Breakthroughs in Coherent Ultrasound Transmission Tomography Systems

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AAPM Annual Meeting, 7/31/2018

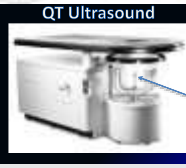
Ultrasonic Computed Tomography

- Medical *ultrasound computed tomography,* taken literally, describes the first *pulse echo* ultrasound images (early 50's).
- The term US CT or UCT is used with systems detecting the *transmitted* waves (as in X CT)
- Late 70's, done with movement of single element transducers, later with arrays
- UCT gives quantitative tissue properties, not possible with Pulse Echo

I hope to convince:

- B mode-images represent boundaries in tissue properties
- The transmission component of UCT systems allows discrimination of tissues by their bulk properties
  - speed of sound (c)
  - attenuation coefficient (α)
  - density (ρ).
- Any other imaging mode can be made better if you have a map of those properties, particularly "c"

FDA Approved Transmission Tomo Systems for Dx



C. Li, N. Duric, P. Littrup, and L. Huang, "In vivo breast sound-speed imaging with ultrasound tomography." *Ultrasound in Medicine & Biology*, vol. 35, no. 10, pp. 1615-1628, Oct. 2009.

Quantitative 3D high resolution transmission ultrasound tomography: creating clinically relevant images (Conference Presentation)
James Wiskin John Klock Elaine Iuanow Dave Borup Robin Terry Bilal Malik Mark Lenox Proc. SPIE. 10139, Medical Imaging 2017: Ultrasonic Imaging and Tomography, | 2 May 2017

Typically with synthetic aperture

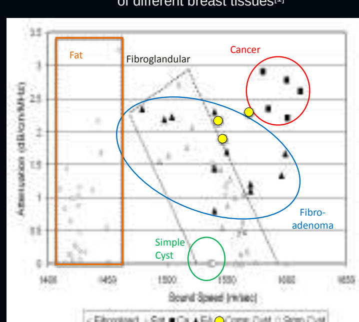
- Virtual synthetic aperture
- Recons Initially straight line like x-ray CT
- Then bent ray
- Then 2D full wave physics
- Now some 3D recons

- By Shaddim - Own work, CC BY-SA 3.0, https://commons.wikimedia.org/w/index.php?curid=44954728

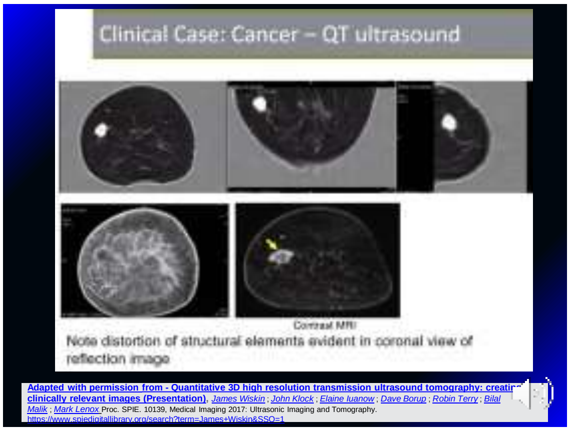
Background

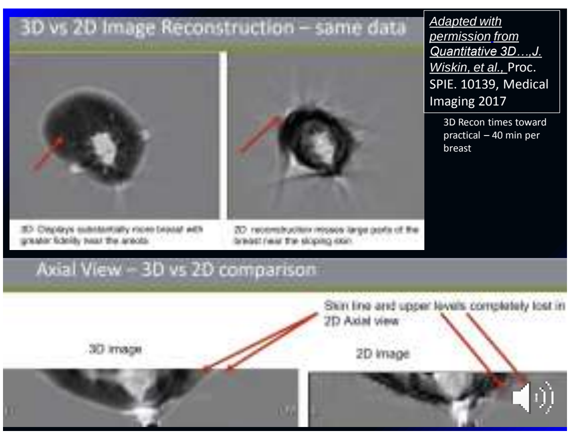
- Malignant lesions typically have an elevated sound speed and attenuation coefficient in comparison to other tissues.

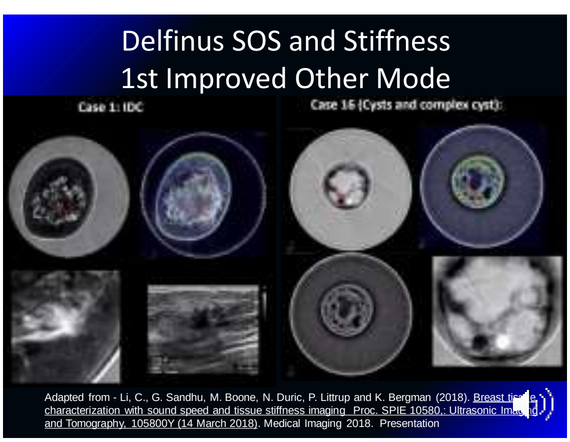
Speed of sound and attenuation coefficient of different breast tissues[1]



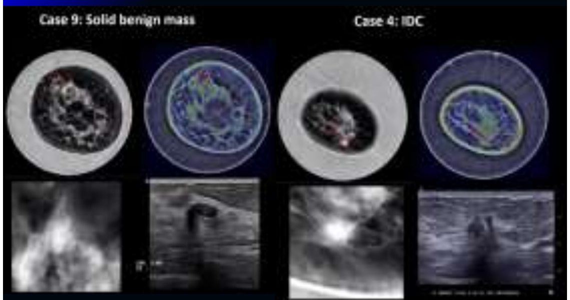
M. P. André, C. H. Barker, N. Sekhon, J. Wiskin, D. Borup, and K. Callahan, "Pre-Clinical experience with Full-Wave Inverse-Scattering breast imaging acoustical imaging," ser. Acoustical Imaging, I. Akiyama, Ed. Dordrecht: Springer Netherlands, 2009, vol. 29, ch. 10, pp. 73-80.


Clinical Case: Cancer – QT ultrasound
Contrast MRI
Note distortion of structural elements evident in coronal view of reflection image
Adapted with permission from - Quantitative 3D high resolution transmission ultrasound tomography: creating clinically relevant images (Presentation), James Wiskin ; John Klock ; Elaine Iuanow ; Dave Borup ; Robin Terry ; Bilal Malik ; Mark Lenox Proc. SPIE. 10139, Medical Imaging 2017: Ultrasonic Imaging and Tomography.
https://www.spiedigitallibrary.org/search?term=James+Wiskin&SSO=1


3D vs 2D Image Reconstruction – same data
Adapted with permission from Quantitative 3D….J. Wiskin, et al., Proc. SPIE. 10139, Medical Imaging 2017
3D Recon times toward practical – 40 min per breast
Axial View – 3D vs 2D comparison
Skin line and upper levels completely lost in 2D Axial view
3D image
2D image


Delfinus SOS and Stiffness
1st Improved Other Mode
Case 1: IDC
Case 16 (Cysts and complex cyst):
Adapted from - Li, C., G. Sandhu, M. Boone, N. Duric, P. Littrup and K. Bergman (2018). Breast tissue characterization with sound speed and tissue stiffness imaging. Proc. SPIE 10580, Ultrasonic Imaging and Tomography, 105800Y (14 March 2018). Medical Imaging 2018. Presentation

SOS-corrected Stiffness Imaging -2



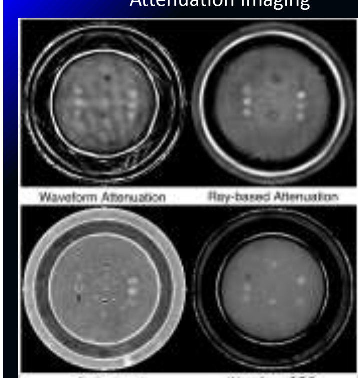
Adapted from - Li, C., G. Sandhu, M. Boone, N. Duric, P. Littrup and K. Bergman (2018). Breast tissue characterization with sound speed and tissue stiffness imaging Proc. SPIE 10580,: Ultrasonic Imaging and Tomography, 105800Y (14 March 2018). Medical Imaging 2018. Presentation

Table 1. Quantitative Sound Speed and BI-RADS Criteria for Different Masses

Mass/Tissue	Shape	Mass Margin	Sound Speed	Stiffness
Cyst	Oval/round	Well circumscribed distinct margin	similar to water	Soft (blue)
Fibroadenoma	usually oval/	Usually circumscribed	similar or higher than water	Stiff or soft
Cancer	Irregular	Microlobulated, indistinct, angular, spiculated	usually greater than water and dense parenchyma	Stiff (redder)
Fatty Tissue	Any shape	n/a	Less than water	Soft
Dense Parenchyma	Any shape	n/a	Greater than water	Medium Stiff

Li, C., G. Sandhu, M. Boone, N. Duric, P. Littrup and K. Bergman (2018). Breast tissue characterization with sound speed and tissue stiffness imaging Proc. SPIE 10580,: Ultrasonic Imaging and Tomography, 105800Y (14 March 2018). Medical Imaging 2018.

Attenuation Imaging

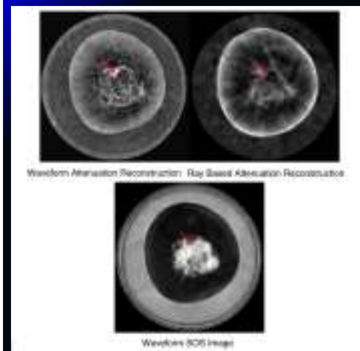


- Attenuation coef. waveform recon is
  - Higher resolution
  - less stable than SOS
  - needs good SNR
- With accurate reflection and SOS images, can use them & known tissue properties to guide the α recon.

Cuiping Li, et al., Breast imaging using waveform attenuation tomography, SPIE Medical Imaging, 2017

In Vivo Images - Cyst

Cuiping Li, et al.



Frequency Domain Waveform Attenuation Recon

Helmholtz Eqn., $k = \omega/c$

$(\nabla^2 + k^2)u(\omega, c) = f(\omega)$

u is FT of complex valued wavefield

Big matrix inversion for inverse problem solution

Minimize cost function

$E(w, c) = 1/2\, \delta d^{\dagger} \delta d$

$\delta d = u - d$ is the data residual, d the measured field.

Complex SOS $c = c_r + ic_i$

Attenuation coeff. α

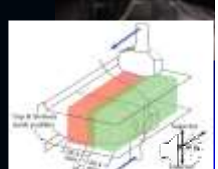
$-20 ln_{10} 2\pi c_i / c_r^2$ (dB/mm)

Semi Summary

- Transmission tomography, only US -> high res. SOS and physical density maps
- These maps necessary to correct other US imaging modes -> high resolution, quantitative, sensitive, spatially correct
  - Doppler, quasistatic and shear wave complex elastography, CEUS, texture and speckle measures, photoacoustics
  - Breast, scrotum; soon brain, limbs
- When we find out how good US can be, …
  - Register whole brain, abdomen, MSK, heart, neck US to CT or MR for corrections
  - Use until body changes too much

Multimodality breast imaging in same and different systems

Breast Light and Ultrasound Combined Imaging (BLUCI) →

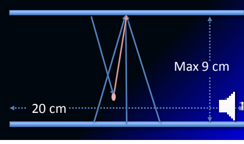


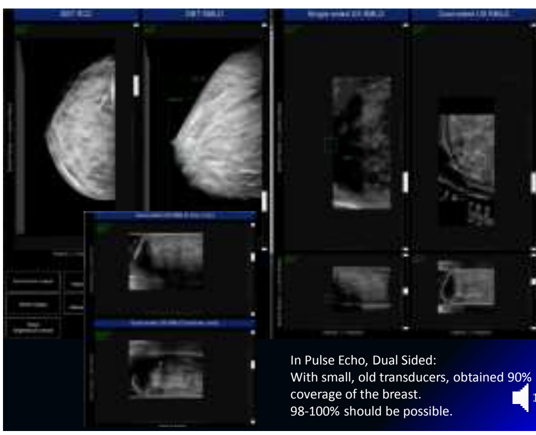
Transmission & Reflection Ultrasound
360º vs Mammo Geometry

- Breast is suspended in H20
- With suction stabilizer, can match breast length from breast CT or MR
- Must be large enough to fit largest breast or parts imaged
- Low enough frequency for high SNR through longest dimension, ~20 cm
- Crawl onto table

22 cm dia

- Combined DBT/Ultras info
- Max thickness 8-9 cm, adjustable
- Allows higher frequency
  - can penetrate
  - Smaller phase shifts
  - Smaller area of sources reaching a detector
- Faster recons?
- Transmission requires *a priori* info.

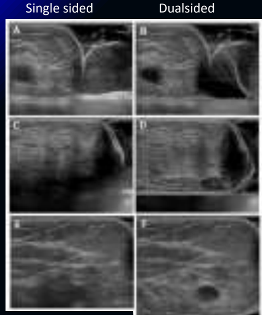




In Pulse Echo, Dual Sided:
With small, old transducers, obtained 90% coverage of the breast.
98-100% should be possible.

16 cases with cysts

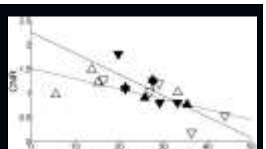
Single sided Dualsided



Case 1

Case 2

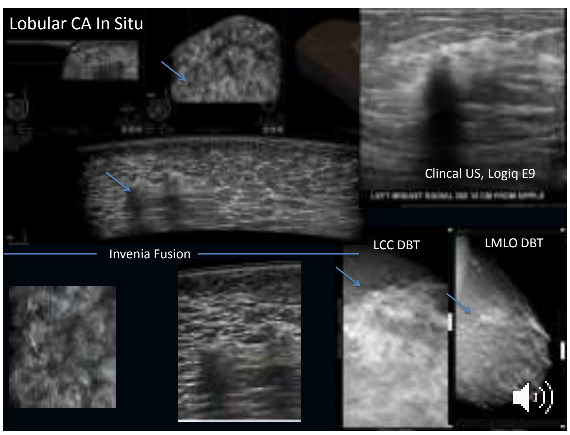
Case 3



^ Linear fits to simple cysts (black) and complex cysts and solid masses (white)

7 cyst cases where mass detectable in single-sided images
Contrast to noise 67% greater in dual sided images

Eric Larson, et al., Ult Med Biol 017



Invenia ABUS – DBT Fusion

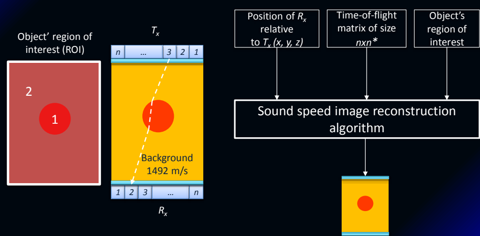
10 Subjects
5 invasive cancers – 4 of them Lobular Carcinomas
All visible on Invenia except:

Lesion	Mammo	DBT	ABUS	Comment
Invasive Lobular Ca (ILC)	N	Y	N	Too deep
6 mm palpable ILC	N	N	N	Too deep, only on hand US
Complex Cyst	Y	Y	N	Too far back

- Results from combined system are much easier to interpret than from separate.
- **Clinical transducer housing limits access near chest wall.**
- Imaging in complex tissues only to 4 cm at 10 MHz.
  - **Use of a lower frequency setting, or dual-sided imaging would be helpful.**

Need dual sided, long transducer, combined system, then could do transmission tomography as well as pulse echo imaging.

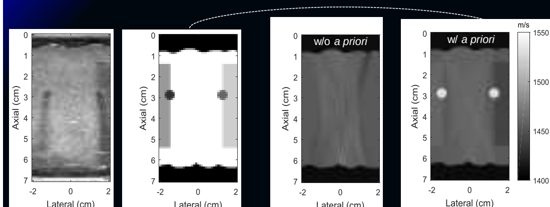
Ray-Based Sound Speed Image Reconstruction Algorithm for Ultrasound Limited Angle Tomography For Mammographic Geometry



- Only 1 experimental number, arrival time
- Wavefield recon. requires full received waveform including some scattering

SOS With Dual-Sided US Scanner

- Transmission mode imaging with *a priori* information (*e.g.* from segmentation of B-mode image) [5]



B-mode image | Segmented B-mode as *a priori* info | Reconstructed speed of sound images

5] Hooi, F. M., & Carson, P. L. (2014). First-arrival traveltime sound speed inversion with a priori information. *Medical physics*, *41*(Part1).

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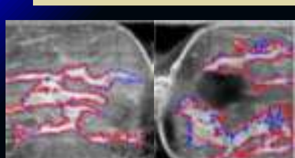
Manually supervised and corrected and automated segmentations of fibroglandular tissues



Automated segmentation agreed with BIRADS density classification by radiologist in 86% of 21 cases.

Manually supervised and corrected classification on 8 cases showed good Pixel by pixel agreement.

SE -- misclassified pixels as % of all breast pixels
TC – Intersection of sets of manual and automated segmented pixels/ union of those sets

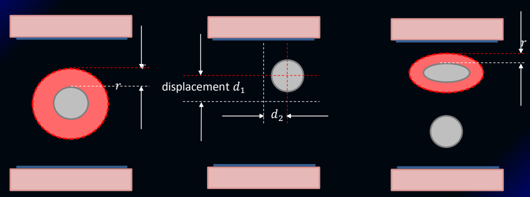
Peng Gu, Won-Mean Lee, Marilyn A. Roubidoux, Jie Yuan, Paul L. Carson, Ultrasonics **65**, 51-58, (2016).

SOS Effects of Mis-Segmentations

Up to ±5% δ SOS for -/+4 mm radius error, r

Up to -3% δ SOS for ±5 mm & ±2.5 mm d_1 & d_2

Up to -2% δ SOS for 5 mm r, d_1 & d_2



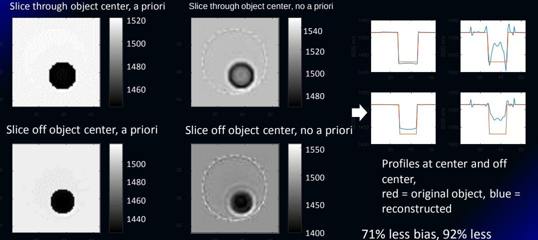
Mis-segmentation of object size

Mis-segmentation of object position

Mis-segmentation of nearby object

Jintamethasawat, R., W. M. Lee, P. L. Carson, F. M. Hooi, M. M. Goodsitt and O. D. Kripfgans (2018). "Error Analysis of Speed of Sound Reconstruction in Ultrasound Limited Angle Transmission Tomography." Ultrasonics **88**(Aug.): 174-184.

Inclusion of a Priori Information in Full-Aperture, Full-wave Inversion Quasi 3D Speed of Sound Image Reconstruction



Profiles at center and off center,
red = original object, blue = reconstructed

SOS images, in and off center slices, with and without *a priori* information, presumably from pulse echo images

71% less bias, 92% less variance of mean SOS in the object, 83% less edge enhancement. More so limited aperture recon.

Yunhao Zhu, Rungroj Jintamethasawat, *et al.*, AIUM, 2017

Existing Reconstruction Algorithm

Speed of Sound Reconstruction Method with *A Priori* Information

$$\min_{\mathbf{c}}\left\{(\mathbf{d}-g(\mathbf{c}))^T\mathbf{C}_\mathbf{D}^{-1}(\mathbf{d}-g(\mathbf{c}))+\underbrace{(\mathbf{c}-\mathbf{c_a})^T\mathbf{C}_\mathbf{M}^{-1}(\mathbf{c}-\mathbf{c_a})}_{\text{Regularizer acting as } a\ priori \text{ information}}\right\}$$

- $\mathbf{C_M}$: covariance matrix adjusting level of tissue homogeneity
- $\mathbf{C_D}$: data covariance matrix
  - $C_{M_{ij}} = \rho_k\sigma^2$ for speed of sound pixels i and j correlated with correlation coefficient ρ_k, where σ is an allowable change of pixel value
- $\mathbf{c_a}$: initial speed of sound guess

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Proposed Reconstruction Algorithm

- For total-variation regularization (smoothing) need to split the objective function. Adding the auxiliary term $\mathbf{u}$:
$$\min_{\mathbf{c},\mathbf{u}}\left\{\left(\mathbf{d}-g(\mathbf{c})\right)^T\mathbf{C}_\mathbf{D}^{-1}\left(\mathbf{d}-g(\mathbf{c})\right)+(\mathbf{c}-\mathbf{u})^T\mathbf{C}_\mathbf{M}^{-1}(\mathbf{c}-\mathbf{u})+\lambda\|\mathbf{E}\nabla\mathbf{u}\|_1\right\}$$

- Then the objective function can be separated into two sub-problems:
$$\min_{\mathbf{c}}\left\{\left(\mathbf{d}-g(\mathbf{c})\right)^T\mathbf{C}_\mathbf{D}^{-1}\left(\mathbf{d}-g(\mathbf{c})\right)+(\mathbf{c}-\mathbf{u})^T\mathbf{C}_\mathbf{M}^{-1}(\mathbf{c}-\mathbf{u})\right\} \quad \text{(sub-problem 1)}$$
$$\min_{\mathbf{u}}\left\{(\mathbf{c}-\mathbf{u})^T\mathbf{C}_\mathbf{M}^{-1}(\mathbf{c}-\mathbf{u})+\lambda\|\mathbf{E}\nabla\mathbf{u}\|_1\right\} \quad \text{(sub-problem 2)}$$

- Both sub-problems are solved alternately

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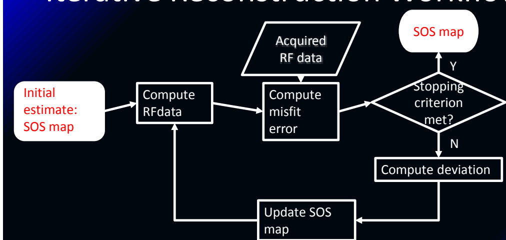
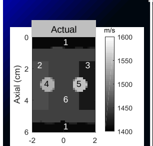
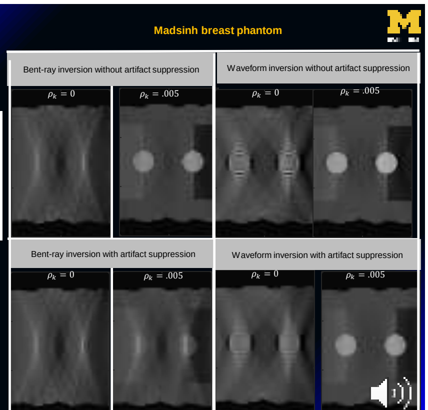
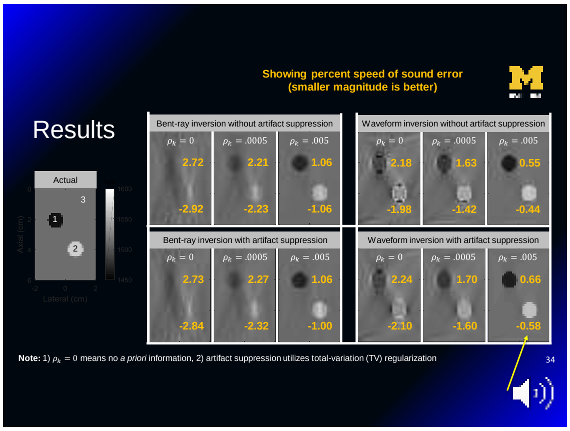
Iterative Reconstruction Workflow



Results






Showing percent speed of sound error
(smaller magnitude is better)
Results
Actual
3
1
2
Axial (cm)
Lateral (cm)
Bent-ray inversion without artifact suppression
Waveform inversion without artifact suppression
$\rho_k = 0$
$\rho_k = .0005$
$\rho_k = .005$
2.72
2.21
1.06
2.18
1.63
0.55
-2.92
-2.23
-1.06
-1.98
-1.42
-0.44
Bent-ray inversion with artifact suppression
Waveform inversion with artifact suppression
2.73
2.27
1.06
2.24
1.70
0.66
-2.84
-2.32
-1.00
-2.10
-1.60
-0.58
Note: 1) $\rho_k = 0$ means no *a priori* information, 2) artifact suppression utilizes total-variation (TV) regularization
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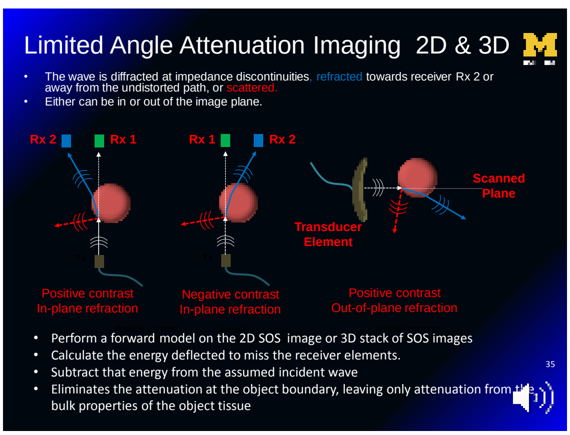
Limited Angle Attenuation Imaging 2D & 3D
The wave is diffracted at impedance discontinuities, refracted towards receiver Rx 2 or away from the undistorted path, or scattered.
Either can be in or out of the image plane.
Rx 2
Rx 1
Rx 1
Rx 2
Scanned Plane
Transducer Element
Positive contrast In-plane refraction
Negative contrast In-plane refraction
Positive contrast Out-of-plane refraction
Perform a forward model on the 2D SOS image or 3D stack of SOS images
Calculate the energy deflected to miss the receiver elements.
Subtract that energy from the assumed incident wave
Eliminates the attenuation at the object boundary, leaving only attenuation from the bulk properties of the object tissue
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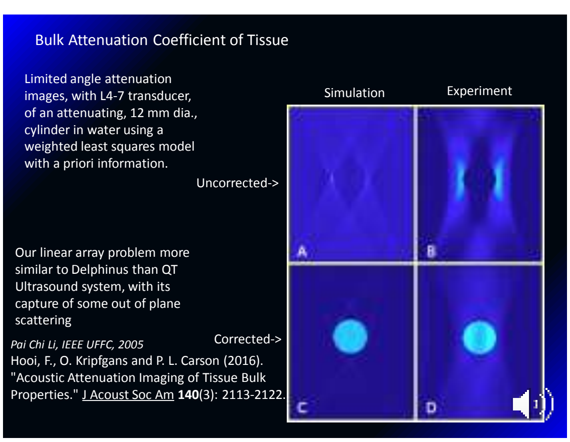
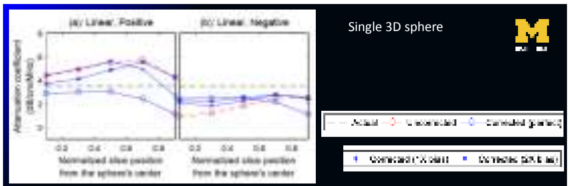
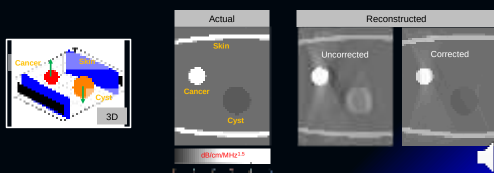

Bulk Attenuation Coefficient of Tissue
Limited angle attenuation images, with L4-7 transducer, of an attenuating, 12 mm dia., cylinder in water using a weighted least squares model with a priori information.
Simulation
Experiment
Uncorrected->
A
B
Our linear array problem more similar to Delphinus than QT Ultrasound system, with its capture of some out of plane scattering
Corrected->
Pai Chi Li, IEEE UFFC, 2005
Hooi, F., O. Kripfgans and P. L. Carson (2016). "Acoustic Attenuation Imaging of Tissue Bulk Properties." J Acoust Soc Am **140**(3): 2113-2122.
C
D

Single 3D sphere



≤ 1 dB/MHz ≤ 2 dB/Mz error for slice out to 0.6 of radius from sphere center

- Numerical breast phantom with masses located off from the imaging plane



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Summary

- Transmission tomography, only US -> high res. SOS and physical density maps
- These maps necessary to correct other US imaging modes -> high resolution, quantitative, sensitive, spatially correct
  - Doppler, quasistatic and shear wave complex elastography, CEUS, texture and speckle measures, photoacoustics
- Breast, scrotum; soon brain, limbs
- When we find out how good US can be, ...
  - Register whole brain, abdomen, MSK, heart, neck US to CT or MR for corrections
  - Use until body changes too much
- Prone US & CT or MR of breast *vs.* combined US & DBT
  - Which is better in which cases– a question between two promising futures
    - Not obvious
      - Short path, low energy vs full aperture in both modalities
      - Convenient standing or sitting vs crawling onto table
    - Do the comparative study, rather than a big one between one of these four modalities and the obvious past, (where much of our meager clinical trials money goes for short term gain).
  - How get there:
    - Public investment, NIH, etc.
    - User Demand, small companies, or big companies invest heavily to replace what they already sell.
  - When is the right time?
    - BCT approved for large clinical research studies in USA (2015), for sale in Canada, Australia, European Union
    - Prone UCT FDA approved
    - Combined US & DBT – 5-6 years out.

Acknowledgements

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Eric Larson

Kai Thomenius
Cynthia Davis, Larry Mo, et al.

Yunhao Zhu
Peng Gu
Jie Yuan