Effect of chemoradiation on cervical cancer tumor oxygenation, using Blood Oxygen Level Dependent (BOLD) MRI

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• TARGET AUDIENCE – Clinical radiologists and scientists involved in the diagnosis and treatment of cervical cancer.

• PURPOSE – Blood oxygen level dependent (BOLD) MRI sequences can non-invasively measure oxygen bioavailability in different tissues throughout the body, including the uterine cervix.[1,2] Previous studies have shown that solid tumors with low oxygenation tend to be more aggressive, as well as more resistant to both radiotherapy and chemotherapy.[3] Tumor hypoxia has been shown to be an independent and powerful prognostic indicator for poor outcomes in cervical cancer as well as other multiple other solid malignancies.[4] Current non-surgical treatment for cervical tumors involves external beam radiotherapy (EBRT) to the pelvis with concurrent cisplatin based chemotherapy, followed by intracavitary high dose brachytherapy (HDR). The goal of our study is to examine the effects of chemoradiation treatment on cervical tumor oxygenation.

• METHODS – This retrospective, HIPAA-compliant study was approved by our institutional human subjects review committee. Eleven patients (35 – 62 years; 50 +/- 8.7 years) with varying stages of cervical cancer (from IB to IIIA) were evaluated with BOLD MRI before treatment, after treatment with chemotherapy and EBRT, and after treatment with intracavitary high dose brachytherapy. All of these patients received chemotherapy and external beam radiotherapy prior to high dose intracavitary radiotherapy. Subjects were imaged with a 1.5 T MR scanner (Signa Excite HD, GE Healthcare, Waukesha, WI, USA) and an 8-channel body coil. MR BOLD images were acquired with a TR/TE/flip angle = 87ms/7-42ms/40°, FOV = 32-34cm, slice thickness 4.0 mm, skip 0.5 mm, and 256x256 matrix. Each slice was acquired in a separate 12-second breath hold. R_2* maps were constructed on a separate GE workstation in Functool®. R_2* (s^{-1}) measurements of oxygen bioavailability were measured from BOLD images by placing a region of interest over the cervical tumor. R_2* measurements of nearby skeletal muscle in the same imaging plane as the tumor were obtained as reference standard values. Values of oxygen bioavailability were compared between groups with a Student's t-test.

RESULTS: Treatment with chemoradiation and subsequent high dose intracavitary brachytherapy resulted in decreased cervical oxygenation. Pretreatment R2* values (23.5 s^{-1} +/- 9.0) are significantly lower (P=.001) than post-treatment R2* values (36.1 s^{-1} +/- 7.8). Pretreatment R2* values are also lower as compared to post-chemo-EBRT values, and although the difference is not statistically significant (P=0.12), the results trended in the expected direction.

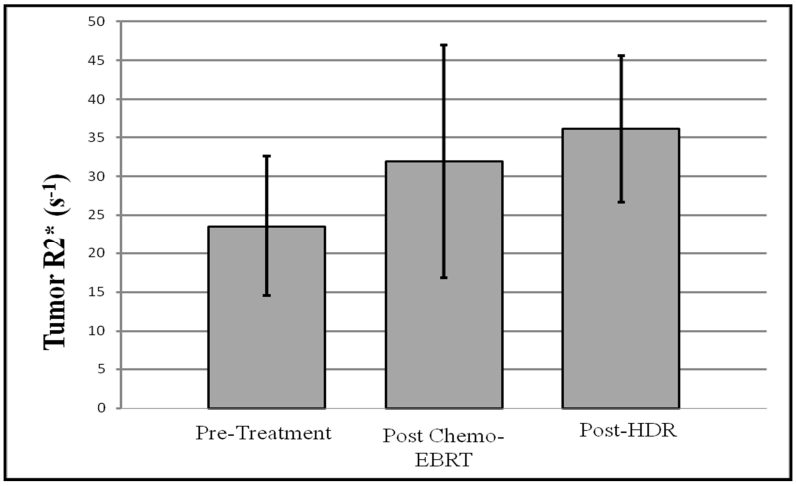

Figure 1: Tumor oxygenation as a function of treatment stage. Post-HDR R2* values are significantly higher than pre-treatment values (P=.001), indicating that tumor oxygenation decreases after treatment is rendered.

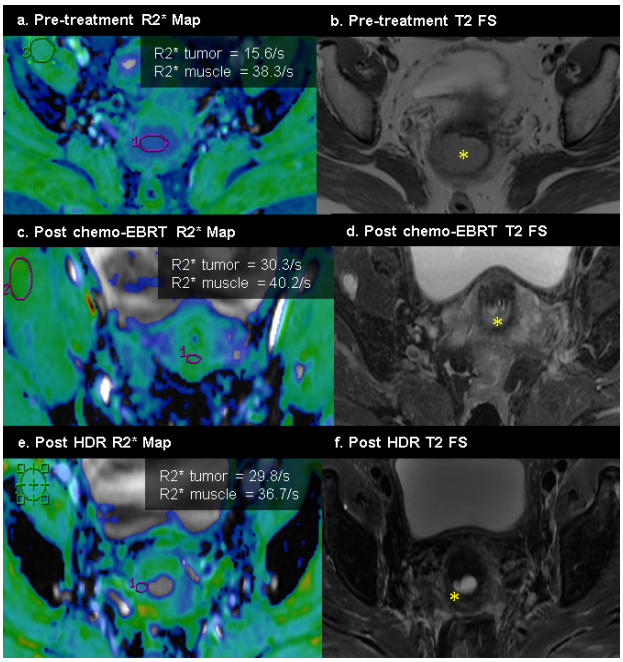

Figure 2: Example of tumor before treatment (A and B), post chmo-EBRT (C and D), and post HDR (E and F). * represents tumor in B, D, and F.

• DISCUSSION / CONCLUSION - Our findings suggest that cervical oxygenation decreases (as seen by higher R2* values) after treatment with chemotherapy / external beam radiation / brachytherapy. The explanation for these results may include reduced angiogenesis, reduced tumor volume, and/or increased fibrotic tissue formation. It has been shown that relatively hypoxic tumors in general respond more poorly to radiotherapy due to decreased radiosensitivity, BOLD MRI may be useful in differentiating between those tumors which will be radiosensitive and those that will not. In the future, BOLD MRI may become a routine, clinically useful method to determine cervical tumor oxygenation status. Limitations of this study include small sample size, unknown patient hemoglobin level during each imaging phase, and its retrospective nature. Further work will be required to determine if there is indeed a difference in the treatment response depending on tumor oxygenation levels.

• REFERENCES –

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