

Radioterapia nel ca prostatico: quali indicazioni? Quali studi clinici in corso?

Sergio Fersino

Unità Operativa Complessa
Radioterapia Oncologica
Direttore: F. Alongi



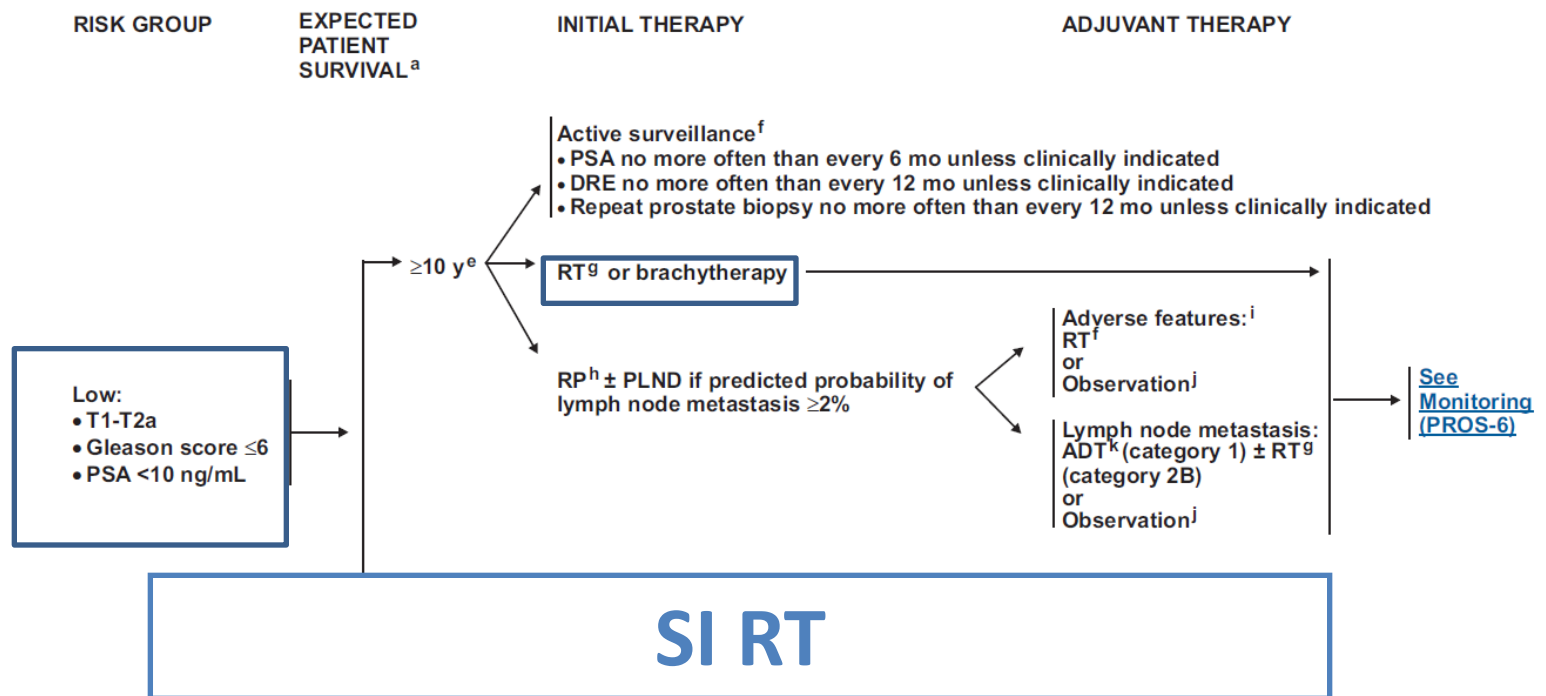
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Trattamento RADICALE

RISCHIO BASSO

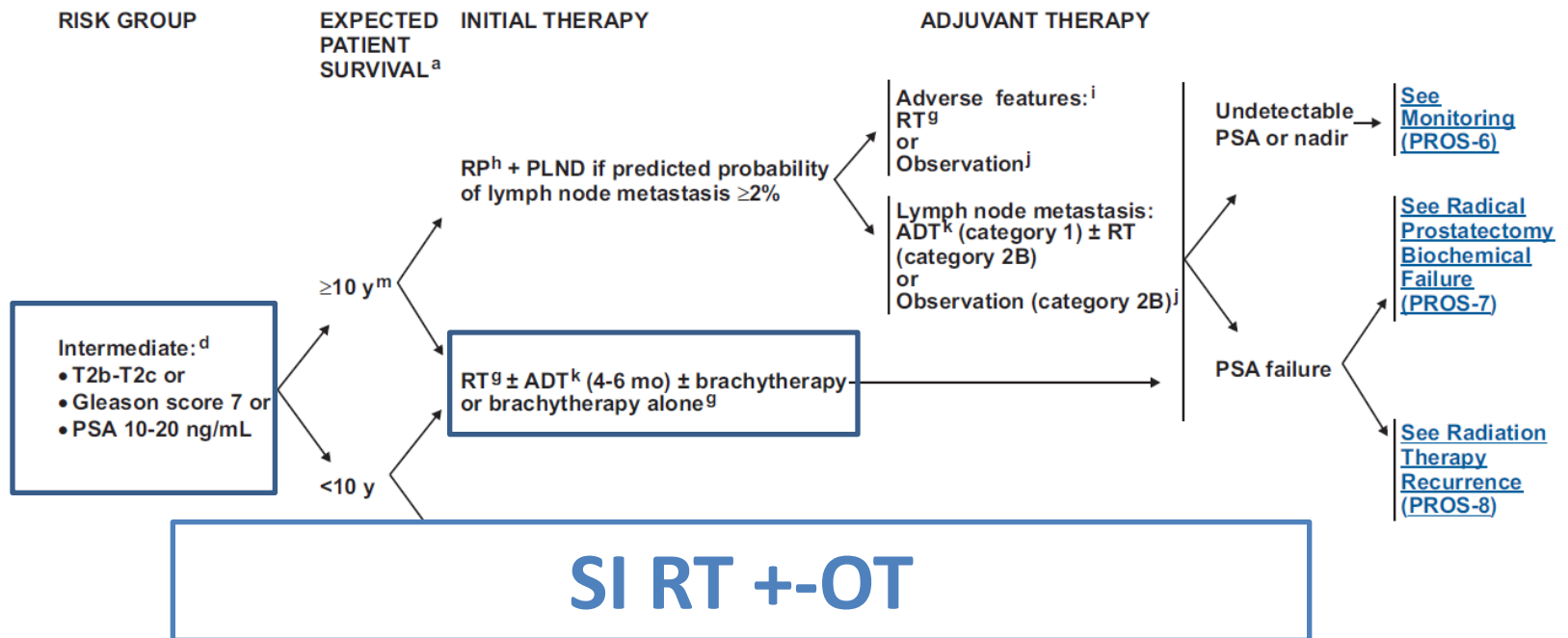


National Comprehensive Cancer Network®
NCCN Guidelines Version 1.2014
Prostate Cancer



Trattamento RADICALE

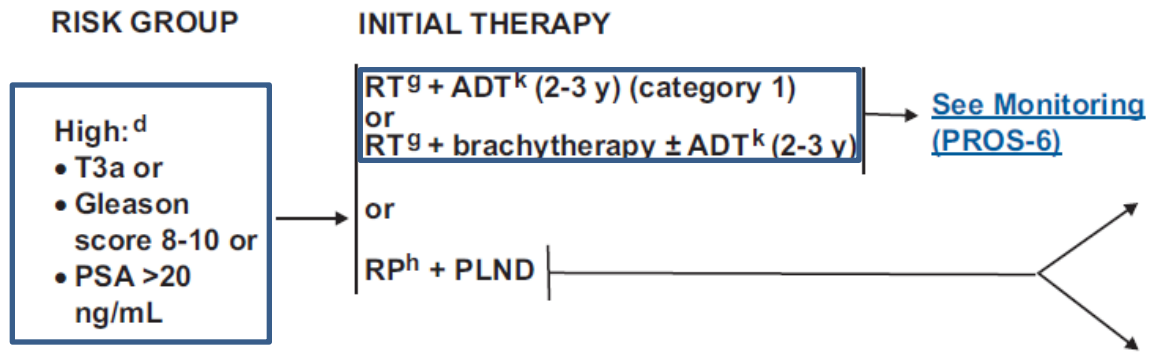
RISCHIO INTERMEDIO



Trattamento RADICALE

RISCHIO ALTO

NCCN National Comprehensive Cancer Network® **NCCN Guidelines Version 1.1**
Prostate Cancer

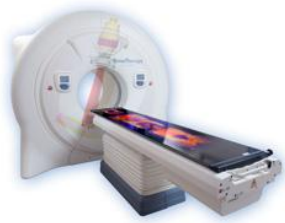


SI RT +OT

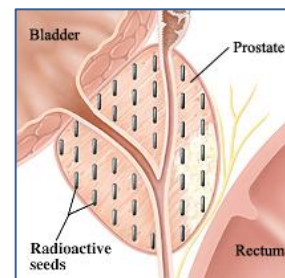
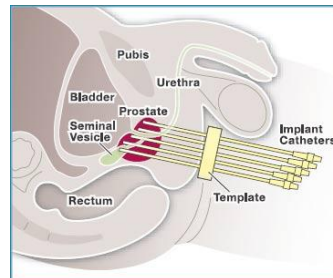


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Trattamento RADICALE: *se si, quale tecnica?*



Radioterapia a fasci esterni: *Tomoterapia, Cyberknife, Rapidarc-TrueBeam, etc*



Brachiterapia: *interstiziale o a permanenza*



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Trattamento RADICALE: *se si, quale tecnica?*

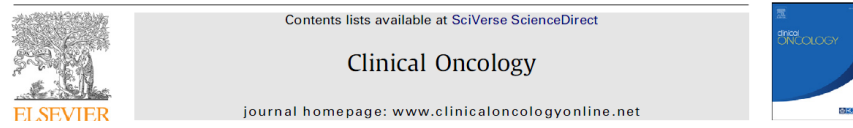
- Radioterapia a fasci esterni:** tutte le tecniche ad
- intensità modulata (IMRT)
 - guidate dalle immagini per ogni seduta (IGRT),

(indipendentemente dalla apparecchiatura usata)



Potrebbero essere preferite per innalzare la dose garantendo una uguale o minore tossicità rettale (EBM livello 1)

Clinical Oncology 24 (2012) 461–473



Guidelines

Intensity-modulated Radiotherapy in the Treatment of Prostate Cancer

G. Bauman^{*}, R.B. Rumble[†], J. Chen[‡], A. Loblaw[§], P. Warde[¶] and Members of the IMRT Indications Expert Panel

Trattamento RADICALE: *se si, quali nuove frontiere?*



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NCCN Guidelines Version 1.2014 Prostate Cancer

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PRINCIPLES OF RADIATION THERAPY

Primary External Beam Radiation Therapy (EBRT)

- **Highly conformal RT techniques should be used to treat prostate cancer.**
- **Doses of 75.6 to 79.2 Gy in conventional fractions to the prostate (\pm seminal vesicles for part of the therapy) are appropriate for patients with low-risk cancers. For patients with intermediate- or high-risk disease, doses up to 81.0 Gy provide improved PSA-assessed disease control.**

DOSE ESCALATION? YES!!



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Trattamento RADICALE: *se si, quali nuove frontiere?*

PRINCIPLES OF RADIATION THERAPY

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- Moderately hypofractionated image-guided IMRT regimens (2.4 to 4 Gy per fraction over 4-6 weeks) have been tested in randomized trials reporting similar efficacy and toxicity to conventionally fractionated IMRT. They can be considered as an alternative to conventionally fractionated regimens when clinically indicated.

**Moderate Hypofractionation (from 35-42 fractions to 20-25)?
YES!!**



Trattamento RADICALE: *se si, quali nuove frontiere?*



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PRINCIPLES OF RADIATION THERAPY

Primary External Beam Radiation Therapy (EBRT)

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- Moderately hypofractionated image-guided IMRT regimens (2.4 to 4 Gy per fraction over 4-6 weeks) have been tested in randomized trials reporting similar efficacy and toxicity to conventionally fractionated IMRT. They can be considered as an alternative to conventionally fractionated regimens when clinically indicated.
- Extremely hypofractionated image-guided IMRT/SBRT regimens (6.5 Gy per fraction or greater) are an emerging treatment modality with single institutional and pooled reports of similar efficacy and toxicity to conventionally fractionated regimens. They can be considered as a cautious alternative to conventionally fractionated regimens at clinics with appropriate technology, physics, and clinical expertise.

**Extreme Hypofractionation (from 35-42 fractions to 3-5)?
YES, but in selected cases and inside protocols!!**

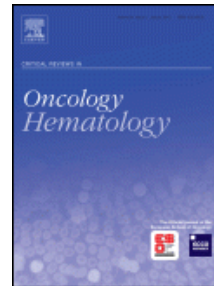


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Trattamento RADICALE: *novità?* **IPOFRAZIONAMENTO ESTREMO**



ELSEVIER



Critical Reviews in Oncology/Hematology xxx (2012) xxx–xxx

CRITICAL REVIEWS IN
*Oncology
Hematology*
Incorporating Geriatric Oncology

www.elsevier.com/locate/critrevonc

Will SBRT replace conventional radiotherapy in patients with low-intermediate risk prostate cancer? A review

Stefano Arcangeli*, Marta Scorsetti, Filippo Alongi

Radiotherapy and Radiosurgery department, Istituto Clinico Humanitas, Humanitas Cancer Center, Rozzano, Milano, Italy

Accepted 23 November 2011



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SBRT and (Extreme) Hypofractionation For Prostate

Alongi *et al. Radiation Oncology* 2013, **8**:171
<http://www.ro-journal.com/content/8/1/171>



RESEARCH

Open Access

Linac based SBRT for prostate cancer in 5 fractions with VMAT and flattening filter free beams: preliminary report of a phase II study

Filippo Alongi^{1,4*}, Luca Cozzi², Stefano Arcangeli¹, Cristina Iftode¹, Tiziana Comito¹, Elisa Villa¹, Francesca Lobefalo¹, Pierina Navarria¹, Giacomo Reggiori¹, Pietro Mancosu¹, Elena Clerici¹, Antonella Fogliata², Stefano Tomatis¹, Gianluigi Taverna³, Pierpaolo Graziotti³ and Marta Scorsetti¹

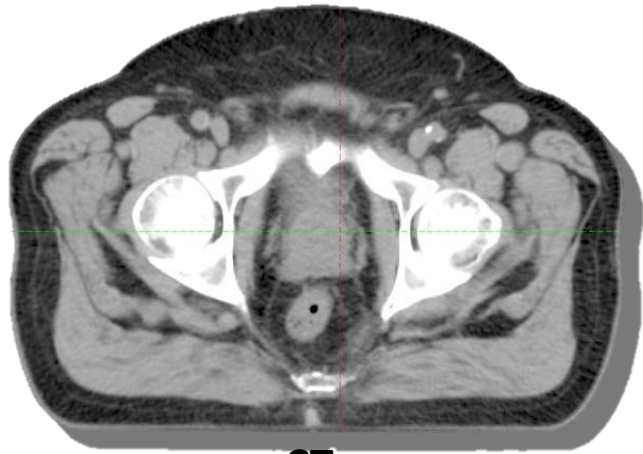


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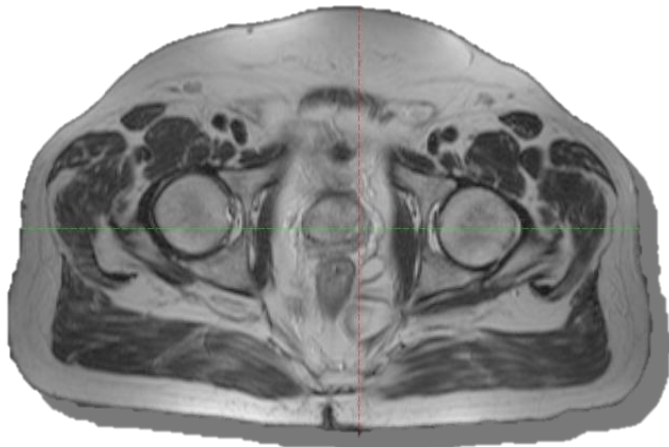
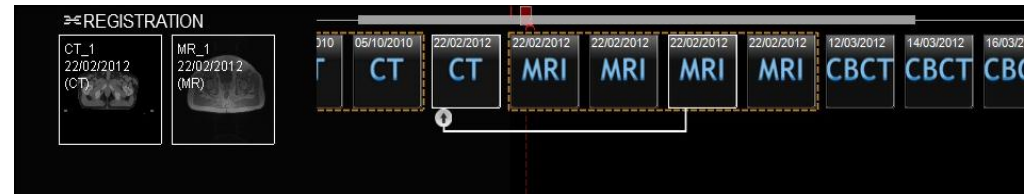
The first **40** patients analysis

SBRT and (Extreme) Hypofractionation For Prostate

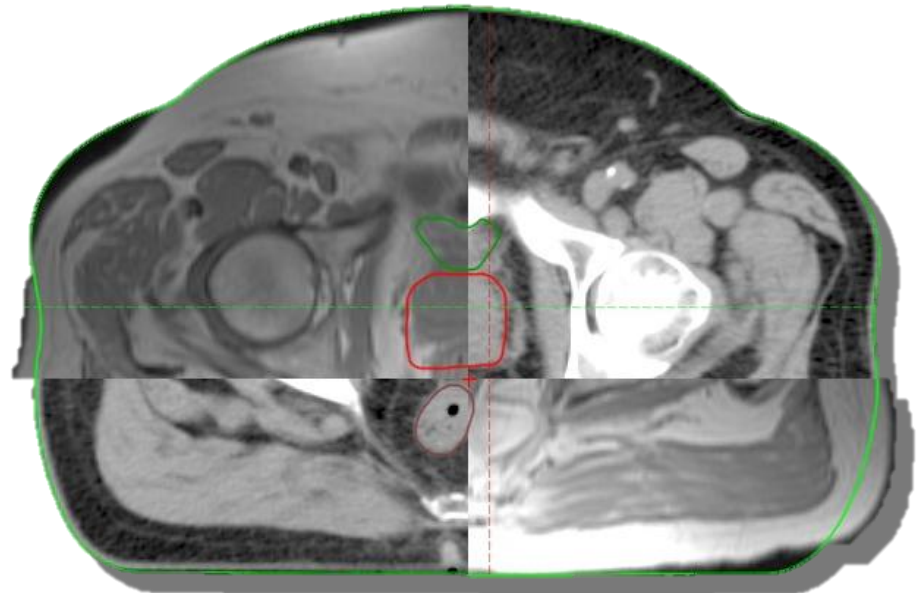
IMAGING and TARGET DEFINITION - 1



CT

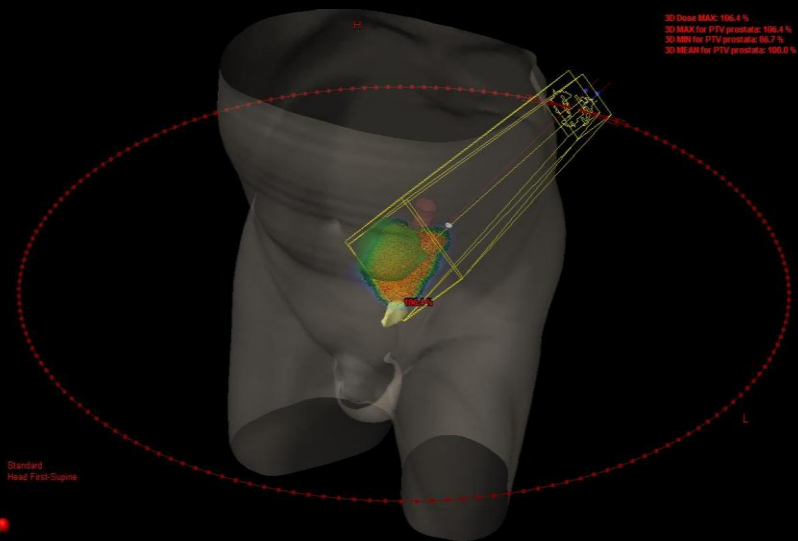
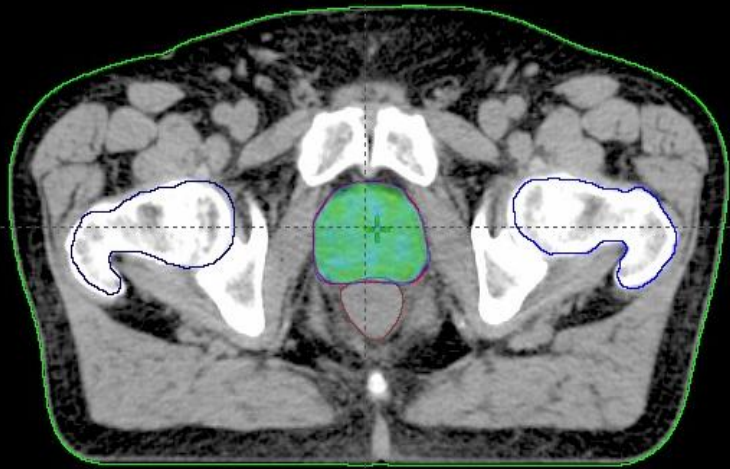


MRI

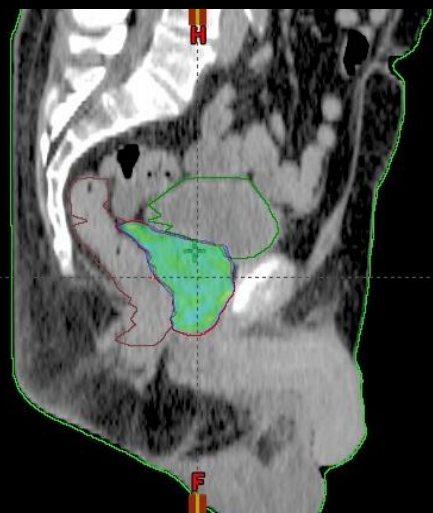


Trattamento RADICALE: *IPOFRAZIONAMENTO ESTREMO in 5 sedute*

70 anni, cT2, iPSA 8, GS 3+4



3D Dose MAX: 106.4 %
3D MAX for PTV prostate: 106.4 %
3D MIN for PTV prostate: 96.7 %
3D MEAN for PTV prostate: 100.0 %



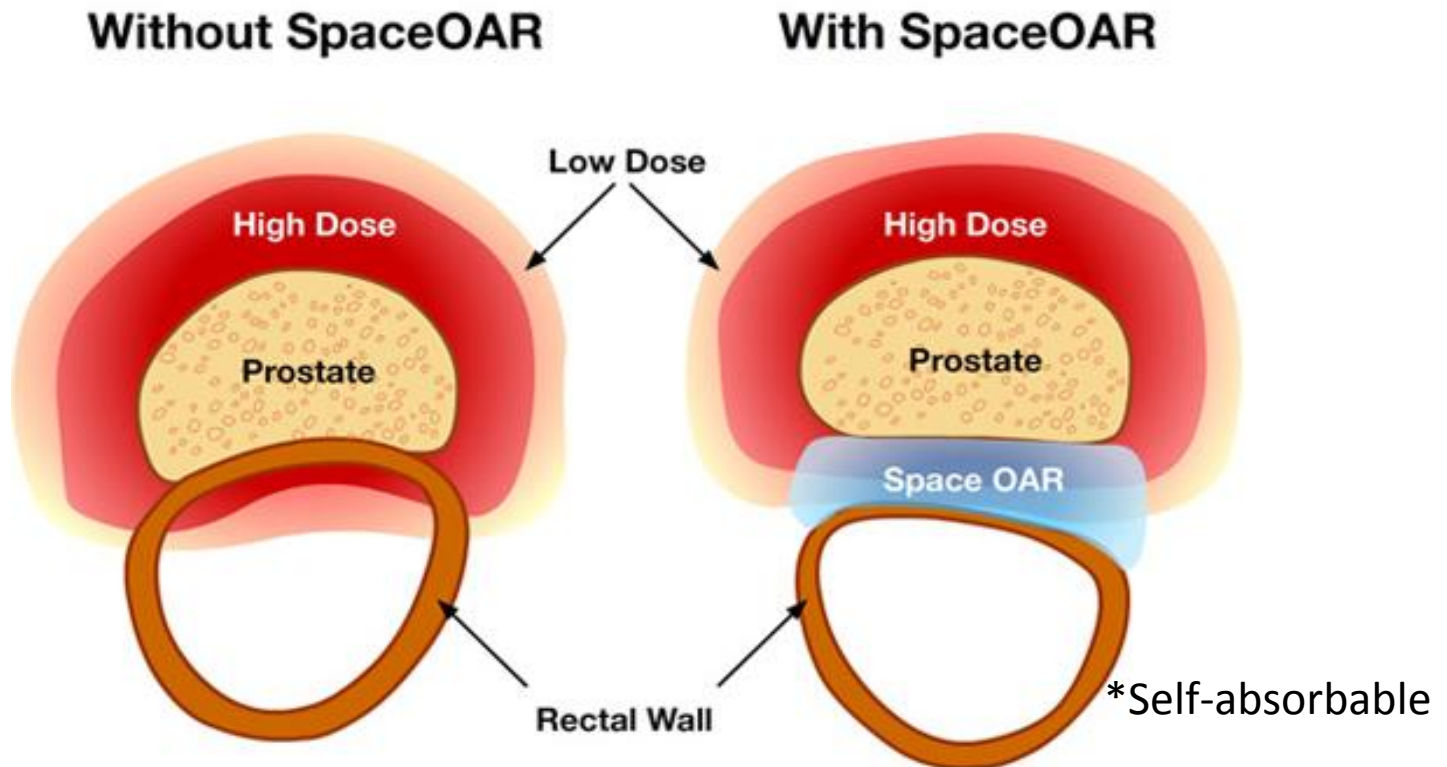
35 Gy in 5 sedute
Tempo di trattamento 120 sec.

.59 cm

SBRT and (Extreme) Hypofractionation For Prostate

SPACEOAR: A SOLUTION

SpaceOAR hydrogel moves the rectum away from the high dose radiation field



SBRT and (Extreme) Hypofractionation For Prostate

SPACEOAR IN HUMANITAS SBRT PROTOCOL

MRI T2 after implant

CT after implant

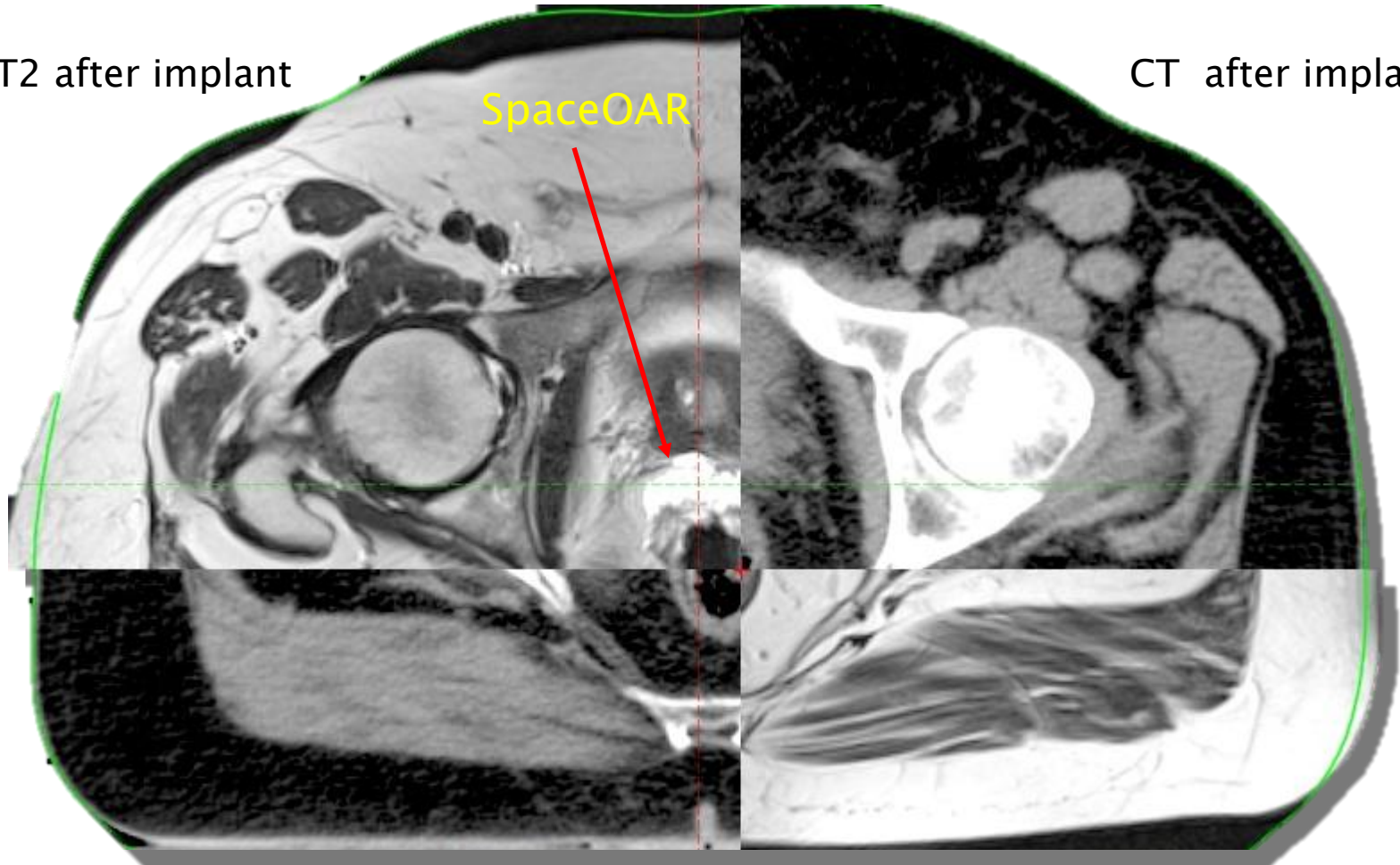
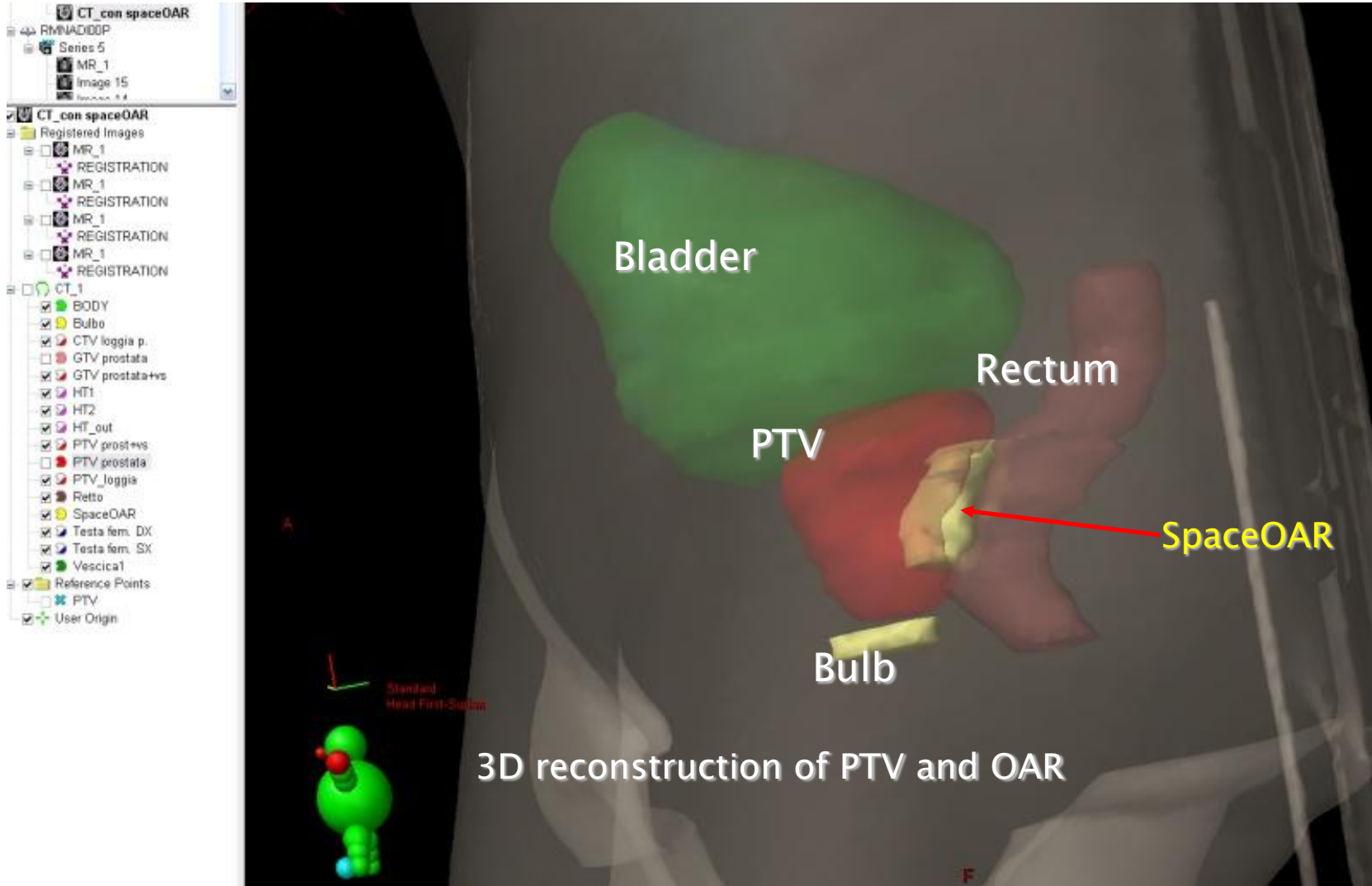


IMAGE FUSION FOR VOLUMES DEFINITION

SBRT and (Extreme) Hypofractionation For Prostate

SPACEOAR IN SBRT PROTOCOL



SBRT and (Extreme) Hypofractionation For Prostate

J Cancer Res Clin Oncol
DOI 10.1007/s00432-014-1732-1

2014

ORIGINAL ARTICLE – CLINICAL ONCOLOGY

Stereotactic body radiotherapy with flattening filter-free beams for prostate cancer: assessment of patient-reported quality of life

Marta Scorsetti · Filippo Alongi · Elena Clerici · Tiziana Comito · Antonella Fogliata ·
Cristina Iftode · Pietro Mancosu · Piera Navarria · Giacomo Reggiori ·
Stefano Tomatis · Elisa Villa · Luca Cozzi

Conclusion

The EPIC QoL questionnaire was administered to a cohort of prostate patients treated in a prospective trial for SBRT with RapidArc and FFF beams. Results demonstrated, in the absence of any statistical significance, some trends to a modest decrease in the urinary and sexual domains with a more marked “perception” (bother) than the actual functional decrease. Present data are not in contrast, given the uncertainties, with other similar studies and suggest for a good compliance and tolerance of the treatment modality.

Table 2 Acute and late toxicity profiles over the cohort of 72 patients in the prospective protocol

	G0	G1	G2	G3	G4
GI acute	49 (68 %)	17 (24 %)	6 (8 %)	0	0
GU acute	22 (31 %)	19 (23 %)	31 (43 %)	0	0
GI late	68 (94 %)	4 (6 %)	0	0	0
GU late	49 (68 %)	22 (31 %)	1 (1 %)	0	0



SBRT and (Extreme) Hypofractionation For Prostate: **Single dose the last frontier.**

Tumori, 100: e87-e86, 2014

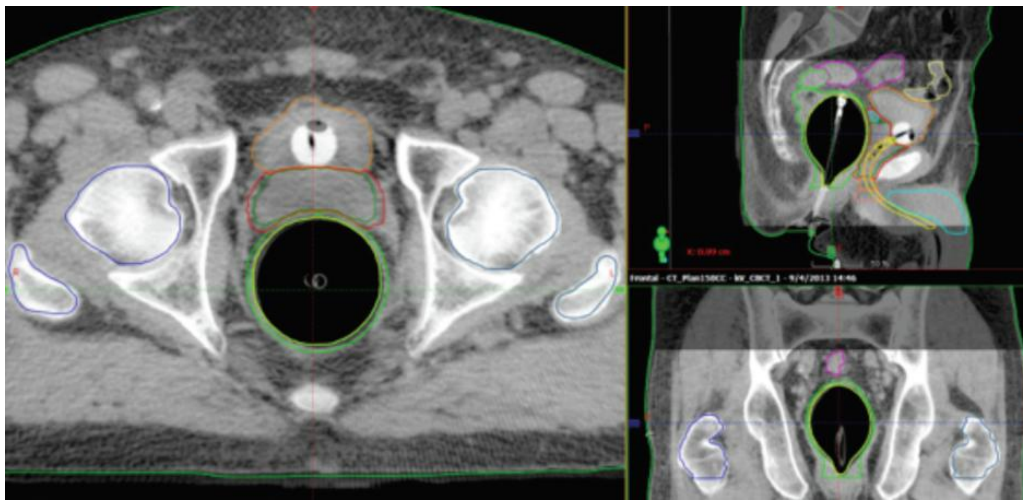
LETTER TO THE EDITOR

Could single-high-dose radiotherapy be considered the new frontier of stereotactic ablative radiation therapy?

Filippo Alongi¹, Berardino De Bari²,
and Marta Scorsetti³

¹Radiation Oncology Department, Sacro Cuore Hospital, Negrar-Verona, Italy; ²Service de Radio-Oncologie, Centre Hospitalier Universitaire Vaudois (CHUV), Lausanne, Switzerland; ³Radiotherapy and Radiosurgery Department, Humanitas Cancer Center, Rozzano, Milan, Italy

In summary, an increasing amount of preliminary data seems to confirm the potential feasibility and efficacy of SABR. Nevertheless, this therapeutic approach should still be considered investigational, as no long-term data exist about clinical outcomes and acute and late toxicity rates. Patient selection is a crucial issue and prospective trials are needed to accumulate evidence and standardize treatments and dose-volume constraints. Future improvements and further data will confirm or refute the effectiveness and good tolerability of the single-dose approach.



Trattamento POST-OPERATORIO: *ADIUVANTE O SALVATAGGIO?*

CRITICAL REVIEW

ADJUVANT VERSUS SALVAGE RADIOTHERAPY AFTER PROSTATECTOMY: THE APPLE VERSUS THE ORANGE



CHRISTOPHER R. KING, PH.D., M.D.

Department of Radiation Oncology, UCLA School of Medicine, Los Angeles, CA

Radioterapia postoperatoria immediata o di
salvataggio non sono stati **mai comparati** in
uno studio prospettico



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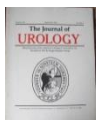
Trattamento POST-OPERATORIO: **ADIUVANTE**

ASTRO/AUA Guideline Statements

STANDARD. Physicians should offer adjuvant radiotherapy to patients with adverse pathologic findings at prostatectomy including seminal vesicle invasion, positive surgical margins, or extraprostatic extension because of demonstrated reductions in biochemical recurrence, local recurrence, and clinical progression.



Trattamento POST-OPERATORIO: **ADIUVANTE**



Studio randomizzato	Pazienti	FUP mediano	Outcome	considerazioni
RTOG 8794 (J Urology 2009)	431	12.7 anni	Metastasis free survival and overall survival a favore di RT	Vantaggio di sopravvivenza solo a lungo termine
EORTC 22911 (Lancet 2012)	1005	10.6 anni	RT meglio di osservazione per PFS e LC a 5 anni, a 10 anni perso il vantaggio della RT vs osservazione.	Margini positivi e età < 70 anni: unici forti fattori prognostici a favore di RT. No vantaggio sopravvivenza
ARO 9602 (European Urology 2014)	388	10 anni	RT meglio di osservazione per PFS	RT riduce il rischio di recidiva biochimica del 51%



Trattamento POST-OPERATORIO: **SALVATAGGIO**

ASTRO/AUA Guideline Statements

RECOMMENDATION. Physicians should offer salvage radiotherapy to patients with PSA or local recurrence after radical prostatectomy in whom there is no evidence of distant metastatic disease.

Radioterapia di salvataggio in caso di **rialzo**
del **PSA**: ma a **quale valore?**



Trattamento POST-OPERATORIO DI **SALVATAGGIO**:
QUANDO CONSIDERIAMO IL PSA COME RECIDIVA BIOCHIMICA?

“A PSA value greater than 0.2 ng/mL is an appropriate cutpoint to define PSA recurrence after RRP”

Freedlan et al, Urology 61 : 365-369, 2003

ASTRO/AUA Guideline Statement

RECOMMENDATION. Clinicians should define biochemical recurrence as a detectable or rising PSA value after surgery that is ≥ 0.2 ng/ml with a second confirmatory level ≥ 0.2 ng/ml.



Trattamento POST-OPERATORIO DI SALVATAGGIO QUANDO? A CHE PSA?



Contents lists available at SciVerse ScienceDirect

Radiotherapy and Oncology

2012

journal homepage: www.thegreenjournal.com



Original article

Salvage radiotherapy after prostatectomy – What is the best time to treat?

Alessandra Siegmann^{a,1}, Dirk Bottke^{b,1}, Julia Faehndrich^a, Maike Brachert^b, Gunnar Lohm^a, Kurt Miller^c, Detlef Bartkowiak^b, Wolfgang Hinkelbein^a, Thomas Wiegel^{b,*}

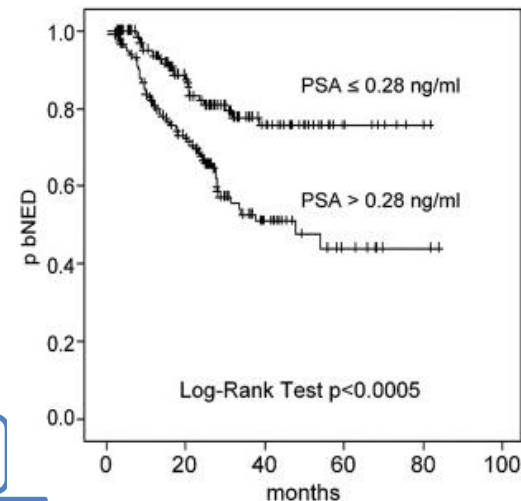
^aDepartment of Radiation Oncology, Charité Universitätsmedizin, Berlin; ^bDepartment of Radiation Oncology, University Hospital Ulm; ^cDepartment of Urology, Charité Universitätsmedizin, Berlin, Germany

Purpose: Salvage radiotherapy (SRT) is applied routinely in patients with biochemical relapse after radical prostatectomy (RP). However, only ~30% of these patients achieve a durable response after 10 years. As a standard, 66 Gy are given, ideally with a PSA below 0.5 ng/ml. We tried to determine more precisely the optimal PSA for starting SRT.

Material and methods: In 301 prostate cancer patients without hormonal treatment, we analysed the impact on the biochemical response (bNED) to SRT of two pre-SRT PSA levels, namely below or above the median of 0.28 ng/ml.

Results: The median follow-up time for the entire group was 30 months. In 151 patients, SRT commenced at a PSA \leq 0.28 ng/ml, in 150 at $>$ 0.28 ng/ml. Eighty-two patients (27%) developed biochemical progression during follow up. The calculated two-year bNED was 74% for the entire group, 78% versus 61% for a PSA \leq or $>$ 0.28 ng/ml, respectively. In multivariate analysis, pT_{3b}, resection status, pre-SRT PSA dichotomized at median, PSA post-SRT undetectable, and PSA doubling time were statistically significant independent predictors of progression after SRT.

Conclusions: Our findings suggest that a PSA of \leq 0.28 ng/ml improves bNED compared with a PSA before SRT of $>$ 0.28 ng/ml.



Quindi, salvataggio si, ma precoce!!!!

Trattamento POST-OPERATORIO : Quindi che fare?

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

2012



Collaborative Review – Prostate Cancer
Editorial on pp. x–y of this issue

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

Evidence synthesis: Conflicting evidence from these trials suggests that adjuvant RT can have a favorable impact on systemic progression, PCa-specific mortality, or overall survival. Observational studies have reported durable responses to salvage RT in a substantial proportion of high-risk patients (provided that it is administered at the earliest evidence of BCR) and reduced PCa-specific mortality. There is consensus that the outcome of patients receiving postoperative RT is best when the prostate-specific antigen (PSA) level is the lowest. However, it is unclear if better outcomes will be achieved administering adjuvant RT to all patients at increased risk for recurrent PCa who have an undetectable postoperative PSA level compared to close observation and timely salvage RT at the earliest indications of BCR.

Conclusions: Given the absence of data from randomized trials demonstrating superiority of one approach over the other in terms of quantity and quality of life, we advocate multidisciplinary input and shared and informed decision making among patients, urologists, and radiation oncologists based on the relative advantages and disadvantages

**DECIDERE INSIEME: MULTIDICIPLINARE E' MEGLIO PER UN
APPROCCIO PERSONALIZZATO MA BASATO SULLE
EVIDENZE!!!!**

THANKS FOR YOUR ATTENTION

