Change in Ultrasonic Backscattered Energy for Temperature Imaging:
I. Simulation with Multiple Scatterers
II. Measurements from In Vivo Images

R. Martin Arthur¹, Jason W. Trobaugh¹, William L. Straube², Jesse Parry², Yuzheng Guo¹, and Eduardo G. Moros³

¹Electrical & Systems Engineering
²Radiation Oncology
Washington University in St. Louis.
St. Louis, MO, 63130, USA
³Radiation Oncology, University of Arkansas

Supported by NIH Grants R21 CA90531, R01 CA107558 and the Wilkinson Trust at Washington University
Objective of Ultrasonic Thermometry

To develop a method to produce 3D temperature maps in soft tissue during hyperthermia cancer treatment

- non-invasively, conveniently at low cost with a single view from standard equipment
- with at least 0.5°C accuracy & 1 cm³ resolution
Change in backscattered energy (CBE) as a monotonic temperature-dependent parameter

- **CBE single-scatterer prediction**
  
  *U Med & Bio, 20:915-922, 1994*

- **CBE from isolated echoes in 1D**
  
  *Medical Physics, 30:1021-1029, 2003*

- **CBE over selected regions in 2D**
  
  *IEEE UFFC, 52:1644-1652, 2005*
Change in backscattered energy (CBE) as a monotonic temperature-dependent parameter

- CBE in selected regions in 2D in 4 liver, 2 turkey & 1 pork samples
- Null tests
  - No heating ($\pm 0.2$ dB)
  - Heating effects on the transducer ($\pm 0.1$ dB)
  - Positioning ($\pm 0.05$ dB)
- CBE in simulations of scatterer collections
I. Simulation of Scatterer Collections

- To provide a theoretical representation for images of multiple scatterers to extend our single-scatterer model
- To study effects of noise
- To establish calibration procedures
- To determine limits on spatial resolution and temperature accuracy
Simulation Methods

Discrete-Scatterer Model

- Superposition of point-spread-functions
- Temperature dependence of individual scatterers from single-scatterer model

Simulated images for heating of 500 lipid and 1000 aqueous temperature-dependent scatterers randomly placed in a liver-like medium

Simulated and Measured CBE

CBE from simulated images computed in the same manner used for actual images
Increase in BE (red)  Decrease in BE (blue)

CBE measured in bovine liver
Single vs Multiple Scatterers

**Numerical Simulation**
Multiple sub-wavelength scatterers
(500 lipid, 1000 aqueous)

**Analytic Prediction**
Single sub-wavelength scatterers

Effect of Backscatter Coefficient
- **Mean of + CBE**
- **Mean of - CBE**

Temperature, °C

CBE, dB

Lipid Scatterer
Aqueous Scatterer
Effect of Noise in Simulated Images

From Single Image with Noise N

- Mean of + CBE
- Mean of - CBE

From Single Image with Noise 2N

- Mean of + CBE
- Mean of - CBE

From 25 Images with Noise 2N

- Mean of + CBE
- Mean of - CBE
- RMS

Average with Standard Error from 25 Images with Noise 2N

- Mean of + CBE
- Mean of - CBE
- RMS
Calibration & Estimation

Calibration Curve
Second-degree Polynomial Fit to CBE from Simulated Images with Noise

Temperature Estimation
Calibration from
• Images with 1500 scatterers with
  • Noise over a
• 0.3 cm³ tissue volume
II. CBE In Vivo

In vivo Experimental Configuration

- 128 Element 7 MHz Linear Array
- Control of temperature from 37 to 45°C and image acquisition with AutoIt®
- Access to RF signals
Measurement of Backscattered Images

In Vitro Ultrasonic Image of Bovine Liver

Motion was compensated over multiple subregions

Added Problems for *in vivo* application of CBE temperature estimation include

- CBE in living tissue
- Perfusion effects
- Added motion
In Vivo Studies

- Performed on nude mice
  - attached to submerged angled tray
  - bilaterally implanted HT29 tumors
  - RTD thermistor in contralateral tumor
- *In vitro* procedure followed
  - from 37.0 to 45.0°C in 0.5°C steps
  - for an experiment of 0.5 hours
- Mice euthanized without recovery
- Images analyzed in a manner similar to that for *in vitro* experiments

37.0°C

Nude Mouse: ti102

spine femur

mpg movie
Non-Rigid Motion

- Arrow lengths are 50 X actual motion field
- Represented as interpolation over image
- Estimated using conventional optimization
Change in Backscattered Energy in Motion—Compensated Images

CBE
Increasing - Red
Decreasing - Blue

Images after Non-Rigid Motion Compensation

mpg movie
CBE with Temperature In Vivo

Measured CBE in mice

Predicted CBE in sub-wavelength scatterers
CBE with Temperature

- CBE is nearly monotonic with temperature
- Calibration of CBE may enable temperature imaging

**In Vitro**

- Bovine Liver
- Turkey Breast
- Pork Muscle

**In Vivo**

- Mouse ti102
- Mouse ti103
- Mouse ti104
- Mouse ti105
Change in backscattered energy (CBE) was nearly monotonic and consistent in magnitude in in vitro and in vivo measurements.

**Predictions**
- Single-scatterer model
- Multiple-scatterer simulations

**Measured values**
- 1D isolated sites in *in vitro* beef liver, turkey breast & pork muscle specimens
- 2D motion-compensated images in *in vitro* beef liver, turkey breast & pork muscle specimens
- 2D motion-compensated images *in vivo* in mice

We expect CBE to enable noninvasive temperature imaging for hyperthermia.
Future Directions for Thermometry Based on Ultrasonic CBE

- Refinement of the CBE model
  - Histological study of scatterer distribution
  - Evaluation of images & CBE using simulation
- Estimation of temperature from simulations and measurements
- Development of clinically relevant heating and measurement systems
  - Small Animal Heating with Ultrasound
  - Scanning Ultrasound Reflector Linear Array

Simulated Images:
- 500 lipid
- 1000 aqueous scatterers
- With Noise
- 0.3 cm³ vol

Temperature, °C

Estimated, °C