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Preliminary Patient Reported Outcomes Analysis of 3DCRT versus IMRT on the High Dose Arm of the Radiation Therapy Oncology Group (RTOG) 0126 Prostate Cancer Trial

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Abstract

Purpose—A preliminary report of patient reported outcomes (PROs) between men receiving high-dose radiation therapy (RT) on RTOG 0126, a phase III dose-escalation trial treated with either 3-dimensional conformal RT (3D-CRT) or intensity modulated RT (IMRT).

Methods—3D-CRT patients received 55.8 Gy to the prostate and proximal seminal vesicles (P+PSV) and allowed for an optional field reduction, then 23.4 Gy to prostate only. IMRT patients received 79.2 Gy to the P+PSV. PROs were assessed at 0 (baseline), 3, 6, 12, and 24 months and included bladder and bowel function assessed with the Functional Alterations due to Changes in Elimination (FACE) and erectile function assessed with the International Index of Erectile Function (IIEF). Analyses included those who completed all data at baseline and at least one follow-up and compared to an imputed data set.

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Results—Of 763 patients randomized to the 79.2-Gy arm, 551 and 595 patients who responded to FACE, 505 and 577 who responded to the IIEF were included in the completed and imputed analyses, respectively. There were no significant differences between modalities for any of the FACE or IIEF subscale or total scores at any time point for either the completed or imputed data sets.

Conclusions—Despite significant reductions in dose and volume to normal structures using IMRT, this robust analysis of 3D-CRT and IMRT showed no difference in PRO bowel, bladder and sexual functions for similar doses delivered to the P+PSV for IMRT compared to 3D-CRT delivered to either the P+PSV or prostate alone.

Introduction

Recent randomized control trials have demonstrated a biochemical disease free survival benefit for men receiving dose-escalated radiation therapy (RT) (doses average of 79 or 80 Gy) for the treatment of prostate cancer.[1,2] Dose escalation can be achieved with either three dimensional conformal radiation therapy (3DCRT) or with intensity modulated RT (IMRT). There is evidence suggesting that IMRT may achieve higher RT doses with no increase or even less dose to normal critical structures such as bowel and bladder compared to 3DCRT.[3–6] However, IMRT may cost more than twice that of 3DCRT due to increased treatment planning.[7] The cost could be significantly adjusted in favor of IMRT *if* IMRT produced greater quality of life improvements compared to 3DCRT. This is particularly important for prostate cancer given its high incidence in the aging male population and the role that RT plays in the primary management of this disease.

A recent analysis using SEER data indicated men treated with IMRT were less likely to have physician reported gastrointestinal (GI) morbidity compared to those treated with 3DCRT but more likely to receive a diagnosis of erectile dysfunction.[8] While the data is intriguing, it is unclear if clinician reports as captured in SEER are congruent with the patient subjective experience of post RT GI and GU symptoms. It has become widely recognized that patient reported outcomes (PROs) are the gold standard for reporting of primarily subjective symptoms. A large body of literature over the last decade has substantiated that validated PRO measures are often more predictive and accurate indicators for the occurrence and magnitude of symptoms compared to physician reported toxicities that do not include diagnostic lab tests or imaging, such as bowel and bladder function.[9,10] Some studies have suggested a benefit in terms of lower physician reported gastrointestinal (GI) and erectile dysfunction toxicities with IMRT compared to 3DCRT, but others have reported higher erectile dysfunction rates with IMRT.[8,11] Only three non-randomized published studies have compared the two RT techniques in terms of PRO data and all three compared lower dose (69.6Gy – 72Gy) 3DCRT to higher dose (76Gy–78Gy) IMRT, with few significant differences especially after 6 months.[12–15] Currently, no published data exist comparing similar doses of 3DCRT to IMRT for patients receiving RT for prostate cancer. Therefore, the purpose of this analysis is to compare high dose 3DCRT to IMRT on three critical functions for patients with prostate cancer: bladder, bowel and erectile function, using symptom self-report. We hypothesize that IMRT is associated with significantly less

negative change from baseline in PROs at specified follow-up time points compared to 3DCRT when patients in both modalities received high dose RT.

Methods

Study Design

The Radiation Therapy Oncology Group (RTOG) 0126 is a randomized prospective phase III trial comparing escalated high dose to conventional dose RT for localized prostate cancer. The primary objective of RTOG 0126 is to determine whether 3DCRT/IMRT to 79.2 Gy in 44 fractions will lead to improved overall survival in patients treated for intermediate risk prostate cancer compared to those treated with 3D-CRT/IMRT to 70.2 Gy in 39 fractions. On the high dose arm, 3D-CRT patients received 55.8 Gy to the prostate and proximal seminal vesicles (P+PSV) then 23.4 Gy to prostate only. After the first 31 fractions (55.8 Gy), per protocol 3D-CRT allowed for an optional field reduction to irradiate only the prostate. IMRT target volume included the prostate and proximal 1 cm of seminal vesicle tissue for the entire 79.2 Gy. This report is a preliminary analysis of PROs on the high dose arm of RTOG 0126. Toxicity data is reported elsewhere.[16]

Sample and Setting

Patients were accrued from both US and Canadian institutions. Major eligibility criteria were: histologically confirmed prostate adenocarcinoma within 180 days of randomization; clinical stage T1b–T2b; a Gleason score of 2–6 and PSA ≥ 10 but < 20 or a Gleason score of 7 and PSA <15; Zubrod Performance Scale 0–1. Major exclusion criteria were: distant metastases; regional lymph node involvement; previous treatments for prostate cancer; previous or concurrent invasive cancers; and major medical or psychiatric illness. Of the 1532 patients enrolled in the trial, 763 patients were randomized to the high dose arm of RTOG 0126.

Measurements

Two PRO measures were used to assess three major pelvic functions: bladder function, bowel function, and erectile function. Bladder and bowel function were assessed with the Functional Alterations due to Changes in Elimination (FACE) and erectile function (EF) was assessed with the International Index of Erectile Function (IIEF) Questionnaire. Both PROs were assessed with a focus on longer-term symptoms beyond the acute phase at 0 (baseline), 6, 12, and 24 months and FACE had an additional 3 month acute phase assessment.

FACE is a 15-item, 5-point Likert-type patient self-rating scale designed to measure the construct of intrusion on daily functioning caused by changes in elimination as measured by two subscales: Changes in Urinary Function (CUF) and Changes in Bowel Function (CBF). Items map well to physician reported toxicities after RT to the prostate such as proctitis/dysuria, urgency and incontinence, however there is no item that maps directly to rectal bleeding. FACE asks the patient to “circle the number of the response which best describes how you feel.” The question is framed in the present, thereby avoiding recall bias.

Scores may range from 0 to 60 for the total scale with lower scores representing better function/less symptom intrusion. The CUF subscale was developed specifically for use in prostate and bladder cancer clinical trials.[17] Internal consistency was demonstrated with a Cronbach's alpha of 0.85 indicating the scale to be reliable. Factor analysis of CUF showed all items loaded on a single factor with item-total correlations ranging from 0.66 to 0.87, demonstrating reliability and construct validity.[17] Subsequent to CUF, a second subscale labeled CBF has been developed and both underwent further psychometric testing with an internal consistency estimate of 0.76 for the total scale, 0.71 for the CUF subscale, and 0.72 for the CBF subscale.[18] Further, criterion validity was assessed in a randomized trial to determine the efficacy of octreotide acetate in preventing the onset of acute diarrhea in patients undergoing chemoRTfor rectal or anal cancer. There was a statistically significant correlation between the CTCAE v3.0 diarrhea grade and FACE (Spearman r = .22, P = .001) total bowel score.[19]

The IIEF is a 15-item patient self-rated questionnaire which includes five scales: erectile function, orgasmic function, sexual desire, intercourse satisfaction, and overall satisfaction.[20] Patients are asked to circle the response that best describes their experience over the past 4 weeks. Scores may range from 5 to 75 for the total scale with a higher score representing better erectile function. Internal consistency represented by Cronbach's alphas for the five scales ranged from .73 to .92 with an overall alpha of .91. Scale reliability was determined with high test-retest correlation coefficients ranged from r = 0.64 to r = 0.84.

Data Analysis

Chi-squared tests were used to compare pretreatment characteristics between patients with completed PRO data and with missing PRO data. Completed PRO data was defined as having completed the baseline questionnaire and also having at least one follow-up form will all items answered. Neither the FACE nor IIEF have published recommendations for management of missing data. Therefore, we conducted both a complete case analysis, including only patients who completed all items for the IIEF and FACE, and an imputed data analysis. For the imputed data analysis patients were included who completed at least 13 out of 15 items for each of the IIEF and FACE. The missing items were imputed by replacing the missing item response with the average item response (correcting for reverse scoring in the FACE) for that patient. The nonparametric Wilcoxon test was used for modality comparisons on bladder, bowel and erectile function. In order to compare the short-term impact of these RT modalities, as well as any differences in recovery from treatment side effects, changes over time from 0 (baseline), to 3, 6, 12, and 24 months were evaluated setting alpha at 0.01 to adjust for multiple comparisons If any comparisons were found to be or trend towards significance, a multi-variable regression model was built to determine the effect of other covariates [age (≤ 70 vs > 70), race (white vs. non-white), and penile bulb median dose (< 52.5 vs ≥ 52.5 Gy)].

Results

Table 1 lists the pretreatment characteristics of patients by modality and who completed FACE and the IIEF. For FACE, 551 patients completed all items at a minimum of one

timepoint. Table 2 includes the comparison of those with completed versus those with imputed FACE data. Imputation permitted analysis of an additional 78 patients for a total of 595 in the imputed analysis. Of these, 48% vs 53%, 63% vs 68%, 74% vs 77%, and 66% vs 72% had the complete vs imputed FACE filled at 3, 6, 12, and 24 months respectively. Of the patients with complete or imputed baseline FACE, 92% were included in at least one of the change from baseline comparisons. Statistically significant differences were found between patients with and without the FACE data. Patients completing FACE were significantly associated with being white, not Hispanic/Latino, having a study entry PSA of < 10 ng/ml, and T2 disease. There were no statistically significant differences between 3D-CRT and IMRT for the total FACE score, or for the urinary (CUF) or bowel (CBF) subscale scores at any of the time points for either the complete or missing case analysis.

For the IIEF 505 patients completed all items at a minimum of one timepoint. Table 3 includes the comparison of those with completed versus those with imputed data. Imputation permitted analysis of an additional 70 patients for an imputed total of 577 patients. Of these, 56% vs 60.8%, 65% vs 69%, and 61% vs 67% had complete vs imputed IIEF data at 6, 12, and 24 months respectively. Of the patients with complete and imputed baseline IIEF data, 85% and 87% (respectively) were included in at least one of the change from baseline comparisons. Statistically significant differences were found between patients with and without the IIEF data. Patients completing IIEF were significantly associated with being white, not Hispanic/Latino, having a Zubrod of 0, and having a study entry PSA < 10 ng/ml.

No statistically significance differences were present at any of the time points comparing 3D-CRT and IMRT for the total IIEF score or any of the five subscales on complete or imputed data.

The average of percent penile dose for 3DCRT was 73.1, 66.8, 59, 47.2 and for IMRT is 45.8, 37.6, 29.3, 19.7 for 40Gy, 50Gy, 60Gy, 70Gy respectively. While percent of penile bulb received was significantly lower for IMRT compared to 3DCRT for 40Gy, 50Gy, 60Gy, and 70Gy (all $p<0.0001$), neither univariate nor a multivariate sensitivity analyses including bulb dose were significantly associated with any of the IIEF outcomes even for men younger than age 70.

Discussion

Patients' demographic and clinical characteristics were fairly well-balanced between those with and without the completed IIEF and FACE data, with the major differences being those with completed data were more likely to be white, and have a study entry PSA of < 10 ng/ml..

This is the first investigation comparing patient-reported outcomes in similar high dose 3DCRT and IMRT. These data show there are no significant differences between IMRT and 3DCRT in bowel or urinary patient reported symptoms between the two treatment modalities at any time point up to 24 months. These findings come in spite of published data showing statistically significant documented lower RT doses to critical normal tissue for patients treated with IMRT in the same patient population.[16] While IMRT provides

statistically lower doses to normal tissue the findings may not be clinically significant. Since the organs at risk were defined per protocol in about 95% of the 3DCRT and 90% of the IMRT cases, it suggests that dose constraints to normal structures can be well met with 3DCRT.[16] A few non-randomized, primarily single institution studies have shown some small but inconsistent differences in favor of IMRT when comparing conventional dose 3DCRT to higher dose IMRT. For instance, Lips et al [13] investigated patient reported GI and genitourinary (GU) symptoms at three time points: before treatment, one month and six months after treatment. There were no significant differences at six months after treatment for either bowel or urinary symptoms measured by the European Organization for Research and Treatment of Cancer prostate-specific quality of life module (EORTC QLQ-PR25), while the urinary symptom score showed a statistical difference at one month after treatment but not at the other time points. Yoshimura et al.[22] reported that higher dose IMRT compared to conventional dose 3DCRT resulted in similar profiles of disease-specific health related quality of life measured by the University of California, Los Angeles Prostate Cancer Index (UCLA PCI) within the first year after the treatment. A marginal difference (p=0.05) for bowel symptoms was found in a 24-month follow-up study conducted by Namiki et al.[23] using UCLA PCI, whereas no difference was found in urinary symptoms. In a 5-year follow-up study conducted by the same research group,[14] bowel function and bother scores were decreased significantly from baseline to 5 years after 3DCRT, whereas no significant decreases in functions between the baseline and any of the post-treatment follow-up time points were found in IMRT group. More recently, Pinkawa and colleagues[15] found that bowel and urinary function (measured by the Expanded Prostate Cancer Index Composite (EPIC)) after dose-escalated IMRT were similar to changes after 3DCRT. Hummel et al[24] summed up the findings in a systematic literature review showing overall patient reported outcomes improved for both treatment groups following either IMRT or 3DCRT, with any modality differences resolved by 6 months after RT.

The current study showed no difference in any aspect of erectile function. In 77 patients treated for localized prostate cancer, Kupelian and colleagues[12] showed that the IMRT group scored better on the sexual summary score of EPIC ($p = 0.003$) at 24 months after treatment. However, Kupelian's study did not report baseline sexual function, and therefore, whether the difference was due to sample bias or treatment is unclear. Two other longitudinal studies from a similar research group found that sexual function had a tendency to decrease after treatment for the 3DCRT group, while the IMRT group showed no significant difference over time.[14,23] Nevertheless, a statistically significant difference between the two treatment groups only existed at 18 months after treatment.[23] Pinkawa and colleagues[15] found sexual function scores more than 1 year after RT were slightly better in IMRT than in 3DCRT. Generally, the results from current and previous studies indicate either a very small or no effect in favor of IMRT over 3DCRT in terms of sexual function given similar dose.

The results from PROs have been supported in part by physician reported toxicities. PRO findings of this study are congruent with toxicity data from the same trial, which showed no significant differences between 3DCRT and IMRT for acute or late, Grade 2+ or 3+ GU toxicities, or for acute Grade 2 + or 3+ GI toxicities. In contrast to the PRO data presented here, physician reported toxicity analysis did show a statistical benefit in favor of IMRT for

late grade 2+ GI toxicities.[16] The reduction in physician reported late GI toxicity was associated with IMRT more frequently (compared to 3DCRT) keeping the volume of rectum from exceeding 70 Gy or 75 Gy to <15% and <10%, respectively. As in the toxicity report, there were significantly more patients who completed the self-report data on bowel symptoms on the IMRT arm who meet these constraints than on the 3DCRT arm: IMRT <15% pV70 - 36%; <10% pV75 - 33% versus 3DCRT <15% pV70 - 13%; <10% pV75: 12% (p=0.001). However, when we compared those who did and did not meet these constraints for both rectal pV70 and pV75 by modality, there were no significant differences in patient reported bowel scores for any of the time points assessed (3, 12 or 24 months) (data not shown).

In order to make sure there were no sampling biases between patient-reported symptoms and physician-observed toxicities (i.e. patients with more severe toxicities are more likely to withdraw from the PRO data than those with less severe toxicities) in this trial, acute and late GU and GI toxicities were compared between patients with completed PRO data and with missing PRO data during the treatment, and no statistically significant difference has been found. Similarly, three other studies did not show statistically significant differences between 3DCRT and IMRT on GU or GI toxicities.[25–27] However, some studies demonstrated that the use of IMRT decreased the rate of GI [28–31] or GU physician reported toxicities.[29,31] While the sum of the toxicity data seems to show similar outcomes between modalities, with the possible exception of physician reported late higher GI grade toxicities, the preponderance of patient reported outcomes data is clear; there are no identifiable differences in notable bowel or bladder symptoms. The toxicity analysis of these patients did not include sexual function so no comparisons can be made with PROs.

A benefit of this analysis is the robustness of these findings. The completed data analysis and the analysis using imputation were the same. In addition, compared to the physician reported toxicities of similar bowel and bladder symptoms reported by Michalski and colleagues,[16] patient reported outcomes were comparable. Further, not even adjustments for penile bulb dose made a difference in sexual function findings.

There are several limitations to this study. The main limitation is that patients were not randomly assigned to either 3DCRT or IMRT. This may introduce a sampling bias, which may lead to imbalances between the two treatment arms. Comparison between the two arms on pretreatment characteristics showed the two arms generally well-balanced, with the exception of race and study entry PSA. Also, the FACE questionnaire does not explicitly address patient concerns regarding rectal bleeding. In the physician reported toxicity paper of the same sample Michalski, et al[16] the most common recorded GI toxicity was rectal bleeding. Without a specific prompt, patients may not report distress related to rectal bleeding and this may partly explain the discordance between physician reported toxicity and the patient reported outcome.

Conclusion

The benefit of IMRT over 3D-CRT in terms of bowel, bladder and sexual functions reported by patients themselves has not been supported by this analysis. It seems reasonable to

continue to push for higher RT dose to tumor with decreasing dose to normal tissues in the experimental setting to see if a threshold can be reached that maintains or improves tumor control but decreases treatment related symptoms to the point patients are able to experience a noticeable improvement.

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Table 1

Pretreatment Characteristics (Answered all 15 questions on IIEF and FACE at baseline)

	IIEF			FACE		
	3DCRT 79.2 Gy (n=338)	**IMRT 79.2 Gy (n=169)**	**p-value**	**3DCRT 79.2 Gy (n=308)**	**IMRT 79.2 Gy (n=191)**	**p-value**
Age (years)						
Median	71	71		71	72	
Min - Max	50 – 88	54 – 83		51 – 88	54 – 82	
Race	n (%)			n (%)		
White	290 (85.8)	135 (79.9)		263 (85.4)	147 (77)	
Black	34 (10)	27 (16)		34 (11)	35 (18.3)	
Other	14 (4.1)	7 (4.1)	0.15*	11 (3.6)	9 (4.7)	0.05*
Ethnicity						
Hispanic or Latino	7 (2.1)	5 (3)		8 (2.6)	5 (2.6)	
Not Hispanic or Latino	322 (95.3)	153 (90.5)		294 (95.5)	178 (93.2)	
Unknown	9 (2.7)	11 (6.5)	0.09	6 (1.9)	8 (4.2)	0.34
Zubrod Performance Status	n (%)			n (%)		
0	318 (94.1)	155 (91.7)		284 (92.2)	175 (91.6)	
1	20 (5.9)	13 (7.7)		24 (7.8)	15 (7.9)	
Unknown	0	1 (0.6)	0.32	0	1 (0.5)	0.82
PSA (Study Entry)						
<10 ng/ml	248 (73.4)	121 (71.6)		225 (73.1)	137 (71.7)	
10–<15 ng/ml	73 (21.6)	37 (21.9)		66 (21.4)	43 (22.5)	
15–20 ng/ml	17 (5)	11 (6.5)	0.78	17 (5.5)	11 (5.8)	0.95
Gleason						
2–6	52 (15.4)	30 (17.8)		41 (13.3)	34 (17.8)	
7	286 (84.6)	139 (82.2)	0.50	267 (86.7)	157 (82.2)	0.17
T Stage						
T1	174 (51.5)	105 (62.1)		160 (51.9)	115 (60.2)	
T2	164 (48.5)	64 (37.9)	0.02	148 (48.1)	76 (39.8)	0.07

	IIEF			FACE		
	3DCRT 79.2 Gy (n=338)	**IMRT 79.2 Gy (n=169)**	**p-value**	**3DCRT 79.2 Gy (n=308)**	**IMRT 79.2 Gy (n=191)**	**p-value**
N Stage						
N0	322 (95.3)	158 (93.5)		292 (94.8)	180 (94.2)	
NX	16 (4.7)	11 (6.5)	0.40	16 (5.2)	11 (5.8)	0.79
M Stage						
M0	330 (97.6)	167 (98.8)		302 (98.1)	187 (97.9)	
MX	8 (2.4)	2 (1.2)	0.51**	6 (1.9)	4 (2.1)	0.99**
Urinary incontinence at study entry (severity)¥						
GRADE 0	320 (94.7)	155 (91.7)		289 (93.8)	176 (92.1)	
GRADE 1	17 (5)	10 (5.9)		17 (5.5)	10 (5.2)	
GRADE 2	0	3 (1.8)		1 (0.3)	3 (1.6)	
GRADE 3	1 (0.3)	0		1 (0.3)	0	
Unknown	0	1 (0.6)	0.20*	0	2 (1)	0.47*
Urinary frequency/urgency at study entry (severity)¥						
GRADE 0	230 (68)	108 (63.9)		206 (66.9)	125 (65.4)	
GRADE 1	92 (27.2)	51 (30.2)		86 (27.9)	55 (28.8)	
GRADE 2	15 (4.4)	10 (5.9)		15 (4.9)	10 (5.2)	
GRADE 3	1 (0.3)	0		1 (0.3)	0	
Unknown	0	0	0.35*	0	1 (0.5)	0.74*
Sexual impotence at study entry (severity)¥						
GRADE 0	181 (54.4)	80 (48.8)		164 (54.1)	93 (50.5)	
GRADE 1	38 (11.4)	27 (16.5)		36 (11.9)	30 (16.3)	
GRADE 2	35 (10.5)	24 (14.6)		31 (10.2)	24 (13.0)	
GRADE 3	79 (23.7)	33 (20.1)	0.19*	72 (23.8)	37 (20.1)	0.32*

Q1 = first quartile; Q3 = third quartile.

*Chi-square for race is White vs. Non White; for urinary incontinence, urinary frequency/urgency, and sexual impotence at study entry is Grade 0 vs. Non Grade 0.

**P-value from Fisher's exact test.

$\gamma_{\text{Physician graded symptoms}}$

Table 2

Comparison by Modality and Complete vs Imputed Data of Patients Response on FACE Total Score, Urinary and Bowel Subscales

	Total Score				Urinary Subscale				Bowel Subscale			
	Completed FACE Data		Imputed FACE Data		Completed FACE Data		Imputed FACE Data		Completed FACE Data		Imputed FACE Data	
	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy
Baseline	n=308	n=191	n=390	n=205	n=308	n=191	n=390	n=205	n=308	n=191	n=390	n=205
Median	2	2	2	2	1	1	1	1	0	0	0	0
Range	(0, 25)	(0, 54)	(0, 25)	(0, 54)	(0, 16)	(0, 27)	(0, 16)	(0, 27)	(0, 11)	(0, 27)	(0, 11)	(0, 27)
Δ from baseline												
3 mos	n=158	n=79	n=224	n=91	n=158	n=79	n=224	n=91	n=158	n=79	n=224	n=91
Median	0.5	0	1	0	0	0	1	0	0	0	0	0
Range	(−9, 25)	(−9, 19)	(−9, 25)	(−9, 24)	(−9, 13)	(−7, 10)	(−9, 13)	(−7, 20)	(−5, 13)	(−11, 12)	(−5, 13)	(−11, 12)
6 mos	n=201	n=113	n=272	n=134	n=201	n=113	n=272	n=134	n=201	n=113	n=272	n=134
Median	0	0	0	0	0	0	0	0	0	0	0	0
Range	(−19, 40)	(−17, 44)	(−19, 40)	(−17, 44)	(−15, 19)	(−13, 23)	(−15, 23)	(−13, 23)	(−9, 21)	(−9, 21)	(−9, 21)	(−9, 21)
12 mos	n=232	n=139	n=301	n=158	n=232	n=139	n=301	n=158	n=232	n=139	n=301	n=158
Median	0	0	0	0	0	0	0	0	0	0	0	0
Range	(−19, 29)	(−19, 21)	(−19, 29)	(−19, 31)	(−12, 15)	(−15, 14)	(−12, 15)	(−15, 22)	(−8, 19)	(−6, 11)	(−8, 19)	(−6, 11)
24 mos	n=211	n=120	n=283	n=147	n=211	n=120	n=283	n=147	n=211	n=120	n=283	n=147
Median	0	0	0	0	0	0	0	0	0	0	0	0
Range	(−18, 105)	(−14, 19)	(−18, 105)	(−14, 25)	(−11, 12)	(−8, 12)	(−11, 17)	(−11, 12)	(−7, 106)	(−9, 9)	(−7, 106)	(−9, 20)

Δ =change; Using Wilcoxon non-parametric test, there's no significant difference existed.

Table 3

Comparison by Modality and Complete vs Imputed Data of Patients Response on IIEF Sexual Desire Subscale and Overall Sexual Satisfaction Subscale

	Erectile Function Subscale				Overall Sexual Satisfaction Subscale			
	Completed IIEF		Imputed IIEF		Completed IIEF		Imputed IIEF	
	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy	3D-CRT 79.2 Gy	IMRT 79.2 Gy
Baseline	n=338	n=169	n=377	n=200	n=338	n=169	n=377	n=200
Median	15.0	12.0	14	11.5	8.0	8.0	8.0	7.5
Range	(1, 30)	(1, 30)	(1,30)	(0,30)	(2, 10)	(2, 10)	(0, 10)	(0, 10)
Δ from baseline								
6 mos	n=195	n=88	n=236	n=115	n=195	n=88	n=236	n=115
Median	−1.0	0.0	0	0	0.0	0.0	0.0	0.0
Range	(−26, 23)	(−26,20)	(−26,23)	(−26,21)	(−8, 7)	(−8, 8)	(−10,7)	(−8,10)
12 mos	n=215	n=112	n=255	n=144	n=215	n=112	n=255	n=144
Median	−1.0	−1.0	−1	−1	0.0	−0.5	−1	0.0
Range	(−28, 28)	(−29, 18)	(−28,28)	(−29,25)	(−8, 7)	(−8, 8)	(−8,7)	(−8,8)
24 mos	n=212	n=98	n=263	n=130	n=212	n=98	n=263	n=130
Median	−2.0	−1.0	−2	−1	−1.0	0.0	−1	0.0
Range	(−29, 23)	(−5, 18)	(−29,23)	(−29,23)	(−8, 5)	(−8, 5)	(−10,7)	(−10,10)

Δ =change; Using Wilcoxon non-parametric test, there's no significant difference existed.

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