Thiel Soft Embalmed Porcine Kidney Perfusion Model for Focused Ultrasound Therapy

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***Abstract*— Thiel soft embalmed porcine kidneys have been used to study the effect of artificial blood flow on focused ultrasound (FUS) therapy. A significant temperature drop is observed when a perfusion is established within the porcine kidneys, compared with the no-flow condition FUS leads to a 2 ~ 4 ºC higher temperature rising. The influence of Thiel soft embalmed Porcine Kidney Perfusion Model for Focused Ultrasound Therapy effect from blood flow must be considered.**

I. INTRODUCTION

A 3D computational model study by P. Hariharan et al. [1] indicates that the blood flow contributed significant reduction in focused ultrasound lesion volume when a vessel is located within approximately a few millimeter width of ultrasound. Considering the representative clinical conditions, compared with no-flow, the formed lesion volume will be reduced by approximately 40% and 20%, when the beam is located parallel and perpendicular to the blood vessel, respectively.

L. Chen et al. [2] performed FUS on in vivo rat livers. The ultrasound induced lesion size become significantly different at exposure durations more than 3 s, compared with normal blood flow and with reduced blood flow (250 ml/100g min^{-1} and 5 ml/100g min^{-1}, respectively).

Thiel fluid is an embalming to preserve natural properties of biological tissues, and it does not cause significant difference on thermodynamics properties. Therefore the Thiel kidney is the ideal specimen for the perfusion and FUS therapy experiment [3].

A pair of porcine kidneys has been processed by using Thiel fluid and the blood circulation rebuild with 0.9 % saline water by using heart lung machine. The MR guided FUS system has been used to perform sonication on the simulator to find the difference of therapeutic results between the conditions with or without blood flow.

II. MATERIALS AND METHODS

A. Materials

The materials used to simulate were fresh porcine kidneys, embalmed in Thiel fluid. The experimental equipment included MR scanner (Signa HDx 1.5 T, GE Healthcare, USA, *Fig. 1 (a)*) with pelvic coil, InSightec ExAblate 2000 sonication system (InSightec, Israel, *Fig. 1 (b)*), Jostra heart lung Machine (Maquet HL30, Germany, *Fig. 1 (c)*). Other associated supplies included transparent waterproof box, rubber tubes and connectors, 0.9 % saline water.

Fig. 1 (a) MR scanner; (b) ExAblate 2000 sonication system; (c) MAQUET Jostra Heart lung machine.

B. Simulator

To prepare the Thiel porcine kidney perfusion simulator, there are two parts of work, the first part is to prepare the Thiel porcine kidneys, and the second part is to build up the circulation of saline water in the Thiel porcine kidneys to accomplish the simulation of blood circulation.

A pair of fresh porcine kidneys has been processed by using Thiel fluid. The blood vessels of fresh porcine kidney are covered by fat and other tissues, they need to be dissected out by removing the fat and other tissues. The renal aorta is used as the inflow while the renal vein is the outflow. The aorta is the most significant vessel, it is used to inject the fluid. To find the outlets of vein and ureter as well as other potential leaking points, 0.9 % saline water has been injected form the aorta access. The hemostat is required to close the distal of the aorta to make sure the whole saline water is perfused into the kidneys' blood circulation network. The inflow access of renal aorta is fixed a pipe connector in order to connect with rubber tubes for circulation, see *Fig. 2*.

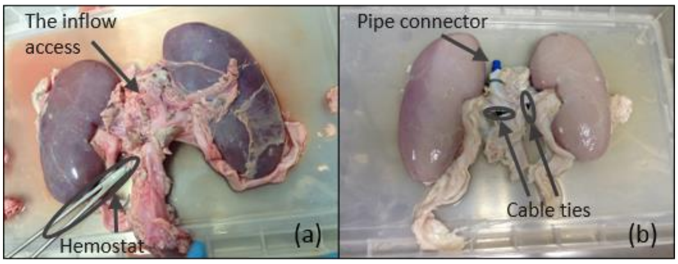

Fig. 2 The preparation of Thiel porcine kidney perfusion simulator: (a) Saline water is injected from the aorta access. The hemostat is required to close the distal of the aorta to make sure the whole saline water is perfused into the kidneys; (b) Leaking points and distal end of the aorta need to be blocked off by using small cable ties and twine.

The kidneys need to be cleaned and perfused with 0.9 % saline water from the access to wash out the remaining blood.. The flux rate of perfusion inflow should not be too quick to damage the vessels, which should be lower than 500 ml/min. After flushing the kidney by saline water, the kidneys need to be perfused by Thiel fluid through the aorta access to prevent decay. The volume of Thiel fluid is approximate 500 ml. Then the kidney is stored in Thiel tank fluid, for 4~5 days to complete the preservation before sonication experiment.

C. *Circulation*

To build the circulation simulator, a pair of kidneys is put into a transparent box, as *Fig. 3*.

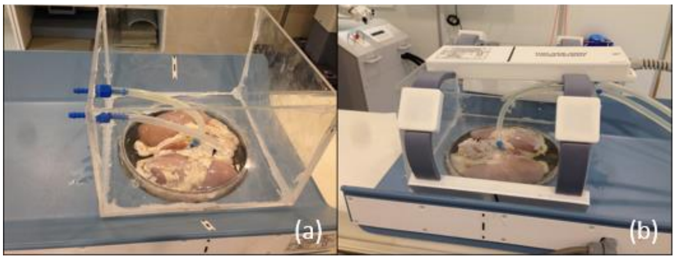

Fig. 3 (a) The transparent box designed for perfusion experiment; (b) Whole set-up model with the InSightec Pelvic MR receiving coil in place.

The box is designed as MR compatible and suitable for ExAblate 2000 FUS therapeutic system. It is equipped with a 220 mm diameter cylinder tube, covered with plastic film, aligning with FUS transducer, which is design to fit to the Pelvic MR receiving coil. The box is waterproof.

The inflow rate is set to approximately 300 ml/min, while the outflow rate should outnumber slightly the inflow rate to prevent leaking caused by too high pressure. The diagram of *Fig. 4* illustrates the whole experimental set-up.

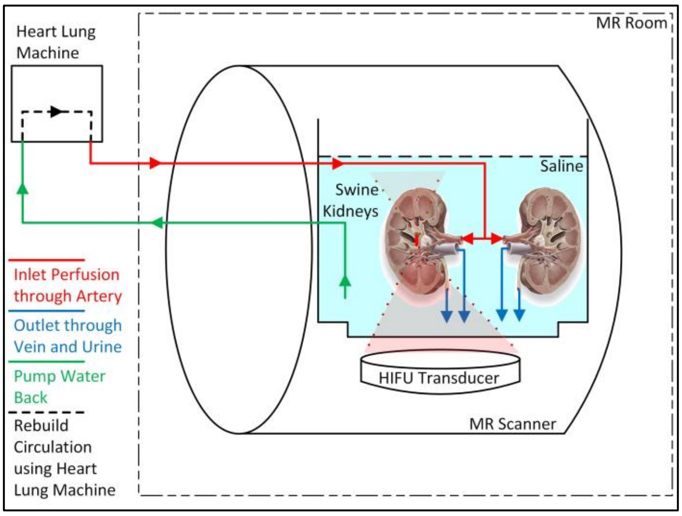

Fig. 4 The diagram of experimental set-up.

D. *Imaging and Sonication*

The GE Signa HDx 1.5 T MR scanner with Pelvic coil (InSightec) has been employed to plan and monitor the FUS therapy. The scan protocol 3D-FIESTA (fast imaging employing steady state acquisition) is used to image the kidneys, and parameters are set as *Table 1*.

Table 1 The parameters for MR scanning

Parameters	Value
TR	3.2 ms
TE	1.3 ms
Flip Angle	60°
Slice Thickness	5 mm

The InSightec ExAblate 2000 sonication system has been used to do the FUS therapy on the perfused porcine kidneys, the parameters of the sonication are shown as *Table 2*.

Table 2 The parameters for sonication

Parameters	Value
Acoustic Power	20 W
Duration Time	20 s

The sonication target position were selected nearby main vessels, approximately 5 mm away from the vessels. Each selected position will have one pair sonication points, one under the condition with blood flow, while another without.

III. RESULTS

The 3D-FIESTA scanning protocol could provide clear image of the blood vessels inside the kidney. Especially with blood flow, the vessels appear much brighter than surrounding tissues, shown as *Fig. 5*.

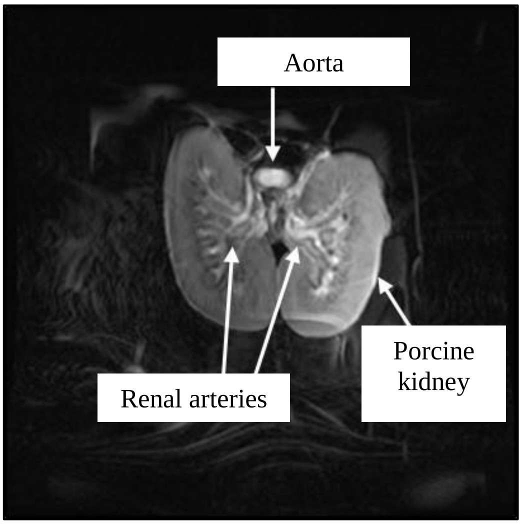

Fig. 5 A coronal MRI scan result, the vessels are visible under flow condition, 1.5 Tesla using 3D-FIESTA imaging protocol.

Five pairs of points (10 spots, pairing by flow or no-flow) are selected to be performed sonication. *Fig. 6* and *Fig. 7* shows the temperature rising results of the sonication performed on a pair of selected points.

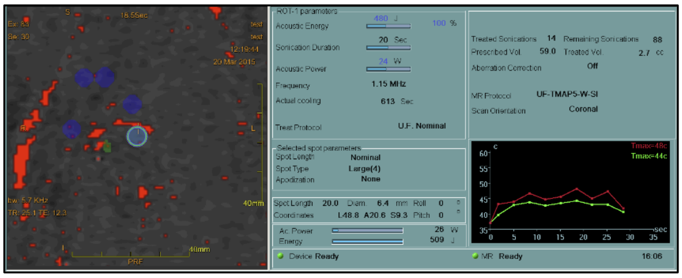

Fig. 6 Result of temperature rising with blood flow.

An example of temperature rising result during sonication on a selected point in *Fig. 6*. The blood flow was present while sonication. The temperature monitoring curve shows the maximum temperature reached 48 °C.

Fig. 7 Result of temperature rising without blood flow.

An example of temperature rising result when sonicating in the same area as *Fig. 7* shows, closest to the paired point which *Fig. 6* shows. The blood flow was stopped by turning off the heart lung machine. The maximum temperature reached 51 °C, which was 3 °C higher compared with the 48 °C, while the blood flow was available.

As mentioned before, at 5 paired points sonication was performed. Three pairs of the selected sonication points showed reasonable results, while the data from the other 2 pairs of points contains too much noisy to analyze. From the comparison of temperature rising of 3 sets of sonication points, a significant temperature drop was observed when a perfusion blood flow is available within the porcine kidneys, and the no-flow condition has a 2 ~ 4 °C higher temperature rising. The 3 sets of results about temperature rising is shown as *Table 3*.

Table 3 A summary of the sonication results

	With flow	Without flow
No. 1	44 °C	46 °C
No. 2	48 °C	51 °C
No. 3	49 °C	53 °C

IV. Discussion

The experiments indicate, that the influence of the blood flow on FUS ultrasound therapy can be simulated in a Thiel soft embalmed porcine kidney. The blood flow has considerable contribution on the tissue cooling adjacent to the sonication spot. The temperature drop requires longer FUS exposure duration.

S. A. Sapareto and W. C. Dewey [4] proposed a reference thermal dose t_{43}. It indicates that the thermal dose of 240 minutes at 43 °C is sufficient to induce necrosis in tissue. Using Sapareto-Dewey thermal dose equation (1), all thermal exposures are converted to "equivalent-minutes" at this reference temperature,

$$t_{43} = \sum_{t=0}^{t=final} R^{(43-\bar{T})} \Delta T \qquad (1)$$

where t_{43} means the equivalent time at 43°C; Δt is time interval between temperature measurements; $\bar{T}$ is the average temperature during the time Δt; and R is defined as a rate, for $R=0.25$ when $T < 43$°C, and $R=0.5$ when $T > 43$°C [4-6].

According to the Sapareto-Dewey thermal dose equation (1) in order to achieve the equivalent biological effect, the exposure duration will reduce by half when every 1 °C temperature rise above 43 °C. For example, the exposure of 1.75 s at 56 °C will cause the same level of thermal damage as the reference thermal dose t_{43} [5, 6].

Using Sapareto-Dewey thermal dose equation (1), the equivalent thermal dose of each temperature at *Table 3* could be calculated. It is assumed that the temperature is constant value as the maximum. And the difference of the two thermal dose of each group 'with flow' and 'without flow' is also shown as *Table 4*.

Table 4 Equivalent thermal dose

	t' /*With flow*	t'' /*Without flow*	$t' - t''$
No. 1	7200 s / *44 °C*	1800 s / *46 °C*	5400 s
No. 2	450 s / *48 °C*	56.25 s / *51 °C*	393.75 s
No. 3	225 s / *49 °C*	14.06 s / *53 °C*	210.94 s

The difference of equivalent thermal dose between ‘with flow’ and ’without flow’ is not negligible, especially the ablate temperature is relatively lower. This result illustrates the influence from blood flow during FUS therapy.

V. Conclusion

From this early-stage experiment, it indicates that the blood flow has influence on FUS ultrasound therapy. The target tissue under FUS therapy has conductive thermal transfer to the surrounding, and the blood flow supplies extra convectional thermal transfer, which has considerable contribution on the tissue cooling down. The experimental results indicate clear temperature drops are observed when a perfusion blood flow is available within the porcine kidneys, compared with a 2 ~ 4 ºC higher temperature rising in the no-flow condition. Therefore it is reasonable to consider the influence from blood flow when decide the thermal dose for FUS therapy if the target tissue is nearby the vessels, especially the main vessels.

VI. Future Work Plan

This experiment is at a preliminary stage, currently only comparing the conditions with and without blood flow. In order to understand the biological effect which is much closer to clinical practice, another experimental plan is to perform the perfusion on fresh porcine kidney as well as Thiel human cadaver kidney. The research plan will include the influence of different velocities of blood flow, different distances between vessel and target focus point, and different relative location of focus point and vessel.

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References

[1] P. Hariharan, M. R. Myers, and R. K. Banerjee, "HIFU procedures at moderate intensities—effect of large blood vessels," *Physics in Medicine and Biology,* vol. 52, p. 3493, 2007.

[2] L. Chen, G. t. Haar, C. R. Hill, M. Dworkin, P. Carnochan, H. Young, *et al.*, "Effect of blood perfusion on the ablation of liver parenchyma with high-intensity focused ultrasound," *Physics in Medicine and Biology,* vol. 38, p. 1661, 1993.

[3] W. Thiel, "[The preservation of the whole corpse with natural color]," *Annals of anatomy= Anatomischer Anzeiger: official organ of the Anatomische Gesellschaft,* vol. 174, pp. 185-195, 1992.

[4] S. A. Sapareto and W. C. Dewey, "Thermal dose determination in cancer therapy," *International Journal of Radiation Oncology*Biology*Physics,* vol. 10, pp. 787-800, 4// 1984.

[5] Z. Qiu, "Development of MRI-compatible Transducer Arrays for Focused Ultrasound Surgery: The Use of Relaxor-PT Piezocrystals," PhD, School of Engineering, Physics and Mathematics, University of Dundee, 2014.

[6] G. Ter Haar, "Acoustic surgery," *Physics Today,* vol. 54, pp. 29-34, 2001.