Transcranial Ultrasound Thrombolysis

Kim Philippi, UC II
Nancy Hahn, UC I
Kenneth Wagner, PhD**
Daniel Kanter, MD **
Thomas Thomsick, MD*
Christy Holland, PhD*
* Dept. of Radiology, University of Cincinnati
** Dept. of Neurology, University of Cincinnati

Objective:
To aid in the development of a Transcranial Ultrasound Thrombolysis System (TUTS), the thickness and ultrasound attenuation of the human temporal bone was compared to that of the pig. In addition, the synergistic thrombolytic effect of tissue plasminogen activator (t-PA) and 1MHz ultrasound was assessed *in vitro*.

Methods:
To determine the thickness of the temporal bone, measurements were made using electronic calipers on CT images of 20 females, 20 males, and an *ex vivo*, 4-wk-old porcine skull. In a 51.5 x 31.5 x 22 cm water tank, the acoustic output from a 1" diameter, 1-MHz transducer was measured in 3 orthogonal planes with a bilaminar PVDF hydrophone. To determine the effect of the temporal bone on the field, a human or porcine skull segment was inserted between the ultrasound transducer and the hydrophone and the attenuated signal was measured. In addition, standard clots were made from 3 mL of citrated porcine blood plus thrombin (3 IU). Fourteen clots were incubated for 3 hrs in a 37 C water bath, refrigerated overnight, blotted, and weighed. Four clots were treated with 0.1 mg/ml t-PA for 30 minutes, and weighed. Ten clots, bathed in 0.1 mg/ml t-PA, were exposed to 1-MHz pulsed ultrasound over a range of duty cycles at two amplitudes for 30 min in a 37 C water bath, and weighed to determine the efficacy of thrombolysis.

Results:
Maximum thicknesses of the temporal bone were: 0.66 (+/- .14 SD) for females, 0.69 (+/- .11) cm for males and 0.71 cm for the porcine skull. Minimum thicknesses of the temporal bone were: 0.22 (+/- .07) cm for females, 0.23 (+/- .05) cm for males and 0.5 cm for the porcine skull. *In vitro* thrombolysis correlated with both t-PA concentration and exposure duration. In addition, 1-MHz ultrasound treatment with a peak-to-peak pressure of 0.2 or 1.1 MPa combined with a t-PA dose of 0.1 mg/ml decreased clot mass by 19-68 %.

Conclusions:
Temporal bone thicknesses are similar between males and females and between 4-wk-old pigs and adult humans. Thus, the juvenile pig may serve as an ideal animal model to test the efficacy of TUTS. Also, our *in vitro* findings suggest that 1-MHz ultrasound improves clot lysis with 0.1 mg/ml t-PA.