

# Is Better Patient Selection the Key to Successful HIFU Therapy for Prostate Cancer?

## Preliminary Results of an Optimization Study Designed to Find the Therapeutic “Sweet Spot”

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### Objectives

High Intensity Focused Ultrasound (HIFU) therapy offers significant advantages over conventional definitive treatments for localized prostate cancer. Side effects from HIFU are substantially reduced compared to radical prostatectomy or radiation therapy and the total cost is considerably less. Efficacy of HIFU, however, remains a question. We developed a model HIFU prostate cancer protocol to improve outcomes using Multi-Parametric (MP) MRI localization and modified patient screening criteria. Early results are presented.

### Advantages of an MP-MRI Prostate Scan

- Offers total gland assessment while improving sensitivity and specificity
- Image advantage over biopsies for anterior and apical cancers
- Provides an excellent metric for determining which patients may need treatment and which are candidates for CDM (Chronic Disease Management) or AS (Active Surveillance) protocols.
- Assesses lymph nodes and bone integrity in the true pelvis

### Clinical Value of an MP-MRI Prostate Scan

- Shows a 98-100% PPV for diagnosing prostate cancer<sup>1</sup>
- Defines the true extent of the disease without trauma or risk to the patient
- MP-MRI scanning takes the guess work out of diagnostics
- In a clinical setting, it enables a better definition of patient selection for AS, as well as an adjunct to surgical intervention including HIFU
- CAPSURE data demonstrates the need for diagnostic help: there is only a 70% success rate with radical prostatectomy and a 63% recurrence rate following radiation treatment
- Understanding the extent of the cancer is critical to the outcome

### Results

After treatment, mean PSA nadir dropped to 0.28 ng/ml. The Phoenix definition for cure (nadir PSA level + 2), often used to determine efficacy of definitive radiation therapy, was used. Urethral narrowing or bladder neck strictures occurred in about 20% of patients but were easily treatable. No other significant side effects from HIFU therapy were noted. There were no reports of incontinence, rectal wall injury, fistulas or new erectile dysfunction. Duration of follow-up was 3 to 72 months. To date, just a single patient (Gleason 6 group) has shown a significant PSA increase since his HIFU procedure. This patient was successfully treated with radiation therapy.

### Conclusions

Excellent diagnostics and outcomes are associated with physician technical skill and imaging skill while using ultrasound and a 3.0 MP-MRI scan. It is reasonable to say that reproducible outcomes will be seen when using the Ablatherm™ HIFU technology in properly selected patients.

### The “Sweet Spot Study”

Authors	Number of Patients	Age	Gleason Score	Pre-RX PSA	Post-RX PSA Nadir	Stage	Follow-up (mo.)	MP-MRI	BDFR	Re-RX Rate .Salvage.
Wheeler 'Sweet Spot Study' in Press	67	61.5 Range: (49-81)	6=36 7(3+4)=22 7(4+3)=6 8=2 9=1	5.2	0.137 ng/ml (mean) (89% nadir ≤ 0.30 ng/ml); Range: 0-.46	T1-T2 N0,M0	85 mo. (Mean: 27.3 mo.) Range: 3-85	Pre-Op (All patients); Scans Post-op If applic.	99% @ 7(+yrs) (Phoenix Definition)	1 (EBT)
Orovan Published: British Journal of Urology-2012	402	62.7 (±7.5)	6=183 7(3+4)=130 7(4+3)=63	6.6 ±7.5	0.38 (0.7) ng/ml nadir Low Risk; 0.35(0.68) ng/ml nadir Intermediate. Risk	T1-T2 N0,M0	48 mo. (mean 24 mo.) Range: 6-48	No Scans; Biopsies 50/78 pts. with PSA nadir >0.5 post-op	72% @ 4yrs (Horowitz) GS 6 -76% GS 7 – 69.5%	12 (HIFU) 6 (RRP) 4 (EBT) 4 (ADT) 7 (AS)

Table 1. The goal was to look for the best candidates to yield the best outcomes. Entry criteria were as follows: Prostate size < 40 g, AP diameter < 32 mm, PSA < 8.5 ng/mL, Gleason Score of 6, 7, 8, or 9, and primary treatment within 3.5 years of diagnosis

### Biopsy Correlation to MP-MRI Scan in the “Sweet Spot Study”

- 54% of patients had a cancer missed by biopsy that was detected by the MP-MRI
- Out of a total of 86 cancers detected in biopsy only three lesions (GS = 6 in two patients) were not detected using MP-MRI, yielding a 97% PPV.
- 28% (19/67) patients treated had bilateral cancer on biopsy; 18/19 of these cancers were detected by MP-MRI
- Of the 67 patients diagnosed with prostate cancer by MP-MRI, only 33% were correctly diagnosed with biopsy

Lt. Biopsy +	Rt. Biopsy +	Biopsy + Bilaterally	Lt. MP-MRI +	Rt. MP-MRI +	Bilateral MP-MRI +
N = 42/67 (63%)	N = 42/67 (63%)	N = 18/67 (27%)	N = 41/42 (98%) Correctly Identified	N = 40/42 (95%) Correctly Identified	N = 55/67 (82%)

### Biochemical Disease Free Rates (BDFR) with Comparison to CAPSURE Data

Research Author(s)	Country	BDF Rates Minimum of 34 months (mean)
Blana, A. et al	Germany (2008)	77% Low and Intermediate Grades at 5 years 69% Low and Intermediate Grades at 7 years
Blana, A., Chaussy, C. et al	Germany (2009)	75% Low and Intermediate Grades
Orovan, W. et al. (Cleveland Clinic) Wheeler, R.	Canada (2012) USA ('Sweet Spot Study' in Press) 2014	76% - Low Grade 69.5% - Intermediate Grade 99% Low, Intermediate and High Grades
Uchida, T., Shoji, S., Nakono, M., et al.	Japan (2008)	84% - Low Grade 64% Intermediate Grade
Crouzet, S. et al.	France (2010)	83% - Low Grade 75% - Intermediate Grade
Agarwal, P., Sadetsky, N., Konety, B. et al.	CAPSURE Data (2008)	37% - All treatment Grades – EBRT 70% - All treatment Stages -Surgical