Permanent prostate seed implant brachytherapy: Report of the American Association of Physicists in Medicine Task Group No. 64[a]

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There is now considerable evidence to suggest that technical innovations, 3D image-based planning, template guidance, computerized dosimetry analysis and improved quality assurance practice have converged in synergy in modern prostate brachytherapy, which promise to lead to increased tumor control and decreased toxicity. A substantial part of the medical physicist's contribution to this multi-disciplinary modality has a direct impact on the factors that may singly or jointly determine the treatment outcome. It is therefore of paramount importance for the medical physics community to establish a uniform standard of practice for prostate brachytherapy physics, so that the therapeutic potential of the modality can be maximally and consistently realized in the wider healthcare community. A recent survey in the U.S. for prostate brachytherapy revealed alarming variance in the pattern of practice in physics and dosimetry, particularly in regard to dose calculation, seed assay and time/method of postimplant imaging. Because of the large number of start-up programs at this time, it is essential that the roles and responsibilities of the medical physicist be clearly defined, consistent with the pivotal nature of the clinical physics component in assuring the ultimate success of prostate brachytherapy. It was against this background that the Radiation Therapy Committee of the American Association of Physicists in Medicine formed Task Group No. 64, which was charged (1) to review the current techniques in prostate seed implant brachytherapy, (2) to summarize the present knowledge in treatment planning, dose specification and reporting, (3) to recommend practical guidelines for the clinical medical physicist, and (4) to identify issues for future investigation. © 1999 American Association of Physicists in Medicine. [S0094-2405(99)00910-4]

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TABLE OF CONTENTS

GLOSSARY OF ABBREVIATIONS

ADCL	Accredited Dosimetry Calibration Laboratory.
D_{100}, D_{90}, D_{80}	Dose to 100%, 90%, 80% of the target volume for dosimetric evaluation.
DVH	Dose-volume histogram.
Gleason score	A pathological grading system for measuring the degree of differentiation of prostate tumors.
MPD	Matched peripheral dose, typically used in conjunction with the ellipsoidal approximation for the prostate volume.
mPD	Minimum peripheral dose. Used in dosimetric planning, the mPD corresponds to the isodose surface that just encompasses the planning target volume. This report recognizes that whereas the mPD usually corresponds to a prescribed dose, D_{100} as determined from postimplant dosimetry may be significantly different from the prescribed dose.
NIST	National Institute of Standards and Technology.
PSA	Prostate specific antigen.
PTV	Planning target volume.
S_{mPD}	Total source strength required to achieve 1 Gy in the mPD, typically used in dosimetric planning and optimization.
TRUS	Transrectal ultrasound.
$V_{200}, V_{100}, V_{90}, V_{80}$	(fractional) Volume of the prostate target for dosimetric evaluation that received 200%, 100%, 90%, 80% of the prescribed mPD.

I. INTRODUCTION

Adenocarcinoma of the prostate is the most common malignancy in man in the United States, excluding skin cancer. The American Cancer Society estimated that 184,500 new cases of prostate cancer would be diagnosed in the U.S. in 1998. Growing emphasis on prostatic specific antigen (PSA) based early detection and changes in the population demographics in the U.S. suggest that the number of newly diagnosed cases would continue to increase each year. In the treatment of prostate cancer, there is now a broad resurgence of interest in the role of permanent interstitial implantation of radioactive seeds. Prostate seed implants are currently performed using iodine-125 and palladium-103 sources under imaging and template guidance to deliver localized irradiation to high doses. For selected patients, seed implantation alone offers a complete course of treatment; for others, it is used in conjunction with external beam radiation therapy to the pelvis. Based on PSA screening data in 1991 to 1993, it was estimated that up to 10% of all newly diagnosed prostate cancer patients would be considered ideal candidates for seed implantation as definitive radiotherapy management.[1]

The techniques for permanent interstitial prostate brachytherapy evolved in two distinct eras. Historically, seed implantation was performed by free-hand placement of seeds in

an open surgical procedure via the retropubic approach.[2] Dosimetric planning was limited to the use of nomographs following intraoperative measurement of the size of the prostate gland.[3–5] The total activity to be implanted was determined using the average dimensions of the prostate. Postimplant dosimetry was analyzed in terms of the matched peripheral dose (MPD), defined as the isodose surface that would cover a spatial volume numerically equal to the volume of the prostate inferred from the ellipsoidal approximation.[6] Overall, the open surgical technique suffered from substantial uncertainties in dosimetric planning, implant execution and dose evaluation. In contrast, contemporary techniques for prostate brachytherapy rely on three-dimensional (3D) image-based treatment planning and real-time visualization of needle insertion and/or seed deposition. Seed implantation is performed under template guidance via a transperineal approach in a percutaneous procedure typically performed in an outpatient surgical setting. Holm *et al.*[7] first described the use of transrectal ultrasound (TRUS) for precise guidance of transperineal seed insertion in 1983. The technique was further popularized by Blasko, Grimm, Ragde and co-workers,[8–10] and has evolved into the most popular modality for prostate seed implantation to date. Characteristic of the technique is the use of TRUS for preoperative dosimetric planning and intraoperative visualization of needle placement. A somewhat different technique, developed by Wallner *et al.*,[11,12] uses computerized tomography (CT) to identify the target volume for treatment planning; intraoperative needle placement is verified under fluoroscopy using the urethra as the primary landmark. Compared to the open surgical technique, these contemporary techniques place considerable emphasis on 3D conformal dosimetric planning and precise placement of the planned seed configuration in the patient. Greater emphasis is also placed on careful patient selection based on serum PSA levels and Gleason scores.

The clinical experience associated with the retropubic technique has been a subject of active investigation.[13–21] The clinical results of long term studies with 10–15 year follow-up have been mixed, partly because the techniques of seed implantation and hence the implant qualities were quite varied. In particular, Zelefsky and Whitmore[20] recently reported the final assessment of the 15-year outcome of the historical series of retropubic freehand implants performed at the Memorial Sloan-Kettering Cancer Center. They concluded that the technique was associated with a greater than expected incidence of local relapse at 15 years, and identified suboptimal dose distribution due to technical limitations as the possible cause of the unfavorable outcome. Nath *et al.*[21] examined the 3D dose distribution of 110 prostate implants performed at Yale–New Haven Hospital in this era. They identified a number of dosimetric quality indicators to which statistically significant differences in local recurrence-free survival could be attributed. Patients in the dosimetrically favorable group had 10-year survival rates higher by a factor of up to 2 compared to those in the unfavorable group. Review of the contemporary transperineal experience using template and image guidance is still ongoing.[22–33] While some early studies[22,31] indicate significant proportions of

tumor-positive biopsies postimplantation and/or distant metastases, most of the large published series[24–26,29] have shown PSA-based control rates comparable to prostatectomy or external beam radiation. A notable study by Vijverberg *et al.*[33] examined biopsy findings postimplantation and the quality of the implant in terms of the minimum dose delivered to the prostate. They reported significant correlation between the implant quality and the resulting negative biopsy, and between the implant quality and the serum PSA during follow-up. One of the major advantages of seed implantation has been the lower morbidity rates compared to radical prostatectomy and external beam radiation therapy. The use of contemporary techniques has further reduced treatment-related morbidities. Urinary or rectal complication and sexual dysfunction are generally reported to be relative low in many recent studies.[34–39] Careful treatment planning and execution are expected to further reduce treatment-related morbidities.

In summary, there is now considerable evidence to suggest that technical innovations, 3D image-based planning, template guidance, computerized dosimetry analysis and improved quality assurance practice have converged in synergy in modern prostate brachytherapy, which promise to lead to increased tumor control and decreased toxicity. A substantial part of the medical physicist's contribution to this multidisciplinary modality has a direct impact on the factors that may singly or jointly determine the treatment outcome. It is therefore of paramount importance for the medical physics community to establish a uniform standard of practice for prostate brachytherapy physics, so that the therapeutic potential of the modality can be maximally and consistently realized in the wider healthcare community.

Prostate seed implantation is the permanent placement of radioactive seeds in the prostate using interstitial brachytherapy techniques. However, it differs from traditional brachytherapy in three important aspects: 3D anatomy-based dosimetric planning, real-time diagnostic imaging guidance and fast dose fall-off due to lower energy radionuclides. In addition, it differs from remote-controlled high dose rate brachytherapy in that the radioactive source strength distribution is less amenable to optimization and alteration. These considerations lead to the unique nature of prostate seed implant, which may be characterized as precision-oriented yet dosimetrically sensitive. To the majority of brachytherapy practitioners, image-guided interstitial implantation is a relatively new treatment technique. A typical implant team consists of the radiation oncologist, the medical physicist, the urologist and/or the ultrasound radiologist. At present, most of the practitioners acquire technical proficiency through a short training course followed by actual patient treatment. There is as yet no uniform requirement either in the training curriculum or within the medical physics profession regarding adequate understanding of the unique physics issues in seed implantation. An extensive survey by Prete *et al.*[40] in the U.S. for prostate brachytherapy revealed alarming variance in the pattern of practice in physics and dosimetry, particularly in regard to dose calculation, seed assay and time/method of postimplant imaging. Because of the large number
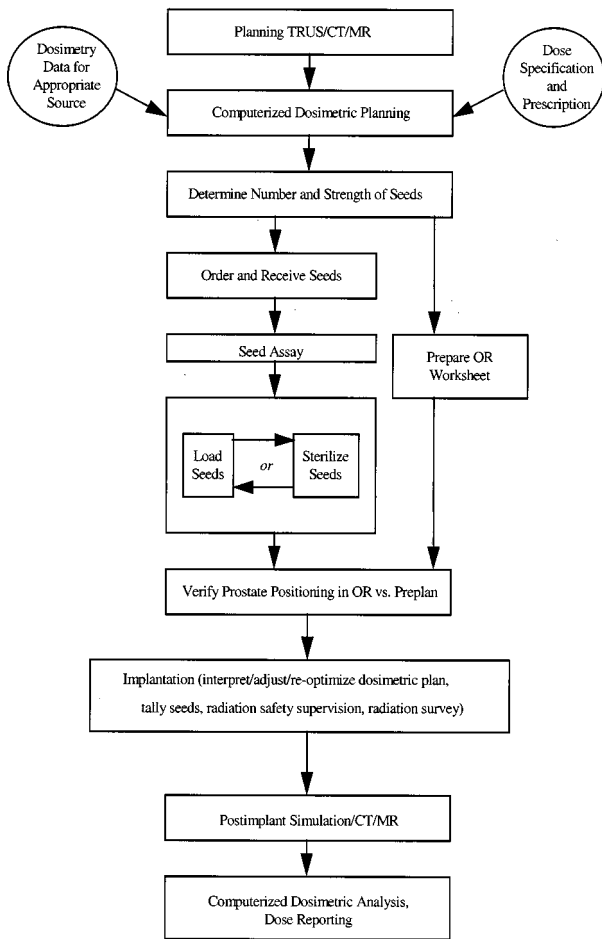
FIG. 1. Process flow diagram for a preoperatively planned prostate seed implant.

of start-up programs at this time, it is essential that the roles and responsibilities of the medical physicist be clearly defined, consistent with the pivotal nature of the clinical physics component in assuring the ultimate success of prostate brachytherapy.

It was against this background that the Radiation Therapy Committee of the American Association of Physicists in Medicine formed Task Group No. 64, which was charged (1) to review the current techniques in prostate seed implant brachytherapy, (2) to summarize the present knowledge in treatment planning, dose specification and reporting, (3) to recommend practical guidelines for the clinical medical physicist, and (4) to identify issues for future investigation. Although high dose rate (HDR) brachytherapy for prostate cancer has certain similarities with permanent seed implantation, the topic is beyond the scope of this Task Group. This report represents the work of the AAPM Task Group No. 64. The report has been approved by the Radiation Therapy Committee and the Science Council.

The dosimetry formalism for interstitial brachytherapy was standardized by the AAPM Task Group No. 43.[41] A code of practice for brachytherapy physics in general was outlined by Task Group No. 56.[42] The present report will address the clinical medical physics issues unique to perma-

nent prostate seed implant. It should be emphasized that this is a rapidly evolving treatment modality and an area of active investigation. Much of our current knowledge in optimized treatment planning, intraoperative uncertainties, the time course of prostate volume change, correlation of radiological studies of the prostate, and postimplantation analysis is based on research efforts which are still ongoing. The intention of this report is therefore to guide the practicing medical physicist in successfully implementing or improving the prostate implant procedure, and to provide a survey of the current standard of practice in this evolving field.

The remaining parts of this document are organized as follows: Sec. II provides a practical review of the current techniques in ultrasound-guided seed implantation; Sec. III reviews the dosimetric aspects of prostate brachytherapy, with an emphasis on the present knowledge in treatment planning, dose specification and reporting; Sec. IV contains the summary of recommendations; Sec. V discusses issues for future consideration.

II. REVIEW OF CURRENT TECHNIQUES

A. Overview of contemporary techniques

The major goal of prostate brachytherapy is to deliver a tumoricidal dose to the cancer-bearing prostate while minimizing urinary and rectal morbidities. The specific aims are to design the optimal treatment plan using 3D anatomical information, to implement the treatment plan intraoperatively with precision, and to analyze the dosimetric outcome postimplantation. Contemporary prostate brachytherapy is a multi-disciplinary treatment modality, in which each member of the implantation team brings specialized knowledge that promotes the clinical goal. Figure 1 delineates the flow of events pertinent to the medical physicist in this treatment modality. The role of the medical physicist spans the entire process of patient treatment, from the planning volume study, dosimetric planning, seed preparation, to intraoperative consultation and radiation safety supervision, and postimplant dosimetry.

B. Treatment planning techniques

Computerized treatment planning plays an important role in modern prostate brachytherapy. Careful dosimetric planning leads to smooth and expedient implantation, and reduces the likelihood or extent of normal tissue radiation damage. The process of dosimetric planning is especially helpful to the implant team in the early stages of implementing the prostate brachytherapy program. It allows the practitioners to contemplate the technical and dosimetric issues presented by each case and make adjustment, if necessary, prior to implantation. Although it is time consuming, the planning process requires the team to give prior consideration to the patient's anatomy and any technical problems it may present. It allows the team to formulate a plan that will: (1) provide coverage of the entire target volume by the prescribed dose while keeping the rectal and urethral doses within acceptable tolerances, (2) control dose inhomogene-

ity, and (3) keep the implant as technically simple as possible. The following topics are important in planning the implant:

1. Ultrasound volume study

The ultrasound volume study used to plan the implant is usually obtained no earlier than 2–3 weeks before implantation, in order to limit changes in the prostate, particularly if the patient is under hormonal therapy. If it is not possible to comply with this time interval (e.g., due to a shortage of seeds), a second volume study and computerized treatment plan may be performed before implantation. The volume study consists of consecutive axial images obtained at 5 mm intervals from the base of prostate to the apex, with the template hole pattern superimposed on each image. Practitioners who enlarge the planning target volume (PTV) beyond the prostate often start 5 mm superior to the base and end 5 mm inferior to the apex. In either case, a sagittal ultrasound image is often obtained for base-apex length measurement to assure that the proper number of slices are obtained. A member of the physics staff is usually present to ascertain that the patient is set up in such a manner that a satisfactory plan can be developed from the volume study. Specific parameters that are checked include: (1) the angle of elevation of the patient's legs in the stirrups; (2) the alignment of the ultrasound probe with respect to the prostate in all of the ultrasound images, such that implant needles, which are inserted parallel to the probe, do not traverse the rectal wall; (3) the superposition of the template hole pattern on the contours of the prostate. In particular, the most posterior aspects of the prostate need to be within or very close to the posterior row of template holes in order to adequately cover the prostate by the prescribed dose.

The planning volume study ideally includes adequate localization of the prostatic urethra on each axial slice. The seed configuration is then designed to avoid implantation at or near the location of the prostatic urethra.

2. Pubic arch

The first consideration in the planning process is to determine the degree of pubic arch interference. The pubic arch may ''shadow'' the anterior and lateral portions of the prostate, making it difficult or impossible to implant seeds in these locations. If this restriction exists, the brachytherapist may angle the template and ultrasound probe assembly to achieve better needle access. However, the ability to correct this problem is limited. Severe pubic arch interference is considered a contraindication for performing the implant.

Both CT and TRUS have been used to detect pubic arch interference. In the CT-based technique, the largest extent of the prostate is manually projected onto the axial slice containing the pubic arch. If significant overlap exists between the two structures, pubic arch interference is likely to be encountered. A shortcoming of this technique is that the patient is not in the lithotomy position during the CT study, thus the relationship between the prostate and the pubic arch may be slightly different during implantation. In the TRUS-

based technique, the ultrasound probe is first moved to an axial slice on which the pubic bone-soft tissue interface is visible. The location of the pubic arch is traced on the ultrasound screen using the cursor. The probe is then moved longitudinally to visualize the entire prostate on successive axial slices, with the tracing of the pubic arch overlaid on the images. The advantage of this technique is that it can be combined with the volume study, with the patient in the treatment position. However, it is harder to precisely identify the pubic arch on ultrasound compared with CT.

3. Seed distribution

Different types of seed distributions are in current use and a consensus on the optimal seed distribution does not exist. The classic approach is to space the seeds 1 cm apart, center-to-center, throughout the prostate. This approach, referred to as *uniform loading*, requires a higher number of lower strength seeds (typically 0.4 to 0.5 U seed for ^{125}I, 1.2 to 1.5 U seed for ^{103}Pd), and is characterized by relatively high doses in the center of the prostate. In *modified peripheral loading*, some seeds in the central portion of a uniformly loaded implant are deleted to reduce the central dose. This may require increasing the strength of the remaining seeds or decreasing the needle to needle or seed to seed spacing in the periphery. *Peripheral loading* is an alternative approach in which the seeds are preferentially limited to the periphery of the prostate. This requires a substantial increase in seed strength (typically 0.75 to 1.0 U/seed for ^{125}I, 2.0 U/seed or higher for ^{103}Pd). The end result is to produce a dose minimum (albeit above the prescribed minimum dose), instead of a dose maximum, at the location of the urethra.

4. Urethra

The prostatic urethra is readily visualized on TRUS and CT studies when a Foley catheter is left indwelling during imaging. Alternatively, aerated gel injected into the urethra can act as a contrast-enhancing agent under TRUS imaging. In order to plan the treatment to avoid direct implantation near the urethra or to calculate the dose received by the urethra, the entire length of the prostatic urethra needs to be visualized. Based on the study by Wallner *et al.*,[38] it appears that the maximum urethral dose and the length of the urethra that receives greater than 360 Gy (converted from 400 Gy of pre-TG43 dose for ^{125}I) are significantly correlated with RTOG grade 2–3 urinary morbidity. In another study, Desai *et al.*[43] reported that acute urinary morbidity in 117 patients treated with ^{125}I implants correlated with the dose-volume histogram of the prostate as well as doses delivered to 5 cm^2 of the urethra as measured by the dose-surface histogram. Additional studies incorporating more patients, different radionuclides and various seed loading patterns will aid the determination of the dose tolerance to the urethra.

Treatment plans are commonly devised to limit the urethral dose whenever possible. To accomplish this goal, seeds are not placed in close proximity to the urethra. In addition, some seeds in an otherwise uniformly loaded implant may have to be deleted to achieve this goal.

5. Rectum

The anterior wall of the rectum is adjacent to the prostate, which makes it difficult to deliver the prescribed dose to the posterior periphery of the prostate without delivering an equivalent dose to the most anterior portion of the rectum. Placing the seeds too close to the rectal wall may increase the risk of ulceration, whereas the extreme posterior portion of the prostate may be underdosed if the seeds are placed too far away. Particular attention is given to the recto-prostatic interface in planning the implant. The physicist aims to cover the entire prostate while keeping the volume of the rectal wall that receives the prescribed dose as small as possible. Special care is taken where seeds must be positioned near the recto-prostatic interface, especially if peripheral loading is employed using higher activity seeds.

According to a dosimetric study by Wallner *et al.*based on CT scans taken 2–4 h after implantation,[38] the rectal surface that receives greater than 90 Gy (Converted from 100 Gy of pre-TG43 dose for ^{125}I) appears to correlate significantly with rectal bleeding or ulceration. This study suggests that either the dose-surface histogram or the amount of the rectal wall that receives greater than 90 Gy is a useful parameter in dosimetric planning and analysis. Again, further studies incorporating more patients, different radionuclides and different seed loading patterns will aid the determination of the rectal dose tolerance.

6. Dose margin

Due to seed placement uncertainties that are inherent to the implant procedure, the percentage of the prostate volume that is covered by the prescribed dose is almost always less than planned. Thus, if the prescribed dose and coverage are to be achieved it may be necessary to ''over plan'' the implant. This is achieved in a variety of ways: by using a planning volume that is larger than the prostate volume (which is also justified by the known incidence of extracapsular extension of disease), by increasing the total activity implanted by about 15%, or by increasing the number of seeds or seed strength until the prescribed isodose line lies several millimeters outside the prostate. All of these methods effectively constitute a planning integral dose escalation. Thus, the decision to plan a dose margin is tied to the prescribed dose itself.

7. Intraoperative planning

Although preoperative dosimetric planning has been a community standard in modern prostate brachytherapy, this two-step process from the planning volume study to implantation contains several sources of uncertainties. The patient position in the planning volume study is difficult to reproduce in the operating room, leading to ad hoc modifications of the treatment plan at the time of implantation. Anesthesia may result in relaxation of pelvic musculature and consequent change in prostate shape compared to the contour obtained in the volume study without anesthesia. Furthermore, the prostate may undergo volume change in the interval between planning and implantation, which invalidates the pre-
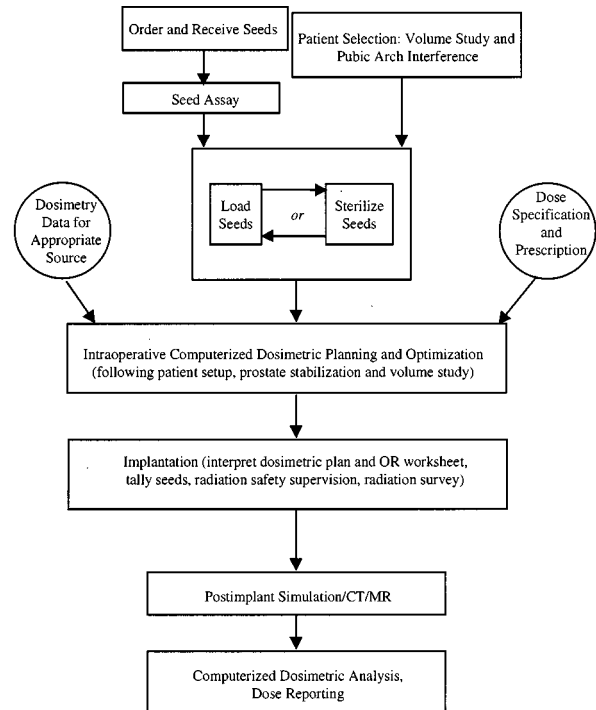
FIG. 2. Process flow diagram for an intraoperatively planned prostate seed implant.

operative plan. Appreciable change in prostatic volume or position can occur following the insertion of stabilizing needles, introducing yet another source of error in implementing the preoperative plan.

These problems can be alleviated by the technique of intraoperative optimized treatment planning.[44] With the patient anesthetized and in the treatment position, the prostate is first stabilized using implantation needles. A complete TRUS volume study follows, from which images are transferred to the planning computer and segmented. The treatment plan-

TABLE I. Equipment requirement for the prostate seed implant program.

Mick applicator technique	Pre-loaded needle technique
Capital equipment	
Well-type ionization chamber	Well-type ionization chamber
GM or scintillation detector	GM or scintillation detector
Ion chamber survey meter	Ion chamber survey meter
Computer treatment planning system	Computer treatment planning system
Ultrasound unit	Ultrasound unit
Stabilization device/attachment	Stabilization device/attachment
Fluoroscopy unit	Fluoroscopy unit
Mick applicator	
Supplies and consumables	
Loading block, cartridges	Needle box, (optional) needle loading device
Seed carrier	Seed sterilization container
Mick-compatible needles	Needles
(Optional) stabilization needles	(Optional) stabilization needles
Reverse action tweezers	Reverse action tweezers
Radioactive seeds	Radioactive seeds
	Spacers and bone wax

ning system is invoked to produce optimized dosimetric plan, which is subsequently reviewed and approved by the physicist and the radiation oncologist in the operating room before seed placement takes place.

Intraoperative computerized planning allows several major steps to be streamlined. Specifically, preoperative planning can be reduced to a screening of pubic arch interference and a volumetric measurement to estimate the maximum total source strength required. Seed inventory can be consolidated to the same batch for a group of patients, which reduces the variance for waste. Figure 2 shows the modified flow of events pertinent to the medical physicist under the intraoperative technique. Most notably, intraoperative dosimetric planning is a critical step in this treatment technique, where the medical physicist occupies an important role in the intense decision-making process.

C. Equipment and applicators

Equipment for ultrasound-guided prostate implants includes the ultrasound machine, the rectal probe, the stepping device/probe carrier, the perineal template, and the stabilizing mechanism (see Table I). The ultrasound machine is typically a portable unit, and contains a seed implant software package such that a grid pattern can be displayed on the screen. The stepping device allows the rectal probe to be attached to the stabilizing mechanism while permitting movement in and out of the patient's rectum in precise steps. The needle template has holes accepting 17 gauge or 18 gauge needles, arranged typically in a 13 by 13 matrix, at 5 mm spacing. The template may be designed to mount directly to the rectal probe in some commercial systems, in which case it moves together with the probe, or it may be mounted on the probe carrier, in which case it remains stationary with respect to the perineum as the probe is moved. In either case, the holes on the needle template correspond to the grid points displayed on the TRUS monitor screen. The stabilizing mechanism immobilizes the entire rectal probe/carrier/template system against the operating table or floor, to prevent unintentional motion of the probe and needle template during the implant procedure. The template is placed at close proximity to the perineum to minimize needle splaying in the target volume.

Ultrasound equipment is now available that can display the sagittal as well as transverse planes of the prostate volume. This feature has been found to be helpful in identifying the superior prostate capsule to guide individual needle insertion, in visualizing the movement of the prostate volume as needles are inserted, and in confirming that the seeds are deposited correctly at the cephalad-most portion of the prostate.[45–47]

Equipment required for the prostate volumetric study includes ''stirrups'' to support the legs and an examination table that allows the mounting of stirrups. The patient is set up in an extended lithotomy position on the examination table, with the thighs at approximately right angles to the body. This rotation of the pelvic bones allows better access to the prostate, and helps avoid needle obstruction by the pubic arch. It is important that similar stirrups are available to achieve the same patient position during the implantation procedure in the operating room, so that the relationship of the prostate and the adjacent organs can be accurately and quickly reproduced. The patient is prepared for the volumetric study using Fleets enema, and may be catheterized using a Foley catheter with saline injected into the bladder and the Foley bulb in order to identify the urethra. Alternatively, aerated gel may be injected as a contrast agent to identify the urethra by ultrasound.

A lubricant (such as K-Y jelly™) is needed to help introduce the rectal probe into the rectum. Topical anesthesia (such as Lidocaine jelly™) may be needed for sensitive patients. A small amount of saline or coupling jelly should be injected into the condom over the rectal probe for improved imaging quality and positioning of the posterior prostate capsule in the ultrasound image. Too much saline in the condom may however cause distortion of the prostate and the neighboring anatomy. The amounts of saline injected into the bladder, the Foley bulb, and the condom may be recorded, to be reproduced in the implant procedure.

D. Source type, assay and preparation

^{125}I and ^{103}Pd sources are comparable in photon energy, capsule dimensions and dose distribution. ^{125}I and ^{103}Pd are encapsulated in titanium and delivered as sealed sources (''seeds''). They are similar in size ($4.5 \, \text{mm} \times 0.8 \, \text{mm}$ outer dimensions for ^{125}I model 6711 seeds and $4.5 \, \text{mm} \times 0.81 \, \text{mm}$ for ^{103}Pd model 200 seeds). Both ^{125}I and ^{103}Pd decay via electron capture. ^{125}I and ^{103}Pd are currently produced by nuclear reactors and cyclotrons, respectively.

The ^{125}I decay scheme results in the emission of photons with energies of 27.4 keV (1.15 photons/disintegration), 31.4 keV (0.25/dis) and 35.5 keV (0.067/dis).[48] At the time of this report, the seed type most commonly used for prostate implants is model 6711, which contains ^{125}I in the form of silver iodide deposited on the surface of a silver rod. This silver rod also serves as a radiographic marker. ^{125}I model 6711 seeds therefore also emit fluorescent x-rays resulting from photoelectric interaction in the silver rod, the energies of which are 22.1 keV (0.15/dis) and 25.5 keV (0.04/dis). The average energy for all emissions is approximately 27.4 keV, which results in a half value layer in lead of approximately 0.025 mm. The self absorption of this assembly is approximately 37.5%. Therefore, contained activity is approximately 1.6 times the apparent activity. The air kerma strength used for prostate implants is commonly between 0.4 and 1.0 U (0.3–0.8 mCi) per seed. The halflife of ^{125}I is 59.4 days; ninety percent of the total dose is delivered in 197 days.

^{103}Pd emits characteristic x-rays of 20.1 keV (0.656/dis) and 23.0 keV (0.125/dis).[48] The half value layer in lead is 0.008 mm. The active radionuclide is plated onto two graphite pellets on either side of a lead radiographic marker within the titanium capsule. Each end of the seed is cupped inward (i.e., it is concave). This is a salient feature of the ^{103}Pd seeds and therefore can be used to uniquely identify ^{103}Pd seeds.

(Other seeds are convex where the two end welds meet the main source body.) The self-absorption of the seed is stated to be 54% by the manufacturer, indicating that the contained activity of ^{103}Pd in each seed is approximately 2.2 times the stated apparent activity. The air kerma strength commonly used for prostate implants is between 1.4 to 2.2 U (1.1 to 1.7 mCi) per seed. The half-life of ^{103}Pd is 16.97 days; 90% of the total dose is delivered in 56 days.

AAPM Task Group No. 56 recommends that 10% of the seeds be assayed.[42] There are several seed assay methods that address the special circumstance in which a large number of loose seeds are contained in a shipment. Seeds can be assayed in bulk, or in cartridges.[49] In addition, an autoradiograph can be taken with a large number of seeds to compare the resulting film density. This film method, in conjunction with the well chamber seed assay, assures that the seeds are of uniform strength. Seeds in suture are delivered sterile, thereby complicating the assay procedure. A calibration check may be performed on single nonsterile seeds from the same batch as a given shipment of seeds in suture and ordered expressly for this purpose. Alternately, a sterile insert to the standard dose calibrator can be used to directly assay seeds in suture, as described by Feygelman *et al.*[50] and by Butler *et al.*[51] The advantage of the latter techniques is that sterility may be maintained while a sufficient number of seeds are assayed.

Unlike seeds in suture, loose seeds are not sterile and need to be sterilized prior to use. The method of sterilization depends on the implantation technique. If preloaded needles are used, the seeds are sterilized prior to loading. After sterilization, the needles are loaded under sterile conditions, often in the operating room. If the Mick applicator is used, the seeds can be loaded into cartridges prior to sterilization. The sterilized cartridges are then taken to the operating room, ready for use.

Seeds are commonly sterilized in an autoclave. Flash sterilization can be used, or longer duration steam sterilization may be opted if time and availability allow. Flash sterilization is done in the autoclave at 270 °F (133 °C) at 30 PSI for at least 3 minutes. The conventional autoclave cycle is 250 °F (121 °C) at 15 PSI for about 30 minutes. Loose seeds can be sterilized in the vial/lead pig in which they are delivered, with the cap loosened. Alternatively, the vial can be uncapped and the open end plugged with cotton. The gravity cycle is preferable to the vacuum cycle when loose seeds are sterilized. The difference between gravity and vacuum cycles is the drying method. The vacuum cycle uses a strong vacuum to achieve drying. The vacuum may displace loose seeds from the container, causing potential radiation hazard. Seeds may also be sterilized using ethylene oxide gas (cold gas). Cold gas sterilization takes considerably more time and is required for seeds in suture material.

Seed preparation requirements depend on the implantation technique adopted, i.e., using the Mick applicator or pre-loaded needles. Table I shows a list of typical equipment required for either technique. The needles used for implantation also differ. The Mick TP200 applicator compatible needles have a blunt needle sheath and a stylet that is slightly longer than the sheath, with a trocar point. Needles used in the pre-loaded technique have a sharp beveled point, and a blunt stylet that is slightly shorter than the needle. A mark is typically present on the end of the needle to indicate the direction of the bevel at the tip. This can be helpful in that the needle track may be made to deflect slightly toward the beveled direction, if so desired. The needles and stylets also have centimeter markings to help visually determine the depth of needle insertion, and the length of the needle that is filled with seeds and spacers. The first 0.5–1 cm of the needle is usually sand-blasted for increased ultrasonic echogenicity. If the image of the needle tip on ultrasound is used to infer the actual needle depth, it is important to assess the precise depth where the needle first appears under ultrasonic imaging; otherwise a systematic positioning error of 0.5–1 cm can occur.

In the Mick applicator technique, ^{125}I or ^{103}Pd seeds are loaded into the Mick-compatible cartridges using the loading block and a pair of reverse action tweezers. The loaded cartridges are then screwed into either the loading block or the seed carrier and sterilized. Some seeds are commercially available in pre-loaded plastic cartridge inserts that are compatible with the Mick applicator. Use of such pre-loaded inserts minimizes radiation exposure to the personnel and the time required for loading the cartridges. The user's well chamber calibration factors may, in this case, be obtained specifically for such pre-loaded cartridge inserts.

The pre-loaded needle technique requires longer time for preparation. In this case, the radioactive seeds and spacers are loaded into sterilized needles as specified by the treatment plan. The loading pattern of seeds vs. spacers for each needle may be printed on a diagram to facilitate the loading process. The needle tip is plugged with a piece of surgical bone wax or rectal suppository. The length of the wax (approximately 5 mm) should be accounted for when depositing the seeds into the prostate. The loaded needles are then placed into a sterilized needle box, ready for implantation. Various needle loading devices are commercially available that aim to reduce the amount of time required for loading the needles, permit visual verification of the loading pattern, and reduce radiation exposure to personnel.

A Geiger–Muller (GM) counter or scintillation detector is used to survey the seed preparation area after completion of the loading process. A running total of the seeds is kept as they are loaded into cartridges or needles.

In early 1995, Amersham Healthcare introduced Rapid Strand™ in which the I-125 seeds are enclosed within a stiff, absorbable suture material that maintains the seeds 1 cm apart center-to-center. The suture material is braided Vicryl™ (polyglactin 910) which is stiffened thermally and sterilized by ethylene oxide. The stiffened Vicryl suture material is hygroscopic and softens and swells when exposed to moisture from body fluids. If not handled properly, the strand may swell and jam in the implant needle making it impossible to expel the strand from the needle. Therefore, it is important that the needle be plugged properly. Bone wax, which is often used to seal the tip of needles loaded with loose seeds and spacers, is too hard to expel without causing

a mechanical collapse of the Vicryl spacing between the seeds. Suppositories, such as Anusol-HC™, are a softer material that partially melts at 37 °C and allows expulsion of the strand without collapsing the Vicryl. The internal bore of the needle must be very smooth. Any roughness of needle wall will catch the Vicryl fibers and jam the needle.

The technique for use of Rapid Strand can be summarized as follows.[52] Place 3 suppositories in a 30 ml glass cup or beaker and flash sterilize in a steam autoclave for 3 min at 140 °C and 2 atm pressure. With aseptic technique, an empty 18 gauge implant needle is dipped vertically into the clear, molten suppository to a depth at least covering the needle bevel and preferably covering the burnished echogenic region of the needle (approximately 5 mm). Upon removing the needle vertically, capillarity and gravity equalize to form a liquid column 7–9 mm long that solidifies in 3–10 min. Once the needles have cooled for 5 min, appropriate lengths of Rapid Strand are cut and inserted into the needles, followed by the stylet. After inserting the needle into the patient, the moisture resistance of the suppository seal persists even though the needle may be retracted and reinserted several times in achieving the desired location. During this time the suppository is warming and melting. Approximately 2–3 min at body temperature are required for the suppository to melt sufficiently around the perimeter of the needle so that the strand can be easily expelled. Two circumstances that may lead to jamming of the strands within the needle are leaving too little time for the suppository to melt sufficiently, or striking the pubic bone, which may dislodge or disrupt the suppository plug.

E. Implantation procedure

Ultrasound-guided prostate implant procedures can be performed in an operating room or an interventional radiology procedure room. After anesthesia, the patient is set up in the dorsolithotomy position, and draped with sterile covers. The perineum is cleaned with Betadine™ and the scrotum is retracted by either sewing it to the drapes or by using a sling. The ultrasound probe is attached to the stepping device and inserted into the rectum. With the exception of the needle template, these instruments are usually nonsterile, but are cleaned prior to use.

The prostate may be first immobilized against lateral and anterior-posterior motion by use of two or more stabilizing needles, inserted under TRUS visualization through carefully chosen template positions.[53,54] Special prostate stabilizing needles with a hook-type mechanism are commercially available, though standard implant needles for stabilization are also effective.[53] In general, three stabilizing needles arranged in a triangular pattern inside the prostate are quite adequate. However, not all brachytherapy practitioners use immobilization needles.

Under the current preoperatively planned implantation technique, the positioning of the prostate on the template grid under TRUS is carefully checked against the treatment plan both before and after the insertion of the stabilizing needles. Offset in the relative position by exactly one grid width (5 mm) is easily corrected by shifting the treatment plan. Other offset amounts need to be remedied by repositioning the patient. Under the intraoperative planning technique, prostate stabilization is followed by TRUS volume study and optimized dosimetric planning, as described in Sec. II B.

For either the Mick applicator technique or the pre-loaded needle technique, a needle loading diagram and/or worksheet is required in the operating room to identify the template coordinates for needle insertion. In the Mick applicator technique, the loading diagram specifies the spacing between the seeds in each needle, the number of seeds in the needle, and the distance of the first seed-drop position from the base of the prostate (or any other reference plane), i.e., the offset from the reference plane. The diagram for the pre-loaded needle technique specifies the offset from the reference plane for each needle.

The operating table ideally allows the placement of a mobile fluoroscopy unit to visualize the implanted area. The use of fluoroscopy during implantation helps in visualizing the needles and seeds as they are inserted in relation to a Foley bulb filled with contrast media, and the patient's bony anatomy.[55] As a needle is inserted into or pulled out of the prostate, the movement of the previously implanted seeds can be readily seen on the fluoroscopy monitor, and adjustment in the needle insertion depth may be made to compensate for such movement.

If needles are to be loaded in the operating room, a sterile table or work area equipped with adequate radiation shielding is set up by a member of the physics staff. Even in the Mick applicator technique, a set of sterile loading and seed handling equipment is kept available in case jammed cartridges need to be reloaded.

During seed placement, the medical physicist interprets the planning information in each incremental step to the clinicians, and records the progress of seed deposition in the patient. Typically, the medical physicist provides verbal instructions on the needle coordinates, the offset from the reference plane, and, if using the Mick applicator, the number of seeds and the seed spacing, as each needle is being placed.

The technique for seed placement requires some degree of manual dexterity. In the pre-loaded needle method, the needle is withdrawn against the stylet such that the seeds remain in the same position in the prostate as the needle is removed. Advancing the stylet will deposit the seeds ahead of their intended locations, while allowing the stylet to retract with the needle will cause the seeds to be deposited behind their intended locations. The Mick applicator method requires the clinician to keep track of each seed deposition. Desired seed spacing is achieved by retracting the needle a known number of steps on the applicator's preset scale. When the needle is retracted too rapidly, the seed tends to follow it due to the suction created by needle retraction. When the stylet is advanced too rapidly, the seed can be injected beyond its intended location in the prostate. Care is taken to ensure that only one seed is allowed to drop from the cartridge at a time, otherwise multiple seeds will be placed at one planned location.

It is often found that preoperative treatment plans require minor or major modifications. Typical scenarios that cause such modifications include discrepancies between expected and actual needle placement, detection of the urethra or adjacent rectal wall close to the intended seed location, prostate volume/position change, or the need to compensate for prior seed misplacement. The medical physicist brings to the operative procedure a special understanding of the dosimetric impact of any such modification, and thus plays an important role in evaluating each circumstance. It should be stressed that while real-time deviation from the preoperative plan is often unavoidable for adequate dose coverage, excessive *ad hoc* deviation can lead to severely suboptimal dose distribution. To acquire a quantitative understanding of the dosimetric characteristics of a preoperative plan, the medical physicist may wish to simulate a number of such ad hoc changes on the planning computer prior to implantation. This is especially helpful in the early stages of a prostate seed implant program.

A running total of the seeds and needles implanted is recorded on the operative worksheet. Any real-time deviation from the planned seed deposition is annotated as it occurs. In the Mick applicator technique, it is good practice to reconfirm the running total of seeds deposited every time the cartridge is emptied, which serves as a checksum for correct seed drop. This is to be facilitated by loading a constant number of seeds per cartridge (except the last cartridge). Note that the checksum method does not guard against accidental placement of multiple seeds at the same location, but will uncover the problem soon after it occurs. A radiation survey should be made for each used needle to confirm that no seed is unintentionally left inside the needle.

After seed placement, the urologist usually performs a cystoscopy to find and retrieve any loose seeds in the bladder. A lead seed container is kept available in the operating room, for use in the event that seeds are retrieved from the bladder, or that seeds are accidentally dropped on the floor. A GM detector or a scintillation detector is kept available to locate misplaced seeds, and to conduct radiation survey in the implantation area following the procedure. The radiation survey includes the floor, waste, linen and all used applicators. All seeds brought to the operating room must be accounted for by the implantation worksheet and the seeds that remain in the possession of the medical physicist at the end of the procedure. A properly calibrated ion chamber survey meter is used to measure the maximum exposure rate at the surface and at 1 m from the implanted patient for documentation.

F. Postimplant dosimetry

1. Rationale

The quality of prostate seed implants is, as in all brachytherapy, dependent upon the skill and experience of the practitioner. Because patients differ in their anatomy, some implants are technically more difficult than others. Hence, a variation in implant quality may occur, even for an experienced practitioner.

Prostate implants are generally planned to deliver a prescribed minimum dose. However, it has been shown that the minimum dose planned can rarely be achieved due to seed placement errors which are inherent in the procedure.[56–58] Furthermore, postimplant edema can further reduce the dose delivered by the implant.[59–61] Hence it cannot be assumed that the patient would receive the dose prescribed in the pretreatment dosimetric plan.

Postimplant dosimetric evaluation was traditionally carried out using multiple radiographs. Although such plane films are adequate for reconstruction of the relative seed positions, they cannot provide the dose delivered to the prostate because the prostate cannot be visualized on a radiograph. Postimplant dosimetry was limited to a calculation of the matched peripheral dose (MPD), a parameter that has been shown to be an unreliable indicator of the dose delivered to the prostate.[62]

The dose delivered to the prostate and other organs can be determined by performing a postimplant CT-based dosimetric analysis. The advantage of CT-based dosimetry is that the prostate and other organs, such as the rectum, can be visualized. This capability allows dose-volume histograms (DVHs) to be generated, which provide detailed information on dose coverage and implant quality.

At present, a postimplant CT study is the most direct method for carrying out quantitative dosimetric evaluation. CT-based dosimetric evaluation is particularly important during the early stages of a new prostate seed implant program to aid the team in progressing up the learning curve as quickly as possible. Continuous evaluation of implant quality permits improvement in techniques as the program develops. Otherwise, problems which compromise implant quality may go undetected and be perpetuated indefinitely.

2. Technical issues

The necessary steps in performing a CT-based dose analysis are (1) outlining the prostate volume for dosimetric evaluation on each CT image, (2) localization of each seed, (3) calculation of the dose to each point in a 3D matrix of grid points in a selected volume which includes the prostate, (4) generation of isodose curves which can be superposed on each CT image, and (5) generation of a DVH for the prostate as well as dosimetric information for the critical structures.

A seed 4.5 mm in length often appears on adjacent CT images spaced at 5 mm intervals, therefore a useful facility in dosimetric analysis is to permit identification of seeds that appear on multiple adjacent CT images. This is usually accomplished by superposing the seed location from the previous image onto the image being analyzed.[62] Seed redundancy algorithms are also helpful, which can reduce the seeds to the number actually implanted using distance-based redundancy likelihood analysis.

A complete CT-based dosimetric evaluation includes the dose delivered to other organs, such as the urethra and rectum. However, there are no standards for specifying the dose to these organs, and each case presents a unique set of circumstances. It is very difficult, if not impossible, to define

the urethra on a CT image unless there is a Foley catheter in the urethra. Distension of the rectum can cause variability in assessing the rectal dose due to the typical large dose gradient in this region.

The determination of the dose to the prostate from a postimplant CT scan is nontrivial. A major problem is defining the prostate volume accurately on the CT images. Outlining the prostate on CT involves subjective judgment because the prostate is not well resolved from other adjacent soft tissue structures. As a result, the volume derived from the CT scan is generally larger than that of the TRUS volume study used to plan the implant.[63–65] The problem this presents is that the dose coverage will be evaluated for a prostate volume which is larger than that used in planning the implant. As a result, the percentage of the ''prostate'' covered by the prescribed dose will generally be less than that planned.

The most notable difficulties in defining the prostate in CT images have been described[63] as (1) an inability to distinguish the posterior portion of the prostate from the anterior wall of the rectum on noncontrast CT. (2) a tendency to confuse the posterior-inferior (apical) portion of the prostate with the anterior portion of the levator ani muscles, and (3) a tendency to include portions of the neurovascular bundles as part of the prostate volume. Because of these difficulties, defining the prostate requires a certain amount of subjective judgment.[63]

Another problem is postoperative edema, which typically increases the prostate volume by 40 to 50% compared to the preoperative volume.[59,60,66] If the postimplant CT scan is obtained immediately after the implant is performed, the dose may be underestimated. The edema increases the distance between the seeds, as well as the volume, thereby lowering the dose rate. On the other hand, if the CT study is obtained after the edema has resolved, the dose may be overestimated because the decrease in dose rate while the prostate was edematous is ignored.

The impact of edema on the postimplant dosimetry is not yet well defined. However, two factors which intuitively contribute are: (1) the magnitude of the edema and (2) the margin used in planning the implant. An example of a margin is an implant planned so that the prescribed isodose line is a few millimeters outside the periphery of the prostate. Such margins are created by the practice of increasing the planned source strength by approximately 15% to compensate for seed placement error.[63] One would expect a greater percentage of the edematous prostate to be covered by the prescribed isodose line when such a margin is incorporated into the plan.

The scheduling of postimplant imaging studies is an important quality assurance issue because of the effect of edema on the postimplant dosimetry. However, the optimal time for obtaining the CT scan has not been established. The optimal time for imaging ^{125}I and [103]Pd implants will differ because their half-lives are different. The duration of edema is a key factor in determining the optimal timing. A recent study[60] based on serial CT scans shows that the edema resolves exponentially with a half-life of from 4 to 25 days

(mean: 9.3 days). Using the mean edema half-life of 9.3 days, the edema will typically resolve to 12.5% of its original value in 28 days. This would appear to be an appropriate time to image an ^{125}I implant because of its 60 day half-life. However, the situation is not so clear with [103]Pd because of its much shorter 17 day half-life.

Although the methodology has not yet been perfected, the TRUS volume study may ultimately become a useful aid in defining the prostate volume in the CT study.[65] This is particularly true if the postimplant CT scan is obtained after the edema is resolved so that the preimplant and postimplant volumes can be assumed to be equivalent. If both studies were imaged at 5 mm intervals, the TRUS study should be useful in identifying the apex in the CT study even before a methodology for registering TRUS and CT images becomes available. Fusion of CT and MR images may also be a viable solution, as MR provides adequate visualization of the prostate while CT provides localization of the implanted seeds.[66,67]

These numerous difficulties and technical challenges notwithstanding, the standards for seed implant quality are being defined in terms of quantitative CT-based dosimetric evaluation. Willins and Wallner[68] reported that, for CT scans obtained on the day of implantation, coverage of 80% or more of the target volume by the prescription dose is probably adequate. Bice *et al.*[69,70] have conducted extensive review of postimplant dosimetry using a wide range of CT-based quality assessment parameters. Stock *et al.*[71] found that dose was the most significant predictor of biochemical failure in a multivariate analysis using dose, PSA, Gleason score and stage in 134 patients treated with ^{125}I implants. A dose response was observed at a level of 140 Gy in D_{90}, the dose that covers 90% of the target volume under CT-based postimplant evaluation. Patients receiving a D_{90} less than 140 Gy had a 4-year freedom from biochemical failure rate of 68%, compared to a rate of 92% for patients receiving a D_{90} greater or equal to 140 Gy ($p = 0.02$).

The clinical correlation of dosimetric evaluators is an ongoing effort. Practitioners of prostate brachytherapy are urged to carefully document the methodology and the time course for each set of postimplant dosimetry, in order to preserve its predictive value.

III. REVIEW OF DOSIMETRIC ASPECTS

This section reviews the dosimetric aspects of treatment planning and postimplant analysis relevant to permanent prostate brachytherapy. The historical circumstances that led to the adoption of the ''160 Gy prescription dose'' are described, so that contemporary practitioners can make an intelligent judgment with regard to the past clinical experience based on the Memorial nomograph. Dosimetric consistency with the AAPM Task Group No. 43 formalism is again stressed. Methods for dosimetric evaluation and optimization are summarized.

A. Historical perspective on dosimetry

Although [222]Rn seeds, [198]Au seeds and even ^{192}Ir seeds have been used in permanent implants of the prostate, the historical background of clinical and physics techniques pertinent to the present report really began with the initial use of ^{125}I seeds for this purpose at New York's Memorial Hospital in the late 1960's.[72] These implants were performed using a retropubic approach, following a midline incision and bilateral lymphadenectomy. Ideally, needles were inserted about 1 cm apart and parallel to one another, avoiding the urethra and stopping short of the rectum by sensing needle pressure on a finger in the rectum. Each needle was withdrawn at least 0.5 cm before the first seed was inserted. The dimensions of the prostate were assessed in the plane perpendicular to the needles as the distance between peripheral needles and along the needle direction by subtracting the average needle protrusion from the overall needle length (15 cm). The total apparent activity (in mCi) to be implanted was determined by multiplying the average dimension (in cm) by an empirically derived factor of 5. Implementation of this procedure was eventually facilitated by a nomograph that specified the number of seeds (of known strength) to be implanted and their approximate spacing within the target.[3]

The dose associated with an implanted activity determined in the above manner was believed to be about 160 Gy and was considered to be the minimum effective dose. However, an early evaluation of the ''dimension averaging'' method had shown that, on the basis of Quimby volume implant data,[73] for which the cumulated activity (mg h) per unit dose is approximately proportional to the square root of the volume treated, dimension averaging may be expected to produce a peripheral dose roughly proportional to the minus one-sixth power of volume.[5] Alternately, if Manchester volume implant data[74] had been invoked, where the cumulated activity per unit dose is explicitly stated to be proportional to the two-thirds power of volume, the expectation would have involved a dose proportional to the minus one-third power of volume. In either of these conjectures, the premise is that ^{125}I seeds display a dose-rate fall-off with distance from the seed similar to that from a radium or radon source. (Dimension averaging had, in fact, been used earlier for radon seed implants.) Although we now know that assumption to be totally unjustified, it is nevertheless clear that adherence to the original dimension-averaging method of planning leads to smaller doses for larger target volumes. During the time this planning method was in use, it was not really appropriate to suggest that it resulted in delivery of a given dose, since target volumes (e.g., prostates) varied significantly in size.

Before the advent of CT imaging, there was no way to evaluate the minimum peripheral dose received by the prostate, since the prostate capsule was not seen on the postimplant stereo-shift radiographs from which dose calculations were generally performed. In order to provide some form of feedback to the brachytherapy clinicians that would reflect the extent to which implant goals were achieved, it became customary at Memorial Hospital to report the dose for which the isodose contour volume was the same as the target vol-

TABLE II. Average dose at total decay from a source with an air kerma strength of 1 U using the point source approximation.

Distance (cm)	Dose at total decay (Gy)		
	[125]I model 6711 1985 NIST Standard	[125]I model 6711 1999 NIST Standard	[103]Pd model 200 TheraSeed®
0.5	70.02	77.98	20.19
1.0	16.83	18.74	3.91
1.5	6.93	7.71	1.33
2.0	3.50	3.90	0.56
2.5	1.97	2.19	0.27
3.0	1.18	1.32	0.13
3.5	0.74	0.83	0.07
4.0	0.49	0.54	0.04
4.5	0.33	0.37	0.02
5.0	0.23	0.26	0.01
5.5	0.17	0.19	
6.0	0.12	0.14	
6.5	0.09	0.10	
7.0	0.07	0.08	

ume inferred from dimensions measured at surgery.[75] The target was usually approximated as an ellipsoid, for which the volume is the product of the three dimensions multiplied by $\pi/6$. Because it involved matching volumes, the dose so reported subsequently came to be called the ''matched peripheral dose'' or MPD. It was obtained by interpolation in a table of volumes computed at uniformly spaced dose levels, each volume representing the sum of voxels for which the dose was greater than the specified dose.

The MPD concept proved helpful in later modifications of the original ''planning'' nomograph to take into account the difference in dose rate falloff with distance between ^{125}I seeds and [222]Rn seeds.[6,76] MPD values evaluated for actual implants were found to decrease significantly with increasing target volume.[77] From the slope of the line fitted to such data on a log–log plot, it was possible to derive the exponent that, if applied to the average dimension in a modified dimension-averaging method, would result in a constant dose as a function of target volume. This exponent was found to be 2.2, where the increase over the 2.0 value that would have been implied by Manchester volume implant data was taken to be due to the much lower penetration of ^{125}I photons relative to those of [222]Rn. The same reasoning was later applied to develop a similar nomograph for [103]Pd seed implants.[4] For [103]Pd, with photons of even lower energy, the corresponding exponent of average dimension was 2.56. For both ^{125}I and [103]Pd nomographs, the ''constant-dose'' formula was applied only for average dimensions greater than 3 cm. For smaller implants, the original dimension-averaging rule was allowed to stand and the dose increased for decreasing volume.

With respect to the ephemeral but pervasive ''160 Gy'' prescription dose for ^{125}I permanent implants, a further observation of interest is that it seems to have survived in spite of major changes in ^{125}I dosimetry. At the time it was first proposed, dose calculations were using a one-dimensional lookup table of dose rate times distance-squared with an en-

try at a distance of 1 cm of 1.7 $cGy\,cm^2\,mCi^{-1}\,h^{-1}$. This value had been arrived at indirectly, making use of TLD measurements of relative dose vs distance in Mix-*D* phantom material. It was considered to be the quotient of total energy emission per mCi h and the product of phantom density and the volume integral of the relative measurements.[78] It was changed, in 1978, to 1.10 $cGy\,cm^2\,mCi^{-1}\,h^{-1}$ on the basis of subsequent measurements and calculations[79] that included averaging the anisotropy (albeit in air) over 4π solid angle. MPD values were reduced to 65% of what they would have been using the previous table.

B. Dosimetry data revision

The history of ^{125}I dosimetry has been reviewed in detail by both the AAPM Task Group 43 (TG43) report[41] and the report of the *ad hoc* Committee of the AAPM Radiation Therapy Committee on ^{125}I sealed source dosimetry.[80] As indicated by Kubo *et al.*,[80] two separate but related events need to be considered in the discussion of dosimetry data revision for ^{125}I seeds:

(1) The adoption of the AAPM Task Group No. 43 recommended dosimetry data for model 6711 ^{125}I seeds, which differs significantly from the dosimetry data of Ling *et al.*[81]
(2) The revision of the NIST calibration standard for the titanium-encapsulated ^{125}I seeds, including both model 6702 and model 6711 seeds. This revision causes the reported air kerma strength value for a calibrated seed to be approximately 10% lower than that under the current NIST calibration standard.

When applied to the dosimetry of permanent prostate seed implants, the isotropic point source approximation is commonly used for the dose calculation model. At distance *r* from the center of the source, the dose delivered at total decay from an ^{125}I or ^{103}Pd seed is

$$D = \dot{D}_0 \times 1.443 \times T_{1/2}, \tag{1}$$

where the initial dose rate $\dot{D}_0$ is given by the TG43 formalism

$$\dot{D}_0 = \frac{S_k \Lambda g(r) \bar{\phi}_{an}}{r^2}, \tag{2}$$

where S_k, Λ, $g(r)$, and $\bar{\phi}_{an}$ are the air kerma strength, dose rate constant, radial dose function, and anisotropy constant, respectively. Table II gives the dose at total decay from an ^{125}I or ^{103}Pd seed with an air kerma strength of 1 U, using the point source approximation. Comparison with the old exposure rate formalism shows that, for a model 6711 ^{125}I seed of given strength, the dose calculated using the TG43 formalism and dosimetry data is approximately 11% lower at 1 cm from the center of the seed in water. Luse *et al.*[82] further compared the isodose distribution for the implant of a 35 cc prostate, using 88 seeds and 20 needles. They found that the contiguous volume of 53 cc receiving 160 Gy, using the Ling *et al.* dosimetry data, would receive 144 Gy when the dose is calculated using the TG43 dosimetry data, corresponding to the 11% difference observed earlier. Luse *et al.* therefore recommends that the prescription dose in prostate implants using ^{125}I seeds be modified downward by 11%, prescribing 144 Gy instead of 160 Gy, when the dosimetry data of TG43 is used in the dose calculations. Another empirical study by Bice *et al.*[83] based on similar comparative analysis also reached the same conclusion.

While there is no timeline constraint on the adoption of the TG43 dosimetry data, early adoption of TG43 will facilitate smooth implementation of the revised air kerma strength standard by NIST. The revision of the NIST I-125 standard will need to be carried out in concert with the manufacturer. This requires a change of the dose rate constant Λ in the user's treatment planning system. Loevinger[84] has reported earlier that this revision would lead to approximately a 10% increase of the dose rate constant. The AAPM Radiation Therapy Committee Ad Hoc Subcommittee on Low-Energy Seed Dosimetry reviewed the available data and recommends[85] that, for I-125 sources calibrated using the 1999 NIST air-kerma-strength standard, the dose rate constants should be revised upward by a factor of 1.114. In particular, it is recommended that dose rate constants of 0.98 cGy/h-U and 1.04 cGy/h-U be used for model 6711 and model 6702 seeds calibrated using the NIST 1999 revised air-kerma-strength standard.

C. Dose specification and reporting

Consistency in dose specification, prescription and reporting is an important step towards establishing a uniform standard of practice in prostatic brachytherapy. Early efforts in this area[86–90] were exclusively limited to idealized representations of the target using cubic, cylindrical, spherical or ellipsoidal volumes. However, these investigations marked the departure from built-in target-size dependence in nomograph-based planning and prescription toward specification or prescription of a desired dose. The early experience with CT-based planning and evaluation for ^{125}I prostate implants at the Memorial Sloan Kettering Cancer Center was reported by Roy *et al.*[62] In their study, the peripheral dose was defined as the isodose surface that encompassed 99% of the target volume, or D_{99}. By analyzing 10 implant cases, they showed that the actual coverage of the target volume by the peripheral dose ranged from 78% to 96%, with an average coverage of 89%. More recently, Willins and Wallner[68] published a follow-up study presenting the analysis of 20 unselected implant cases performed by an experienced clinical team. In this study, dose was prescribed to the planned minimum peripheral dose (mPD); postimplant dosimetry was carried out using CT taken on the day of implantation. The actual coverage of the target volume by the prescribed mPD ranged from 73% to 92%, with an average of 83%. The actual D_{100} delivered to the target volume was 43%±8% (±1 SD) of the prescribed mPD. The authors identified subjectivity in interpreting postimplant CT scans and prostatic swelling as extraneous uncertainties, which would compound with any seed placement errors to result in apparently poor

coverage by the mPD. The reliance on the mPD for dose prescription and reporting was discussed by Yu *et al.*[56] Based on simulated distributions of common seed placement errors, they concluded that generally 90% of the original PTV could be covered by the prescribed mPD when the average dimension of the PTV was greater than 3 cm. No consistent pattern was found for the magnitude of underdosage between the planned mPD and the realized D_{100}; however, underdosage from the planned mPD to the realized D_{100} could easily exceed 20% due to common seed displacement.

Although the mPD as a dose specification parameter displays excessive sensitivity, it is the most direct measure of dosimetric coverage under 3D image-based treatment planning. Less sensitive dosimetric parameters have been proposed for prescription and/or reporting, including the net minimum dose,[89] the average peripheral dose,[88] the harmonic mean dose,[90] and the widely cited matched peripheral dose. However, these parameters by definition do not provide the essential information on isodose coverage of the PTV. The practice of prescribing the treatment dose to the mPD is also consistent with modern external beam radiation therapy. The problem of achieving consistency between dose specification for prescription and dose reporting is closely related to the uncertainties in defining the PTV, which are discussed in more detail in Sec. III D.

It must be concluded at this time that the present techniques for permanent seed implantation do not yet allow the planned mPD to be reproduced with any consistency; however, the percent coverage of the PTV by the planned mPD isodose surface is a reasonably consistent indicator of implant quality. Furthermore, the mPD required for clinical control of disease and avoidance of morbidity is currently unknown.

With regard to regulatory compliance, this body of research work strongly suggests that apparent underdosage from the prescribed mPD to the realized D_{100} for a given implant cannot be taken alone as evidence of poor administration of brachytherapy.

D. Dosimetric uncertainties

Three major sources of uncertainties are now widely recognized: seed displacement, prostate edema postimplantation, and difficulty in defining the target volume based on CT. These uncertainties can potentially compound to cause gross dosimetric variability and ultimately to affect the treatment outcome.

Seed displacement refers to the deviation in the positions of the implanted seeds from the planned locations. The dosimetric impact of seed displacement has been well documented.[56,57,68,91] In particular, Roberson *et al.*[57] classified seed displacement in terms of needle placement error, source-to-source spacing variability, and seed splaying. These errors arise because (1) the patient position during the planning volume study is not always reproducible in the operating room; (2) the prostate volume may have changed since the planning study, particularly for patients under hormonal therapy; (3) prostate movement occurs during implan-

tation, even with stabilizing needles in place. Use of rigidly spaced source strands will partially alleviate the seed displacement uncertainties. However, a complete solution to the above problems is unlikely to result until intraoperative computerized real-time dosimetry is widely available.

Dosimetric uncertainties as a result of prostate edema and difficulty in defining the target volume based on CT are unique to dose analysis and reporting postimplantation. These issues are discussed in detail in Sec. II F.

E. Treatment plan evaluation

Methods for dosimetric evaluation are necessary in order to select competing treatment plans during the traditional planning process, in ranking computer-optimized plans, or in postimplant dosimetry analysis. At present, little clinical correlation has been published between the planning dosimetry evaluators and treatment outcome, due in part to the difficulty of achieving the planned parameters in actual implants. To that extent, the dosimetric evaluators are pragmatic constructs to quantify the treatment plan evaluation process.

1. S_{mPD}

The total source strength required to deliver 1 Gy of the mPD, S_{mPD}, is implicitly or explicitly used in treatment planning to select the seed distribution that yields the maximum tumor dose. Intuitively, the dose distribution within a given PTV is also most uniform when S_{mPD} is minimized, for otherwise some source strength can be removed from the nonuniform region without reducing the mPD. The concept of S_{mPD} can be traced back to the Manchester system of implant dosimetry. For prostate seed implants using ^{125}I and ^{103}Pd seeds, the following fitted results provide minimized values of S_{mPD} as functions of the average dimension d of the PTV:[56,92]

$$^{125}\text{I} \quad S = 0.014 \ d^{2.05} \ \text{U/Gy-mPD}, \tag{3}$$

$$^{103}\text{Pd} \quad S = 0.056 \ d^{2.22} \ \text{U/Gy-mPD}. \tag{4}$$

These relationships do not take into account any irregularities in the shape of the target volume, and therefore should only be used as idealized estimates of S_{mPD}. Most clinical treatment plans are likely to yield higher values of S_{mPD}. For the purpose of benchmarking comparison with the idealized model, the three largest orthogonal dimensions of the isodose surface selected for prescription may be used to obtain the average dimension.

For reference, the following fitted results are obtainable from Ref. 4 for the total source strength implanted per Gy of MPD:

$$^{125}\text{I} \quad S = 0.012 \ d^{2.2} \ \text{U/Gy-MPD}$$

$$\text{(converted to TG43 dose).} \tag{5}$$

$$^{103}\text{Pd} \quad S = 0.36 \ d^{2.56} \ \text{U/Gy-MPD}. \tag{6}$$

For average dimensions d between 3 and 5 cm, Eqs. (3)–(4) and Eqs. (5)–(6) agree to within 10% for ^{125}I or ^{103}Pd. It is well known that the mPD is substantially lower than the MPD. However, Eqs. (5)–(6) were derived from the dosim-

etric analysis of past clinical cases, i.e., arising from postoperative analysis, whereas Eqs. (3)–(4) were results of optimized ideal seed placement, i.e., arising from preoperative planning. The apparent agreement of the two sets of fitted equations is therefore rather incidental.

2. Dose uniformity

The full-width at half-maximum (FWHM) of the differential dose-volume histogram or the ''natural'' dose-volume histogram[93] has been used as an indicator of dose uniformity for prostate implants.[62,94] Greater dose uniformity throughout the target volume would be associated with a reduced FWHM. Roy *et al.*[62] reported 307 Gy±73 Gy (±1 SD) in FWHM of the DVH postimplantation for 10 cases in 1993. Although they did not report the FWHM in the corresponding preoperative plans, the parameter is likely to increase from the plan to the postimplant dosimetry because seed displacement tends to spread out the peak of the DVH. A simpler construct is the uniformity number (UN), defined as the ratio of the mean peripheral dose to the mean tumor dose, both calculated as harmonic means in the PTV to avoid numerical instability.[90] The UN is about 0.7 for idealized implants, and should be relatively insensitive to seed displacement. Dose profiles have also been used to measure uniformity in two dimensions through the target volume.[95]

The notion of achieving dose uniformity is related to the concept of sterilizing a uniform distribution of tumor cells throughout the PTV, which is also an implicit assumption in most external beam treatment of prostate cancers. With the possible exception of minor dose heterogeneity,[96] high doses within the PTV in excess of that required to produce sufficient cell kill is assumed to add risk without benefit to therapy.

3. Dose conformity

Dose conformity measures the closeness between the isodose surface chosen for prescription and the PTV in three dimensions. It is different from dose uniformity, as demonstrated in the following example. If the PTV is a sphere, then a point source located in the center will achieve perfect conformity, but the dose distribution is severely nonuniform throughout the target. Thus dose conformity alone does not fully define the objectives for optimizing prostate implant treatment plans.

The most common measure of dose conformity is the root-mean-square deviation of the peripheral dose from a selected dose level. This evaluator is often used in conjunction with computerized optimization. Another conformity indicator is the peripheral uniformity number (PUN), defined as the ratio of the mPD to the mean peripheral dose calculated in the harmonic formalism.[90] For planned seed configurations optimized for ^{125}I and ^{103}Pd, the PUN is on average equal to 0.67. A higher PUN is indicative of better conformity in the treatment plan. The PUN is likely to undergo severe degradation after seed displacement due to the volatility in the mPD. A third parameter proposed in the literature is the conformation number (CN), which is applicable to both external

beam and brachytherapy.[97] When calculated at the level of the mPD, the CN is simply the ratio of the volume of the PTV to the volume enclosed by the mPD isodose surface. For prostate seed implants, the CN is on average 0.72, compared to 0.65 for a 3-field external beam boost treatment of the prostate.

The notion of dose conformity is based on the assumptions that a well-defined and clinically relevant PTV can be precisely identified, and that there is reasonable expectation of delivering the conformal dose distribution as planned. In some institutional protocols, the PTV includes an expanded dosimetric margin around the true prostate to encompass extracapsular extension and in anticipation of dose degeneration subsequent to seed misplacement. Treatment planning then aims to conform to the expanded PTV. However, distortion of the planned isodose surface invariably occurs due to seed placement uncertainties. Until a technique becomes available that substantially accounts for these uncertainties in real time, dose conformity remains an evaluator only of idealized treatment plans.

4. Dose-volume histogram

Compared to single scalar evaluators, the DVH (including ''natural'' DVH) provides substantially more information for quantitative evaluation of the dose distribution associated with a given plan or actual implant. Variations of the DVH concept include the coverage, external-volume and heterogeneity indices,[21,56,98] and the dose nonuniformity ratio.[98] In particular, the coverage index (CI) shows the percentage of the target volume covered by any isodose level. In the preoperative treatment plan, CI at the mPD dose level is by definition 100%; in the actual implant, the corresponding CI at the same dose level should be approximately 90% under the current implantation techniques, and is expected to be higher with better techniques.[56]

F. Treatment plan optimization

It was recognized from the early days of image-based 3D planning that template-guided prostate implants were amenable to computerized optimization. Roy *et al.* first reported the Memorial experience of CT-based optimized planning, in which the seed loading patterns were determined by a least-square method to maximize the dose conformity;[99] the needle patterns were selected on the basis of clinical judgment. This method is therefore semi-automatic, in that the treatment planner needs to design a needle pattern (and in their initial approach, needle orientation) as a starting point for computer optimization. Even so, the authors reported a factor of 10 reduction in the planning time compared to the manual planning experience. The optimal seed loading rules were explored by Narayana *et al.*[100] When the effects of potential seed displacement and prostatic volume change were taken into account, peripheral loading appeared to be the optimal strategy.

A number of robust optimization schemes have since been applied to prostate implants. Pouliot *et al.*[101] used simulated annealing (SA) to optimize a cost function that took into

account both dose conformity and dose uniformity. The genetic algorithm (GA) has been adapted for inverse planning to minimize S_{mPD} and maximize dose conformity, while keeping the number of needles at a customary range.[92,102] Chen *et al.*[103] devised an ad hoc method in which one seed was placed at a time until S_{mPD} was minimized. Overall, these optimization techniques were able to produce improved treatment plans, as measured by the respective evaluators, without extensive human intervention and within 1–15 min run time on modern computers. In addition, both SA and GA are stochastic, ''intelligent'' optimization schemes, capable of search for optimality as defined by realistic objective functions.[104,105] The potential for incorporating seed displacement uncertainties in such an intelligent optimization scheme was explored.[102,106] It is quite likely that some of these techniques will be translated into mainstream treatment planning and intraoperative dosimetric guidance in the near future.

IV. CURRENT RECOMMENDATIONS

Based on the rationale and the empirical evidence outlined in the foregoing sections, the AAPM recommends the following practical guidelines as a basis for promoting a level of quality standards in prostate brachytherapy physics that is necessary to ensure that the anticipated clinical outcomes are reproducible and uniform on a large scale. Practitioners of existing prostate seed implant programs are urged to compare these guidelines with their institutional protocols, carefully evaluate and justify any departures, and make modifications to their programs if necessary. For new prostate seed implant programs, it is recommended that these guidelines be implemented as part of the quality assurance protocols.

It is recognized that modern prostate brachytherapy is a multi-disciplinary effort that involves radiation oncology, diagnostic radiology and urology. Successful implementation and continued improvement of a prostate brachytherapy program rely on effective teamwork and ongoing quality assurance review of the entire program. The physics aspects of quality assurance as outlined in this section are an integral part of this multi-disciplinary effort.

This section of the document uses three distinct levels of imperatives with strictly defined meanings:

(1) *Shall* or *Must* indicates a recommendation that is necessary to ensure a minimum standard of safety and effectiveness in prostate seed implantation;
(2) *Should* indicates a recommendation that is necessary to meet the baseline standard of practice in prostate seed implantation;
(3) *Recommend* indicates an advisory recommendation that is to be applied when practicable.

A. Equipment

The medical physicist *should* be directly involved in the selection, acceptance-testing and quality assurance of any equipment acquired for the prostate seed implant program

(see Table I). The quality assurance of equipment that affects the dosimetric consequences of seed implantation *must* be performed by the medical physicist.

Imaging: Verification *shall* be made (e.g., in phantom) to ensure that the grid pattern on the ultrasound image corresponds to the physical locations given by the perineal template. The fluoroscopy unit used in the operating room *should* display minimal distortion in a screen area that adequately encompasses the implant region. It is *recommended* to identify and follow a set of acceptance testing and ongoing quality assurance procedures described in the Report of AAPM Ultrasound Task Group No. 1[107] that are relevant to TRUS imaging, especially with regard to spatial resolution, grayscale contrast, geometric accuracy, and distance measurement.

Accessories: Proper functioning of applicators, accessories and stabilizing devices *should* be verified before each implantation procedure.

Treatment planning system: The medical physicist *shall* verify that the treatment planning system reproduces the values shown in Table II for the dose at total decay from an ^{125}I model 6711 or [103]Pd seed, calculated using the TG43 data in the point source approximation.[40] This test serves as a necessary indication that the planning system complies with the dosimetric formalism recommended by TG43. The medical physicist *shall* verify that the treatment planning system performs the correct dose summation at one or more locations in a simple configuration of multiple seeds. We endorse the recommendations of the AAPM Task Group No. 40[108] regarding quality assurance of treatment planning systems. In particular, the above tests *shall* be performed before the computer treatment planning system is put into clinical use, and at each subsequent software release.

Dosimeters: The medical physicist *shall* establish the calibration of dosimeters for the assay of each type of seed used in the prostate brachytherapy program. The user's well chamber *shall* be calibrated at an ADCL with direct traceability to NIST. Alternatively, individually calibrated seeds *shall* be obtained from the ADCL to establish a calibration factor for the particular geometry being used. In either case, the constancy of the user's dosimeter *shall* be confirmed using a long-lived radionuclide before each use. Proper functioning of the ion chamber survey meter and radiation detector *shall* be verified using a long-lived test source before each use in the operating room.

B. New radionuclide designs

New supplies of ^{125}I, [103]Pd or other low energy sources for permanent implantation need to become commercially available to meet the increasing demand for radioactive seeds. However, it must be stressed that for any new therapeutic radionuclide, the dosimetry for the source design *must* be established. Ideally, a national air kerma strength standard *should* be established, and the parameters for the TG43 formalism *should* be measured and independently confirmed.

The dosimetry of low energy photon-emitting brachytherapy sources such as ^{125}I and [103]Pd is sensitive to the

source geometry, encapsulation and internal structure due to self-absorption effects. These factors can be particularly sensitive to the quality of the manufacturing process during seed fabrication. It is inappropriate to use the dose rate constants, radial dose functions, anisotropy functions, anisotropy factors or constants published in the TG43 report for new source designs. Regarding a source intended for wide use, the vendor *shall* have the responsibility to provide a calibration of source strength that is traceable to a standard, and the medical physicist *shall* have the responsibility to ensure that the clinical dosimetry parameters have been validated by independent investigators other than the vendor.

C. Seed assay

Radioactive seeds may be obtainable in loose seeds, ready-loaded cartridges, or absorbable suture. In whatever form the seeds are procured, the manufacturer's assay *must* be independently confirmed. As recommended by AAPM Task Group No. 56,[41] a random sample of at least 10% of the seeds in the shipment *should* be checked. Discrepancies of 3% or more between the mean of the assay and the manufacturer's calibration *should* be investigated. Unresolved discrepancies of 5% or more *should* be reported to the manufacturer.

As discussed by the Ad Hoc Committee of the AAPM Radiation Therapy Committee on ^{125}I sealed source dosimetry, the revision of the NIST standard for ^{125}I *must* be taken into account as soon as it becomes available.

D. Changes to the dose value due to TG43

To promote uniformity in the clinical adoption of the TG43 formalism, it is *recommended* to scale the prescribed dose such that a pre-TG43 value of 160 Gy becomes 145 Gy. This recommendation is based on the discussion in Sec. III B but with the dose rounded from 144 Gy to 145 Gy. The clinically optimal dose and the method of prescription are not yet definitive. In cases where a pre-TG43 prescribed dose other than 160 Gy needs to be converted to the TG43 value, it is *recommended* to use the scaling ratio of 0.9.

E. Dosimetric planning

Treatment planning *must* be carried out for all patients prior to the insertion of radioactive seeds. In this context, treatment planning refers equivalently to intraoperative planning or conventional preoperative planning. It is *recommended* to generate the isodose distributions superposed on the contours of the prostate in selected planes, and to construct the DVH for the prostate. It is *recommended* to generate the DVH or ideally the dose-surface histogram (DSH) for the rectum. It is *recommended* to adequately identify the entire length of the prostatic urethra, and to calculate the dose profile along the urethra.

Prior to implantation, the dosimetric plan *should* be checked using an independent procedure or by a second member of the physics staff, and *must* be reviewed by the radiation oncologist.

F. Implantation procedure

A member of the physics staff *shall* be present in the operating room during prostate seed implantation. The physics personnel *must* be familiar with the treatment plan and the dosimetric consequences of any deviation from the plan. If the implantation technique relies upon preoperative plans based on prior volume studies, the position of the prostatic gland relative to the template coordinates *must* be verified in more than one imaging plane. If deviation from the planned position is detected, the physics personnel *should* evaluate whether modification to the setup and/or treatment plan is required, and recommend corrective action.

An account of the needles and seeds implanted *shall* be kept as the procedure progresses. At the end of implantation and after cystoscopy, the physics personnel *shall* confirm the total number of seeds implanted in the patient and the number of seeds remaining, which *must* add up to the total number brought into the operating room.

A scintillation detector or GM counter *must* be available in the operating room. For implants using loose seeds, it is *recommended* to survey each needle after it is withdrawn from the patient, to verify that no seed is unintentionally left in the needle core. At the completion of the procedure, a complete radiation survey *must* be conducted, which includes the vicinity of the implant area, the floor, waste, linen and all used applicators. The exposure rate at the surface and at 1 m from the patient *should* be measured by a properly calibrated ion chamber survey meter, and documented in accordance with pertinent federal and state regulations.

The physics personnel *should* be familiar with any institutional policies and procedures regarding sterile techniques and the operative environment.

G. Patient release

The medical or health physicist *shall* routinely review the patient survey results postimplantation to confirm that the prostate seed implant program continually satisfies all pertinent federal and state regulations regarding the release of patients with radioactive sources. NCRP Commentary No. 11, ''Dose Limits for Individuals Who Receive Exposure from Radionuclide Therapy Patients,'' provides additional information that may be of use in this context.

For obvious reasons, the institution's accountability of radioactive sources for a permanent prostate seed implant ends at the time of patient release. However, basic instructions to the patient on identifying the seeds and on radiation protection principles should be provided. It is not necessary to require the patient to strain urine and return dislodged seeds.

H. Postimplant analysis

A quantitative dose analysis *must* be carried out for each patient postimplantation. This statement is based on the premise that it is as important to know and document the dose delivered by a permanent seed implant as by an external beam treatment. The importance of a postimplant analysis cannot be overemphasized for the purposes of multi-

institutional comparison, improving techniques, evaluating outcome, and identifying patients who might benefit from supplemental therapy or be at risk for long-term morbidity.

The postimplant analysis *should* include two-dimensional dose distributions on which the target volume for dose evaluation is outlined. In addition, it is *recommended* to construct the DVH for this target volume, and to document the dose levels that cover 100%, 90% and 80% of the target volume for postimplant evaluation, i.e., D_{100}, D_{90} and D_{80}, and the fractional volume receiving 200%, 100%, 90% and 80% of the prescribed dose, i.e., V_{200}, V_{100}, V_{90} and V_{80}. Current literature suggests that imaging studies for dosimetric evaluation are ideally obtained 2–3 weeks postimplantation for [103]Pd implants and approximately 4 weeks postimplantation for ^{125}I implants. However, it is recognized that logistic considerations sometimes preclude such uniform timing of postimplant imaging for all patients. In addition, future technology may permit immediate postimplant dosimetry assessment in the operating room. In any case, the time course of postimplant dosimetric evaluation *should* be recorded for all patients.

For dosimetric evaluation performed at the optimum imaging time, it is *recommended* to use D_{90}, in comparison to the prescribed dose, as an indicator of implant quality in dose coverage. An implant with good coverage is characterized by D_{90} equal to or greater than the prescribed dose.

It is recognized that such dosimetric analysis is sensitively dependent upon the definition of the target volume for postimplant evaluation. Therefore a consistent radiological interpretation of the target volume should be used and documented to facilitate future interpretation of the dosimetric outcome.

It is *recommended* to construct the DVH or ideally the DSH for the rectal wall. Furthermore, it is *recommended* to adequately identify the location of the prostatic urethra, and to document the dose to the urethra. We recognize that visualization of the urethra at the recommended imaging time, rather than immediately postimplantation, may involve additional catheterization. It is hoped that a more convenient contrast-enhancing technique will become available in the near future.

I. Training requirement for physics personnel

For a member of the physics staff to perform independent work in permanent prostate brachytherapy, it is *recommended* that a minimum of five documented cases be performed under the direct supervision of an experienced physicist. In this context, an experienced physicist is one (a) who satisfies the above training requirement, or (b) who has performed a minimum of 20 documented cases independently.

J. Recommendations regarding commercial treatment planning systems

It is *recommended* that the TG43 dose calculation formalism be *explicitly* represented in commercial treatment planning systems for prostate seed implantation. This implies that the half-life, the dose rate constant, the radial dose function,

and as a minimum the anisotropy constant are separately specified in the source data library. Thus if future changes are to occur on any of the parameters for a given radioactive source, they can be easily and uniformly updated by the user of the system with the least confusion.

It is *recommended* that software facilities be implemented to generate the DVH for the target volume and the DSH for the rectal wall, both in preoperative planning and for postimplant evaluation.

In addition to these practical guidelines, the medical physicist should observe the recommendations of AAPM Task Group No. 56 with regard to the code of practice for brachytherapy physics,[42] and of AAPM Task Group No. 40 with regard to quality assurance for radiation oncology in general.[108]

V. ISSUES FOR FUTURE CONSIDERATION

This section contains a discussion of some dosimetric and radiobiologic effects on which consensus understanding does not yet exist among investigators of prostate brachytherapy. In addition, areas of current and future investigation are identified to aid practising medical physicists in designing their clinical seed implant programs.

A. Anisotropic dose calculation

The AAPM TG43 report[41] contains extensive tabulation of the anisotropy functions for ^{125}I and [103]Pd single seeds. In principle, it is not difficult to incorporate the anisotropy function formalism at the planning stage. However, in so doing one needs to make certain assumptions about the orientation of the radioactive seeds, e.g., being perfectly aligned along the needle insertion direction. Such an assumption is probably quite valid in the case of seed strands compared to loose seeds, but for any given case it is impossible to predict the extent and direction of splaying that will occur. On the other hand, the anisotropy constant is an averaged quantity weighted by the solid angle, and therefore represents the best estimate of the dose surrounding a radioactive seed of indeterminate orientation. Use of the anisotropy function formalism in postimplant dosimetry is technically more difficult, since the orientation of each seed must be determined by locating both ends of the seed. Until automated seed reconstruction software becomes widely available, the point source approximation appears to be the more appropriate formalism.

The dosimetric effects of anisotropy for ^{125}I were discussed by Ling *et al.*[109] There appear to be rather large differences in the dose distribution and the mPD between the anisotropy function formalism and the point source approximation widely used at present. To maintain uniform standard of dose reporting in prostate seed implant, investigators are urged to document the dose calculation formalism in their planning and/or postimplant dosimetry procedures.

B. Interseed effect

Mutual attenuation by neighboring seeds has been reported to be significant.[110,111] Meigooni *et al.*[111] performed

Solid Water measurement and Monte Carlo calculations to examine the dose perturbation in a two-plane implant of 3 $\times$ 3 seed arrays. They concluded that the inter-seed effect would reduce the peripheral dose by 6% for ^{125}I seeds. While the dosimetric impact of the inter-seed effect may be of clinical concern in simple, regular configurations, the overall effect in prostate implants is not clear. In practice, only the nearest-neighbor seeds are likely to produce appreciable dose perturbation. The solid angle sustained by a seed at 1 cm average distance is sufficiently small that the volume of perturbation is for most purposes negligible.

C. Tissue heterogeneity

The major cause of tissue heterogeneity is calcified deposits in the prostate gland, which occur in a small percentage of patients. The calcification presents on TRUS and CT studies as hyperechoic and high density regions, in contrast to the surrounding fibromuscular tissue. In the energy range of ^{125}I and ^{103}Pd radionuclides, where the photoelectric effect is the dominant absorption process, the presence of calcium ($Z = 20$) in fibromuscular tissue ($Z = 7.6$) leads to three dosimetric effects: (a) the dose rate constant is different in the two media, resulting in different absorbed dose; (b) the radial dose function is modified by the increased attenuation of the high Z material; (c) increased dose deposition occurs in the soft tissue at the interface of heterogeneity, due to a greater number of photoelectrons, which have a range of about 10 μ.[112–117] The overall dosimetric effect depends on the extent and the microscopic structure of calcification and the implant configuration. As a first approximation, the ratio of mass energy attenuation coefficients of calcium to muscle is 24 at 30 keV, and 23 at 20 keV. At present, there is no clinical study to gauge the actual impact of such tissue heterogeneity. It is prudent to identify patients who present with tissue heterogeneity under planning radiological studies, and to evaluate the efficacy and the optimal strategy of seed implantation on an individual basis.

The same physical principles may lead to variability of dose deposition in malignant versus normal histologies due to different elemental compositions. It is not yet clear whether the physical laws translate to a therapeutic advantage for adenocarcinoma of the prostate, and if so, what the magnitude of such advantage is.

D. Biological models

The linear-quadratic cell-kill model was extended by Dale to take into account (a) the decaying dose rate in brachytherapy, (b) dose rate difference across dosimetric inhomogeneity, (c) tumor cell proliferation, and (d) repair of sublethal damage for low dose-rate radiation.[118,119] This model was used by Ling *et al.* to examine the effect of dose heterogeneity in prostate seed implants.[96] The authors concluded that there might be some advantage in dose heterogeneity at about 20% above the prescribed dose, but beyond that, dose would be ''wasted'' in terms of producing cell kill. The biologically effective dose (BED) and cell surviving fractions predicted based on the model have been used as endpoints to

compare alternative treatment plans in prostate implant optimization.[92] Assumptions on the following parameters must be made to apply the Dale model: the α-to-β ratio, the value of α, the potential doubling time for tumor cells (T_{pot}), and the mean time for repair of sublethal damage. Given the uncertainties in these parameters, it must be concluded that the biological models should not be taken as quantitatively predictive, but rather as a guide of the relative efficacy of competing treatment plans. In addition to the cell surviving fraction, the tumor control probability (TCP) can be calculated based on the BED with additional assumptions on prostate tumor dose response data.[96,120]

The commonly quoted prescription dose of 115 Gy for ^{103}Pd implants is the dose estimated to have the same ''time-dose-factor'' (TDF)[121] as that corresponding to 145 Gy (converted from 160 Gy of pre-TG43 dose) from ^{125}I implants. Using the linear quadratic model to compare the relative cell kill effectiveness of the two radionuclides for these doses, Ling[122] has shown that ^{103}Pd may be more effective for T_{pot} of a few days and that ^{125}I may be more effective for longer T_{pot}. The determination of the most efficacious dose for each type of implants involves ongoing analysis of clinical outcome, dosimetric specification and radiobiological modeling.

E. Relative biological effectiveness

The relative biological effectiveness (RBE) was measured by Ling *et al.*[123] for ^{125}I and ^{103}Pd and by Freeman *et al.*[124] and Marchese *et al.*[125,126] for ^{125}I. Relative to ^{60}Co and at dose rates relevant to permanent prostate implant, the RBE was reported to be about 1.4 for ^{125}I and about 1.9 for ^{103}Pd.[123] The enhanced cell inactivation for a given dose reflects the additional biological effects of the radiation that are not described by the physical quantities.

These radiobiological effects are currently not taken into account in the clinical dosimetry for prostate seed implant, and are considered theoretical advantages of this modality.

F. Time course of target volume change

Work is continuing on characterizing the time course of prostatic volume change subsequent to seed implantation. A more complete understanding of this issue will have a strong impact on optimal dosimetric planning and postimplant analysis. Any significant differences in the pattern of gland swelling and resolution may be dosimetrically compensated for in planning for the specific radionuclide used, thus reducing the variance in the effective treatment dose delivered across the patient population.

G. Differential dose planning and delivery

The notion of planning the dose distribution to encompass the primary foci of the tumor in a high dose region is often an attractive one in treatment planning. It is justified radiobiologically on the basis that higher dose is required to eradicate higher tumor cell density. Advances in tumor imaging for prostate cancer will lend more credibility to the concept of differential interstitial irradiation. It is the nature of

brachytherapy to accept certain high dose regions in the treatment volume in order to achieve reasonably uniform dose coverage at a lower isodose level. With computerized optimization strategies, it is possible to routinely achieve this goal by placing the high dose volume at the focal area of the gross tumor. If the goal is achieved without sacrificing any other aspects of the clinical treatment plan, then it may be hypothesized that differential dose planning offers a therapeutic advantage compared to dosimetric planning without regard to the locations of tumor foci.

H. Intraoperative seed localization and dosimetry

While postimplant dosimetry is important for quantitative evaluation of dosimetric outcome, prostate brachytherapy ultimately will benefit from intraoperative seed localization followed by real-time computerized dosimetry, all performed with the patient still under anesthesia and in the treatment position. Thus any significant underdosage can be discovered and remedied by additional implantation before the end of the procedure. There is then a reasonable expectation that every implant will deliver the intended dose, where the only dosimetric variability is due to ongoing edematous reaction.

I. Correlation of dosimetric and clinical outcomes

A number of studies[21,33,38,71] suggest that the dosimetric outcome of a prostate seed implant ultimately plays a major role in predicting the likelihood of local relapse and/or long-term treatment-related morbidity. The natural progression of the disease is such that extensive follow-up is required for clinical outcome analysis. Such clinical correlation with dosimetric predictors will be aided by more consistent postimplant analysis and quantitative, organ-specific dose evaluation on a larger scale. Careful treatment plan optimization and dosimetric outcome analysis will in turn provide an early indication of treatment effectiveness for a prostate seed implant. Such is the goal of the present effort in seeking wide success of interstitial implantation in the management of prostate cancer.

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