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Clinical Outcome of Patients Treated with 3D Conformal Radiation Therapy 3D-CRT for Prostate Cancer on RTOG 9406

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Abstract

Purpose—Report of clinical cancer control outcomes on RTOG 9406, a 3D conformal radiation therapy (3DCRT) dose escalation trial for localized adenocarcinoma of the prostate.

Methods and Materials—RTOG 9406 is a Phase I/II multi-institutional dose escalation study of 3DCRT for men with localized prostate cancer. Patients were registered on five sequential dose levels: 68.4Gy, 73.8Gy, 79.2Gy, 74Gy and 78Gy with 1.8Gy/day (levels I through III) or 2.0Gy/day (levels IV & V). Neoadjuvant hormone therapy (NHT) from 2 to 6 months was allowed. Protocol specific, ASTRO, and Phoenix biochemical failure definitions are reported.

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Results—Thirty-four institutions enrolled 1084 patients and 1051 patients are analyzable. Median follow-up for levels I, II, III, IV and V was 11.7, 10.4, 11.8, 10.4, and 9.2 years, respectively. Thirty-six percent of patients received NHT. The 5-year overall survival was 90%, 87%, 88%, 89%, and 88% for dose levels I-V. The 5-year clinical disease-free survival (excluding protocol PSA definition) for levels I-V is 84%, 78%, 81%, 82%, and 82%, respectively. By ASTRO definition, the 5-year disease-free survivals were 57%, 59%, 52%, 64% and 75% (low risk); 46%, 52%, 54%, 56%, and 63% (intermediate risk); and 50%, 34%, 46%, 34%, and 61% (high risk) for levels I-V, respectively. By the Phoenix definition, the 5-year disease-free survivals were 68%, 73%, 67%, 84%, and 80% (low risk); 70%, 62%, 70%, 74%, and 69% (intermediate risk); and 42%, 62%, 68%, 54%, and 67% (high risk) for levels I-V, respectively.

Conclusion—Dose escalated 3DCRT yields favorable outcomes for localized prostate cancer. This multi-institutional experience allows comparison to other experiences with modern radiation therapy.

Keywords

Prostate cancer; 3D radiation; PSA outcomes; Dose escalation; Conformal radiation

INTRODUCTION

The primary objective of RTOG 9406 was to determine whether 3D CRT can allow safe administration of higher doses of radiation in men with prostate cancer. We have previously reported and published results on treatment toxicity. ^{1–4} Three dose levels were initially planned, 68.4 Gy, 73.8 Gy, and 79.2 Gy. Because dose limiting toxicity was not identified in the first three dose levels, the study remained open to accrue patients to two additional dose levels, 74 Gy and 78 Gy. The dose per fraction was increased to 2 Gy/day to minimize the elapsed treatment time associated with the dose escalation. In this paper we report the 5 and 10 year biochemical control and clinical outcomes in patients treated in this trial at all five dose levels.

METHODS AND MATERIALS

Study design

Details regarding the clinical study, radiation dose prescription and quality assurance has been described. RTOG 9406 is a Phase I/II dose escalation with 3D conformal radiation therapy for Stages T1 through T3 nonmetastatic carcinoma of the prostate. For quality assurance purposes, all participating institutions were required to register at least one patient to the first dose level of 68.4 Gy minimum dose to the planning target volume in 1.8 Gy/day fractions. Once institution compliance to the protocol was established by the 3D QA Center (now Image Guided Therapy quality assurance Center, ITC), registration to higher dose levels was allowed.

Patient eligibility

Patients with previously untreated biopsy-proven adenocarcinoma of the prostate, 1992 American Joint Committee on Cancer clinical stages T1 through T2 were eligible, except for patients with T1b-c or T2a-b with Gleason sums 5 and PSA 4. The upper limit of prostate specific antigen (PSA) for eligibility on this study was 70 ng/ml and it must have been obtained within 3 months prior to study entry or initiation of hormone therapy and more than 10 days following a prostate biopsy. Neoadjuvant androgen blockade beginning 2–6 months prior to registration was allowed as long as a pre-hormonal PSA was available.

All tumors were assigned a Gleason score. Centralized review of prostate biopsy specimen was not required. All patients had a complete blood count, biochemistry survey including serum BUN, creatinine, alkaline phosphatase, testosterone, and PSA. Pelvic nodal assessment was not required if the risk of lymphatic metastasis was 15%.⁵ Patients with a risk of nodal metastasis > 15% were required to undergo either a preregistration diagnostic pelvic imaging and/or pelvic lymphadenectomy to rule out nodal metastases.

Treatment planning

Standardized nomenclature as published by the International Commission on Radiation Units and Measurements (ICRU 50) ⁶ was used.

Patients were stratified into three treatment groups according to their risk of seminal vesicle invasion. Group 1 patients had clinical stage T_{1, 2} cancers with a calculated risk of seminal vesicle invasion of less than 15%. Group 2 patients had a risk of seminal vesicle invasion exceeding 15%. Group 3 patients were those with T₃ stage.

Target volume and critical normal structure definition

The gross tumor volume (GTV) was defined by the treating physician as encompassing all known disease identified by the planning CT, urethrogram, and clinical information. At a minimum, the GTV included the entire prostate gland. Elective seminal vesicle irradiation was included as a clinical target volume (CTV1) in patients with group 2 disease. The ICRU6 reference point doses were to be located in the central part of the planning target volume (PTV) on or near the central axis of the beam intersections. Normal tissue volumes contoured included the bladder, rectum, bilateral femora, and skin. These organs were contoured as solid organs. The tissue within the skin and excluding all other critical normal structures and target volumes was designated as unspecified tissue. The PTV consisted of the respective CTVs with a 0.5 to 1.0 cm margin to account for treatment uncertainties from set up or internal organ motion.

3D treatment planning

Treatment was administered to the PTVs using 3D conformal fields shaped to exclude as much of the bladder and rectum as possible. Elective pelvic nodal irradiation was not allowed. Group 2 patients received treatment initially to PTV1 that encompassed the prostate and seminal vesicles with an uncertainty margin. These patients had a treatment volume reduction after 54 Gy on the 2 Gy arms or 55.8 Gy on the 1.8 Gy arms that excluded the seminal vesicles. After that dose, the PTV2 received the assigned minimum study dose. Group 1 patients had no elective seminal vesicle irradiation. DVHs were generated for all critical normal structures and the unspecified tissues. Portions of the bladder and rectum by necessity received the full dose to the PTV because the PTV overlapped with these organs. Careful 3D planning was encouraged to ensure that the volume of the bladder and rectum receiving the full dose was kept to a minimum. No specific dose constraints were described in the protocol.

At the start of the trial, radiation doses were prescribed as a minimum to the PTV. This convention would assure complete coverage of the clinical target volume by the prescribed study dose over the entire course of radiation therapy. This PTV minimum dose prescription resulted in the isocenter or ICRU reference point being approximately 4% higher than the minimum PTV dose. As the study proceeded to dose level III (79.2 Gy) concerns were raised about the risks of rectal toxicity that might be encountered without additional measures to reduce rectal dose. For dose level III (79.2 Gy at 1.8 Gy/day) only, the prescription convention was changed to a minimum dose to the GTV/CTV while maintaining the minimum PTV dose to at least 73.8Gy. In practice, a minimum GTV dose

prescription kept the isocenter dose 2-3% higher than 79.2 Gy (average ICRU reference dose 81.6 Gy) and the minimum dose the PTV received was 1-2% lower than 79.2 Gy (average PTV minimum dose 77.2 Gy). After dose level III the study returned to a minimum PTV dose prescription for dose levels IV and V, 74 Gy and 78 Gy, respectively.

Disease control definition—The protocol specified criteria for local failure are progression (increase in palpable abnormality) at any time, failure of regression of a palpable tumor by two years, and redevelopment of a palpable abnormality after complete disappearance of previous abnormalities. For this study, unique biochemical definitions of local and non-local control were specified in the protocol prior to the establishment of the 1997 ASTRO consensus definition. Protocol biochemical criteria for failure of local therapy is failure of PSA to fall below 4 ng/ml 14 months (The protocol states 12 months following the start of radiation therapy, but the window was increased to allow for late case report forms.) following the start of radiation therapy or two consecutive rises (at least one month apart and at least 0.2 ng/ml) in PSA during first 14 months after start of treatment (or start of hormone therapy after one increase value of at least 0.2 ng/ml). For PSA less than 4 ng/ml, a rising PSA to double nadir value or a rise of 1 ng/ml in the absence of clinical or bone scan evidence of this metastases, is considered a local failure.

For comparison of biochemical control rates to others reported in the literature, two additional, non-protocol specified biochemical failure definitions were used. The ASTRO definition of 3 consecutive PSA rises back dated between the nadir and first PSA rise was used and the start of salvage hormones was also considered an ASTRO biochemical failure. A PSA value exceeding 2.0ng/ml over the current nadir (nadir + 2) with date of failure reported as the call date is included, the so-called Phoenix definition. 8-10

Biochemical disease-free survival rates by the ASTRO definition and Phoenix criteria are reported with respect to a three tiered risk categorization that utilizes pretreatment PSA, biopsy Gleason score and clinical tumor stage as described by D'Amico. ¹¹

Statistical considerations

Local failure rate was estimated using the cumulative incidence method. 12 Disease-free and overall survival was estimated using the Kaplan-Meier method. 13 The study was not designed, nor powered to make statistical comparisons between treatment arms for efficacy endpoints. Therefore, no comparisons are presented between treatment and groups.

RESULTS

Between August 23, 1994 and October 30, 2000, Thirty-four institutions enrolled 1084 patients, of which 1055 were eligible and 1051 of them are analyzable for outcome. The dataset for this analysis was created in December 2010. The 29 cases were excluded from efficacy analyses for the following reasons: no protocol treatment received (13), ineligible (12), withdrawn consent (4) and the 4 cases entered onto dose level I/disease group 3 was considered too small of a sample to include. The nominal study (and ICRU) prescription doses were level I 68.4 Gy (71.3 Gy) level II 73.8 Gy (77.1 Gy), level III 79.2 Gy (81.6 Gy), level IV 74 Gy (77.1 Gy) and level V 78 Gy (80.8 Gy). The PTV size was significantly smaller for level III than the other levels. The mean margin for dose level III was not different from dose levels I or II but the margin was significantly smaller for dose level IV and V. Pretreatment characteristics for all eligible patients are shown in Table 1. Three hundred eighty-two (36%) patients received neoadjuvant hormone therapy (median duration 6.13 months). Median follow up for levels I, II, III, IV and V was 11.7 years, 10.4 years, 11.8 years, 10.4 years, and 9.2 years, respectively.

The 5-year/10-year overall survival rates were 90%/70%, 87%/66%, 88%/76%, 89%/70%, and 88%/69% for dose levels I-V, respectively (Table 2). The 5-year/10-year cause specific survival rates were 99%/93%, 97%/93%, 99%/96%, 98%/92%, and 99%/92% for dose levels I-V, respectively. The 5-year/10-year clinical disease-free survival (excluding the protocol PSA definition) rates for levels I-V are 84%/60%, 78%/56%, 81%/67%, 82%/64%, and 82%/67%, respectively.

Outcome by protocol criteria

The 5 and 10-year rates of protocol specified failure of local therapy by dose level and risk group are presented in Table 3. According to the protocol definition, the 5-year rates for failure of local therapy (defined by the original 9406 specific PSA criteria) for levels I-V are 45%, 39%, 34%, 28%, and 28%, respectively. When using a purely clinical definition (no PSA) the actuarial incidence of local failure at 5-years for levels I-V was 5%, 10%, 6%, 6%, and 3%, respectively.

Outcome by ASTRO and Phoenix definitions

The 5 and 10-year rates for biochemical disease-free survival by ASTRO and Phoenix definitions for all patients, regardless as to whether or not they received neoadjuvant hormone therapy, are summarized in Table 4 by D'Amico risk group. By the ASTRO definition, the 5-year disease-free survivals for low risk patients were 57%, 59%, 52%, 64% and 75% for levels I–V, respectively. By the Phoenix definition, the 5-year disease-free survivals for low risk patients were 68%, 73%, 67%, 84%, and 80% for levels I–V, respectively.

By the ASTRO definition, the 5-year disease-free survivals for intermediate risk patients were 46%, 52%, 54%, 56%, and 63% for levels I–V, respectively. By the Phoenix definition, the 5-year disease-free survivals for intermediate risk patients were 70%, 62%, 70%, 74%, and 69% for levels I-V, respectively.

By the ASTRO definition, the 5-year disease-free survivals for high risk patients were 50%, 34%, 46%, 34%, and 61% for levels I–V, respectively. By the Phoenix definition, the 5-year disease-free survivals for high risk patients were 42%, 62%, 68%, 54%, and 67% for levels I–V, respectively.

The 5 and 10-year rates for biochemical disease-free survival by ASTRO and Phoenix definitions for patients that received neoadjuvant hormone therapy are summarized in Table 5. The 5 and 10-year rates for biochemical disease-free survival, by ASTRO and Phoenix definitions, for patients that did not receive hormone therapy, are summarized in Table 6.

Discussion

The primary objective of RTOG 9406 was to determine the maximal tolerated dose of radiation that could be delivered to the prostate gland and the immediate surrounding tissues using 3D CRT. Our prior publications have demonstrated that treatment to doses as high as 79.2 Gy and 78 Gy in 1.8 Gy and 2.0 Gy fractions, respectively, resulted in lower than expected rates of grade 3 toxicities. ^{1–4}

This is the first report of tumor control outcome in this series of patients. The overall survival, cause specific survival, and local failure rates are excellent and comparable to other modern series employing 3DCRT. 14–16

When this study was designed in 1994, there was no consensus on the appropriate definition of biochemical control following definitive radiation therapy for prostate cancer..^{7, 9, 17} The

biochemical definition of failure of local therapy described by the study committee was an effort to recognize the importance of PSA in the evaluation of patients treated with radiation therapy. The results by this unique study specific PSA definition of failure of local therapy are reported to comply with the original study description. Compared to modern failure definitions, the protocol considered any 2 consecutive rises or the doubling of the PSA at any level as a failure therefore inappropriately declaring some patients as having a failure who actually experienced benign PSA spikes or bounces. The unique nature of this original study definition does not allow meaningful comparisons to other reported experiences and therefore will not be discussed further.

In order to allow comparison of our results with other past and future series, we are reporting the clinical results using both the ASTRO definition and a Phoenix definition of nadir PSA plus 2.0ng/ml.^{7, 9, 17, 18} While the overall survival and cause specific survival rates are excellent, the lower than expected 10 year biochemical failure rates raise some concern about the durability of cancer control with external beam radiation therapy alone. Whether further technological innovations such as image guidance, further dose escalation with external beam radiation or brachytherapy, or risk adapted use of adjuvant systemic hormone therapy improves outcomes remain the topics of investigation. Biochemical failure does impact patient management with salvage local and systemic therapies that carry considerable side effects and morbidity.

During the period of this dose escalation trial several changes occurred in the radiotherapeutic management of men with localized prostate cancer. That neoadjuvant hormone therapy confers a local control and disease-free survival benefit in patients with bulky or high risk cancers became recognized.¹⁹ Furthermore, better algorithms and nomograms to predict the risk of tumor spread beyond the prostate became established and prognostic categories became better defined.^{11, 20}

In this 9406 dose escalation series, 4–6 months of neoadjuvant hormone therapy was allowed at the discretion of the treating physician after 1996. The administration of hormone therapy was not defined by protocol nor was it a stratification variable. It was felt by the study committee that the elective use of hormone therapy would not interfere with the primary objective of toxicity assessment but it would make interpretation of the clinical outcome more problematic. The data are reported collectively (Table 4) and by whether the patients did (Table 5) or did not (Table 6) receive hormone therapy. In addition, we report the data by recognized prognostic risk groups in addition to the original stratification categories.

In the recently completed RTOG 0126 randomized study, the study has been powered to determine if there is a significant improvement in overall survival with escalated doses of conformal radiation therapy. This randomized trial also collected quality of life data to determine if there is an impact on dose escalation to patient reported outcomes. There is some suggestion that the early administration of salvage hormone therapy for biochemical failures may have a positive impact on overall survival. ²¹ If salvage hormone therapy reduces the rate of death from prostate cancer then any biochemical disease free survival advantage seen with dose escalation, and consequent avoidance of the need for hormonal therapy, may need to be balanced against the relative impact of radiation toxicity on quality of life.

Several prospective randomized phase 3 clinical trials have been reported that demonstrate an advantage to dose escalation with respect to biochemical disease free survival. 22–25 Whether or not dose escalation leads to an improvement in survival will require both more follow up and results from the RTOG randomized trial.

Conclusion

The overall survival and clinical disease-free survival of men treated with 3D conformal radiation therapy on the RTOG dose escalation trial is comparable to that of single institutional series. The RTOG has completed accrual to a prospective randomized controlled trial in North America to determine if higher radiation doses (79.2Gy in 44 fractions) will lead to improved biochemical, disease-free and overall survivals.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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• Report of clinical cancer control outcomes on RTOG 94-6, a 3D CFT dose escalation trial for localized adenocarcinoma of the prostate.

- Thirty-four institutions enrolled 1051 analyzable patients on five sequential dose levels.
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- This multi-institutional experience allows comparison to other experiences with modern radiation therapy.

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Table 1

Pretreatment characteristics

		Dose Level I (68.4Gy @ 1.8Gy/Fraction)	I (68.4Gy Fraction)	Dose @]	Dose Level II (73.8Gy @ 1.8Gy/Fraction)	.8Gy on)	Dose Level @ 1.8Gy/	Dose Level III (79.2Gy @ 1.8Gy/Fraction)	Dose Level IV (74Gy @ 2.0Gy/Fraction)	IV (74Gy Fraction)	Dose Level V (78Gy @ 2.0Gy/Fraction)	V (78Gy raction)
Variable	Levels	$\begin{array}{c} Group \ 1 \\ (n=75) \end{array}$	Group 2 (n=33)	$\begin{array}{c} Group \ 1 \\ (n=97) \end{array}$	Group 2 (n=108)	Group 3 (n=95)	Group 1 (n=104)	Group 2 (n=63)	Group 1 (n=115)	Group 2 (n=141)	Group 1 (n=119)	Group 2 (n=101)
Age	< 70 70	53% 47%	39% 61%	43% 57%	48% 52%	54% 46%	67% 33%	56% 44%	51% 49%	43% 57%	54% 46%	48% 52%
T-Stage	T1 T2 T3	56% 44% 0%	27% 73% 0%	67% 33% 0%	29% 71% 0%	0% 0% 100%	54% 46% 0%	27% 73% 0%	65% 35% 0%	40% 60% 0%	68% 32% 0%	46% 54% 0%
Institutional Gleason	2–6 7 8–10	93% 7% 0%	36% 36% 27%	95% 5% 0%	41% 41% 19%	28% 44% 27%	94% 6% 0%	22% 46% 32%	91% 9% 0%	21% 56% 23%	87% 13% 0%	12% 71% 17%
Initial PSA	$ \begin{array}{c} 10 \\ 11-20 \\ 20 \end{array} $	75% 24% 1%	42% 33% 24%	81% 19% 0%	43% 35% 22%	35% 37% 28%	87% 13% 1%	43% 38% 19%	86% 14% 0%	50% 32% 18%	77% 23% 0%	43% 41% 17%
Induction Hormones	Yes No	8% 92%	15% 85%	20% 80%	48% 52%	87% 13%	30%	68% 32%	22% 78%	52% 48%	8% 92%	34% 66%
D'Amico Risk Groups	Low Intermediate High	68% 31% 1%	12% 42% 45%	76% 24% 0%	16% 48% 36%	0% 0% 100%	81% 18% 1%	2% 56% 43%	77% 23% 0%	2% 59% 39%	65% 35% 0%	3% 66% 31%
Median Follow-up	Years (min,max)	11.6 (1.5,15.7) (0.1) 11.7 (0.1,15.7)	11.8 (0.1,15.7) .7 [5.7)	11.0 (1.3,14.9)	9.3 (0.9,15.2) 10.4 (0.2,15.2)	10.4 (0.2,14.2)	11.8 (1.1,13.7) (3.5) (1.1,13.7) (1.8)	11.7 (3.5,13.4) 8 13.7)	10.9 (1.2,12.1) (0.9) 10.4 (0.9,12.1)	10.0 (0.9,11.9) :4 12.1)	9.3 (0.1,10.5) (0.5) 9.2 (0.1,10.7)	9.2 (0.5,10.7) 2 0.7)

*
Low risk: PSA 10ng/ml and a Gleason Score of 2–6 and T1-T2c; intermediate risk: 10ng/ml<PSA 20ng/ml and/or Gleason Score 7; and high risk: PSA>20 and/or Gleason 8–10 and/or T3.

Table 2

Overall and Clinical Disease Free Survival (excludes any biochemical failure)

Dose level	Study Group	n	Estimated 5-Year Rate Overall	Estimated 10-Year Rate Overall	Estimated 5-Year Rate Clinical DFS	Estimated 10-Year Rate Clinical DFS
	All	108	%06	%0 <i>L</i>	84%	%09
68.4 Gy	1	75	%76	71%	88%	%79
	2	33	%58	%19	75%	24%
	All	300	%L8	%99	78%	%95
12 0 0:	1	26	%18	64%	84%	%LS
/3.8 Gy	2	108	%08	%29	%02	%05
	3	95	%76	%ZL	%08	%79
	All	167	%88	%9 <i>L</i>	81%	%29
79.2 Gy	1	104	%L8	%6L	%08	72%
	2	63	%68	71%	83%	%09
	All	256	%68	%0 <i>L</i>	82%	%49
74 Gy	1	115	%76	% <i>LL</i>	88%	%EL
	2	141	%98	64%	78%	%LS
	All	220	%88	%69	82%	%L9
78 Gy	1	119	%88	73%	85%	%ZL
	2	101	%68	64%	%82	%19

Table 3

Protocol defined Failure of Local Therapy (includes protocol specific PSA failure criteria), by Dose Level and D'Amico Risk Group

Dose Level	D'Amico Risk Group	n	Estimated 5-Year Rate	Estimated 10-Year Rate
68.4 Gy	Low	55	42%	58%
	Intermediate	37	38%	55%
	High	16	69%	75%
73.8 Gy	Low	91	33%	44%
	Intermediate	75	46%	59%
	High	134	39%	55%
79.2 Gy	Low	85	35%	41%
	Intermediate	54	31%	43%
	High	28	36%	39%
74 Gy	Low	92	21%	34%
	Intermediate	109	27%	35%
	High	55	40%	54%
78 Gy	Low	80	27%	29%
	Intermediate	109	27%	35%
	High	31	32%	39%

Table 4

Biochemical Disease Free Survival, All Patients by D'Amico Risk Group - ASTRO and Absolute Nadir + 2 Definitions

Estimated Estimated 5-Year Rate 10-Year Rate D'Amico Risk Group n ASTRO ASTRO
55 57% 26% 37 46% 25% 16 50% 21%
91 59% 37% 75 52% 34% 134 34% 23%
85 52% 48% 54 54% 42% 28 46% 16%
92 64% 45% 109 56% 31% 55 34% 13%
80 75% 61% 109 63% 45% 31 61% 50%

Table 5

Biochemical Disease Free Survival, Patients by D'Amico Risk Group with induction hormones – ASTRO and Absolute Nadir + 2 Definitions

3	D'Amico Risk Group	п	Estimated 5-Year Rate ASTRO	Estimated 10-Year Rate ASTRO	Estimated 5-Year Rate Nadir + 2	Estimated 10-Year Rate Nadir + 2
I Inter F	Low Intermediate High	7 8 1	43% 67% 100%	29% - 100%	71% 100% 100%	14% 67% 100%
Inter Inter	Low Intermediate High	19 29 106	53% 45% 36%	46% 35% 25%	74% 62% 68%	56% 32% 41%
Inter	Low Intermediate High	23 25 26	47% 44% 46%	40% 32% 13%	77% 69%	71% 47% 34%
Inter	Low Intermediate High	18 46 35	33% 52% 34%	28% 39% 15%	67% 69% 51%	50% 57% 41%
I Inter	Low Intermediate High	3 24 17	67% 63% 64%	67% 50% 57%	67% 77% 64%	67% 57% 64%

Table 6

Biochemical Disease Free Survival, Patients by D'Amico Risk Group without induction hormones - ASTRO and Absolute Nadir + 2 Definitions

Dose Level	D'Amico Risk Group	u	Estimated 5-Year Rate ASTRO	Estimated 10-Year Rate ASTRO	Estimated 5-Year Rate Nadir + 2	Estimated 10-Year Rate Nadir + 2
68.4 Gy	Low Intermediate High	48 34 15	60% 44% 47%	26% 25% 16%	68% 38%	40% 26% 23%
73.8 Gy	Low	72	61%	34%	73%	40%
	Intermediate	46	56%	34%	63%	35%
	High	28	22%	15%	41%	15%
79.2 Gy	Low	62	55%	51%	63%	54%
	Intermediate	29	62%	51%	72%	54%
	High	2	50%	50%	50%	50%
74 Gy	Low	74	72%	50%	88%	59%
	Intermediate	63	59%	26%	77%	45%
	High	20	35%	10%	60%	25%
78 Gy	Low	77	75%	60%	80%	63%
	Intermediate	85	63%	44%	67%	48%
	High	14	57%	43%	71%	43%