GUIDING NANOPARTICLE ENHANCED PHOTOTHERMALTHERAPY FOR CANCER WITH PHOTOACOUSTIC THERMAL IMAGING AND DIFFUSE OPTICAL TOMOGRAPHY

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Key Words: photothermal therapy, photoacoustic, diffuse optical tomography, thermometry, nanoparticles.

Recent advances in magnetic resonance thermal imaging have begun to enable minimally invasive alternatives to conventional cancer treatment, including Photothermal Therapy (PTT). PTT is a promising technique where thermal tumor destruction is facilitated by NIR laser light delivered through thin optical fibers. As such, this therapeutic method avoids the negative side-effects of surgery, radiation, and chemotherapy, which represent significant hardships for the patient as well as high cost to the health care system. Our ongoing phase II clinical trial of MRI-guided PTT for prostate cancer (PCa) shows promise but suffers from complex, indirect, and slow imaging guidance[1]. This is particularly problematic when treatment is near critical structures like the rectal wall where just a few millimeters of overtreatment may lead to serious injury. Out of abundance of caution the operating surgeon may terminate the treatment prematurely. These drawbacks are contributing to an approximately 30% tumor undertreatment rate in our trial, along with increased risk of recurrence, and are preventing widespread adoption and benefits of PTT.

To maximize the potential impact of PTT as well as other thermal therapies, we are developing a photonics-based PTT guidance platform with the direct precision of hand-held functionality and simultaneous real-time imaging of the tumor location, treatment intensity, and treatment response, embodying the 3 main requirements for PTT until now provided only by MRI. Here we share recent results from our prototype photoacoustic (PA) PTT-guidance system as well as our hybrid magnetic resonance-diffuse optical tomography (MR-DOT) prostate-specific probe and system designed for *in-human* MR-guided PTT validation studies.

Characterization of the instrument platform included deep tissue real-time PA thermal mapping during PTT in tissue mimicking polyacrylamide coagulating phantoms and *ex-vivo* tissue. Tumor-localizing porphysome nanoparticle PA imaging was evaluated in a vascular phantom at clinically relevant depths. Our MR-DOT guidance system capability was assessed with *in-patient* MR-DOT measurements during clinical PTT for PCa.

The prototype guidance platform PA thermometry during 5-watt and 2-watt PTT in coagulating phantoms and ex-vivo tissue, respectively, was found to be in good agreement with the expected 55°C coagulation temperature (Figure 1). Furthermore, real-time (10 Hz) wide-field (5-cm x 5-cm) porphysome imaging at depths of up to 4 cm was achieved highlighting clinically appropriate depth and field-of-view performance.

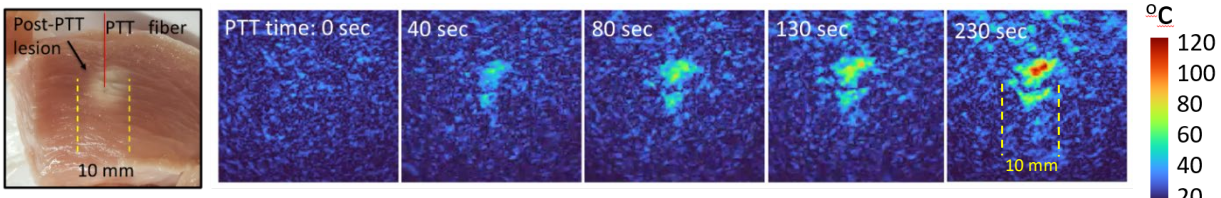

Figure 1 – Real-time photoacoustic thermometry in ex-vivo poultry tissue during 2-watt PTT

Results from our MR-DOT scans during *in-patient* PTT for prostate cancer showed consistent >60% tissue coagulation-induced attenuation indicating direct system sensitivity to treated tissue extent.
Our biophotonics-based guidance platform uniquely embodies all 3 requirements for PTT, but with direct real-time feedback for efficient functionality and accuracy. The intuitive precision of hand-held imaging simultaneously specifying tumor location, treatment zone temperature, and extent of treated tissue will spare nearby critical tissues while ensuring complete treatment of the tumor mass. As such, the proposed imaging platform represents both high translational potential as well as high impact on cancer treatment.

[1] Lindner U, et al. Image guided photothermal focal therapy for localized prostate cancer: phase I trial. J Urol. 2009 Oct;182(4):1371-7