Prostatectomy as salvage therapy

Paul Cathcart - Guy’s & St Thomas’ NHS Trust, London
Outcomes After Prostate Brachytherapy Are Even Better Than Predicted

Steven J. Frank, MD; Lawrence B. Levy, MS; Marco van Vulpen, MD, PhD; Juanita Crook, MD; John Sylvester, MD; Peter Grimm, DO; Thomas J. Pugh, MD; and David A. Swanson, MD

Table 1. Patient Characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Princess Margaret Hospital (n = 683)</th>
<th>University Medical Center Utrecht (n = 731)</th>
<th>Seattle Prostate Institute (n = 402)</th>
<th>Totals (n = 1816)</th>
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<tbody>
<tr>
<td>Gleason sum score</td>
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<td>110</td>
<td>528</td>
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<td>731</td>
<td>301</td>
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<td>Pretreatment PSA level, ng/mL</td>
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<td>Minimum</td>
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<td>Mean</td>
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<td>10.3</td>
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<tr>
<td>Maximum</td>
<td>18.4</td>
<td>100.0</td>
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</tbody>
</table>

Abbreviations: PSA, prostate-specific antigen.
Quality of Life and Satisfaction with Outcome among Prostate-Cancer Survivors

Martin G. Sanda, M.D., Rodney L. Dunn, M.S., Jeff Michalski, M.D., Howard M. Sandler, M.D., Laurel Northouse, R.N., Ph.D., Larry Hembroff, Ph.D.,

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**Table D: Patient Interview Completion Rates**

<table>
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<th>Before Treatment</th>
<th>Follow-up (mo)</th>
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<tr>
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<tr>
<td>No. of patients</td>
<td>1201</td>
<td>1201</td>
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<tr>
<td>No. of patients who completed the interview</td>
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**Graph A:**
- Prostatectomy
  - Nerve-sparing
  - Non-nerve-sparing

**Graph B:**
- Radiotherapy
  - Radiotherapy alone
  - Radiotherapy plus NHT

**Graph C:**
- Brachytherapy
  - Brachytherapy alone
  - Brachytherapy plus radiotherapy, NHT, or both

**Graph D:**
- Sexual Score
- Urinary Incontinence Score
- Bowel or Rectal Score
- Visceral Hemorrhage Score
• Attributes of brachytherapy appeal to young men who place high utility on genitourinary function

• At risk of recurrent disease for decades following prostate cancer treatment

• Salvage treatment very important issue
Definition of biochemical failure

- PSA nadir + 2
- Predicts prostate cancer:
  - metastases
  - Death
- Does not predict local recurrence
- Chance of cure from local therapy low
  - Identifying patients too late
- Confounding factors
  - PSA bounce (15%), expected rise in PSA after stopping hormones
Local versus systemic recurrence

• Local recurrence
  • Rising PSA confirmed on repeat evaluation
  • Positive prostate biopsy
    • Need to wait at least 18 months after primary treatment
  • Negative metastatic screen

• Systemic disease
  • Rapid PSA DT (<3 months)
    • Only 10% of patients
  • Positive metastatic evaluation
Evaluation for local salvage therapy

• Is the cancer curable?
  • Pre-primary treatment characteristics
    • Gleason 7 or less, Organ confined, PSA less than 20
  • Pre-salvage characteristics
    • Gleason 7 or less, Organ confined, PSA less than 20

• Is the patient appropriate
  • Good health, life expectancy>10 years
  • Highly motivated, willing to accept risk of salvage surgery

• Would the treatment be safe?
  • No evidence of radiation cystitis or proctitis – often brachytherapy patients do not have unlike EBRT

• Conclusion – patients opting for brachytherapy as primary prostate cancer therapy often good candidates for salvage prostatectomy
Work-up

• Need to identify local recurrent disease from metastatic disease
  • (a proportion have micrometastatic disease)

<table>
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<th>PSA recurrence after RT</th>
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<tr>
<td>Perform prostate mpMRI only in patients who are considered candidates for local salvage therapy, use mpMRI to localise abnormal areas and guide biopsies.</td>
<td>3</td>
<td>B</td>
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<tr>
<td>Choline PET/CT imaging is recommended to rule out lymph nodes or distant metastases in patients fit enough for curative salvage treatment.</td>
<td>2b</td>
<td>B</td>
</tr>
<tr>
<td>Perform bone scan and/or abdominopelvic CT only in patients with PSA &gt;10 ng/mL, or with adverse PSA kinetics (PSA-DT &lt; 6 months, PSA velocity &gt; 0.5 ng/mL/month).</td>
<td>3</td>
<td>A</td>
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</table>

PSMA PET imaging the most useful tool
Needle biopsy of limited value within 12 months of radiation due to tumour cell death

Slow tumour death after radiation due to EBRT causing necrosis only after cell has undergone a cell division

Only treat patients with a Gleason gradable prostate cancer

Need to differentiate from prostatic adenocarcinoma with severe radiation change
Biopsy

- Avoid the rectum
- Go transperineal
Distant/local recurrence after brachytherapy – how common?

- 2869 men
- 7% (213) experienced BCF (Phoenix definition)
  - 30% positive post-treatment biopsy
  - PSA doubling time most predictive of a positive biopsy
- 10 year MFS - 70% in men with BCF

Overall
- 1/3 harbour a component of local failure
- 1/4 demonstrate clinical metastases

Stone et al.
THE IMPORTANCE OF LOCAL CONTROL IN EARLY STAGE PROSTATE CANCER: OUTCOMES OF PATIENTS WITH A POSITIVE POST-RADIOThERAPY BIOPSY TREATED ON RTOG 9408

Daniel J. Krauss, MD1, Chen Hu, PhD2, Jean-Paul Bahary, MD3, Luis Souhami, MD1, Elizabeth M. Gore, MD3, Susan Maria Jacinta Chafe, MD3, Mark H. Leibenhaut, MD1, Samir Nareyek, MD3, Javier Torres-Roca, MD3, Jeff Michalski, MD1, Kenneth L. Zeltzer, MD1, Viroon Donavanik, MD1, Howard Sandler, MD1, David G. McGowan, MD1, Christopher U. Jones, MD1, and William U. Shipley, MD1,4

![Graphs showing disease-specific survival, overall survival, and distant metastasis](chart)

- **Disease-Specific Survival (%):**
  - Rebiopsy Negative: 100%
  - Rebiopsy Positive: 98.5%
  - Failed: 13/585 (2.3%)
  - Total: 20/246 (8.1%)

- **Overall Survival (%):**
  - Rebiopsy Negative: 100%
  - Rebiopsy Positive: 99%
  - Dead: 171/585 (29.1%)
  - Total: 246/246 (100%)

- **Distant Metastasis (%):**
  - Rebiopsy Negative: 0%
  - Rebiopsy Positive: 0.5%

- **Failure Rates:**

  - **Total Patients at Risk:**
    - Rebiopsy Negative: 585
    - Rebiopsy Positive: 246
  
  - **Years at Risk:**
    - Rebiopsy Negative: 585
    - Rebiopsy Positive: 246

- **Statistical Significance:**
  - Disease-Specific Survival: p=0.0001 (Gray)
  - Overall Survival: p=0.1194 (Log-Rank)
  - Distant Metastasis: p=0.0008 (Gray)

**Legend:**
- GS 7-10: Rebiopsy Neg Failed 9 Total 179
- GS 7-10: Rebiopsy Pos Failed 17 Total 100

**Note:**
- The graphs illustrate the impact of rebiopsy on patient outcomes, with significant improvements in disease-specific and overall survival rates for patients with negative rebiopsies compared to those with positive rebiopsies. The data suggest that rebiopsy can be a valuable tool in assessing the effectiveness of radiotherapy in the management of early stage prostate cancer.
Salvage surgery
Difficulty of salvage surgery

- Hierarchy of salvage surgery difficulty (hardest – easiest)
  - Post EBRT plus Brachytherapy therapy boost
  - Post EBRT
  - Post brachytherapy
  - Post cryotherapy
  - Post HIFU/electroporation/PDT

- Hierarchy of salvage surgery outcomes (Best-worst)
  - Post HIFU/electroporation/PDT
  - Post brachytherapy (dependant on placement of seeds at apex)
  - Post Cryotherapy
  - Post EBRT
  - Post EBRT plus Brachytherapy therapy boost
Progression Free Probability (PFP) after salvage surgery

Fig. 1 – Kaplan-Meier probability of freedom from recurrence following salvage prostatectomy.
Death after salvage surgery

Fig. 3 – Cumulative incidence of death from prostate cancer following salvage prostatectomy.

Prostate Cancer
Oncologic Outcome and Patterns of Recurrence after Salvage Radical Prostatectomy
Philippe Paparel, Angel M. Cronin, Caroline Savage, Peter T. Scardino, James A. Eastham
Clinical Local recurrence after salvage surgery

• 124 men
  • 75 free of BCR
  • Only 1 patient experienced clinical local recurrence
  • (hormone refractory with bone mets)
  • Urinary obstruction: TURP after salvage RP
  • Specimen Gleason 5+5=10
Results

• At 10 years after salvage surgery
  • BCR-free: 37% (95% CI: 31%-43%)
  • Metastasis-free: 77% (95% CI: 71%-82%)
  • PCSS: 83% (95% CI: 76%-88%)

• Long-term progression-free probability by pathological stage is comparable to standard radical prostatectomy
  • Many not organ-confined
• Urinary incontinence 29-90%
• Sexual dysfunction up to 100%
• Anastomotic stricture 7-41%
• Rectal injury 0-28%
• Major complication 0-25%
• Time trends suggest complication rate improving
• Not so for anastomotic stricture
  • The robot may help

Less for salvage surgery
post brachytherapy
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<th>First author</th>
<th>Yr</th>
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<th>Technique</th>
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<th>Pre-SRP EF, %</th>
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</table>

SRP = salvage radical prostatectomy; EF = erectile function; SCP = salvage cystoprostatectomy; RCP = radical cystoprostatectomy; Ex = exenteration; PLND = pelvic lymph node dissection; SRP/Cath = SRP with urinary catheterizable reconstruction.

* With sildenafil.

University of California, Los Angeles, Prostate Cancer Index.

Cancer Control and Functional Outcomes of Salvage Radical Prostatectomy for Radiation-recurrent Prostate Cancer: A Systematic Review of the Literature

Debre C. Chade, James Eastham, Markus Graefen, Jim C. Ha, R. Jeffrey Karmes, Laurence Knize, Francesco Montorsi, Hendrik van Poppel, Peter T. Scardino, Shitrook Hoffman, Shariat
Locally recurrent prostate cancer after initial radiation therapy: A comparison of salvage RP versus cryotherapy

• Retrospectively reviewed patients
  • Surgery at the Mayo clinic, cryotherapy at MD Anderson
• Eligibility criteria
  • PSA <10
  • Post biopsy Gleason score <8
  • Prior radiation therapy alone without hormone therapy

Pisters et al. 2009 182 (2):517-527
Conclusion

• Young healthy patients with recurrent prostate cancer after radiation therapy should consider salvage surgery as it offers superior biochemical disease free survival and potentially offer the best chance of cure

• ‘Best’ long-term oncological outcomes
• Higher rates of incontinence and BNC

Pisters et al. 2009 182 (2):517-527
Cases

Posterior
• 45 year old IT worker presented in 2013
• PSA 13.2, 14ml prostate, Gleason 4+3=7, 3/12 cores on TRUS, MCCL 5mm, PIRAD 2 on MRI
• PMH – Diabetes, raised Cholesterol
• TP biopsy for assessment for brachytherapy
  • Gleason 4+4=8, 2/24, MCCL 1mm
• Dynamic prostate brachytherapy boost
  • (optimised implant), 145 Gy

<table>
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<th>Prostate</th>
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<td>Volume (cm³)</td>
<td>27.98</td>
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<td>V100 (%)</td>
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<td>92.99%</td>
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<td>D90 (Gy)</td>
<td>149.88 (103.37%)</td>
<td>159.37 (109.91%)</td>
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</table>
• PSA dynamics
  • 7.5, 2.6, 1.5, 4.6, 5.7, 13.5, 14.6
• MRI
  • Diffuse non-specific uptake
• Choline PET
  • Small intense focus left of midline of prostate
  • Also identified a polp in bowel (low grade adenoma)
• TP prostate biopsy
  • 14/24 cores, Gleason 4+4=8, 6/6 sites, MCCL 12mm
• Patient self-referred to Professor Jelle Barentsz, Nijmegen, Radboud University
  • Combidex (ferumoxtran-10) MRI (nano-sized iron oxide particles)
    • No metastatic disease evident
PET imaging very useful
• Management
  • Radical prostatectomy
  • Bilateral nerve sparing procedure

• Immediate Outcome
  • Pathology
    • Gleason 4+4=8, T2, 0/13 nodes, margins clear
  • No complications
    • 1 post-op night in hospital

• Longer-term Outcome
  • Oncological
    • PSA<0.03 at 3 and 6 months
  • Functional
    • Continent – no pads at 8 weeks
    • Pump, pills, Erectile function improving sufficient for intercourse
Anterior disease

Prostate brachytherapy in 2004
PSA nadir of 0.2 documented in 2009

MRI anterior lesion
• The PSMA PET CT scan indicates avidity within the right anterior prostate
• Targeted Transperineal biopsies - Gleason 4+3
• Significant radiation effect noted
Doesn’t show much
T3b disease
Retroperitoneal disease post-op
• The surgery is difficult
• Few urologists perform salvage prostate surgery
• The surgery requires unique principles to be applied
• The robot is just a tool and unlikely to make a huge difference to outcome of salvage prostate surgery
Recurrent Prostate Cancer (RPC) clinic

Overview

Prostate cancer is the most common cancer to affect men in the UK with over 40,000 men being diagnosed with the disease each year. Common primary treatments employed to treat prostate cancer include surgery to remove the prostate, radiation therapy (external beam radiation therapy (EBRT), brachytherapy), cryotherapy and High Intensity Focused Ultrasound (HIFU).

Regardless of the initial treatment, a proportion of men will experience primary treatment failure exhibiting evidence of recurrent prostate cancer (RPC), usually demonstrated by a rising PSA (Prostate Specific Antigen) reading after therapy.

The proportion of men experiencing recurrent prostate cancer (RPC) after primary treatment ranges from 10 to 50% depending on the initial treatment they received in addition to the extent and aggressiveness of their prostate cancer at initial diagnosis.
Recurrent Prostate Cancer (RPC) team

Surgeons
Mr Paul Cathcart
Mr Rick Popert

Clinical Oncology
Dr Stephen Morris
Dr Teresa Guerrerourbano

Medical Oncology
Dr Simon Chowdhury

Radiology/Nuclear medicine
Dr Giles Rottenberg
Professor Gary Cooke
Making a referral to the recurrent prostate cancer (RPC) clinic

Referral contacts

Guy's Hospital
Department of urology
1st floor, Southwark Wing
Great Maze Pond
London SE1 9RT

Tel: 020 7188 7338
Email:

Email: prostatecns@gstt.nhs.uk,
linda.boorman@gstt.nhs.uk,
paul.cathcart@gstt.nhs.uk

Who can refer?

Referrals to the recurrent prostate cancer (RPC) clinic are welcomed from GPs or specialists in the patient's local hospital. Direct approaches from patients by email are also accepted.