Available online at www.sciencedirect.com

ScienceDirect

journal homepage: http://www.elsevier.com/locate/rpor

Original research article

Treatment outcomes and late toxicities of intensity-modulated radiation therapy for 1091 Japanese patients with localized prostate cancer

Hidekazu Tanaka[a,*], *Takahiro Yamaguchi*[a], *Kae Hachiya*[a], *Shingo Kamei*[b], *Satoshi Ishihara*[b], *Masahide Hayashi*[c], *Shinichi Ogawa*[c], *Hironori Nishibori*[c], *Satoshi Goshima*[a], *Masayuki Matsuo*[a]

[a] *Department of Radiology, Gifu University Graduate School of Medicine, Yanagido 1-1, Gifu 501-1194, Japan*
[b] *Department of Urology, Kizawa Memorial Hospital, Shimokobi 590, Kobicho, Minokamo 505-8503, Japan*
[c] *Department of Radiology, Kizawa Memorial Hospital, Shimokobi 590, Kobicho, Minokamo 505-8503, Japan*

ARTICLE INFO

Article history:
Received 23 August 2017
Accepted 26 November 2017

Keywords:
Prostate cancer
Intensity-modulated radiation therapy
External beam radiation therapy

ABSTRACT

Aim: This study aimed to evaluate the treatment result of intensity-modulated radiation therapy (IMRT) in a large number of Japanese patients with prostate cancer.
Background: A total of 1091 patients with localized prostate cancer were recruited between March 2006 and July 2014. The patients were stratified into low- ($n = 205$ [18.8%]), intermediate- ($n = 450$ [41.2%]), high- ($n = 345$ [31.6%]), and very high-risk ($n = 91$ [8.3%]) groups according to the National Comprehensive Cancer Network classification. All patients were irradiated via IMRT at a dose of 74–78 Gy with or without androgen-deprivation therapy. The mean follow-up period was 50 months (range, 2–120 months).
Results: The biochemical failure-free rate (BFFR), the clinical failure-free rate, and the overall survival rate at the 5-year follow-up for all patients was 91.3%, 96.2%, and 99.1%, respectively. In univariate analysis, the prostate-specific antigen (PSA) levels (≤20 vs. >20 ng/ml) were significantly correlated with BFFR. A trend toward higher BFFR was noted in patients with a Gleason score (GS) of ≤7 than in patients with GS ≥8. In multivariate analysis, only PSA (≤20 vs. >20 ng/ml) was significantly correlated with BFFR. The cumulative incidence rate of gastrointestinal and genitourinary toxicity (≥grade 2) at the 5-year follow-up was 11.4% and 4.3%, respectively.
Conclusions: The findings of this study indicate that IMRT is well tolerated and is associated with both good long-term tumor control and excellent outcomes in patients with localized prostate cancer.

* *Corresponding author.*
E-mail address: htanaka-gif@umin.ac.jp (H. Tanaka).
https://doi.org/10.1016/j.rpor.2017.11.002

1. Background and aim

In 2012, the world wide incidence of prostate cancer was approximately 1,095,000 cases, resulting in 307,000 deaths.[1] In Japan, prostate cancer is the most commonly diagnosed cancer in men, with a projected incidence of 92,600 cases (16% of 576,100 cancer cases at all primary sites) in 2016. In 2014, 11,507 patients died of prostate cancer.[2]

Among the optimal treatment options for prostate cancer is external beam radiotherapy[3]; it is less invasive than other treatment modalities and can be administered to patients with comorbidities for which surgery is contraindicated. Intensity-modulated radiation therapy (IMRT) has been widely used for external beam irradiation of localized prostate cancers. Several studies have revealed that IMRT is safer than three-dimensional conformal radiation therapy (3D-CRT), particularly in terms of gastrointestinal (GI) adverse events.[4–7] The safety of IMRT also allows dose escalation, leading to better tumor control.[8] However, most large, single-institution studies on the efficacy of IMRT for localized prostate cancer have been performed in Western institutions. To the best of our knowledge, studies with more than 1000 patients with prostate cancer treated with IMRT are yet to be performed in Japan. Because the physique and prostate glands of Asians are smaller than those of Westerners, the outcomes and toxicity might differ between Asian and Western patients. Accordingly, this retrospective study aimed to evaluate the outcomes and late toxicity associated with IMRT among Japanese patients with prostate cancer.

2. Material and methods

2.1. Patients

Between March 2006 and July 2014, 1252 patients with prostate cancer were treated with IMRT at our institution. Patients with lymph node and distant metastases and those whose prostate-specific antigen (PSA) levels were not measured at least once after IMRT were excluded. As a result, 1091 patients were included in this analysis. Patient characteristics are shown in Table 1. All tumors were histologically confirmed as adenocarcinomas. The median patient age was 70 years (range, 38–80 years). The median PSA level at diagnosis was 8.53 ng/ml (range, 2.65–370.00 ng/ml). A total of 427 (39.1%), 331 (30.3%), 38 (3.5%), 125 (11.5%), 122 (11.2%), 39 (3.6%), and 9 (0.8%) patients had cT1c, T2a, T2b, T2c, T3a, T3b, and T4, respectively. The patients had a Gleason Score (GS) of ≤6 (n = 316 [29.0%]), 7 (n = 482 [44.2%]), 8 (n = 175 [16.0%]), 9 (n = 104 [9.5%]), and 10 (n = 14 [1.3%]). Following the National Comprehensive Cancer Network (NCCN) classification, 205 (18.8%), 450 (41.2%), 345 (31.6%), and 91 (8.3%) patients belonged to the low-, intermediate-, high-, and very high-risk groups, respectively.[9] Low-risk was defined as T1c–T2a, PSA levels <10 ng/ml, and GS ≤6. Intermediate-risk was defined as T2b–T2c, GS = 7, or PSA levels of 10–20 ng/ml. High-risk was defined as T3a, ≤3 cores with GS 8–9 (primary GS ≠ 5). Very high-risk was defined as T3b–T4, primary GS = 5, or >4 cores with GS = 8–10. The mean follow-up period was 50 months (range, 2–120 months).

Table 1 – Patient characteristics (N = 1091).

Median age (range) (years)	70 (38–80)
Median initial PSA (range) (ng/ml)	8.53 (2.65–370.00)
<10	630 (57.7%)
≥10, ≤20	281 (25.8%)
>20	180 (16.5%)
Clinical stage	
T1c	427 (39.1%)
T2a	331 (30.3%)
T2b	38 (3.5%)
T2c	125 (11.5%)
T3a	122 (11.2%)
T3b	39 (3.6%)
T4	9 (0.8%)
Gleason score	
≤6	316 (29.0%)
7	482 (44.2%)
8	175 (16.0%)
9	104 (9.5%)
10	14 (1.3%)
NCCN classification	
Low risk	205 (18.8%)
Intermediate risk	450 (41.2%)
High risk	345 (31.6%)
Very high risk	91 (8.3%)
ADT use	
Yes	646 (59.2%)
No	445 (40.8%)

PSA: prostate-specific antigen, NCCN: National Comprehensive Cancer Network, ADT: androgen-deprivation therapy.

2.2. Treatment planning

Patients were instructed to empty their bladder 60 min prior to the treatment. Each patient was positioned supine on a couch within the immobilization devices and underwent computed tomography (CT). Axial CT images of 2.5-mm thickness were obtained from the superior border of the sacroiliac joint to 5 cm below the ischial tuberosity.

The IMRT plans were created using the TomoTherapy Treatment Planning System (TomoTherapy Inc., Madison, WI, USA). The IMRT plans with helical tomotherapy (HT) were created using an inverse treatment planning system. The CT datasets with structures and contours in Pinnacle[3] (Hitachi Medical Co., Tokyo) were transferred to the HT planning workstation. The clinical target volume (CTV) was defined as the prostate and the proximal portions of the seminal vesicles in patients with T1–T3a cancers. For patients with T3b cancers, the entire seminal vesicle was included in the CTV. The planning target volume (PTV) margin was set at 5 mm in all directions. For low- and intermediate-risk patients with biopsy-positive core rate ≤50%, the prescribed dose was 74 Gy; for intermediate-risk patients with biopsy-positive core rate >50%, it was 76 Gy; and for high- and very high-risk patients, it was 78 Gy. The daily fraction dose was 2.0 Gy, 5 times a week. The dose constraints for PTV were as follows: the dose administered to 95% of the PTV was >90% (>95% is preferable); the PTV receiving at least 90% of the prescribed dose was >96% (>98 is preferable); and the maximum dose was <110% of the prescribed dose. The rectum was delineated from 15 mm superior to 15 mm inferior to the PTV. As such, a rectal wall thickness of 3 mm and a bladder wall thickness of 3 mm were created. The rectum