Preliminary Study of the Conformal Radiation Therapy in Prostate Carcinoma

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Abstract **Objective** To observe the outcome and complications of three-dimension conformal radiation therapy (3DCRT) in the treatment of prostate carcinoma. **Methods** 7 patients with prostate carcinoma underwent 3DCRT. The first 40~46Gy was administered using large fields, the boost was given conformally to the prostate and seminal vesicles. Another 45 patients treated by conventional radiation therapy during 1990-1999 served as control. **Results** Median fellow-up was 24 months. The 2- year prostate specific antigen (PSA) relapse free rate was 100%. 4 patients experienced grade 1 acute gastrointestinal (GI) side effects, grade 2 and grade 3 were one patient respectively. Late GI morbidity were grade 1, one patient; and grade 3, one patient. Only one patient had late genitourinary(GU) grade 3 complication. **Conclusion** The outcome of 3DCRT was satisfied. On the basis of accurately staging and target defining, 3DCRT through the whole treatment was advantageous to protect the rectum and increase doses.

Key Words Prostate neoplasms; radiotherapy; Three-dimensional conformal; Prognosis

The implementation of conformal radiation therapy for the treatment of prostate cancer has provided an approach to increase radiation dose and decrease normal tissue complication. From December 1999 to December 2000, 7 patients with prostate cancer received three-dimensional conformal radiotherapy. The present study was to evaluate the outcome of 3D-CRT in prostate cancer.

METHODS AND MATERIALS

Clinical data

From December 1999 to December 2000, 7 patients were treated with three-dimensional conformal radiotherapy (3D-CRT). The mean age of the patients was 67.6 years old (ranged 57~72 years). Pretreatment diagnostic evaluation included disease history, body examine, KPS, serum prostate-specific antigen (PSA) and free serum prostate-specific antigen (f-PSA) examine, blood routine, liver and kidney function. Chest X-ray, bone scan, pelvis CT, and B-ultrasound of the abdomen and pelvic were performed as staging procedures in all patients. The prostate cancer were staged according to TNM classification[1]: T2 stage in 5 patients, T3 in 1 patient, T4 in 1 patient. All patients had a histological diagnosis of prostate adenocarcinoma. The median of pretreatment PSA was 3.1ng/mL (range, 0.1~113.5 ng/mL). The clinical data are summarized in Table 1.

Methods of treatment

All patients were received radiation therapy in combination with androgen suppression. Treatment for prostate cancer had included irradiation of the whole pelvis followed by a boost dose to the prostate and seminal vesicles, the whole pelvis was treated to 40~46Gy by conventional radiation technique (four-field box) and the prostate plus seminal vesicles then boosted to 70Gy by 3D-CRT.

The patients were immobilized in the supine position using a polyurethane foam cast extended from inferior abdomen to the upper thigh. The immobilization device was the same one that used during treatment. The metal marks were placed on the skin and cast. With rectum and bladder empty, the patients were then CT scanned in the cast with 1cm thick from the bottom of the ischial tuberosities to the juncture between the fourth and fifth lumbar vertebrae, and 5mm thick for the prostate plus seminal vesicles. The images were transferred

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to the Cadplan 6.0.8 treatment planning system and the algorithm was Bathe Methods. The responsible radiation oncologist contoured the target, the normal tissues that included the rectum, bladder, and the femoral heads on every CT slices. The clinical target volume (CTV) was defined as prostate plus seminal vesicles, the planning target volume (PTV) encompassed 1-cm outside throughout CTV except that 0.5cm in posterior border. A 0.5cm margin was left between the fields edge and the PTV outer margin for all fields to allow for penumbra. This margin was determined by beam´s eye views (BEV) to assure the target volume encompassed by the geometric borders of all treatment fields. The CTV was encompassed by 95% iso-dose contour and the variation of the dose distribution across target volume was less than 5%.

The treatment techniques consisted of five isocenter fields in the transaxial plane, with two lateral, two anterior oblique (50°and 310°) and one posterior field, using photon of 6MV from Varian 2300 C/D linear accelerator. The median prescribed does was 70.0Gy (ranging 65.9~71.1Gy).

Portal films were taken prior in the first day treatment and once a week during the course of treatment. The treatment planning assurance was performed by comparing the portal films, the simulator films and digitally reconstructed radiographs (DRR), which generated from the simulation CT image sets on TPS.

Criterion of jugement

The patients were followed up from the first day irradiation to the censored date. The PSA failure was defined according to the American Society of Therapeutic Radiation Oncology (ASTRO)consensus as three consecutive rising PSA values from the nadir value[2]. The radiation oncologist used the American National Cancer Institute (NCI) Common Toxicity Criteria (CTC v. 2.0) scoring systems to describe morbidity during the course of or within 90 days of the completion of radiation [3]. CTC v. 2.0 is a more comprehensive and improved reference for the grading of acute toxicity for all modalities. The advantages of the CTC v. 2.0 were the opportunity to score acute radiation toxicities not include or well-defined in the previous RTOG system and allow more specific scoring of individual toxicities. Late complications were defined as those developing more than 90 days after the completion of irradiation or those that started prior to and persisted for longer than 90 days after completion of treatment. Late complications were scored according the LENT/SOMA scale of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment Cancer (EORTC)[4].

Statistics

Survival rate was estimated by the Kaplan – Meier method, using SPSS 10.0 software. The comparison between 3D-CRT group and conventional radiation group previously described 5 was done by χ^2 test.

RESULTS

All patients were followed up from the first day irradiation to the censored date. Median follow-up was 24 months (rang, 18~30 months). The 2-year freedom from arising PSA (biochemical, no evidence of disease) survival was 100%.

The distribution of acute reaction and late complication for both Gastrointestinal (GI) and Genitourinary (GU) was shown in Table 2. Four patients of all seven patients experienced Grade 1 acute GI toxicities(57.1%), one patient had Grade 2 (14.3%) and another patient developed Grade 3 (14.3%). No patient experienced acute GU symptoms. For late complications, one patient had Grade 1 GI-related symptoms (14.3%) and one had Grade 3 rectum complications (14.3%), only one patient experienced Grade 3 GU complication (14.3%). The mean age of the patients in conventional radiation group previously reported was 70 years old (rang, 53~82 years). The median tumor dose was 68.3Gy (range, 50.4Gy/29fx/46d~75.9Gy/38fx/55d). Except KPS, there were no differences between the comparisons with the 3D-CRT group (Table 3).

The complications were analyzed by comparing Grade 1 and Grade $\geqslant$2 between the conventional group and the 3D-CRT group. Except acute GU toxicities, no statistically significant difference was observed between the two groups (Table 2).

DISCUSSION

Since the 1980s, the 3D-CRT was introduced to increase the radiation dose with a concomitant decrease in the risks of normal tissue complications. The 3D-CRT used sophisticated computer-aided treatment planning to accurately conform the distri-

Table 1. Patients characteristics

	range	median
Age (years)	57~72	70
KPS	80~100	90
Pre-irradiation PSA in ng/mL	0.1~113.5	3.1
Pre-irradiation fPSA in ng/mL	0.5~3.3	1.1
Metastatic lymphadenopathy	0	
Metastasis	1(bone)	
Stage		
T2	5	
T3	1	
T4	1	
Androgen suppression		
Orchiectomy	2	
Orchiectomy+Flutamide	2	
Flutamide+Zoladex	3	
The interval between radiotherapy and androgen suppression (months)	1~24	1

Table 2. Factors associated with complications

	Age (years)		KPS		Prescribed dose (Gy)		Large field in cm^2 (AP)		Large field in cm^2 (RL)	
	Range	Median	Range	Median	Range	Median	Range	Median	Range	Median
Conventional group	53-82	70	80-90	80	50.4-75.9	68.3	99-376	210	70-238	144
3D-CRT group	57-72	70	80-100	90	65.9-71.1	70.0	207-418	240	143-200	150
χ^2	0.70		8.06		2.01		3.08		0.79	
P	>0.05		<0.05		>0.05		>0.05		>0.05	

Table 3. Comparison of complications between the conventional radiotherapy group and the 3D-CRT group

	Gastrointestinal				Genitourinary			
	Acute		Late		Acute		Late	
	Grade 1≥	Grade 2	Grade 1 ≥	Grade 2	Grade 1 ≥	Grade 2	Grade 1 ≥	Grade 2
3D-CRT group	4	2	1	1	0	0	0	1
Conventional group	23	7	7	3	18	2	10	3
χ^2	0.86		0.49		4.73		0.02	
P	>0.05		>0.05		<0.05		>0.05	

bution of prescribed radiation dose to anatomical boundaries of the prostatic target volume in the entire 3D configuration. This concept must take into account tumor location, patient immobilization and set up varieties, including patient motion, machine output uncertainties, dose calculation, algorithm uncertainties, variations in machine parameters, and the effect these variations have on the dose distribution. The irradiation portal was designed to conform the geometric shape of the involved target volume and displayed with the beam´s eye view (BEV) technique. The target volume included three parts, the most central proportion was defined the Gross Tumor Volume (GTV) that consisted of primary tumor, metastatic lymphadenopathy, or other metastases. Clinical experience indicated that around

the GTV there was generally subclinical involvement, i.e., individual malignant cells, small cell clusters, or microextensions, which cannot be detected by the staging procedures. The volume surrounding the marcroscopic tumor had usually a high tumor cell density towards the periphery of this volume. The GTV together with this surrounding volume of local subclinical involvement was the Clinical Target Volume (CTV). To ensure that all tissues in the CTV receive the prescribed dose, the Planning Target Volume (PTV) was geometrically larger volume than the CTV, and defined to select appropriate beam sizes and beam arrangements, taking into consideration the effect of all the possible geometrical variations such as organ movements, treatment setups. Surrounding by the rectum and the bladder, the movement of the prostate was smaller than other organs and suitable for the 3D-CRT. Many trials had confirmed a clinically significant outcome[6–12].

Radiotherapy planning studies have confirmed that 3D-CRT reduces the volume of normal tissue within the high does volume compared the conventional radiotherapy. Epstein et al [6] reported a high-grade toxicity rate of less than 1% in conformally treated patients at median 13 months compared with 6.3% of 156 patients treated with conventional fields. Stopey et al[7] initiated a prospective Phase Ⅲ randomized trial. There were 189 patients randomized with a minimum follow–up of 2 years. All patients were initially treated with 4-field box to an isocenter dose of 46-Gy at 2-Gy per fraction. In the 70-Gy arm, treatment was continued to a reduced volume using a 4-field box technique. In the 78-Gy arm, treatment was continued to a reduced volume using a conformal 6-field arrangement. The overall rate of complications was similar in both treatment arms.

Although the cases of this study are limited, the result show that the rate of 2-year freedom from arising PSA is rather satisfactory, and there are no statistic difference between the comparison with the conventional radiotherapy group previously reported in the complications. Because most patients have the symptoms of genitourinary, there are no obvious influences on change of the presenting symptoms in the treatment course, so that no acute genitourinary toxicities observed. It is noticeable that a patient developed grade 3 late gastrointestinal complication, but no grade 3 toxicity observed in the conventional radiotherapy group. Of course it is correlated with the limit of follow up in the conventional radiotherapy group, but the DVH demonstrate that the dose of rectum is as high as the dose of target volume, and a little influence on the dose of rectum with 3D-CRT boost after large field irradiated to 46Gy.

Hartford et al.[8] estimated the dose-volume histograms (DVH) of 41 patients treated with conformal radiotherapy and found statistical correlation between the risk of late rectal wall bleeding and the combination of the dose and volume irradiated. The dose-volume combination proved to be statistically significant combination distinguishing between bleeders and nonbleeders, ranging contiguously between 60CGE (Cobalt Gray Equivalent) to 70% of the anterior rectal wall and 75CGE to 30%. This observation demonstrated that relatively lower doses to higher volumes contributed to late rectal complications as did higher doses to lower volumes, neither excluded the other. Boersma et al.[9] founded a significant higher actuarial incidence of sever rectal bleeding in patients where more than 40% and 50% of the rectal wall volume received at least 65Gy (P=0.02). Other significant cutoff levels were a rectal wall volume of 30% receiving at least 70Gy (P=0.008), and a rectal wall volume of 5% receiving at least 75Gy(P=0.02). Skwarchuk et al.[10] retrospectively analyzed 743 patients with T_{1C}~T_3 prostate cancer treated with 3D-CRT. A multivariate logistic regression model showed the correlation between the probability of ≥grade 2 late rectal bleeding and the following variables: the total rectal wall volume, the maximum dose to the rectal wall, enclosure of the outer rectal contour by the 50% isodose line (P<0.01). Obviously, in the basis of accurate staging and target contour, it is possible to protect the rectum and increase the radiation dose using 3D-CRT in the whole treatment course.

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