

Definitive Focal Therapy: Are we Ready to Compete with Cryotherapy, HIFU and Laser Ablation Techniques?

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Disclosures

Speaking Honorarium

Received honorarium and travel support for participation in this meeting

Research Collaborations

Montefiore Medical Center maintains ongoing research collaboration agreements with Accuray and Varian Medical Systems

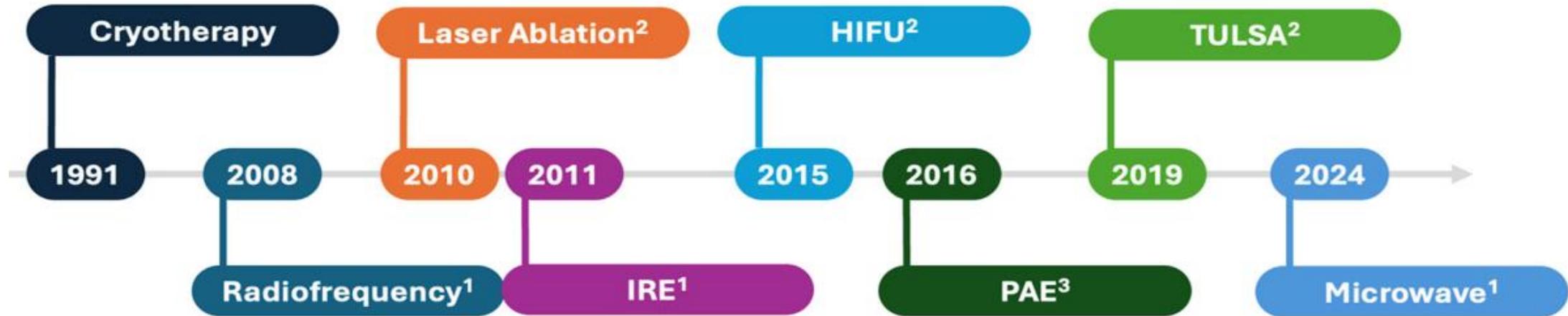
Outline

- **Focal Therapy**
 - Modalities
 - Indications
 - Outcomes: QOL, Cancer

- **Can we deliver Focal Therapy using Radiation?**
 - Data on focal brachytherapy-HDR & LDR
 - Data on focal EBRT/SBRT
 - Technical considerations

What is focal therapy?

A targeted delivery of ablative energy to a region of cancer in the prostate (subtotal) with the intention of inducing cell death



Focal Therapy- Modalities

Cryotherapy (CT)

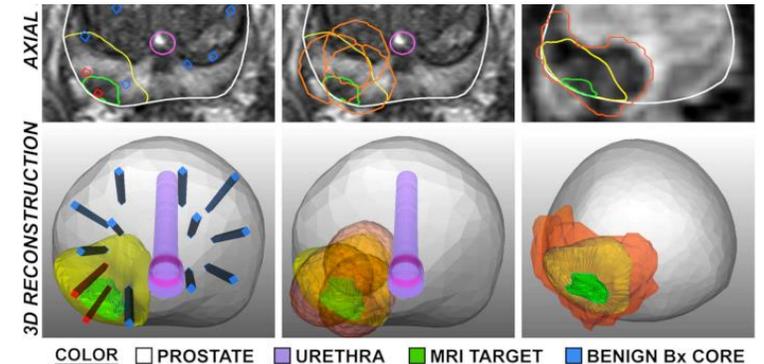
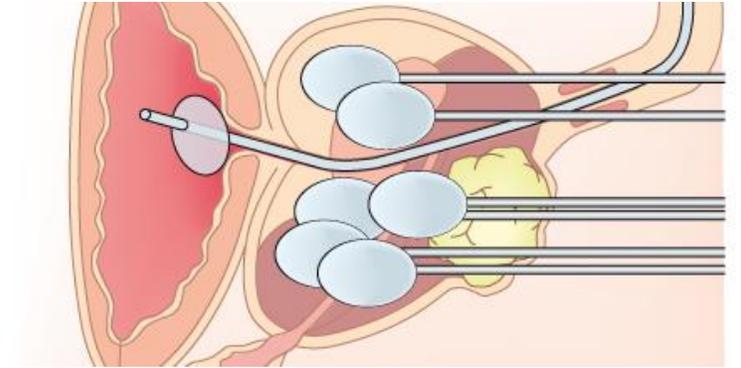
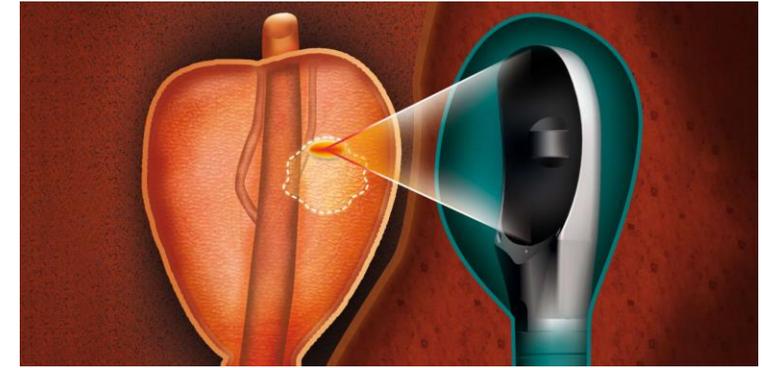
- Extremely low temperatures - cellular damage
- Trans-perineal probes/needles
- Sedation- Local or General
- Anterior/Apical tumors

High Frequency Ultrasound (HIFU)

- High frequency ultrasound - thermal ablation
- Transrectal or trans-urethral probe
- Sedation-Local or General
- Posterior tumors

Laser Ablation (LA)

- Focused laser energy (thermal) - vaporize/coagulate
- Trans-perineal or trans-rectal
- Sedation- Local or General
- Better temperature control



COLOR □ PROSTATE □ URETHRA □ MRI TARGET □ BENIGN Bx CORE

Focal Therapy-Modalities

Photodynamic Therapy (PDT)

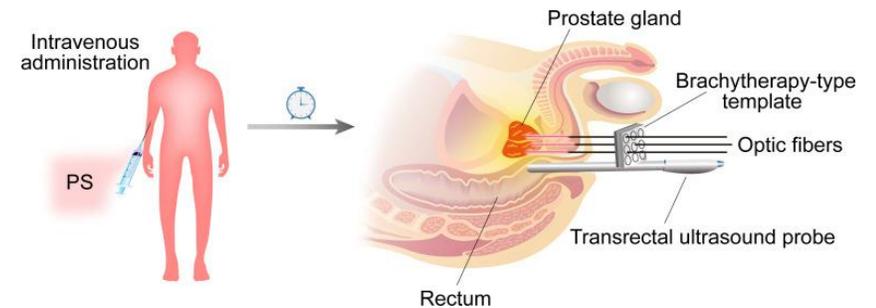
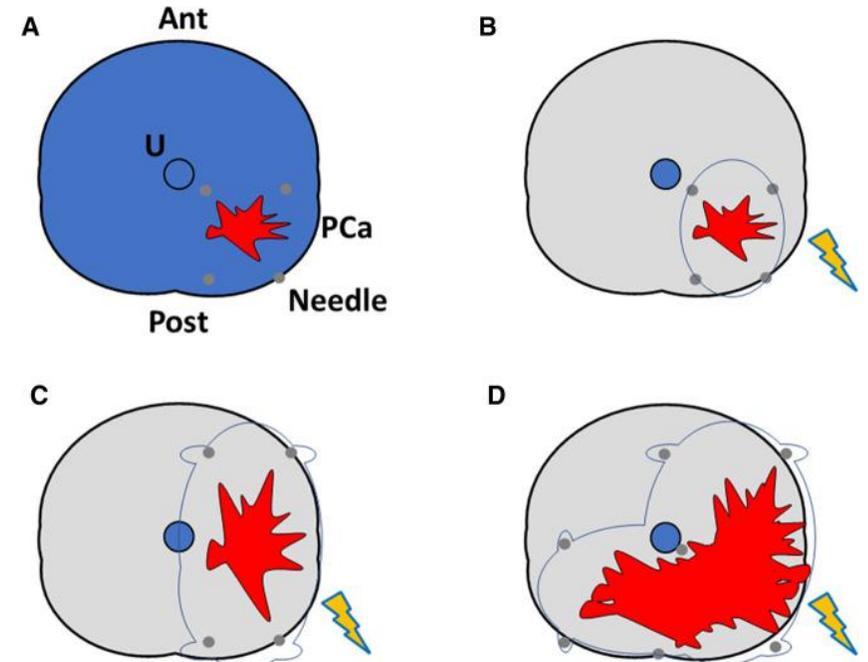
- Light activated photosensitizer-ROS
- Trans-perineal needles
- Sedation- Local or General
- Selective tumor targeting

Radiofrequency Ablation (RFA)

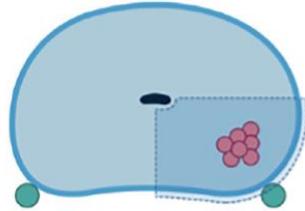
- High frequency electric current- Thermal injury
- Trans-perineal needles
- Sedation- Local or General

Irreversible Electroporation (IRE)

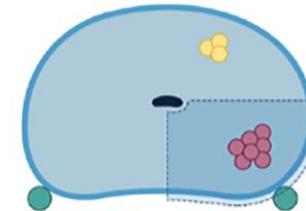
- Electric pulses- nanopores in cell membrane
- Non-thermal
- Trans-perineal
- Sedation: General or complete neuromuscular blockade



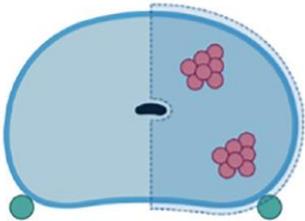
Types of Ablation



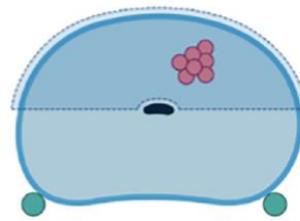
Quadrant ablation



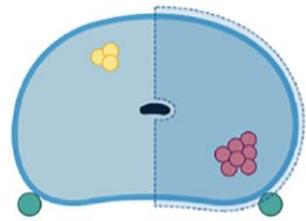
Quadrant ablation with untreated low risk disease



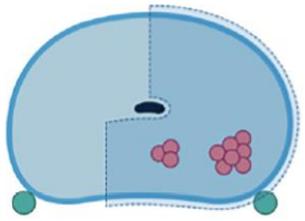
Hemi- ablation



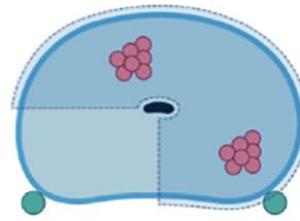
Hemi- ablation



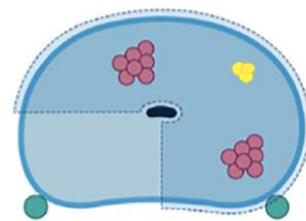
Hemi- ablation with untreated low risk disease



Hockey- Stick ablation



Hockey- Stick ablation



Hockey- Stick ablation with included low risk disease

Overview of focal therapy technologies for prostate cancer

Modality	Device name	Manufacturer	Technology features	Imaging integration	Regulatory approvals	Procedural cost (USD) (US and Europe estimates)	Equipment purchase cost (USD)
HIFU	Ablatherm	EDAP TMS	Noninvasive, ultrasound-guided, thermal ablation	MRI, Ultrasound	FDA, CE	\$15,000–\$25,000	\$300,000–\$500,000
	Sonablate	SonaCare					
	Focal One	Medical				\$20,000–\$30,000	\$500,000–\$700,000
	TULSA-PRO	Profound Medical					
Cryotherapy	Boston Scientific (visual ICE)	Boston Scientific	Freeze–thaw cycles, transperineal/transrectal approach	MRI, Ultrasound	FDA, CE	\$12,000–\$20,000	\$180,000–\$300,000
	Cryocare	Endocare				\$10,000–\$20,000	\$150,000–\$250,000
	Galil SeedNet	Galil Medical					
IRE	NanoKnife	AngioDynamics	Nonthermal, electric field–induced cell death	Ultrasound, CT, MRI	FDA, CE	\$20,000–\$35,000	\$250,000–\$400,000
	Dophi™ N3000	SurgNova, China				\$5,000–\$8,000	\$80,000–\$120,000
LA	Visualase	Medtronic	Minimally invasive, fiberoptic laser delivery	MRI, Ultrasound	CE	\$12,000–\$22,000	\$200,000–\$350,000
	EchoLaser	Elesta					
PDT	TOOKAD	Steba Biotech	Light-activated photosensitizer for tumor ablation	MRI	EMA (EU), Phase III trials ongoing	\$18,000–\$30,000	Varies (drug-based pricing model)
RFA	STARmed	STARmed	Electromagnetic energy–induced hyperthermia	Ultrasound, CT, MRI	CE	\$10,000–\$18,000	\$100,000–\$200,000
	Medtronic Emprint	Medtronic					

Summary of Oncological Outcomes

Study	Energy source	Biopsy	Imaging	PSA drop	Recurrence outcome	Follow-up (months)
Bakavicius et al. ⁴⁵ (20 studies, 4,209 patients)	HIFU	Target and systematic	mpMRI	Median PSA reduction 53% to 84%	In-field recurrence: 5% to 22%; out-of-field progression: 2% to 29%	6 to 56
Cribbs et al. ⁴⁶ (55 studies, 12,655 patients)	IRE and HIFU	–	mpMRI	Mean reduction of 74.7% HIFU vs. 57.3% in IRE	IRE: Lower mean PSA reduction, higher in-field negative biopsy rates, and better potency preservation.	–
Hopstaken et al. ⁴⁷ (72 studies, 5,827 patients)	8 energy sources	Target and systematic	mpMRI	Not specified; PSA monitoring included in follow-up	Median csPCa in treated area: HIFU: 14.7%, IRE: 8.5%, PDT: 10%, Cryoablation: 15%, FLA: 17%	Relatively short numbers
Nicoletti et al. ⁴⁴ (124 studies, 8,000+ patients)	10 energy sources	Target and systematic	mpMRI	BCR range: 2% (Focal Brachytherapy) to 67.5% (HIFU)	Salvage treatment rates range from 1% (IRE) to 54% (HIFU)	Varies across studies (median: 24)
Slusarczyk et al. ⁴⁸ (50 studies, 4,615 patients)	7 energy sources	Target and systematic	mpMRI	Not specified; median baseline PSA 6.5 ng/ml	12-mo csPCa RFS: 86%; 24-mo csPCa RFS: 81%; 5-yr radical/systemic treatment-free survival: 82%	Median: 21 (IQR: 12–34)

Summary of Functional Outcomes

Study	Energy modality	ED rate	UI rate	Assessment method	Follow-up (months)
Bakavicius et al. ⁴⁵ (20 studies, 4,209 patients)	HIFU	80% retained sufficient erections	98% totally continent	IPSS, ICSmaleSF, IIEF, EPIC, FACT-P	3 to 73
Cribbs et al. ⁴⁶ (55 studies, 12,655 patients)	IRE, HIFU	Higher potency maintenance with IRE than HIFU	IRE 94% continent at 3 months, 100% at 7 months. HIFU 100% continent at 3 months.	IPSS, IIEF, EPIC	–
Hopstaken et al. ⁴⁷ (72 studies, 5,827 patients)	8 energy sources	ED rates: 0–40% (varied by energy type)	UI rates: <1% at 1 year	IPSS, ICSmaleSF, IIEF-5, EPIC	3 to 89
Tay et al. ⁴⁹ (49 studies, 6,172 patients)	HIFU, IRE, Cryotherapy	45.7% low, 48.6% moderate, and 5.7% severe impact	97.1% reported low impact	IPSS, ICSmaleSF, IIEF-15, EPIC, FACT-P	6 to 63
Slusarczyk et al. ⁴⁸ (50 studies, 4,615 patients)	7 energy sources	New ED in 11% (95% CI: 4–18%)	Pad-requiring UI increased by 3 % (95% CI: 0–6%)	–	6 to 85

PRINCIPLES OF FOCAL/SUBTOTAL THERAPY OR WHOLE GLAND ABLATIVE THERAPY

- **Patients should be counseled prior to receiving FT or whole gland ablative therapy as follows:**
 - ▶ **HIFU, TULSA, FLA, RFA, IRE, PDT, and histotripsy are not FDA approved or cleared for the treatment of prostate cancer.**
 - ▶ **Currently, no treatment delivered as FT, including radiotherapy or partial prostatectomy, have demonstrated superiority or non-inferiority to guideline-recommended therapies in randomized trials with long-term follow-up. The importance of long-term follow-up is of increased importance in this setting given the high rates of secondary therapy after FTs and potential for increased toxicity.**
 - ▶ **For patients with low- and intermediate-risk disease¹⁻⁷:**
 - ◊ **Biopsy-detected (any) cancer after FT is common within 2 years post-treatment (20%–70%).**
 - ◊ **Erectile dysfunction (10%–40%) and urinary incontinence (0%–20%) have been reported to occur of variable severity within 2 years post-treatment.**
 - ▶ **FT or whole gland ablative therapy may impact the safety and/or efficacy of subsequent local therapy.**
- **Moderate toxicity (grade 2) is common, and severe toxicity (grade 3 or higher) is possible with reported rates in trials from approximately 4%–17% in the first 2 years post-FT.¹⁻⁷**
- **There is no evidence-based, universally agreed upon follow-up protocol after FT. Patients often undergo serial imaging.**

• **“Focal therapy has not demonstrated superiority or non-inferiority in randomized trials”**



PRINCIPLES OF FOCAL/SUBTOTAL THERAPY OR WHOLE GLAND ABLATIVE THERAPY

General

- 
- Ablative therapy refers to the use of a device to destroy tissue that can be directed at part of the prostate gland (termed partial gland, hemigland, or focal therapy [FT]) or the whole prostate gland.
 - FT includes ablative therapies and non-ablative therapies, such as partial prostatectomy and focal radiation therapy.^a
 - Presently, FT is an experimental and emerging technology for the initial treatment of localized prostate cancer that lacks randomized controlled trial evidence with long-term follow-up showing its superiority or noninferiority to current recommended management strategies. As such, FT meets the criteria as an alternative therapy, or a non-standard treatment.

Newly Diagnosed or Previously Untreated Prostate Cancer

- 
- Pathologic confirmation of prostate cancer and risk stratification is required prior to consideration of ablative or FT.
 - Active surveillance is the preferred treatment for low-risk prostate cancer, and ablative and focal therapies are discouraged in this population.
 - The Panel also believes that ablative FT should be discouraged in patients with high- or very-high-risk, regional, or metastatic prostate cancer outside of a clinical trial.
 - There is currently insufficient comparative effectiveness evidence for FT to be recommended for patients with intermediate-risk prostate cancer, and the Panel believes there is uncertainty about the long-term efficacy and toxicity of these treatments. Therefore, ablative and focal therapies in this population should be utilized only in the context of a clinical trial.
 - The following device categories are currently FDA approved or cleared for the initial treatment of prostate cancer, but randomized evidence to the superiority in long-term cancer control and/or quality of life are lacking when delivered as focal rather than whole gland therapy. These treatments may be considered as FT for patients with previously untreated, localized prostate cancer only in the context of a clinical trial:
 - ▶ External beam radiotherapy^a
 - ▶ Brachytherapy
 - ▶ Cryotherapy ablation
 - The following device categories are currently not FDA approved or cleared for the treatment of prostate cancer as focal or whole gland therapy, and should only be used for patients with previously untreated, localized prostate cancer in the context of a clinical trial:
 - ▶ High-intensity focused ultrasound (HIFU)
 - ▶ Transurethral ultrasound ablation (TULSA)
 - ▶ Focal laser ablation (FLA)
 - ▶ Radiofrequency ablation (RFA)
 - ▶ Irreversible electroporation (IRE)
 - ▶ Photodynamic therapy (PDT)
 - ▶ Histotripsy
 - ▶ Partial prostatectomy

Ongoing clinical trials currently in the active or recruitment phase

Trial name	Trial ID	Study type	Study groups	Primary endpoint measure	Primary endpoint timeline (months)	Clinical objective
CHRONOS ⁵²	NCT04049747	–	–	–	–	–
CHRONOS-A	–	RCT	FT (HIFU/Cryo) vs. RT/BT/RP.	PFS	60	FT alone is noninferior compared to radical therapy in terms of PFS
CHRONOS-B	–	RCT	FT (HIFU/Cryo) vs. FT + neoadj treatment	FFS	60	FT combined with neoadj treatment compared to FT alone in terms of PFS.
ENHANCE ⁵³	NCT03845751	Single arm	HIFU + Short-course ADT	Treatment failure	12	Enhance oncological outcomes of HIFU-ADT combination
ENFORCE ⁵⁴	NL-OMON55975	RCT	FT (HIFU/TULSA/IRE) vs. RP/RT	Oncological effectiveness, QoL	48–60	Assess oncological effectiveness and QoL of FT vs. radical treatment
ATLANTA ⁵⁵	NCT03763253	RCT	SOC vs. SOC + FT (HIFU vs. Cryo) vs. SOC + RP/RT	Efficacy (biopsy findings), safety and PFS	24–48	Improve survival with local and metastases-directed therapy
NeoADT-TULSA ⁵⁶	NCT05917860	Single arm	Neoadjuvant ADT + TULSA	PSA reduction and oncological response	24	Investigate neoadjuvant ADT with TULSA for intermediate-risk PCa
EMERHIT ⁵⁷	NCT05710861	Single arm	HIFU vs. RP	Cost-utility comparison of HIFU vs. RP	60	Compare cost-utility of HIFU vs. RP for localized PCa
CAPTAIN ⁵⁸	NCT05027477	RCT	TULSA vs. RP	Cancer control and functional outcomes	60	Compare oncological and functional outcomes of TULSA vs. RP
WATER IV PCa ⁵⁹	NCT06651632	RCT	Aquablation vs. RP	Safety and Efficacy	120	Assess safety and efficacy of Aquablation in. PCa
TMA ⁶⁰	NCT06262633	Single arm	TMA	PFS	6	Investigate efficacy and complications of TMA

Focal Radiation Therapy

- Has been successfully delivered using brachytherapy (LDR and HDR) for definitive or salvage treatment of prostate cancer
 - Meta-analysis
- Re-Irradiation using EBRT is feasible and safe in prostate cancer
 - SBRT for re-irradiation
 - SBRT as definitive treatment

Focal Brachytherapy

- 26 studies reporting on 1492 patients were included in this review.
- Fourteen studies reported on monotherapy, 10 on salvage, and two on boost.

BJR, 2025, 98, 354–367
<https://doi.org/10.1093/bjr/tqae254>
Advance access publication: 19 December 2024
Systematic Review



Partial or focal brachytherapy for prostate cancer: a systematic review and meta-analysis

Enrique Gutiérrez-Valencia, MD, MHA¹, Inmaculada Navarro-Domenech, MD¹, Kailee Zhou¹, Marc Barcelona, MD¹, Rouhi Fazelzad, MIST¹, Matthew Ramotar, HBSc¹, Irving Sanchez, MD, MHA², Victor Ruiz, MD², Robert Weersink, PhD¹, Rachel Glicksman, MD¹, Joelle Helou, MD, MSc³, Alejandro Berlin , MD¹, Peter Chung, MD¹, Ronald Chow, MS¹, Srinivas Raman , MD, MASc^{*,1}

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Focal Brachytherapy

- **Definitive:**

- 10 LDR Studies
 - Median dose- 145 Gy
- 4 HDR Studies
 - 19-24 Gy in one fraction
- Target delineation
 - MRI
 - Biopsy
- Margins
 - 5 mm –10 mm
 - Hemigland
- Biochemical Control (BC)
 - 97% (95% CI: 86%-99%) at 24 months
 - 82% (95% CI: 65%-92%) at 60 months.

- **Salvage:**

- 3 LDR Studies
 - Median dose- 145 Gy
- 7 HDR Studies
 - 19-27 Gy in 1-2 fraction(s)
- Target delineation
 - MRI
 - Biopsy
 - PET-CT
- Margins
 - 3mm –5 mm
- Biochemical Control (BC)
 - 67% (95% CI: 62%-72%) at 24 months
 - 35% (95% CI: 17%-58%) at 60 months.

Focal EBRT/SBRT

- Has been successfully deployed to deliver higher doses to dominant lesion
 - Flame-hypo trial
 - Delineate trial
- Focal SBRT studies

SBRT- Focal Boost

- 100 Patients with Intermediate- or high-risk PC
- The planning target volume (PTV) was created by adding an isotropic margin of 4–5 mm to the CTV (Prostate +/- SV).
- Tumor lesions on mpMRI were contoured as GTV in collaboration with an experienced uro-radiologist.
- All patients were treated with 35 Gy in 5 weekly fractions to the whole prostate gland (CTV) with an iso-toxic integrated boost up to 50 Gy to the multiparametric MRI-defined tumor (GTV).
- If the dose constraints to the normal tissues would be exceeded, these were prioritized over the focal boost dose.

Results:

- Median follow-up of 61 months.
- 5-year bDFS (95 % CI) was 93 % (86 % to 97 %).
- At 5 years, the prevalence of grade 2 + genitourinary and gastrointestinal toxicity was 12 % and 4 %, respectively.



Original Article

Stereotactic body radiotherapy with a focal boost to the intraprostatic tumor for intermediate and high risk prostate cancer: 5-year efficacy and toxicity in the hypo-FLAME trial

Cédric Draulans^{a,*}, Karin Haustermans^{a,b}, Floris J. Pos^c, Uulke A. van der Heide^c, Lisa De Cock^a, Jochem van der Voort van Zyp^d, Hans De Boer^d, Robert J. Smeenk^e, Martina Kunze-Busch^e, Evelyn M. Monnikhof^f, Robin De Roover^b, Sofie Isebaert^b, Linda G.W. Kerkmeijer^{d,e}

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Characteristic	Total study cohort, No. (%) (n = 100)
Age, median (range), year	73 (57 – 84)
EAU risk group	
Intermediate	25
High	75
NCCN risk group	
Favorable intermediate	11
Unfavorable intermediate	21
High	45
Very high	23
Initial PSA, median (range), ng/mL	10.8 (3.0 – 29.0)
AJCC 7th edition clinical tumor stage	
T1c	3
T2a	25
T2b	11
T2c	14
T3a	44
T3b	3
ISUP grade group	
1	18
2	33
3	24
4	15
5	10
Intended androgen deprivation therapy	
LHRH agonists/antagonists	59
Antiandrogens	3
None	38
Intended androgen deprivation therapy duration	
None	38
Short term (≤ 6 months)	31
Long term (6 – 36 months)	31

SBRT-Focal Boost

CLINICAL INVESTIGATION

Stereotactic Body Radiation Therapy to the Prostate With Focal Boost: Analysis of the Primary Endpoint in the DELINEATE Trial Cohort E

Julia Murray, FRCR,^{a,b} Laura Satchwell, MSc,^a Zayn Rajan, MSc,^a Annie Gao, MSc,^{a,b} Helen McNair, PhD,^{a,b} Angela Pathmanathan, MD(Res),^{a,b} Chris Parker, FRCR,^{a,b} James Talbot, MSc,^a David Dearnaley, FRCR,^b and Alison Tree, MD(Res)^{a,b}

^aThe Royal Marsden National Health Service (NHS) Foundation Trust, Sutton, United Kingdom; and ^bDivision of Radiotherapy and Imaging, The Institute of Cancer Research, Sutton, United Kingdom

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- Intermediate or high-risk prostate cancer
- 49 patients
- Single-institution, prospective phase 2 trial, DELINEATE cohort E
- SBRT to a dose of 36.25 Gy, with a simultaneous integrated boost to the tumor (s) up to 45 Gy in 5 fractions
- Median follow-up was 48.8 months.
- The median(IQR) boost volume was 1.9(IQR,1.4-2.81)cm³
- All patients received at least short course hormone therapy.
- The highest rate of acute RTOG gastrointestinal(GI) and genitourinary (GU) of grade 2+ was seen at weeks 3 and 4, respectively, settling to baseline levels by week 12.
- Cumulative 1-year incidence of RTOG grade ≥ 2 GI late toxicity was 6.1% (90% CI,2.4%-15.1%).
- There was no reported late grade 3 or worse bowel toxicity using RTOG or CTCAE scales.

SBRT-Focal Salvage

Original Reports | Genitourinary Cancer

Salvage Reirradiation for Locally Recurrent Prostate Cancer: Results From a Prospective Study With 7.2 Years of Follow-Up

Christian Ekanger, MD¹; Svein Inge Helle, MD, PhD¹; Lars Reisæter, MD, PhD^{2,3}; Liv Bolstad Hysing, MSc, PhD^{1,4}; Rune Kvåle, MD, PhD^{1,5}; Alfred Honoré, MD⁶; Karsten Gravdal, MD, PhD⁷; Sara Piilskog, MSc, PhD^{1,4}; and Olav Dahl, MD, PhD^{1,8}

DOI <https://doi.org/10.1200/JCO.23.01391>

- 38 patients with biopsy-proven locally recurrent PC >2 years after previous treatment and absence of grade 2-3 toxicity from the first course of radiation were included.
- The treatment was 35 Gy in five fractions to the MRI-based target volume
- 6 months of androgen-deprivation therapy starting 3 months before radiation.
- Results:
 - bRFS were 81% (95%CI, 69 to 94) and 58% (95%CI, 49 to 74), at 2-year and 5-year respectively.
 - Local recurrence-free survival was 93% (95% CI, 82 to 100),
 - Metastasis-free survival was 82%(95%CI, 69 to 95), and
 - Overall survival was 87% (95% CI, 76 to 98) at 5 years.
 - Two patients (5%) had durable grade 3 genitourinary toxicity, one combined with GI grade 3 toxicity.
- A PSA doubling time \leq 6 months at salvage, a Gleason score >7, and a PSA nadir \geq 0.1 ng/mL predicted a worse outcome.

SBRT-Salvage



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Clinical and Translational Radiation Oncology

journal homepage: www.sciencedirect.com/journal/clinical-and-translational-radiation-oncology



Review Article

Re-irradiation to the prostate using stereotactic body radiotherapy (SBRT) after initial definitive radiotherapy – A systematic review and *meta-analysis* of recent trials

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- 14 publications were included in the systematic review.
- Dose- 30-40 Gy in 5-6 fractions
- 6 studies with focal SBRT
- The pooled rate of acute GU and GI toxicity \geq G2 were 13 % (95 % CI: 7–18 %) and 2 % (95 % CI: 0–4 %).
- For late GU and GI toxicity \geq G2 the pooled rates were 25 % (95 % CI: 14–35 %) and 5 % (95 % CI: 1–9 %).
- The pooled 2-year biochemical recurrence-free survival was 72 % (95 % CI: 64–92 %).

Focal SBRT- definitive

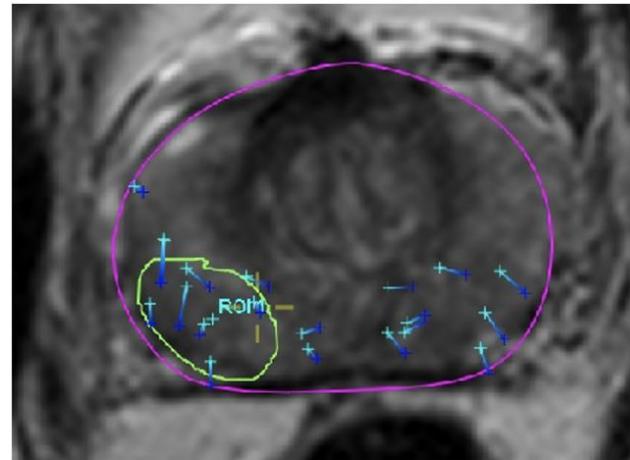
- Patients with pathologic focal Gleason 6–7 disease and a corresponding PIRADS 4–5 lesion on mpMRI underwent targeted and comprehensive biopsies using MRI/ultrasound fusion under electromagnetic sensor navigation.
- After rigorous analysis for imaging biopsy concordance, five of 18 patients were eligible to proceed to f-SBRT
- Absolute concordance was 43.8% (95% CI: 0.20, 0.64). Patterns of discordance included additional sites of ipsilateral disease, bilateral disease, and negative target. Five were upstaged to a new NCCN risk category necessitating treatment escalation.
- The five patients with concordant pathology completed three fraction f-SBRT with sparing of the surrounding normal structures (including contralateral neurovascular bundle), with no reported grade 2+ toxicities and favorable PSA responses (mean: 41% decrease).

“Image-guided confirmatory biopsies frequently revealed additional disease, suggesting the need for caution in partial-gland therapy. For truly focal disease, f-SBRT provided excellent dosimetry, minimal toxicity, and encouraging biochemical response”

Focal Prostate Stereotactic Body Radiation Therapy With Correlative Pathological and Radiographic-Based Treatment Planning

Elisha Fredman^{1*}, Bryan Traughber^{1,2}, Michael Kharouta¹, Tarun Podder¹, Simon Lo³, Lee Ponsky⁴, Gregory MacLennan⁵, Raj Paspulati⁶, Bradley Ellis¹, Mitchell Machtay^{1,2} and Rodney Ellis^{1,2}

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Targeted and repeat whole-gland biopsies using the UroNav needle guidance system.



Focal SBRT-Definitive

Stereotactic focal radiotherapy as an alternative treatment for low-risk prostate cancer: Results of a single-arm monocenter Phase-II trial

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Number of patients	24
Median age, years	66 (55 – 79)
Gleason score	22 (91.7%)
6	2 (8.3%)
7 (3 + 4)	
Clinical stage	12 (50%)
T1c	9 (37.5%)
T2a	3 (12.5%)
T2b	
PSA level, ng/ml	7.08 (2.4–13.0)
Median PSA	19 (79.2%)
<10	5 (20.8%)
≥10	
Percent biopsy cores positive for cancer	22 (91.7%)
< 34%	2 (8.3%)
≥ 34%	
Risk group, CAPRA score	7 (29.2%)
1	8 (33.3%)
2	9 (37.5%)
3	
Median treatment time, days	10 (9 – 13)

Variable	Baseline	Last FU	P value*
IPSS	2.90 (± 2.84)	3.29 (± 3.83)	p>0.05
U-QOL	0.70 (± 0.69)	0.67 (± 0.92)	p>0.05
IIEF-5	16.1 (± 9.08)	17.0 (± 9.27)	p>0.05

*P values for change relative to baseline, as determined by Mann-Whitney U test.

[†]U, follow-up; IIEF-5, International Index of Erectile Function-5 Scale; IPSS, International Prostate Symptom Score; U-QOL, Urinary Quality of Life questionnaire.

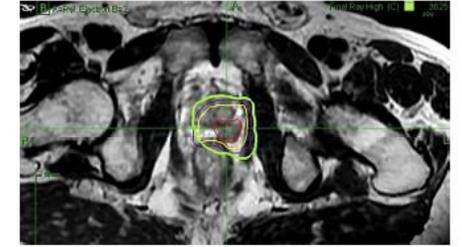
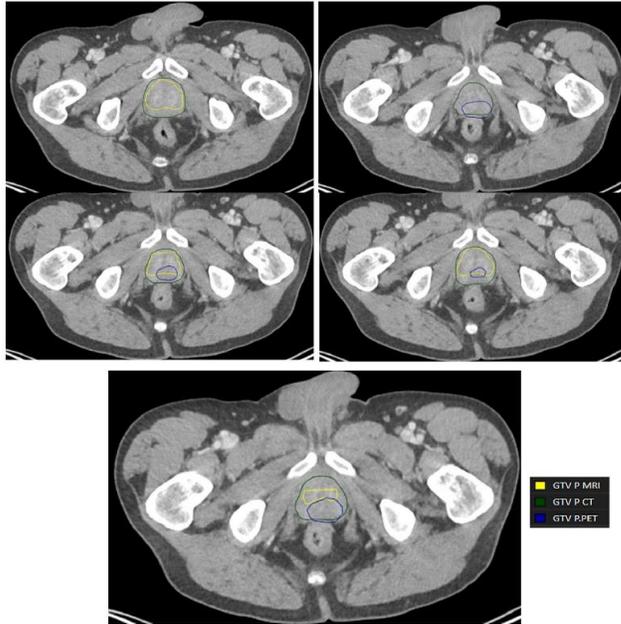


FIGURE 2
Example of a delineated focused stereotactic treatment on the MRI T2 sequence axial view. Red = gross target volume. Yellow = clinical target volume. Purple = planning target volume. Green = 36.25 Gy isodose.

- Patients with localized CAPRA ≤ 3 prostate adenocarcinoma; an isolated PIRADS ≥ 4 macroscopic tumor on MRI;
- Dose: 36.25 Gy (80% isodose prescription) were delivered in 5 fractions every other day using Cyberknife M6.
- Over a median follow-up of 36 months, Three-year biochemical progression-free survival was 96%.
- Acute/late grade ≥ 3 toxicities did not occur: all acute toxicities were grade-1 genitourinary (38% patients), grade-2 genitourinary (8%), or grade-1 rectal (13%) toxicities. There was one (4%) late grade-1 genitourinary toxicity. QOL was unchanged at last follow-up, as shown by IPSS (2.86 to 3.29, p>0.05),

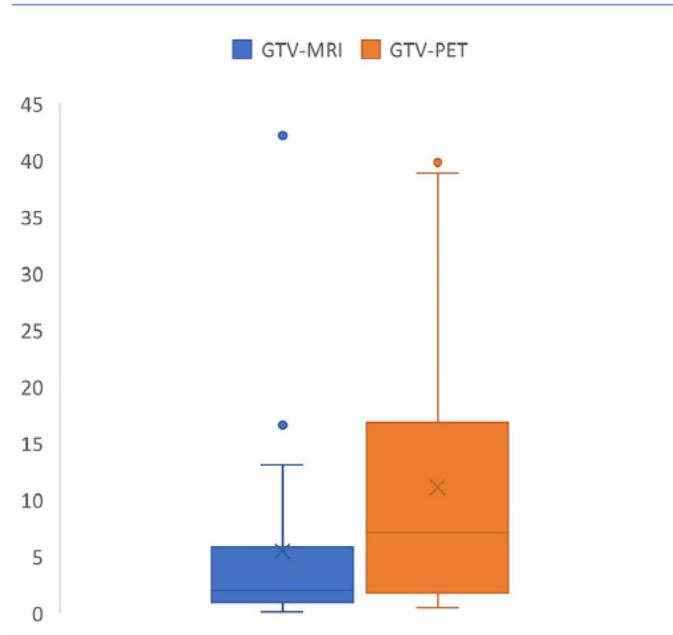
Identifying the “Lesion/Area”

- MRI Vs PET



Scientific Article

Comparative Analysis of ⁶⁸Ga-Prostate-Specific Membrane Antigen Positron Emission Tomography/Computed Tomography and Multiparametric Magnetic Resonance Imaging for Gross Tumor Volume Delineation in Radiation Therapy Planning of Prostate Cancer

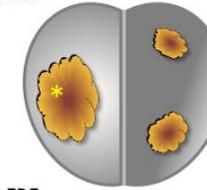


Prostate cancer is a multi-focal disease

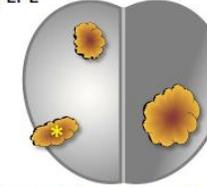
- Prostate cancer is a highly heterogeneous disease with spatial and temporal heterogeneity.
- “Multifocal primary prostate cancer displays high heterogeneity both within and between different foci”

(A-C) Current varying definitions of index tumor (*)

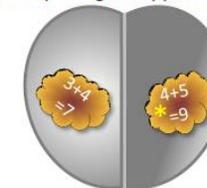
A) Size



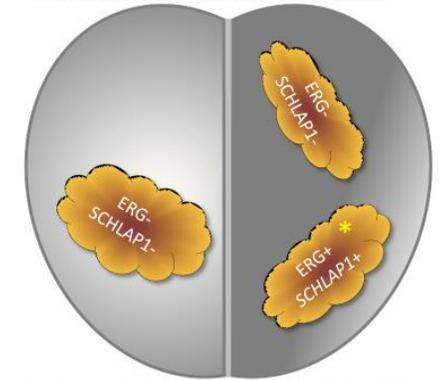
B) EPE



C) Morphological appearance



D) Molecular definition of index tumor



Extensions may include other alterations in RNA, proteins, somatic mutations, epigenetics, microenvironment, and/or metabolomics



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Review Article

Prostate cancer: Molecular aspects, consequences, and opportunities of the multifocal nature

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How precise is Prostate SBRT?

- When intra-fraction motion is accounted for, adequate CTV coverage can be maintained with PTV margins reduced to 2 mm in all directions

TABLE 5 Average gamma pass rates for Delta4 diode measurements using a gamma criteria of 3%, 2 mm, 10% threshold dose for uncorrected and corrected/gated measurements with the Radixact and Truebeam systems, respectively

Motion type	Radixact Synchrony		Truebeam Marker Match	
	Uncorrected (St. Dev)	Corrected (St. Dev)	Uncorrected (St. Dev)	Gated (St. Dev)
Stable	99.7% (0.2%)	100.0% (0.1%)	99.9% (0.2%)	99.8% (0.5%)
Drifting	73.5% (6.1%)	90.0% (4.7%)	81.7% (5.5%)	99.7% (0.4%)
Erratic	77.9% (2.5%)	95.3% (1.7%)	87.1% (4.2%)	98.0% (1.9%)
High frequency	84.1% (3.2%)	93.7% (3.8%)	80.1% (4.8%)	90.2% (5.8%)

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Open Access Original Article

Real-Time Adaptive Motion Management in Prostate Stereotactic Body Radiation Therapy: Clinical and Dosimetric Analysis of 25 Patients

Lee C. Goddard^{1,2}, Jonathan Cabrera¹, Justin Tang¹, Madhur K. Garg¹, Wolfgang A. Tome^{1,2}

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RADIATION ONCOLOGY PHYSICS

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MEDICAL PHYSICS

Reducing PTV margins for prostate SBRT with motion compensation and gating techniques

Lee Goddard^{1,2} | Kyoungkeun Jeong^{1,2} | Justin Tang^{1,2} | Madhur Garg^{1,2} | Wolfgang A. Tome^{1,2}

Future directions

Recruiting ⓘ

Focal Therapy With Stereotactic Body Radiation Therapy (SBRT) for Patients With a Single Prostate Tumor

ClinicalTrials.gov ID ⓘ NCT05616650

Sponsor ⓘ National Cancer Institute (NCI)

Information provided by ⓘ National Institutes of Health Clinical Center (CC) (National Cancer Institute (NCI)) (Responsible Party)

Last Update Posted ⓘ 2025-12-31

Are we ready to compete with Focal therapies such as Cryotherapy, HIFU and Laser?

YES!

Should be done on a clinical trial

Technical Considerations:

Identification and delineation of the target: mpMRI and PET-CT

Intra-fraction Motion: Fiducials, Synchrony, MR-Linac

Rectal Spacer might help reduce rectal dose in posterior lesions

Urethral sparing with proper urethral delineation on MRI/CT