



RTOG P0011: Phase III Randomized Trial of Adjuvant Therapy for High Risk pT2/3N0 Prostate Cancer Patients

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Issues

- Surveillance with PSA before initiating treatment
 - Long-term results are poor (durable control: 20 to 40%)
 - Selection of patients varies by institution
 - 2/3 of patients with rising post-op PSA never receive RT
- The role of adjuvant radiation therapy for bad pTN0
 - T2-T4 ± surgical margins
 - High Gleason score (>6) and pre-op PSA (> 10 ng/ml)
- Data indicate acceptable and safe dose of radiation to the prostate bed



Biochemical and Clinical Outcome of 36 Matched-pairs

	Failure			Median F/U (Months)		Salvage TX
	PSA	Local	Distant	Until Failure	After Failure	
Adjuvant	4	0	0	41	12	1HT
Observation	17	3	0	19	30	6RT/9HT

Valicenti IJROBP,45:1999



PSA Control: Salvage XRT for Postoperative PSA Failure

<u>Author</u>	<u>No.</u>	<u>Response</u>	<u>bNED</u>
Lange, 90	29	82%	53%
Link, 92	18	60%	32%
Schild, 94	27	89%	48%
McCarthy, 94	15	53%	33%
Wu, 95	53	58%	30%
Valicenti, 98	27	81%	44%
ASTRO Consensus		70%	27-45%



Survival: pT3 After Adjuvant XRT

<u>Author</u>	<u>Follow-up</u>	<u>Survival</u>	
		<u>5-yr</u>	<u>10-yr</u>
Gibbons, 86	9 yr	59%	NS
Shevlin, 89	5.5 yr	92%	76%
Eisbruch, 94	5 yr	75%	46%
Anscher, 95	10 yr	88%	62%
Schild, 96	32 mo	92%	NS
Petrovich, 98	5 yr	92%	83%



RTOG 9019: Acute Toxicity

- Adjuvant XRT vs. No adjuvant XRT for pT3(C)
- \geq Grade 3 GU toxicity 6/141(4.3%)
 - Incontinence 2/141 (1.4%)
- \geq Grade 3 GI toxicity 4/141 (2.8%)



EORTC 22911:Urinary Incontinence after Adjuvant XRT

- Objective pad weighing test and patient interview

<u>Treatment</u>	<u>NO.</u>	<u>% Totally Dry</u>
Adj XRT(60Gy)	48	77%
Observation	52	83%

- None had GI/GU side effects ≥ 3



Postoperative 3D Conformal XRT: Late Effects, Zelefsky, 1997

GU effects

Grade I 9/42 (21%)

Grade II 1/42 (2%)

Grade III 1/42 (2%)

GI effects

Grade II 2/42 (5%)



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SCHEMA

S
T
R
A
T
I
F

Y

Seminal Vesicle Invasion

1. No
2. Yes

PSA

1. ≤ 10 ng/ml
2. > 10 ng/ml

Grade (Gleason Score)

1. 2 – 6
2. 7
3. 8 – 10

Positive Surgical (inked) Margins (+)

1. No
2. Yes

Neoadjuvant Hormonal Therapy

1. No
2. Yes

R
A
N
D
O
M
I
Z
E
D

Radiation therapy
to 63-66.6 Gy
plus LH-RH
agonist x 2 years

Vs.

Radiation therapy
to 63-66.6 Gy



Eligibility

- Postoperative PSA ≤ 0.2 ng/ml
- High risk pT2
 - Positive margins
 - Gleason >8
 - Preoperative PSA ≥ 10 ng/ml
- High risk pT3
- NHT up until 10 months before surgery



High Risk pT3N0 Prostate Cancer: (5 yr bNED 20 to 70% after RRP alone)

- Gleason score ≥ 7 and one or more
 - T3b
 - Positive margins
 - PSA > 10 ng/ml
- Gleason < 7 and two or more
 - T3b
 - Positive margins
 - PSA > 10 ng/ml



Objectives

- Primary endpoint
 - Does the addition of 2 years of androgen suppression to adjuvant RT improve overall survival?
- Secondary endpoints
 - DFS
 - bNED
 - DM
 - Toxicity



Study Accrual

- Study opened on 7/1/01 as three arm trial with androgen suppression-only arm
- 9 cases entered to study as of August 2002
 - Adjusted design by dropping androgen suppression-only arm
 - On 2/12/03, the trial became two arm Study: adjuvant RT + 2 yrs HT vs. adjuvant RT only
- As of 6/23/03, 29 cases entered
 - Accrual picking up substantially since dropping third arm
- Goal: 75 cases by 12/31/03