

Farmaci innovativi e ipofrazionamento

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30 settembre, 1-2 ottobre 2016

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SALVAGE IMAGE-GUIDED STEREOTACTIC SECOND RE-IRRADIATION OF LOCAL RECURRENCE IN PROSTATE CANCER:

SOMETHING VENTURED, COULD SOMETHING BE GAINED?

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BACKGROUND

Second most common cancer in men (SEER, 2016)

Prostate cancer represents 10.7% of all new cancer cases in the U.S.



Estimated New Cases in 2016	180,890
% of All New Cancer Cases	10.7%
Estimated Deaths in 2016	26,120
% of All Cancer Deaths	4.4%

Prostate cancer is most frequently diagnosed among men aged 65-74.

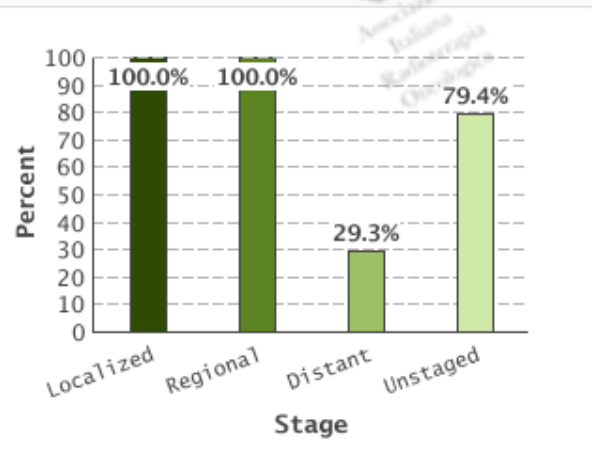
Median Age At Diagnosis	66
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The percent of prostate cancer deaths is highest among men aged 75-84.

Median Age At Death	80
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Diagnosis: the earlier the better → 80% of new diagnosis are in early stage, 12% local stage, 4% metastatic stage, 4% unknown stage

5-Year Relative Survival

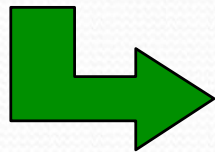


Year	1975	1980	1985	1990	1995	2000	2004	2008
5-Year Relative Survival	66.0%	70.2%	75.0%	88.5%	95.7%	98.8%	99.7%	99.1%

BACKGROUND

Biochemical Failure: Phoenix definition (ASTRO and the Radiation Therapy Oncology Group, 2005) → PSA rise of at least 2 ng/mL above the nadir

Positive Digital Rectal Exploration



RECURRENCE

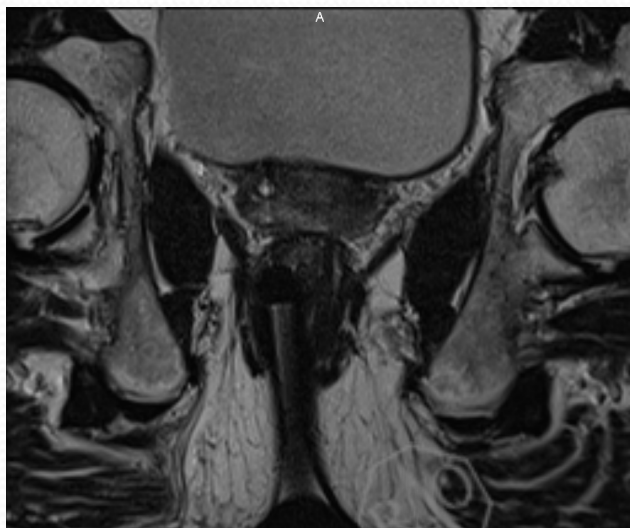


RE- STAGING (NCCN 2016)

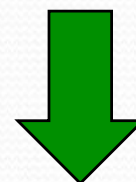
- Bone scan
- Prostate MRI
- Consider:
 - TRUS biopsy
 - Abdominal/ pelvic CT/ MRI
 - C-11 choline PET

BACKGROUND

Intraprostatic failure after primary EBRT \pm ADT: 22- 69% (Neppele- Huber 2012, Kuban 2003)



COULD THE PATIENT
BE A CANDIDATE FOR LOCAL
THERAPY?



- Original clinical stage T1- T2, Nx or N0
 - Life expectancy > 10 years
 - PSA now < 10 ng/mL



Salvage therapy of intraprostatic failure after radical external-beam radiotherapy for prostate cancer: A review

Filippo Alongi^a, Berardino De Bari^{b,*}, Franco Campostrini^c, Stefano Arcangeli^d,
Deliu Victor Matei^e, Egesta Lopci^f, Giuseppe Petralia^g, Massimo Bellomi^g, Arturo Chiti^f,
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THERAPEUTIC OPTIONS:

- ADT (Androgen Deprivation Therapy)
 - Salvage prostatectomy
 - Cryotherapy
 - High-intensity focused ultrasound (HIFU)
- External-beam radiation therapy (EBRT)
 - Brachytherapy (BRT)



BACKGROUND

CRYOTHERAPY

- Urinary incontinence 73%
- Sexual impotence 72%
- Obstructive symptoms 67%
- Severe perineal pain 8%
- Rectal fistulas 1-3%

HIFU

- Late urethral stricture 7.8- 36%
- Urinary incontinence 7- 50%
- Recto- urethral fistula 2- 6%

Cancer/Radiothérapie 20 (2016) 275–281

Original article

Stereotactic body re-irradiation therapy for locally recurrent prostate cancer after external-beam radiation therapy: Initial report



Ré-irradiation stéréotaxique robotisée de récurrence locale de cancer de prostate après radiothérapie externe : résultats préliminaires

G. Janoray^{a,b,*}, A. Reynaud-Bougnoux^{a,b}, A. Ruffier-Loubière^{a,b}, G. Bernadou^{a,b}, Y. Pointreau^{a,b}, G. Calais^{a,b}

BJR

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FULL PAPER

Salvage image-guided intensity modulated or stereotactic body reirradiation of local recurrence of prostate cancer

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PATIENTS AND METHODS

n= 3

Mean age= 76 years

Mean PSA at relapse = 3.7 ng/mL

Mean biochemical PFS from first re- EBRT= 27.8 months

Relapse diagnosed by mpMRI and/ or choline- PET

No distant metastasis

Clinical evaluation: No genitourinary (GU) or gastro- intestinal (GI) symptoms from previous radiation courses (RTOG/ EORTC)



Società Italiana di Radiobiologia
MATERIALE NON RIPRODUCIBILE

PATIENTS AND METHODS

	<u>Treated Volume</u>	<u>Technique</u>	<u>Total Dose; Dose/ fraction</u>	<u>BED ($\alpha/\beta = 1.5 \text{ Gy}$)</u>
Patient 1				
Sept- Nov 2005 (67 ys)	Prostate+ 1/3 Seminal Vescicles	3D- CRT	76 Gy; 2 Gy/ fract.	177.3 Gy
Feb 2010 (72 ys)	Prostate	SBRT CyberKnife®	30 Gy, 6 Gy/ fract.	150.0 Gy
Sept- Oct 2013 (75 ys)	Intraprostatic lesion (apex)	SBRT CyberKnife®	25 Gy, 5 Gy/ fract.	108.3 Gy
Patient 2				
Jan- March 2005 (65 ys)	Prostate+ 1/3 Seminal Vescicles	3D- CRT	76 Gy, 2 Gy/ fract.	177.3 Gy
March 2012 (72 ys)	Prostate	SBRT CyberKnife®	25 Gy, 5 Gy/ fract.	108.3 Gy
Sept 2015 (76 ys)	Intraprostatic lesion (left lobe)	SBRT CyberKnife®	30 Gy, 6 Gy/ fract.	150.0 Gy
Patient 3				
Feb- March 2003 (52 ys)	Prostate	3D- CRT + Brachytherapy	50 Gy; 2 Gy/ fract.+ 100 Gy I-125 seeds	N.E.
Apr- May 2010 (59 ys)	Prostate	3D- CRT	30 Gy; 6 Gy/ fract.	150.0 Gy
Jul 2012 (61 ys)	Peri- prostatic node	SBRT VERO®	24 Gy 8 Gy/ fract.	152.0 Gy

BED: Biologically Effective Dose; 3D- CRT: 3 Dimensional- Conformal Radiation Therapy; SBRT: Stereotactic Body Radiation Therapy; NE: Not Evaluable

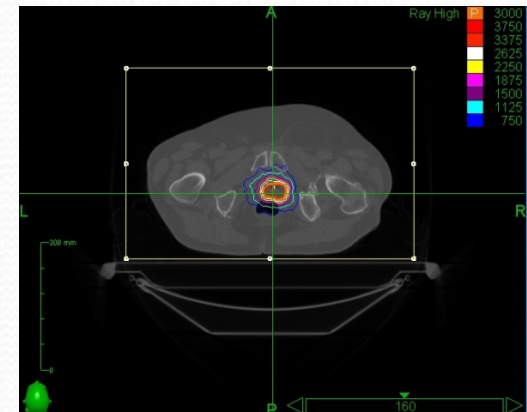
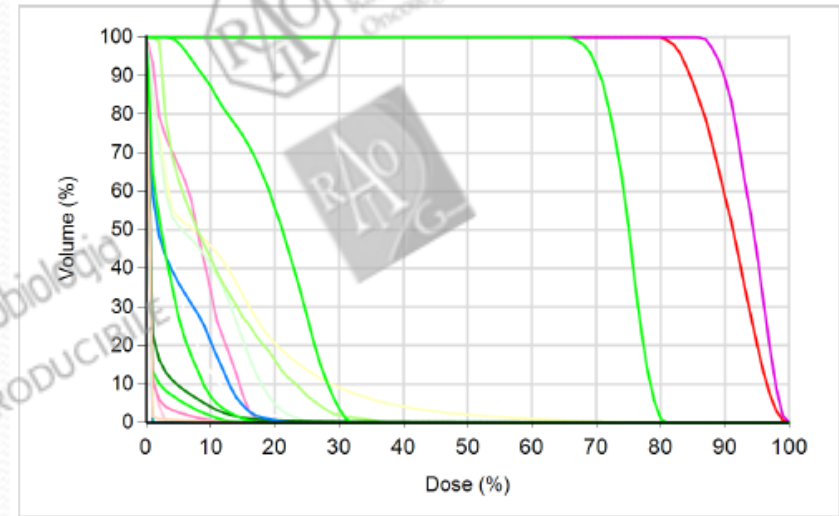
PATIENTS AND METHODS

- Previous treatment plans analysis

- Modified constraints for re-irradiation
 - Bladder: $D_{30\%} < 10.6 \text{ Gy}$
 - Rectum: $D_{30\%} < 13.5 \text{ Gy}$
 - Femoral heads: $V_{40\%} < 5\%$
 - Penile bulb: $D_{29\text{Gy}} < 50\%$

- High precision technology: IGRT+ Stereotactic technique
 - Better dose delivery
 - Set-up verification
 - Control of organ motion and inter-fraction variability

DVH: Relative Dose



RESULTS

Mean follow-up time from 2nd Re- EBRT = 28.9 months

- Toxicity (RTOG/ EORTC):
 - No acute GU or GI event
 - No late GU or GI event
- Efficacy of 3rd RT course → Biochemical and clinical response in **all** patients

Biochemical relapse: 1 pt (PFS = 22 months)

3rd Local relapse: 1 pt (PFS= 23 months)

No Evidence of Disease: 1 pt

CONCLUSIONS



- ✗ Need for larger case series
- ✗ Need for longer follow- up
- ✗ Sub- optimal disease control?
- ✗ Radioresistance issues → Radiobiology?

- ✓ Safety: no acute or late toxicity reported
- ✓ (Still) sub- optimal disease control?
- ✓ Radiosensitivity issues → Radiobiology?

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GRAZIE PER L'ATTENZIONE!



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