# Concetto di approccio multimodale per l'Urologo: Chirurgia di salvataggio dopo RT?


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OSPEDALE POLICLINICO SAN MARTINO

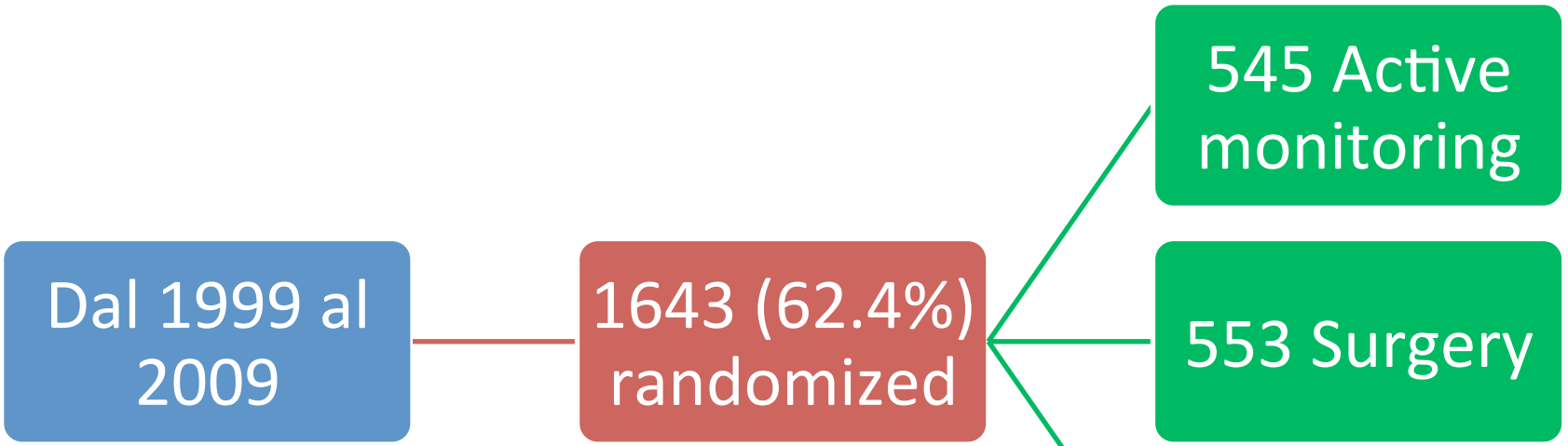
Sistema Sanitario Regione Liguria

# 10-Year Outcomes after Monitoring, Surgery, or Radiotherapy for Localized Prostate Cancer

The NEW ENGLAND JOURNAL of MEDICINE

F.C. Hamdy, J.L. Donovan, J.A. Lane, M. Mason, C. Metcalfe, P. Holding, M. Davis, T.J. Peters, E.L. Turner, R.M. Martin, J. Oxley, M. Robinson, J. Staffurth, E. Walsh, P. Bollina, J. Catto, A. Doble, A. Doherty, D. Gillatt, R. Kockelbergh, H. Kynaston, A. Paul, P. Powell, S. Prescott, D.J. Rosario, E. Rowe, and D.E. Neal, for the ProtecT Study Group*

2016;375:1415–24




Of the 405 men who started radiotherapy within 9 months after treatment assignment, 55 (14%) had an increase in the PSA level of 2 ng per milliliter or more above the nadir after radiotherapy,

National Comprehensive Cancer Network®

# NCCN Guidelines Version 2.2017
# Prostate Cancer

NCCN Guidelines Index
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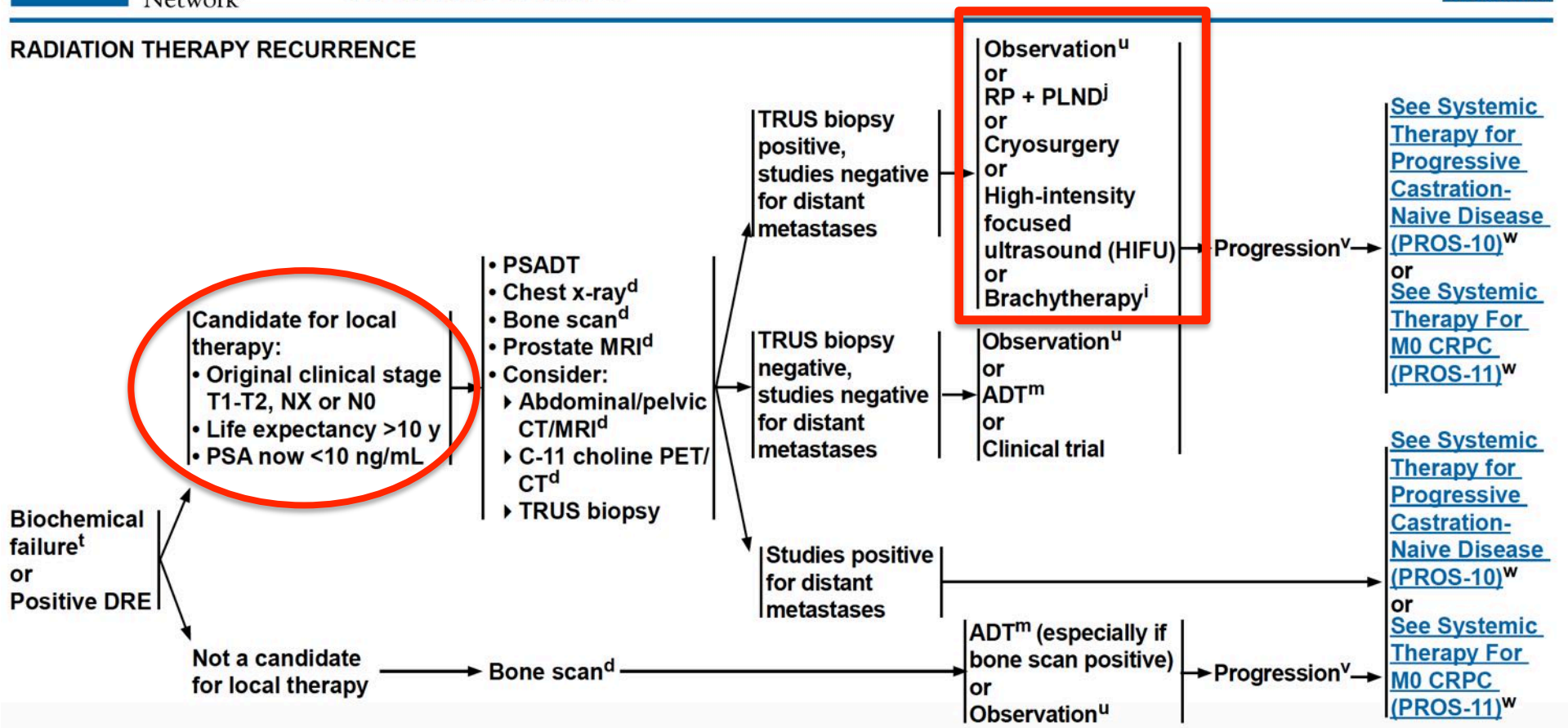
Discussion

## RADIATION THERAPY RECURRENCE



# EAU - ESTRO - ESUR - SIOG Guidelines on

# Prostate Cancer

*6.9.6.2 Summary of salvage radical prostatectomy*

In general, SRP should be considered only for patients with low comorbidity, a life expectancy of at least ten years, a pre-SRP PSA < 10 ng/mL and biopsy Gleason score ≤ 7, no LN involvement or evidence of distant metastatic disease pre-SRP, and who's initial clinical staging was T1 or T2 [701]. A meta-regression analysis suggested that SRP may be associated with worse continence outcomes than non-surgical approaches [707].

| **Recommendations for biochemical recurrence after radiotherapy** | | |
|---|---|---|
| Treat highly selected patients with localised PCa and a histologically proven local recurrence with salvage radical prostatectomy (SRP). | 3 | B |
| Due to the increased rate of side effects, perform SRP in experienced centres. | 3 | A |
| Offer/discuss high intensity focused ultrasound, cryosurgical ablation and salvage brachytherapy to/with patients without evidence of metastasis and with histologically proven local recurrence. Inform patients about the experimental nature of these approaches. | 3 | B |

UROLOGIC ONCOLOGY

# Underutilization of local salvage therapy after radiation therapy for prostate cancer[1]

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Urologic Oncology: Seminars and Original Investigations 32 (2014) 701–706

**Objective:** To evaluate the rates at which patients are offered and receive local salvage therapy (LST) after failure of primary radiotherapy for localized prostate cancer, as it is the only potentially curative treatment for localized recurrence but appears to be underutilized when compared with androgen-deprivation therapy (ADT) or observation.

**Materials and methods:** Patients with localized prostate cancer who received primary radiotherapy with curative intent between 1999 and 2000 were identified in the British Columbia Tumour Registry. Exclusion criteria included patient age >72 years, prostate-specific antigen >40 ng/ml, and clinical stage T4 at diagnosis. Data on clinicopathologic features, primary therapy, prostate-specific antigen kinetics, and salvage therapy were collected retrospectively. Radiation failure was defined as biochemical recurrence according to the Phoenix criteria or by initiation of salvage therapy.

**Results:** Of 1,782 patients treated in the study period, 1,067 met inclusion criteria. Of these, 257 failed radiation therapy. Radiation therapy failure was managed with observation (>12 mo) in 126 patients and ADT in 119. Of the observed patients, 66 subsequently received ADT. Five patients (1.8%) received LST (3 radical prostatectomy and 2 brachytherapy).

**Conclusions:** Only 2% of patients relapsing after radiation therapy for localized prostate cancer received LST. Although the benefits of LST are unproven, these findings reveal a possible underutilization of LST and indicate a need for enhanced collaboration between specialties to optimize care of this challenging cohort.

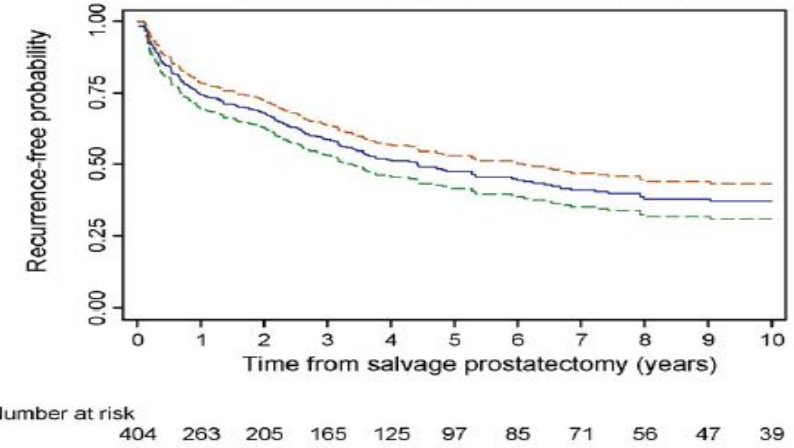
# Salvage Radical Prostatectomy for Radiation-recurrent Prostate Cancer: A Multi-institutional Collaboration

Chade DC et al. *Eur Urol.* 2011 August ; 60(2): 205–210.

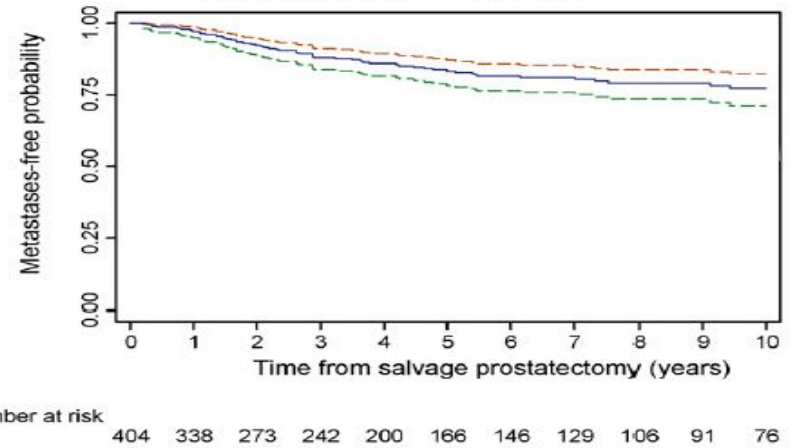
**Design, setting, and participants**—This is a retrospective, international, multi-institutional cohort analysis. There was a median follow-up of 4.4 yr following SRP performed on 404 men with radiation-recurrent PCa from 1985 to 2009 in tertiary centers.

**Intervention**—Open SRP.

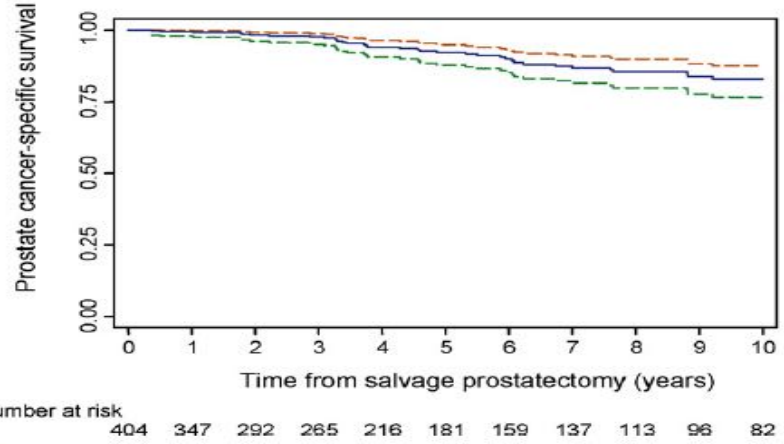
(a) Biochemical recurrence-free: all patients



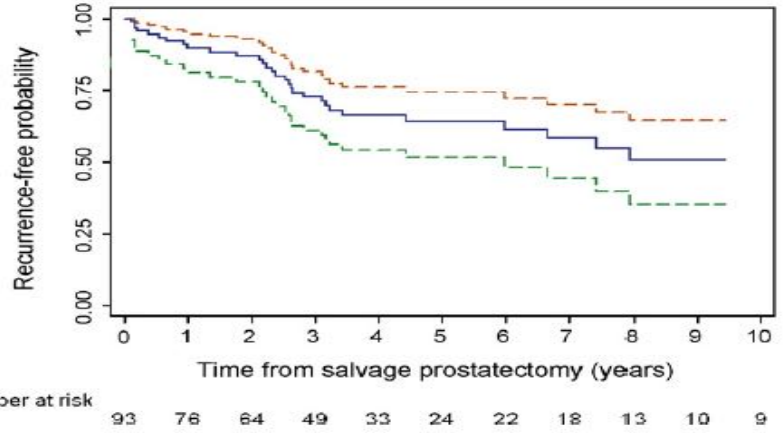

(b) Metastasis-free: all patients




(c) Prostate cancer-specific survival: all patients




(d) Biochemical recurrence-free: low-risk group
(pre-SRPPSA ≤ 4ng/mL and pre-SRP biopsy Gleason score ≤ 7)



EUROPEAN UROLOGY 57 (2010) 437–445

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European Association of Urology

Prostate Cancer

# Prognostic Parameters, Complications, and Oncologic and Functional Outcome of Salvage Radical Prostatectomy for Locally Recurrent Prostate Cancer after 21st-Century Radiotherapy

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January 2004 and August 2008: 55 men with biopsy-proven, locally recurrent PCa underwent Salvage Radical Prostatectomy and lymph node dissection after radiotherapy.

| Characteristics | Before RT | Before SRP |
|---|---|---|
| Clinical TNM | | |
| ≤cT2b | 39 (70.9%) | 44 (80%) |
| ≥cT3a | 16 (29.1%) | 11 (20%) |
| Median no. of biopsies | 8 (6–22) | 10 (8–24) |
| Biopsy Gleason score | | |
| ≤6 | 34 (61.8%) | 37 (67.3%) |
| 7 | 17 (30.9%) | 8 (14.5%) |
| 8–10 | 4 (7.3%) | 10 (18.1%) |
| PSA | | |
| <10 ng/ml | 29 (52.7%) | 45 (81.8%) |
| 10.1–20 ng/ml | 11 (20%) | 10 (18.2%) |
| >20 ng/ml | 15 (27.3%) | 0 |
| Androgen deprivation | | |
| Neoadjuvant | 12 (21.8%) | 0 |
| Adjuvant | 0 | 0 |

PSA = prostate-specific antigen; RT = radiotherapy; SRP = salvage radical prostatectomy.

**Table 2 – Pathohistologic findings of the salvage radical prostatectomy specimens**

| Variable | *n* |
|---|---|
| Pathologic stage | |
| pT2a-c pN0 SM– | 31 (71.1%) |
| pT2a-c pN0 SM+ | 1 (2.2%) |
| pT3a pN0 SM– | 3 (6.7%) |
| pT3a pN1 SM– | 1 (2.2%) |
| pT3a pN1 SM+ | 1 (2.2%) |
| pT3b pN0 SM+ | 1 (2.2%) |
| pT3b pN1 SM+ | 2 (4.4%) |
| pT3b pN1 SM– | 5 (11.1%) |
| Total PSMs | 5 (11.1%) |
| Total lymph node metastases | 9 (20%) |
| Specimen Gleason score | |
| ≤6 | 15 (33.3%) |
| 7 | 21 (46.7%) |
| 8–10 | 9 (20%) |

PSM = positive surgical margin.

# Continence

- 19 (34.5%) at the time of discharge.
- 34 (61.8%) at 3 mo postoperatively.
- 44 (80%) at 1 yr postoperatively.
- 11 (20%) remained incontinent.

Restoration of continence strongly correlated with the type of previous RT:

- 9.5% patients following seed implantation,21.1% and 33% patients following EBRT or EBRT plus brachytherapy, respectively, remained incontinent.

# EF

15 (26.7%) men with unimpaired preoperative

erections underwent nerve sparing prostatectomy.

- 4 men had a preservation of EF.
- 6 of 15 (40%) patients achieved erections with the use of PDE5-Is.

45 of 55 (81.8%) patients remained impotent.

# Oncological outcomes

The median follow-up 23 mo:

None patients

- died as a result of PCa or other non–cancer-related causes.
- had asymptomatic or symptomatic local recurrences.
- of the good-risk group developed biochemical recurrence (BCR) or clinical recurrences.

7 (35%) patients in the poor-risk group developed recurrences.

5 men experienced PSA progression after a median follow up of 12 mo.

2 patients (4.4%) developed bone metastases (received LHRH analogues).

ELSEVIER

Seminars in
RADIATION
ONCOLOGY

# Cancer Control and Complications of Salvage Local Therapy After Failure of Radiotherapy for Prostate Cancer: A Systematic Review

Arti Parekh, BA, Powell L. Graham, AB, and Paul L. Nguyen, MD

The National Comprehensive Cancer Network guidelines currently endorse salvage local therapy as a reasonable alternative to observation or androgen-deprivation therapy for select men with a biopsy-proven local recurrence after definitive radiation for prostate cancer. Patients being considered for salvage therapy should have had localized disease at presentation, a prostate-specific antigen < 10 at recurrence, a life expectancy >10 years at recurrence, and a negative metastatic workup. In this systematic review, we synthesize the current literature describing the oncologic efficacy and toxicity profile of salvage brachytherapy, prostatectomy, cryotherapy, and high-intensity focused ultrasound. We found 5-year biochemical control rates to be similar across treatments, in the range of 52%-56%, although patient selection and definition of failure was variable. Toxicity profiles were also distinct between local salvage modalities.
Semin Radiat Oncol 23:222-234 

Current National Comprehensive Cancer Network (NCCN) guidelines endorse the use of salvage local therapy consisting of:

- radical prostatectomy
- brachytherapy
- cryotherapy
- high-intensity focused ultrasound (HiFU).

Selected PubMed studies between January 1, 1990 and September 1, 2011.

**Total Included**
- 24 prostatectomy
- 13 brachytherapy
- 16 cryotherapy
- 7 HIFU

**Table 5** Toxicity and 5-year FFS by Salvage Therapy Type FFS: failure-free survival

| Salvage Therapy | Incontinence | Bladder Neck Stricture | Fistula |
|---|---|---|---|
| Brachytherapy | 6.16% | 7.48% | 3.09% |
| Prostatectomy | 49.69% | 26.09% | 2.43% |
| Cryotherapy | 16.40% | 4.15% | 1.61% |
| HiFU | 36.94% | 17.22% | 3.61% |

| | Number of studies reviewed with 5-year FFS | Total number of patients | 5-year FFS |
|---|---|---|---|
| Brachytherapy | 9 | 223 | 55.63% |
| Prostatectomy | 16 | 980 | 52.18% |
| Cryotherapy | 2 | 335 | 56.07% |
| HiFU | 1 | 22 | 52.00% |

- The cancer control rates do not differ substantially between the salvage modalities.
- Radical prostatectomy, however, carried the highest rates of both incontinence and bladder neck stricture.

It is difficult to compare the outcomes of the 4 salvage treatment modalities:

- there is no standard definition of failure within or across modalities.
- toxicities are not standardly reported or recorded.
- there is huge variation in the length of follow-up time between both modalities.

→ The toxicity profiles of each modality are distinct.

EUROPEAN UROLOGY FOCUS 2 (2016) 158–171

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


Platinum Priority – Review – Prostatic Disease

# Comparative Oncologic and Toxicity Outcomes of Salvage Radical Prostatectomy Versus Nonsurgical Therapies for Radiorecurrent Prostate Cancer: A Meta–Regression Analysis

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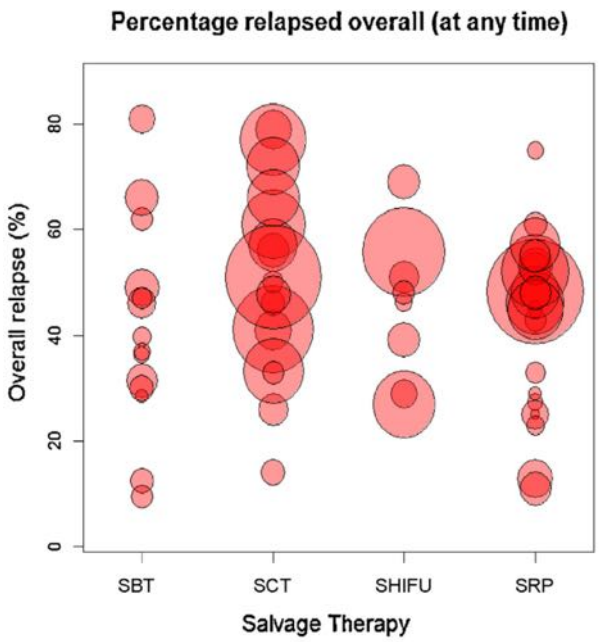
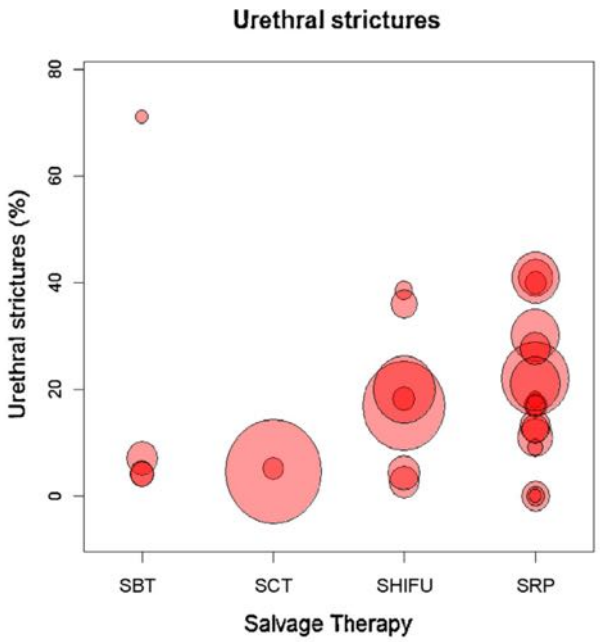
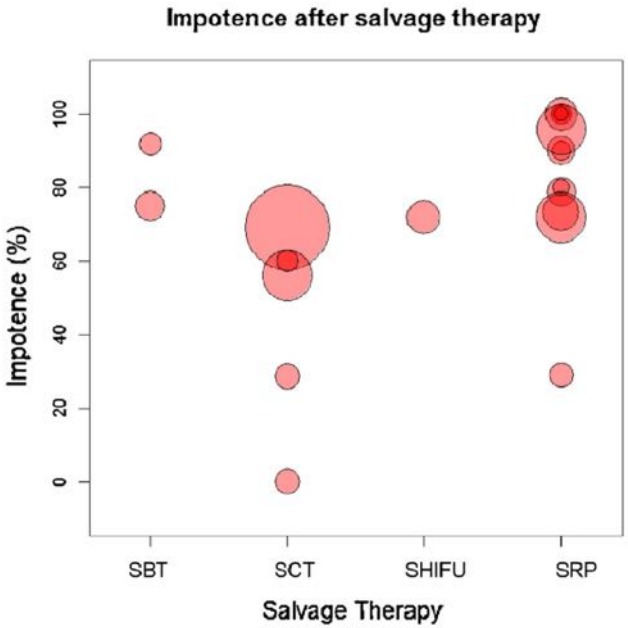
[a] *Department of Surgery, Basildon and Thurrock University Hospital, Essex, UK;* [b] *Health Services Research Unit University of Edinburgh, Edinburgh, UK;* [c] *Department of Urology, Addenbrooke's University Hospital, Cambridge, UK;* [d] *Academic Urology Group, Department of Surgery and Oncology, University of Cambridge, Cambridge Biomedical Campus, Cambridge, UK*

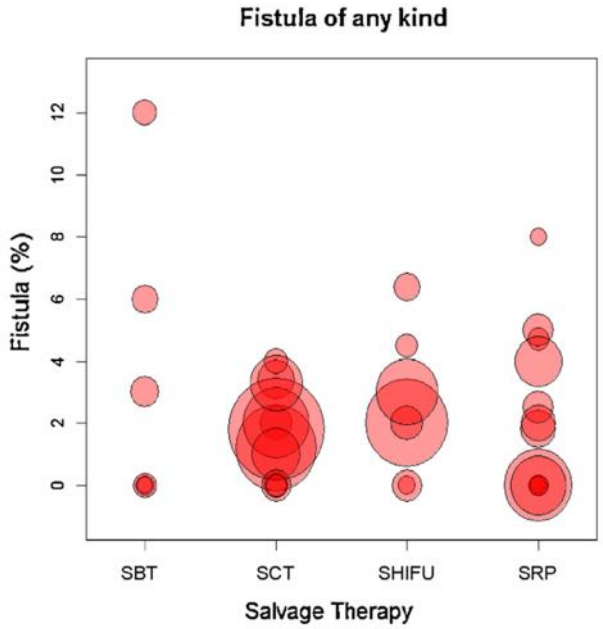
*Evidence acquisition:* We performed a systematic review of PubMed/Medline citations according to the Preferred Reporting Items for Systematic Review and Meta-analysis (PRISMA) statement. We included 63 articles in the analysis (25 on SRP, 8 on SHIFU, 16 on SCT, 14 on SBT).

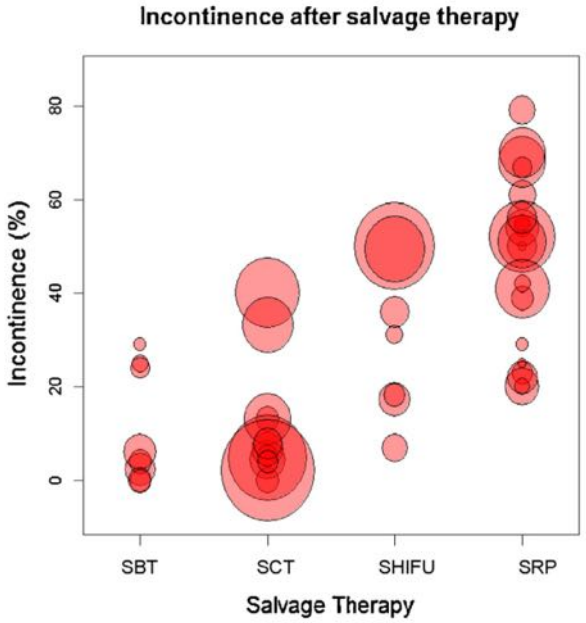
**Conclusions:** current salvage modalities appear to have similar oncologic and toxicity outcomes. In particular, SRP does not appear to confer any added benefit in terms of disease control compared with more minimally invasive approaches but instead may potentially increase functional debility.




SBT = salvage brachytherapy;
SCT = salvage cryotherapy;
SHIFU = salvage high-intensity focused ultrasound;
SRP = salvage radical prostatectomy.

Online version at http://www.minervamedica.it

Minerva Urologica e Nefrologica 2017 February;69(1):26-37
DOI: 10.23736/S0393-2249.16.02797-1

REVIEW

# Salvage robotic prostatectomy for radio recurrent prostate cancer: technical challenges and outcome analysis

Homayoun ZARGAR [1, 2], Alastair D. LAMB [3], Bernardo ROCCO [4], Francesco PORPIGLIA [5], Evangelos LIATSIKOS [6], John DAVIS [7], Rafael F. COELHO [8], Julio M. POW-SANG [9], Vipul R. PATEL [10], Declan G. MURPHY [2, 3]

EVIDENCE SYNTHESIS: We report on ten case series including 197 men undergoing sRARP after varying modalities of radiotherapy. Over two thirds are recurrence free at the time of follow-up but with continence rates of only 60% and potency rates of only 26%. Complications requiring intervention are few at 16% though higher than primary RARP.

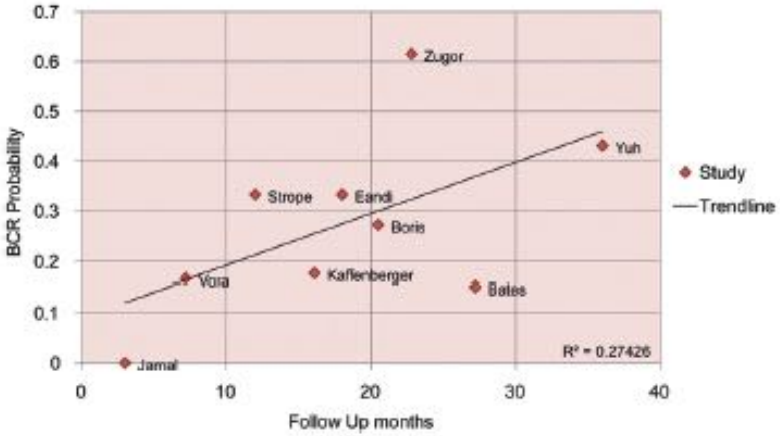



Figure 3.—BCR rates are higher in those series with longer follow-up. This suggests that follow-up duration is important for establishing the oncological durability of sRARP.

# C.R.M. - 69aa

APR: CardioASA in prevenzione primaria, no comorbidità.

ANAMNESI UROLOGICA:

2015 PSA 10,6 ng/ml: biopsia prostatica: 5 prelievi a sinistra negativi; 5 prelievi a destra con adenoca Gleason 3+4. cT1

Aprile 2015: Brachiterapia (LDR)

Ottobre 2015: PSA 0,89 ng/ml; Gennaio 2016: 0,59 **Aprile 2016: 0,43** Ottobre 2016: 0,88

Aprile 2017: 1.63 → PETCol: Negativa - **Luglio 2017: 3,62**

E.O: complessivamente negativo

DRE: esiti Brachiterapia

Ripetute PET colina, TC e scinti: negative

24/8/2017 Prostatectomia radicale retropubica + LAD con EI: ypT2c (5% del tessuto prostatico)-pN0 (18 N), Gleason score non attribuibile.

Dimesso in IV GPO, CV rimosso in VII GPO. A 3 mesi: continenza urinaria 1-2 pads/die, scarsa funzione erettile (sta assumendo inibitori di PDE-5). PSA a 1 mese dall'intervento: 0,03. PSA a 3 mesi dall'intervento: 0,03

Persistente dolore perineale postoperatorio. Eseguita RM pelvica: assenza di raccolte in pelvi e di reperti che potrebbero indicare la causa della sintomatologia.

Iniziato trattamento con corticosteroidi per os con successivo lieve miglioramento della sintomatologia

# S.P. – 74 anni

- 2011 PSA 59 ng/ml -> Bp Adk Prostatico G.S. 4+4 in tutti i prelievi.
- Radioterapia (76 Gy, senza linfonodi) dal luglio 2011 al settembre 2011 + Bicalutamide per 6 mesi.
- Nadir PSA Maggio 2012: 0,09 ng/ml.
- Dicembre 2014 PSA 2,8 ng/ml –> Inizia Decapeptyl mensile con PSA a Maggio 2015 0,3 ng/ml.
- Da Novembre 2016 ripresa della crescita del PSA. Ultimo PSA Novembre 2017: 4,1 ng/ml. Tempo raddoppiamento < 6 mesi. Testosterone soppresso.
- Gennaio 2015 scintigrafia ossea negativa.
- Ottobre 2017 TC torace e addome neg. (senza m.d.c.): negativa.
- PET con colina (11/17): ipercaptazione ampia in sede prostatica sinistra, non altre ipercaptazioni.
- ER: prostata con aumento di consistenza lobo sinistro con limiti indistinti
- Ottobre 2017 Creat 1,6 mg/dL.

# Prostatectomia radicale di salvataggio

## Cardine: la selezione del paziente

- Non comorbidità importanti
- Conferma istologica di recidiva locale
- Informazione sulle conseguenze dell'intervento e sui possibili affetti avversi
- Malattia curabile prima del trattamento primario: stadio < T3b, PSA preoperatorio <10-15 ng/ml, GS <8, cN0, cM0
- PSA doubling time >12 mesi
- Intervallo libero da recidiva dopo terapia primaria di almeno 2 (se RT) o 3 anni (se brachiterapia)
- Assenza di gravi sintomi urinari o incontinenza

Rozet et al. CCAFU French guidelines 2016-2018 on prostate cancer. Prog Urol 2016; 27: S95-143

## Problematiche tecniche:

- Fibrosi
- Perdita dei piani chirurgici
- Danno vascolare → ridotta capacità di guarigione dei tessuti

## Problematiche del paziente:

- Età più avanzata rispetto al pz ''standard'' → maggiori comorbidità
- Gleason score e stadio clinico-patologico più sfavorevole