Int. J. Radiation Oncology Biol. Phys., Vol. 51, No. 5, pp. 1422–1430, 2001

0360-3016/01/$–see front matter

ELSEVIER

PII S0360-3016(01)01616-9

PHYSICS CONTRIBUTION

INTRAOPERATIVE PLANNING AND EVALUATION OF PERMANENT PROSTATE BRACHYTHERAPY: REPORT OF THE AMERICAN BRACHYTHERAPY SOCIETY

SUBIR NAG, M.D.,* JAY P. CIEZKI, M.D.,† ROBERT CORMACK, PH.D.,‡ STEPHEN DOGGETT, M.D.,§ KEITH DEWYNGAERT, PH.D.,‖ GREGORY K. EDMUNDSON, M.S.,¶ RICHARD G. STOCK, M.D.,# NELSON N. STONE, M.D.,# YAN YU, PH.D.,** AND MICHAEL J. ZELEFSKY, M.D.††, for the Clinical Research Committee, The American Brachytherapy Society, Oak Brook, IL

*Ohio State University, Columbus, OH; †Cleveland Clinic Foundation, Cleveland, OH; ‡Harvard Medical School, Boston, MA; §Radiation Oncologist, Tustin, CA; ‖New York University, New York, NY; ¶William Beaumont Hospital, Detroit, MI; #Mount Sinai School of Medicine, New York, NY; **University of Rochester, Rochester, NY; ††Memorial Sloan-Kettering Cancer Center, New York, NY

Purpose: The preplanned technique used for permanent prostate brachytherapy has limitations that may be overcome by intraoperative planning. The goal of the American Brachytherapy Society (ABS) project was to assess the current intraoperative planning process and explore the potential for improvement in intraoperative treatment planning (ITP).

Methods and Materials: Members of the ABS with expertise in ITP performed a literature review, reviewed their clinical experience with ITP, and explored the potential for improving the technique.

Results: The ABS proposes the following terminology in regard to prostate planning process:

- **Preplanning—Creation of a plan a few days or weeks before the implant procedure.**
- **Intraoperative planning—Treatment planning in the operating room (OR): the patient and transrectal ultrasound probe are not moved between the volume study and the seed insertion procedure.**
- **Intraoperative preplanning—Creation of a plan in the OR just before the implant procedure, with immediate execution of the plan.**
- **Interactive planning—Stepwise refinement of the treatment plan using computerized dose calculations derived from image-based needle position feedback.**
- **Dynamic dose calculation—Constant updating of dose distribution calculations using continuous deposited seed position feedback.**

Both intraoperative preplanning and interactive planning are currently feasible and commercially available and may help to overcome many of the limitations of the preplanning technique. Dosimetric feedback based on imaged needle positions can be used to modify the ITP. However, the dynamic changes in prostate size and shape and in seed position that occur during the implant are not yet quantifiable with current technology, and ITP does not obviate the need for postimplant dosimetric analysis. The major current limitation of ITP is the inability to localize the seeds in relation to the prostate. Dynamic dose calculation can become a reality once these issues are solved. Future advances can be expected in methods of enhancing seed identification, in imaging techniques, and in the development of better source delivery systems. Additionally, ITP should be correlated with outcome studies, using dosimetric, toxicity, and efficacy endpoints.

Conclusion: ITP addresses many of the limitations of current permanent prostate brachytherapy and has some advantages over the preplanned technique. Further technologic advancement will be needed to achieve dynamic real-time calculation of dose distribution from implanted sources, with constant updating to allow modification of subsequent seed placement and consistent, ideal dose distribution within the target volume. © 2001 Elsevier Science Inc.

Prostate, Brachytherapy, Treatment planning, Dose calculation, Intraoperative.

Reprint requests to: Subir Nag, M.D., Chief of Brachytherapy, Ohio State University, 300 West Tenth Ave., Columbus, OH 43210. Tel: (614) 293-3246; Fax: (614) 293-4044; E-mail: nag.1@osu.edu

Financial disclosure: Dr. Steven Doggett is a consultant for Burdette Medical Systems. Dr. Nelson Stone and Dr. Richard Stock have financial interest in ProSeed Inc. The software developed in the PIPER system has been licensed to RTek Medical Systems by the University of Rochester. The Research Corporation of the University of Rochester holds an equity interest in RTek Medical Systems on behalf of the University of Rochester and Dr. Yan Yu.

Acknowledgments—The authors express their gratitude to David Carpenter for editorial assistance. The authors acknowledge the support of the Board of Directors of the American Brachytherapy Society and thank Drs. Dan Ash, Jan Batterman, John Blasko, Cliff Burdette, Anthony D'Amico, Louis Denis, Rodney Ellis, Ronald Ennis, Jay Friedland, Nilendu Gupta, Robert Jackson, Ted Jackson, Gyorgy Kovacs, Deborah Kuban, Yeh-Chi Lo, Gregory Merrick, Paul Schellhammer, Terry Stupar, Kent Wallner, Allan Wilkinson, and Marco Zaider for their valuable suggestions.

Received Dec 27, 2000, and in revised form Mar 20, 2001. Accepted for publication Apr 17, 2001.

INTRODUCTION

Prostate brachytherapy is rapidly gaining popularity in the United States as a method of treating early prostate cancer. Historically, the prostate has been implanted using a preplanned dosimetric method in most centers (1). A planning transrectal ultrasound (TRUS) prostate volume study is performed a few weeks before the procedure, and the physician outlines the prostate contour. A treatment plan containing needle locations and the number and strength of seeds in the needles is prepared using contiguous transverse images of the prostate from the TRUS. On the day of the implant, the intraoperative patient positioning and setup should match the pre-implant planning study as closely as possible. The prostate is then implanted according to the preplan. The preplanned method has a number of potential disadvantages:

- Alterations in the prostate volume and shape occur between the time of the preplan and the implant procedure, because of changes in patient position and relaxation of pelvic musculature induced by anesthesia or as a result of hormonal therapy. Hence, these changes can introduce inaccuracies in an implant based solely on the preplan.
- The patient positioning, setup, and images acquired during the actual implant should be matched with those obtained during the pre-implant planning study. These can occasionally be difficult to replicate in the operating room (OR).
- The preplanned method requires a separate TRUS imaging planning study, which is cumbersome and sometimes difficult to schedule. Furthermore, a separate pubic arch obstruction evaluation study is required in some preplanned techniques.

To overcome the disadvantages of the preplanned method, the recently published American Brachytherapy Society (ABS) recommendations for prostate dosimetry noted that, "Ideally, one should strive for on-line, real-time intraoperative dosimetry to allow for adjustment in seed placement to achieve the intended dose" (2). A few institutions are currently performing and refining intraoperative treatment planning (ITP) with a goal of achieving this ideal (3–16). The use of a portable computer in the OR to perform treatment planning and calculation of dose distribution in real time is a new technology in the evolution of prostate brachytherapy. This technology is still in the early phase of development and practiced in only a few centers, to allow the formation of a consensus on guidelines. However, the ABS feels that the time is opportune to critically assess the current state of the art, explore the potential for improvement in ITP, and suggest a focus of further technologic development for both investigators and industry.

METHODS AND MATERIALS

A panel meeting was held August 12–14, 2000 in New York City. Members of ABS with expertise in ITP performed a literature review, reviewed their clinical experiences, critically assessed the current state of the art of ITP, and explored the potential for technologic improvement. Representatives from the industry were invited to provide input during the brainstorming sessions. A preliminary report was then drafted. This initial report was revised based on the comments of external experts, including some who were not ABS members. The board of directors of the ABS approved this final document.

RESULTS

The results of the deliberations of the ABS panel on the potential for improvement are given in the following sections.

Terminology

There are several methods of ITP; however, there is no uniform terminology for the various methods. The ABS therefore proposes the following nomenclature in regard to the prostate planning process:

Preplanning. Creation of a plan a few days or weeks before the implant procedure.

Intraoperative planning. Treatment planning in the OR; the patient and TRUS probe are not moved during the time between the volume study and seed insertion procedure.

1. Intraoperative preplanning: Creation of a plan in the OR just before the implant procedure, with immediate execution of the plan.
2. Interactive planning: Stepwise refinement of the treatment plan using computerized dose calculations derived from image-based needle position feedback.
3. Dynamic dose calculation: Constant updating of calculations of dose distribution using continuous deposited seed position feedback.

The elements of ITP and their current availability are tabulated in Table 1.

Intraoperative preplanning

Intraoperative preplanning eliminates the preplanning patient visit by bringing the planning system into the OR. Because there is no preplan on which to base seed ordering, the approximate number of seeds to be ordered is determined from a nomogram or table based on the prostate volume obtained from a CT scan or ultrasound. TRUS is performed in the OR, and the images are imported in real time into the treatment planning system. The target volume, rectum, and urethra are contoured on the treatment planning system either manually or automatically, and a treatment plan is generated. The prostate is implanted according to the plan.

Wilkinson *et al.* (10) have reported that, using the ABS dose evaluation indices (2), ITP-based implants were of better quality than those in patients treated with the conventional preplanned method. When ITP was compared to the preplanned method, the median D_{90} (dose to 90% of the

Table 1. Elements of an intraoperative planning system

Level*	Description	Commercially available	Under development
1,2,3	Treatment planning in operating room	X	
1,2,3	Image acquisition	X	
1,2,3	Target definition	X	
1,2,3	Organ segmentation (draw contours manually)	X	
1,2,3	Identify needle position in relation to prostate	X	
2	Intraoperative optimization based on imaged needle location	X	
2	Estimate seed positions from imaged needle position	X	
2	Update dose calculation based on imaged needle location	X	
3	Auto organ segmentation	X	
3	Capturing deposited seed positions in real time		X
3	Optimization based on deposited seed location		X
3	Dynamic updating of dose calculation based on actual seed position		X
3	Account for motion of prostate during placement		X
3	Account for intraoperative edema		X
3	Postimplant dose calculation at time of surgery		X
3	Account for postoperative edema		X

* Levels

1. *Intraoperative preplanning* refers to the creation of a plan in the OR just before the implant procedure with immediate execution of the plan.
2. *Interactive planning* refers to stepwise refinement of the treatment plan using dose calculations derived from image-based needle position feedback.
3. *Dynamic dose calculation* refers to constant updating of dose calculations of implanted sources using continuous seed position feedback.

prostate volume) increased from 120.5 Gy to 136.5 Gy, the V_{80} (volume of the prostate receiving 80% of the prescribed dose) increased from 90.4% to 95.6%, and the V_{100} (volume of the prostate receiving 100% of the prescribed dose) increased from 76.2% to 84.9% (10). These improvements were statistically significant. Similar results were confirmed by Gewanter *et al*. (5). However, it must be noted that these were prospective but nonrandomized studies and are therefore subject to selection bias. In addition, studies comparing ITP to historic controls cannot distinguish between improvements due to ITP and those due to improved physician skill or to use of radioisotope with larger total activity.

Intraoperative preplanning has some advantages over the two-step preplanned method. It avoids the need for two separate TRUS procedures and for reproducing patient positioning, and setup is obviated. However, intraoperative preplanning does not account for intraoperative changes in prostate geometry or deviations of needle position from the preplan (13).

Interactive planning

The process of seed ordering, image acquisition, target definition, and organ contouring is similar to the intraoperative preplanning method. An optimized treatment plan is then performed, the dose–volume histogram (DVH) is generated, and the plan is examined. If necessary, seeds may be added or deleted manually, and the new isodose distributions and DVH displays are regenerated. The needles are inserted as per plan. In interactive planning, it is critical that the dose calculation is updated based on estimated seed positions derived from actual (imaged) needle positions (6, 9, 12, 14–16). The needles are repositioned, or subsequent needle positions are altered in the plan if there are adverse dosimetric consequences. The dose calculation is then updated based on actual needle location. The interval at which the dose distribution is recalculated is operator dependent. Various interactive planning systems exist; some are commercially available, whereas others are institution based. Commercially available systems include the Interplant system (Burdette Medical System, Champaign, IL), PIPER (RTek, Pittsford, NY), SPOT (Nucletron Corporation, Veenandaal, Netherlands), Strata (Rosses Medical Systems, Columbia, MD), and VariSeed (Varian Medical Systems, Palo Alto, CA). The institution-based systems include those at Memorial Sloan-Kettering Cancer Center (MSKCC) and Brigham and Women's Hospital in Boston. A brief description of some of these systems is included here to illustrate the differences between them. The reader should refer to the original publications for details.

In the technique used by Stock *et al*. (17, 18) and Stone *et al*. (7, 19) using the VariSeed system (modified version 6.7), the implantation begins with insertion of needles, 1 cm apart, into the periphery of the gland using the largest TRUS transverse diameter cut as a guide. The position of the needles is determined on the acquired TRUS images by identifying the echo bright markings ("acroflash") of the implanted needles. The planning system assumes that the needles run straight and do not deviate. Seventy-five percent of the seeds are then implanted through these peripheral needles using a Mick applicator. The seed positions are marked on the planning system along the needle track, and isodoses are generated. The remaining 25% of the seeds are

implanted using about 6 to 8 needles in the prostate interior such that they remain 0.5–1 cm from the urethra and cover the periphery of the base and apex. The needle positions in the interior are optimized to limit dose to normal structures (urethra, rectum) and minimize cold or hot areas within the prostate. DVH constraints for prostate D_{90}, urethral D_{30}, and the volume of the rectum irradiated by the prescription dose are used to adjust interior seed numbers and positions.

The MSKCC technique (9, 14) relies on an inverse planning optimization program, which uses a genetic algorithm optimization system. The genetic algorithm optimizer (20–23) attempts to find seed positions on a grid of available, or potentially available, sites that satisfy the dose constraints for the normal organs, such as the urethra and rectum, while maintaining maximal target coverage with the prescription dose to the prostate. This iterative optimization process analyzes more than 10^6 possible seed locations to achieve the ideal fit and solution and requires approximately 5–10 min for completion in the operating program. The computer determines the ideal seed location that meets the predetermined dose constraints for the urethra, rectum, and target (9, 14, 24). The seeds are loaded using a Mick applicator according to the seed-loading pattern dictated by the plan.

In the PIPER (Prostate Implant Planning Engine for Radiotherapy) system (12, 16), an automatic segmentation algorithm is used to contour the prostate, rectum, and urethra on TRUS images, reducing the contouring time to less than 2 minutes (25). The dosimetric planning is accomplished within 2 minutes using the inverse planning engine (or optimization). The ITP evaluation is a continuous, interactive process of isodose review, DVH analysis, and assessment of the feasibility of the needle placement plan (e.g., avoiding the urethra) during the actual procedure, by taking into account needle placement deviations as observed on live ultrasound. An assumption is made that the seeds are deposited along the actual needle track identified on live TRUS at the planned retraction distances (i.e., the *x* and *y* coordinates of each seed are displaced to reflect the observed needle deviation, but the *z* coordinate remains faithful to the plan).

The Interplant System (Burdette Medical System, Champaign, IL) has a built-in optical encoder in the probe-stepping mechanism that permits the real-time ultrasound images to be spatially registered against the position of the probe and template, thereby allowing instant operator feedback of the probe position within the prostate (6). Multiple loading configurations based on the dose constraints for the target, urethra, and rectum are preprogrammed in the system, allowing in the OR the comparison of several plans, if required. The plan is updated based on the seed position as estimated from the probe position and the needle track.

Although the previous methods rely on TRUS for imaging, interactive planning can also be performed using a split-ring MRI, as in the method developed at Brigham and Women's Hospital (11, 13, 26, 27). The split-ring MRI located in a surgical suite allows imaging in the lithotomy position. The placement of source-bearing needles is guided by dosimetric feedback (15). Interactive planning incorporates the actual needle placement, determined by the needle's MR (magnetic resonance) artifact observed on real-time images. Dosimetric consequences of needle placement are calculated with the needle in the patient, and the plan is modified, if necessary, before the sources are deposited.

Dosimetric outcome data. Zelefsky *et al.* demonstrated consistent excellent dose coverage of the prostate with the 144 Gy isodose line (V_{100}), with a median of 96%, and median D_{90} values of 116% of the prescription dose with the use of ITP (9). In a comparative dosimetric analysis of three implant techniques used at MSKCC, lower maximal urethral doses were observed significantly more frequently with the intraoperative computer-generated conformal plan in comparison to a CT preplan approach or an intraoperative ultrasound manual optimized approach (9, 14). Using this ITP approach, intraoperative dose intensification has been accomplished by directing higher doses toward regions showing active disease on MR spectroscopy without exceeding dose constraints on the urethra and rectum (21).

Lo *et al.* (8) compared the dosimetry results generated intraoperatively to CT-based evaluation performed 1 month postimplant in 70 patients, (37, I-125 alone; 33, boost Pd-103). This revealed a good correlation between intraoperative and postimplant results. The mean D_{90} results intraoperatively compared to those seen postimplant were 178 Gy vs. 188.5 Gy for I-125 implants and 98 Gy vs. 98.5 Gy for boost Pd-103 implants, respectively (8).

Interactive planning represents an improvement over intraoperative preplanning, and potentially would allow for a shortening of the learning curve for inexperienced brachytherapists, and the technical outcome of the procedure would be less operator dependent. However, in interactive planning the calculated dose distribution is based on implanted needle position, and hence interactive planning may not account for seed movement after deposition.

Dynamic dose calculation

At this time, dynamic dose calculation is not available for permanent prostate brachytherapy, because it is difficult to image individual seeds on TRUS. However, dynamic dose calculation has been used for high-dose-rate prostate brachytherapy (28, 29), and it is possible that some of its components could be adapted for permanent prostate dynamic dose calculation. Dynamic dose calculation is feasible for high-dose-rate prostate brachytherapy, because it requires imaging the needles, not the individual seeds, with TRUS. There is rapid development in this field, and it is possible that some of the features of dynamic dose calculation may become available by the time this report is published.

In comparison to interactive planning, dynamic dose calculation requires the following additional components. The essential feature is that the deposited seed positions are captured in real time, and the optimization is based on deposited seed location (rather than needle location). The dose distribution is updated dynamically based on actual

positions as the seeds are deposited. The motion of the prostate during placement, as well as changes in prostate size and shape due to intraoperative edema, are accounted for. Postimplant evaluation is performed at time of surgery, obviating a separate postimplant dose-calculation procedure.

Future directions in ITP

ITP addresses many of the limitations of current permanent prostate brachytherapy. However, current methods do not as yet allow for localization of the seeds, which is essential for dynamic dose calculation. If dynamic dose calculation is to be achieved, the advances in ITP must include the following: improvements in target visualization, ability to account for dynamic changes in prostate contour, improved seed detection, and better delivery systems. Although some of these potential improvements in ITP may seem far-fetched now, they are presented here to suggest directions in which the industry might focus its efforts.

Improved ultrasound technology

Sonoelasticity imaging. Sonoelasticity imaging is an ultrasound-based technique that holds promise for both seed localization and prostate–tissue segmentation. The basic principle is to transfer a mechanical vibration to the imaging area containing materials of different vibration properties and to detect such differences in Doppler mode ultrasound (30, 31). Sonoelastic imaging may be used to detect seeds and to distinguish the prostate itself from surrounding tissues by virtue of its ability to adjust resonance frequencies in the vibration harmonics. In addition, sonoelastic imaging may be used to more accurately localize prostatic tumors, thus allowing possible tumor dose intensification.

Automatic segmentation of the prostate boundary. A number of methods can be used for automatic segmentation (contouring) of the prostate boundary. These include the use of genetic algorithm (32), radial bas-relief method (33), multiscale edge detection algorithm with nonlinear Laplace filtering (34, 35), and a trainable method for TRUS segmentation (25). This would allow faster, automatic contouring of the prostate gland.

Transurethral ultrasound. Transurethral ultrasound devices, based on intravascular ultrasound currently in clinical use, may offer improved visualization of prostate anatomy and seed position. This is due primarily to the increased resolution of the image, allowing better differentiation of the seeds from the surrounding tissue. The merging of this imaging technology with dose calculation software may help develop intraoperative source-based dose calculation methods.

Fusion of ultrasound and fluoroscopy

The availability of both radiography and ultrasound imaging in the OR leads naturally to consideration of fusion of these two imaging modalities. TRUS is used to image the prostate, and the fluoroscope or flat panel radiograph is used to image the seeds. The seeds are identified automatically, and their positions are reconstructed and registered (fused) with the TRUS image. Solutions to the problems of automatic seed matching and reconstruction are well documented; most involve a 3-film approach (36–41). Using captured fluoroscopic images to replace the film radiographs in this approach would provide an automated system for capture, identification, and reconstruction of the seed position. Research is currently ongoing to solve the technical problems resulting from image distortion, organ motion, and spatial shifts.

Improved CT technology

CT technology currently joins the prostate implant process primarily for postimplant evaluation of the procedure. Automated source localization from volumetric CT data is straightforward. However, the physical constraints of current CT scanners restrict the use of this modality in intraoperative procedures. Current efforts may lead to CT devices that can improve the implant procedure. Using cone beam techniques and amorphous silicon detectors may allow CT imaging of the prostate and sources with the patient in the treatment position. This could be used for end-of-procedure evaluation of the implant while allowing placement of additional sources to fill in underdosed regions. Registration of an intraoperative CT data set (which can localize sources well) into the ultrasound planning system (which can visualize the prostate well) could allow incorporation of CT-derived source locations into the planning process. Alternatively, with increased availability of CT scanners, CT may be used for the entire implant process: initial imaging, planning, and source-based evaluation.

Improved MRI technology

MR technology is not widely used in the prostate implant process, though its soft-tissue resolution is well suited for visualizing the anatomic structures of interest, including the prostate and its subsections, urethra, rectum, and neurovascular bundles. Registration of diagnostic MR images onto intraoperative TRUS images could allow the integration of MR information into the ITP process. However, it should be recognized that if the MR images are obtained without the TRUS probe in place, not only is there an image registration/fusion problem but a soft-tissue deformation problem as well. Further research is ongoing in the area of deformable image registration. Interventional MR units, which are becoming more common, could allow MR imaging in the treatment position with the TRUS probe in place and provide the means for more generally available MR-guided implants. In the postimplant setting, MR may be fused to CT data sets to allow source-based calculation of dose distribution derived from CT data to be overlaid on MR images for visualization of the anatomy. Improvements in MR scanning techniques may lead to the ability to use MR to find sources directly from the MR imaging data, although this approach may be limited by the spatial distortions that are present in the MR modality.

Accounting for target geometry changes

There are changes in the target (prostate) geometry that are induced by needle insertion, by intraoperative edema/hemorrhage, and by postimplant edema. Some of these may be accounted for.

Changes due to needle insertion. The *z* axis (cranial-caudal) movement of the prostate can be compensated for by continuous monitoring of needle positions via TRUS and updating needle positions at selected intervals during the procedure. Sagittal ultrasound imaging is well suited for this. Altering the needle coordinates can compensate for the lateral intraoperative swelling of gland. At the present time, the need to add activity to compensate for prostate volume changes remains unclear.

Changes induced by intraoperative edema. The extent of intraoperative edema can be decreased by decreasing the number of needles used, decreasing the number of needle punctures, and using needles with sharper bevels, designed to reduce trauma.

Accounting for postimplant edema. Postimplant edema is prevalent within 24 hours and usually resolves at 4–6 weeks postimplant (42–46). Postimplant edema can be accounted or adjusted for by increasing target dose or target volume and by increasing the total activity or air-kerma (42). In the future, computer programs may be able to account for intraoperative and postoperative edema by adjusting the cumulative seed activity and position to deliver the prescription dose to the target over the lifetime of the implant.

Improvements in delivery system

Improvements in ITP may be achieved by further refinements in source delivery systems, such as the following:

- Improvements in needle loading can be achieved with the use of an autoloader, which can speed the process and improve the consistency of the seed positions within the needle.
- Fixed-space sources such as RapidStrand can be improved to decrease the "compressibility" of the strand and remove the limitations inherent in the fixed 10-mm spacing between the sources. Strengthening the strand by changing the material or adding a hardener immediately before implantation should help "hold" the seeds in their intended positions. A mechanism to vary the seed spacing along the strand will improve the flexibility of planning the implant.
- A more automated system of seed insertion should include higher-capacity cartridges, a seed-counting mechanism, and an improved withdrawal format.
- A motorized device could automatically push the needle tip a predetermined distance to facilitate the implant procedure (47). Optical encoders would allow feedback of the needle position. This would allow robotic placement, minimizing operator dependence.
- Seeds ("smart seeds") can be designed to incorporate computer chips that emit unique signals; these can be detected three-dimensionally external to the patient, allowing seed localization independent of the imaging modality used.
- The surface of the seeds could be "dimpled," enhancing their echogenicity ("echo-bright") and allowing them to be more readily identified on TRUS during the implant.
- Diodes could be placed within needles to autodetect source position as they are being deposited, and the information could be used to update the dose calculation.

Improved target localization

Currently, the entire prostate gland is considered to be the target volume for implantation, because the tumor cannot be definitively visualized. The use of functional imaging may allow better localization of tumor within the prostate, thus allowing dose intensification by directing higher doses toward regions showing active disease on MR spectroscopy, radiolabeled monoclonal antibody scan, ultrasonic spectrum analysis, or positron emission tomography (21, 25, 26, 48, 49).

DISCUSSION

Historically, the prostate has been implanted using a preplanned dosimetric method in most centers. However, the preplanned technique has a number of limitations. These include the need to match patient positioning, TRUS probe setup, and images acquired during the actual implant with those obtained during the preimplant planning study. Occasionally, these can be difficult to replicate. Changes in the prostate volume and shape occur between the time of the preplan and the implant procedure because of alterations in patient position, relaxation of pelvic musculature induced by anesthesia, or as a result of hormonal therapy. Hence, an implant based solely on the preplan can be inaccurate. Furthermore, the preplanned method requires a separate TRUS imaging planning study and occasionally a separate pubic arch obstruction evaluation study, which are time-consuming, cumbersome, and sometimes difficult to schedule. Intraoperative treatment planning can overcome some of the drawbacks of the preplanned method (see Table 2).

With ITP, reproducing patient and ultrasound probe positions is unnecessary, because ultrasound images are captured in the OR immediately before implant with the patient in the treatment position. Furthermore, any changes in size and shape of the prostate due to hormone therapy, muscle relaxation, or prostate movement can be accounted for. If pubic arch interference is encountered, the probe can be repositioned, a replan done, and the implant continued, making a separate pubic arch interference study unnecessary. There are disadvantages with ITP: (*1*) It adds about 10–20 min to the OR time, which can be expensive; (*2*) The physicist must plan under pressure because of time constraints.

The number of seeds to be ordered for ITP cases is based on the prostate volume obtained from a CT scan or TRUS. Hence, although a complete TRUS planimetric study is not

Table 2. Comparison of preplanning with intraoperative planning

	Preplanning	Intraoperative planning
Preprocedure TRUS	Full volumetric study and planning	Not required or limited to volume measurement
Preprocedure CT	Not done	Required if TRUS not done
Pubic arch obstruction evaluation	Usually required	Not required
Reproducing preplan in OR	Sometimes difficult to reproduce	Not required
Time and manpower requirements in OR	Less	More
Treatment planning environment	Low-pressure with greater time available for QA	High pressure with time constraints
Account for changes in prostate size and shape due to hormonal therapy or anesthetic muscle relaxation	No	Yes
Account for needle deviation from plan	No	Yes
Account for seed movement after seed deposition	No	No (for interactive planning) Yes (for dynamic dose calculation)
Account for postimplant prostate edema	No	No

Abbreviations: OR = operating room; QA = quality assurance; TRUS = transrectal ultrasound.

required, as in the preplanned method, a prostate CT scan or a limited TRUS study is needed to estimate the prostate volume. Some brachytherapists order 5–10% more seeds to account for changes in volume encountered in the OR. Hence it is possible that some of the ordered seeds may not be required. These will be wasted if the manufacturer refuses to accept returns. Some brachytherapists (who are accustomed to the preplanned technique) may not initially be comfortable in changing over to ITP. If so, they may wish to have an additional preplan until they are confident with ITP.

Some brachytherapists currently perform prostate implants using "manual" intraoperative treatment planning. No preplanning is done. Seeds are ordered based on a nomogram. In the OR and without a computer, the seeds are inserted according to a predetermined seed distribution pattern within the prostate. The seeds could be distributed using a peripheral, uniform, modified peripheral, or modified uniform distribution pattern. The use of a portable computerized treatment planning system in the operating room would be invaluable to further refine technique. Conversely, for those using computerized ITP, the use of a nomogram could serve as a valuable quality assurance check of the intraoperative computer-based dose calculations.

Currently, only intraoperative preplanning and interactive planning are commercially available. Intraoperative preplanning has produced improved dosimetric results when compared to those seen with preplanned techniques performed at the same center (5, 10). However, it is not clear if this dosimetric improvement was solely due to intraoperative planning or whether it represented (at least partly) the experience gained during the learning curve (i.e., the investigators started with the preplanned method, gained experience, and later went to the ITP). While interactive planning is based on the position of the needles and not on the position of the implanted seeds, the initial dose calculation results agree well with the post-CT results (8). The full potential of real-time intraoperative dose calculation will, however, be realized only with the implementation of dynamic dose calculation based on deposited seed position. Current treatment planning must be improved to allow autoregistration, autocontouring of the target (prostate), and autosegmentation of the normal tissues, and current imaging technology (ultrasound, CT, or MRI) must be improved to allow localization of individual seed position within the tumor. The isodose calculations must be rapidly performed, optimized, and updated as subsequent seeds are implanted. This real-time dynamic dose calculation will permit identification of areas of underdosage and allow modification of subsequent seed placement to obtain ideal dose distribution within the target volume. Another advantage of intraoperative computer-optimized treatment planning is that the learning curve for the inexperienced brachytherapists can be potentially shortened, and the technical outcome of the procedure would be less operator dependent, allowing the necessary dose distribution to be achieved, even by the novice. Further, once dynamic dose calculation becomes a reality, and individual seeds can be imaged, the postimplant evaluation can be performed in the OR, thus eliminating a separate postimplant dose calculation procedure.

CONCLUSION

ITP is another step in the evolution of permanent prostate brachytherapy. It addresses some of the limitations of current permanent prostate brachytherapy and has some advantages over the preplanned technique. Both intraoperative preplanning and interactive planning are currently feasible and commercially available. In interactive planning, the dosimetric feedback based on imaged needle positions can be used to modify the treatment plan. However, current technology cannot quantify the changes in prostate size and shape or the alterations in seed positions that occur during the implant. The major current limitation of ITP is the inability to localize the seeds in relation to the prostate. Use of ITP does not obviate the need for postimplant dosimetric

analysis, and it will not do so until the technology is developed to achieve dynamic dose calculation. This will allow constant updating of dose calculations of implanted sources and modification of subsequent seed placement to consistently obtain the ideal dose distribution within the target volume. The advantages of ITP need to be confirmed through correlation with dosimetric, toxicity, and efficacy outcome studies.

REFERENCES

1. Nag S, Beyer D, Friedland J, *et al*. American Brachytherapy Society (ABS) recommendations for transperineal permanent brachytherapy of prostate cancer. *Int J Radiat Oncol Biol Phys* 1999;44:789–799.
2. Nag S, Bice W, DeWyngaert K, *et al*. The American Brachytherapy Society recommendations for permanent prostate brachytherapy post-implant dosimetric analysis. *Int J Radiat Oncol Biol Phys* 2000;46:221–230.
3. Nag S. Transperineal Iodine-125 implantation of the prostate under fluoroscopic and transrectal ultrasound control. *Endocuriether Hypertherm Oncol* 1985;1:207–211.
4. Nag S, Martinez-Monge R, Fernandes PS. Transperineal Pd-103 brachytherapy as the sole treatment modality for good prognostic prostate cancer. *Rev Med Univ Navarra* 2000;44: 12–20.
5. Gewanter RM, Wuu S, Laguna JL, *et al*. Intraoperative preplanning for transperineal ultrasound-guided permanent prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48: 377–380.
6. Doggett S. Image registered real-time intraoperative treatment planning: Permanent seed brachytherapy. *Radiother Oncol* 2000;55(Suppl. 1):4 (Abstr.).
7. Stone NN, Stock RG, DeWyngaert JK, *et al*. Prostate brachytherapy: Improvements in prostate volume measurements and dose distribution using interactive ultrasound guided implantation and three-dimensional dosimetry. *Radiat Oncol Investig* 1995;3:185–195.
8. Lo YC, Stock RG, Hong S, *et al*. Prospective comparison of intraoperative real-time to post-implant dosimetry in patients receiving prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48(Suppl. 1):359–360 (Abstr.).
9. Zelefsky MJ, Yamada J, Cohen G, *et al*. Postimplantation dosimetric analysis of permanent transperineal prostate implantation: Improved dose distributions with an intraoperative computer optimized conformal planning technique. *Int J Radiat Oncol Biol Phys* 2000;48:601–608.
10. Wilkinson D, Lee EJ, Ciezki J, *et al*. Dosimetric comparison of pre-planned and OR planned prostate seed brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48:1241–1244.
11. Cormack RA, Kooy HM, Tempany CM, D'Amico AV. A clinical method for real-time dosimetric guidance of transperineal I-125 prostate implant using IMR imaging. *Int J Radiat Oncol Biol Phys* 2000;46:207–214.
12. Yu Y, Zhang Y, Brasacchio RA, *et al*. Automated treatment planning engine for prostate seed implant brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;43:647–652.
13. Cormack RA, Tempany CM, D'Amico AV. Optimizing target coverage by dosimetric feedback during prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48:1245–1249.
14. Zaider M, Zelefsky MJ, Lee EK, *et al*. Treatment planning for prostate implants using magnetic resonance spectroscopy imaging. *Int J Radiat Oncol Biol Phys* 2000;47:1085–1096.
15. D'Amico AV, Cormack R, Tempany C, *et al*. The use of real time MR guided interstitial brachytherapy in select patients with localized prostate cancer. *Int J Radiat Oncol Biol Phys* 1998;42:507–515.
16. Messing EM, Zhang Y, Rubens DJ, *et al*. Intraoperative optimized inverse planning for prostate brachytherapy: Early experience. *Int J Radiat Oncol Biol Phys* 1999;44:801–808.
17. Stone NN, Ramin SA, Wesson MF, *et al*. Laparoscopic pelvic lymph node dissection combined with real-time interactive transrectal ultrasound guided transperineal radioactive seed implantation of the prostate. *J Urol* 1995;153:1555–1560.
18. Stock RG, Stone NN, Wesson MF, *et al*. A modified technique allowing interactive ultrasound-guided three-dimensional transperineal prostate implantation. *Int J Radiat Oncol Biol Phys* 1995;32:219–225.
19. Stock RG, Stone NN, Lo TC. Intraoperative dosimetric representation of the real-time ultrasound-guided prostate implant. *Tech in Urol* 2000;6:95–98.
20. Lee EK, Gallagher RJ, Silvern D, Wuu CS, Zaider M. Treatment planning for brachytherapy: An integer programming model, two computational approaches and experiments with permanent prostate implant planning. *Phys Med Biol* 1999;44: 145–165.
21. Yu Y, Schell MC. A genetic algorithm for optimization of prostate implants. *Med Phys* 1996;23:2085–2091.
22. Sloboda RS. Optimization of brachytherapy dose distributions by simulated annealing. *Med Phys* 1992;19:955–964.
23. Silvern D, Lee EK, Gallagher RJ, *et al*. Treatment planning for permanent prostate implants: Genetic algorithm versus integer programming. *Med Biol Eng Comput* 1997;35:850.
24. Zelefsky MJ, Cohen G, Zakian K, *et al*. Intraoperative conformal optimization for transperineal prostate implantation using magnetic resonance spectroscopic imaging. *Ca J Sci Am* 2000 (in press).
25. Cheng G, Liu H, Rubens DJ, *et al*. Automatic segmentation of the prostate in transrectal ultrasound imaging. *Radiology* 2001;218:612.
26. Schenck FJ, Jolesz FA, Roemer RB, *et al*. Superconducting open-configuration MR imaging system for image-guided therapy. *Radiology* 1997;202:219–226.
27. Silverman SG, Jolesz FA, Newman RW, *et al*. Perspective: Design and implementation of an interventional MR imaging suite. *Am J Radiol* 1997;168:1465–1471.
28. Edmundson GK, Yan D, Martinez AA. Intraoperative optimization of needle placement and dwell times for conformal prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1995; 33:1257–1263.
29. Stromberg J, Martinez A, Gonzalez J, *et al*. Ultrasound-guided high dose rate conformal brachytherapy boost in prostate cancer: Treatment description and preliminary results of a phase I/II clinical trial. *Int J Radiat Oncol Biol Phys* 1995;33: 161–71.25.
30. Rubens DJ, Hadley MA, Alam SK, *et al*. Sonoelasticity imaging of prostate cancer: In vitro results. *Radiology* 1995;195: 379–383.
31. Lerner RM, Huang SR, Parker KJ. "Sonoelasticity" images derived from ultrasound signals in mechanically vibrated tissues. *Ultrasound Med Biol* 1990;16:231–239.
32. Arambula CF, Davies BL. Automated prostate recognition: A key process for clinically effective robotic prostatectomy. *Med Biol Eng Comput* 1999;37:236–243.
33. Kwoh CK, Teo MY, Ng WS, *et al*. Outlining the prostate boundary using the harmonics method. *Med Biol Eng Comput* 1998;36:768–771.
34. Aarnink RG, Pathak SD, de la Rosette JJ, *et al*. Edge detection

in prostatic ultrasound images using integrated edge maps. *Ultrasonics* 1998;36:635–642.
35. Aarnink RG, Giesen RJ, Huynen AL, *et al*. A practical clinical method for contour determination in ultrasonographic prostate images. *Ultrasound Med Biol* 1994;20:705–717.
36. Amols H, Rosen I. A three-film technique for reconstruction of radioactive seed implants. *Med Phys* 1981;8:210–214.
37. Rosenthal M, Nath R. An automatic seed identification technique for interstitial implants using three isocentric radiographs. *Med Phys* 1983;10:475–479.
38. Niroomand-Rad A, Thomadsen B. Evaluation of the reconstruction of seed positions from stereo and orthogonal radiographs for routine radiotherapy planning. *Radiat Med* 1990; 8:145–151.
39. Altschuler M, Kassaee A. Automatic matching of corresponding seed images of three simulation radiographs to allow 3-D triangulation of implanted seeds. *Phys Med Biol* 1997;42:293–302.
40. Metz C, Fencil L. Determination of three-dimensional structure in biplane radiography without prior knowledge of the relationship between the two views: Theory. *Med Phys* 1989; 16:45–51.
41. Fencil L, Metz C. Propagation and reduction of error in three-dimensional structure determined from biplane views of unknown orientation. *Med Phys* 1990;17:951–961.
42. Potters L, Wang XH, Yamada Y. A nomogram to compensate for intraoperative prostate edema during transperineal brachytherapy. *Tech Urol* 2000;6:99–103.
43. Waterman F, Yue N, Corn B, *et al*. Edema associated with I-125 or Pd-103 prostate brachytherapy and its impact on post-implant dosimetry: An analysis based on serial CT acquisition. *Int J Radiat Oncol Biol Phys* 1998;41:1069–1077.
44. Yue N, Dicker A, Corn B, *et al*. A dynamic model for the estimation of optimum timing of computed tomography scan for dose evaluation of ^{125}I or ^{103}Pd seed implant of prostate. *Int J Radiat Oncol Biol Phys* 1999;43:447–454.
45. Prestidge BP, Bice W, Kiefer E, *et al*. Timing of computed tomography-based postimplant assessment following permanent transperineal prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 1998;40:1111–1115.
46. Merrick G, Butler WM, Dorsey AT. Influence of timing on the dosimetric analysis of transperineal ultrasound-guided prostatic conformal brachytherapy. *Radiat Oncol Invest* 1998;6: 182–190.
47. Kovacs G, Galalae R, Wirth B, *et al*. Optimization of interstitial brachytherapy for locally advanced prostate cancer by a new implantation technique. *Strahlenther Oncol* 1995;171(12): 685–688.
48. Ellis RJ, Sodee DB, Spirnak JP, *et al*. Feasibility and acute toxicities of radioimmunoguided prostate brachytherapy. *Int J Radiat Oncol Biol Phys* 2000;48:683–687.
49. Feleppa EJ, Fair WR, Tsai H, *et al*. Progress in two-dimensional and three-dimensional ultrasonic tissue-type imaging of the prostate based on spectrum analysis and nonlinear classifiers. *Molecular Urol* 1999;3:303–310.