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High-dose-rate brachytherapy boost for prostate cancer: Comparison of three different fractionation schemes

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ABSTRACT

PURPOSE: Dose escalation for prostate cancer can be achieved with a combination of external beam radiotherapy (EBRT) and brachytherapy (BT) boost to increase local control. For high-dose-rate (HDR)-BT, optimal fractionation remains under debate. The objective was to assess the clinical outcome of three schemes of HDR-BT boost.

METHODS AND MATERIALS: Retrospective single institution data collection was performed. Patients received 46 Gy EBRT then an HDR-BT boost: 3 × 6 Gy, 2 × 9 Gy, or 1 × 14 Gy. HDR needles were placed under general anesthesia with endorectal ultrasonography guidance. CT-scan and treatment were performed postoperatively.

RESULTS: Between 2009 and 2012, 159 patients were included. Nine patients (5.7%) were low, 32 (20.1%) intermediate, and 118 (74.2%) high risk (D'Amico classification) without significant difference between the three BT schemes. With a median followup of 61 months, 5-year biochemical relapse−free survival, 5-year local relapse−free survival, 5-year metastases-free survival, and 5-year overall survival rates were 86.6% (SE 2.7%), 98.3% (SE 1%), 95.3% (SE 1%), and 96.5% (SE 1.5%), respectively, with no significant difference between the BT schemes. The rates of acute ≥ G2 genitourinary and ≥G2 gastrointestinal toxicities were 11.3% and 6.3%, respectively (p = NS). The rates of late genitourinary ≥ G2 and gastrointestinal ≥ G2 toxicities (at last follow-up) were 9.4% and 0.6% with, respectively, 0.6% and 0% of G4 (p = NS).

CONCLUSIONS: Hypofractionation up to a single-fraction HDR-BT boost for prostate cancer yields similar results in terms of biochemical control and late toxicity compared with two or three-fraction schemes. Single fraction HDR-BT appears acceptable for boosting prostate cancer after definitive EBRT. © 2017 American Brachytherapy Society. Published by Elsevier Inc. All rights reserved.

Keywords: Prostate cancer; High-dose-rate; Brachytherapy; Boost

Introduction

Radiotherapy is a standard curative treatment for localized prostate cancer, and its technique and results have improved over the last 30 years. With the technological advances, dose delivery precision and conformality have greatly improved, translating into higher control rates with over 90% of biochemical-free relapse rates at 10 years after treatment (1, 2).

To increase local control, dose escalation can be achieved by using a combination of external beam

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radiation therapy (EBRT) and brachytherapy (BT) boost. With its low alpha/beta ratio and anatomical location, prostate cancer is an ideal target for a high-dose-rate (HDR)-BT boost. Indeed, due to its intrinsic hypofractionation sensibility, biologic equivalent dose delivered to the prostate with a BT boost can be dramatically increased while conforming to the prostate volume and sparing adjacent organs.

Recently, the American Society of Clinical Oncology and the Cancer Care Ontario published a joint guideline update recommending to offer BT boost for intermediate- and high-risk prostate cancer patients when treated by definitive EBRT based on the data from three randomized controlled trials providing this evidence (EBRT vs. EBRT + BT) (3). However, currently for HDR-BT, different therapeutic schemes (total dose and fractionation) are reported, and there is no clear consensus regarding the right fractionation to use (4).

The main objective of our study was to assess the late clinical outcome (efficacy and toxicity) of three different schemes of an HDR-BT boost after EBRT for localized prostate cancer.

Methods and materials

A retrospective single institution data collection was performed in the Antoine Lacassagne cancer center in Nice, France. Data were collected from patients' files. This study was approved by the local ethic committee.

Inclusion criteria were: histologically proven localized prostate cancer, treated with EBRT combined with an HDR-BT boost. Exclusion criteria were: previous radiotherapy and metastases at time of diagnosis, sever urinary obstructive syndrome, and contraindication to general anesthesia. All patients consecutively treated between 2009 and 2012 were included. According to local guidelines, patients underwent clinical examination, prostate-specific antigen blood test, CT scan and/or MRI, and bone scan at the time of diagnosis. Tumors were staged using the UICC-cTNM classification (7h edition, 2009) and assessed using the D'Amico classification. Short (6 months) or long-term (24−36 months) androgen deprivation therapy was proposed to intermediate- and high-risk patients, respectively. Toxicity analysis focused on genitourinary (GU) and gastrointestinal (GI) side effects using CTCAE, version 3.0 criteria (National Cancer Institute Common Toxicity Criteria). Toxicity assessment was performed weekly during EBRT course, 1 month after HDR-BT boost, then every 6 months during the first 5 years of followup, then annually. The cutoff between acute and late toxicities was fixed to 6 months after the end of HDR-BT. Late toxicities were evaluated using their highest grade at any given consultation starting 6 months after treatment and latest grade at followup

External beam radiation therapy

Planning CT-scan was performed in treatment position with slices of 2.5 mm. Radiation therapy was delivered with a Varian linear accelerator CLINAC 21EX (Varian Medical Systems, Inc., Palo Alto, CA). Three-dimensional conformational radiotherapy was planned using ISOgray (DOSIsoft, Cachan, France). Intensity-modulated radiation therapy (IMRT) planning was performed using Eclipse treatment planning system (Varian Medical Systems, Varian Medical Systems, Inc., Palo Alto, CA). A total dose of 46 Gy in 23 fractions was delivered to the prostate. The dose was prescribed to the International Commission on Radiation Units and Measurements point in case of three-dimensional conformational radiotherapy and to the planning target volume ($D_{50\%}$) for IMRT, leading to consider that all the patients received the same dose delivered to the prostate. According to the calculated risk of lymph node involvement using the Memorial Sloan Kettering Cancer Center nomogram (5), the clinical target volume (CTV) was the whole pelvis or the prostatic fossa (prostate and seminal vesicles) for high (≥15%) and low risk (<15%) of lymph node involvement, respectively. The planning target volume was defined as a 1-cm margin around the CTV in all directions and reduced to 5 mm at the prostate rectal interface.

High-dose-rate brachytherapy boost

HDR-BT was performed within the month following EBRT completion. Patients treated in 2009 received 18 Gy in three fractions (3 × 6 Gy group): first fraction on the day of implant and the following two fractions the next day with at least 6 h apart. Patients treated in between 2010 and 2011 received 18 Gy in two fractions (2 × 9 Gy group): first fraction on the day of implant and the second fraction on the next day. Patients treated from 2011 and onward received 14 Gy in a single fraction (1 × 14 Gy group) on the day of implant.

To clean the rectum, a 2-day fiber-free diet was proposed, and enema was performed the day before and 1 h before procedure. Under general anesthesia, a triple-lumen catheter was first introduced into the bladder, then needles (Sharp Needles; Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden) were implanted transperineally (with endorectal ultrasonography guidance) using a dedicated perineal template sutured to the skin. After recovery, postimplant planning CT-scan was performed in the radiation oncology department for treatment planning purposes. CTV was the whole prostate with no expansion, whereas organs at risk (urethra and rectum) were delineated. Dose−volume adaptation was manually achieved using graphical optimization by dwell location and time variation (OncentraBrachy, Nucletron, an Elekta company, Elekta AB, Stockholm, Sweden). For the 3 × 6 Gy and 2 × 9 Gy groups, a contemporary CT-scan and dose planification were performed before each fraction. Considering α/β 1.5 Gy for prostatic tissue, EQD2 (equivalent dose at 2 Gy/fraction) was 39 Gy, 54 Gy, and

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