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

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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)**  
**ABLAHERM (EDAP-TMS)™**

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients (n)</th>
<th>Pre-RX PSA (ng/ml)</th>
<th>Gleason Score</th>
<th>Stage</th>
<th>Follow-up</th>
<th>Negative Bx. Rate</th>
<th>Biochemical Disease Free Rates, (PHX)</th>
<th>Re-Treatment Rate</th>
</tr>
</thead>
</table>
| Blana, et al  
Germany | 140 | ▶15.0 (Mean = 7) | ≤ 7 | T1-T2 (N0M0) | 5-7 yrs. | 86.4% | 77% @ 5 yrs. 69% @ 7 yrs. | 29.3% |
| Blana, et al  
Germany | 163 | ≤ 20.0 (Mean = 7) | ≤ 7 | T1-T2 (N0M0) | 4.8±1.2 yrs. | 92.7% | 75% @ 5 yrs. | 20.8% |
| Orovan, et al  
(Cleveland Clinic)  
Toronto, CA | 402 | ▶ 20.0 Mean6.6(3.1) Size ▶ 40 ccs  
≤ 7 GS 6(n=183) GS 7(n=219) | ≤ 7 GS 6(n=183) GS 7(n=219) | T1-T2 (N0M0) | .5–4 yrs. | 64% | 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) | ≤ 9 GS 6 (n=57) GS 7 (n=42) GS 8 (n=8) GS 9 (n=5) | T1-T2 (N0M0) | .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)**

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

<table>
<thead>
<tr>
<th>Lt. Biopsy +</th>
<th>Rt. Biopsy +</th>
<th>Biopsy + Bilaterally</th>
<th>Lt. MP-MRI +</th>
<th>Rt. MP-MRI +</th>
<th>Bilateral MP-MRI +</th>
</tr>
</thead>
<tbody>
<tr>
<td>N = 42/67 (63%)</td>
<td>N = 42/67 (63%)</td>
<td>N = 18/67 (27%)</td>
<td>N = 41/42 (98%) Correctly Identified</td>
<td>N = 40/42 (95%) Correctly Identified</td>
<td>N = 55/67 (82%)</td>
</tr>
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</table>
# BIOCHEMICAL DISEASE FREE RATES (BDFR) WITH A COMPARISON OF HIFU TO CAPSURE DATA

<table>
<thead>
<tr>
<th>Research Author(s)</th>
<th>Country</th>
<th>BDF Rates Minimum of 34 months (mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blana,A. et al</td>
<td>Germany (2008)</td>
<td>77% Low and Intermediate Grades at 5 years&lt;br&gt;69% Low and Intermediate Grades at 7 years</td>
</tr>
<tr>
<td>Blana,A., Chaussy,C. et al</td>
<td>Germany (2009)</td>
<td>75% Low and Intermediate Grades</td>
</tr>
<tr>
<td>Orovan,W. et al. (Cleveland Clinic)</td>
<td>Canada (2012)</td>
<td>76% - Low Grade&lt;br&gt;69.5% - Intermediate Grade</td>
</tr>
<tr>
<td>Wheeler,R</td>
<td>USA ('Sweet Spot Study' in Press) 2014</td>
<td>99% Low, Intermediate and High Grades</td>
</tr>
<tr>
<td>Uchida,T., Shoji,S., Nakono,M., et al.</td>
<td>Japan (2008)</td>
<td>84% - Low Grade&lt;br&gt;64% Intermediate Grade</td>
</tr>
<tr>
<td>Crouzet,S. et al.</td>
<td>France (2010)</td>
<td>83% - Low Grade&lt;br&gt;75% - Intermediate Grade</td>
</tr>
<tr>
<td>Agarwal,P., Sadetsky,N., Konety,B. et al.</td>
<td>CaPSURE Data (2008)</td>
<td>37% - All treatment Grades – EBRT&lt;br&gt;70% - All treatment Stages -Surgical</td>
</tr>
</tbody>
</table>
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 to late to learn!! Training courses are available ... Call me!
• “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
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”.