Novel Ultrasound Biomarkers: Acoustic Backscatter Coefficient and Related Features

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Outline

1. Quantitative ultrasound (QUS) background
2. Backscatter coefficient (BSC) theory
3. Experimental BSC measurements
4. BSC measurement limitations
5. Recent successful BSC/QUS studies
6. Perspectives and conclusions

Thanks and acknowledgments - First

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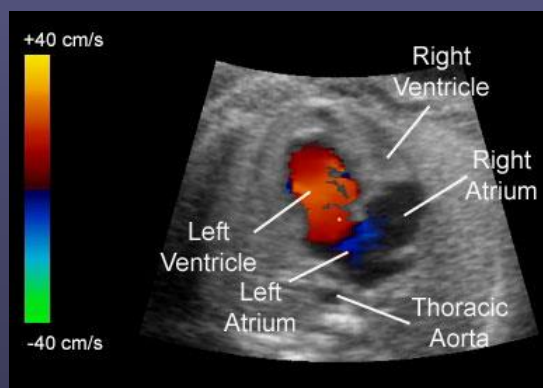
Quantitative Ultrasound (QUS) Background

QUS refers to any quantitative measure (i.e., biomarker) obtained using ultrasound data which is

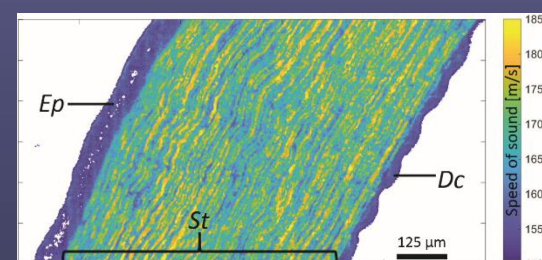
- User independent
- System independent
- Repeatable

-> Measures true tissue/organ property

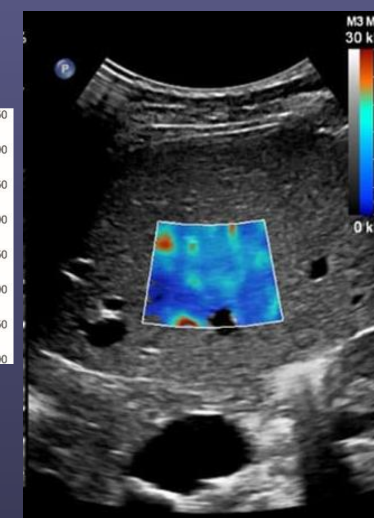
Ovarian cyst measurement



Fetal echocardiography



500-MHz acoustic microscopy in pig eye



Young's modulus in liver

In this presentation, we will focus on QUS methods based on the acoustic backscatter coefficient (BSC)

BSC Theory

BSC definition: $$\sigma_d = \frac{r^2 I_{sc}}{V I_{inc}}$$

In an inhomogeneous medium: $$\sigma_d = \frac{k^4 \langle \gamma^2 \rangle}{16\pi^2 V} \int_V b_\gamma\left(\overrightarrow{\Delta r}\right) e^{-j\vec{K}\cdot\overrightarrow{\Delta r}} d\,\overrightarrow{\Delta r}$$

BSC is proportional to the spatial Fourier transform of the autocorrelation $b_\gamma\left(\overrightarrow{\Delta r}\right)$ of the tissue in terms $\gamma \approx 2\Delta z/z_0$

BSC depends on tissue microsctructure (spatial distribution, size, shape, and acoustic properties of scatterers).

BSC is a frequency dependent function and has units of 1/m/str.

r:	Distance from the source
V:	Scattering volume,
I_{sc} and I_{inc}:	Scattered and incident acoustic intensity, respectfully
z and z_0:	Acoustic impedance and average acoustic impedance
K:	Wavenumber

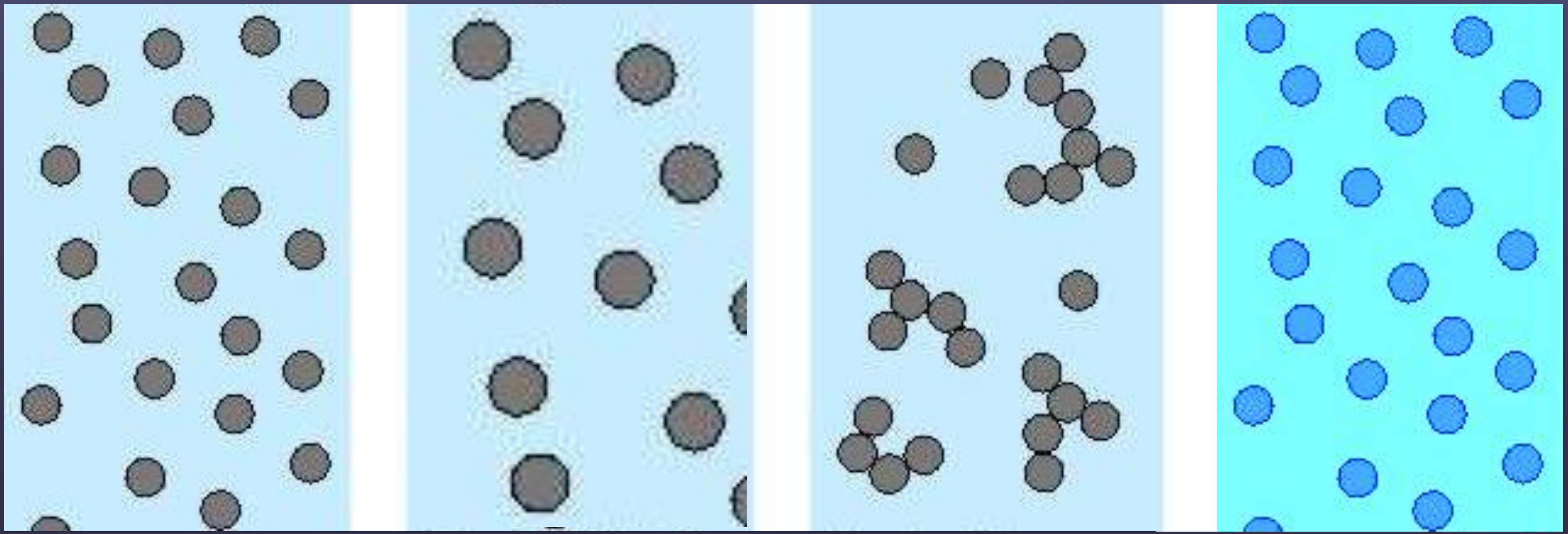
BSC Theory

BSC definition:

$$\sigma_d = \frac{r^2 I_{sc}}{V I_{inc}}$$

Use BSC to infer quantitative information about tissue:

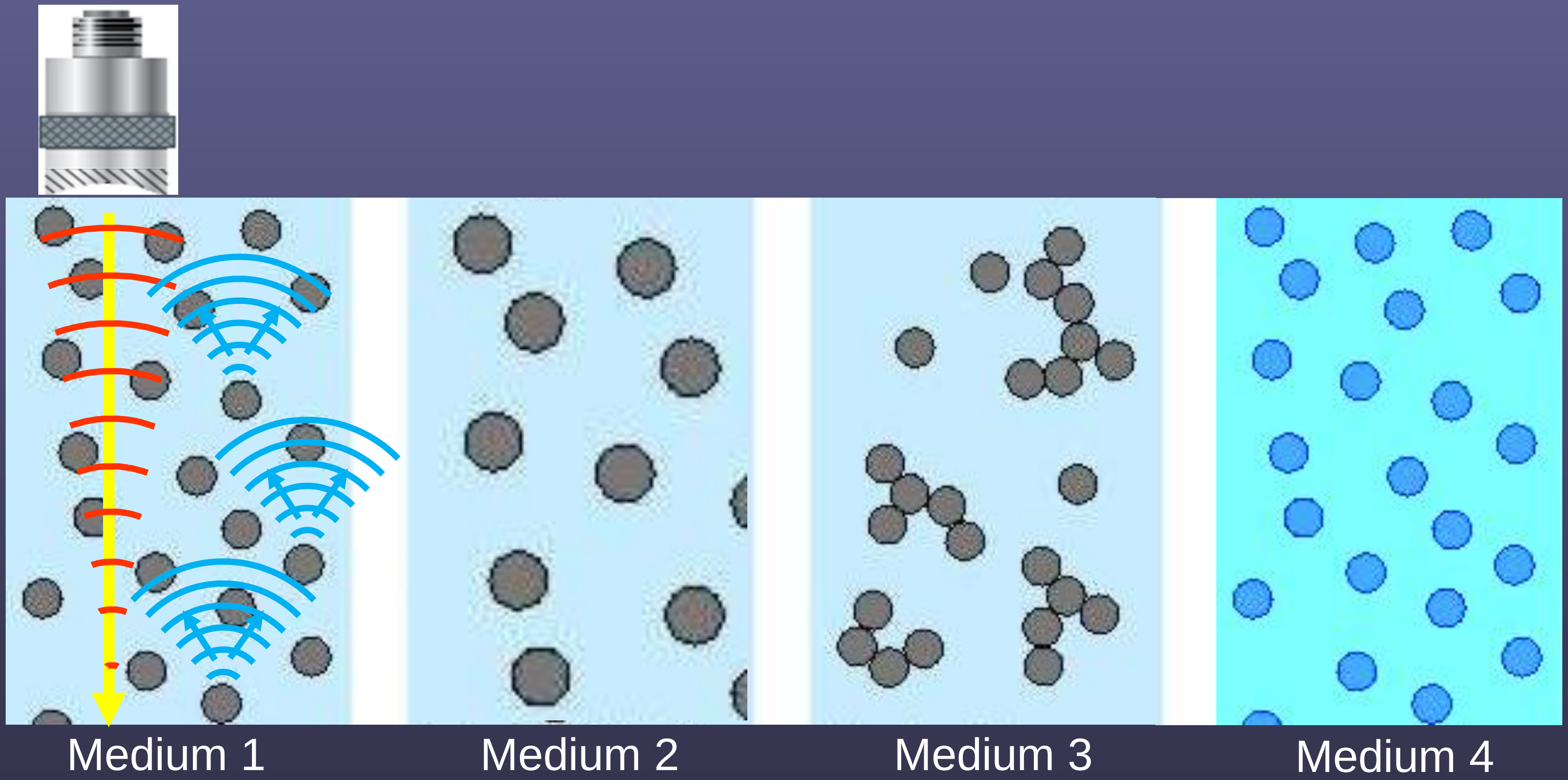
- BSC quantifies tissue microstructural organization (i.e., < wavelength)
- BSC provides new contrast mechanisms
- Model-based or model-free methods
- Raw BSC values or fit parameters are used to monitor disease progression, diagnose, characterize tissue, assess new treatment options, etc.



Medium 1 Medium 2 Medium 3 Medium 4

Experimental BSC Measurements

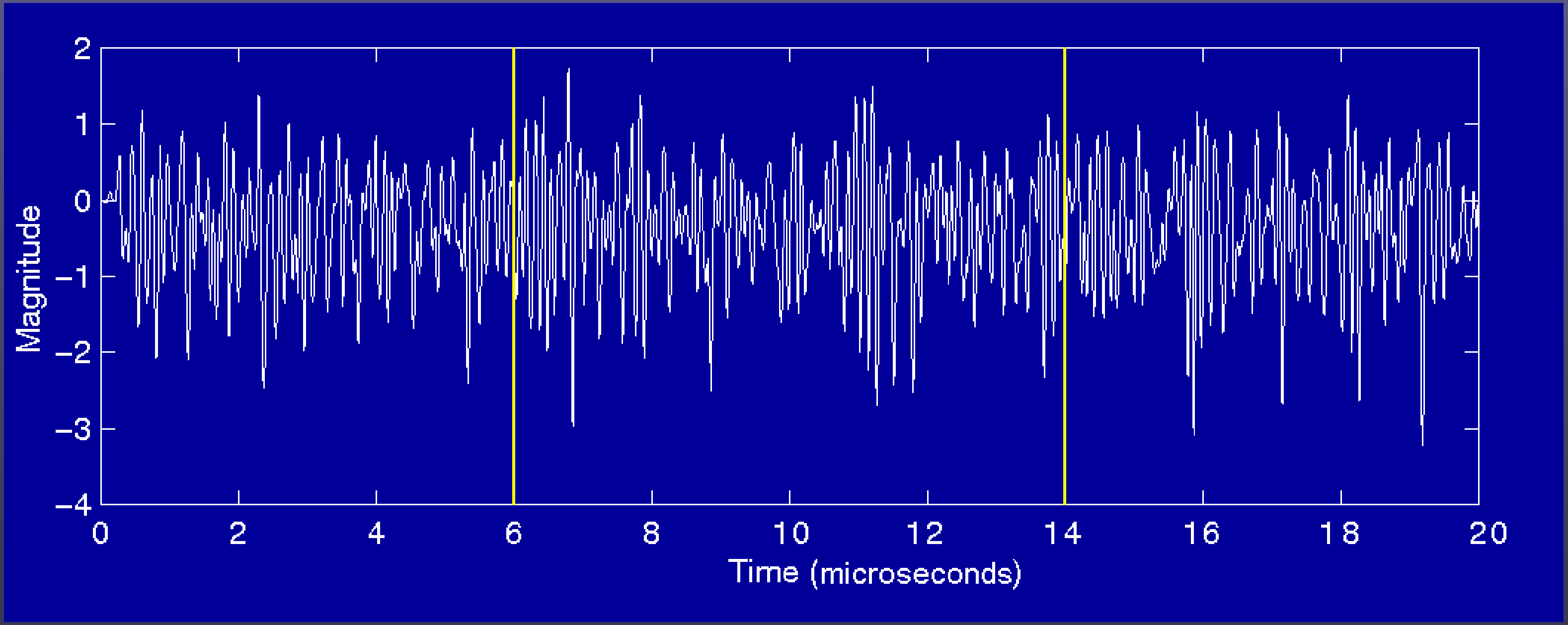
- Pulsed ultrasound beam is emitted
- Scattering occurs in the tissue



All four media would have a very different BSC

Experimental BSC Measurements

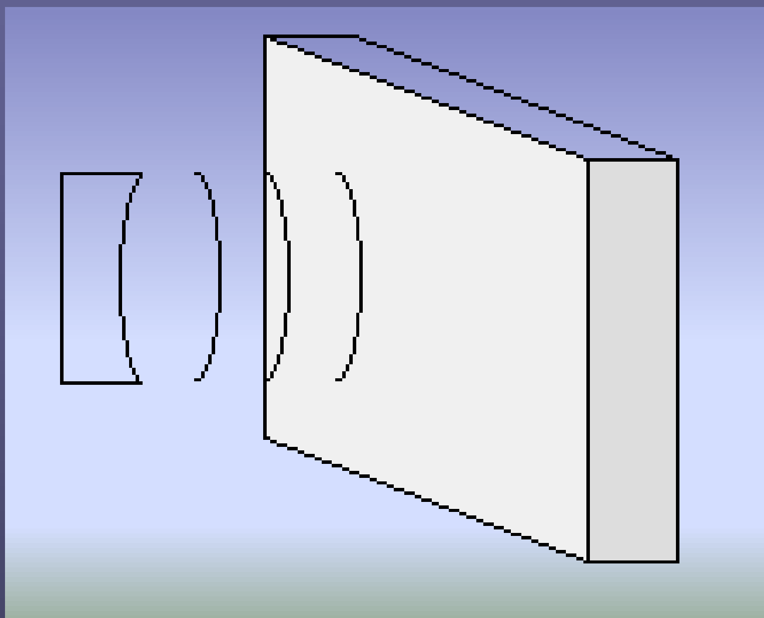
- Pulse ultrasound beam is emitted
- Scattering occurs in the tissue
- Backscattered radio-frequency (RF) echo signals are recorded



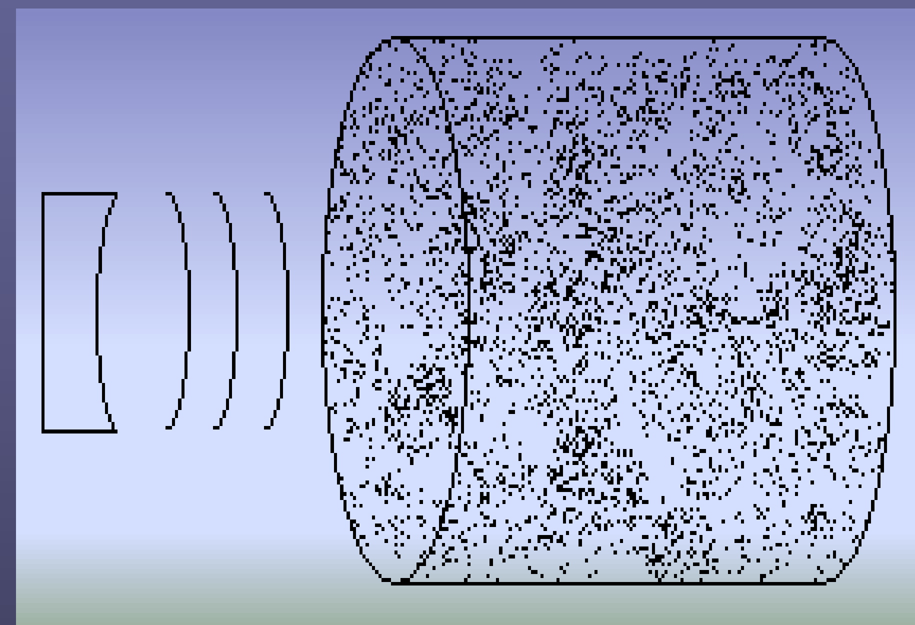
- Adjacent RF lines are gated and average power spectrum is computed
- BSC is computed using calibration methods

BSC Calibration Methods:

Two methods exist to remove system and user dependence:



Planar Reflector Technique

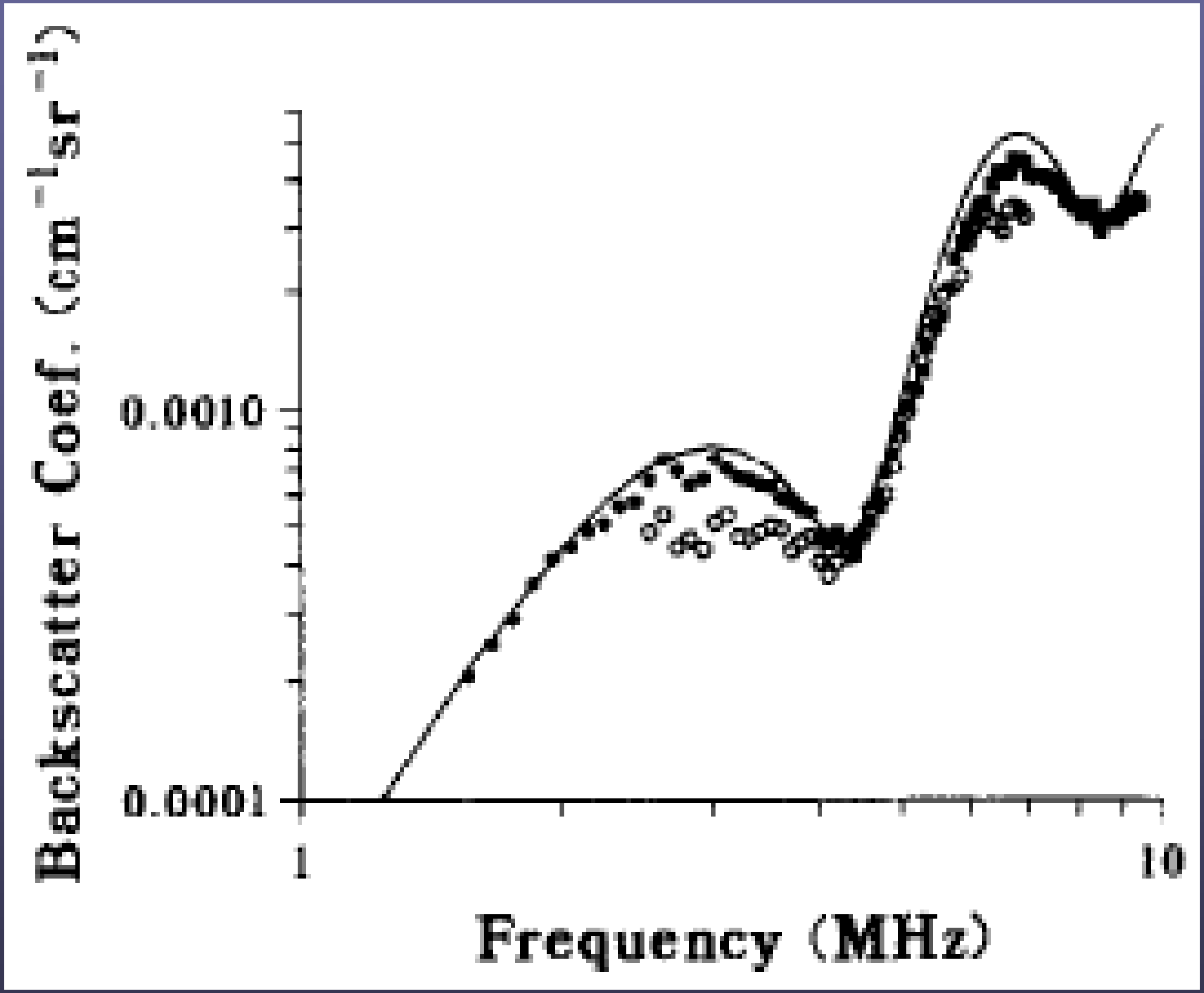


Reference Phantom Technique

- Planar surface of known reflectivity
- Use same settings used for sample
- Works for weakly focused single-element sources, not good for arrays are highly focused sources

- Well-characterized reference phantom (i.e., known attenuation and theoretical BSC)
- Use same settings used for sample
- Can be used with all transducer types and arrays

Experimental vs. Theoretical BSC



Comparison with Faran's theory for backscatter from glass spheres (Hall et al., UMB, 1996)

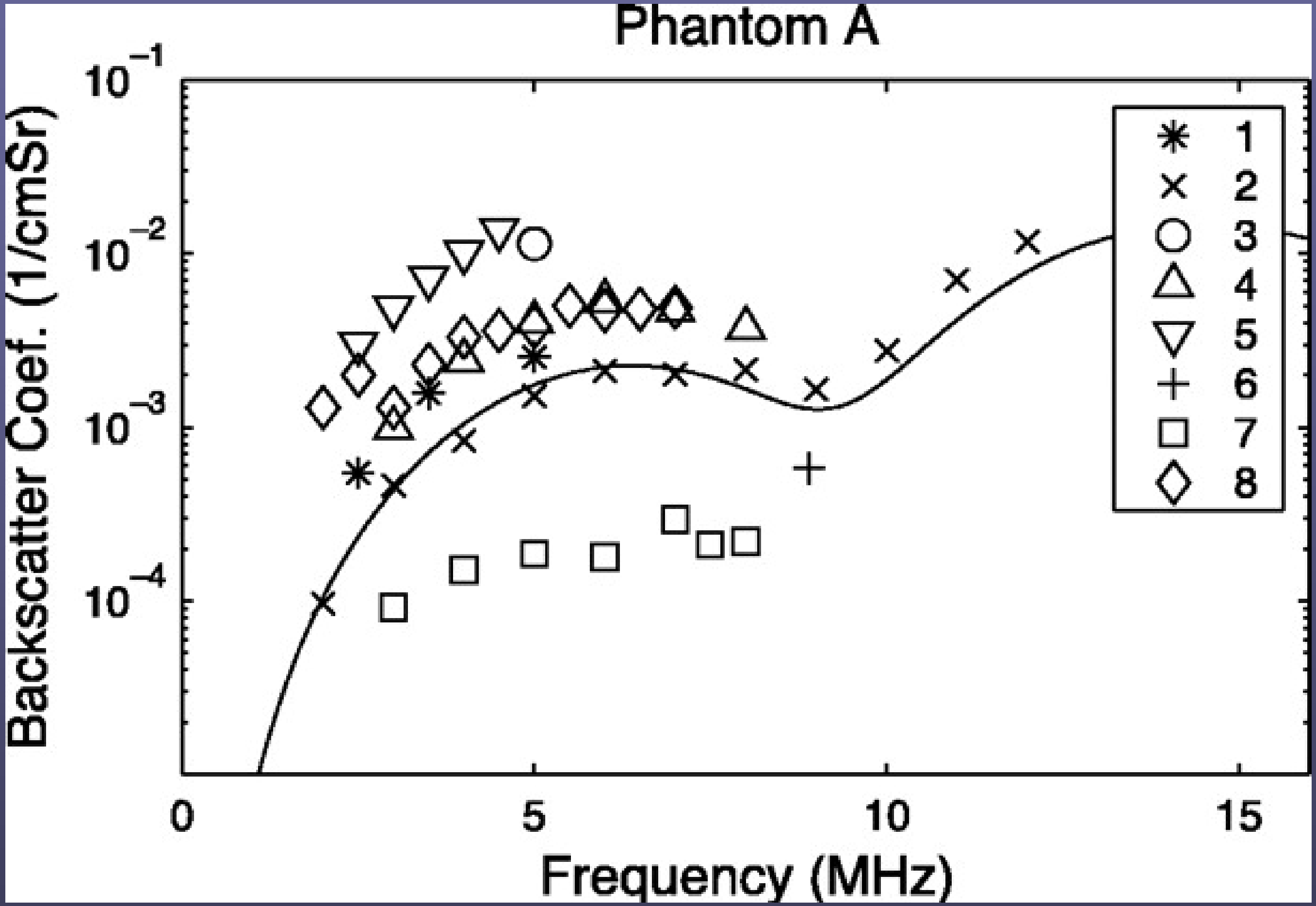
BSC Measurements Limitations

- Attenuation compensation
- Calibration needed
- Reference phantom specific: speed of sound differences
- Reference phantom specific: increased variance
- Spatial resolution
- Non-linear propagation
- Multiple scattering and Born approximation

- Requires RF data

Generally speaking: BSC as a biomarker is not clinically available today, but a mature research field with numerous success stories exist!

BSC Measurements Limitations



75-90 μm glass beads
5/mm^3
Gel background

0.4 dB/cm-MHz

Solid curve: Theoretical BSC based on Faran theory using size, concentration, and properties of the beads

Symbols: Experimental BSC from 8 laboratories (blinded to the true properties)

Interlaboratory Comparison of Ultrasonic Backscatter Coefficient Measurements From 2 to 9 MHz (Wear et. Al., JUM 24: 1235-1250, 2005)

Successful and recent BSC/QUS Studies

Foundation studies:

- New theoretical and experimental developments
- Phantom studies

Oncology: Prostate, lymph node, breast, thyroid, etc.

Premature birth: Cervix

Osteoarthritis: Cartilage

Blood: Blood aggregation

Ophthalmology: tumors, Myopia

Liver: Fatty liver disease

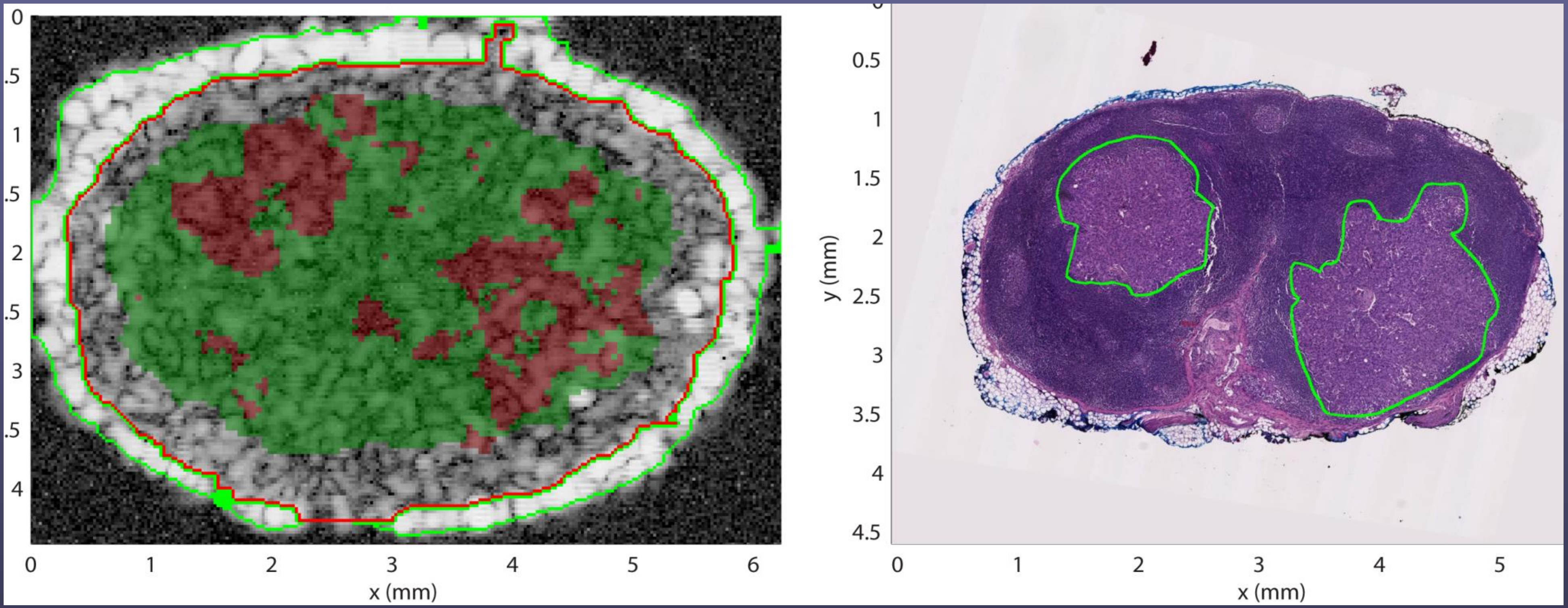
Thermal therapy monitoring

And many more!

Ex vivo BSC-based image in a human lymph node

BSC-based cancer imaging

H&E Histology



26-MHz BSC-based image of human cancerous lymph node

Green -> BSC-based cancer probability < 50%
Red -> BSC-based cancer probability > 50%

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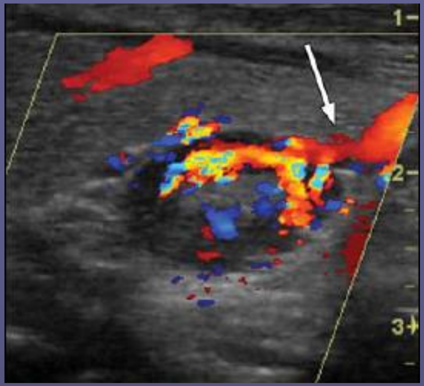
Saegusa-Beecroft et al., Journal of Surgical Research, 2015

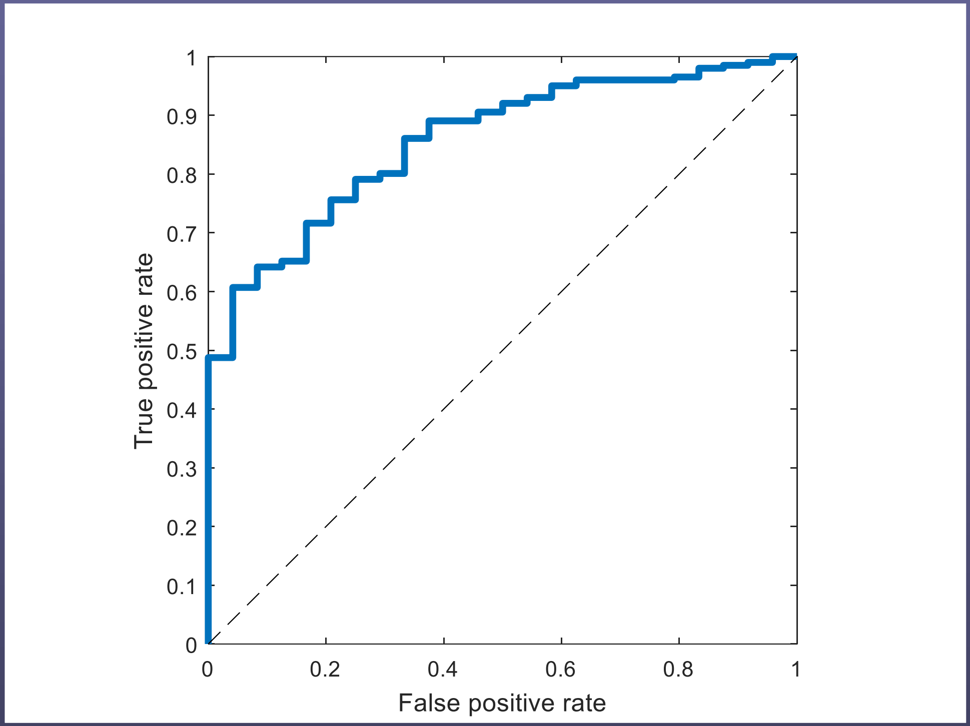
In-vivo BSC Classification of human thyroid nodules

Microcalcification

Doppler Imaging



225 ultrasound nodules from 167 patients



Linear combination of QUS AUC: 0.857 ± 0.033

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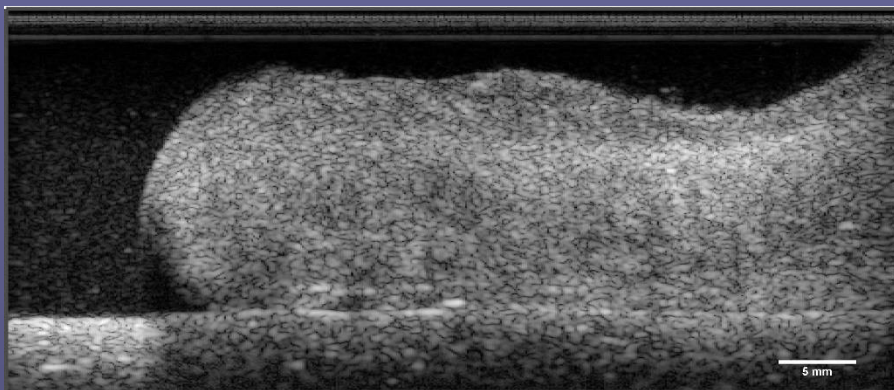
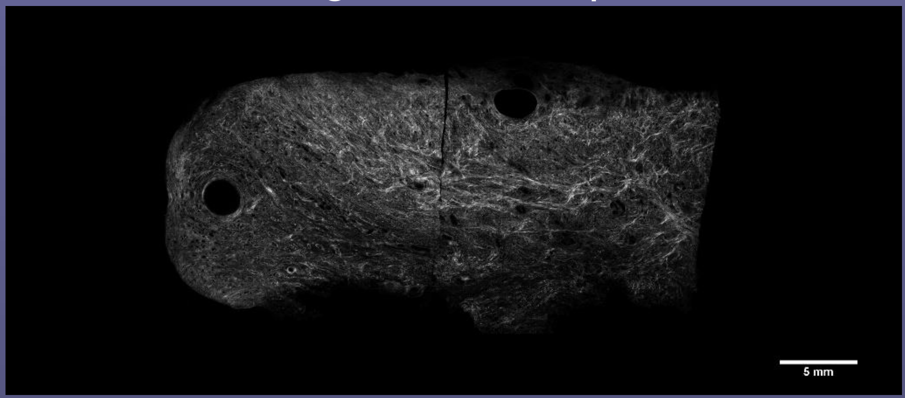
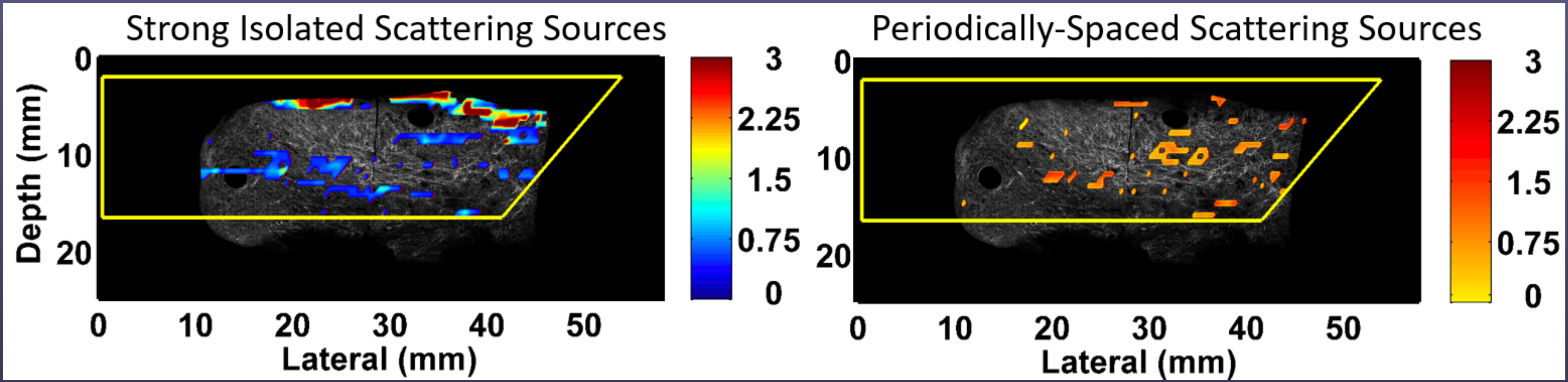
Illustrative BSC-based image in *ex vivo* human cervix

B-mode Ultrasound



Second harmonic generation optical microscopy



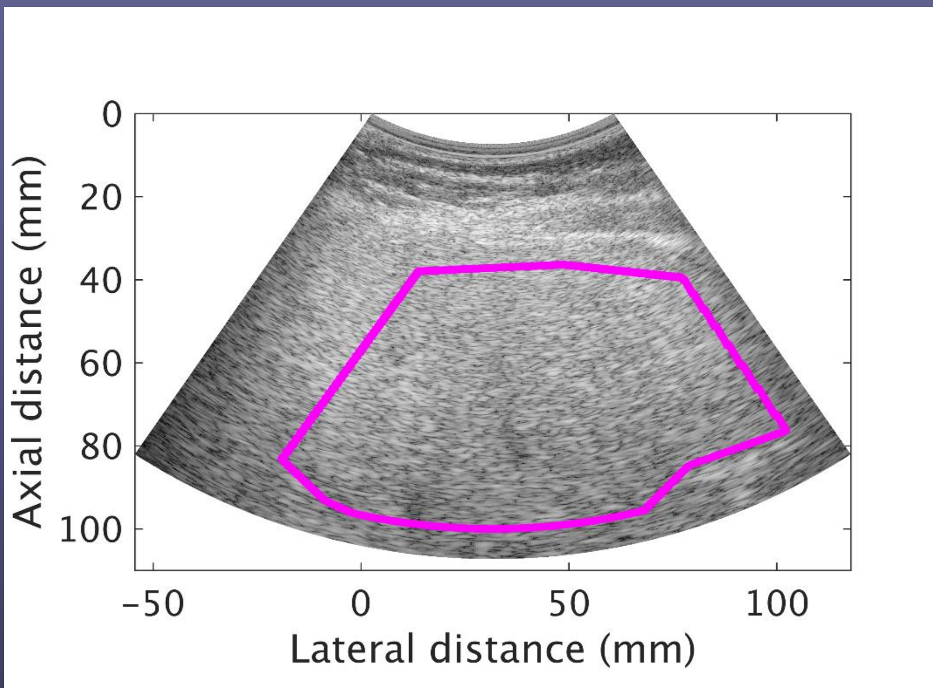


BSC to understand changes in normal cervix during pregnancy towards predicting preterm birth risk

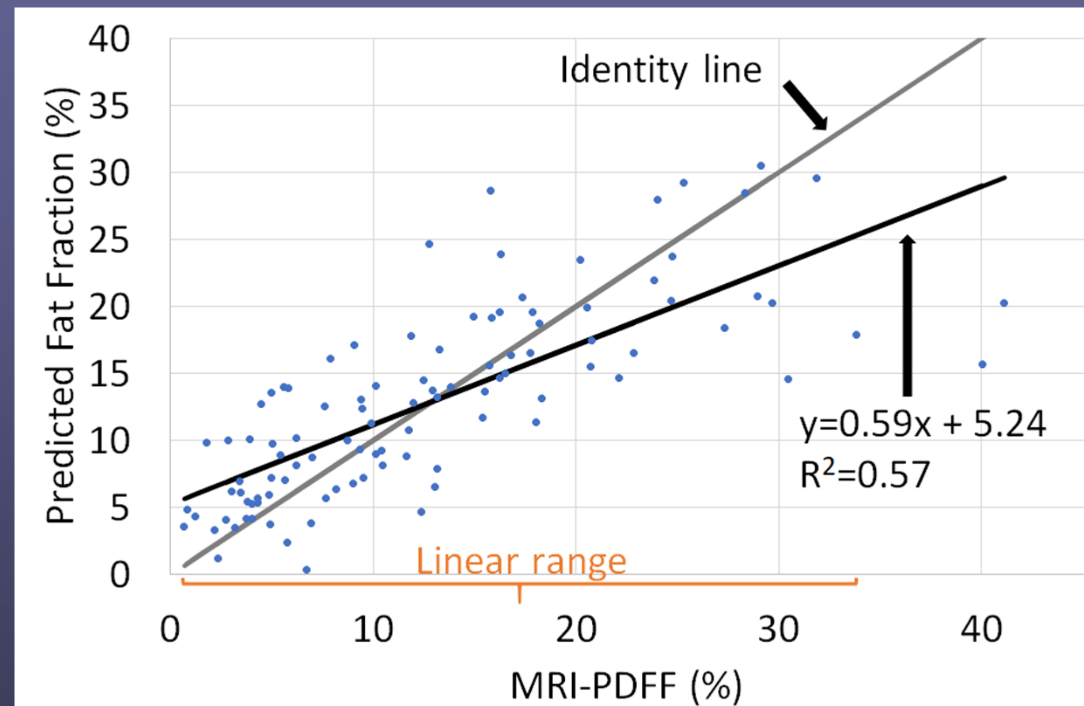
- Reusch LM, et al. “Nonlinear Optical Microscopy and Ultrasound Imaging of Human Cervical Structure,” J Biomed Optics , 2013.
- Rosado-Mendez IM, et al. “Analysis of coherent and diffuse scattering using a reference phantom,” IEEE TUFFC, 2016.
- Guerrero QW, et al., “Quantitative Ultrasound Biomarkers Based on Backscattered Acoustic Power: Potential for Quantifying Remodeling of the Human Cervix during Pregnancy,” UMB, 2018.

Liver Fat Quantification

In-vivo human study of 102 participants with known/suspected Nonalcoholic fatty liver disease (NAFLD)



Liver B-mode with a Field of Interest from a 68-year-old man with NAFLD (MRI-PDFF = 25.3%).



Multi-parametric QUS-predicted fat fraction (cross-validated) versus MRI-PDFF scatterplot

Han A et al. Published Online: February 4, 2020
https://doi.org/10.1148/radiol.2020191152
Radiology

Conclusions

- BSC is a true quantitative “tissue-describing” quantity
- Requires careful methods for experimental computation
- Requires calibration data

- Very sensitive to tissue microstructure and organization

Great potential as a biomarker for a wide range of diseases!

Thank you for your attention!