Purpose:
Motivated by the need of alleviating tumor hypoxia-related resistance to radiation therapy, we propose to develop a magnetic resonance imaging (MRI) guided focused ultrasound system (MRgFUS) incorporating positron emission tomography (PET) hypoxia imaging to detect and coagulate the hypoxic areas in mouse tumors before radiation treatment. We plan to use this system to test the hypothesis that thermal coagulation of evidently hypoxic regions of a tumor can improve radiotherapy outcome.

Methods:
A prototype system was established to seamlessly integrate the processes of PET imaging and MRgFUS ablation. It includes (1) A small animal specialized MR-compatible FUS applicator using a spherically-focused ultrasound transducer. (2) 18F- fluoromisonidazole microPET imaging (Siemens) to acquire and correlate the uptake of 18F-miso tracers to hypoxic tissue in tumors. (3) A small animal positioning and immobilization device that is compatible both to PET and MRI, and can facilitate anesthesia supply, breathing sensor and FUS applicator. (4) An effective method to register PET images with MRI images so that the regions of hypoxic, necrotic, and normoxic tissue can be delineated within a tumor. (5) MRgFUS ablation of the segmented tumor hypoxic areas with the guidance of MRI-acquired (7.0 T Bruker) temperature maps. To test the robustness of this system, we conducted in vivo experiments on six A/J mice bearing 4T1 tumors.

Results:
The tumor hypoxic regions can be clearly distinguished by 18F-miso PET scans of mouse tumors with i.v. injection of 1 mCi/mouse and 1.5-2 hours of uptake. The positioning and immobilization device allowed accurate registration of PET and MRI images. Accurate targeting and heating (error <2 mm) was achieved with MRI-temperature guidance (resolution: 0.2×0.5mm, per 4 s).

Conclusions:
The overall system/approach has proven the feasibility of PET+MRgFUS and should be useful in the study of combined treatment strategies incorporating radiation and thermal therapy using small animals.