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<u>Magnetic Resonance Guided High Intensity Focused Ultrasound: A Novel Noninvasive Technique to Treat Soft Tissue Tumors of the Extremity.</u>

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INTRODUCTION: Local control treatment modalities for soft tissue tumors such as radiation and **s**urgery are associated with morbidity which may include wound infections, scarring, nerve injury, joint stiffness, and prolonged recovery. Over the last few decades there have been relatively few improvements in surgical treatments for soft tissue tumors. Magnetic resonance guided high intensity focused ultrasound (MRgHIFU) thermal ablation is a relatively new noninvasive treatment modality that can ablate solid tumors while sparing surrounding normal tissues (Figure 1). MRgHIFU is FDA approved for treating uterine fibroids and metastatic bone disease and the purpose of our study is to adapt this technology to treat soft tissue tumors of the extremity.

BACKGROUND: MRgHIFU is based on the physical properties of sound. When propagating through human tissue, the acoustic energy of the sonic pressure wave causes tissue shearing on a microscopic level that leads to frictional heating. In most circumstances, ultrasound travels through human tissues with very little energy deposition and no detectable rise in temperature or other harmful effects. However, when multiple acoustic pressure waves converge onto a designated focal point, sufficient energy is deposited into a focused volume to cause heating and thermal necrosis of the tissue. Because heating only occurs where the ultrasound waves converge, the surrounding tissue remains unaffected. When treating tumors in a clinical setting, multiple treatment foci are targeted within the tumor in an overlapping manner such that at the completion of therapy the sum of all the ablations results in complete tumor thermal necrosis. MR thermometry is done in real time during the HIFU treatment and allows direct visualization and temperature mapping of the target tissue (Figure 2). This technology is a potentially a new noninvasive treatment modality for ablating soft tissue tumors in the extremity. Research to understand its effectiveness and safety must be performed.

PURPOSE: The purpose of this study was to determine the feasibility of using MRgHIFU technology to treat soft tissue tumors of the extremity and to report our experience using MRgHIFU in 5 patients with desmoid tumors. We specifically asked: (1) can we use commercially available MRgHIFU equipment to accurately ablate a predetermined target volume within a human cadaver extremity? and (2) What are the preliminary results of MRgHIFU treatment in human patients with desmoids tumors?

METHODS: We used a commercially available HIFU system to perform thermal ablation of simulated tumor volumes in four human cadaver extremities. The simulated tumor volumes were created by percutaneously inserting plastic intravenous catheters in a predetermined geometric pattern into the cadaver muscle. These catheters are visible on MR imaging and define the boundary of the simulated tumor. We conducted the ablations using standard settings of the MRgHIFU device which included a frequency range of 0.9MHz to 1.35MHz and energy deposition of 800J-2900J per sonication. The goal of treatment was to ablate the simulated tumor volume. Upon we then dissected each cadaver limb and measured the actual area of tissue ablation and compared that to the intended area of ablation. Accuracy was determined by measuring the location error according to the International Organization of Standards (ISO). The location error is defined as the longest vertical distance between the predicted ablation plane and the farthest point of actual ablation. We examined each specimen for complications such as skin burns and unintended nerve or vascular burns. After completion of the cadaver studies we obtained approval from our institution's ethics committee to perform MRgHIFU on 5 patients with desmoid tumors. Two patients had progressive disease in spite of exhausting standard treatments, and 3 patients declined surgery, radiation, and systemic treatment. All patients were extensively counseled and signed a comprehensive consent document.

RESULTS: The ablation accuracy for the four cadaver extremities was 5mm, 3mm, 8mm, and 8mm. There were no gross neurovascular structure burns. In a lower leg specimen where the target volume was in the soleus muscle we noticed unanticipated burning along a thick portion of the gastrocnemius aponeurosis. In all five patients the treated portion of the tumor, which avidly enhanced with contrast prior to treatment did not enhance after treatment. Average followoup was 12 months. There were no major complications. In one patient the tumor completely resolved and the remaining 4 patients the tumors stopped growing or became smaller (Figure 3). Overall function using the MSTS outcome score either improved or was stable after completion of treatment.

CONCLUSION: MRgHIFU can be used to accurately ablate tumor volumes in the extremity. Initial experience treating desmoid tumors is encouraging and warrants further investigation.

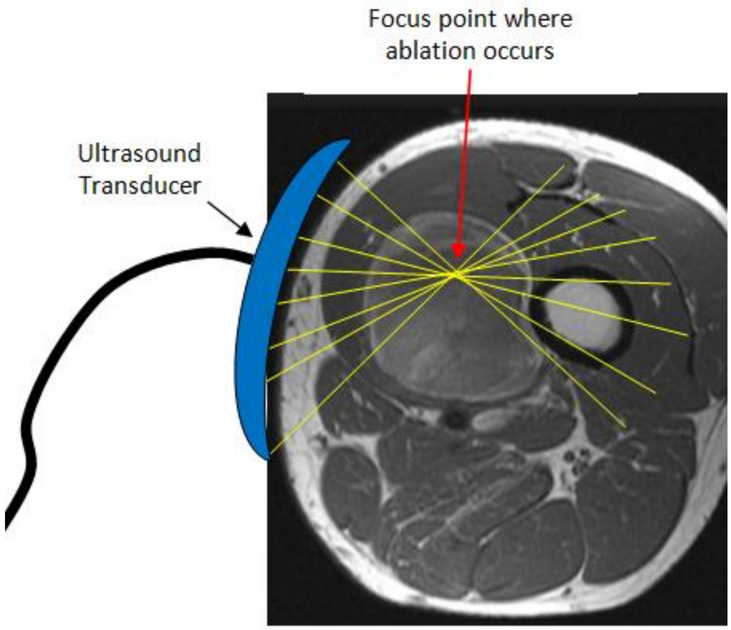

Figure 1 Schematic of a HIFU treatment of sarcoma located in the vastus medialis. The yellow lines represent ultrasound waves that propogate through the thigh without causing. At the focus the waves converge and cause heating of the target tissue while the surrounding tissue are unharmed. The heat is sufficient to ablate a volume approximately the size of a grain of rice. Multiple sonications are performed until the desired volume of tissue is ablated.

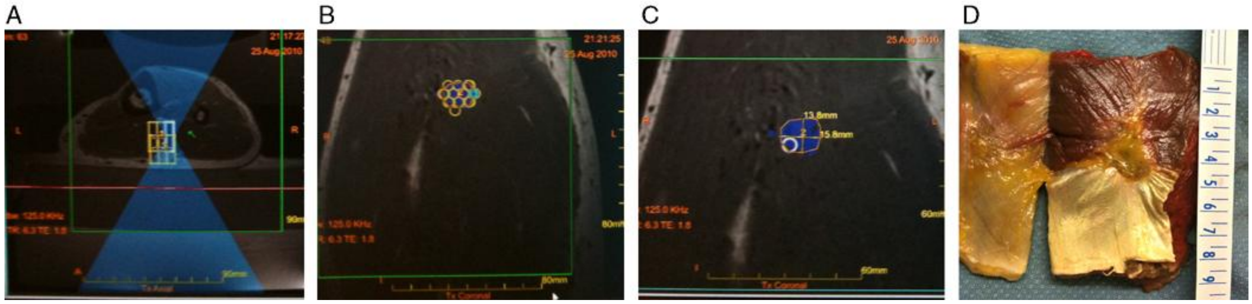

Figure 2. MR guided high-intensity focused ultrasound (HIFU) ablation in a cadaver lower leg. (A) Axial T1 MR image of a human cadaver lower leg undergoing HIFU planning. The yellow cylinders represent planned areas of sonication, in this case where the rice noodles were placed as fiducials. The blue hourglass represents the trajectory of the ultrasound energy with the focus located at the waist. (B) Coronal T1 MR image. The yellow circles represent the coronal view appearance of the same areas to be sonicated. (C) Coronal T1-weighted image of the area treated (blue) by MR thermometry. (D) Tissue specimen showing treated area.

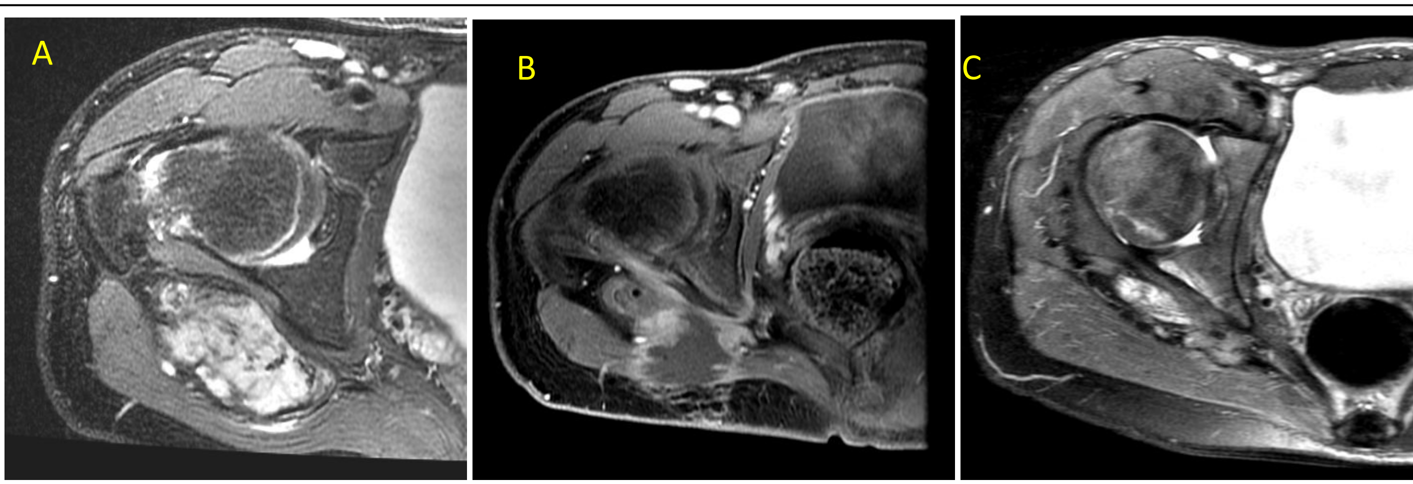

Figure 3. Twelve year old boy who had (A) an enlarging desmoid tumor of his right buttock as seen on this T2 weighted MR image. He had local recurrences after two operations including a left above knee ampuation. He had stable disease while on chemotherapy but progessive disease when he stopped systemic treatment. He underwent two MRgHIFU treatments with (B) T1 fat suppressed post contrast MRI showing necrosis of the tumor and (C) near complete resolution of the tumor as seen on a 4 month followup T2 weigted MRI.