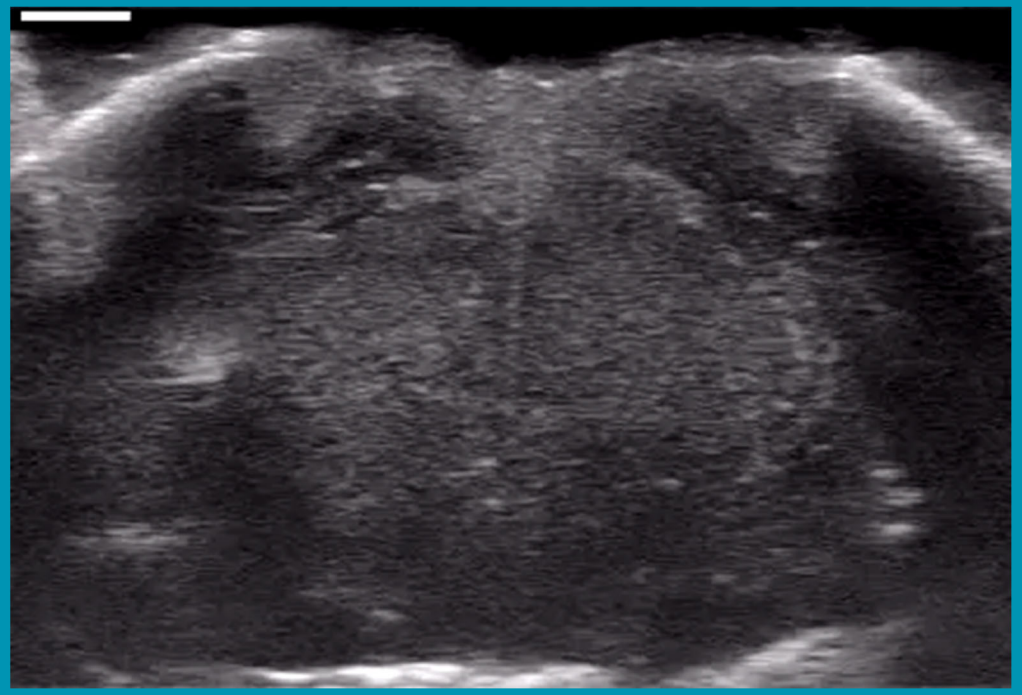
THE 2022 TECHMED EVENT

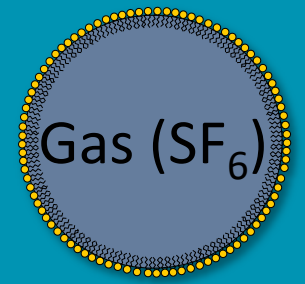
Breast cancer imaging by ultrasound localization microscopy

Georg Schmitz
Ruhr University Bochum

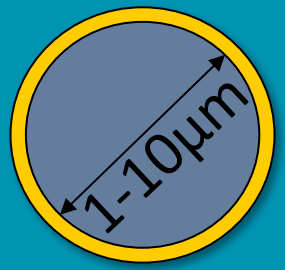
THE 2022 TECH-MED EVENT

Contrast enhanced ultrasound imaging (CEUS)





Soft-shelled
(e. g. phospholipids)
Sonovue, MicroMarker

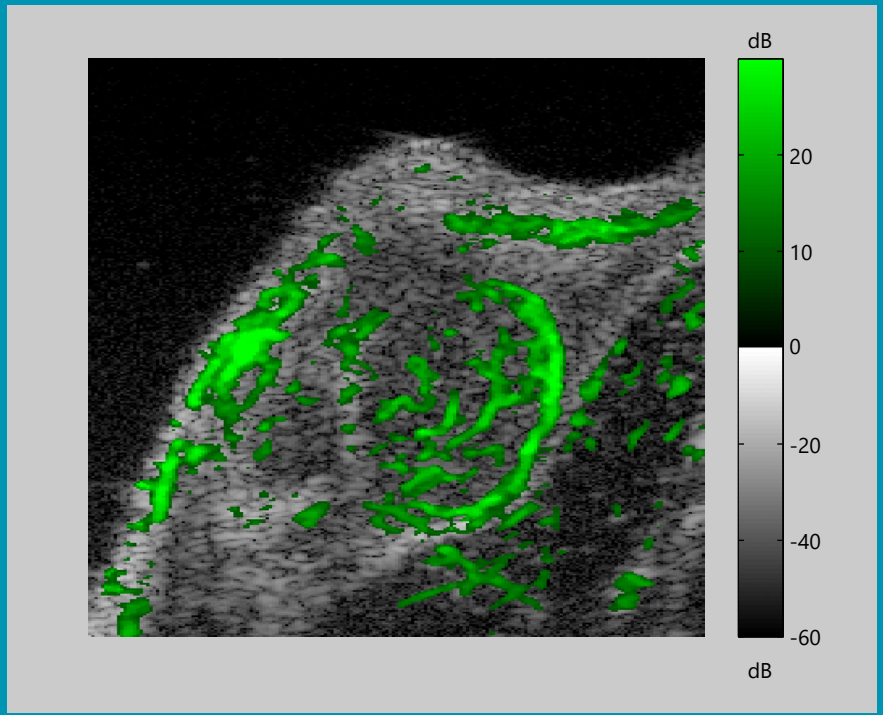


Hard-shelled
(e. g. cyanoacrylate)
PBCA ExMI RWTH Aachen

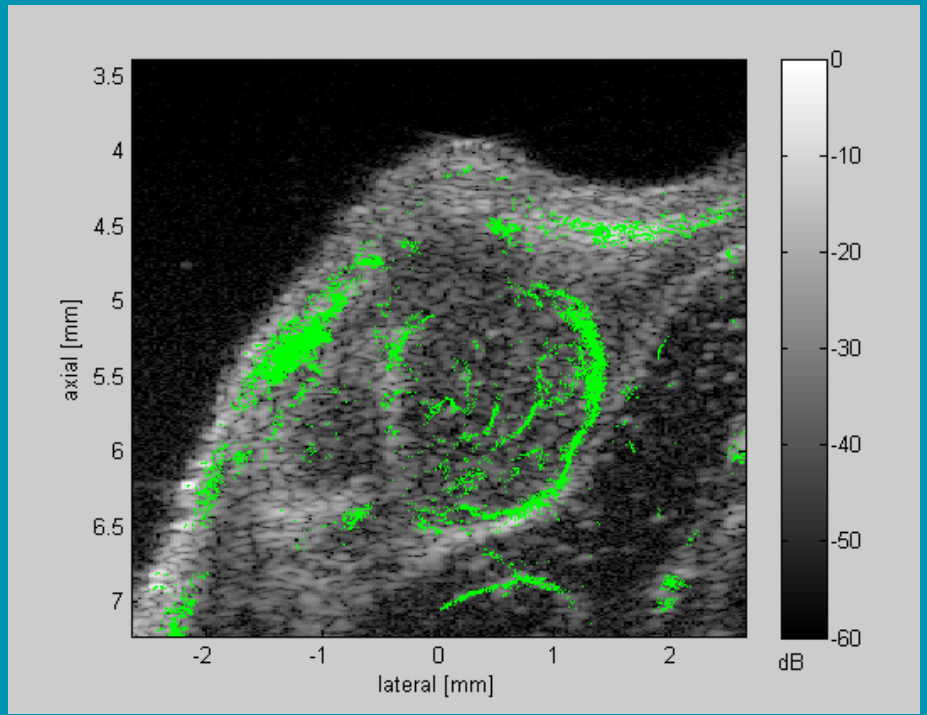
- strong scattering, power $\sim f^4$
- resonance in the ultrasound frequency range
- nonlinear oscillation response (soft-shelled more than hard-shelled)

First in-vivo small animal imaging (2011)

Human Breast Cancer Xenograft induced in CD1 nude mouse Vevo 2100, MS550D Transducer (40 MHz)



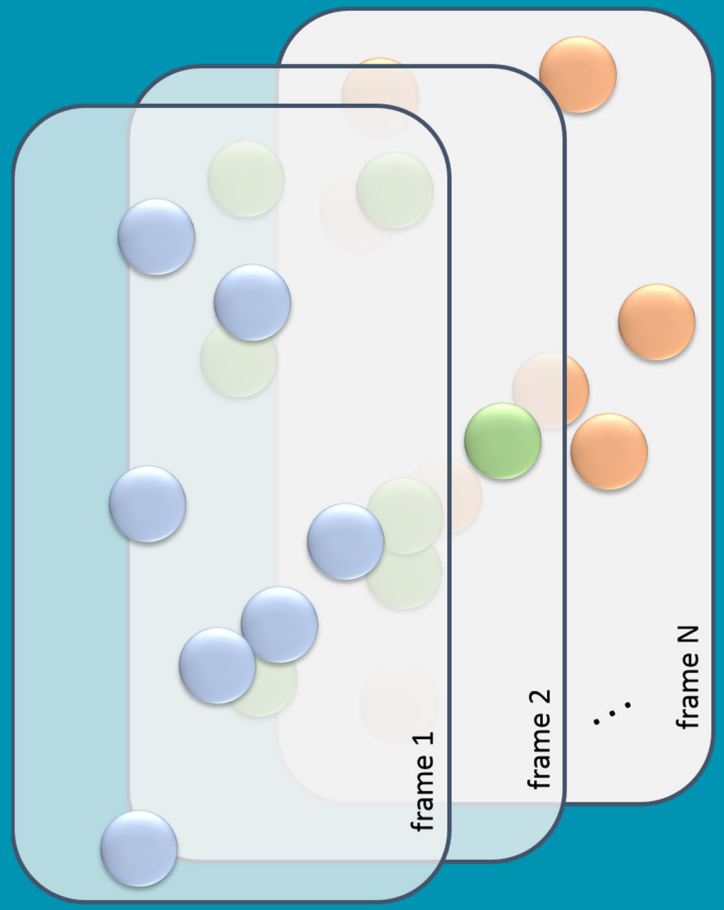
Maximum Intensity Persistence image



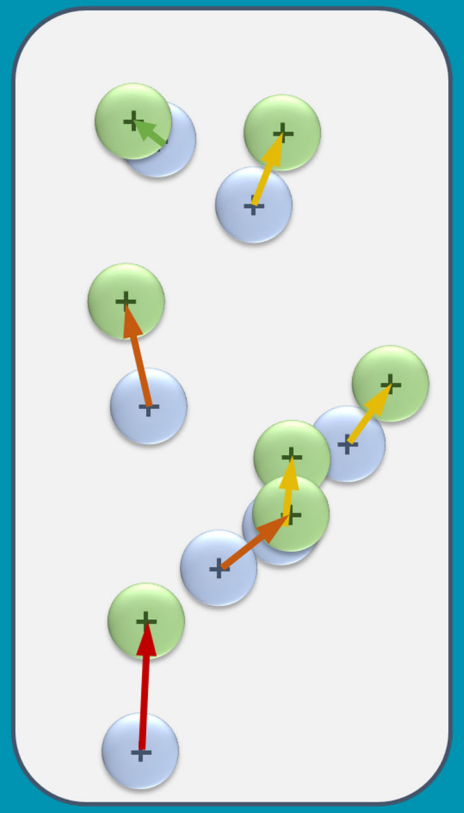
MB centroids plotted onto the grayscale B-Mode image

M. Siepmann, J. Bzyl, M. Palmowski, F. Kiessling, and G. Schmitz, 'Imaging tumor vascularity by tracing single microbubbles', Oct. 2011, pp. 1906–1909, doi: 10.1109/ULTSYM.2011.0476.

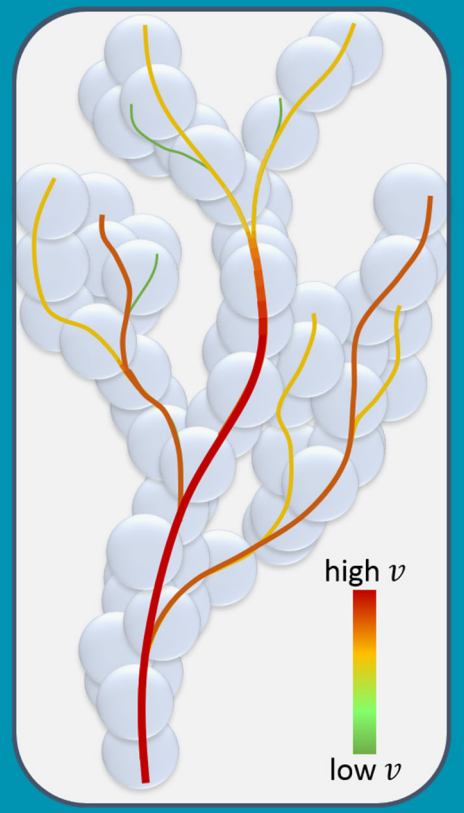
Ultrasound Localization Microscopy (ULM)



Microbubble images with diffraction-limited resolution

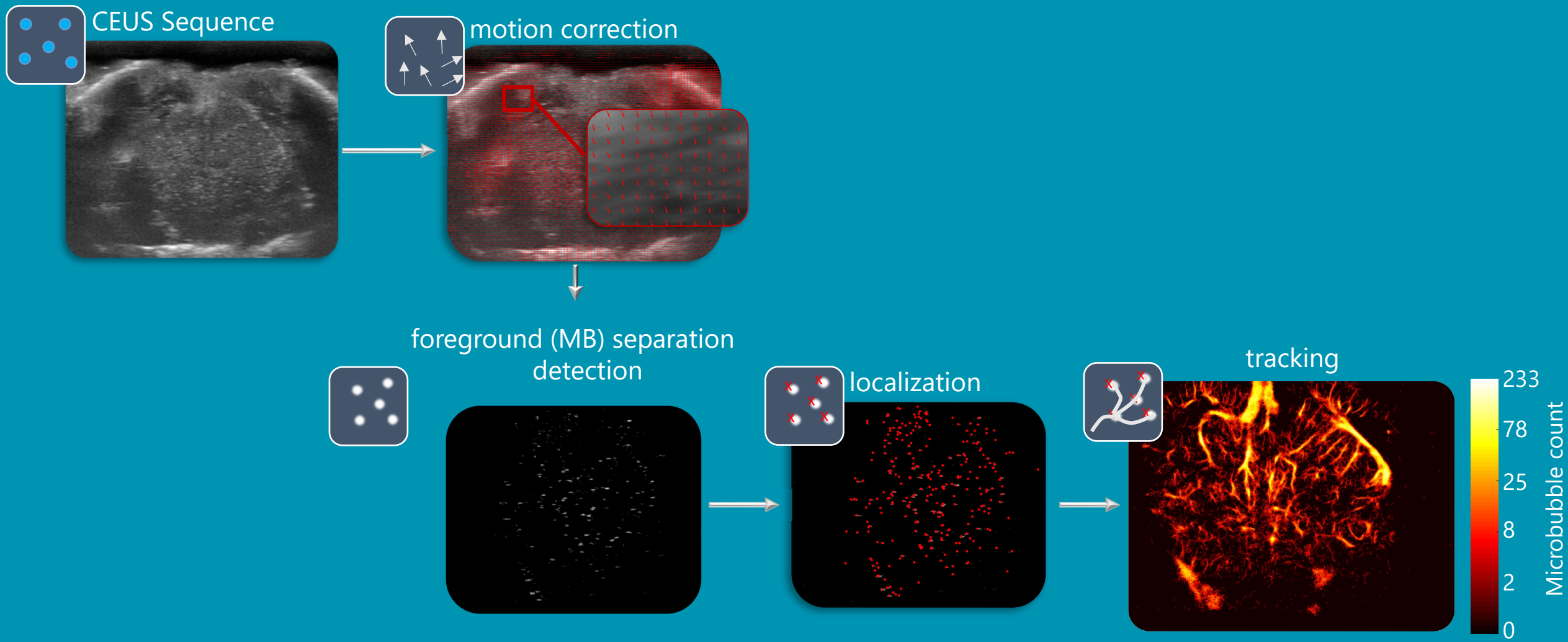


Localization and track: precision beyond the diffraction limit



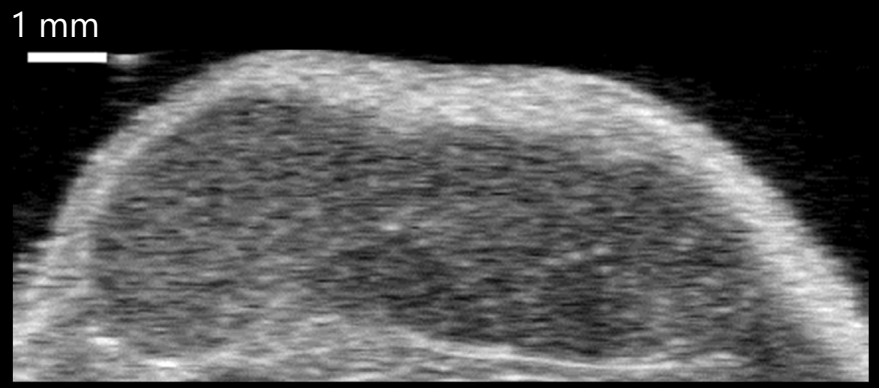
Accumulate and show density, velocity, direction

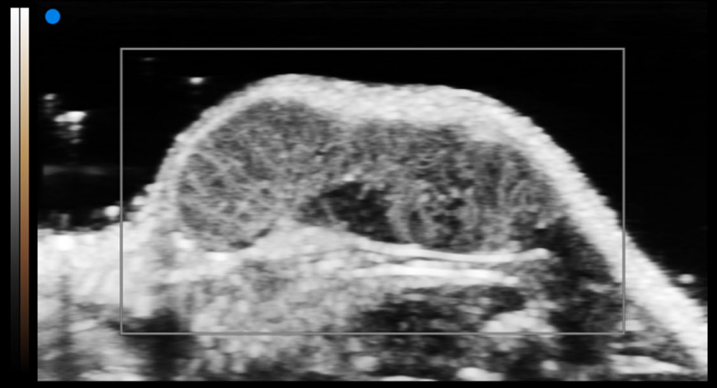
Ultrasound Localization Microscopy (ULM)

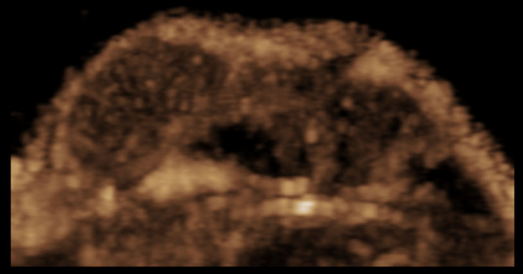


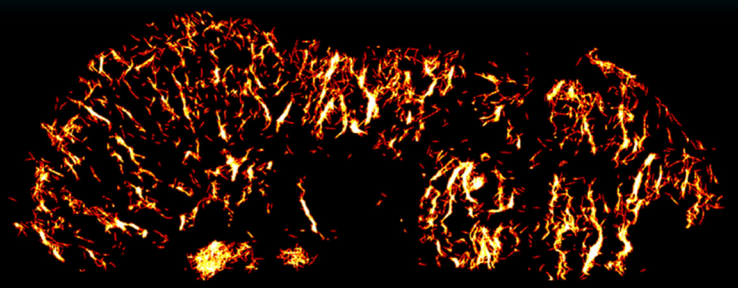
Murine subcutaneous tumor

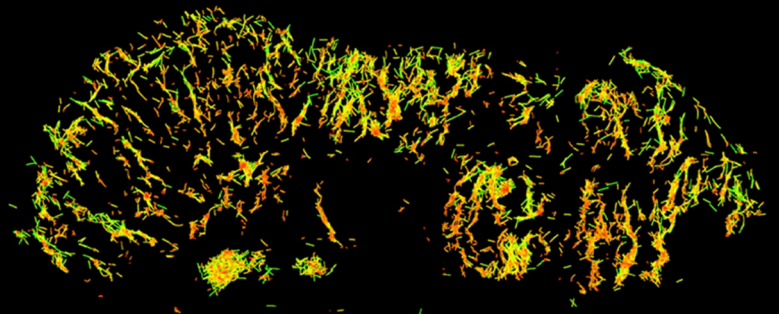
low transducer frequency

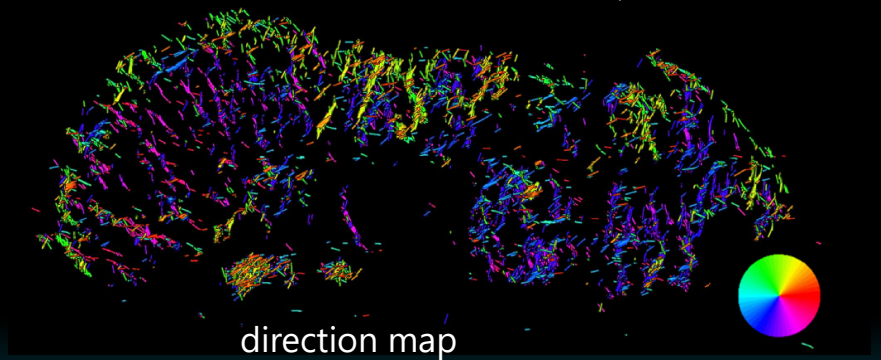






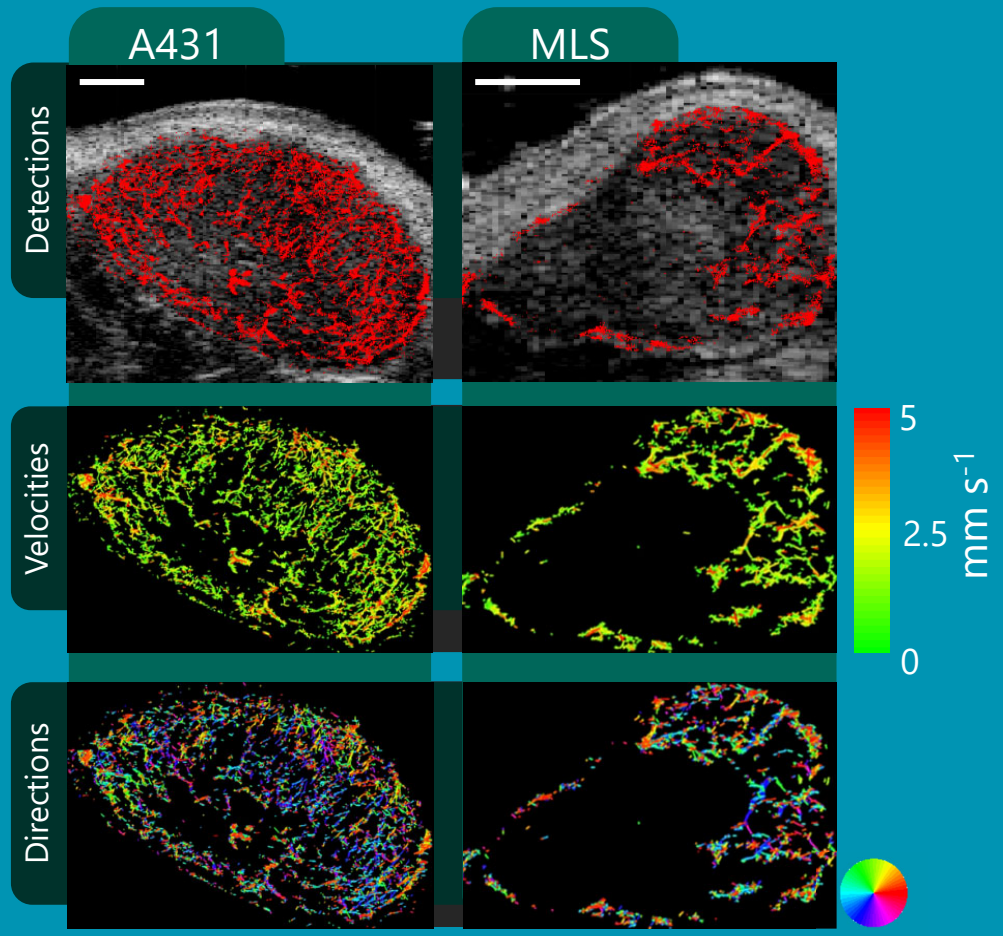


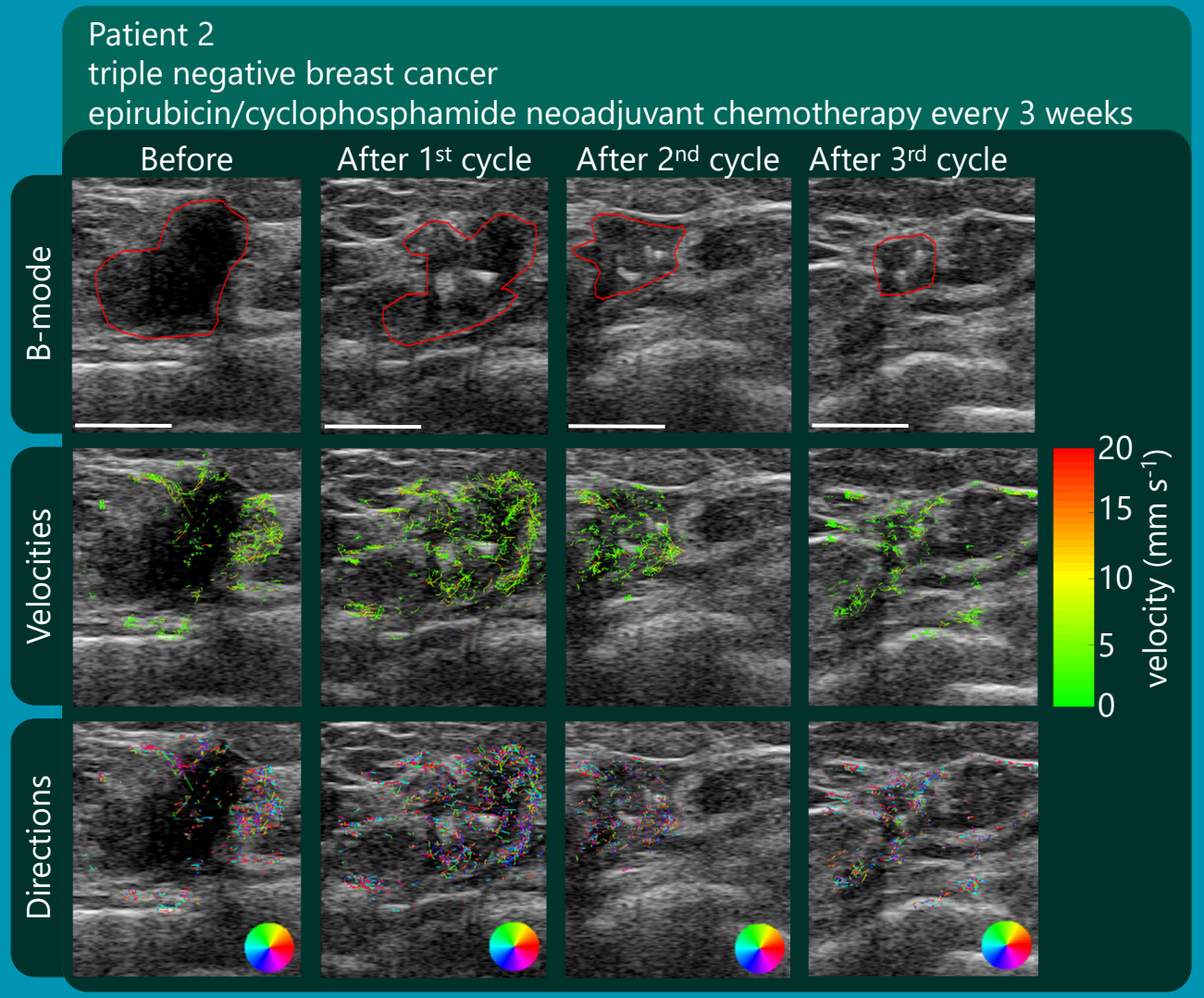




$f_0 =$ 18 MHz, $f_s =$ 25 Hz (4075 frames, 163 s acquisition)

Super-resolution imaging (2018)





T. Opacic, S. Dencks et al, "Motion Model Ultrasound Localization Microscopy for Preclinical and Clinical Multiparametric Tumor Characterization," Nat. Comm., vol. 9, 2018.

What we know to be optimal

- Use RF or IQ data (linear superposition)
- High framerate, e.g., 500 Hz or more
- Moderate concentration and injection speed
- Minimal motion, no out-of-plane motion for 2D

But we quickly want to use the method in clinical studies:
Go with the clinical systems we have

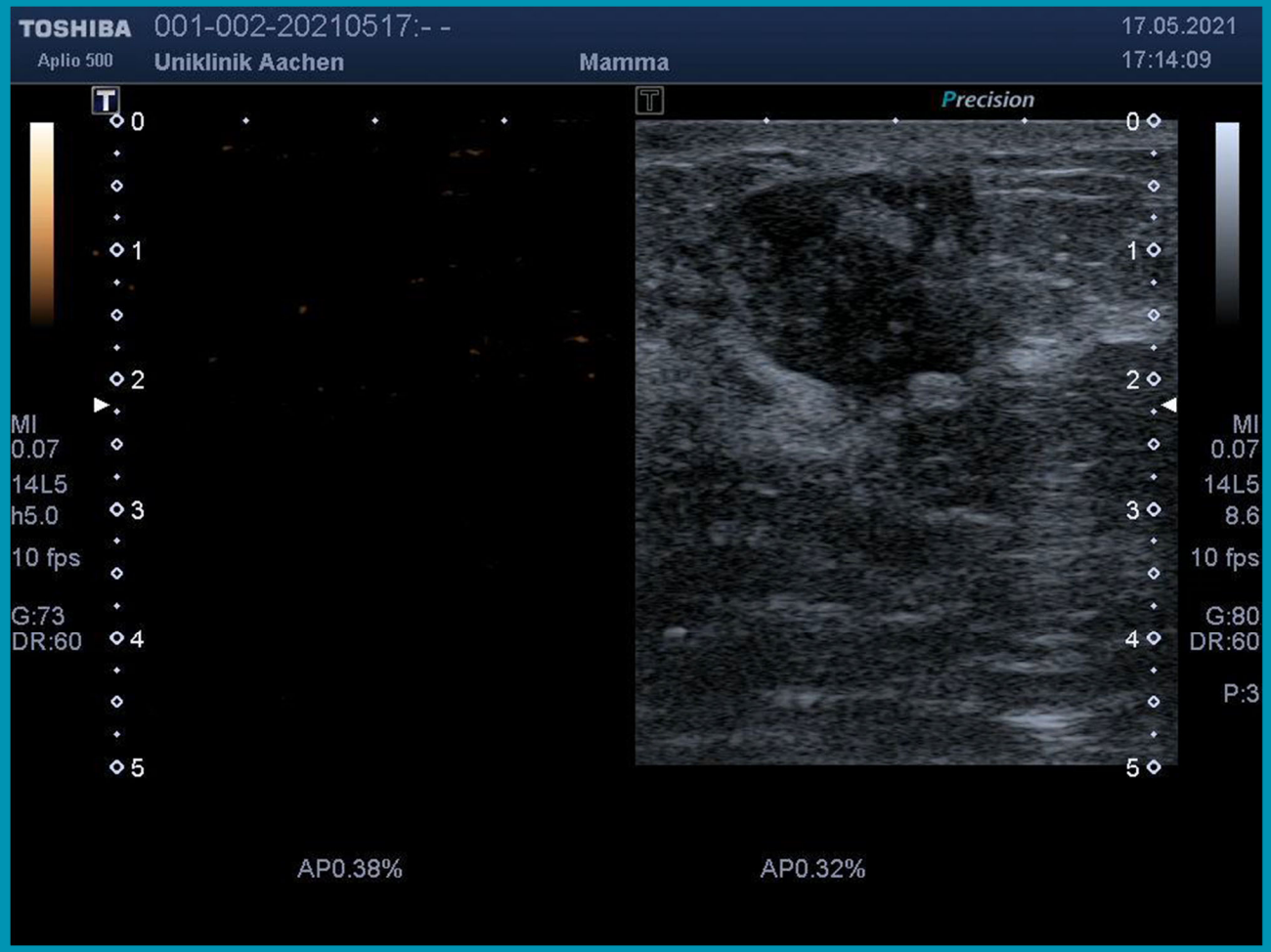
What we know to be optimal

- Use RF or IQ data (linear superposition)
- High framerate, e.g., 500 Hz or more
- Moderate concentration and injection speed
- Minimal motion, no out-of-plane motion for 2D

What we get in our clinical proof-of-concept study

- B-mode videos from DICOM
- low framerate
- Varying concentrations and injection speeds
- Considerable motion, also out of plane

Breast cancer study | Patient 2



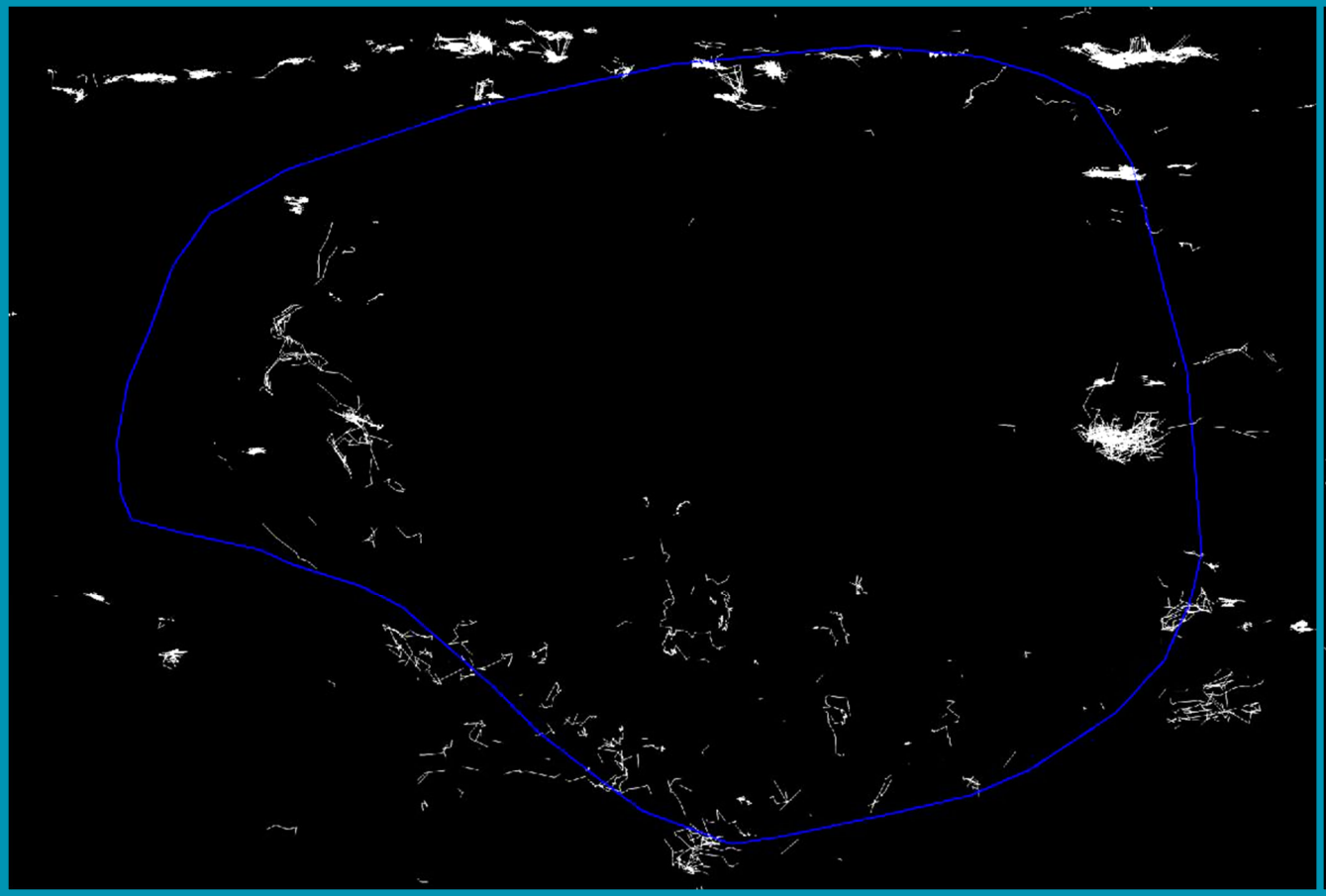
- Study of monitoring neoadjuvant chemotherapy in breast cancer

- Step 1: determine protocol; dose and injection speed
  - 16 patients
  - Two injection speeds: 50 µl/s | 100 µl/s
  - Two dose levels: 0.075 ml/kg | 0.015 ml/kg
  - Canon (Toshiba) Aplio 500 / 14L5 transducer
  - B-mode / contrast mode double view (DICOM)

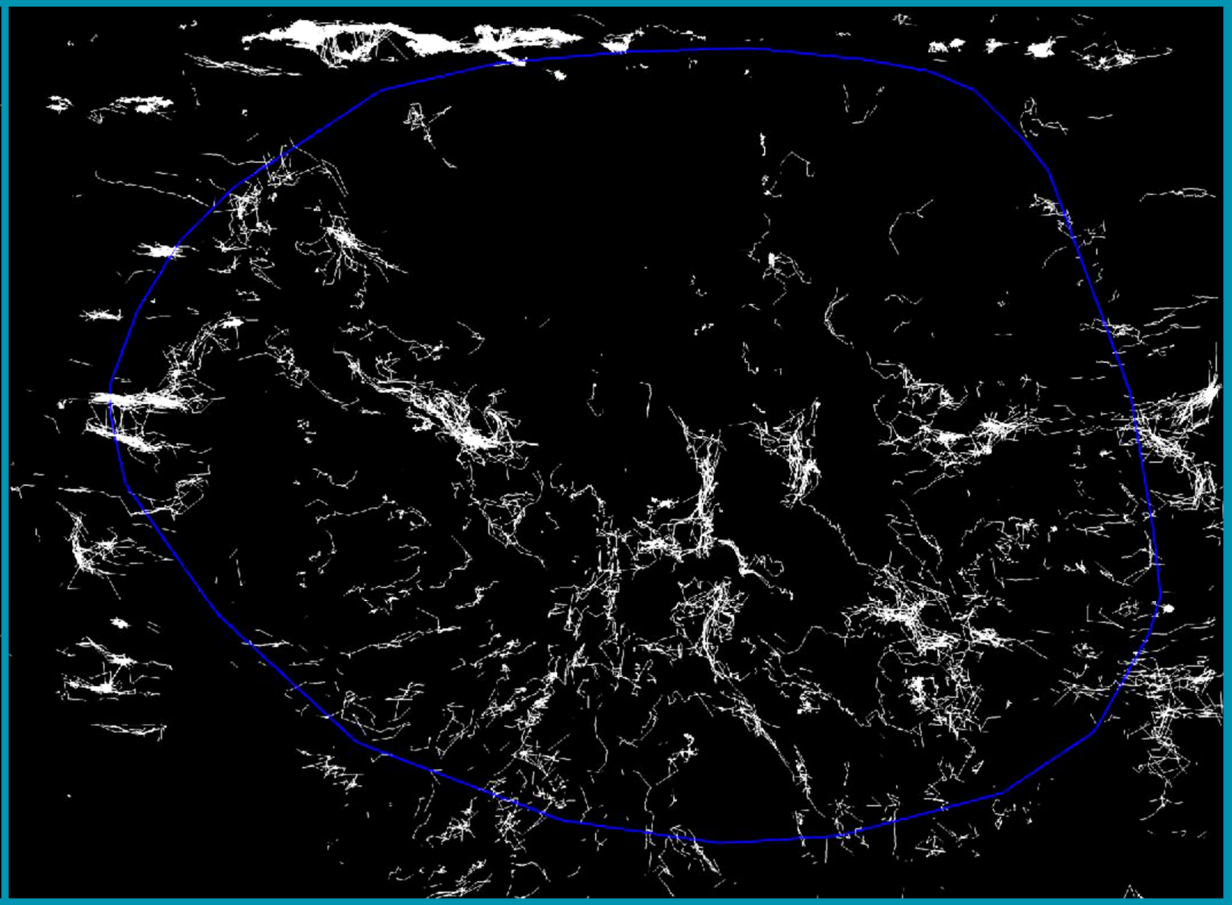
Breast cancer study / tumor ROI / Preliminary results Patient 2

High injection speed

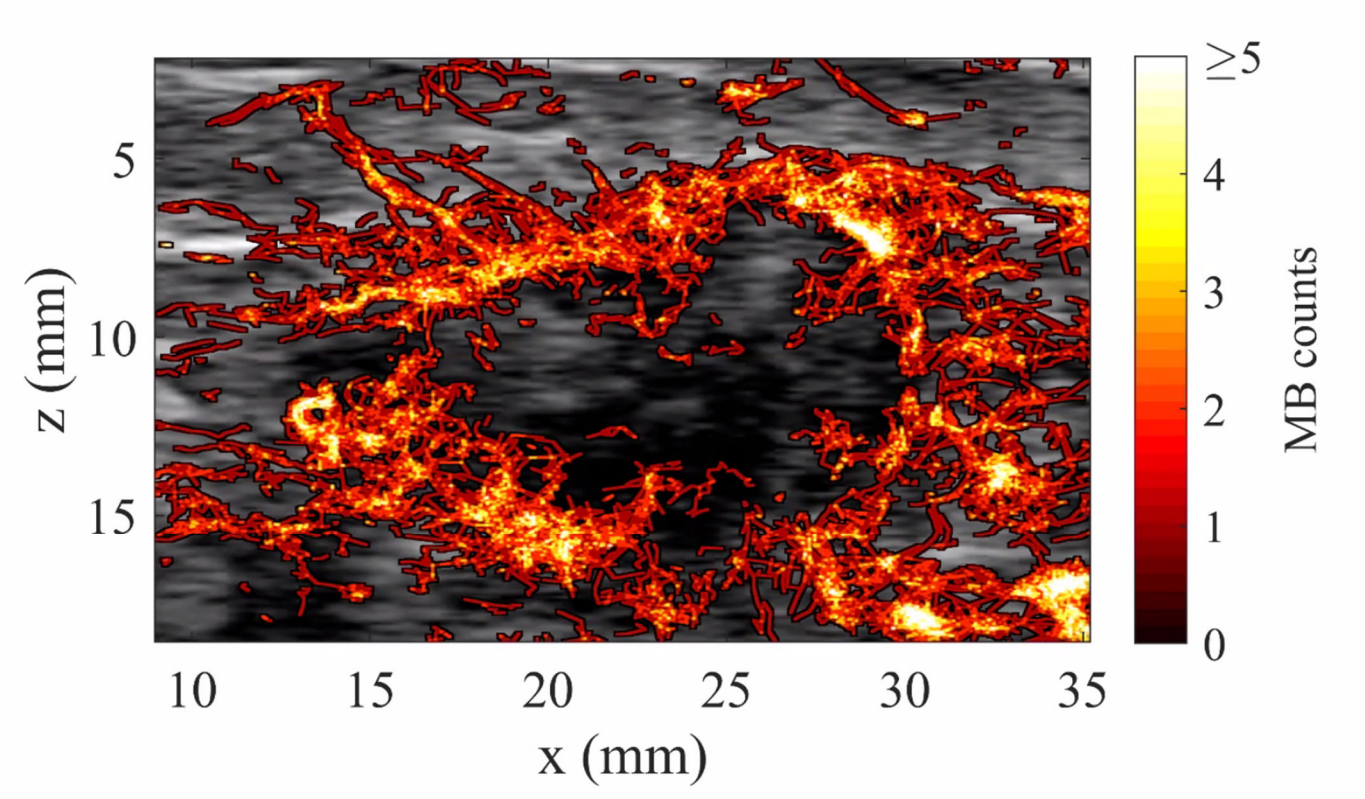
Low concentration

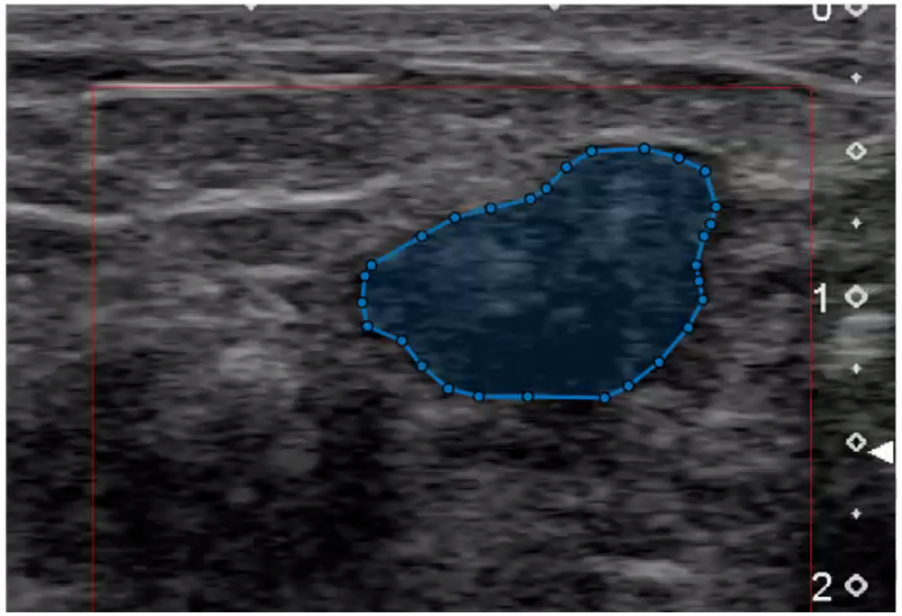


High concentration



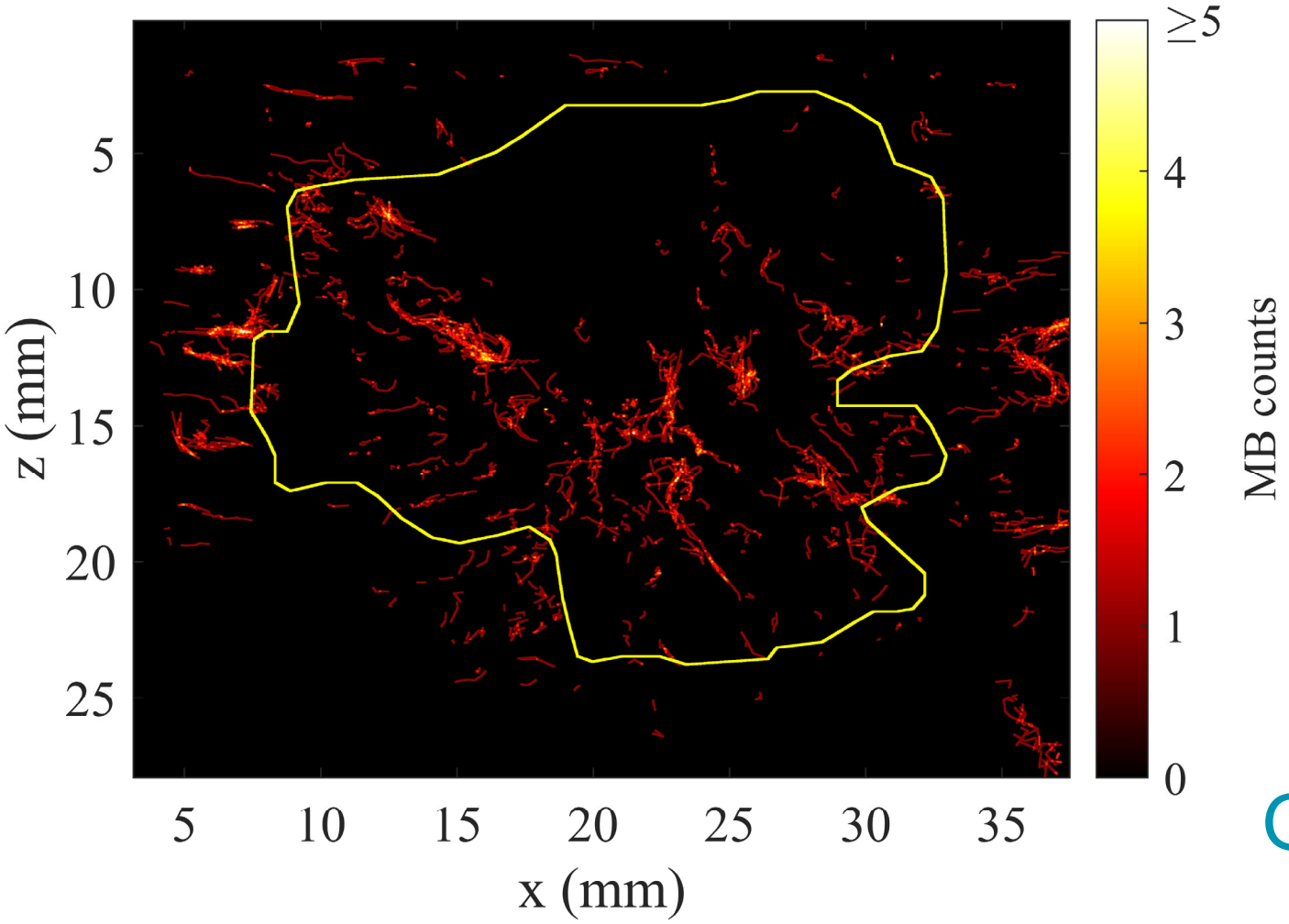
Patient 1 | Dose study | High concentration

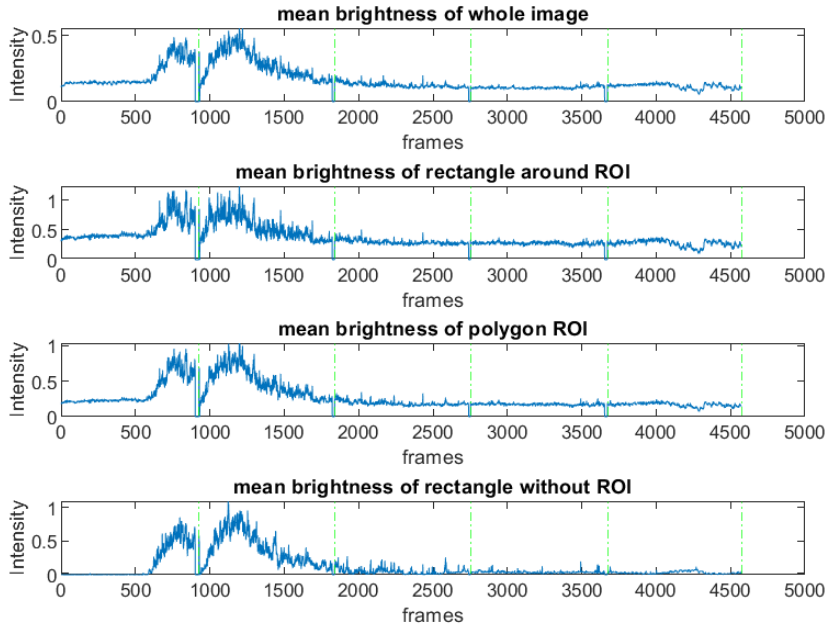




- Few frames usable
- Motion correction not completely solved

Patient 2 | Dose study | High concentration





Go for 3D real-time imaging!

Conclusions

- Clinical use: real-time 3D imaging and motion correction are crucial
- Localization precision can be optimized,
- but clinical system's pixel/voxel sizes or far from optimal
- Using clinical systems with no dedicated modes will limit the method
- Clinical protocols that are manageable in clinical routine are needed
- Can unmet clinical needs be addressed with ULM?

THE 2022 TECHMED EVENT