

Challenges in appropriately selecting men for partial gland ablation

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• None



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Overview

- Where do we stand?
- Rationale for partial gland ablation
- Energy modalities
- Outcomes
 - Functional
 - Oncological
- Mechanism for failure
- Future directions

Remarkable Progress



Welch et al. 2019 NEJM

Not All Tumors Are Equal



Adapted from a figure courtesy of H. Gilbert Welch, Dartmouth Medical School

> prevention.cancer.gov NCI Division of Cancer Prevention

Consequences of Local Therapy



Donovan et al NEJM 2016

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- New York-Presbyterian

P<0.001

P<0.001

60

Functional Outcomes Vary By Surgeon





Momnu et al JAMA Surg 2021

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Conversion to Therapy



Hamdy et al NEJM 2016



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Moving Forward

- Identify intermediate risk patients
 - Need treatment now to prevent metastasis in future (5-10 years)
- Oncological control
 - Cure
 - Reducing number needing radical therapy
 - Without risking progression
- Maintain sexual and urinary quality of life

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Preserving Critical Structures



Biological Rationale



Ahmed, H et al, Lancet Oncology 2012

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Biological Rationale



Liu W et al Nature Medicine 2009

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• THERMAL

- High Intensity Focused Ultrasound (HIFU)
- Cryotherapy (Cryo)
- Focused Laser Ablation (FLA)
- Radiofrequency ablation (RFA)

NON-THERMAL

- Irreversible electroporation (IRE)
- Vascular Targeted Photodynamic Therapy (VTP)
- Focal Brachytherapy

• High Intensity Focused Ultrasound (HIFU)

- Thermal, ultrasound energy
 - Coagulative necrosis
 - Internal Cavitation
- FDA approved for prostate ablation in 2015
- Rectal probe and delivered transrectally
- MR Guided (in bore) vs. US Guided
- Limitations:
 - Anterior tumors
 - Prostate calcifications
 - Requires anesthesia

• Cryotherapy

- Thermal, alternating freeze/thaw cycles
 - Cellular membranes become permeable
 - Results in apoptosis and cell death
- Probes are placed transperinally
- Can easily visualize ice-ball forming in real time
- Can be done under local anesthesia
- Limitations:
 - Posterior tumors close to the rectum
 - "Collateral damage" if radical surgery needed



Shah et al Eur Urol 2019

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MRI-guided focused ultrasound focal therapy for patients with intermediate-risk prostate cancer: a phase 2b, multicentre study

Behfar Ehdaie, Clare M Tempany, Ford Holland, Daniel D Sjoberg, Adam S Kibel, Quoc-Dien Trinh, Jeremy C Durack, Oguz Akin, Andrew J Vickers, Peter T Scardino, Dan Sperling, Jeffrey Y C Wong, Bertram Yuh, David A Woodrum, Lance A Mynderse, Steven S Raman, Allan J Pantuck, Marc H Schiffman, Timothy D McClure, Geoffrey A Sonn*, Pejman Ghanouni*

MRI Guided HIFU

	Patients (n=101)
Age, years	63 (58–67)
Prostate-specific antigen, ng/mL	5.7 (4.2–7.5)
Race	
White	87 (86%)
Black	7 (7%)
Other	7 (7%)
Clinical classification ≤T1C	84 (83%)
Grade group	
2	79 (78%)
3	22 (22%)
Baseline patient-reported functional outcomes	5
Functional erection: IIEF-15≥24	58/99 (59%)
Urinary continence: ICIQ<10	98/100 (98%)
Treatment parameters	
Duration, min	110 (79–141)
Number of sonications	15 (12–18)
Data are median (IQR) or n (%). IIEF=International Ir CIQ=International Consultation on Incontinence Qu	ndex of Erectile Function. Juestionnaire.

Ehdaie et al Lancet Oncology 2022

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MRI Guide HIFU

	Targeted a	rea only	Whole prostate gland		
	6 months (n=101)	24 months (n=89)*	6 months (n=101)	24 months (n=98)†	
Oncological efficacy					
No evidence of grade group ≥2	96 (95%)	78 (88%)	77 (76%)	59 (60%)	
Biopsy outcome					
No evidence of cancer	92 (91%)	71 (80%)	41 (41%)	39 (40%)	
Grade group 1	4 (4%)	7 (8%)	36 (36%)	20 (20%)	
Grade group 2	4 (4%)	6 (7%)	18 (18%)	24 (24%)	
Grade group 3	1(1%)	2 (2%)	3 (3%)	9 (9%)	
Grade group 4	0	1(1%)	2 (2%)	3 (3%)	
Grade group 5	0	2 (2%)	1(1%)	3 (3%)	

Data are as n (%). *There was one patient with a grade group 2 or higher result in the treatment region at 6 months and missing data at 24 months; this patient was assumed to be grade group 2 or higher at 24 months. †There were nine participants with grade group 2 or higher results outside of the treated area at 6 months and missing data at 24 months; these participants were assumed to be grade group 2 or higher at 24 months.

Table 2: Detection of prostate cancer from the combined MRI-targeted and systematic biopsy at 6 and at 24 months

Ehdaie et al Lancet Oncology 2022

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Functional Outcomes

Modality Number of Erectile function patients		Erectile function	Urinary function	Reference	
Thermal					
HIFU	625	15% new ED	83% pad-free at 3 y	Guillaumier et al, 2018	
	164	18% new ED	0% new incontinence	Mistry et al, 2017	
	149	14% new ED	0.6% new incontinence	Hanna et al, 2018	
	111	22% new ED	3% new incontinence	Rischmann et al, 2017	
Cryotherapy	301	No change	Improved flow rates	Bianco et al, 2018	
	122	16% new ED	No change	Shah et al, 2019	
	107	N/A	N/A	Barret et al, 2018	
FLA	98	No change	No change	Feller et al, 2018	
	25	No change	No change	Lepor et al, 2015	
	18	No change	N/A	Elkhoury et al, 2018	
RFA	21	No change	No change	Taneja et al, 2018	
	20	No change	No change	Orczyk et al, 2018	
Nonthermal					
VTP	206	No change	No change	Azzouzi et al, 2015	
	21	No change	No change	Taneja et al, 2018	
Brachytherapy	354	N/A	N/A	King et al, 2018	
IRE	25	No new ED	No change	Murray et al, 2016	
	63	Mild decrease in scores (EPIC)	No change	van de Bos et al, 2018	

Fainberg et al 2021

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Prostate MRI



Stabile et al Nature Reviews Urology 2019

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Detection of Cancer



Figure 2: Diagnostic accuracy for detection of clinically significant cancer (primary definition) between MP-MRI and TPM-biopsy

MP-MRI=multi-parametric MRI. TPM-biopsy=template prostate mapping biopsy. Pie charts represent actual MP-MRI scores 1–5. Sensitivity 93% (95% CI 88–96), positive predictive value 51% (46–56), specificity 41% (36–46), negative predictive value 89% (83–94).

Ahmed et al Lancet 2017

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Underestimating Disease Volume

Image Guided Focal Therapy for Magnetic Resonance Imaging Visible Prostate Cancer: Defining a 3-Dimensional Treatment Margin Based on Magnetic Resonance Imaging Histology Co-Registration Analysis

Julien Le Nobin,* Andrew B. Rosenkrantz, Arnauld Villers, Clément Orczyk, Fang-Ming Deng, Jonathan Melamed, Artem Mikheev, Henry Rusinek and Samir S. Taneja†

- Treatment zone needs to be approximately 20% larger than MRI lesion to include all tumor
- Recommend a 9 mm noncapsular margin and a 3 mm capsular margin





Comparing MRI to Radical Prostatectomy



Nassiri et al J Urol 2018

Comparing MRI to Radical Prostatectomy

Table 2. Sensitivity and specificity of fusion biopsy predictionof focal therapy eligibility vs whole mount findings

	No. Wh		
Fusion Biopsy*	Eligible	Ineligible	Total No.
Eligible Ineligible	12 3	13 36	25 39
Totals	15	49	64

* Sensitivity 80.0%, specificity 73.5% and accuracy 75.0%.

Nassiri et al J Urol 2018

Repeat biopsies show different levels of risk



Fasulo et al Eur Onc 2022

Grade Discordance

Table 2.	Fusion	biopsy	Gleason	grade	group	compared	to
radical pr	ostatec	tomy G	leason gr	ade gr	oup		

	RP Gleason Grade Group				
TBx Gleason Grade Group	1	2	3	4	5
1	8	8	1		
2	10	40	10		
3	1	12	16	7	1
4		2	3	3	8
5			1	2	7

Patel et al Urol 2020

Urethral Distance



В

Patel et al J Urol 2023

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Lesions Cross the Midline



Johnson et al Cancer 2019

Smaller High-Grade Lesions Can Be Missed



Johnson et al Eur Urol 2019

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Evolution of Therapy



Adjuvant Breast and Bowel Project; PDT, photodynamic therapy; RCT, randomized controlled trial; XRT, radiotherapy.

Labbate et al J Urology 2022

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Unanswered Partial Gland Ablation Outcomes

- Surveillance after treatment
 - PSA
 - MRI
 - Biopsy
- Define treatment success (and what to compare it to)
 - Overall survival
 - Metastasis free survival
 - Local recurrence
 - Avoiding radical therapy

Conclusion

- Partial gland ablation is a potential treatment options that could provide effective cancer control and preserve functional outcomes
- Still in the early phases of understanding its role in the management of localized prostate cancer
- While adoption is already increasing substantially, it is critical to perform studies that:
 - Ensure oncologic control is not inferior to current standard of care
 - Understand how to best follow patients and when to salvage
 - Refine techniques to push the field forward