Focal Laser Ablation for Prostate Cancer Followed by Radical Prostatectomy: Validation of Focal Therapy and Imaging Accuracy


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Abstract
An increased incidence of low-risk prostate cancer (PCa) has led investigators to develop focal therapy as a management option for PCa. We evaluated the effects of focal laser ablation (FLA) on PCa tissue and the accuracy of magnetic resonance imaging (MRI) in determining ablated lesion volume by comparing the whole-mount histology and MRI in four patients that underwent FLA followed by radical prostatectomy. Ablated areas were characterized by homogeneous coagulation necrosis. The MRI-calculated ablated volume correlated well with histopathology. We found that FLA creates confluent ablation with no evidence of viable cells in treated regions. Postablation MRI is able to determine the ablation accurately.

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1. Case report
Prostate cancer (PCa) remains a significant burden to society. More younger men are being diagnosed [1], and more men are diagnosed at an earlier stage [2]. Focal therapy (FT) is emerging as an option because of its low risk for the lifestyle-altering complications associated with radical treatment yet it also aims to achieve oncologic control. For FT to gain acceptance as a management option for men with low-risk PCa, however, many issues need to be addressed [3].

Our principal objective in this study was to validate laser energy as an ablative modality by analyzing results using imaging and histopathology in definitive radical prostatectomy (RP) specimens.

Four men were prospectively enrolled to undergo RP for PCa and a focal laser ablation (FLA) procedure 1 wk prior to surgery. Our goal was to validate whether we could ablate a specific volume of PCa, create a homogeneous (confluent) ablative zone, and obtain an accurate image showing the effect of ablation using posttreatment magnetic resonance imaging (MRI).
FLA was performed as previously reported [4]. One week following FLA, patients underwent posttreatment MRI to evaluate the size of the ablated lesion followed by standard open RP on the same day. Necrosis was defined as a new confluent zone demonstrating <10% enhancement compared with the baseline pretreatment contrast-enhanced MRI [5].

The prostate was cut at 3-mm intervals [5] (Fig. 1). Whole-mount slides were stained with hematoxylin and eosin (H&E) in addition to immunostaining for cytokeratin 8 (CAM 5.2), a vital stain for prostatic tissue [6]. Stained slides were scanned using ScanScope XT slide scanning systems (Aperio Technologies, Vista, CA, USA), which allow for pathologic-grade images. Images were reviewed by a single experienced uropathologist (TVK).

All post-FLA magnetic resonance (MR) images were reviewed by an experienced uroradiologist (MAH) blinded to pathology results. The ablation zone and the prostate were contoured. The volumes of ablated tissue were compared with the calculated volumes of ablated tissue in the MR images.

The ablation zone was characterized by homogeneous areas of coagulation necrosis. At the border of the necrotic area, a small hemorrhagic rim was often identified. The cytokeratin 8 staining similarly displayed this abrupt transition of positive (vital) glandular tissue and negative (ablated) glands, and no patches of vital glandular tissue were identified within the necrotic areas. No viable cells were found on pathologic examination in the area ablated between the two fibers (Fig. 2). We were able to ablate all the way to the capsule both laterally and posteriorly (Fig. 3).

Comparison of the ablated volume traced on H&E stained pathology images with the ablated volume traced on the post-FLA MR images revealed on average that MRI-measured volume was 1.4 times pathology measurements (range: 1–1.6; Fig. 4). The Pearson correlation index between the two sets of measurements was $r = 0.79$.

Comparison of the ablated volume traced on the vital stain with the volume traced on the MR images indicated that the ablation volume measured on the MR images was on average 1.1 times larger than the ablation size calculated using vital stain histopathology images (range: 0.96–1.29; $r = 0.89$).

### Table 1 – Patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, y</td>
<td>64</td>
<td>73</td>
<td>68</td>
<td>61</td>
</tr>
<tr>
<td>PSA, ng/ml</td>
<td>2.9</td>
<td>14.8</td>
<td>4.9</td>
<td>3.5</td>
</tr>
<tr>
<td>No. of cores positive</td>
<td>3/12</td>
<td>3/11</td>
<td>3/12</td>
<td>1/12</td>
</tr>
<tr>
<td>Biopsy Gleason grade</td>
<td>3 + 3</td>
<td>4 + 3</td>
<td>4 + 3</td>
<td>3 + 3</td>
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<tr>
<td>No. of laser fibers used</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>No. of ablations (burns)</td>
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<td>3</td>
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<tr>
<td>Laser energy, J</td>
<td>3260</td>
<td>4014</td>
<td>3516</td>
<td>5900</td>
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<tr>
<td>Nerve-sparing RP</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Estimated blood loss, ml</td>
<td>400</td>
<td>500</td>
<td>600</td>
<td>250</td>
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<tr>
<td>Final Gleason score</td>
<td>3 + 3</td>
<td>4 + 4</td>
<td>4 + 3</td>
<td>3 + 3</td>
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<tr>
<td>Ablated volume on MRI, cm$^3$</td>
<td>4.5</td>
<td>2.7</td>
<td>2.5</td>
<td>4.5</td>
</tr>
<tr>
<td>Ablated volume on histopathology H&amp;E, cm$^3$</td>
<td>3.1</td>
<td>2.6</td>
<td>1.5</td>
<td>2.8</td>
</tr>
<tr>
<td>Ablated volume on histopathology vital stain, cm$^3$</td>
<td>4.5</td>
<td>2.8</td>
<td>2</td>
<td>3.5</td>
</tr>
</tbody>
</table>

H&E = hematoxylin and eosin; MRI = magnetic resonance imaging; PSA = prostate-specific antigen; RP = radical prostatectomy.
prostate tumors are found in the peripheral zone adjacent to the rectum.

Studies with various other modalities advocated for FT have performed ablation followed by RP. With whole-gland cryotherapy, in all patients studied there were areas of persistent viable PCa within the target volume [7,8].

In two studies “subtotal” high-intensity focused ultrasound preceded RP [9,10]. In these studies viable tumor was found surrounding the focal treatment zone, and limitations with targeting and ablating dorsal tissue were revealed.

Our second goal was to address the role of imaging in ascertaining treatment effect. We found that the ablated volume measured on MRI was larger than the volume traced on H&E pathology images but correlated well with the vital stain ablation volume. The high degree of correlation between MR images and the vital stain images confirms the hypothesis that lack of contrast enhancement on MRI correlates with nonviable tissue on histopathology, even if the tissue seems to retain some normal morphologic features (eg, nuclei on H&E staining). Apparently, the cytokeratin 8 staining is more sensitive for detection of necrosis than the H&E staining.

In similar designed trials, radiofrequency energy has created intraprostatic lesions demonstrating good correlation between MR-calculated volume and H&E-calculated volume [11]. Larson et al found a strong correlation ($r = 0.92$) between MR volumetric assessment of damage and H&E assessment of damage when using different forms of minimally invasive treatment modalities [12]. We also found a strong correlation between MR ablation zone and histopathology calculated ablation for FLA. Our meticulous way of processing the pathologic specimen lends added weight to these findings.
Although the additional demands on the patients in this trial resulted in limited patient accrual, valuable results were obtained. Based on this study and previous studies, MRI appears critical in FLA procedures and might prove to be the sole imaging modality for targeting the index PCa lesion, facilitating laser fiber placement for ablation and monitoring the ablation in real time using thermometry and immediately following the treatment to verify complete lesion ablation by the absence of viable tissue in the ablated area.

Conflicts of interest: The authors have nothing to disclose.

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**EU ACME Question**

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Question:
Which energy modalities have been used in the focal treatment setting?

A. Cryotherapy.
B. High-intensity focused ultrasound (HIFU).
C. Laser.
D. All of the above.

**References**