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

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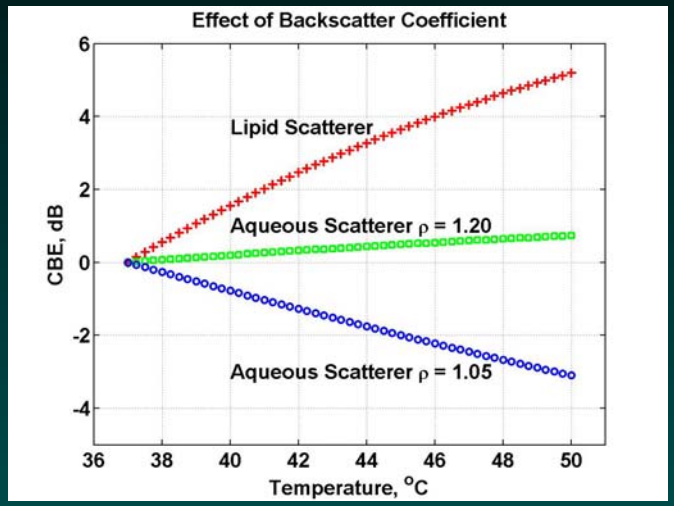
Objective of Ultrasonic Thermometry

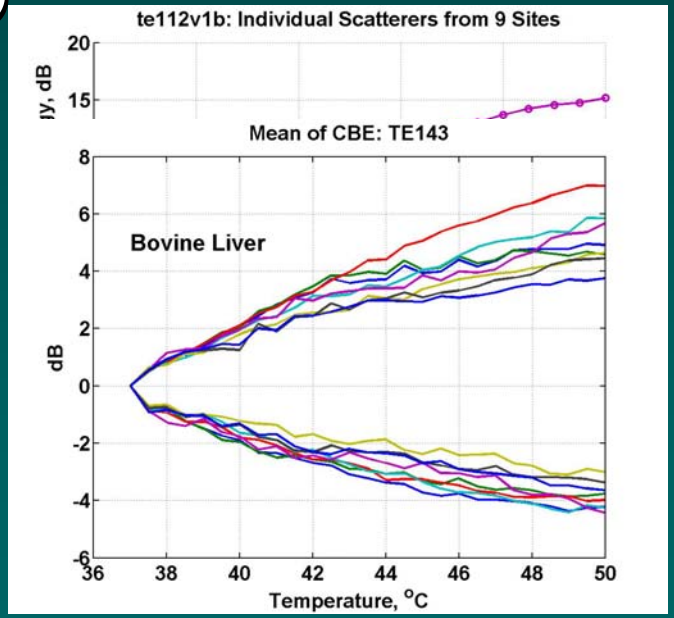
To develop a method to produce 3D temperature maps in soft tissue during hyperthermia cancer treatment

- non-invasively, conveniently at low cost with a single view from standard equipment
- with at least 0.5°C accuracy & 1 cm^3 resolution

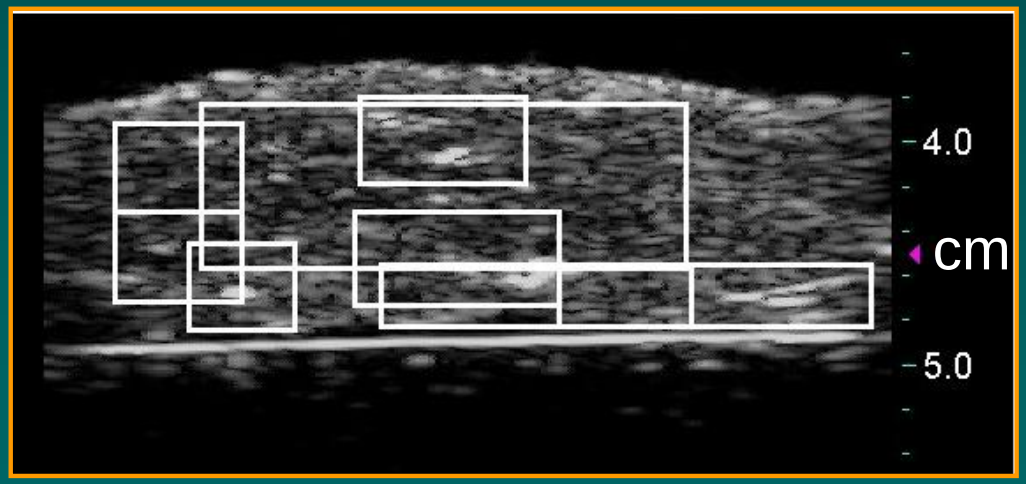
Change in backscattered energy (CBE) as a monotonic temperature-dependent parameter

- 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



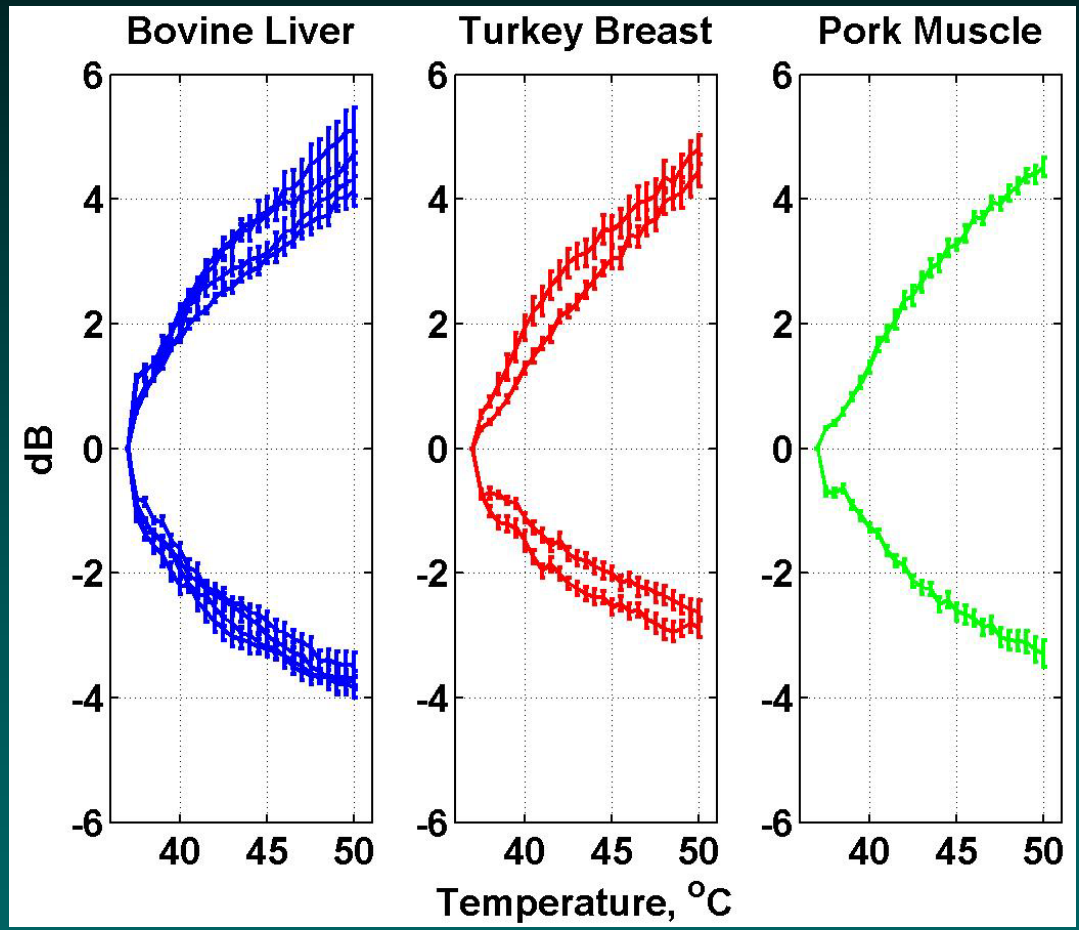


Bovine Liver



Change in backscattered energy (CBE) as a monotonic temperature-dependent parameter

- CBE in selected regions in 2D in 4 liver, 2turkey & 1 pork samples
- Null tests
  - –No heating (<±0.2 dB)
  - –Heating effects on the transducer (<±0.1 dB)
  - –Positioning (<±0.05 dB)
- CBE in simulations of scatterer collections



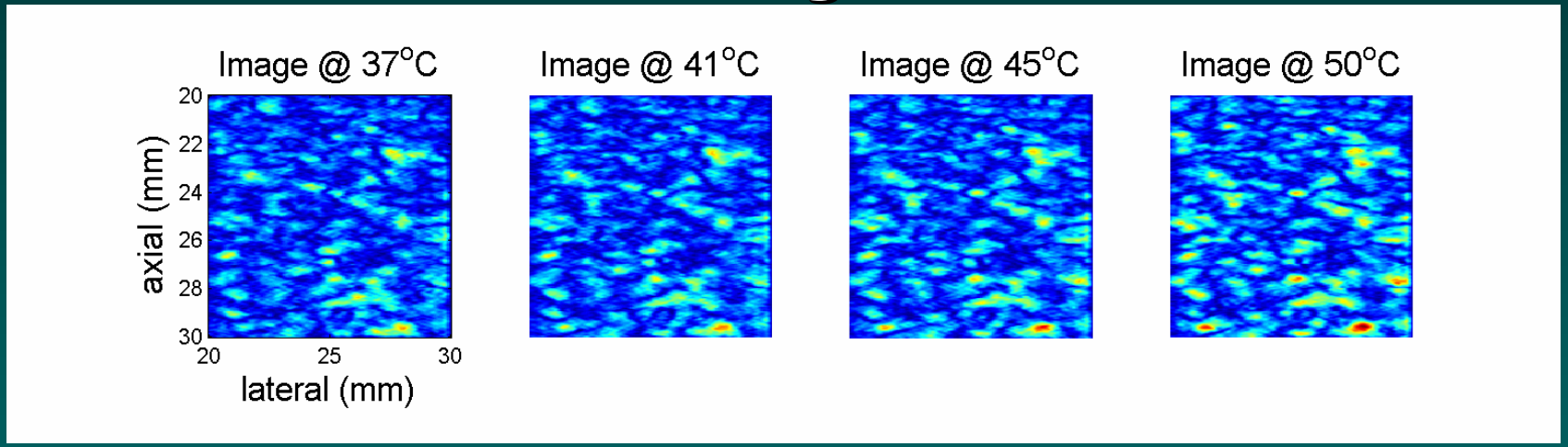
I. Simulation of Scatterer Collections

- 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

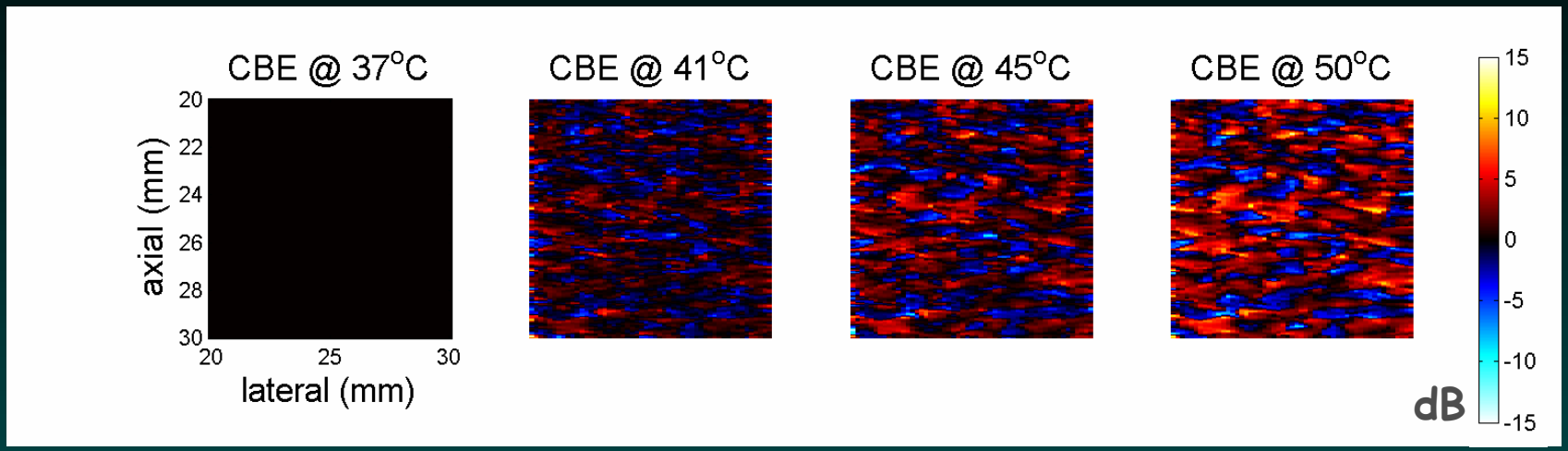
- Superposition of point-spread-functions
- Temperature dependence of individual scatterers from single-scatterer model



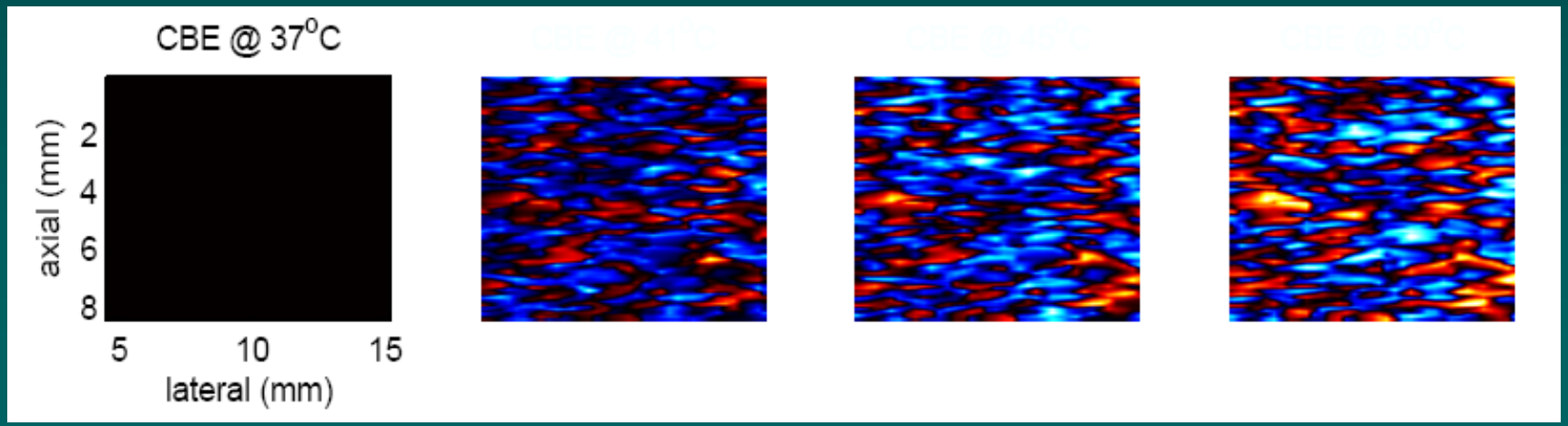
Simulated images for heating of 500 lipid and 1000 aqueous temperature-dependent scatterers randomly placed in a liver-like medium

Trobaugh & Arthur, *IEEE Trans. UFFC*, 48:1594-1605, 2001

Simulated and Measured CBE

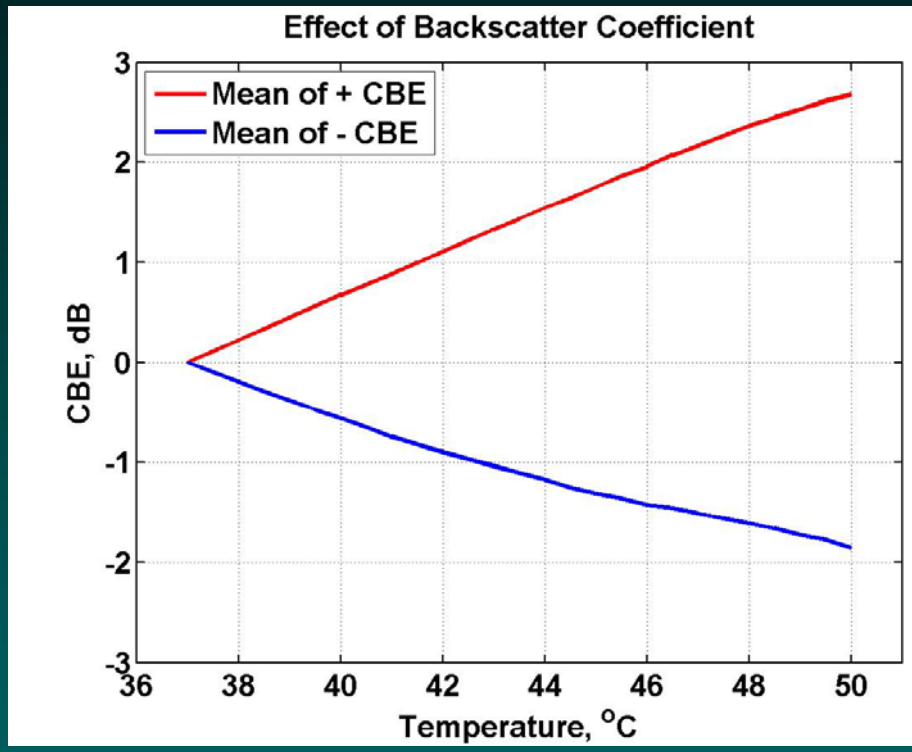


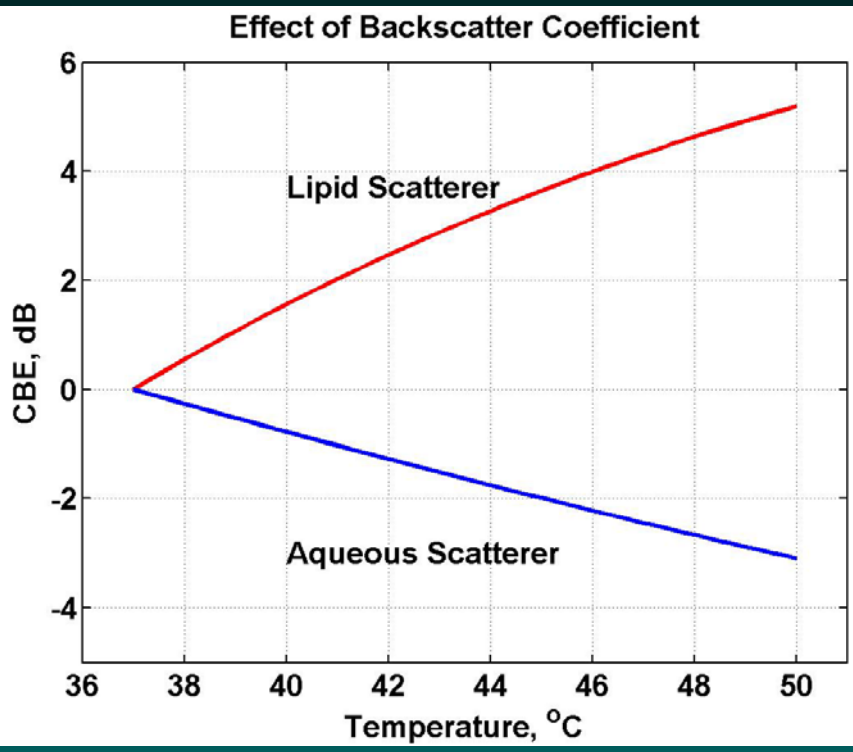
CBE from simulated images computed in the same manner used for actual images
Increase in BE (red) Decrease in BE (blue)



CBE measured in bovine liver

Single vs Multiple Scatterers

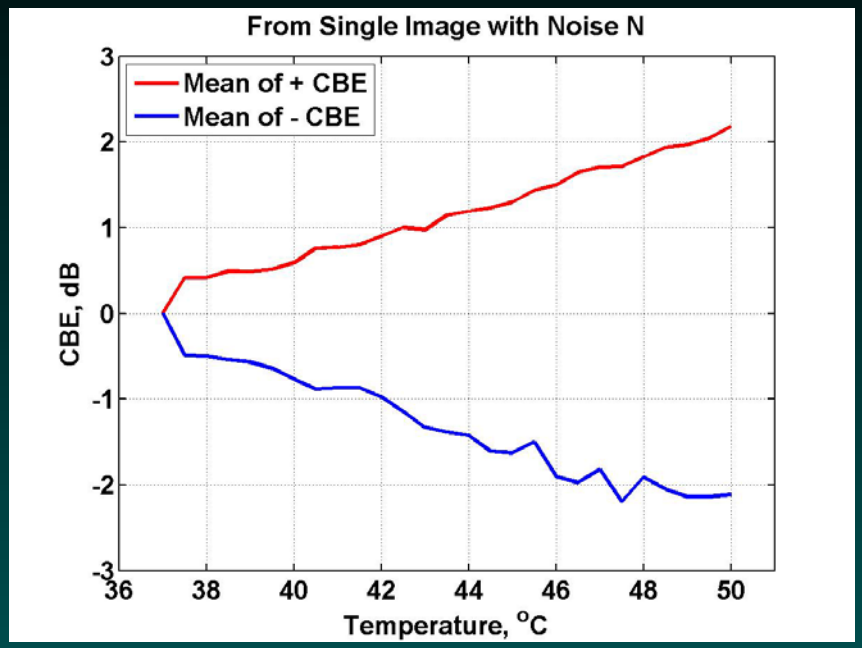




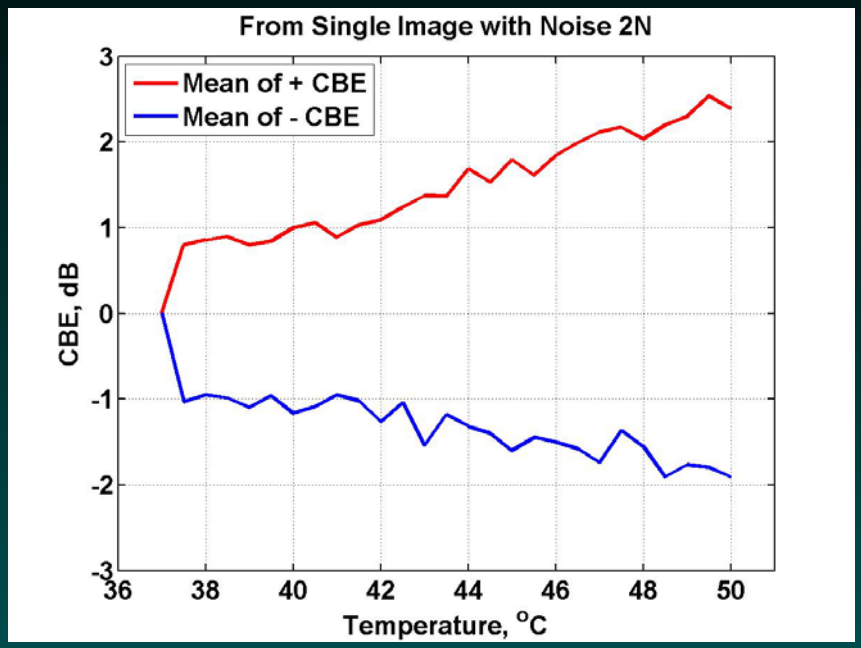
Numerical Simulation
Multiple sub-wavelength scatterers
(500 lipid, 1000 aqueous)

Analytic Prediction
Single sub-wavelength scatterers

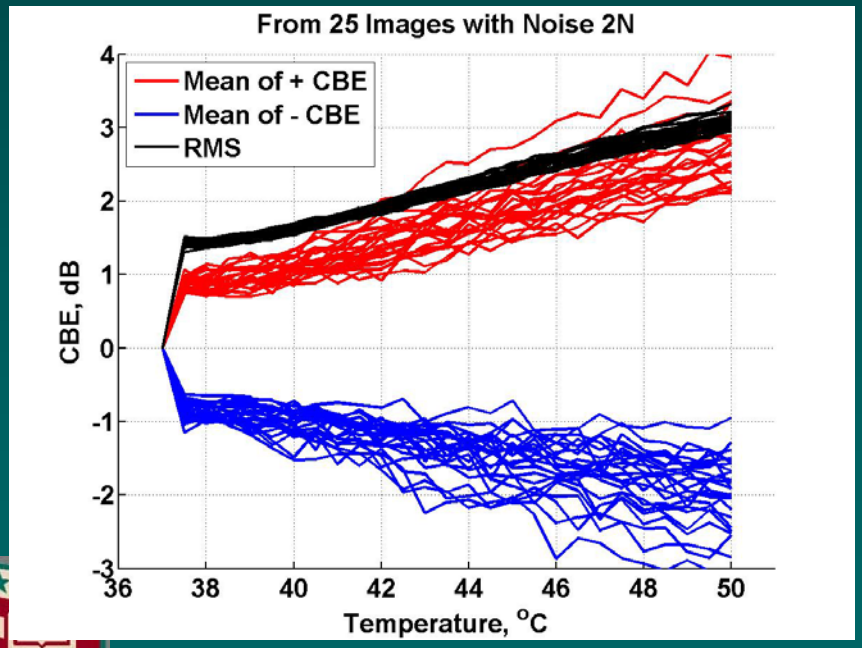
Effect of Noise in Simulated Images



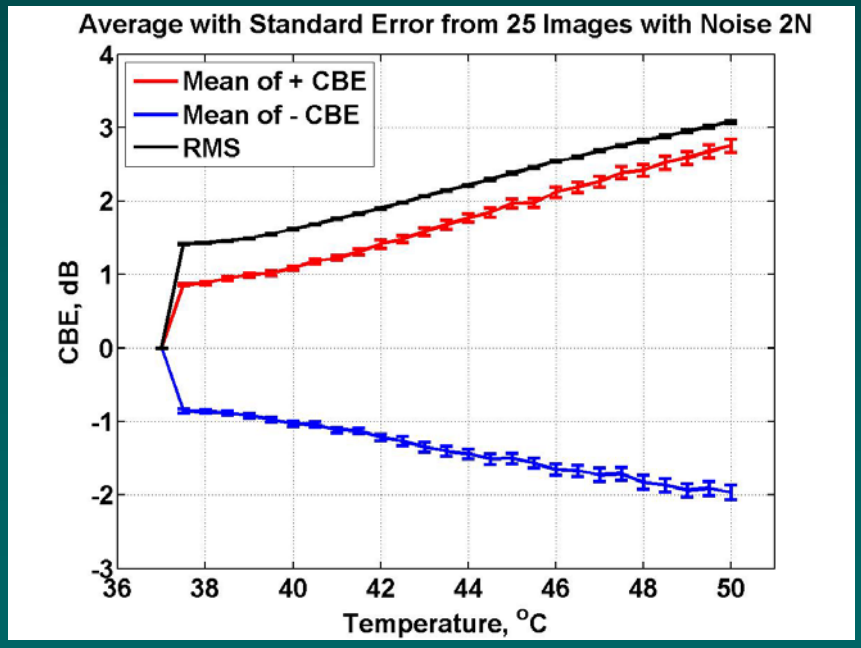
1 Image with Noise Level N



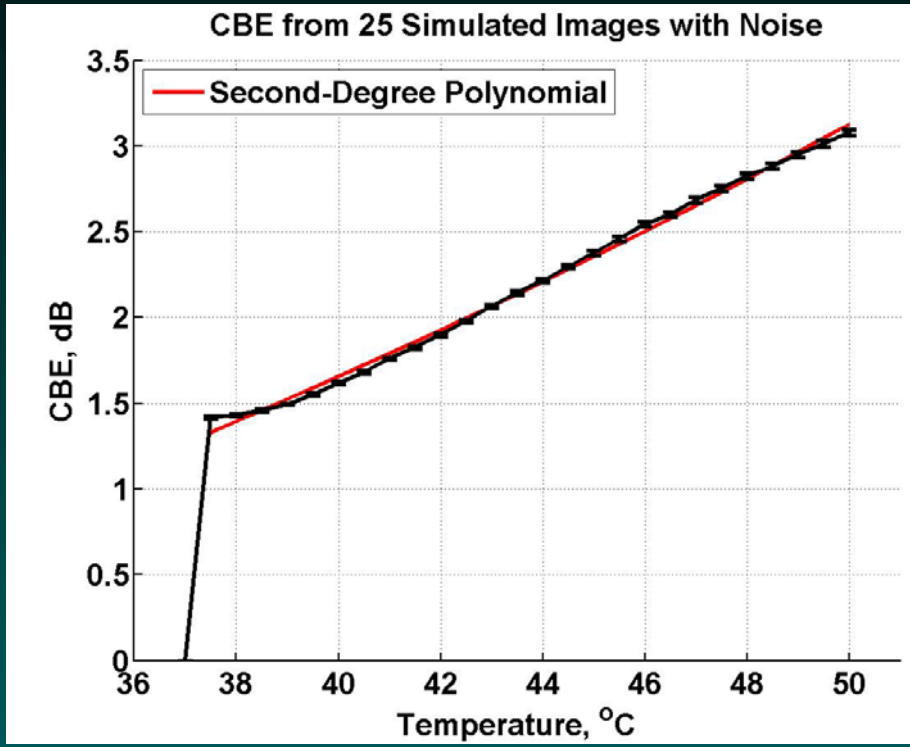
2N

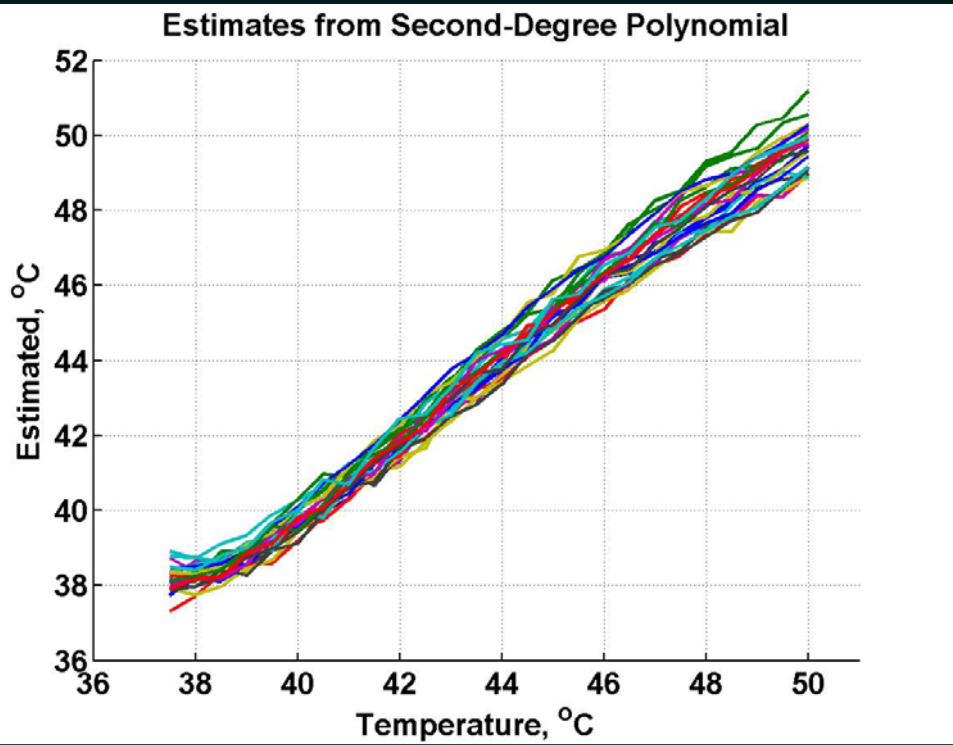


25 Images with Noise Level 2N



Calibration & Estimation





Calibration Curve

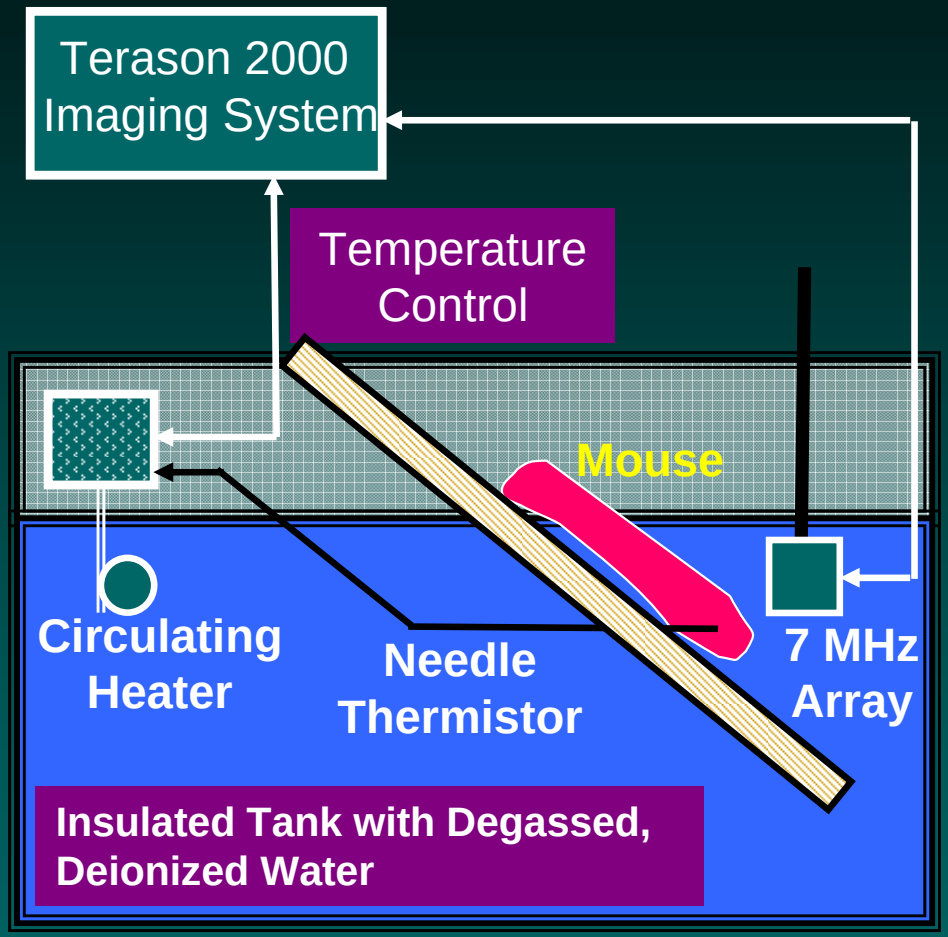
Second-degree Polynomial Fit to CBE from Simulated Images with Noise

Temperature Estimation

Calibration from

- Images with 1500 scatterers with
- Noise over a
- 0.3 cm^3 tissue volume

II. CBE *In Vivo*

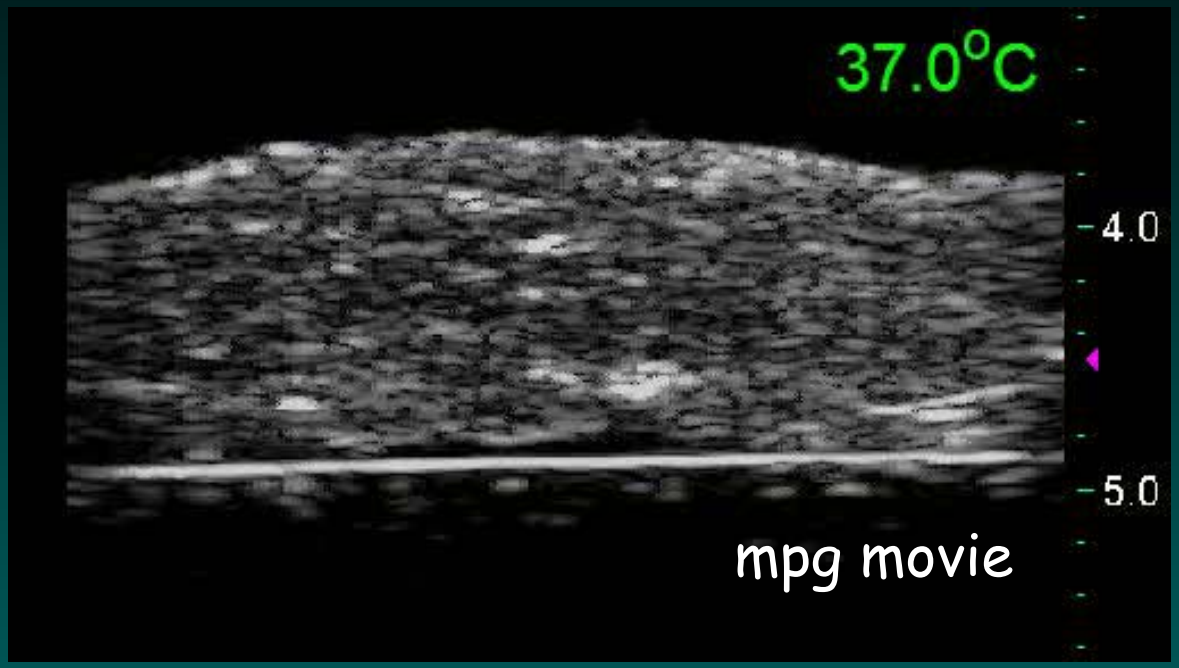


In vivo Experimental Configuration

Terason 2000 (Teratech, Corp., Burlington, MA)

- 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

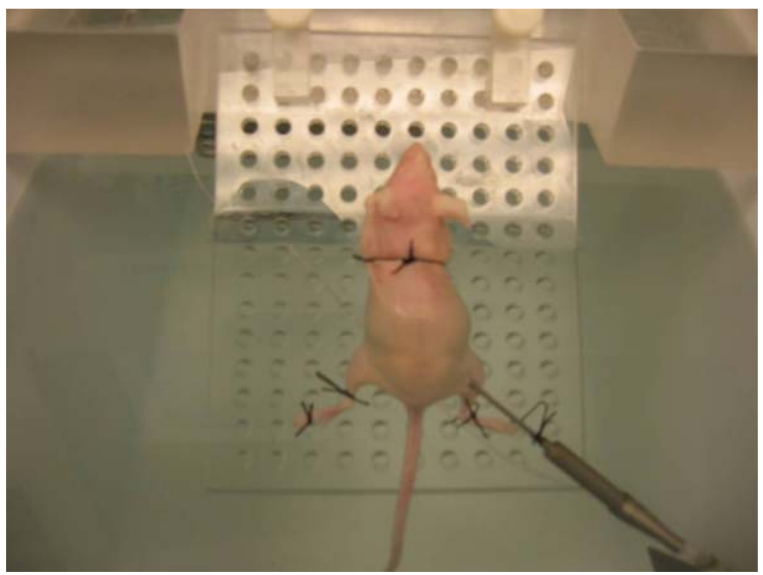
Motion was compensated over multiple subregions

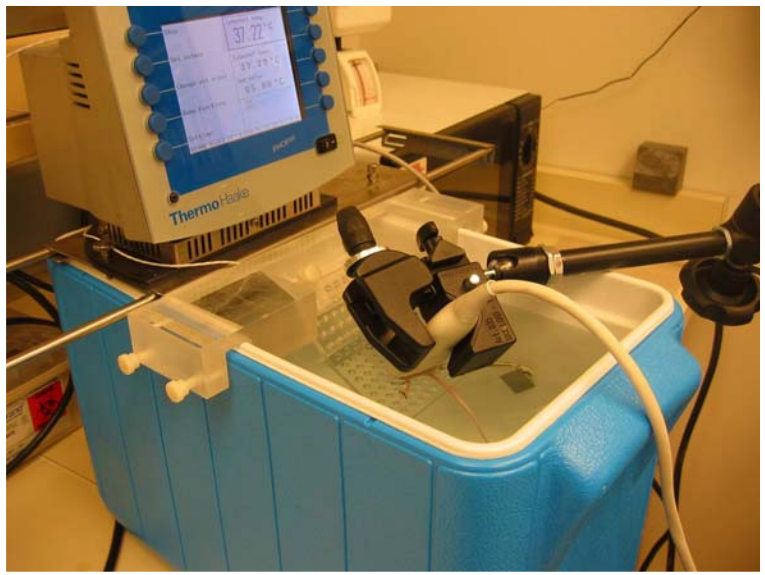
Added Problems for *in vivo* application of CBE temperature estimation include

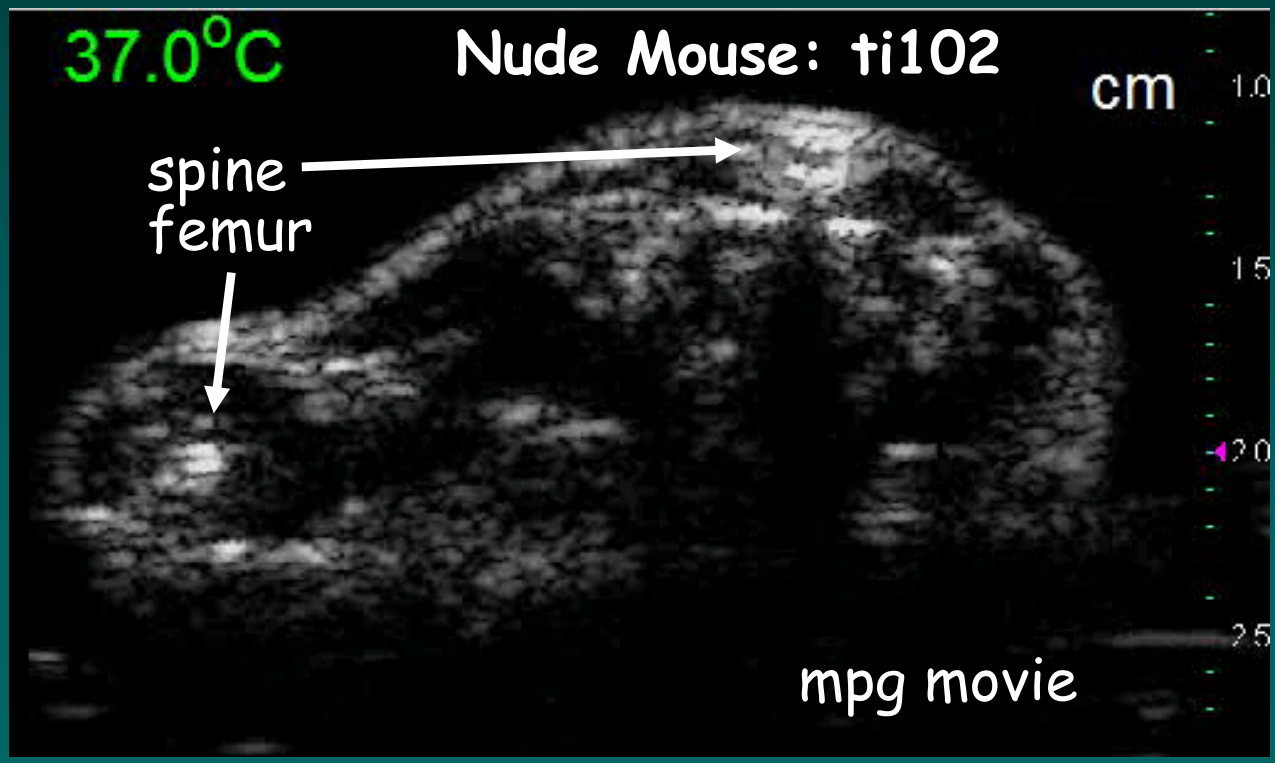
- CBE in living tissue
- Perfusion effects
- Added motion

In Vivo Studies

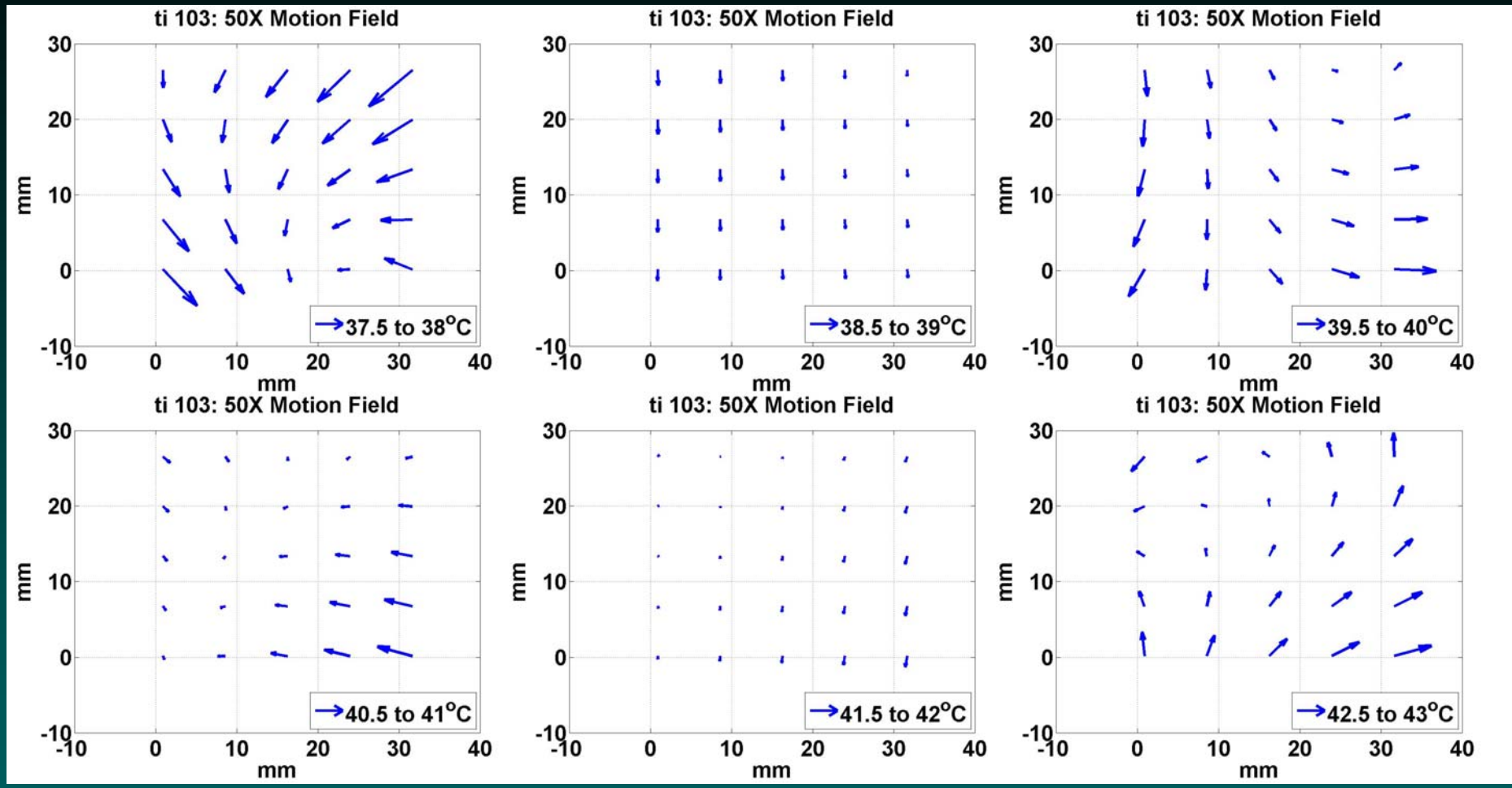
- Performed on nude mice
  - attached to submerged angled tray
  - bilaterally implanted HT29 tumors
  - RTD thermistor in contralateral tumor
- *In vitro* procedure followed
  - from 37.0 to 45.0°C in 0.5°C steps
  - for an experiment of 0.5 hours
- Mice euthanized without recovery
- Images analyzed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





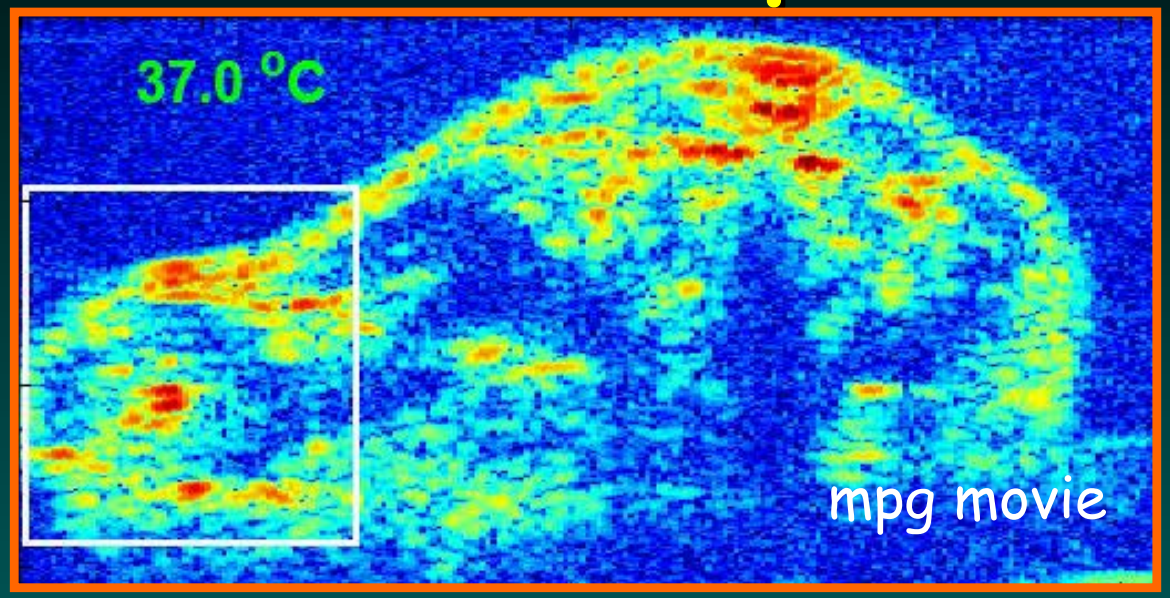


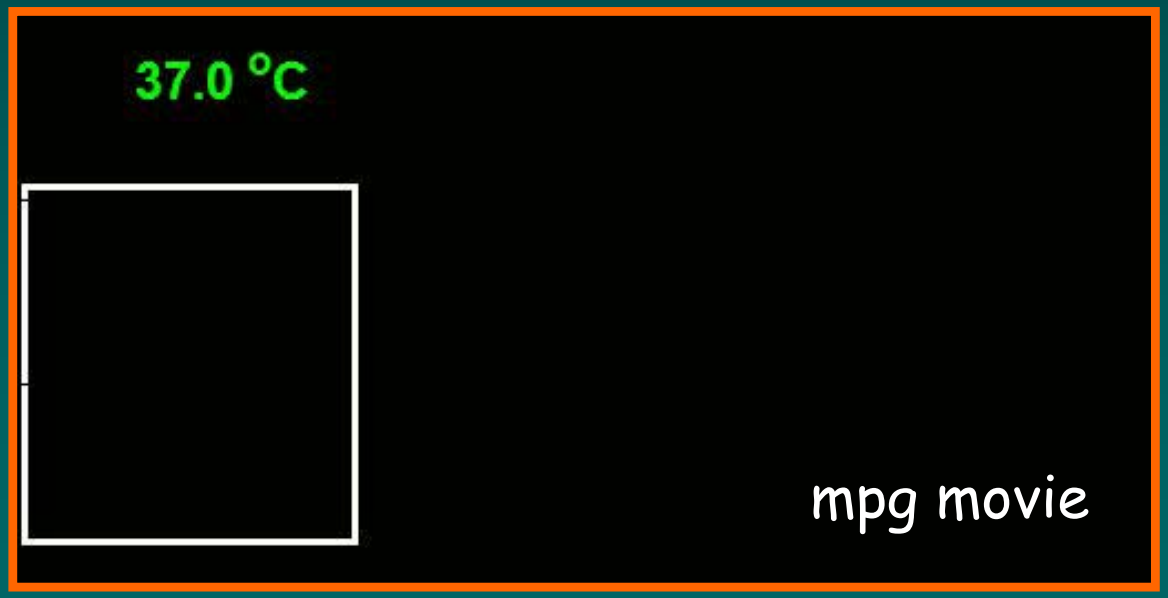
Non-Rigid Motion



- 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





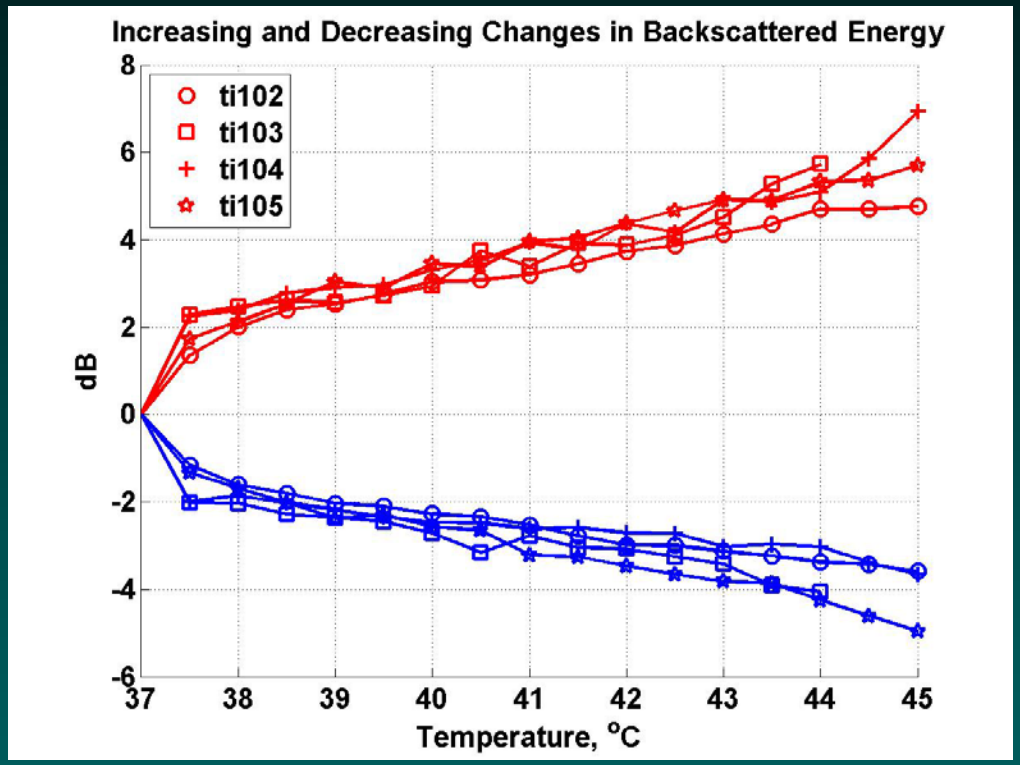
Images after Non-Rigid Motion Compensation

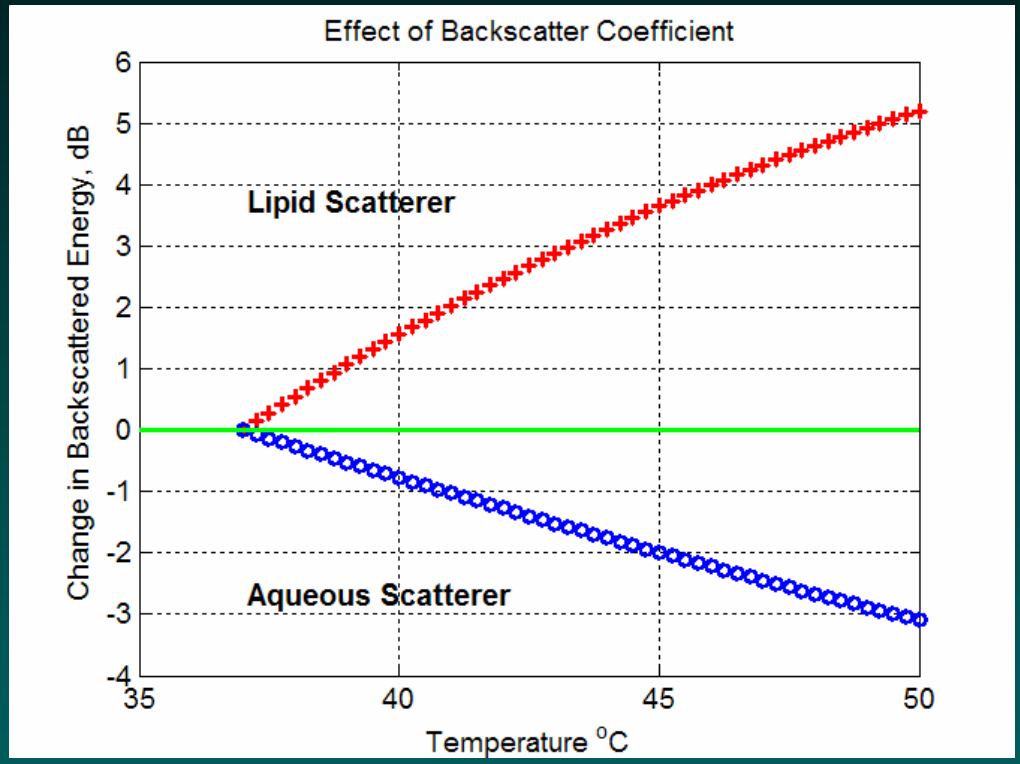
CBE

Increasing – Red

Decreasing – Blue

CBE with Temperature *In Vivo*

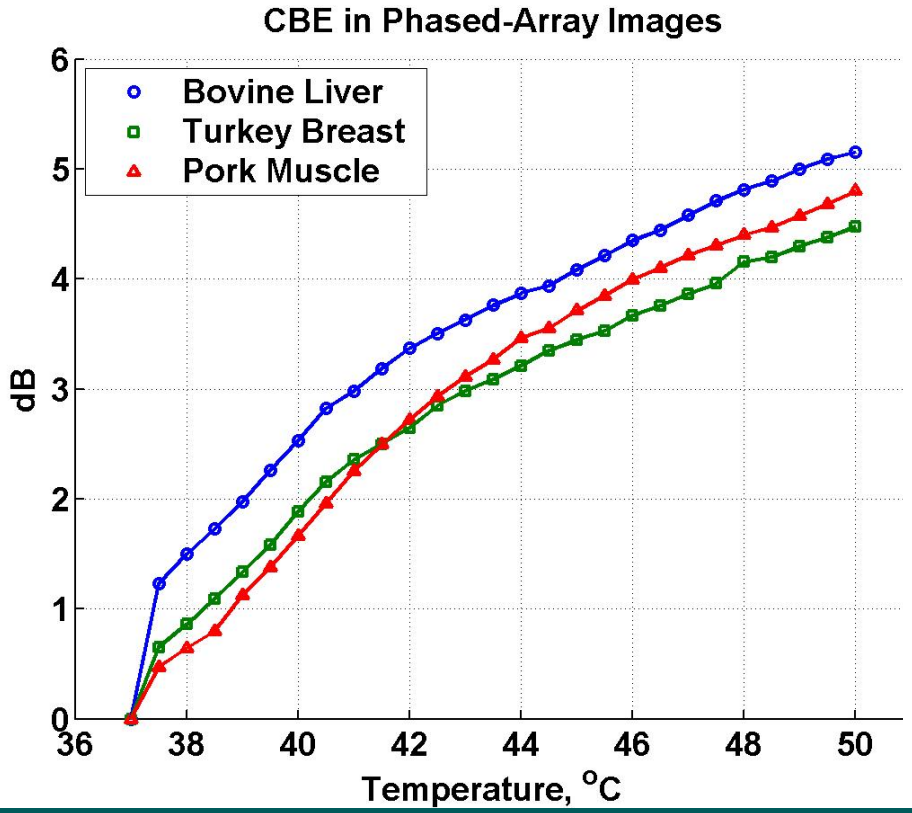


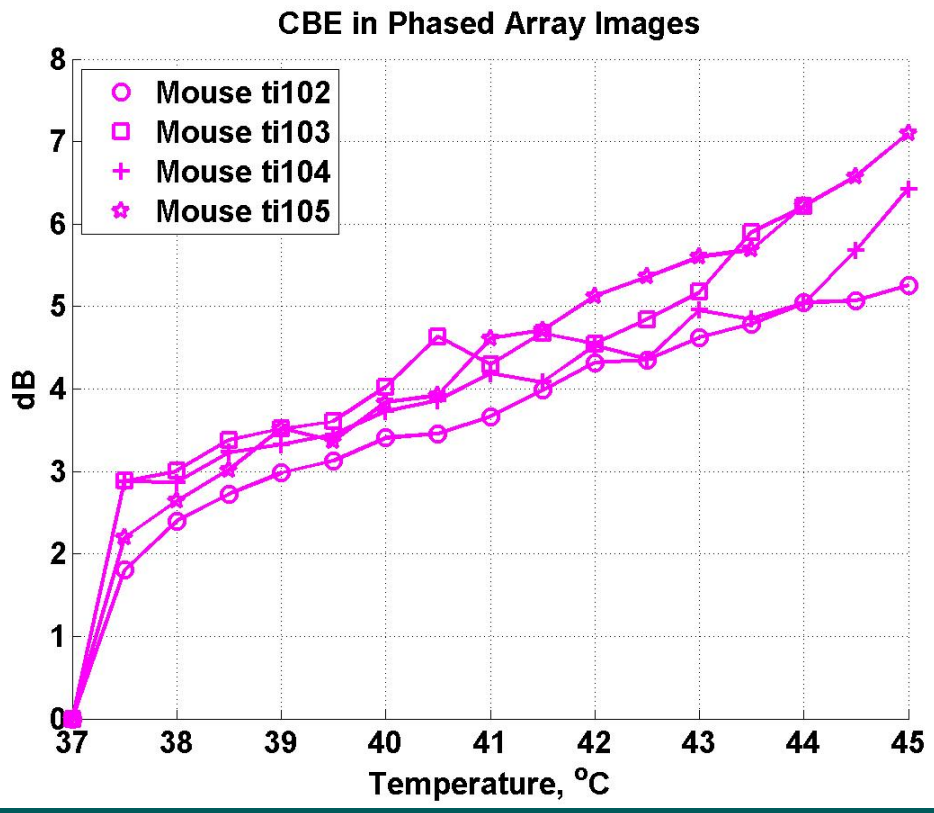


Measured CBE in mice

Predicted CBE in sub-wavelength scatterers

CBE with Temperature





In Vitro *In Vivo*

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

Summary & Conclusions

- Change in backscattered energy (CBE) was nearly monotonic and consistent in magnitude in
  - 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