe diabetes, previous pelvic irradiation, and high AUA score are at increased risk of developing postoperative complications.

Patients who have previously undergone a TURP should be evaluated carefully. A large TURP defect can allow loss of seeds and significantly alter the resultant dosimetry. In addition, TURP patients may be at greater risk for urethral necrosis, stricture, and urinary incontinence (8); hence, patients with large or poorly healed TURP defects should be excluded from brachytherapy. Patients with smaller TURP defects may be implanted using peripheral seed loading. It is prudent to wait at least 2–3 months before performing an implant on post-TURP patients, to allow some tissue regeneration in the defect (24–26). However, longer follow-up is required to evaluate the effect of urethral sparing techniques on tumor control and morbidity.

Glands larger than 60 cc (at the time of implantation) are often technically more difficult to implant because of pubic arch interference and because they require a large number of seeds (8). These patients often become good implant candidates after cytoreduction with hormonal therapy. Patients with large median lobes are difficult to implant and may not achieve satisfactory distribution of seed. Patients with positive seminal vesicles are at risk for extra-capsular extension, lymph node involvement, and gross disease beyond the confines of an implant volume, and therefore may be at greater risk for failure (27). They are not suited for treatment with implant alone, but may be treated with combination of brachytherapy and EBRT. There is only limited data on the use of brachytherapy as monotherapy for patients with previous pelvic irradiation or with proven positive pelvic lymph nodes (24, 28). Patients with high American Urological Association (AUA) scores may experience worsening obstructive symptoms and are at a higher risk of going into urinary retention (29).

Patients with high likelihood to have disease well encompassed by implant are candidates for seed implantation alone. Patients with a significant risk of disease outside the implant volume may benefit from the addition of EBRT or hormonal therapy. Examination of radical prostatectomy specimen and correlation with clinical parameters indicate the risk factors for extracapsular disease to be 40–50% for early-stage prostate cancer patients (25, 30–58). Although lymph node (LN) and seminal vesicle (SV) involvement precludes local therapy (i.e., surgery or implant), the presence of extracapsular penetration (ECP) does not. In many patients with ECP, the disease is confined to a surgical

volume (35). Because the radiation dose can extend a few millimeters beyond the prostate capsule, some patients with ECP can be successfully treated with brachytherapy.

Significant pretreatment factors, predictive of ECP, LN, and SV involvement, include stage, grade, and prostate specific antigen (PSA) (34, 40, 42, 44, 49, 50, 59, 60). Other factors and tests may have an additional role in assessing the extent of disease (30, 32, 36, 38, 41, 45, 47, 55, 61). The nomogram produced in the Partin study, the largest study to date analyzing pretreatment factors predictive of extraprostatic disease, correlated patient subsets to the risk of LN, SV involvement, and ECP (44). From the Partin tables, the risk of LN, SV, and ECP for an individual patient can be determined; and the risk of disease beyond an implant volume can be calculated (59, 60).

The Partin tables and clinical results to date suggest that T1 to T2a patients with PSA < 10 ng/ml and Gleason score ≤ 6 would generally be good candidates for implant alone (8) (Table 1). Patients with Stage T2c and higher or Gleason scores of 8–10 or PSA > 20 ng/ml should receive combined EBRT and brachytherapy. Patients falling between these two risk groups must be evaluated individually and other factors such as perineural invasion, multiple positive biopsies, tumor location, and MRI findings may influence the decision to add EBRT and/or hormonal therapy.

Perineural invasion on biopsy has been associated with capsular penetration in 49–93% of cases (32). At present, perineural invasion is an important factor for predicting capsular invasion, but its value in predicting which patients have disease outside a surgical or an implant volume is limited. Tumors at the base adjacent to the neurovascular bundle have a higher propensity for ECP than do lesions away from the neurovascular bundle (35, 43, 48, 54). Tumors arising in the transition zone are bounded by a surgical capsule, limiting the likelihood of spread into the central and peripheral zones and capsule (39, 49). The risk of capsular penetration is high when contralateral or 4 or more biopsies are positive (62, 63). Ploidy adds little over grade in its predictive value, and therefore has limited clinical significance (31).

The role of MRI in seed implantation is unclear (64). If seed implantation alone is being considered for Gleason score 7–10 tumors, MRI may be of value in detecting extraprostatic spread, especially if the tumor is palpable at the prostatic base near the neurovascular bundle. Patients with Gleason score of 5–7 and PSA between 10 and 20 may also similarly benefit from this examination (65).

Pre-implant treatment planning

The ABS recommends that dosimetric planning of the implant be carried out for all patients before seed insertion. The pre-implant treatment planning is commonly performed a few weeks before the brachytherapy procedure (14, 14, 66–69), but can be performed on the day of the procedure (intraoperative treatment planning) (17, 69, 70). The current standard of practice is to use the transrectal ultrasound (TRUS) to perform the volume study before the implant in

order to prepare a treatment plan containing needle locations, number, and strength of seeds in the needles using contiguous, transverse images of the prostate from the TRUS. However, some have used CT guidance with success (18, 71). The ABS recommends the use of TRUS for both pre-implant planning and guidance during the needle implantation procedure.

Typically, implantation before the 1990s relied on a Quimby-type distribution, with even spacing of sources leading to uneven dose distributions within the implanted volume with the central region of the implant receiving a higher dose (72). The "average dimension" method using the Memorial nomogram was useful in the retropubic era, in that the total activity could be quickly obtained from an intraoperative measurement of the three dimensions of the gland (73). The original Memorial nomogram has been shown to provide an inadequate amount of activity per volume to achieve the desired dose in actual implants (70). However, modifications of these nomograms in combination with real-time TRUS imaging and planning have enabled the desired dose to be achieved (17, 69, 70). Recent innovations in treatment planning systems and computerized tomography have led to greater reliance on a more peripheral distribution of radionuclide in an effort to minimize the central "hot" spots. This method has sometimes been called the modified peripheral loading method. Reducing the central dose (or, more precisely, not having a "hotter" center) compared to the periphery is considered important because of the possibility of urinary complications with a high urethral dose. Although urethral tolerance dose is not precisely known, doses in excess of 400 Gy with ^{125}I sources have shown higher complication rates (16). In the absence of better dosimetric data, the ABS recommends that modified peripheral method be used for prostate implants and that urethral doses be carefully examined in an effort to minimize the length of urethra receiving $> 200\%$ of the prescribed dose (6, 15, 66, 74, 75). This is particularly important if a prostate is implanted post-TURP (6). Additional recommendations may be forthcoming from the AAPM task group No. 64 which is currently developing recommendations for prostate seed implant brachytherapy (Yu *et al.*, personal communication).

Intraoperative procedure

The standard procedure for seed implantation is to use a transperineal approach under guidance of a template and TRUS (22, 66). The intraoperative patient positioning and the setup including the TRUS-probe angle need to match the pre-implant planning study as closely as possible. Alternatively, when using an interactive technique, the patient should be positioned to allow full visualization of the prostate in longitudinal and transverse imaging (17, 69, 70). TRUS is usually performed using a 5.0–7.5 MHz frequency probe. It is preferable to use a high-resolution biplanar ultrasound system with dedicated prostate brachytherapy software. The needles can also be inserted under CT guidance, but this is only performed in a few centers (71, 76). Fluoroscopy can be helpful especially if there is poor image

quality on the TRUS (9, 67, 68, 77, 78). An immobilization apparatus with a "stepping unit" that allows the probe to be moved in and out in 0.5-cm increments should be used. Intraprostatic calcifications and other anatomic landmarks often help in aligning the TRUS probe angle and position such that the 0.5-cm interval images match the pre-implant planning TRUS study as closely as possible. The immobilization device and external template/grid must be periodically calibrated in a water bath in order to ensure that the external grid matches the electronic grid seen on the TRUS monitor.

The prostate gland may move during the implant procedure. Stabilizing needles may be used to help minimize prostate motion during the implant procedure (79, 80). The implant needles are then inserted one at a time into the external template/grid.

The seed insertion can be performed in a variety of ways. Some clinicians place one needle at a time and then deposit the seeds planned for that needle. Others place a row of needles prior to depositing the seeds from those needles, and yet others place all the implant needles and then proceed to deposit the seeds. The seeds can be placed using preloaded needles, or seed in suture (e.g., RAPID StrandTM) or by using a Mick applicator (4, 77, 81). The ABS does not favor any particular seed deposition technique over the other.

Revision of ^{125}I doses

In 1995, the American Association of Physics and Medicine (AAPM) Task Group No. 43 (TG-43) recommended changing the algorithm used to calculate dose from ^{125}I and ^{103}Pd sources (82). The ABS endorses the use of the TG-43 recommendation for ^{125}I dosimetry. Using TG-43, an ^{125}I implant calculated to receive 160 Gy using earlier methodology, will now be calculated to receive 144 Gy, using the point source approximation (83–85). In other words, with no change in the implant, activity, or geometry, the new dose will be reported as approximately 10% less. The ABS recommends that TG-43 be adopted. Thus, the 160 Gy dose prescription of pre-TG-43 era, for ^{125}I should now be 144 Gy. There is great potential for confusion as new prescribed doses are published. Clinicians need to critically read any literature to determine whether the doses were stated as pre- or post-TG-43 modification to avoid misunderstanding when using ^{125}I . The recommendations of TG-43 did not significantly alter the ^{103}Pd dosimetry.

Dose selection

Unfortunately, the precise radiation dose necessary for the eradication of prostate cancer by brachytherapy has not yet been clearly established. Most publications simply report the intended (prescribed) dose, rather than the dose actually achieved. Several important concepts can be derived from both the retropubic era and the transperineal TRUS experience.

Morton and Peschel (86) published the Yale retropubic results in 1988. They noted that patients who received a homogeneous minimum tumor dose of 100 Gy (90 Gy by TG-43) achieved a local control rate of 82%, versus 58% if

the implant was judged as inadequate (either inhomogeneous or inadequate dose). Of note, is that they found that patients with very large prostates, which necessitated an implant of more than 25 mCi, had significantly higher complication rates.

Fuks *et al.* (87) published the Memorial Sloan-Kettering Cancer Center retropubic ^{125}I interstitial prostate implant results in 1991. They treated 879 patients with Stages B and C prostate cancer. In their study, they noted that patients who received a matched peripheral dose of 140 Gy (126 Gy by TG-43) or more achieved a 10-year local control rate of 60%. In contrast, those patients with a matched peripheral dose of less than 140 Gy (126 Gy by TG-43) had a 10-year local control rate of only 20%. Furthermore, they noted that patients who had homogeneous dose distributions within their implants had improved local control rates. Zelefsky *et al.* (88) updated the study with the same conclusions at 15-year follow-up. Major limitations of these studies included the reliance on match peripheral dose (MPD) calculations, use of digital rectal examinations (DRE) to assess local control and the lack of PSA-based treatment endpoint.

In 1996, Stock *et al.* (14) using a transperineal ^{125}I TRUS guided technique with a prescribed minimal peripheral dose of 160 Gy (144 Gy by TG-43), presented PSA-based analysis of their results. They used the concept of D_{90} , which is the dose that 90% of the prostate volume received from the implant. In their series, when the D_{90} was more than 120 Gy (108 Gy by TG-43), the resultant biochemical control (bNED) rate was 100%. In contrast, if the D_{90} was less than 120 Gy (108 Gy by TG-43), bNED rate declined to 65%. In an updated analysis of their study, Stock *et al.* (17) revised the required D_{90} value to 140 Gy (by TG-43), regardless of stratification by baseline PSA value.

Based on the available data, the ABS makes the following recommendations for dose prescription (Table 2). For patients treated with brachytherapy alone, the prescription dose is 115–120 Gy for ^{103}Pd (66, 67, 77, 89) and 144 Gy (TG-43) for ^{125}I . The ^{125}I dose recommendation is based on the dose prescription of 160 Gy (pre-TG-43) commonly reported in the medical literature (2–4, 57, 69, 77, 90, 91), which is approximately 144 Gy if calculated using the TG-43 methodology (82).

Patients with high-risk prostate cancer are to be treated with combined EBRT and ^{103}Pd or ^{125}I brachytherapy as a boost. The recommended EBRT dose to the prostate and periprostatic area is 40–50 Gy in 1.8–2 Gy per fraction

(4–6, 21, 22, 66, 77). For ^{103}Pd , the prescription dose for brachytherapy as a boost is 80–90 Gy (2, 4, 7, 10, 77). For ^{125}I , the prescription dose for brachytherapy as a boost is 100–110 Gy (TG-43), which is once again based on pre-TG-43 published doses of 110–120 Gy (4, 5, 10, 66). Though EBRT is generally performed before brachytherapy by some clinicians, the ABS has no recommendation regarding the timing of brachytherapy to EBRT due to paucity of published data. It should be clearly recognized that the above recommendations for dose prescription is different from the dose actually delivered to the entire prostate (see section on post-implant dosimetry evaluation for details). The dose required for eradication of prostate disease is not known and awaits analysis of long-term control results with CT-based dosimetry.

Choice of radionuclides— ^{103}Pd or ^{125}I

In addition to the continued use of ^{125}I for prostate brachytherapy, ^{103}Pd was introduced in 1986. The physical differences between ^{103}Pd and ^{125}I are listed in Table 3. The lower energy of photons emitted by ^{103}Pd sources results in a more rapid tissue attenuation, hence the seed spacing is critical for ^{103}Pd (92, 93).

Ling *et al.* (94) compared the effectiveness of iodine based on a theoretical radiobiologic model. Using the linear-quadratic model it was concluded that at clinically prescribed doses, the predicted cell kill is better for ^{103}Pd in rapidly proliferating tumors, with an advantage for ^{125}I in slower-growing tumors. Animal studies by Nag *et al.* suggest that ^{103}Pd was more effective than ^{125}I in poorly-differentiated tumor, while this superiority was less marked in well-differentiated cancers (95, 96). Based partly on these assumptions, ^{125}I is most commonly used in lower grade (Gleason score 2–6) tumors and ^{103}Pd used for higher grade (Gleason score > 6) malignancy in the US (22). It must be recognized that these assumptions may not be true, because a recent cell kinetics study (97) on human prostate biopsy samples demonstrated no correlation between tumor histology and cell kinetics. Hence, some physicians use either ^{103}Pd or ^{125}I exclusively (22). *In vitro* laboratory studies reveal a difference in relative biological effectiveness (RBE) for ^{125}I (approximately 1.4) compared to 1.9 for ^{103}Pd (98). The significance of these differences is not clinically apparent.

The ABS does not recommend the use of one radionuclide over the other, because clinical studies have not shown any difference in any subgroup of patients based on outcome or complications. The ABS recommends additional

Table 2. ABS prescription dose guidelines*

Radionuclide	Brachytherapy dose for monotherapy (Gy)	Brachytherapy dose to boost 40–50 Gy EBRT (Gy)
^{125}I (pre TG-43)	160	110–120
^{125}I (TG-43)	144	100–110
^{103}Pd	115–120	80–90

*It should be recognized that the prescription dose is different from the dose actually delivered to the entire prostate.

Table 3. Physical differences between ^{125}I and ^{103}Pd

	^{125}I	^{103}Pd
Year introduced	1965	1986
Photon energy (KeV)	28	21
Seed spacing	Not so critical	< 1.7 cm
Half-life (days)	59.4	17
Initial dose rate (for monotherapy)	7 cGy/h	18–20 cGy/h
RBE	1.4	1.9

clinical research to further elucidate the role of ^{125}I vs ^{103}Pd in prostate cancer.

Post-implantation procedures

A cystoscopy may be performed after the procedure. The advantages of cystoscopy include removal of any blood clots and misplaced seeds in the urethra or bladder, and prediction for potential postoperative complications and detection of other pathology (e.g., bladder tumors). However, the use of cystoscopy is not mandatory. Fluoroscopy or an antero-posterior radiograph may be obtained intraoperatively to assess the adequacy of seed placement.

Radiation precautions should be explained to the patient and written guidelines given. It is common practice to advise the avoidance of prolonged close contact with children (under 18 years) and pregnant women for one half-life of the radionuclide. These guidelines are conservative and generally exceed the regulatory requirements. From a radiation safety perspective, the patient may sleep in the same bed with his partner, and sexual intercourse may be resumed. Although there is no published report of ejaculation of a seed, there have been anecdotal cases. Though the risk of radiation injury from a single seed is minimal, some authors advise patients to abstain from intercourse for 1–2 months, or to wear condoms or masturbate for the first few ejaculations to prevent the unlikely passage of a seed into the partner.

Patients should be advised that there is a low risk of seed migration to the lung, and that this has not been shown to have any clinically adverse effects (67, 99–102). The seeds take approximately 1 day to migrate to the lungs (101); therefore, a chest radiograph is advised at the first follow-up visit (not on the day of implant) to scan the lungs for embolized seeds. The patients should be advised of their presence if detected (67, 99–102).

Postoperative anti-inflammatory drugs, antibiotics, and alpha-blockers are used by many brachytherapists prophylactically, while others prescribe them only as needed (22, 77, 103). The ABS does not support one position over the other, due to insufficient evidence in the literature. Urinary anesthetics, antispasmodics, analgesics, perineal ice packs, and stool softeners may be added in symptomatic patients. Severe urinary obstructive symptoms are uncommon. When they do occur, they are to be managed by intermittent or continuous bladder drainage (foley catheter or suprapubic cystostomy). In the majority of patients, these symptoms resolve by the above temporary measures. The use of transurethral incision of prostate (TUIP) should be avoided in the first 6 months post-implant. If the temporary measures are not successful after this time period, TUIP or minimal TURP may be considered, recognizing that risk of urinary incontinence may exist following these procedures (104).

EVALUATION OF POST-IMPLANT DOSIMETRY

The ABS recommends that postoperative dosimetry be performed for each patient. Without this information, it is impossible to confirm the actual dose delivered or to iden-

tify any variance from the treatment plan. Additionally, careful assessment will provide the brachytherapist an objective measure of implant quality allowing for continued technical improvement. There is a “learning curve” for the procedure (13, 14, 78, 96). Ongoing feedback from critical review of dosimetry is a necessary link in this learning process.

Post-implant dosimetry may be performed using a variety of techniques. Each has its own advantages and disadvantages, which must be understood. The simplest approach is to use orthogonal, three-film autosort, or stereo-shifted radiographs to localize the seed placement. Using these methods, it is possible to accurately report the dose distribution in relation to the implanted seeds. The obvious limitation is that even with the use of contrast, the anatomic boundaries of the prostate cannot be delineated on the radiograph; hence, the dose delivered in relation to the prostate cannot be determined. Therefore, dosimetry obtained by these techniques alone is not sufficient to adequately evaluate the dose delivered to the prostate. It is therefore necessary to use CT evaluation to demonstrate the relationship of the seeds and the prostate (20, 71, 76, 105–107). However, few dosimetry systems currently support this function. Use of MRI scanning is also being investigated (64, 106, 108, 109). The ABS recommends the use of CT-based treatment planning system whenever possible.

Several reports (110, 111) have documented a consistent discrepancy in the measured gland size by ultrasound and CT-imaging studies. For a number of reasons, including difficulty in delineating the prostate boundary at the apex, base, and periprostatic venous plexus; measurements using CT exceed by 20–40% the ultrasound volumes. Following brachytherapy, there is further enlargement of the prostate as seen on CT, possibly resulting from edema or bleeding (112, 113). Therefore, dosimetry based on CT scan performed too early may overestimate the gland size, and thus underestimate the prostate dose. However, CT scans performed several weeks after implantation may more accurately reflect the baseline gland size. The optimal timing for obtaining the post implant CT scan is not known (66, 69, 77, 112). Recent studies suggest that it may be about 4 weeks (112, 113). However, early imaging is often preferred for its practicality.

Roy *et al.* (107, at Memorial Sloan-Kettering, have shown that the dose values D_{99} and D_{100} covering 99% and 100% of the target volume are highly sensitive to small perturbations in seed locations and/or target definition. It should be noted that D_{100} is also the strict definition of the minimum peripheral dose. Yu *et al.* (114) and Stock *et al.* (14, 17) have shown that the dose covering 90% of the target volume (D_{90}) is a much more realistic parameter for dose specification. Willins and Wallner (115) have suggested that inclusion of at least 80% of the target within the prescribed isodose volume (D_{80}) is probably adequate.

The current state of the art is a CT-based dosimetry whereby the source positions, prostate, and normal organs are directly obtained from the CT images (105). However, because few centers have this capability, the following is a

possible approach for post-implant dosimetry. The prostate volume from the pre-implant volume study using TRUS can be superimposed upon the post-implant CT images of the prostate. For registration of the TRUS and CT images, the posterior border of the prostate and/or urethra can be used. Care must be taken to use the correct magnification factors for the two images before superimposition. The calculated isodose curves can then be superimposed upon the combined TRUS and CT images. The dose volume histogram (DVH) could then be calculated for the distribution of dose over the volume of prostate as determined by the TRUS.

The ABS recommends that the following be reported and correlated with outcome data.

1. The prescribed (intended) dose.
2. The dose that covers 100% of the prostate volume (D_{100}), which is the strict definition of minimum peripheral dose. However, there is some uncertainty associated with delineation of the prostate boundaries on a CT scan (105).
3. The dose that covers 90% of the prostate volume (D_{90}). A D_{90} value of greater than or equal to the prescribed dose is a measure of a good implant quality.
4. The percentage of prostate volume that received the prescribed dose (V_{100}). If the dosimetry suggests significant underdosage in some portion of the prostate, the patient may be considered for additional EBRT or a second implant as soon as reasonably feasible. The ABS has formed a task force to formulate the evaluation and reporting criteria for post-implant dosimetry (S. Nag, personal communication).

Follow-up

Close postoperative follow-up with digital rectal examinations (DRE) and PSA at regular intervals is recommended. Routine ultrasound guided biopsies are not required. Biopsies can be performed if recurrence is suspected due to rising PSA or palpable nodule on DRE and salvage therapy contemplated (2, 8, 9, 67, 77, 116). The PSA nadir reached in the post-implant period correlates with outcome. Currently, there is controversy whether a PSA nadir of 1.0, 0.5, or even 0.2 is required to achieve long-term control of prostate cancer (2, 3, 5, 14, 16, 17).

DISCUSSION

Prostate brachytherapy is not new (117, 118). The previous retropubic technique of ^{125}I prostate brachytherapy

achieved inconsistent results with high long-term failure rates if the seeds did not adequately encompass the prostate (26, 72, 86–88, 119–125). The transperineal technique was introduced in an attempt to improve the homogeneity and accuracy of seed placement (4, 66–71, 126–132). Modern transperineal brachytherapy techniques using ultrasound guidance with either ^{103}Pd or ^{125}I offer good alternatives for management of localized prostate cancer in appropriately selected patients. This modality allows delivery of a higher localized radiation dose than that achievable by conventional EBRT. The nonsurgical, outpatient basis of permanent, ultrasound-guided transperineal prostate brachytherapy is convenient, has high patient appeal, offers minimal morbidity in appropriately selected patients, and generally results in minimal impairment of the patient's lifestyle (2–6, 8, 9, 11, 13–15, 17–19, 77, 132).

The high degree of accuracy achievable in prostate implants nowadays is partly due to technological improvements, but quality implants still require skill, adequate training, and attention to detail (2, 4, 14, 66, 69, 75–78, 81, 90, 126). The ABS suggests development of real-time, on-line dosimetry to allow immediate feedback that could result in better implant dosimetry.

Whether acceptable prostate brachytherapy can be performed in community hospitals, or whether it will be limited to centers of excellence remains to be demonstrated. However, since prostate cancer is a relatively slow growing malignancy, a longer (10–15 years) follow-up will be required to accumulate the data needed to reach a resolution and to determine the eventual efficacy of this treatment.

CONCLUSION

The indications, techniques, treatment regimens, and dosimetry being used for brachytherapy of prostate cancer vary widely between radiation oncologists. The current clinical guidelines for permanent TRUS-guided brachytherapy of the prostate should be a practical guide for clinicians performing prostate brachytherapy. The final place of brachytherapy in the armamentarium of prostate cancer treatment awaits the maturation of long-term, controlled clinical trials. This is a constantly evolving field and the recommendations are subject to modifications as new data becomes available. These broad recommendations are intended to be technical and advisory in nature, but the responsibility for the medical decisions ultimately rests with the treating physician.

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