Quantitative Lung Ultrasound Beyond Artifact Imaging

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THERE IS A NEED TO MONITOR CHRONIC INTERSTITIAL LUNG DISEASES

Pulmonary fibrosis affects 200,000 in the US

Cardiogenic pulmonary edema: congestive heart failure affects 6.2 million Americans

Covid-19 related pneumonia: over 29 million COVID cases in the US

Current modalities have limitations

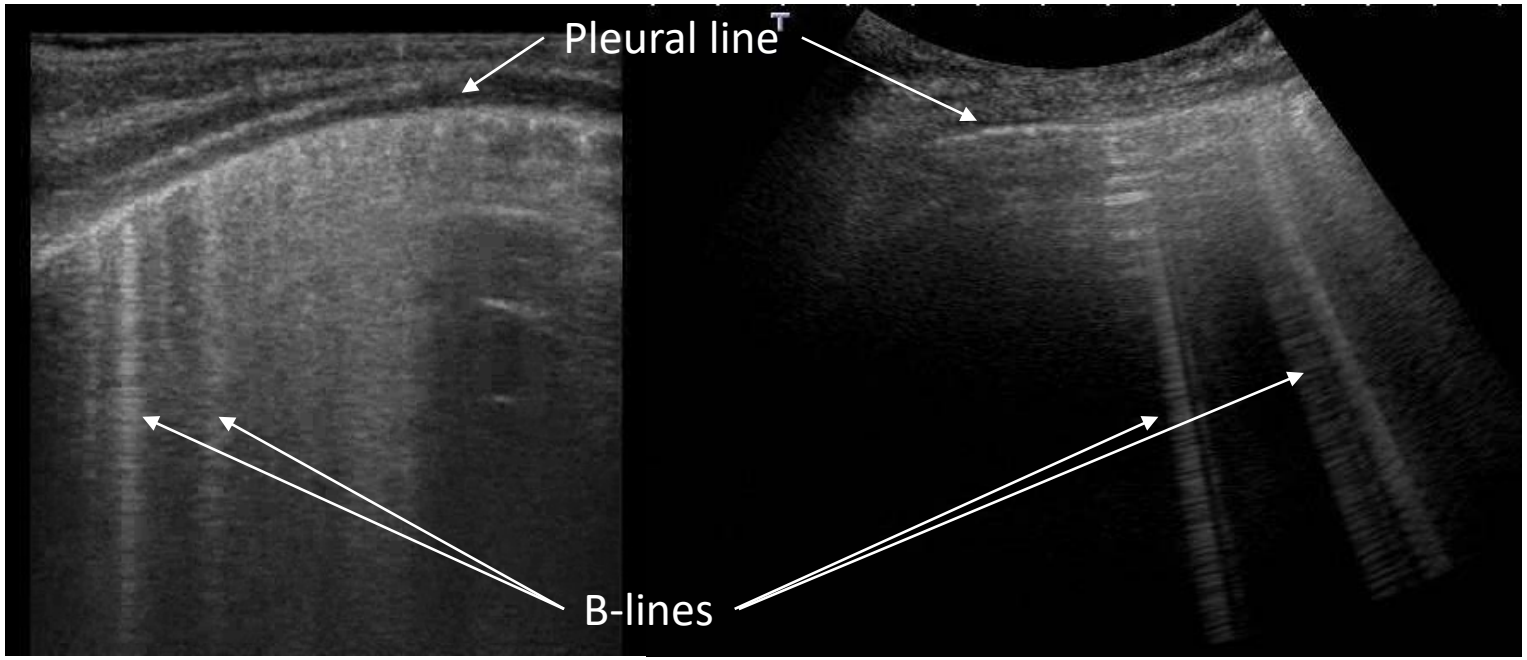
Chest X-Ray
CT scanning
Pulmonary function tests

ULTRASOUND COULD BE A HIGHLY ATTRACTIVE ALTERNATIVE

LIMITATIONS OF LUNG CONVENTIONAL ULTRASOUND

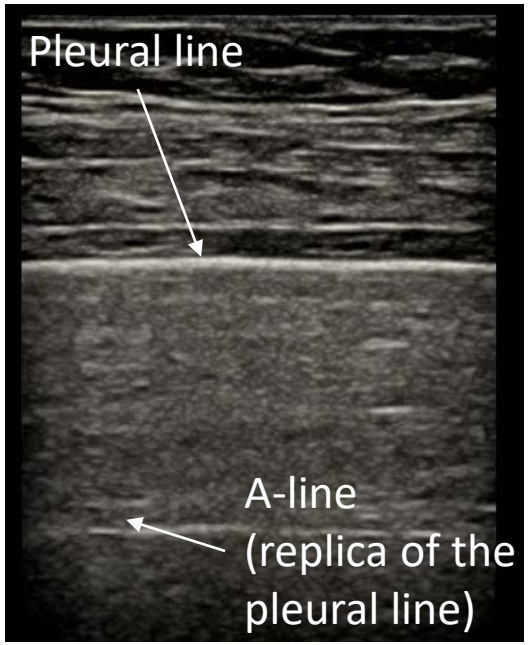
Linear probe

Convex probe

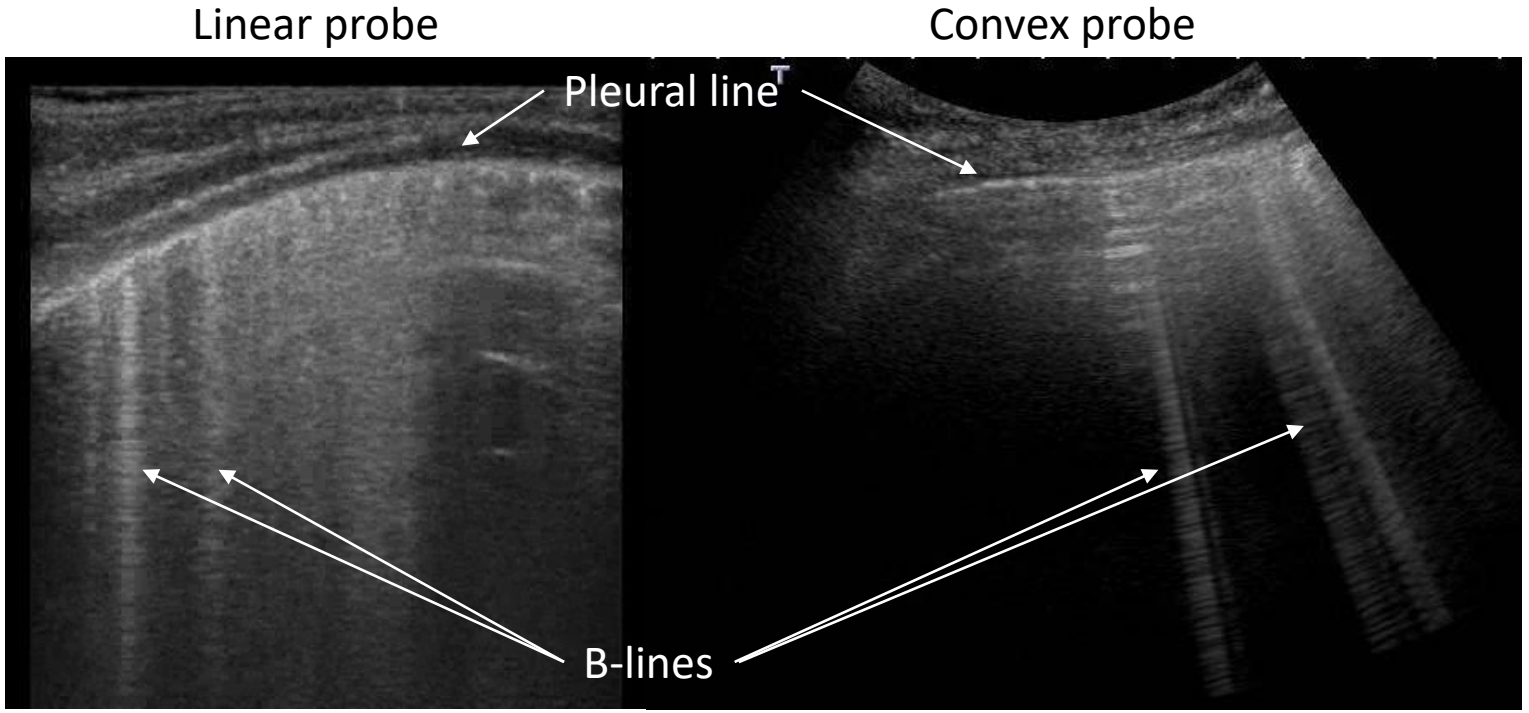


Courtesy of L. Demi, Univ. of Trento

Linear probe



LIMITATIONS OF LUNG CONVENTIONAL ULTRASOUND



Courtesy of L. Demi, Univ. of Trento

"B-line artefact is defined as discrete laser-like vertical hyperechoic reverberation artefacts that arise from the pleural line, which extend to the bottom of the screen without fading"

Dietrich et al, (2016). Lung B-line artefacts and their use. *Journal of thoracic disease*, *8*(6), 1356.

Evidence that the appearance of B-lines could be frequency-dependent

Mento et al (2020). On the influence of imaging parameters on lung ultrasound B-line artifacts, in vitro study. *The Journal of the Acoustical Society of America*, *148*(2), 975-983.

LIMITATIONS OF LUNG CONVENTIONAL ULTRASOUND

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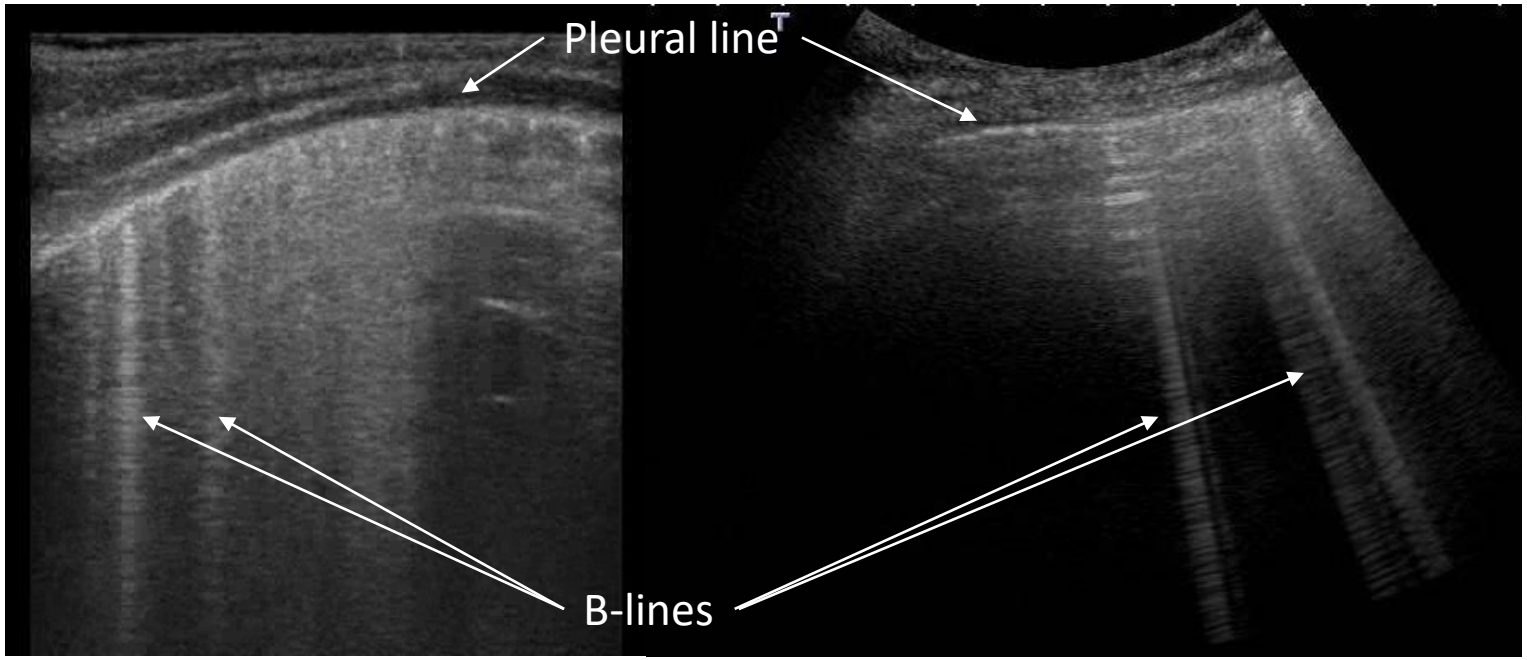
Convex probe



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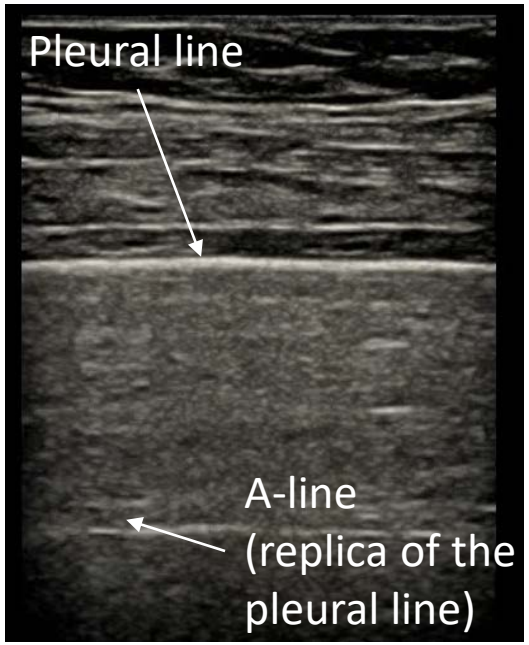
Linear probe



QUALITATIVE
NON-SPECIFIC → **Not well suited for monitoring**
DEPENDENT ON IMAGING PARAMETERS (Mento et al, JASA 148(2), 2020)
→ **WE NEED BIOMARKERS**

QUANTITATIVE LUNG ULTRASOUND BIOMARKERS

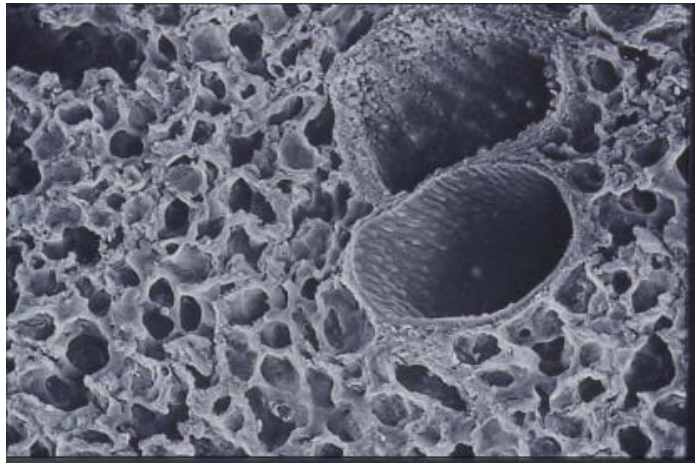
→ Longitudinal follow up, monitoring of chronic lung diseases

→ Monitoring response to treatment

→ Better management of chronic respiratory diseases

HOW CAN THIS BE ACHIEVED?

WHY IS LUNG ULTRASOUND *IMAGING* ELUSIVE?



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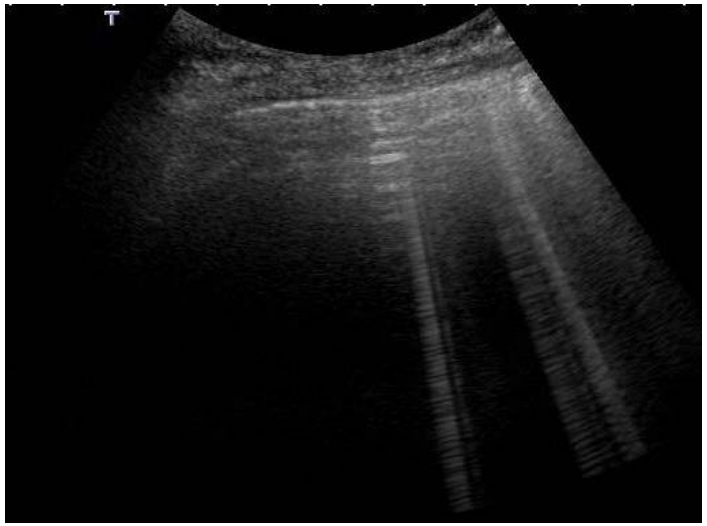

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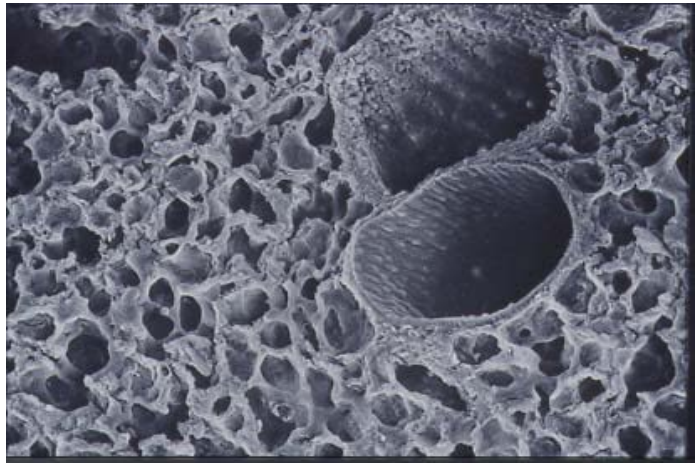

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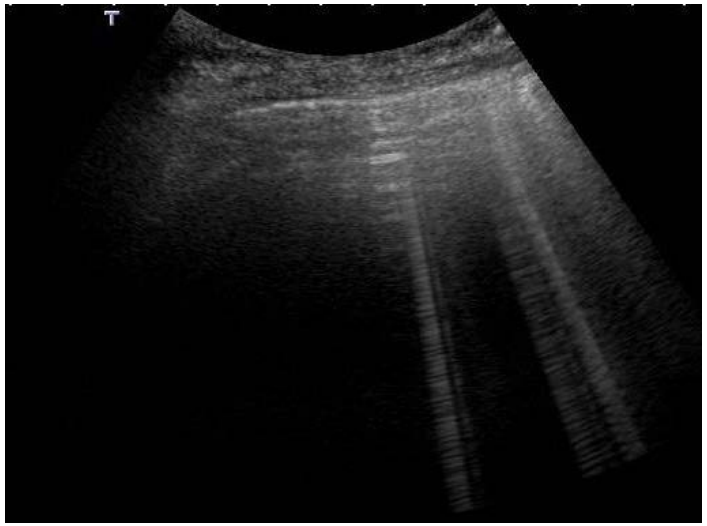
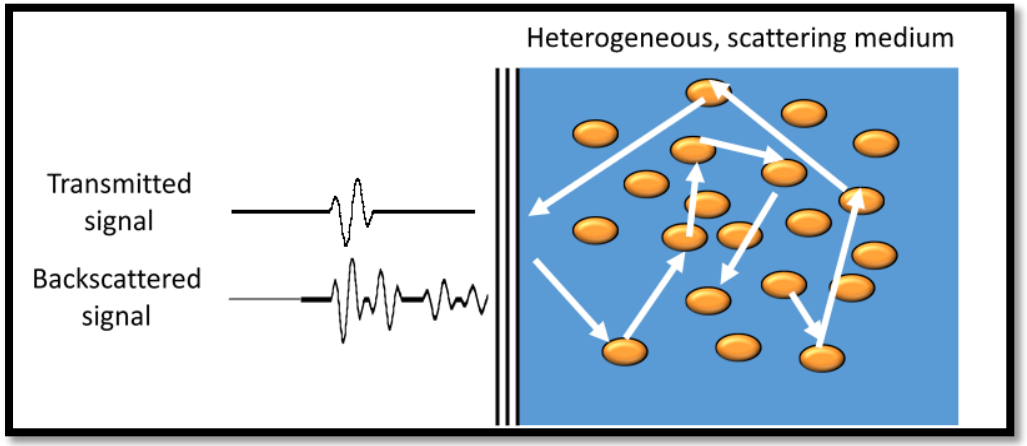


MULTIPLE SCATTERING

No linear relationship between time and distance

→ No imaging!!!

Usually neglected in weakly scattering tissue



ULTRASOUND BIOMARKERS OF INTERSTITIAL LUNG DISEASES

TAKE ADVANTAGE OF MULTIPLE SCATTERING!!!
By leveraging the complexity of wave propagation in highly heterogeneous media

→ **Extract information on the microstructure**
→ **CAN MULTIPLE SCATTERING BE A NEW SOURCE OF CONTRAST?**

DIFFUSION: RANDOM WALKERS IN A FOREST

DIFFUSION: RANDOM WALKERS IN A FOREST

DIFFUSION CONSTANT D

The higher the diffusion constant, the faster the wave will diffuse in the medium

TRANSPORT MEAN FREE PATH L*

Mean distance at which the wave has lost memory of initial direction

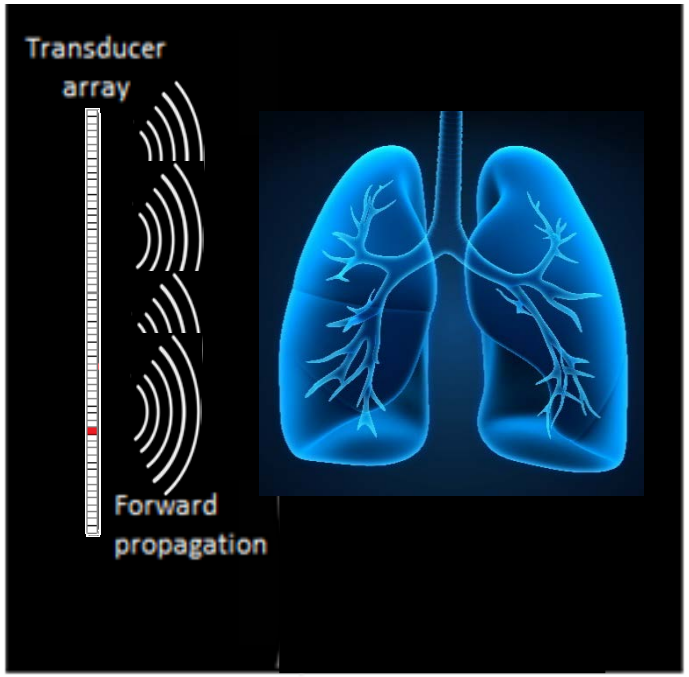
$$D = \frac{V_E \times L^*}{3}$$

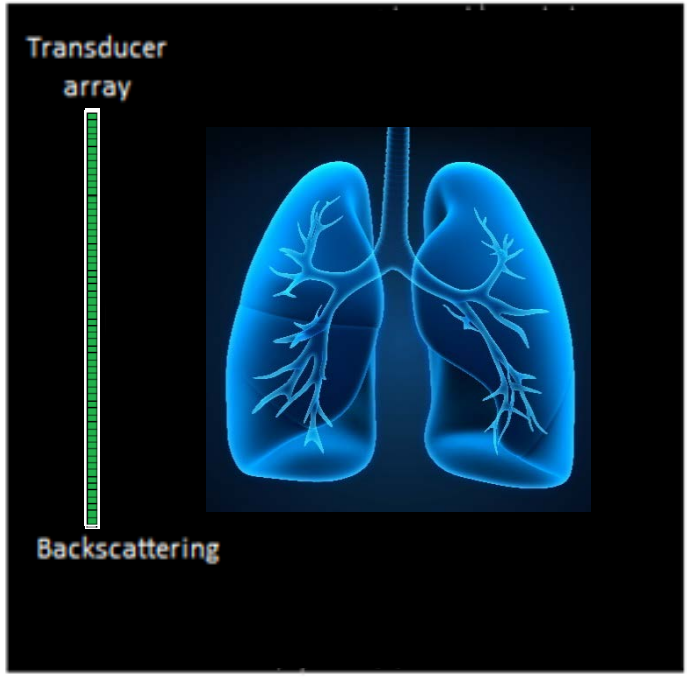
ATTENUATION

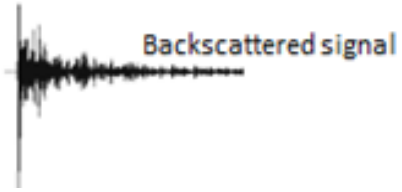
Relate attenuation to microstructure?

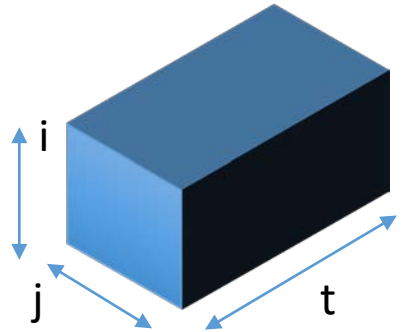
DIFFUSION MEASUREMENT

Per-channel use of ultrasound probe





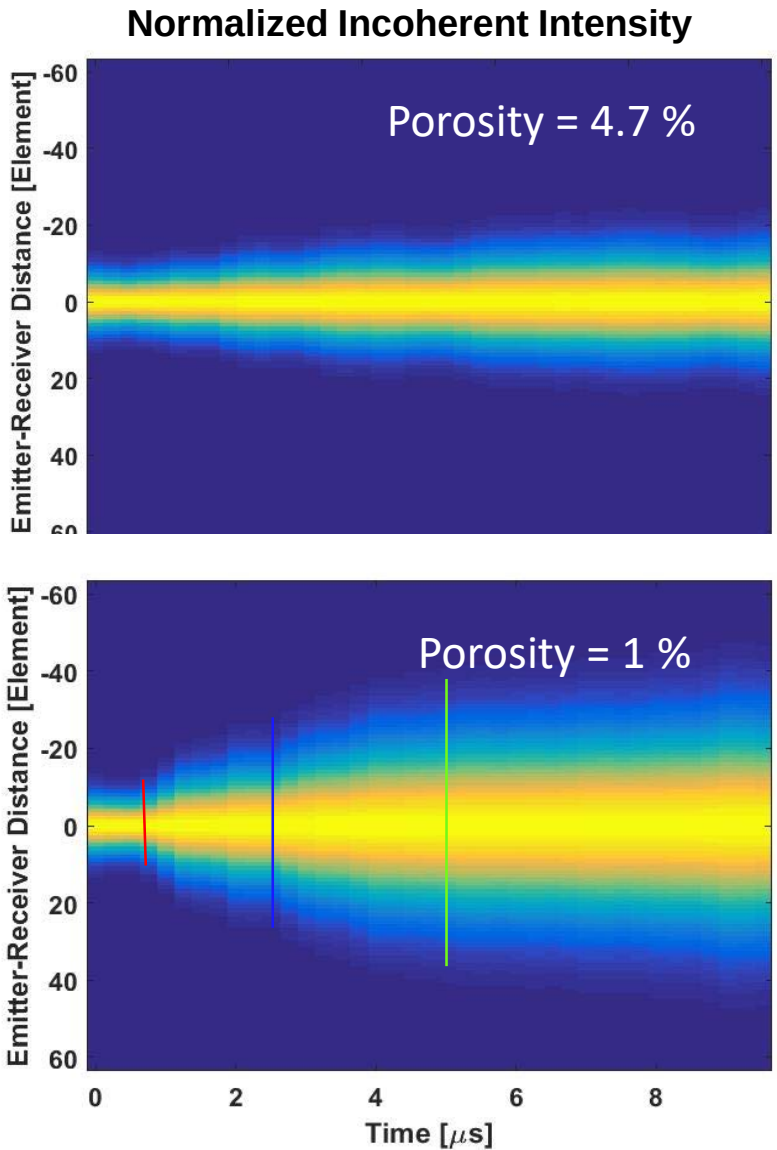


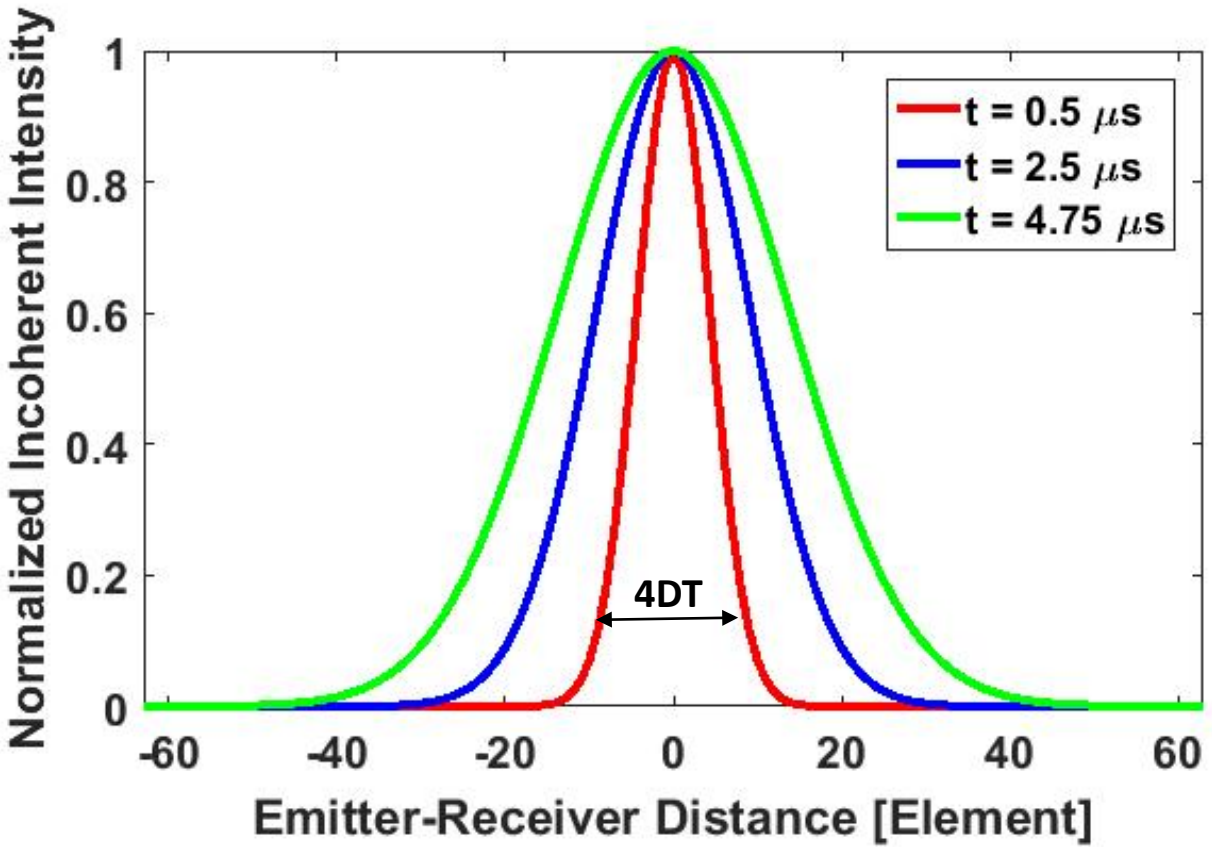


Inter-element response matrix

DIFFUSION MEASUREMENT

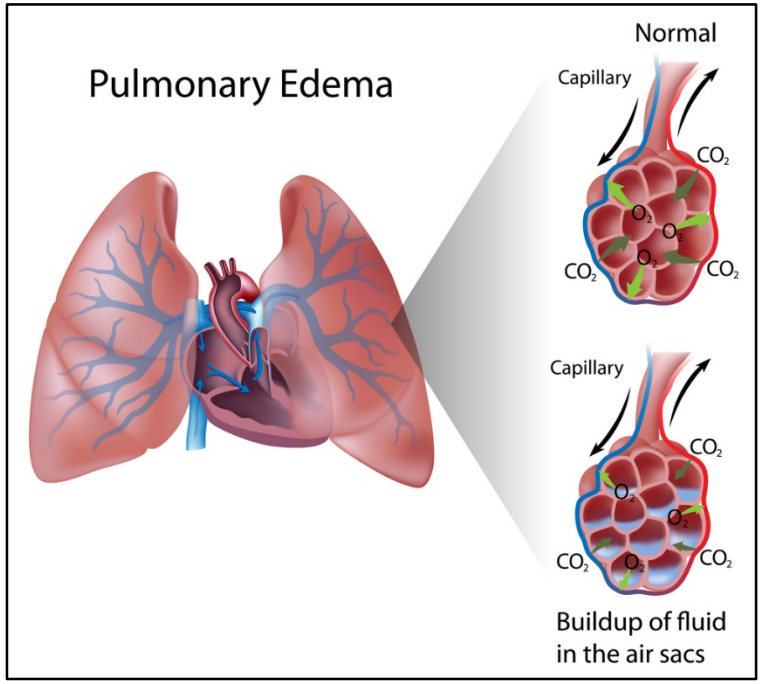
INCOHERENT INTENSITY



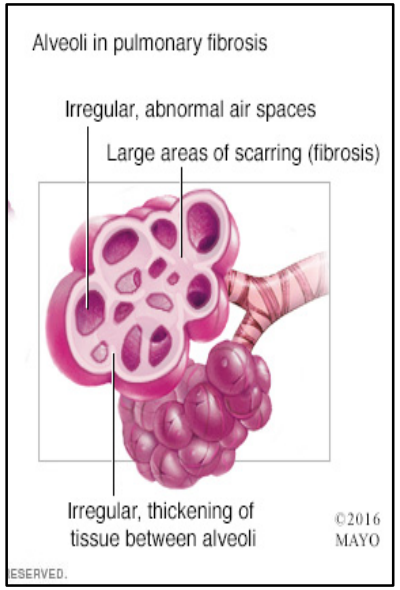


PULMONARY EDEMA, PULMONARY FIBROSIS

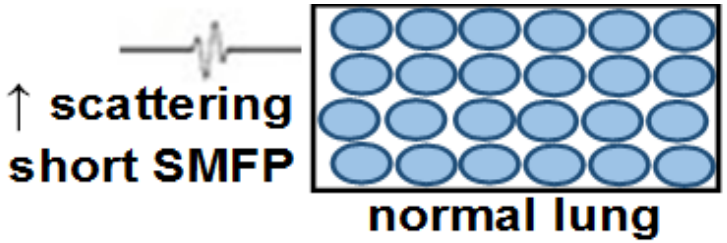
Affect the alveolar spatial distribution

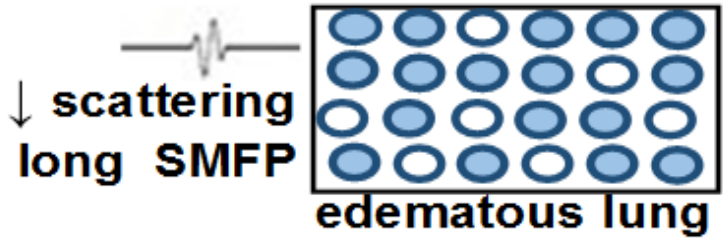


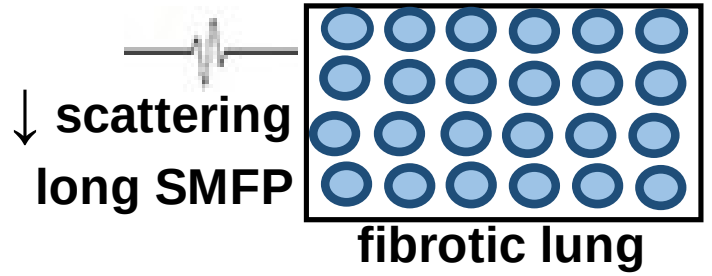
Edema



Fibrosis







QUANTITATIVE BIOMARKERS?

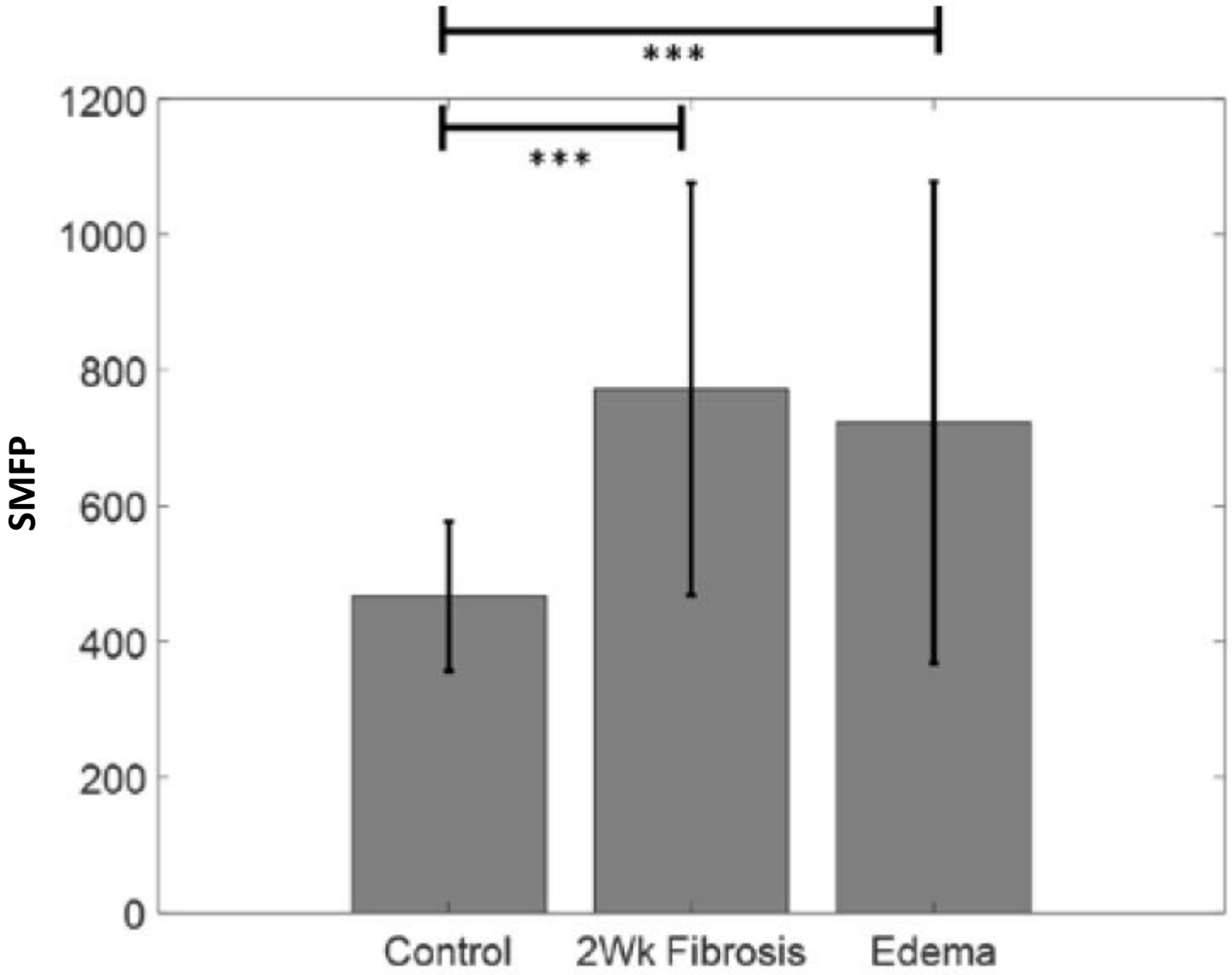
PULMONARY EDEMA, PULMONARY FIBROSIS

18 In-Vivo Sprague-Dawley Rats

- 6 Pulmonary fibrosis induced using Bleomycin
- 6 Pulmonary edema induced using ischemia-reperfusion injury
- 6 Controls

Euthanized after measurement → MicroCT, Histology, Wet/Dry ratio

PULMONARY EDEMA, PULMONARY FIBROSIS

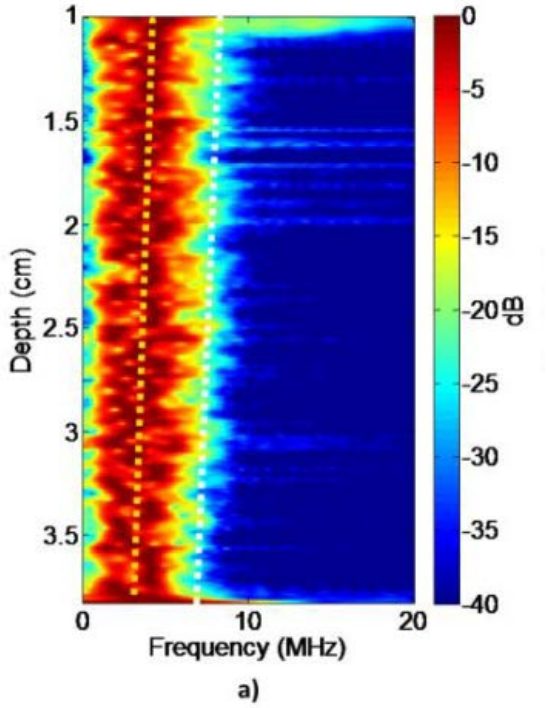


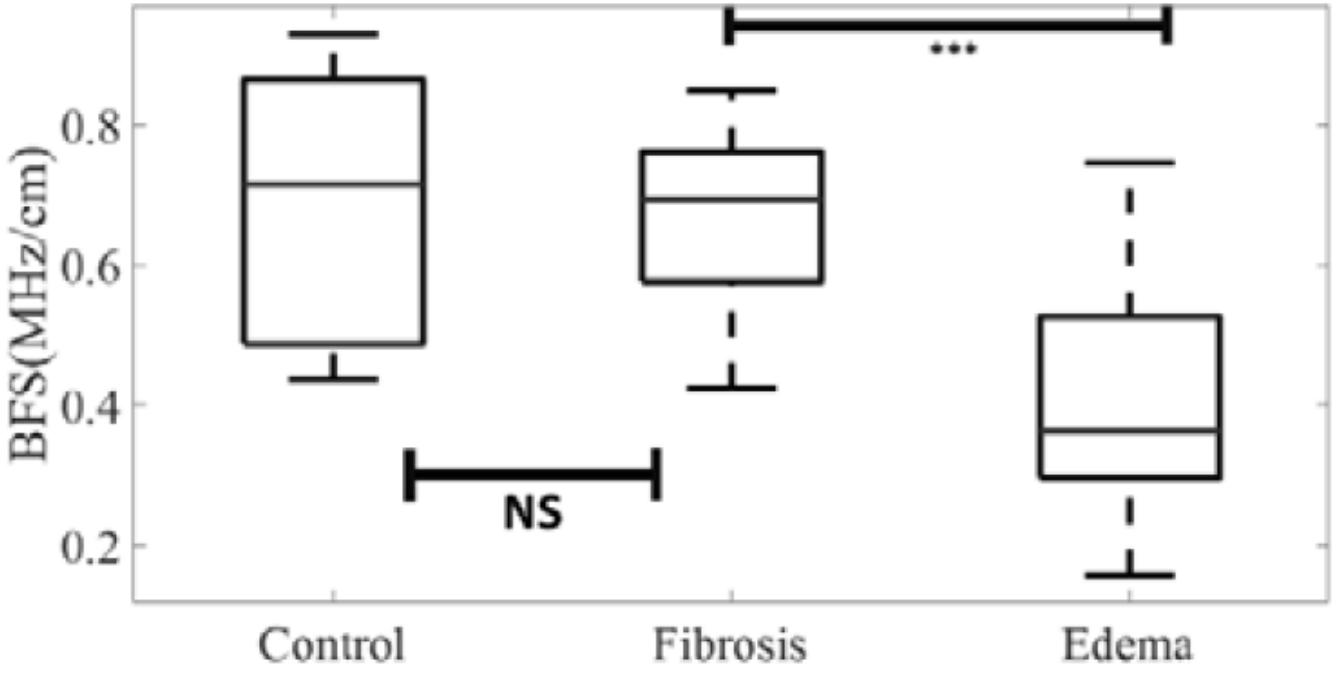
- Significant differences between control and fibrosis
- Significant differences between control and edema
- Discriminate fibrosis from edema?

PULMONARY EDEMA, PULMONARY FIBROSIS

Backscatter Frequency Shift

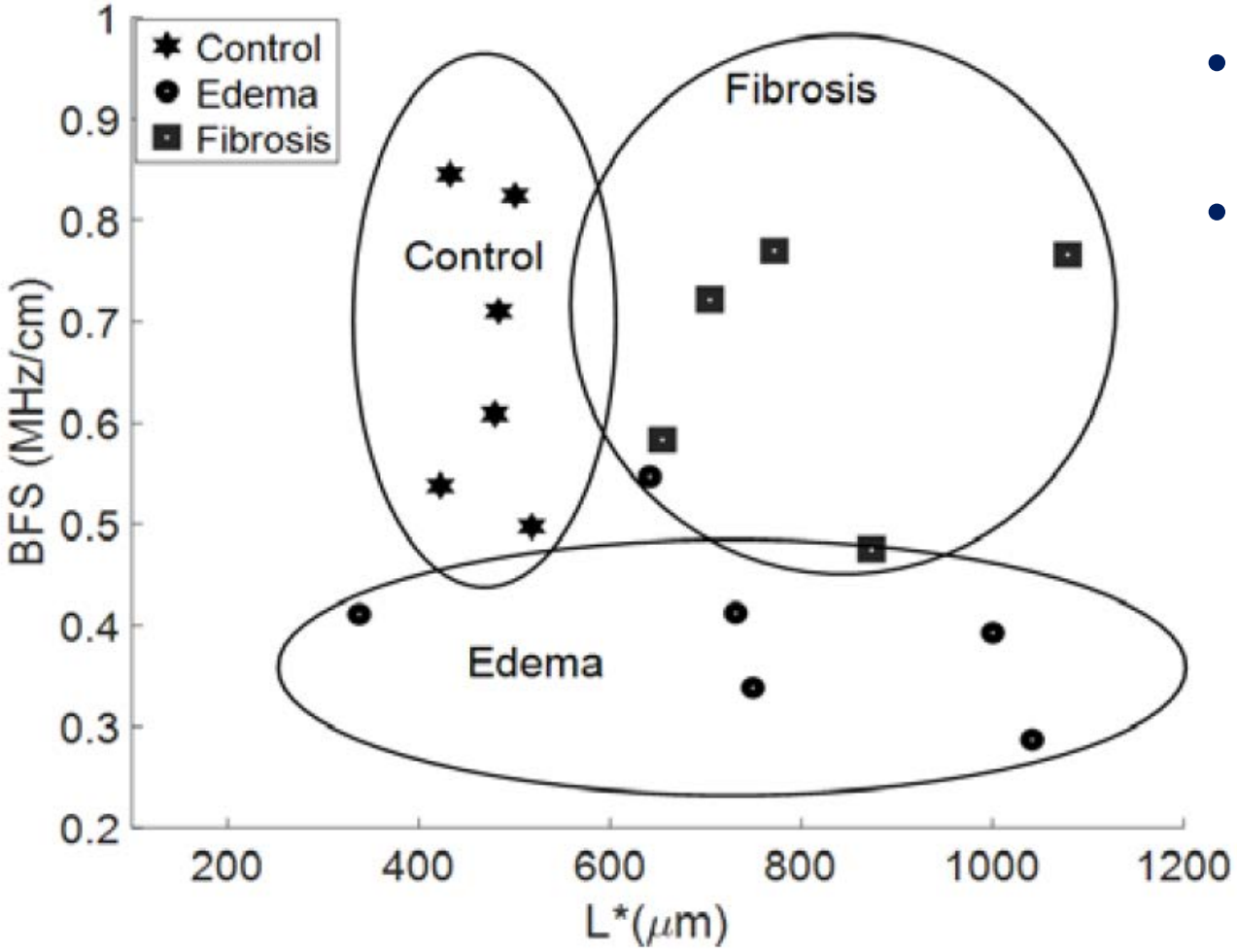
- Attenuation in fibrosis tissue should differ from attenuation in water
- Spectral power analysis
- Isolate frequencies at which maximum amplitude is observed
- Plot frequency vs depth





PULMONARY EDEMA, PULMONARY FIBROSIS

2 parameter space

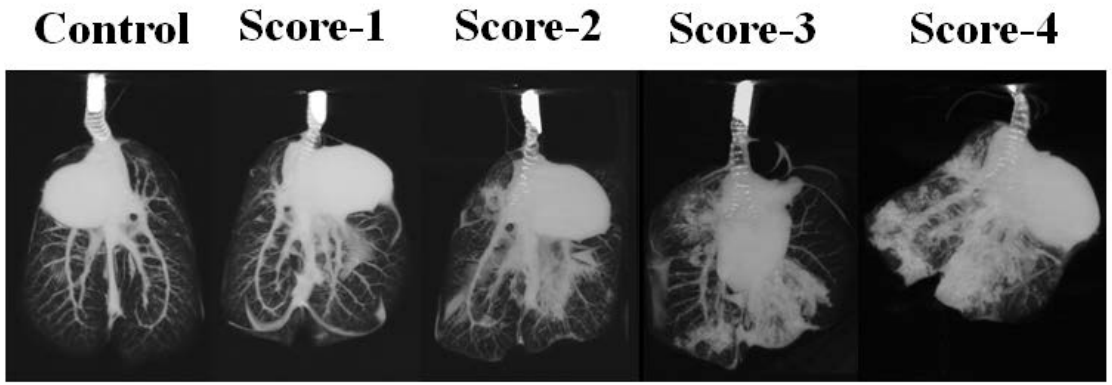


- **SMFP**: Discriminates healthy from interstitial disease
- **BFS**: Discriminates fibrosis from edema

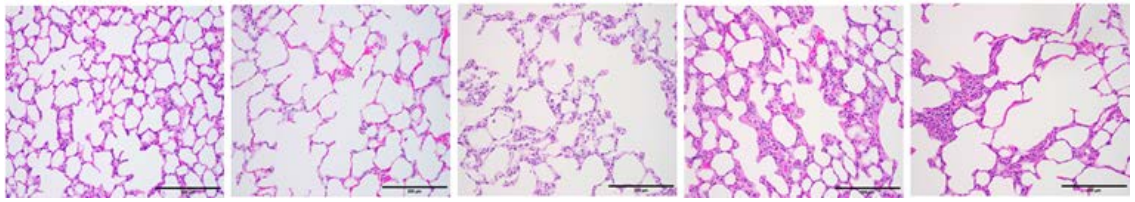
→ **SPECIFICITY**

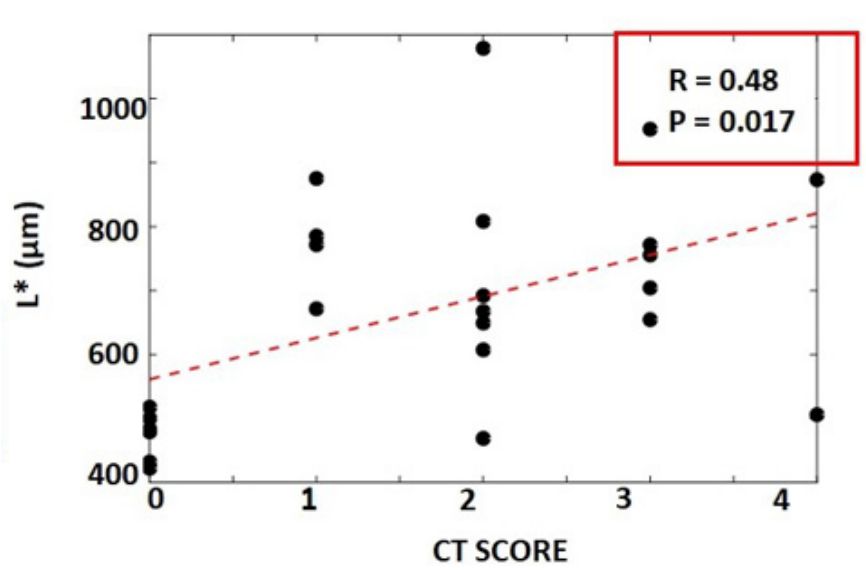
QUANTITATIVE FIBROSIS BIOMARKER? (STAGING)

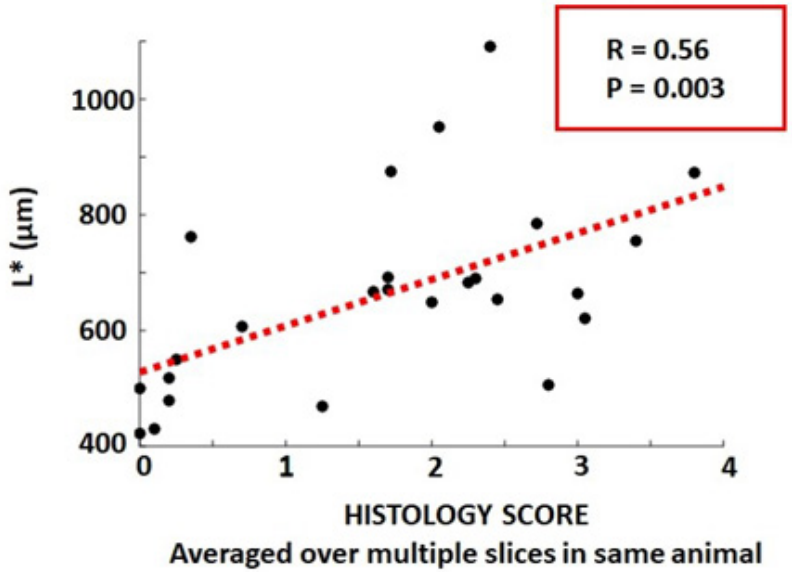
CT SCORING



HISTOLOGY SCORING





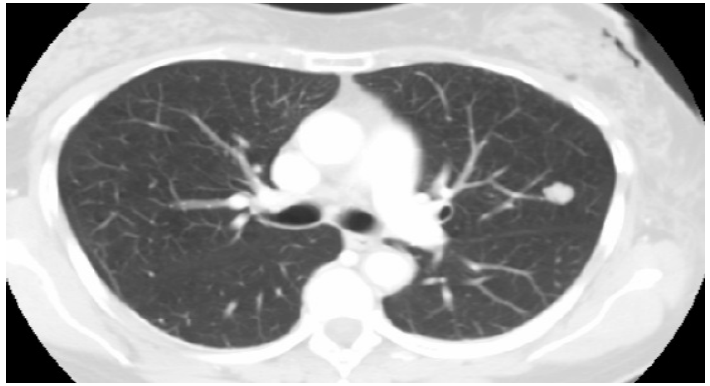


PULMONARY NODULES

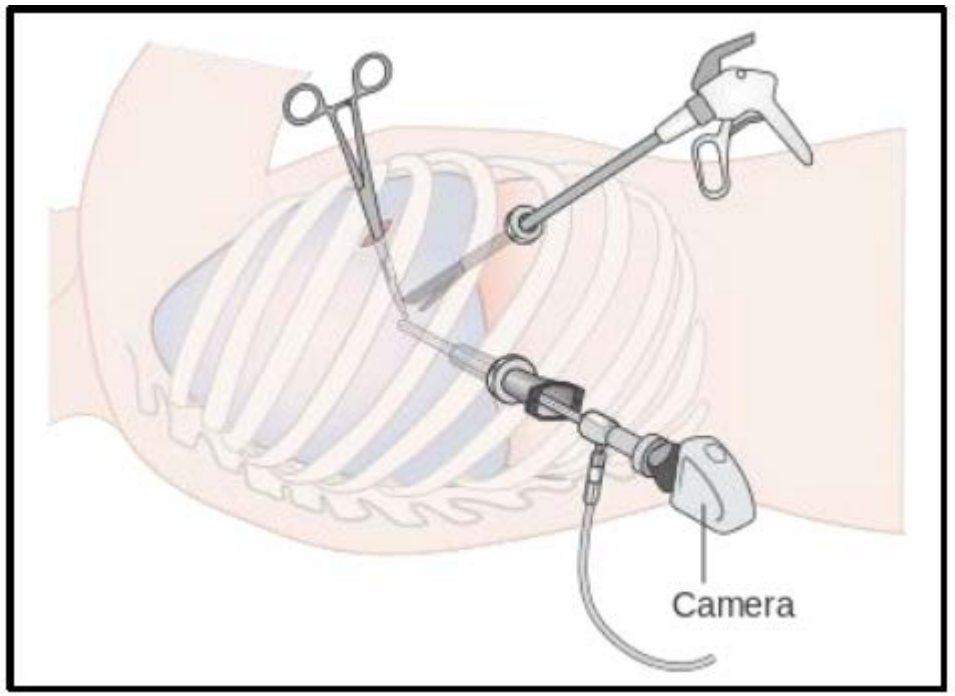
CAN WE MAKE THE DIFFUSION MEASUREMENT MORE LOCAL?

→ IMAGING

CT scan of lung nodule that would be challenging to feel and resect.



VIDEO ASSISTED WEDGE RESECTION

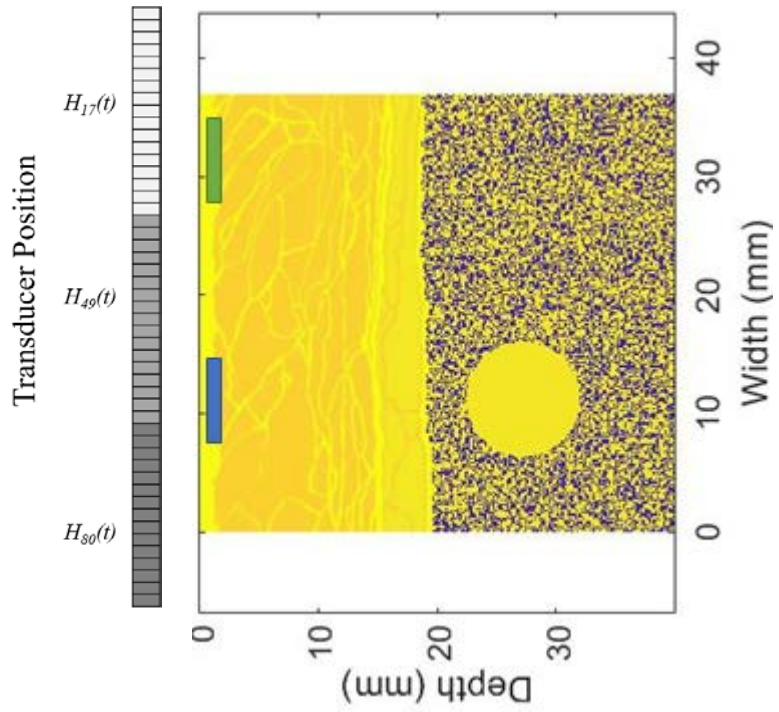


PULMONARY NODULES

By essence, the diffusion process is not local

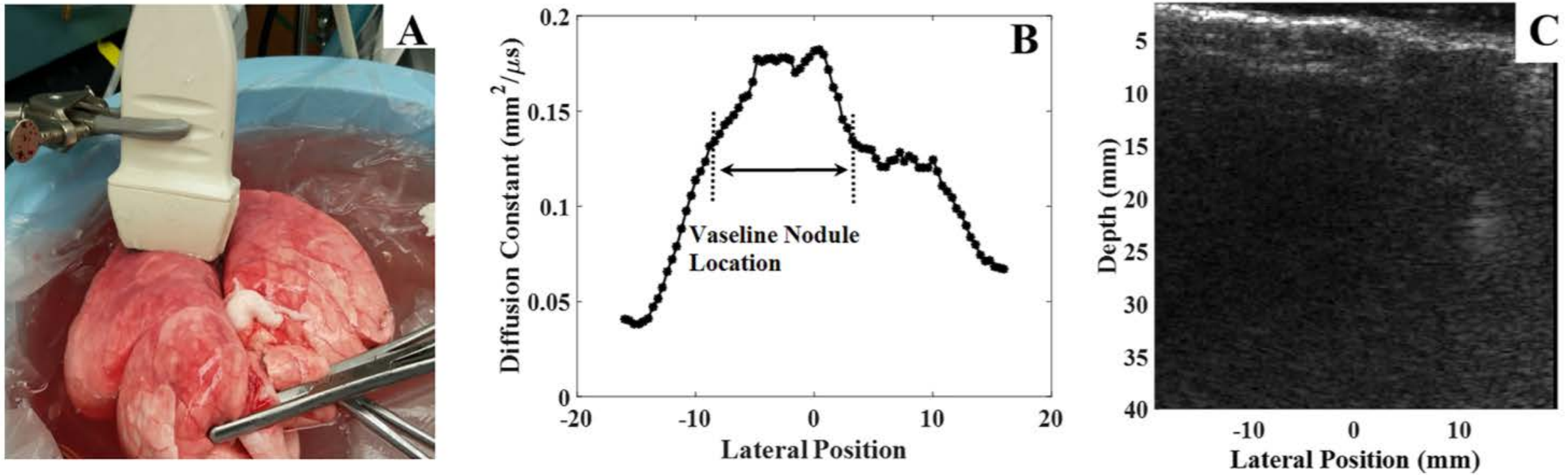
But we can measure the diffusion constant semi locally

- Use sub-arrays of ultrasound probes
- Calculate the incoherent intensity for each sub-IRM



PULMONARY NODULES- PIG LUNG EX VIVO

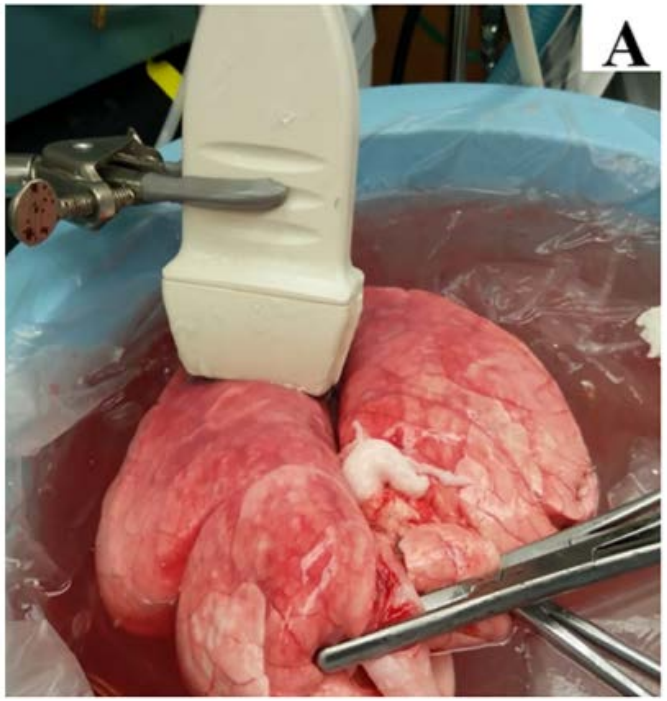
5 weeks old pig lungs connected to a disposable resuscitator
Petroleum Jelly nodule; size : 10 mm ; Depth: 10 mm

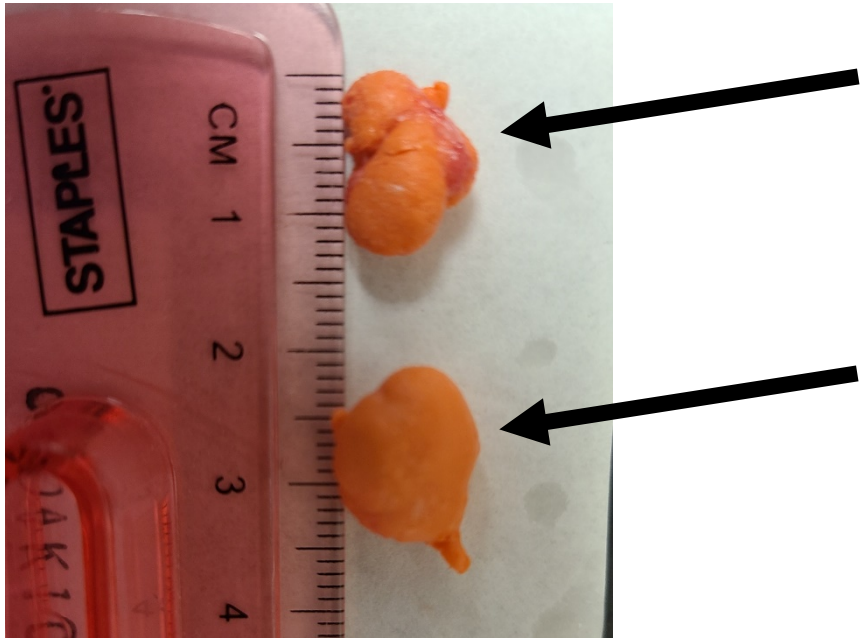


Mohanty, K., Blackwell, J., Masuodi, S. B., Ali, M. H., Egan, T., & Muller, M. (2018). *Applied Physics Letters*, *113*(3), 033704.

PULMONARY NODULES- PIG LUNG EX VIVO

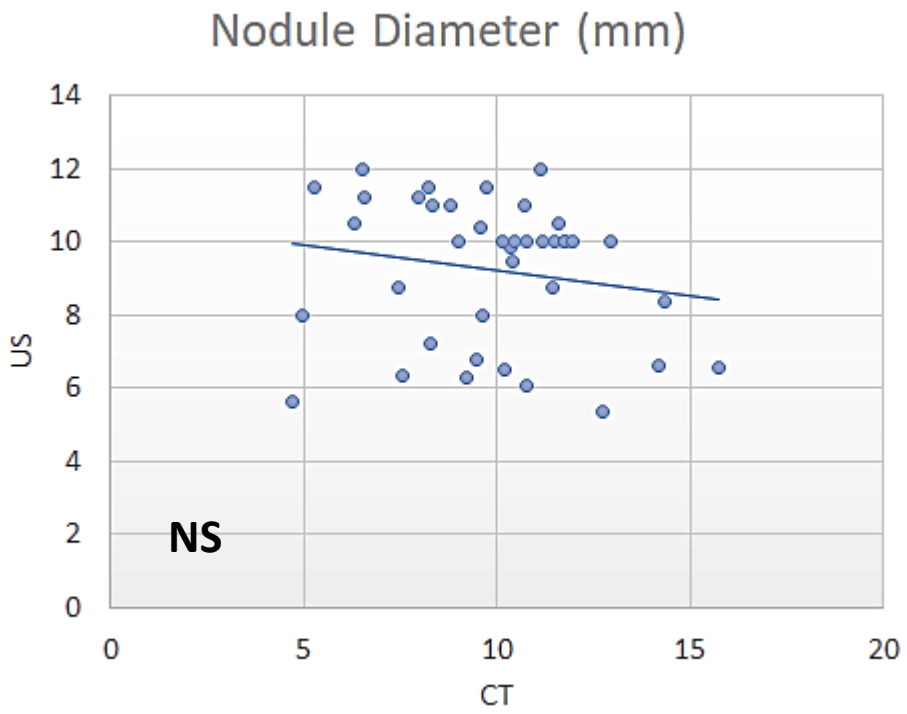
- Artificial nodules implanted inside dog/pig lungs.
- Distinguishable amounts of MS in nodule vs. parenchyma.
- Singular Value Decomposition to separate SS and MS contributions + depression detection algorithm

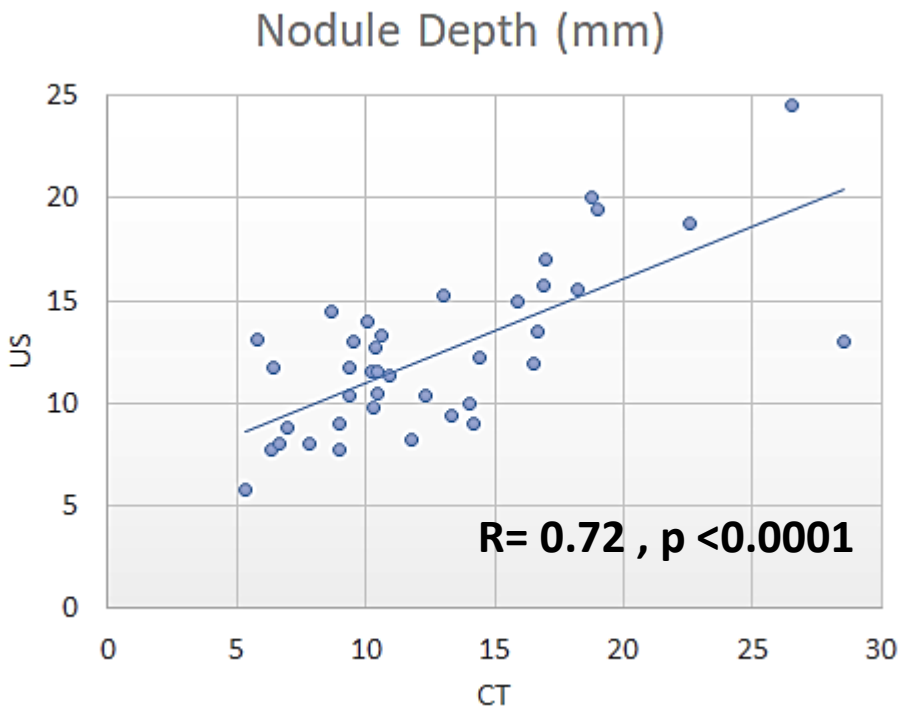




PULMONARY NODULES- PIG LUNG EX VIVO

- 39 out of 40 nodules detected.
- Ultrasound results compared with CT scan values.
- Good estimation of nodule depth. Nodule diameter estimation needs to be improved.





Conclusion

Quantitative characterization of lung parenchyma

- To detect information that wasn't available before

- Sensitive AND specific (EDEMA, FIBROSIS)
  - Differentiate healthy from fibrotic lung and correlates to histology
  - Differentiate healthy from edematous lung

- Use as new source of contrast to detect and localize pulmonary nodules

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