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High-dose-rate brachytherapy as monotherapy for prostate cancer

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ABSTRACT

PURPOSE: To review and analyze the published data on high-dose-rate brachytherapy as monotherapy in the treatment of prostate cancer.

METHODS: A literature search and a systematic review of the high-dose-rate (HDR) brachytherapy (monotherapy) prostate literature were performed on PubMed using ''high-dose-rate, brachytherapy, prostate, monotherapy'' as search terms. More than 80 articles and abstracts published between 1990 and 2013 were identified. Data tables were generated and summary descriptions created. Commentary and opinion was formulated through discussion and consensus based on the critical review of the literature and the author's combined personal experience and knowledge.

RESULTS: Thirteen articles reported clinical outcome and toxicity with followup ranging from 1.5 to 8.0 years. Results were available for all risk groups. A variety of dose and fractionation schedules were described. Prostate-specific antigen progression−free survival ranged from 79% to 100% and local control from 97% to 100%. The toxicity rates were low. Genitourinary toxicity, mainly frequency/urgency, was 0−16% (Grade 3). Gastrointestinal toxicity was 0−2% (Grade 3). Erectile function preservation was 67−89%. The radiobiological, clinical, and technical features of HDR brachytherapy were reviewed and discussed.

CONCLUSIONS: Consistently high local tumor control and low complications rates are reported with HDR monotherapy. It provides reproducible high-quality dosimetry, it has an advantage from a radiobiology perspective, and it has a good radiation safety profile. HDR brachytherapy is a safe and effective local treatment modality for prostate cancer.

Keywords: Prostate; Prostate cancer; High-dose-rate brachytherapy; Radiation therapy; Monotherapy

Introduction

A literature search and systematic review of the high-dose-rate (HDR) brachytherapy (monotherapy) prostate literature was performed on PubMed using ''high-dose-rate, brachytherapy, prostate, monotherapy'' as search terms. More than 80 articles and abstracts published between 1990 and 2013 were identified. Data tables were generated and summary descriptions created. Historical information was derived from the literature and the author's combined personal experiences and knowledge. Commentary and opinion was formulated through discussion and consensus.

HDR prostate brachytherapy began in 1986 at Kiel University in Germany and soon after in the United States, independently at the Seattle Prostate Institute in 1989 and in 1991 at the California Endocurietherapy Cancer Center (CET) in Oakland, California, and William Beaumont Hospital (WBH) in Royal Oak, Michigan (1−6). HDR was initially used only as a boost in conjunction with external beam radiation therapy (EBRT) because of concerns about the effect of large doses per fraction on normal tissues. Dose escalation studies by Martinez *et al.*, however, established the safety and efficacy range for HDR in the context of combined EBRT and HDR (7−9). During the 1990s, ultrasound image guidance and computer treatment planning technology evolved, clinical experience accumulated, and outcomes of HDR prostate brachytherapy began to be reported. The clinical rationale for HDR monotherapy for prostate cancer was derived from organ-specific treatments such as radical prostatectomy and permanent seed monotherapy. Recognition of the technical capabilities of HDR to reliably treat the prostate (and seminal vesicles) with a margin of surrounding tissue and to simultaneously control the dose to adjacent normal tissues led to the development

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of HDR prostate monotherapy clinical trials, which were initiated in the mid-1990s at WBH and CET for low- and intermediate-risk groups, and in Osaka, Japan for all risk groups (9–11).

Why HDR?

HDR brachytherapy and improvements in EBRT evolved simultaneously. Conformal EBRT and intensity modulated radiation therapy are two technologies, which allow physicians to deliver higher total doses and achieve better tumor control rates. However, three major drawbacks of conformal EBRT or intensity modulated radiation therapy are day-to-day variations in internal anatomy secondary to organ motion (interfraction motion), organ deformation and other variations in internal anatomy during radiation therapy delivery (intrafraction motion), and daily setup inaccuracies (setup errors). To overcome these limitations, HDR brachytherapy was identified as a potentially advantageous vehicle for dose-escalation.

HDR technology combines a number of favorable qualities of brachytherapy with the sophisticated treatment planning developed for EBRT. HDR brachytherapy procedures are performed under general or spinal anesthesia, are usually done through a perineal template guide, and use ultrasound guidance similar to low-dose-rate (LDR) permanent seed implants. Organ motion and setup inaccuracies are not an issue with HDR either because they do not occur, or because they can be corrected with interactive online dosimetry during the procedure, or modified during simulation and treatment planning before dose delivery. There is no need to add treatment volume (margins) beyond the intended target to account for patient motion or variations in beam delivery.

Common problems associated with permanent seeds implants such as discrepancy between planned and actual seeds distribution, inability to correct seeds position or to optimize the dose delivered once the seeds are in place, and operator dependency are relatively low in HDR brachytherapy, particularly with the introduction of intraoperative online HDR treatment planning and delivery (12, 13).

Important features of HDR brachytherapy

1. HDR catheters are relatively easy to visualize with transrectal ultrasound (TRUS), and they can be safely implanted outside the prostate capsule and into the seminal vesicles without the risk of seed migration.
2. HDR avoids uncertainties in dosimetry (target dose) associated with prostate volume changes that occur with permanent seed brachytherapy. Immediate swelling and subsequent gland shrinkage due to fibrosis are irrelevant.
3. Real-time dose modulation HDR planning software offers immediate feedback for the physician and physicist to achieve optimal implant catheter distributions.
4. HDR planning provides multiparametric dose optimization through modulation of catheter geometry, dwell position, and dwell time. HDR dosimetry is "high density" because there are approximately twice as many HDR dwell positions as seeds in the typical permanent seed prostate (LDR) implant.
5. The versatility of intratarget dose modulation inherent to brachytherapy can be controlled and directed with HDR to deliver high doses to gross disease (concomitant boost), or it can be used to selectively reduce the dose to parts of the prostate or organs-at-risk (OARs) as in partial prostate irradiation (focal therapy). This process is sometimes described as dose sculpting or dose painting.
6. HDR dosimetry is prospective (known and approved before treatment delivery), and it consistently provides good target coverage and normal organ sparing (14).
7. The low alpha/beta ratio (estimated 1.2–4) means that the large fraction sizes used in HDR have a relatively high biological effectiveness for prostate cancer (15–17).
8. HDR is applicable to a wide range of clinical circumstances in prostate cancer.
9. A single radioactive source may deliver treatment to large numbers of patients and it can be used for many disease sites. The modality can be deployed in a cost-effective manner.
10. HDR treatment courses are of short duration, and recovery from acute side effects is comparatively brief.
11. HDR radiation safety is good because patients are not radioactive after the procedure. As such, patients do not need to follow special precautions such as limiting distance or duration of contact with other adults, children, or pregnant women. Likewise, there are no issues in handling radioactive sources by pharmacy or medical personnel.
12. Because androgen deprivation therapy (ADT) has not been shown to enhance disease control with prostate HDR monotherapy, and as ADT is usually not required for downsizing of prostate volume with HDR brachytherapy, it can usually be omitted, at least in low- and intermediate-risk group cases.

Patient and case selection

Patients whose disease is confined to the prostate or immediate surrounding tissue are ideal candidates for locally directed treatments such as prostatectomy, EBRT, or brachytherapy alone. National Comprehensive Cancer Network defined low- and intermediate-risk cases are more likely to have disease confined to the prostate region and, therefore, are logically the best candidates for local treatment (National Comprehensive Cancer Network guidelines version 1.2014 at www.nccn.org/professionals/physician_gls/pdg/prostate.pdf).