

SERVIZIO SANITARIO REGIONALE
EMILIA-ROMAGNA
Azienda Ospedaliero - Universitaria di Parma

Neoplasie prostatiche

- *Radioterapia: le nuove strategie*

Dr. PL Losardo

U.O.C di Radioterapia

*Azienda Ospedaliero-Universitaria di
Parma*

Parma, 19.5.2015

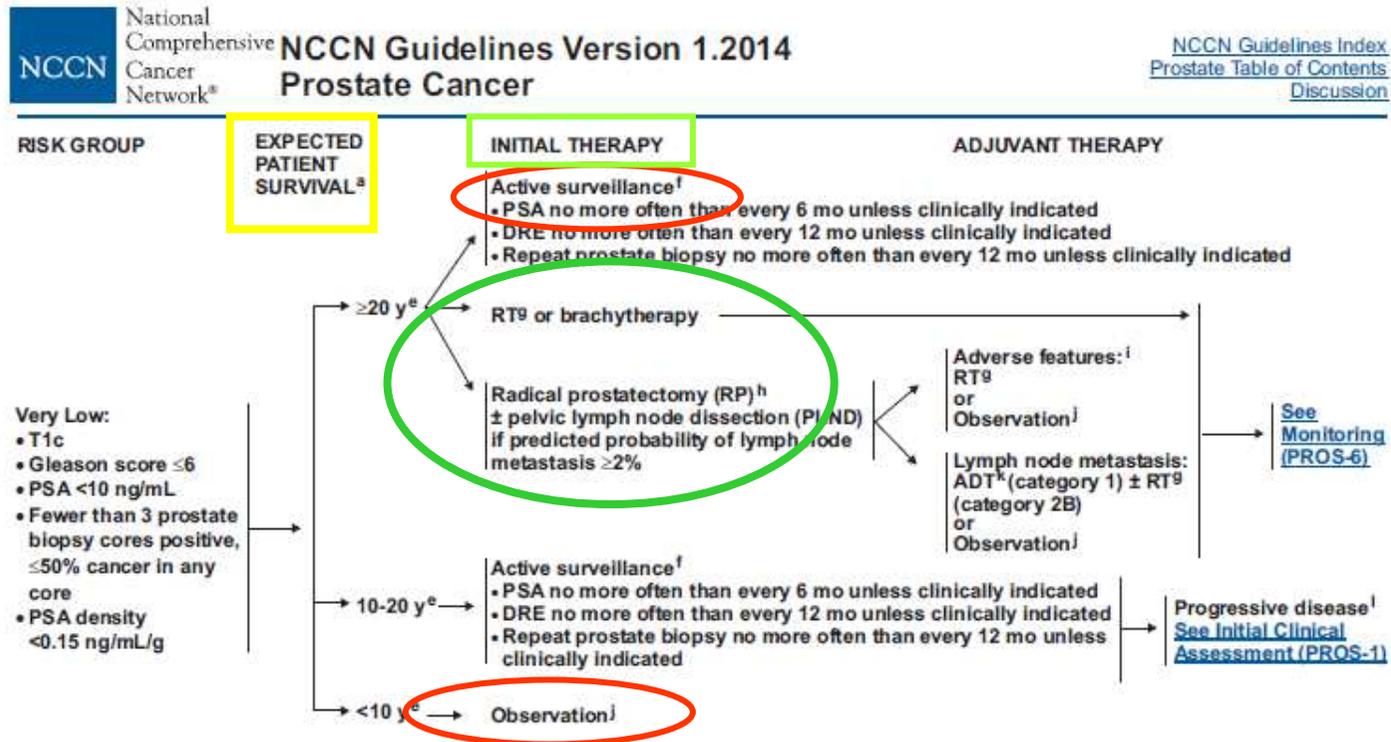


VS



Very Low risk

Printed by pier luigi losardo on 2/3/2014 12:31:38 PM. For personal use only. Not approved for distribution. Copyright © 2014 National Comprehensive Cancer Network, Inc., All Rights Reserved.



^aSee Principles of Life Expectancy Estimation (PROS-A).

^eThe Panel remains concerned about the problems of over-treatment related to the increased diagnosis of early prostate cancer from PSA testing. See NCCN Guidelines for Prostate Cancer Early Detection. Active surveillance is recommended for these subsets of patients.

^fActive surveillance involves actively monitoring the course of disease with the expectation to intervene with potentially curative therapy if the cancer progresses. See Principles of Active Surveillance and Observation (PROS-C).

^gSee Principles of Radiation Therapy (PROS-D).

^hSee Principles of Surgery (PROS-E).

ⁱAdverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

^jObservation involves monitoring the course of disease with the expectation to deliver palliative therapy for the development of symptoms or a change in exam or PSA that suggests symptoms are imminent. See Principles of Active Surveillance and Observation (PROS-C).

^kSee Principles of Androgen Deprivation Therapy (PROS-F).

^lCriteria for progression are not well defined and require physician judgement; however, a change in risk group strongly implies disease progression.

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

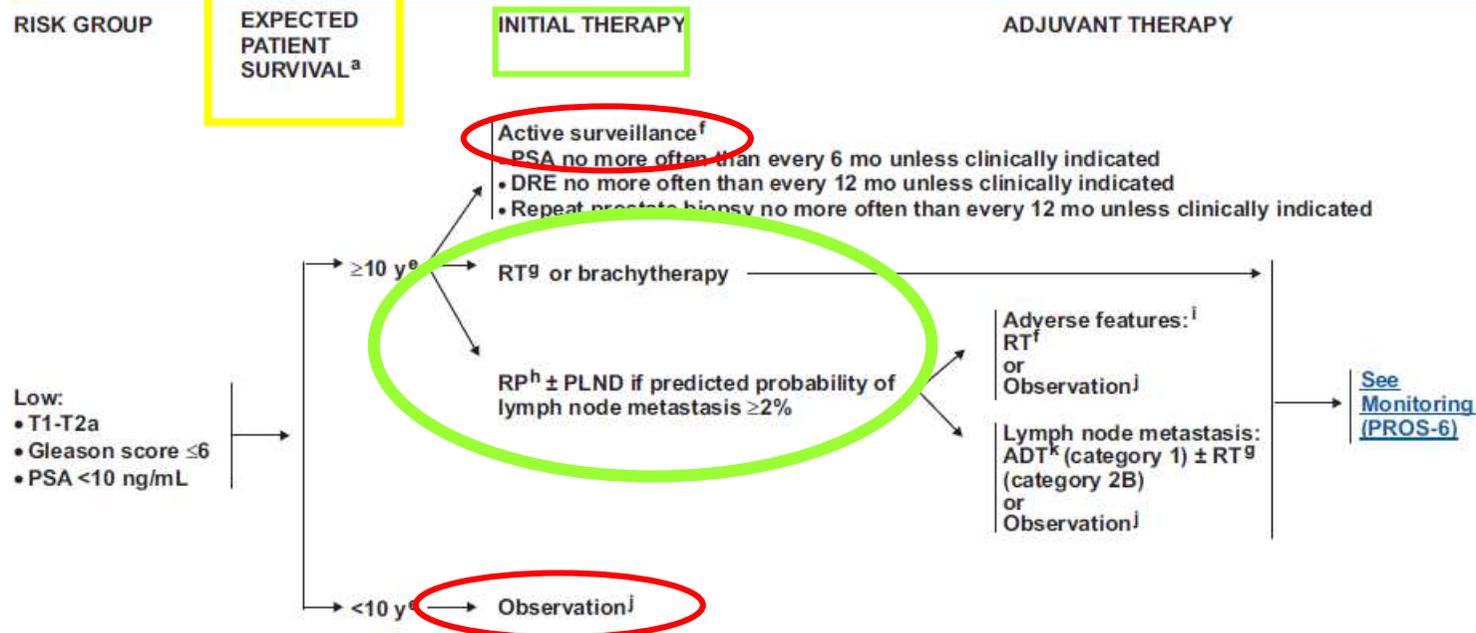
Low risk

Printed by pier luigi losarolo on 2/3/2014 12:31:38 PM. For personal use only. Not approved for distribution. Copyright © 2014 National Comprehensive Cancer Network, Inc., All Rights Reserved.



NCCN Guidelines Version 1.2014 Prostate Cancer

[NCCN Guidelines Index](#)
[Prostate Table of Contents](#)
[Discussion](#)



^a See [Principles of Life Expectancy Estimation \(PROS-A\)](#).

^e The Panel remains concerned about the problems of over-treatment related to the increased diagnosis of early prostate cancer from PSA testing. See [NCCN Guidelines for Prostate Cancer Early Detection](#). Active surveillance is recommended for these subsets of patients.

^f Active surveillance involves actively monitoring the course of disease with the expectation to intervene with potentially curative therapy if the cancer progresses. See [Principles of Active Surveillance and Observation \(PROS-C\)](#).

^g See [Principles of Radiation Therapy \(PROS-D\)](#).

^h See [Principles of Surgery \(PROS-E\)](#).

ⁱ Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

^j Observation involves monitoring the course of disease with the expectation to deliver palliative therapy for the development of symptoms or a change in exam or PSA that suggests symptoms are imminent. See [Principles of Active Surveillance and Observation \(PROS-C\)](#).

^k See [Principles of Androgen Deprivation Therapy \(PROS-F\)](#).

Note: All recommendations are category 2A unless otherwise indicated.

Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

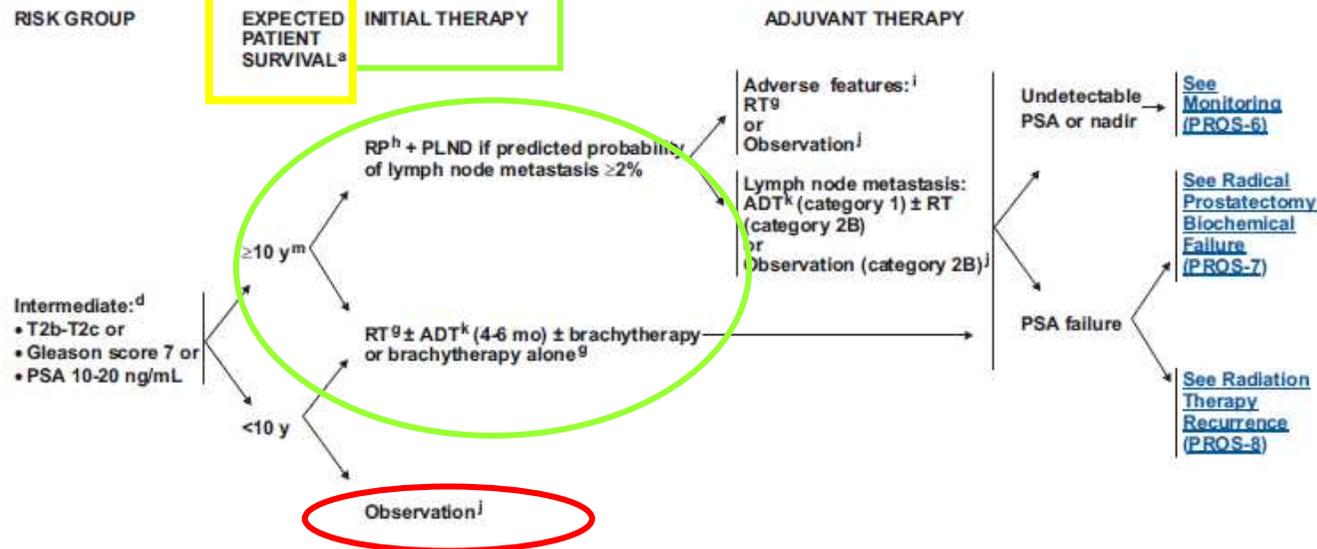
Intermediate risk

Printed by pier luigi losardo on 2/3/2014 12:31:38 PM. For personal use only. Not approved for distribution. Copyright © 2014 National Comprehensive Cancer Network, Inc., All Rights Reserved.



NCCN Guidelines Version 1.2014
Prostate Cancer

[NCCN Guidelines Index](#)
[Prostate Table of Contents](#)
[Discussion](#)



^a See Principles of Life Expectancy Estimation (PROS-A).

^d Patients with multiple adverse factors may be shifted into the next highest risk group.

^g See Principles of Radiation Therapy (PROS-D).

^h See Principles of Surgery (PROS-E).

ⁱ Adverse laboratory/pathologic features include: positive margins, seminal vesicle invasion, extracapsular extension, or detectable PSA.

^j Observation involves monitoring the course of disease with the expectation to deliver palliative therapy for the development of symptoms or a change in exam or PSA that suggests symptoms are imminent. See Principles of Active Surveillance and Observation (PROS-C).

^k See Principles of Androgen Deprivation Therapy (PROS-F).

^l Criteria for progression are not well defined and require physician judgement; however, a change in risk group strongly implies disease progression.

^m Active surveillance of intermediate and high-risk clinically localized cancers is not recommended in patients with a life expectancy >10 years (category 1).

Note: All recommendations are category 2A unless otherwise indicated.
Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

High risk

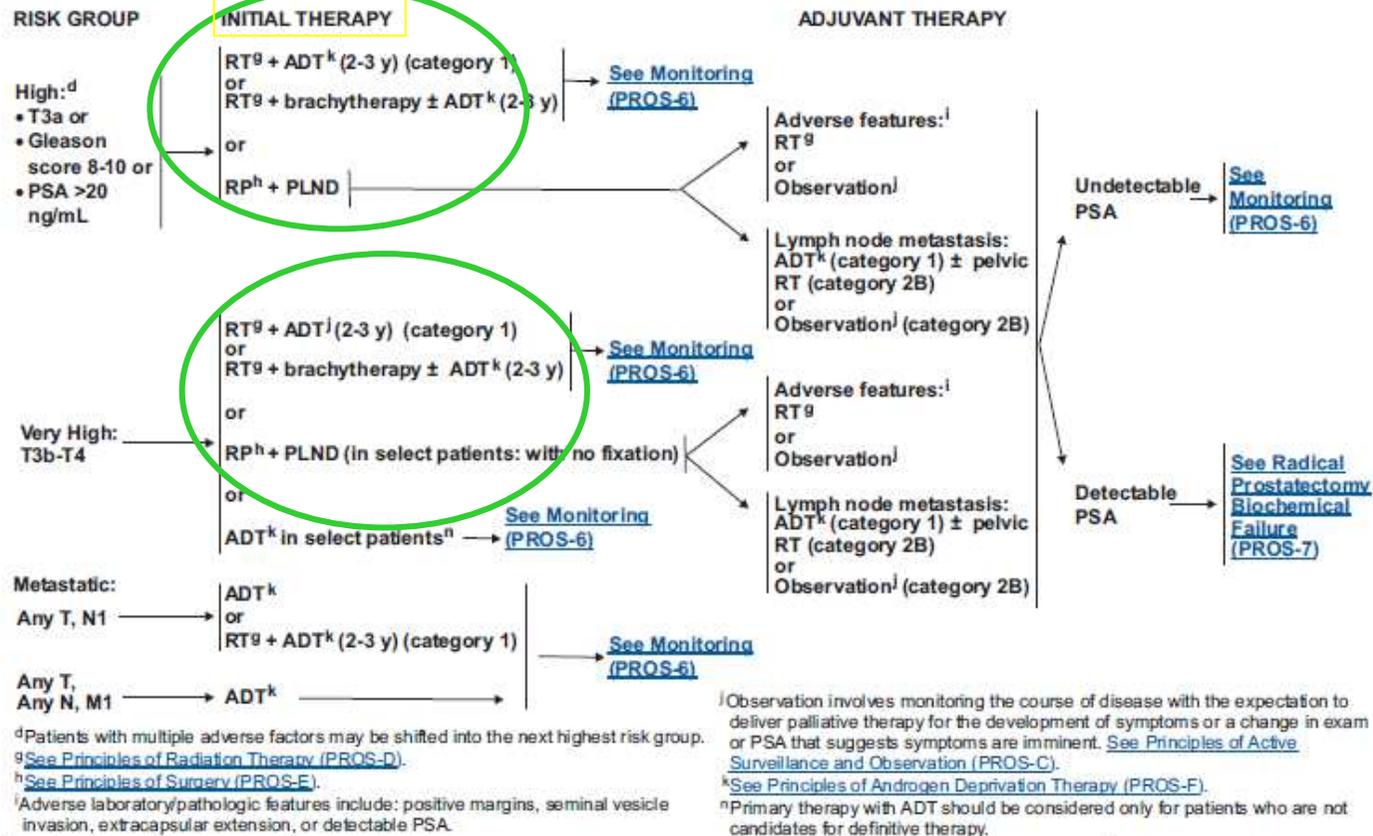
Printed by pier luigi losardo on 2/3/2014 12:31:38 PM. For personal use only. Not approved for distribution. Copyright © 2014 National Comprehensive Cancer Network, Inc., All Rights Reserved.



National
Comprehensive
Cancer
Network®

NCCN Guidelines Version 1.2014 Prostate Cancer

[NCCN Guidelines Index](#)
[Prostate Table of Contents](#)
[Discussion](#)



Note: All recommendations are category 2A unless otherwise indicated.
 Clinical Trials: NCCN believes that the best management of any cancer patient is in a clinical trial. Participation in clinical trials is especially encouraged.

Version 1.2014, © 2014 National Comprehensive Cancer Network, Inc. 2014. All rights reserved. The NCCN Guidelines® and this illustration may not be reproduced in any form without the express written permission of NCCN®.

Outcomes

Surgery versus radiotherapy: wha's better?

No randomized trials

2 RTCs:

- the Canadian **START** phase III (active surveillance vs **RP vs RT**)
- **British ProtecT** trial



EBRT — **Everywhere**

Brachi — **Few center**
Limited indications

BRACHITHERAPY

- Implant in prostate gland of radioisotopes (I-125; Pd-103) Dose 145-150 Gy
- Selection criteria (American Society of Brachiterapy)
 - Clinical stage T1-T2a
 - PSA \leq 10 ng/ml
 - GS $<$ 7
 - Prostatic volume $<$ 50 cc
 - Life expectancy \geq 10 years

RT (EBRT, BRT) vs no initial treatment

No randomized trials



Uncertain effectiveness with RT
Only 1 study improvement disease specific survival by BRT



Increased urinary (BRT>EBRT) or bowel problems



Low risk treated with BRT
Intermediate risk treated with EBRT

Comparative Evaluation of Radiation Treatments for Clinically Localized Prostate Cancer: An Updated Systematic Review

Raveendhara R. Bannuru, MD; Tomas Dvorak, MD; Ndidiama Obadan, MD, MSc; Winifred W. Yu, MS, RD; Kamal Patel, MPH, MBA; Mei Chung, PhD, MPH; and Stanley Ip, MD

Background: Radiation therapy is one of many treatment options for patients with prostate cancer.

Purpose: To update findings on the clinical and biochemical outcomes of radiation therapies for localized prostate cancer.

Data Sources: MEDLINE (2007 through March 2011) and the Cochrane Central Register of Controlled Trials (2007 through March 2011).

Study Selection: Published English-language comparative studies involving adults with localized prostate cancer who either had first-line radiation therapy or received no initial treatment.

Data Extraction: 6 researchers extracted information on study design, potential bias, sample characteristics, interventions, and outcomes and rated the strength of overall evidence. Data for each study were extracted by 1 reviewer and confirmed by another.

Data Synthesis: 75 studies (10 randomized, controlled trials [RCTs] and 65 nonrandomized studies) met the inclusion criteria. No RCTs compared radiation therapy with no treatment or no initial treatment. Among the 10 RCTs, 2 compared combinations of radiation

therapies, 7 compared doses and fraction sizes of external-beam radiation therapy (EBRT), and 1 compared forms of low-dose rate radiation therapy. Heterogeneous outcomes were analyzed. Overall, moderate-strength evidence consistently showed that a higher EBRT dose was associated with increased rates of long-term biochemical control compared with lower EBRT dose. The body of evidence was rated as insufficient for all other comparisons.

Limitations: Studies inconsistently defined and reported outcomes. Much of the available evidence comes from observational studies with treatment selection biases.

Conclusion: A lack of high-quality comparative evidence precludes conclusions about the efficacy of radiation treatments compared with no treatments for localized prostate cancer.

Primary Funding Source: Agency for Healthcare Research and Quality.

Ann Intern Med. 2011;155:171-178.

For author affiliations, see end of text.

This article was published at www.annals.org on 7 June 2011.

www.annals.org

Key Questions

We focused this report on 2 key questions:

1. What are the benefits and harms of radiation therapy for clinically localized prostate cancer compared with no treatment or no initial treatment (watchful waiting, active surveillance, or observation)?
2. What are the benefits and harms of different forms of radiation therapy for clinically localized prostate cancer?

Outcomes

Surgery versus radiotherapy: wha's better?

About 3000 pts T1-T2; 10 years BFS

Conclusion: The biochemical failure rates were similar among PI, high-dose (≥ 72 Gy) EBRT, COMB, and RP for localized prostate cancer. The outcomes were significantly worse for low-dose (<72 Gy) EBRT.

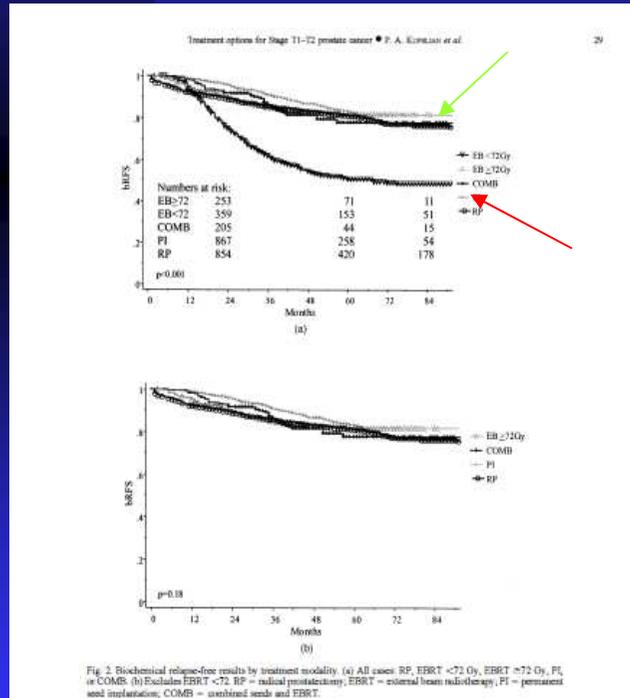


Fig. 2. Biochemical failure-free results by treatment modality. (a) All cases: RP, EBRT <72 Gy, EBRT ≥ 72 Gy, PI, or COMB. (b) Excludes EBRT <72 Gy. RP = radical prostatectomy; EBRT = external beam radiotherapy; PI = permanent seed implantation; COMB = combined seeds and EBRT.

Int. J. Radiation Oncology Biol. Phys., Vol. 58, No. 1, pp. 25-33, 2004
Copyright © 2004 Elsevier Inc.
Printed in the USA. All rights reserved.
S0360-3016/04/\$ - see front matter
doi:10.1016/S0360-3016(04)00704-3

CLINICAL INVESTIGATION **Prostate**

RADICAL PROSTATECTOMY, EXTERNAL BEAM RADIO THERAPY <72 Gy, EXTERNAL BEAM RADIO THERAPY ≥ 72 Gy, PERMANENT SEED IMPLANTATION, OR COMBINED SEEDS/EXTERNAL BEAM RADIO THERAPY FOR STAGE T1-T2 PROSTATE CANCER

PATRICK A. KUPELIAN, M.D.,* LOUIS POTTERS, M.D.,† DEEPAK KHURITA, M.D.,‡ JAY P. CREEKI, M.D.,‡ CHANDANA A. REDDY, M.S.,‡ ALBYN M. RUTHER, M.P.H.,‡ THOMAS P. CARLSON, M.D.,‡ AND ERIC A. KLEIN, M.D.‡

*Department of Radiation Oncology, M. D. Anderson Cancer Center (Orlando, Orlando, FL); †Department of Radiation Oncology, Memorial Sloan-Kettering at Mercy Medical Center, Rockville Centre, NY; ‡Department of Radiation Oncology and the Urological Institute, Cleveland Clinic Foundation, Cleveland, OH

Purpose: To review the biochemical relapse-free survival (BRFS) rates after treatment with permanent seed implantation (PI), external beam radiotherapy (EBRT) <72 Gy, EBRT ≥ 72 Gy, EBRT ≥ 72 Gy, EBRT ≥ 72 Gy, combined seeds and EBRT (COMB), or radical prostatectomy (RP) for clinical Stage T1-T2 localized prostate cancer treated between 1990 and 1998.

Methods and Materials: The study population comprised 1991 consecutive patients treated at the Cleveland Clinic Foundation or Memorial Sloan-Kettering at Mercy Medical Center. All cases had pretreatment prostate-specific antigen (PSA) levels and biopsy Gleason scores (GGS). Neoadjuvant androgen deprivation for ≤ 6 months was given in 617 cases (31%). No adjuvant therapy was given after local therapy. RP was used for 1034 patients (52%), EBRT <72 Gy for 484 (24%), EBRT ≥ 72 Gy for 301 (15%), PI for 253 (13%), and COMB for 122 patients (6%). The RP, EBRT <72 Gy, EBRT ≥ 72 Gy, and 154 PI patients were treated at Cleveland Clinic Foundation. The median radiation doses in EBRT <72 Gy and EBRT ≥ 72 Gy cases was 60.4 and 70.8 Gy, respectively. The median follow-up time for all cases was 70 months (range 11-145). The median follow-up times for RP, EBRT <72 Gy, EBRT ≥ 72 Gy, PI, and COMB were 96, 75, 49, 47, and 46 months, respectively. Biochemical relapse was defined as PSA level > 0.2 for RP cases and three consecutive rising PSA levels (American Society for Therapeutic Radiology Oncology consensus definition) for all other cases. A multivariate analysis for factors affecting the BRFS rates was performed using the following variables: clinical T stage, PSA, GGS, androgen deprivation, year of treatment, and treatment modality. The multivariate analysis was repeated excluding the EBRT <72 Gy cases. Results: The 5-year BRFS rates for RP, EBRT <72 Gy, EBRT ≥ 72 Gy, PI, and COMB were 51%, 51%, 51%, 51%, and 51%, respectively ($p < 0.001$). The 10-year BRFS rates for RP, EBRT <72 Gy, EBRT ≥ 72 Gy, PI, and COMB were 40%, 40%, 40%, 40%, and 40%, respectively. Multivariate analysis, including all cases, showed PSA ($p < 0.001$), GGS ($p < 0.001$), year of therapy ($p < 0.001$), and treatment modality ($p < 0.001$) to be independent predictors of relapse. Because EBRT <72 Gy cases had distinctly worse outcomes, the analysis was repeated after excluding these cases to discover any differences among the other modalities. The multivariate analysis excluding the EBRT <72 Gy cases revealed PSA ($p < 0.001$), GGS ($p < 0.001$), and year of therapy ($p = 0.001$) to be the only independent predictors of relapse. Treatment modality ($p = 0.95$), clinical T stage ($p = 0.09$), and androgen deprivation ($p = 0.50$) were not independent predictors for failure. Conclusion: The biochemical failure rates were similar among PI, high-dose (≥ 72 Gy) EBRT, COMB, and RP for localized prostate cancer. The outcomes were significantly worse for low-dose (<72 Gy) EBRT. © 2004 Elsevier Inc.

Localized prostate cancer, Radiotherapy, Surgery, Relapse free survival.

Advantage High dose EBRT
VS
conventional dose EBRT
Confirmed by randomized studies

- Pollack, 2002
- Lukka, 2005
- Peeters, 2006
- Zietman, 2010

High risk

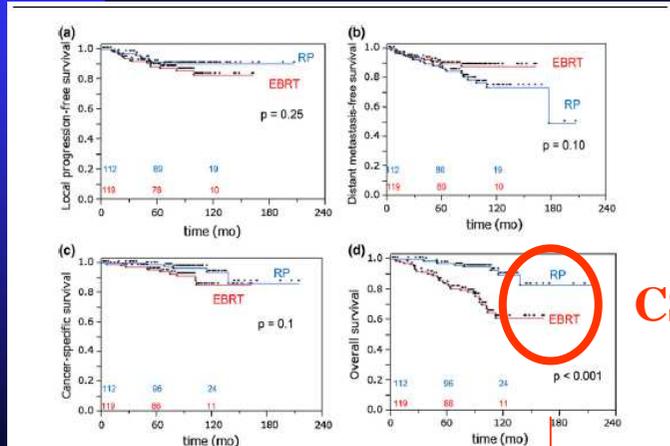


Fig. 1 Kaplan-Meier local progression-free (a), distant metastasis-free (b), cancer-specific (c) and overall (d) survival curves of patients with clinical T3 prostate cancer treated by radical prostatectomy (RP) or external-beam radiation therapy (EBRT). Numbers above X-axis (red EBRT, blue RP) Numbers of patients at risk at 0, 5, and 10 years

Older pts, low dose RT

CSS (survival cancer specific) at 10-15 years between 80-90%; studies (Ward 2005, Hsu 2009)

Int J Clin Oncol
DOI 10.1007/s10147-013-0654-2

ORIGINAL ARTICLE

Long-term oncological outcome in men with T3 prostate cancer: radical prostatectomy versus external-beam radiation therapy at a single institution

Shinya Yamamoto · Satoru Kawakami · Junji Yonese · Yasuhisa Fujii · Shinji Urakami · Shinichi Kitsukawa · Hitoshi Masuda · Yuichi Ishikawa · Takuyo Kozuka · Masahiko Oguchi · Atsushi Kohno · Iwao Fukui

Received: 4 July 2013 / Accepted: 2 December 2013
© Japan Society of Clinical Oncology 2013

Conclusion In cT3 PCA, both RP and EBRT provide an excellent long-term oncological outcome. cT3b was the strongest predictor of oncological outcome for the patients with locally advanced PCA who underwent the definitive therapy.

EURURO-5500; No. of Pages 8

ARTICLE IN PRESS

EUROPEAN UROLOGY XXX (2014) XXX-XXX

available at www.sciencedirect.com
journal homepage: www.europeanurology.com



EAU
European Association of Urology

Prostate Cancer

Stratification of High-risk Prostate Cancer into Prognostic Categories: A European Multi-institutional Study

Steven Joniau^{a,*}, Alberto Briganti^{b,1}, Paolo Gontero^c, Giorgio Gandaglia^b, Lorenzo Tosco^a, Steffen Fieuws^d, Bertrand Tombal^e, Giansilvio Marchioro^f, Jochen Walz^g, Burkhard Kneitz^h, Pia Baderⁱ, Detlef Frohneberg^j, Alessandro Tizzani^c, Markus Graefen^g, Paul van Cangh^d, R. Jeffrey Karnes^k, Francesco Montorsi^b, Hein Van Poppel^g, Martin Spahn^k, European Multicenter Prostate Cancer Clinical and Translational Research Group (EMPaCT)

^aDepartment of Urology, University Hospitals, Leuven, Belgium; ^bSan Raffaele Scientific Institute, Urological Research Institute, Department of Urology, Milan, Italy; ^cDepartment of Urology, University of Turin, Turin, Italy; ^dDepartment of Biostatistics, University Hospitals, Leuven, Belgium; ^eDepartment of Urology, Université Catholique de Louvain, Brussels, Belgium; ^fDepartment of Urology, University of Piemonte Orientale, Novara, Italy; ^gDepartment of Urology, University Medical Centre Eppendorf, Hamburg, Germany; ^hDepartment of Urology, Julius Maximilians Universität Würzburg, Würzburg, Germany; ⁱDepartment of Urology, Community Hospital Karlsruhe, Karlsruhe, Germany; ^jDepartment of Urology, Mayo Clinic, Rochester, MN, USA; ^kDepartment of Urology, University of Bern, Bern, Switzerland

High risk

Only 1 Randomized study (Akakura 2006)
Too many bias

1318 RP, 1062 EBRT 81Gy,
Freedom from mts progression at 8 years
97% vs 93%

VOLUME 28 • NUMBER 3 • MARCH 20 2010

JOURNAL OF CLINICAL ONCOLOGY ORIGINAL REPORT

Metastasis After Radical Prostatectomy or External Beam Radiotherapy for Patients With Clinically Localized Prostate Cancer: A Comparison of Clinical Cohorts Adjusted for Case Mix

Michael J. Zelefsky, James A. Eastham, Angel M. Cronin, Zvi Fuks, Zhigang Zhang, Yoshiya Yamada, Andrew Vickers, and Peter T. Scardino

ABSTRACT

Purpose
We assessed the effect of radical prostatectomy (RP) and external beam radiotherapy (EBRT) on distant metastases (DM) rates in patients with localized prostate cancer treated with RP or EBRT at a single specialized cancer center.

Patients and Methods
Patients with clinical stages T1c-T3b prostate cancer were treated with intensity-modulated EBRT (≥ 81 Gy) or RP. Both cohorts included patients treated with salvage radiotherapy or androgen-deprivation therapy for biochemical failure. Salvage therapy for patients with RP was delivered a median of 13 months after biochemical failure compared with 69 months for EBRT patients. DM was compared controlling for patient age, clinical stage, serum prostate-specific antigen level, biopsy Gleason score, and year of treatment.

Results
The 8-year probability of freedom from metastatic progression was 97% for RP patients and 93% for EBRT patients. After adjustment for case mix, surgery was associated with a reduced risk of metastasis (hazard ratio, 0.35; 95% CI, 0.19 to 0.65; $P < .001$). Results were similar for prostate cancer-specific mortality (hazard ratio, 0.32; 95% CI, 0.13 to 0.80, $P = .015$). Rates of metastatic progression were similar for favorable-risk disease (1.9% difference in 8-year metastasis-free survival), somewhat reduced for intermediate-risk disease (3.3%), and more substantially reduced in unfavorable-risk disease (7.8% in 8-year metastatic progression).

Conclusion
Metastatic progression is infrequent in men with low-risk prostate cancer treated with either RP or EBRT. RP patients with higher-risk disease treated had a lower risk of metastatic progression and prostate cancer-specific death than EBRT patients. These results may be confounded by differences in the use and timing of salvage therapy.

J Clin Oncol 28:1508-1513. © 2010 by American Society of Clinical Oncology

RP patients with higher-risk disease treated had a lower risk of metastatic progression and prostate cancer-specific death than EBRT patients. These results may be confounded by differences in the use and timing of salvage therapy. **Median 13 vs 69 months**

Technical evolution



Technical evolution

High complex:

Classic IMRT, VMAT (RapidArc), Tomotherapy
IGRT (image guided radiotherapy)

Fogarty et al. *Radiation Oncology* 2011, 6:108
<http://www.ro-journal.com/content/6/1/108>

RADIATION ONCOLOGY

RESEARCH Open Access

Volumetric modulated arc therapy is superior to conventional intensity modulated radiotherapy - a comparison among prostate cancer patients treated in an Australian centre

Gerald B Fogarty^{1*}, Diana Ng¹, Gullin Liu¹, Lauren E Haydu^{2,3} and Nastik Bhandari¹

Abstract

Background: Radiotherapy technology is expanding rapidly. Volumetric Modulated Arc Therapy (VMAT) technologies such as RapidArc[®] (RA) may be a more efficient way of delivering intensity-modulated radiotherapy-like (IM) treatments. This study is an audit of the RA experience in an Australian department with a planning and economic comparison to IM.

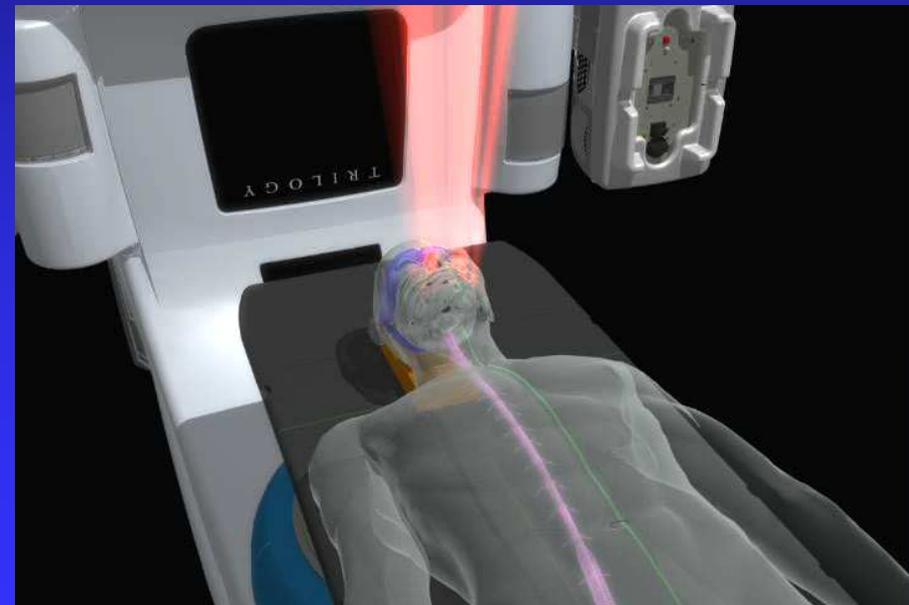
Methods: 30 consecutive prostate cancer patients treated radically with RA were analyzed. Eight RA patients treated definitively were then completely re-planned with 3D conformal radiotherapy (3D); and a conventional sliding window IM technique; and a new RA plan. The acceptable plans and their treatment times were compared and analyzed for any significant difference. Differences in staff costs of treatment were computed and analyzed.

Results: Thirty patients had been treated to date with eight being treated definitively to at least 74 Gy, nine post high dose brachytherapy (HDR) to 50.4Gy and 13 post prostatectomy to at least 64Gy. All radiotherapy courses were completed with no breaks. Acute rectal toxicity by the RTOG criteria was acceptable with 22 having no toxicity, seven with grade 1 and one had grade 2.

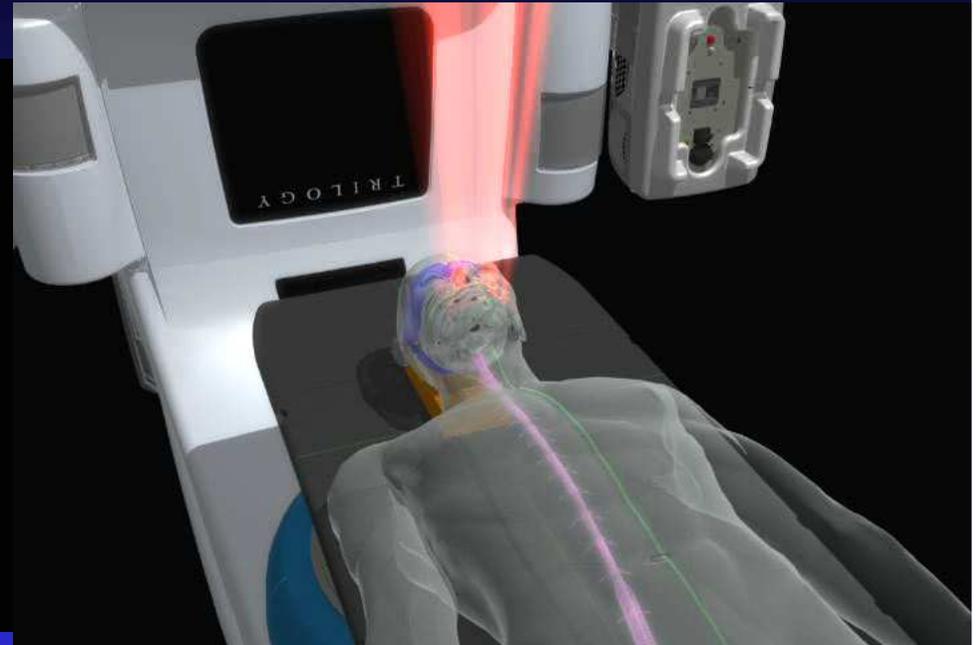
Of the eight re-planned patients, none of the 3D (three-dimensional conformal radiotherapy) plans were acceptable based on local guidelines for dose to organs at risk. There was no statistically significant difference in planning times between IM and RA ($p = 0.792$). IM had significantly greater MUs per fraction (1813.9 vs 590.2 $p < 0.001$), total beam time per course (5.2 vs 3.1 hours, $p = 0.001$) and average treatment staff cost per patient radiotherapy course (\$AUD489.91 vs \$AUD315.66, $p = 0.001$). The mean saving in treatment staff cost for RA treatment was \$AUD174.25 per patient.

Conclusions: 3D was incapable of covering a modern radiotherapy volume for the radical treatment of prostate cancer. These volumes can be treated via conventional IM and RA. RA was significantly more efficient, safe and cost effective than IM. VMAT technologies are a superior way of delivering IM-like treatments.

Keywords: Intensity-modulated radiotherapy, Volumetric modulated arc therapy, three-dimensional conformal radiotherapy, Australia, health care cost



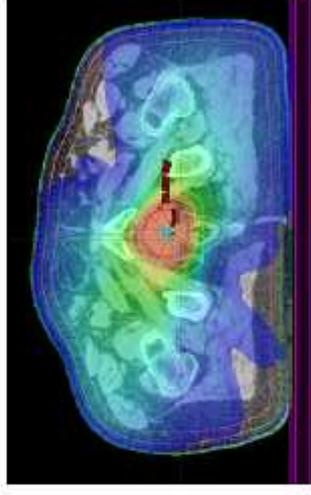
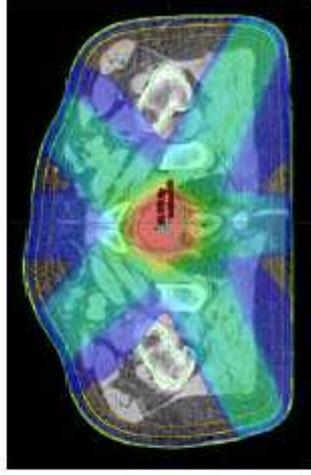
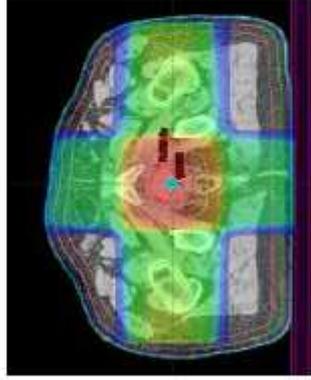
Rapid Arc treatment



Radiobiological aspects on IMRT/RapidArc

- Irradiated volume

Prostate cancer



3D-CRT

IMRT

Rapidarc

IMRT/RapidArc prostate cancer (patient with protesis)

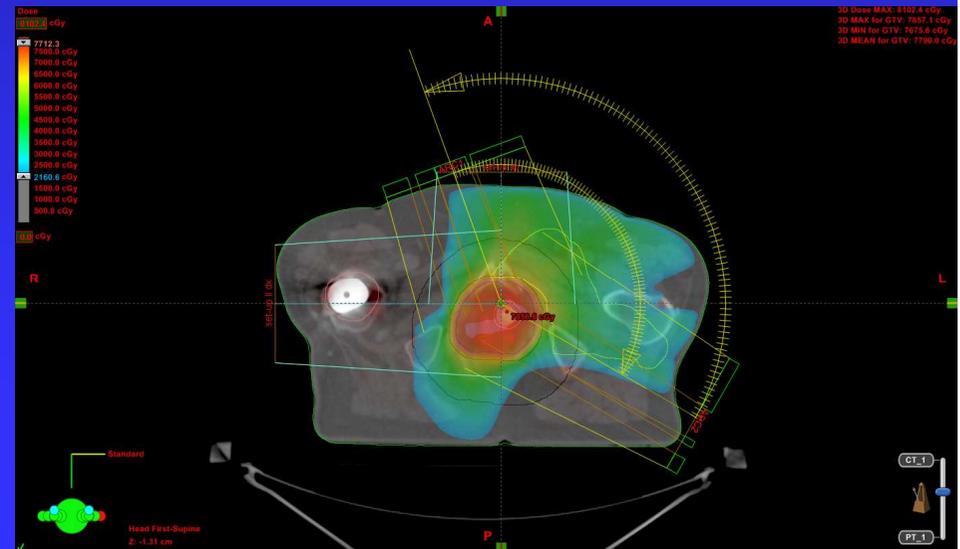
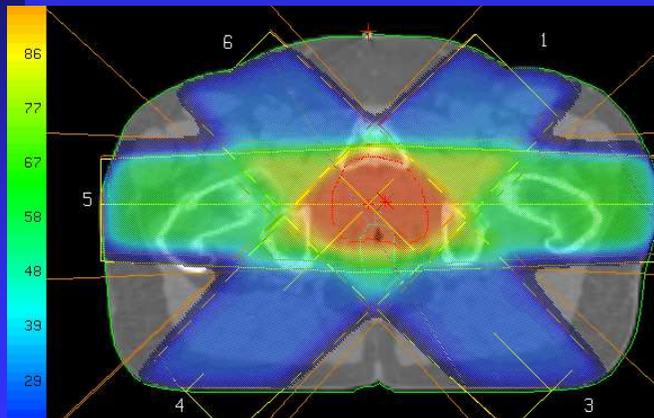
Intermediate risk
74 yrs

PTV 78Gy

Left femur mean dose 26
max dose 45

Protesis mean dose 8
max dose 22

Rectum V70 20%



IGRT (image guided radiotherapy)

NAL protocol (No Action Level)

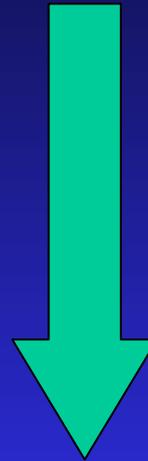
Portal images for N-fractions
Mean error vector -> set-up correction
Reduction of systematic error



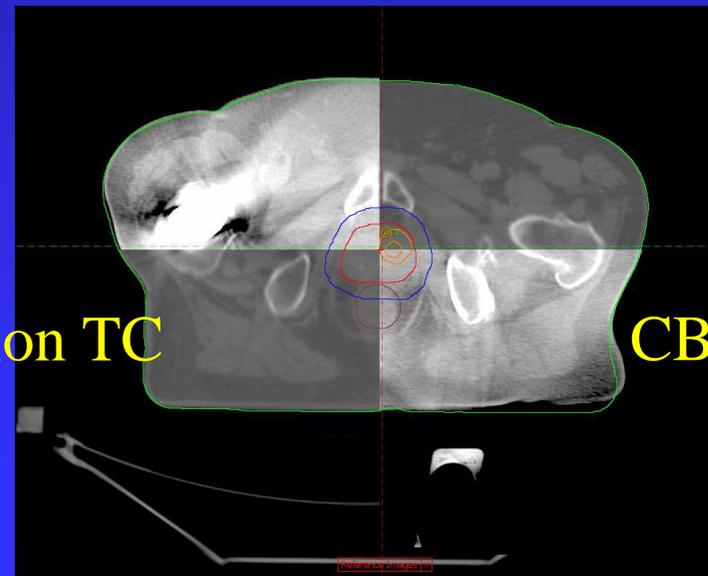
KV-KV

ON-LINE correction

They aim to reduce the margin CTV->PTV,
Systematic and random error.
Reduce set-up errors both in a single session
(intrafraction) that in the course of
treatment (interfraction). Reduce errors due
to organ motion



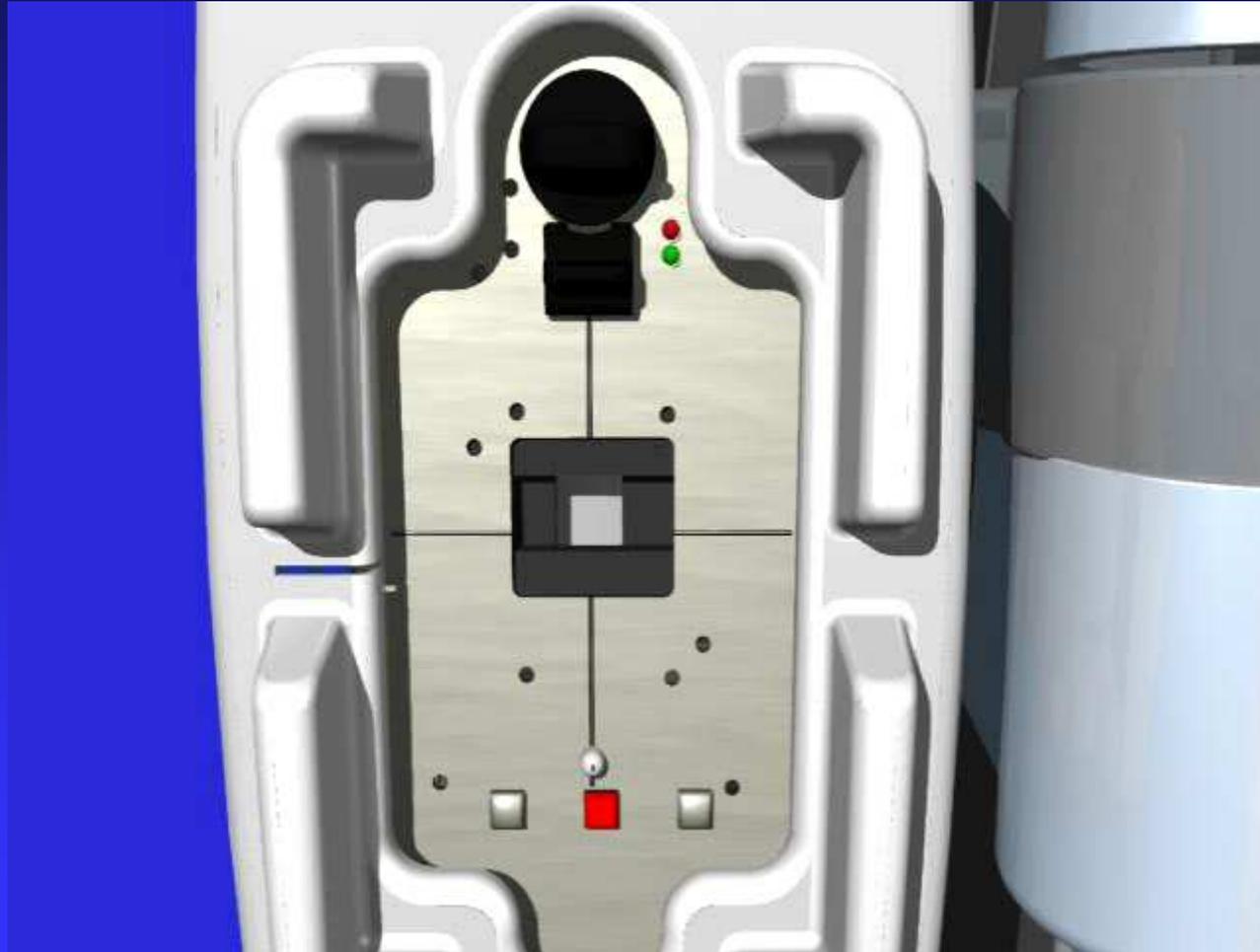
Simulation TC



CBCT

CBCT

IGRT (image guided radiotherapy)



NEOADJUVANT ADT: WHEN?

- cT2-T3 large prostate volume
- High risk patients/ locally advanced disease (cT3b-cT4, cN0)
- Timinig: three months before RT

NEOADJUVANT ADT: BENEFIT

Endocrine treatment, with or without radiotherapy, in locally advanced prostate cancer (SPCG-7/SFUO-3): an open randomised phase III trial

Anders Widmark, Olbjørn Klepp, Arne Solberg, Jan-Erik Damber, Anders Angelsen, Per Fransson, Jo-Åsmund Lund, Ilker Tasdemir, Morten Hoyer, Fredrik Wiklund, Sophie D Fosså, for the Scandinavian Prostate Cancer Group Study 7 and the Swedish Association for Urological Oncology 3

Short-Term Neoadjuvant Androgen Deprivation Therapy and External-Beam Radiotherapy for Locally Advanced Prostate Cancer: Long-Term Results of RTOG 8610

Mack Roach III, Kyoung-hwa Bae, Joycelyn Speight, Harvey B. Wolkov, Phillip Rubin, R. Jeffrey Lee, Colleen Lawton, Richard Valicenti, David Grignon, and Miljenko V. Pilepich

Decrease cancer-related mortality

POST-OPERATIVE RT

- ADJUVANT: patients at high risk of local failure
- SALVAGE: biochemical relapse that indicates local failure

ADJUVANT RADIO THERAPY

- After 12-16 weeks
- The aim: Eradicate residual clonogenic cells in surgical bed
- Dose: 66-70 Gy

ADJUVANT RADIOTHERAPY

- POSITIVE MARGINS!!
 - PSA persistence after surgery (salvage)
 - Patological stage \geq T3
- PERPLEXITIS: perineural invasion,
presence of negative prognostic findings
(Initial PSA, PSADT < 10 months, GS)



Postoperative Radiation Therapy for Pathologically Advanced Prostate Cancer After Radical Prostatectomy

Andrew J. Stephenson^{a,*}, Michel Bolla^b, Alberto Briganti^c, Cesare Cozzarini^d, Judd W. Moul^e, Mack Roach III^f, Hein van Poppel^g, Anthony Zietman^h

Phase III randomized controlled trials evaluating adverse pathologic features → pT3, R+



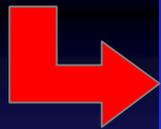
Benefit on biochemical progression with adjuvant RT

First author (yr)	Study design; median follow-up; PSA requirement	Conclusions	Comments
Thompson (2009) [17]	pT3 and/or positive margins with or without adjuvant RT; 152 mo; not specified (33% PSA >0.2 ng/ml)	Improved PSA control, metastasis-free survival, and overall survival	Longest follow-up with one-third receiving salvage therapy with a similar magnitude of benefit
Bolla (2005) [18,42]	pT3 and/or positive margins with or without adjuvant RT; 127 mo; not specified (30% PSA >0.2 ng/ml)	Improved PSA control and local failure; no difference in overall survival, metastasis-free survival, or clinical progression-free survival	Long follow-up; benefit restricted to those with positive surgical margins; poor consistency of pathology on central review
Wiegel (2009) [19]	pT3 and/or positive margins with or without adjuvant RT; 54 mo; undetectable PSA (20% PSA >0.1 ng/ml in intention-to-treat analysis)	Improved PSA control; too few events to assess metastasis and survival end points	Benefit restricted to those with positive surgical margins; inadequate follow-up and/or study size to address survival

SALVAGE RADIOOTHERAPY

DEFINITION:

RT administered with a PSA level recurrence after RP in patients with no evidence of metastatic disease



Biochemical recurrence is typically defined as PSA level >0.2 ng/ml (confirmed by 2 sequential PSA)

Variation in the Definition of Biochemical Recurrence in Patients Treated for Localized Prostate Cancer: The American Urological Association Prostate Guidelines for Localized Prostate Cancer Update Panel Report and Recommendations for a Standard in the Reporting of Surgical Outcomes

Michael S. Cookson,^{*,†} Gunnar Aus,[‡] Arthur L. Burnett,[§] Edith D. Canby-Hagino, Anthony V. D'Amico, Roger R. Dmochowski,^{||} David T. Eton, Jeffrey D. Forman, S. Larry Goldenberg, Javier Hernandez, Celestia S. Higano, Stephen R. Kraus,[¶] Judd W. Moul,^{**} Catherine Tangen, J. Brantley Thrasher^{††} and Ian Thompson^{‡‡}

SALVAGE RADIO THERAPY

- Predictive factors of biochemical failure after salvage RT:
 - GS (8-10)
 - PSA levels pre RT > 2ng/ml
 - PSADT < 10 mesi
 - Negative surgical margins
 - IVS

Following factors are not predictive of biochemical failure after salvage RT: PSA levels pre PR, ECE, free disease survival < 12 months, radiation dose



Early Salvage Radiotherapy Following Radical Prostatectomy

David Pfister^{a,*}, Michel Bolla^b, Alberto Briganti^c, Peter Carroll^d, Cesare Cozzarini^e, Steven Joniau^f,
Hein van Poppel^f, Mack Roach^g, Andrew Stephenson^h, Thomas Wiegelⁱ, Michael J. Zelefsky^j

EARLY SALVAGE RT → pre-RT PSA ≤ 0.5
ng/ml

10 retrospective studies
Dose > 60 Gy (better 66-70)
↓

**Improved 5-yr BRF5 rates for patient who receive
Early salvage RT**

(Take home points 1)

- **IMRT can decrease intestinal and urinary toxicity at the same doses : excellent treatment compliance (no interruption for toxicity)**
- **IMRT/IGRT could improves risk of secondary neoplasms**

(Take home points 2)

■ it is useful for surgery and planning IMRT treatment, the integration of imaging (RNM, PET-TC)

■ All cases treated with IMRT benefit from IGRT, not only using images of KV to control the set-up, but also those of CBCT for verification

of treatment volumes
(Adaptive Radiotherapy)



International Journal of
Radiation Oncology
biology • physics
www.ijrojournal.org

Physics Contribution

Dosimetric and Radiobiological Consequences of Computed Tomography—Guided Adaptive Strategies for Intensity Modulated Radiation Therapy of the Prostate

Jerry J. Battista, PhD,^{*1,2} Carol Johnson, BSc,² David Turnbull, PhD,² Jeff Kempe, MSc,² Karl Bzdusek, MSc,³ Jacob Van Dyk, MSc,^{*1,2} and Glenn Bauman, MD^{*1,2}

Departments of ^{*}Medical Biophysics and ¹Oncology, Western University, London, ON, Canada; ²London Regional Cancer Program, London Health Sciences Centre, London, ON, Canada; and ³Philips Healthcare (Radiation Oncology Systems), Fitchburg, Wisconsin

Received May 1, 2013, and in revised form Jan 25, 2013. Accepted for publication Jul 6, 2013

Thank you for your attention!

