General Inclusion Criteria:

Clinical Stage
- T1-T3b and selected T4

Gleason Score
- Gleason score 2-10

PSA
- No upper limit, but in almost all cases, patient does not have documented distant metastasis (TxA0M0)

Exclusion Criteria:

Relative Contraindications
- Severe urinary obstructive symptoms
- Extensive TURP defect or TURP within 6 month
- Collagen vascular disease

Absolute Contraindications
- Unable to undergo anesthesia (general, spinal, epidural, or local)
- Unable to lay flat

Physics and Dosimetry:

Sources
- Ir-192

Treatment Planning System
- Commissioned prior to first use with source-specific documentation and quality assurance

Image-based Treatment
- Volumetric base upon contiguous slice acquisition (CT, MR, US)
- Slice spacing appropriate to resolution requirements
  - Typical intraoperative procedures: $\leq 5$ mm
  - Typical planning evaluation: $\leq 3$ mm

- Three-dimensional calculation
- DVH-based analysis

Dosimetry
- Air kerma strength of each new source should be independently measured and compared to vendor specifications

Dose calculation
- Dosimetry in accordance with TG43 (1999) and revised TG43U1 (2004) formalisms
- The prescribed dose will be the intended minimum dose delivered to planning target volume (PTV)
Volume quantifiers for structures with ill-defined extent (urethra and rectum) should be cited in cubic centimeters

**Intraoperative Procedure:**

**Anesthesia**
The implant procedure may be done under epidural, spinal or general anesthesia. Epidural or patient controlled analgesia (PCA) should be used during the post-op period for pain control if inpatient.

**Implant**
After loading catheters must be placed with TRUS guidance. The implant catheters must be CT/MR compatible if CT/MR is used for planning. During the implant, attention should be given to keep the catheters in the prostate without perforating the urethra. Posterior rows of catheters may be advanced into the seminal vesicles. No fewer than 14 catheters must be in the clinical target volume for adequate coverage without excessive hot spots.

**Cystoscopy**
Evaluation of the depth of catheter insertion and avoid perforation of the bladder should be done by flexible cystoscopy.

**Fiducial Marker**
To facilitate with the identification of target and normal structures, fiducial marker seeds should be placed under TRUS guidance at the base and the apex of the prostate. A Foley catheter should be inserted in the urethra at the conclusion of the implant procedure to help identify the urethra.

**Treatment Planning:**

**Treatment Planning Scan**
Perform after the implant procedure. The treatment planning CT/MR scan should be performed with the patient in the treatment position with the Foley catheter in place. Metallic obturators or non-CT compatible dummy ribbons must be removed prior to the CT/MR scan to reduce imaging artifacts. The scan thickness must be \( \leq 0.3 \) cm and the slices must be contiguous. The brachytherapy target volume and critical structures should be outlined on all slices. The scan should include the entire prostate and the area at least 3 slices (9 mm) above and below the prostate and include the perineum to allow visualization of the catheters from tips to outside the patient. The tips of all the catheters must be included. The patient’s external body contours should not be included in the field of view (FOV) in order to maximize the image quality.

**Dwell Selection and Dwell Time Optimization**
The dwell time in dwell positions located outside of the PTV should be turned down to minimize normal tissue irradiated.
A dwell time optimization program based on geometric or inverse planning algorithm should be used. Manual optimization is also accepted.

**Brachytherapy Target Volume**

The definition of volumes will be in accordance with ICRU Report 58: Dose and Volume Specification for reporting interstitial therapy. The Clinical Target Volume (CTV) is defined by the physician on the treatment planning scan. For T1c-T2b, the brachytherapy CTV includes the prostate only and for T3a-T3b, the brachytherapy CTV includes the prostate and extra-capsular extension. The brachytherapy Planning Target Volume (PTV) is identical to the CTV.

**Critical Structures**

Critical structures to be contoured include the bladder, rectum, and urethra. When contouring the bladder and rectum, the outer most border of the mucosa must be contoured. For the urethra, the outer surface of the Foley catheter must be contoured. Critical structures should be contoured on every CT slice that contains a target volume and in at least 3 slices (9 mm) above and below the CTV.

**Dose Specifications**

The prescription dose will be given only to the PTV. The goal is to deliver the prescription dose to at least 90% of the PTV (V100 prostate >90%). However, the dose to critical normal structures should be kept at or below limits.

The volume of bladder and rectum receiving 75% of the prescription dose should be kept to less than 1 cm³ (V75 rectum and V75 bladder < 1 cm³) and the volume of urethra receiving 125% of the prescription dose should be kept to less than 1 cm³ (V125 urethra < 1 cm³).

If the dose to critical normal structures cannot be kept below the specified level, we recommend readjusting the implant or repeating the implant procedure until a more optimal implant is obtained.

**Contours and Isodose Distributions**

Isodose distributions of 50%, 100%, 150% of the prescription dose, with contours of the PTV and critical structures should be used to evaluate the treatment plan.

**Dose Volume Histograms**

The number of sample points used in these calculations should be stated. A minimum of 5,000 points should be sampled for the calculation of each cumulative DVH.

**Treatment Delivery:**

**Dose Delivery**

The first HDR fraction should be delivered on the day of the catheter placement. If multiple fractions are delivered, consecutive fractions should be delivered within 24 hours after the first treatment, but no less than 6 hours between treatments.

**Catheter Position Verification**
Visual inspection of the catheters prior to delivery of each treatment is required. Fluoroscopy or CT may be used to verify the position of the catheters. The physician should adjust the catheters if catheter displacement is identified prior to the treatment. If the catheters cannot be satisfactorily repositioned and cannot be corrected by a new plan, then the treatment should be postponed until a satisfactory implant may be done.

Radiation Safety
Room and patient should be surveyed using a radiation survey monitor immediately after each dose delivery.

Catheter Removal
After completion of the treatment all catheters should be removed.

**Patient Selection Criteria:**

**Monotherapy:**
Clinical T1b-T2b and Gleason score ≤ 7 and PSA ≤ 10 ng/mL

**Boost:**
Patients with high risk features such as T3-T4, Gleason score 7-10, and/or PSA > 10 ng/mL
Selected patients with “bulky” T1-2b tumor (inadequate information exists to clearly define bulky tumor based on DRE, TRUS, percentage positive biopsies)

**Prescription Doses:**

**Monotherapy**
10.5 Gy x 3
8.5-9.5 Gy x 4
6.0-7.5 Gy x 6

**Boost**
15 Gy x 1 (with 36-40 Gy XRT)
9.5-10.5 Gy x 2 (with 40-50 Gy XRT)
5.5-7.5 Gy x 3 (with 40-50 Gy XRT)
4.0-6.0 Gy x 4 (with 36-50 Gy XRT)

**Supplemental EBRT:**

**Target Volume**
Prostate and seminal vesicles with margin
Prostate, seminal vesicles and pelvic lymph nodes with margin
Role of pelvic radiotherapy is controversial.

**XRT Technique**
Conventional
3-dimensional conformal
Intensity modulated
Image guided

**Timing**
Goal is to complete both XRT and HDR in 7 weeks
Before
Androgen Deprivation Therapy:

Accepted regimens
- LHRH agonist with or without an anti-androgen

Indications
- Role of hormonal therapy with HDR brachytherapy boost is controversial.
- Neoadjuvant and concurrent for intermediate risk Gleason score 7
- Neoadjuvant, concurrent and adjuvant for Gleason score 8-10

Post-Treatment Evaluation:

Biochemical assessment:
- Serial PSA measurements – baseline at 3-6 months and then every 3-6 months and/or per institutional protocol

Physical examination:
- Role of routine DRE is controversial

Quality of life assessment:
- Urinary, bowel and sexual function should be prospectively assessed at follow-up visits

Post-Treatment biopsy
- Should be reserved for protocol settings or in clinical situation where salvage local therapy is being considered

Selected Reading

Overview


Radiobiology


Brenner, D., Martinez, A.A., Edmundson, G., et al., Direct evidence that prostate tumors show high sensitivity to fractionation (low a/b ratio), similar to late-responding normal tissue. International Journal of Radiation Oncology, Biology, Physics, 52: p. 6-13, 2002


Concomitant Boost IMRT versus IMRT Combined with Brachytherapy, Radiotherapy and Oncology 88: 46-52, 2008

Physics and Dosimetry


Kim, Y., Hsu, I-C., Lessard, E., Pouliot, J., Vujie, J., Dose Uncertainty Due to Computed Tomography (CT) Slice Thickness in CT-based High Dose Rate Brachytherapy of the Prostate Cancer, Med Phys. 31(9)2543-2548, 2004.

Hsu, I-C., Lessard, E., Weinberg, V., Pouliot, J., Comparison of Inverse Planning Simulated Annealing and Geometrical Optimization for Prostate High Dose Rate Brachytherapy, Brachytherapy, 3(3):147-152, 2004


Alterovitz, R., Lessard, E., Pouliot, J., Hsu, I-C., O'Brien, J., Goldberg, K., Optimization of HDR Brachytherapy Dose Distributions Using Linear Programming with Penalty Costs, Medical Physics, 33(11);4012-4019, 2006


Clinical Results


Grills, I., Martinez, A., Hollander, M., Huang, R., Goldman, K., Chen, P., Gustafson, G., High Dose Rate Brachytherapy As Prostate Cancer Monotherapy Reduces Toxicity Compared to Low Dose Rate Palladium Seeds, Journal of Urology, 171:1098-1104, 2004


Astrom, L., Pedersen, D., Mercke, C., Holmang, S., Johansson, K., Long-Term Outcome of High Dose Rate Brachytherapy in Radiotherapy of Localised Prostate Cancer, Radiotherapy and Oncology 74: 157-161, 2005


Hsu, I-C., Cabrera, AR., Weinberg, V., Speight, J., Gottschalk, AR., Roach, M., Shinohara, K., Combined Modality Treatment with High Dose Rate Brachytherapy Boost for Locally Advanced Prostate Cancer, Brachytherapy, 4:202-206, 2005

Vargas, C., Ghilezan, M., Hollander, M., Gustafson, G., Korman, H., Gonzalez, J., Martinez, A., A New Model Using Number of Needles and Androgen Deprivation to Predict Chronic Urinary Toxicity for High or Low Dose Rate Prostate Brachytherapy, Journal of Urology, 174:882-887, 2005


Niehoff, P., Loch, T., Nurnberg, N., Galalae, R., Egberts, J., Kohr, P., Kovacs, G., Feasibility and Preliminary Outcome of Salvage Combined HDR Brachytherapy and External Beam Radiotherapy (EBRT) for Local Recurrences After Radical Prostatectomy, Brachytherapy 4: 141-145, 2005


Rades, D., Schwarz, R., Todorovic, M., Thurmann, H., Graefen, M., Walz, J., Schild, S., Dunst, J., Alberti, W., Experiences with a New High-Dose-Rate


Duchesne, G., Williams, S., Das, R., Tai, K., Patterns of Toxicity Following High-Dose-Rate Brachytherapy Boost for Prostate Cancer: Mature Prospective Phase I/II Study Results, Radiotherapy and Oncology 84: 128-134, 2007

Hoskin, P., Motohashi, K., Bownes, P., Bryant, L., Ostler, P., High Dose Rate Brachytherapy in Combination withExternal Beam Radiotherapy in the Radical Treatment of Prostate Cancer: Initial Results of a Randomised Phase Three Trial, Radiotherapy and Oncology 84: 114–120, 2007


Thurairaja, R., Pocock, R., Crundwell, M., Stott, M., Rowlands, M., Srinivasan, R., Sheehan, D., Brachytherapy for Advanced Prostate Cancer Bleeding, Prostate Cancer and Prostate Disease 1-4, 2008

The American Brachytherapy Society (ABS) high dose rate prostate cancer task group has developed generalized criteria for the use of brachytherapy in the management of prostate cancer. These criteria are intended to guide radiation oncologists, urologists and physicists in making decisions regarding therapy. The complexity and severity of a patient’s clinical condition should dictate the selection of appropriate treatment. The availability of equipment and/or personnel may influence therapy. Approaches classified as investigational by the U.S. Food and Drug Administration (FDA) has not been considered in developing these criteria. The ultimate decision regarding the appropriateness of any treatment must be made by the attending physician.