Sympathetic Renal Denervation using MR guided Focused Ultrasound in a Porcine Model: a Feasibility Study

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PURPOSE: Drug-resistant hypertension remains a significant cardiovascular risk factor for millions of people. Renal sympathetic nerves, wrapping around the renal artery wall, have been identified as a key factor in initiating and maintaining systemic hypertension[1,2]. Recently, invasive catheter-based techniques have gained prominence in their ability to ablate the sympathetic nerves through the lumen of the main renal artery, demonstrating a significant reduction of blood pressure sustained up to 12 months[3]. Further, a non-invasive extracorporeal focused ultrasound system used under ultrasound guidance has been used effectively in renal sympathetic denervation[4]. This abstract presents a feasibility study of performing renal denervation using magnetic resonance guided focused ultrasound (MRgFUS) in a porcine model. ***TARGET AUDIENCE:*** Clinicians and physicists interested in renal denervation and the expansion of MRgFUS applications.

METHODS

At the time of submission, renal denervation had been performed on three normotensive female Yorkshire pigs (40-50 kg). Baseline invasive blood pressure measurements were obtained before the ablation procedure. All animals underwent unilateral renal denervation using a pre-clinical MRgFUS system (256-element phased-array transducer, f=1 MHz, IGT, Inc., Pessac, France) in a Siemens Trio 3T MRI scanner (Erlangen, Germany). After the animal was anesthetized, a fiberoptic temperature probe (Qualitrol, Quebec, Canada) was placed inside the target renal artery under fluoroscopy guidance. The purpose of the probe was to provide an independent measure of energy delivery and target confirmation during the ablation procedure. The pig was placed on top of the MRgFUS system in a custom support holder with an integrated 9-channel RF receive coil in a lateral supine position (Figure 1). MR imaging was used to evaluate the acoustic window, plan the sonication locations around the target renal artery (Figure 2), monitor the near-field heating of the treatment using MR thermometry imaging (3D Seg-EPI sequence, TR/TE=35/11 ms, 2x2x3 mm, 8 slices/25% oversampling, 25° FA, fat saturation, 752 Hz/pixel) and post-treatment evaluation. Several single point sonications (80-100W, 10-20 seconds) were applied to the regions at a close anatomical proximity to the renal arteries. Post-treatment invasive blood pressure measurements were obtained 5-7 days after the MRgFUS treatment and the animal was sacrificed. Histological analysis was performed on both treated and untreated renal arteries that served as controls and surrounding tissues. This study was approved by the local Institutional Animal Care and Use Committee.

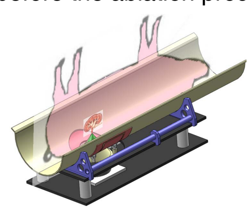

Figure 1*: Schematic of the pig placement on the MRgFUS system.*

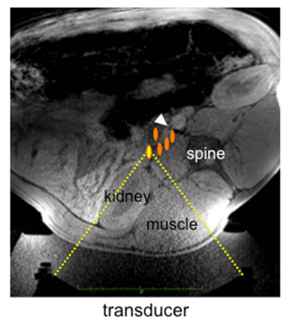

Figure 2*: Axial image of pig on MRgFUS device. Transducer, acoustic window (yellow dashed-line), and approximate sonication sites (orange) are shown. Temperature probe can be seen in the renal artery (white arrow).*

RESULTS

All animals tolerated the procedure well with no apparent adverse side effects. A mean systolic and diastolic blood pressure change of -11.5±13.4 and -23.5±0.7 mmHg was seen in two of the animals 5-7 days post-renal denervation (post-treatment measurements had not yet been obtained on the 3rd animal at the time of submission). The temperature response measured by the fiberoptic temperature probe during a single 20-second ablation is shown in Figure 3. The near-field around the spine was monitored during the ablation procedure. No temperature rise was observed. There were distinct differences in the histological appearance of the nerve bundles located in the adventitia between the treated and non-treated sides (Fig. 4). In contrast there was no indication of damage to either arterial wall.

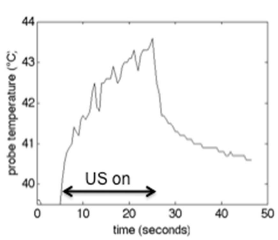

Figure 3*: Reading of temperature probe in renal artery during location shown in yellow (Fig. 2)*

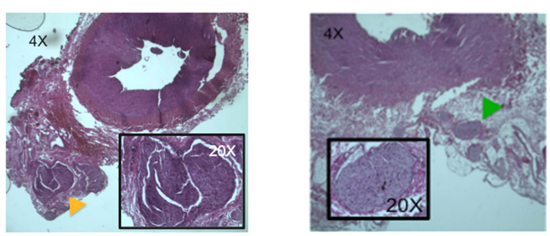

Figure 4: *Histological analysis of nerve bundles day 5 post-denervation treatment. The left image is from the treated artery and the right image is from the control side. The nerves surrounding the treated artery (orange arrow) have enhanced cellular infiltrate, indicative of damage, compared with the nerves (green arrow) surrounding the untreated artery.*

DISCUSSION & CONCLUSIONS

Our initial results presented here demonstrate that MRgFUS can be effectively and safely used to perform renal denervation in a porcine model. Both animals evaluated had a decrease in blood pressure, though the measurements were made while the animal was under anesthesia. Using MRI to guide and monitor the non-invasive FUS procedure can potentially ensure accurate targeting and visualization of the entire acoustic window increasing the overall safety of the procedure, eliminating invasive catheter procedures and use of radiation.

REFERENCES

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