



IMPROVING PROSTATE CANCER OUTCOMES FROM HIFU THERAPY USING MP-MRI LOCALIZATION: EARLY RESULTS FROM A PILOT PROGRAM

LESLIE, S., WHEELER*, R., GRUBBS, G., WHEELER, B., FERNANDEZ, H.
CREIGHTON UNIVERSITY & THE DIAGNOSTIC CENTER FOR DISEASE

MP-MRI (MULTI-PARAMETRIC MAGNETIC RESONANCE IMAGING) PROSTATE SCAN: KEY SEQUENCES

T2Weighted Images

DWI & ADC Map (Diffusion Weighted Imaging
& Apparent Diffusion Coefficient map)

DCE (Dynamic Contrast Enhancement or
Perfusion)

ADVANTAGES TO AN MP-MRI PROSTATE SCAN:

- Total Gland assessment while improving Sensitivity and Specificity of Cancer Detection
- Capsular Integrity assessment at NVBs and Seminal Vesicles to R/O ECE
- Image advantage over biopsies for Anterior Cancers and Apical cancers
- Best metric to determine which patients may need treatment and which patients are candidates for CDM (Chronic Disease Management) or AS (Active Surveillance) protocols
- Advantages in validating stability of patients on CDM
- Assesses Lymph Node disease and bone integrity of the true pelvis
- Cost effective, accurate comparative and atraumatic (patient friendly)

CLINICAL VALUE OF MP-MRI PROSTATE SCANNING:

- MP-MRI scanning is the most sophisticated diagnostic scanning device we have available
- MP-MRI prostate scans have a 98-100% PPV for diagnosing prostate cancer (Ref:Turkbey, Choyke et al NIH, 2011)
- MP-MRI scans define the true extent of disease without trauma or risk to the patient; (Saturation biopsies are barbaric, high risk to patients and therefore will lose favor with patients and 3rd party payers)
- Capsure Data* proves we need help diagnostically: Success with Radical Prostatectomy is 70% while there is a 63% recurrence following Radiation treatment including risk of bladder and colon cancers
- Failure is associated with a lack of understanding for the totality of cancer present due in part to the use of ill advised CAT Scans being used commonly with a lack specificity
- MP-MRI scanning takes the guess work out of diagnostics and the luck out of treatment outcome success
- In a clinical setting, it is like 'diagnostics on steroids' enabling a quantum leap in defining patient selection for Active Surveillance as well as an adjunct to Surgical intervention including HIFU
- Urologists must get involved or else Interventional Radiologists will be doing HIFU cases

HIFU COMPARISON: LOCALIZED PROSTATE CANCER

(PRIMARY THERAPY)

ABLATHERM (EDAP-TMS)TM

| Author | Patients (n) | Pre-RX PSA (ng/ml) | Gleason Score | Stage | Follow-up | Negative Bx. Rate | Biochemical Disease Free Rates, (PHX) | Re-Treatment Rate |
|--|--------------|--|---|-----------------|---------------|---|--|---|
| Blana, etal Germany | 140 | ◀15.0 (Mean = 7) | ≤ 7 | T1-T2 (NOM0) | 5-7 yrs. | 86.4% | 77% @ 5 yrs. 69% @ 7 yrs. | 29.3% |
| Blana, etal Germany | 163 | ≤ 20.0 (Mean = 7) | ≤ 7 | T1-T2 (NOM0) | 4.8±1.2 yrs. | 92.7% | 75% @ 5 yrs. | 20.8% |
| Orovan, etal (Cleveland Clinic) Toronto, CA | 402 | ◀ 20.0 Mean 6.6(3.1) Size ▶ 40 ccs | ≤ 7 GS 6(n=183) GS 7(n=219) | T1-T2 (NOM0) | .5–4 yrs. | 64% n=50/78Bi opsied if nadir > 0.5 | 68% Stuttgart 72% Horowitz -over all 4 yr. rate 76%, 139(6) & 69.5%,152 (7) | 30% (112) 12 (HIFU) 6 (RRP) 4 (EBT) 4 (ADT) 7 (AS) |
| Wheeler London & Cancun | 112 | ◀44.6 Range:.5-44.6 Mean = 9.1 | ≤ 9 GS 6 (n=57) GS 7 (n=42) GS 8 (n=8) GS 9 (n=5) | T1-T2 (NOM0) | .25-7(+) yrs. | MP-MRI: Pre-op & Utilized If PSA fails- PHX | 80% @ 7 yrs. GS(6) 83%,47 GS(7) 86% ,36 GS(8) 63%,5 GS(9) 40%,2 | 6% (7) |

MORBIDITY USING THE HIFU TECHNOLOGY

- **Impotency:** Dependent on Physician Skill in Imaging; Ask about this
- **Incontinence:** Dependent on Physician Skill in Treatment Planning
- **Bowel Injury (Fistula):** Should never occur; Ask about this
- **Inability to kill all the cancer cells:** Dependent on Physician Skill in treatment as well as amount of energy used
- **Urethral Narrowing/Stricture or BNC:** (15-25%); Easily Remedied
- **Injury or Death secondary to Supra-Pubic tube placement:** Should never occur; ask about this

'SWEET SPOT STUDY' USA VS. CANADA

ENTRY CRITERIA: LOOKING FOR THE BEST CANDIDATES TO YIELD THE BEST OUTCOMES

PROSTATE SIZE ≤ 40 GRAMS; AP DIAMETER ≤ 32 MM

PSA ≤ 8.5 NG/ML ... GLEASON SCORE: 6,7,8,9

PRIMARY TREATMENT WITHIN 3.5 YEARS OF DIAGNOSIS

ABLATHERM™ TECHNOLOGY (EDAP-TMS)/SONABLATE 500 (SONACARE)

| 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) |

BIOPSY CORRELATION TO A MP-MRI SCAN IN THE SWEET SPOT STUDY

WHEN BIOPSIES WERE IDENTIFIED AS UNILATERAL OR BILATERAL THERE WAS ONLY 2 CASES IN 67 PATIENTS WHERE THE CANCER WAS NOT RECOGNIZED ON MP-MRI SCANNING AND THESE TWO CASES REPRESENTED A GS OF 3+3=6 SUGGESTING INDOLENT CANCERS

OUT OF A TOTAL OF 86 CANCERS DETECTED ON BIOPSY ONLY 3 LESIONS (GS = 6 IN 2 PATIENTS) WERE NOT FOUND USING MP-MRI YIELDING A 97% PPV

54% OF BIOPSIED PATIENTS HAD A CANCER MISSED WHICH THE MP-MRI FOUND SUGGESTING FOCAL THERAPY WOULD HAVE BEEN THE WRONG TREATMENT FOR THE MAJORITY OF THE PATIENTS HAD A SCAN NOT BEEN PERFORMED

28% (19/67) OF PATIENTS TREATED HAD BILATERAL CANCER ON BIOPSY. OF THIS NUMBER 18/19 WERE IDENTIFIED ON MP-MRI WITH THE LONE FAILURE TO DETECT BEING A GS = 6

OF THE 67 PATIENTS DIAGNOSED WITH PROSTATE CANCER, ONLY 33% WERE CORRECTLY DIAGNOSED WITH A BIOPSY WHILE 67% OF MEN WERE UNDER DIAGNOSED

| 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 A COMPARISON OF HIFU 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) | Canada (2012) | 76% - Low Grade 69.5% - Intermediate Grade |
| Wheeler,R | USA ('Sweet Spot Study' in Press) 2014 | 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 |

CONCLUSIONS:

- Excellence in Diagnostics and outcomes are associated with Physician technical skill and Imaging skill using ultrasound and a 3.0 T MP-MRI Scan
- HIFU (while robotic using the Ablatherm™ model) is not Lithotripsy
- MP-MRI prostate scans have a 98% PPV for diagnosing prostate cancer (Ref:Turkbey, Choyke et al. NIH, 2011)
- Reproducible outcomes using the Ablatherm™ HIFU technology in properly selected patients is a virtual certainty when knowledgeable & experienced physicians participate
- It is never too late to learn!! Training courses are available ... Call me!

MP-MRI REFERENCES: PROSTATE

- “Yearly MP-MRI Scans are used routinely to follow all patients on active surveillance (AS)”; (without the need for additional biopsies)!!

Julio Pow-Sang (Urologist) USF, Department of Urology

MP-MRI REFERENCES (PROSTATE):

- MP-MRI improves higher risk Prostate Cancer detection using an MRI based diagnostic pathway

“almost eliminates the diagnosis of low risk cancer”

Leslie C.Thompson, MBBS, Fracs, Urologist

Wesley Hospital & Research Institute

Brisbane, Australia

Renal & Urology News; Volume 13, Issue 5, May 2014

RADIOLOGY CORNER – AUANEWS - MAY 2014

Study compares MP-MRI of the prostate to the PCPT Risk Calculator in predicting prostate cancer.

“We found that MP-MRI improved prostate cancer detection compared to the PCPT Risk Calculator. We also demonstrated the MP-MRI outperformed the ‘Risk Calculator’ in predicting clinically significant prostate cancer (MP-MRI AUC (0.84) vs. PCPT AUC (0.68). **Ultimately, MP-MRI was less likely to miss clinically significant prostate cancers”.**

Authors: Simpa S. Salami, M.D., MPH and Art R. Rastinehad, D.O., New Hyde Park, New York