

## Sound Medicine

Some contemporary and prospective uses of acoustics in medicine

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Cleveland Clinic UEC CUL

## Overview: Acoustics

Velocity: ~345 m/s in air, ~1500 m/s in water, ~1540 m/s in tissue, ~3000m/s bone

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## Overview: Ultrasound

Imaging

Broadband

High peak pressure

Low time-average power

High Frequency

Therapy

Continuous Wave

High intensity

High time-average power

"Low" Frequency

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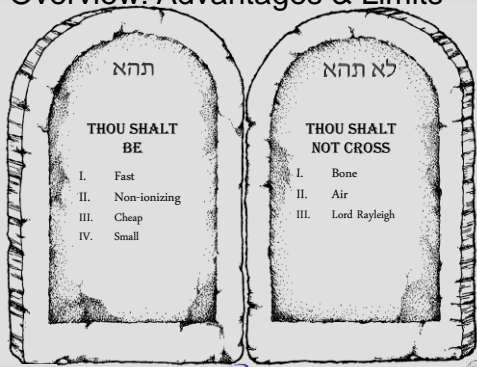
## Overview: Ultrasound

2D Echocardiography Image Courtesy Dr. A. Stoylen

Philips X7 3D Matrix Probe

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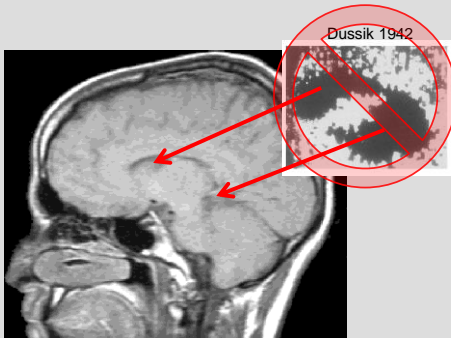
### Overview: Advantages & Limits



### I. Bone



### I. Bone

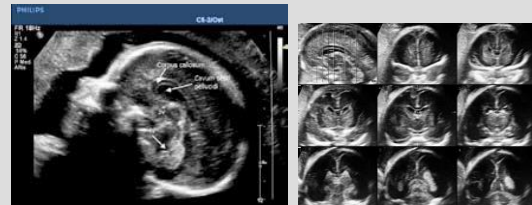


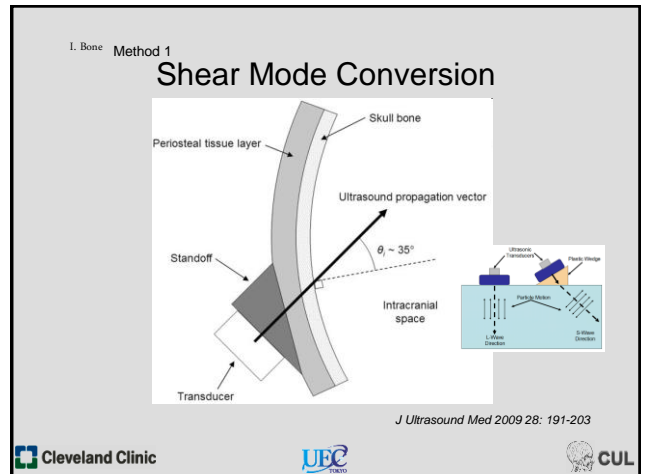
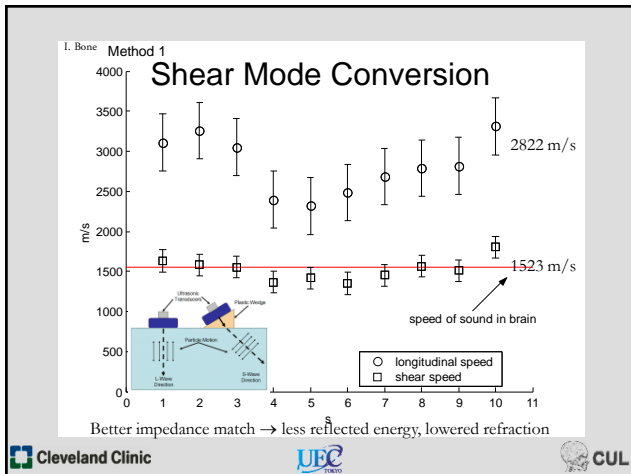
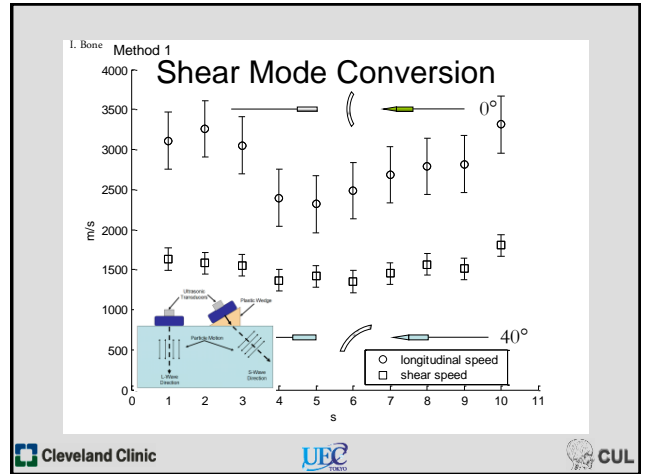
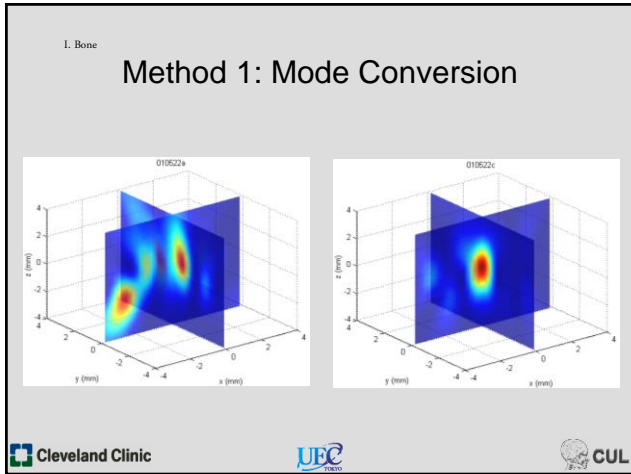
I. Bone

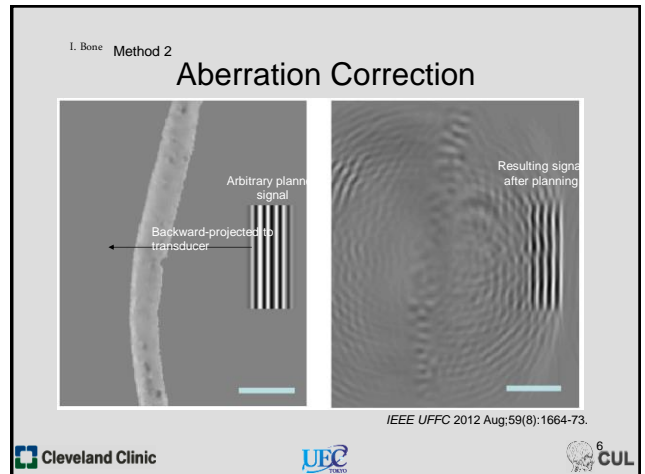
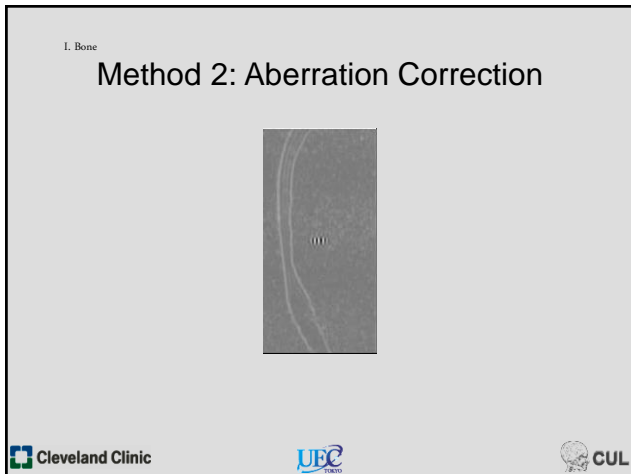
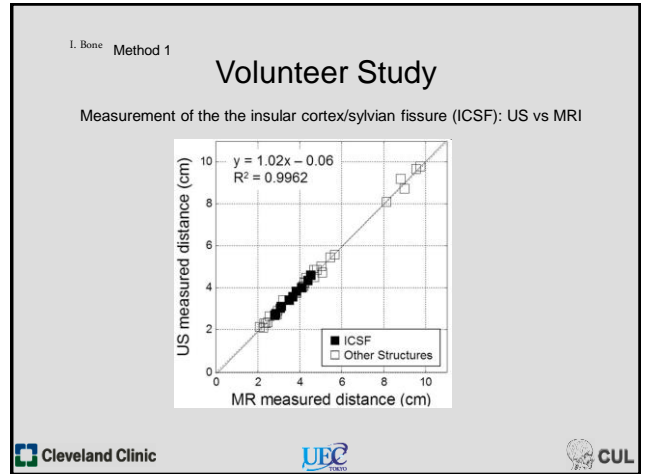
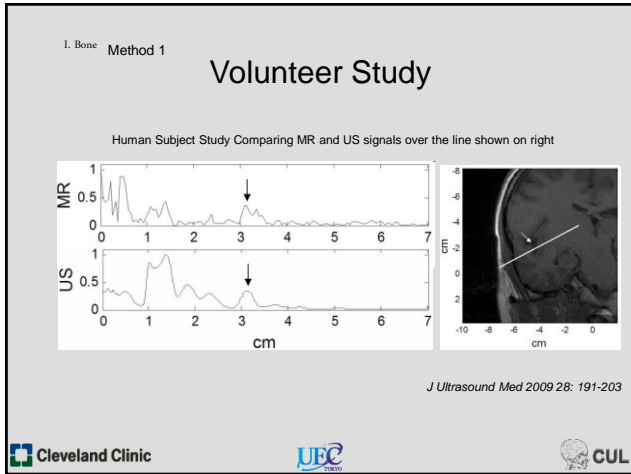
### Brain Imaging

Locations of major anatomical structures (e.g. midline falx, mesencephalic brainstem, ventricle margins, etc.) can already be accurately and precisely imaged, but only after craniotomy, or in pediatric cranial ultrasound (cUS) through the fontanelle.

Ongoing research aims to perform equivalent imaging through the skull.







I. Bone Method 2

## Full Brain Tomography

- Diffraction tomographic approach

Photo      Predicted with phase correction      Predicted, no correction

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I. Bone

## Method 3: The Next step...

- Replace tomography with more generalized approach

512 element ring array (1MHz, 1-3 composite with matching layer)

500+ element conformal array (here, unwired) (0.5 MHz, Random Fiber Composite)

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## Method 3: The Next step...

- Full Inverse Scattering

500+ element conformal array (here, unwired) + "generalized" tomography

G.T. Clement *Inverse Problems* (2014)

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## Focused Ultrasound Surgery

"The devise was made in the form of a double-deck arrangement"

"Four ultrasound beams could be brought into coincidence to produce focal point"

From: Fry et al., *J Exp Med.* 1956, 1;104(3):337-60.

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I. Bone FUS


## A resurged interest

1991 - Magnetic Imaging Guidance and Monitoring

1990's - High power phased arrays

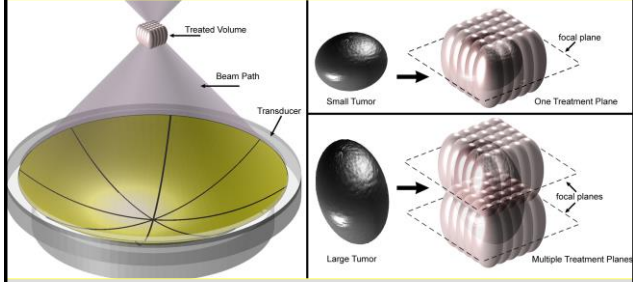

⇓

1. Excellent Targeting
2. On-line Temperature Monitoring and Exposure Quantification
3. On-line Tissue Effect Evaluation
4. Array Control & Correction





I. Bone FUS

## Therapy



I. Bone FUS

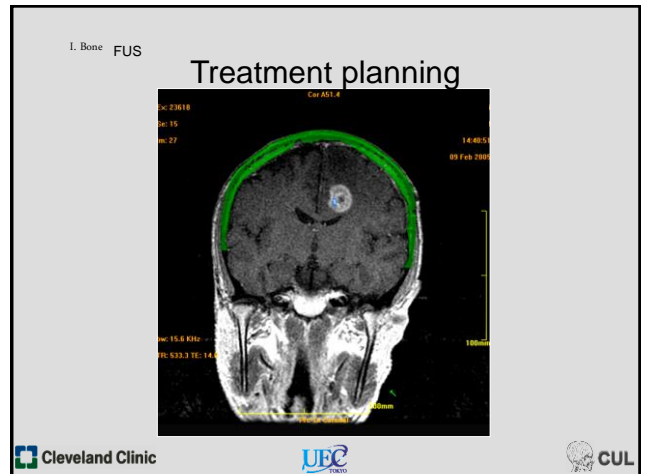
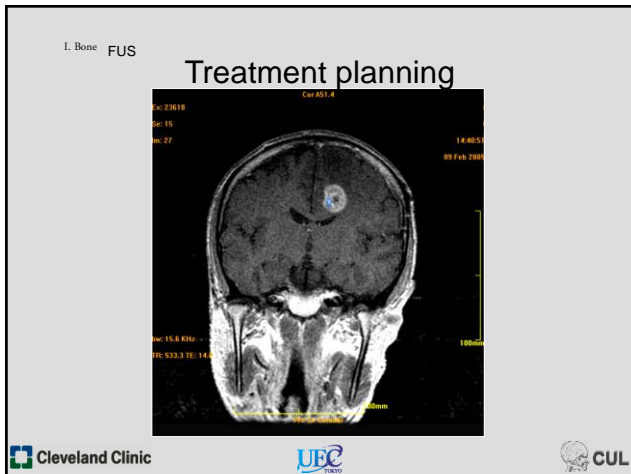
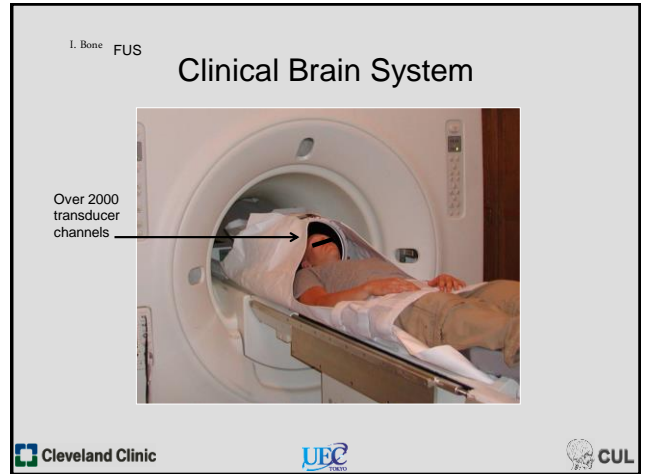
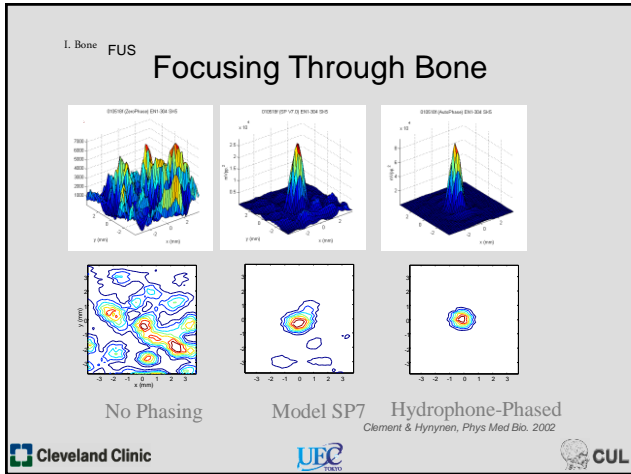
## MR-Guided Treatment

I. Bone FUS

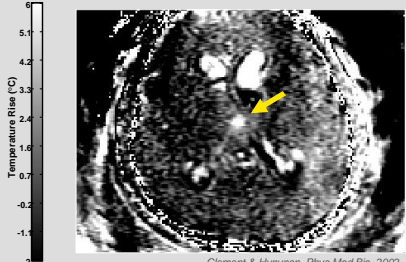
## Original Brain array



I. Bone FUS

### Clinical trials



Temperature Rise (°C)

*Clement & Hyrynen, Phys Med Bio, 2002*

**Initial patients:**

- Demonstrated focal heating through intact skull without overheating the skull
- Sufficient temperatures appeared possible, but somewhat limited by available power

**Ongoing:**

- Clinical studies for Essential Tremors, Brain Cancer, Neuropathic Pain, Parkinson's

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### Transcranial US: Issues, solutions

**Skull heating:**

- Distribute energy over as much skull area as possible
- Lower US frequency
- Active cooling with circulated water

**Focal shifting/distortion:**

- Model-based Phased array correction

**Targeting, Monitoring:**

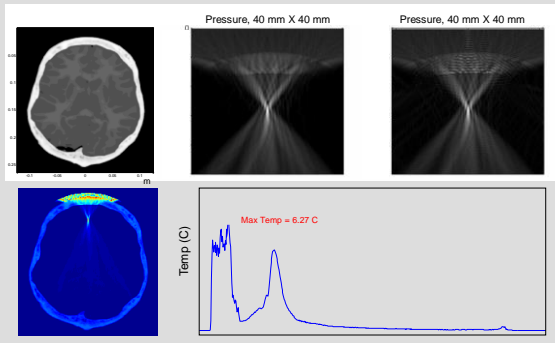
- MRI

**2 key remaining issues: Variability and "Treatment Envelope"**

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### PseudoSpectral WVFD



Pressure, 40 mm X 40 mm

Pressure, 40 mm X 40 mm

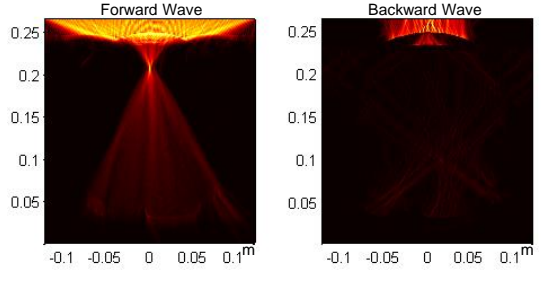
Temp (C)

Max Temp = 6.27 C

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### PseudoSpectral WVFD



Forward Wave

Backward Wave

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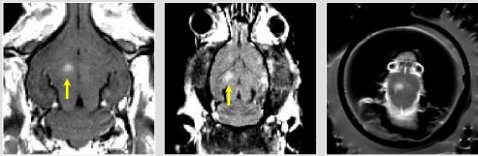
## Early Clinical trials

### Opening the Blood Brain Barrier


- Low-power, pulsed exposures
- Combined with ultrasound contrast agent (Optison, Definity)
- Temporary (~hours), localized, non-invasive



Trypan blue in rat



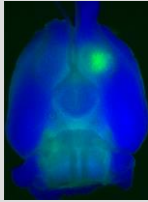
rabbit rat mouse



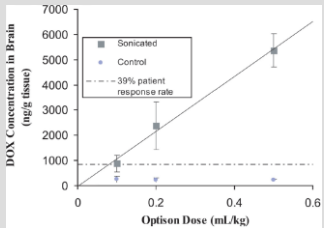
I. Bone FUS

## Early Clinical trials

### Delivery of Doxil (liposomal doxorubicin, rats)



Fluorescent image showing targeted Doxil delivery to the rat brain




Optison Dose (mL/kg)	DOX Concentration (ng/g tissue) - Sonicated	DOX Concentration (ng/g tissue) - Control
0	0	0
0.1	~1000	~500
0.2	~2500	~500
0.5	~5500	~500

Legend: ■ Sonicated, ● Control


--- 39% patient response rate

Treat et al., Int J Cancer (2007)




## II. Air

$p^2/\rho c$

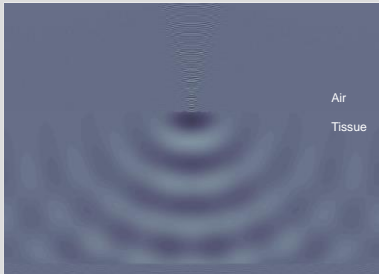


Air  
Tissue


(reflections omitted for clarity)

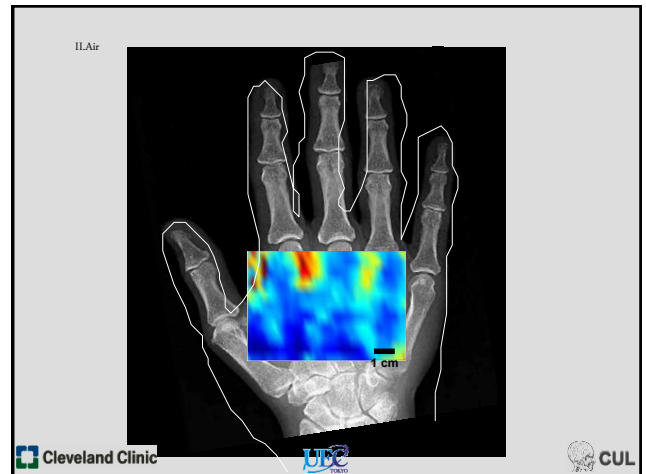
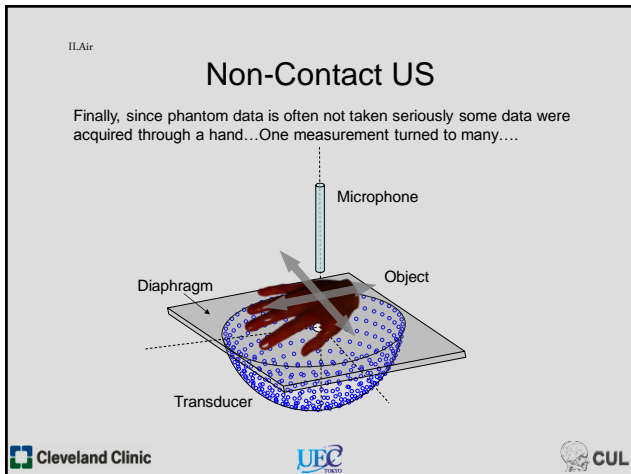
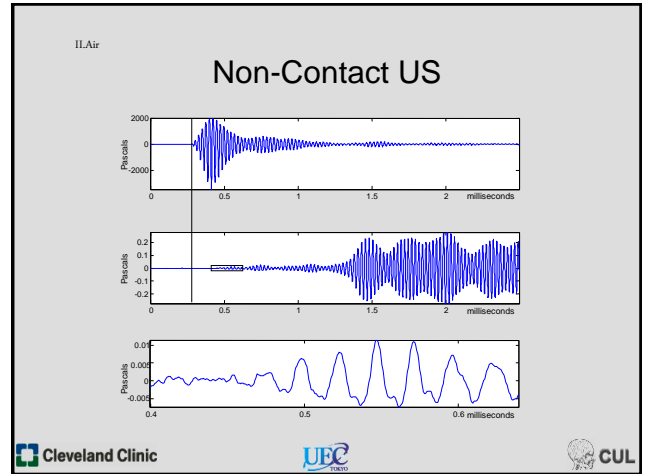
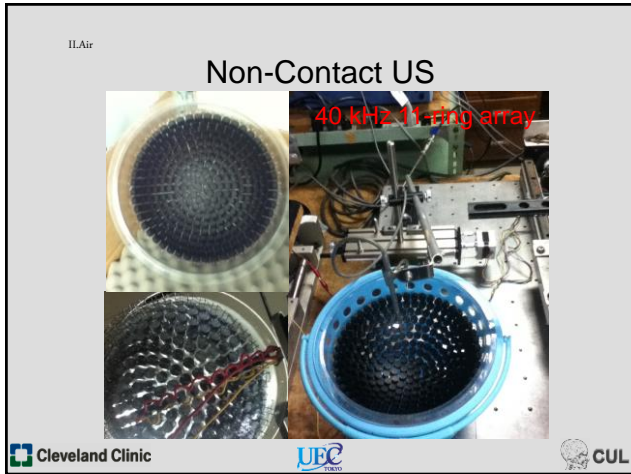


## II. Air



Air  
Tissue





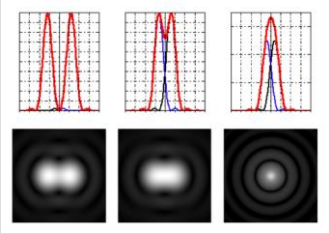

II.Air

## Next Steps...

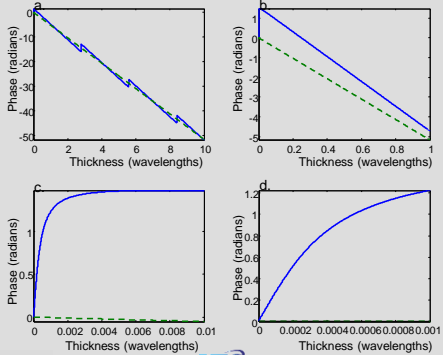

- Demonstration at 400kHz in medical (tissue) phantom
- Development of sensitive receiver
- Improvement of reconstruction methodology



## III. Rayleigh

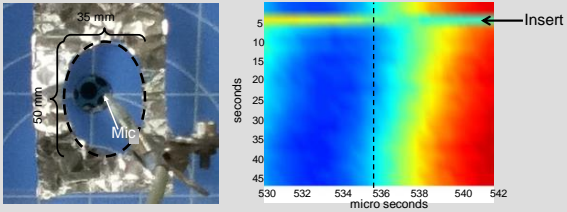




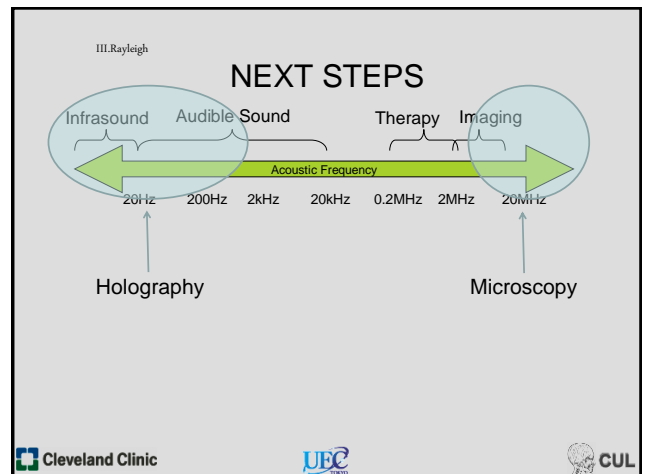
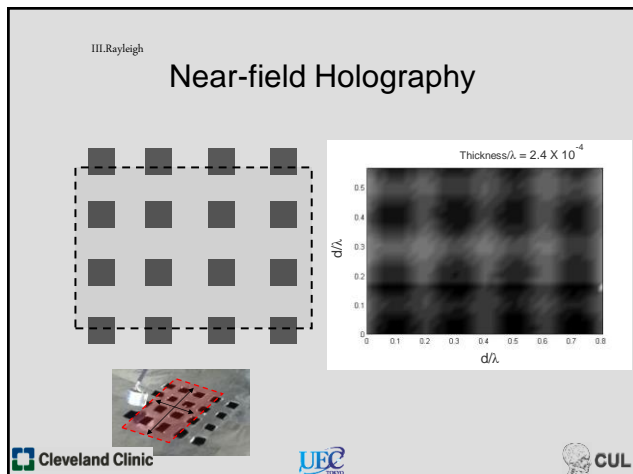
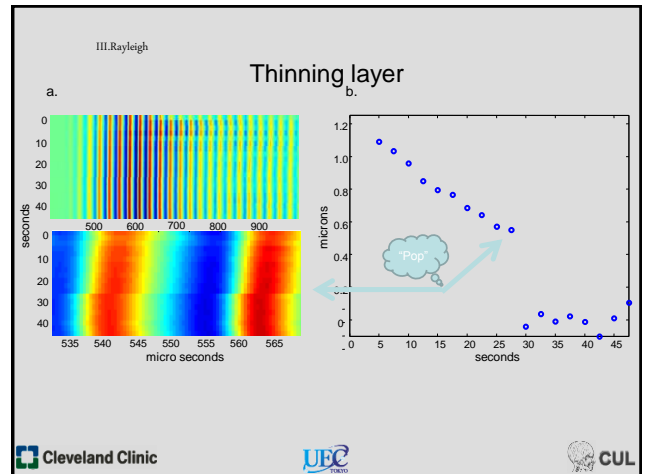
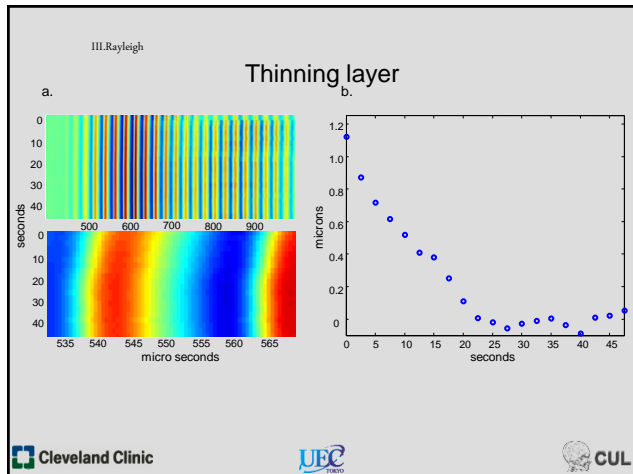
### III.Rayleigh

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## Sub-micron detection at 40 kHz



## Acknowledgements

### University of Electro-communications, Tokyo

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### Cleveland Clinic

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More information at  
[www.focused-ultrasound.org](http://www.focused-ultrasound.org)

