Proton/Ion-acoustic imaging

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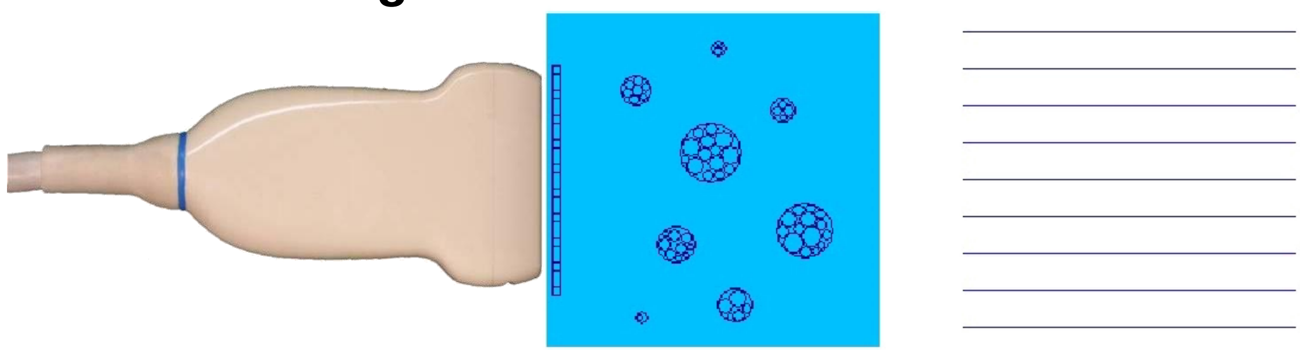
Modern Ultrasound Imaging

Transducer generates pulses of ultrasound waves that travel into the body

Echoes from tissue structures return at a time and with a wave curvature dependent on their depth and lateral position

Echoes are recorded simultaneously by arrays of multiple transducer elements and used to reconstruct images of the **location and strength of acoustic scattering**



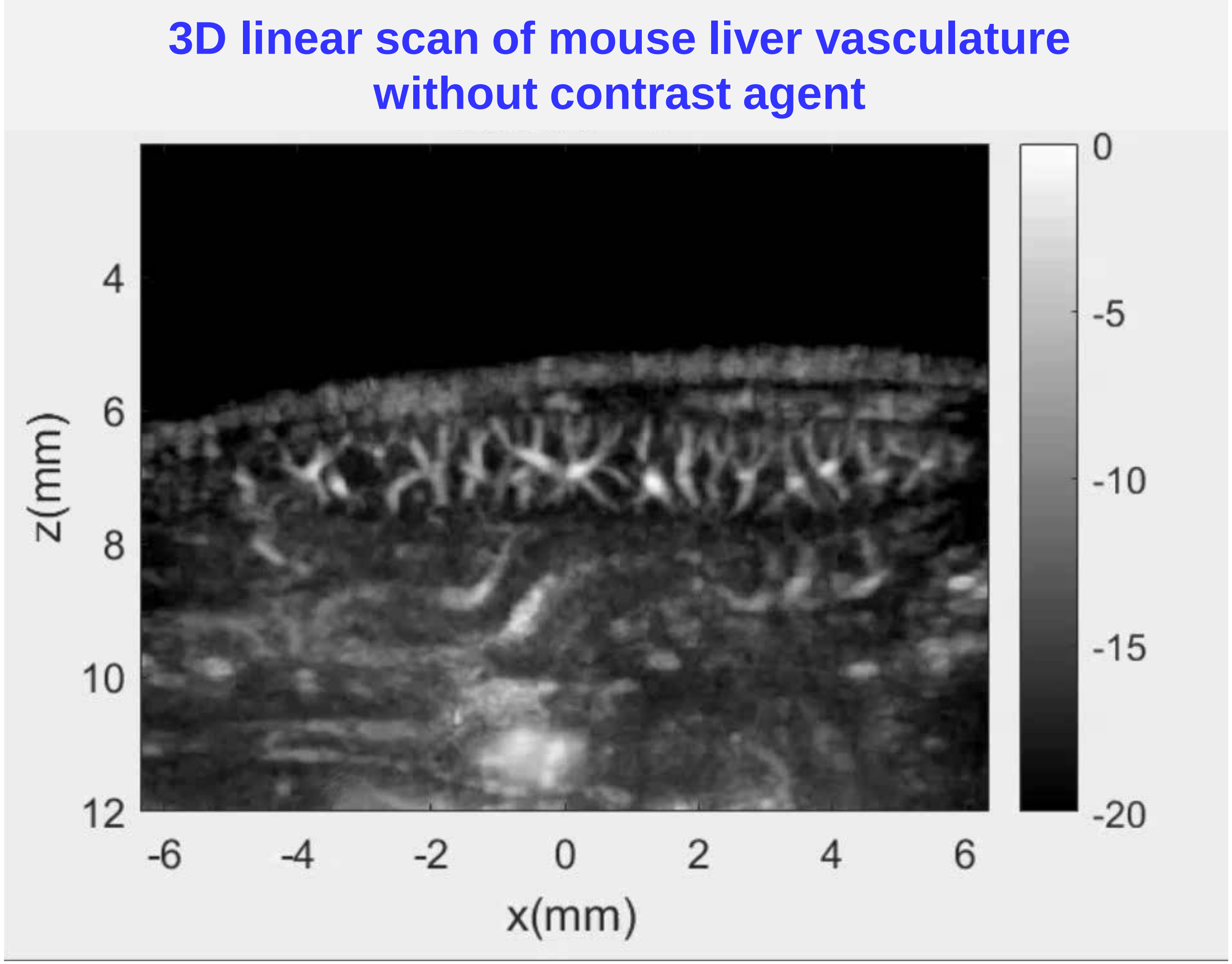
Full aperture focusing ➔ high resolution over whole field simultaneously

1 pulse per image ➔ frame rates < 20 kHz ➔ <u>powerful noise reduction</u>

Other processing:

- **Microbubbles** recognised by pulse sequences that recognise nonlinear scattering (DCE-US); plane wave imaging for bubble sparing and rapid volume acquisition
- Doppler shift allows **blood velocity imaging**
- **Tissue motion tracking** and deformation for **biomechanical properties**

Aperture sub-division processing combined with ultrafast Doppler for further noise reduction

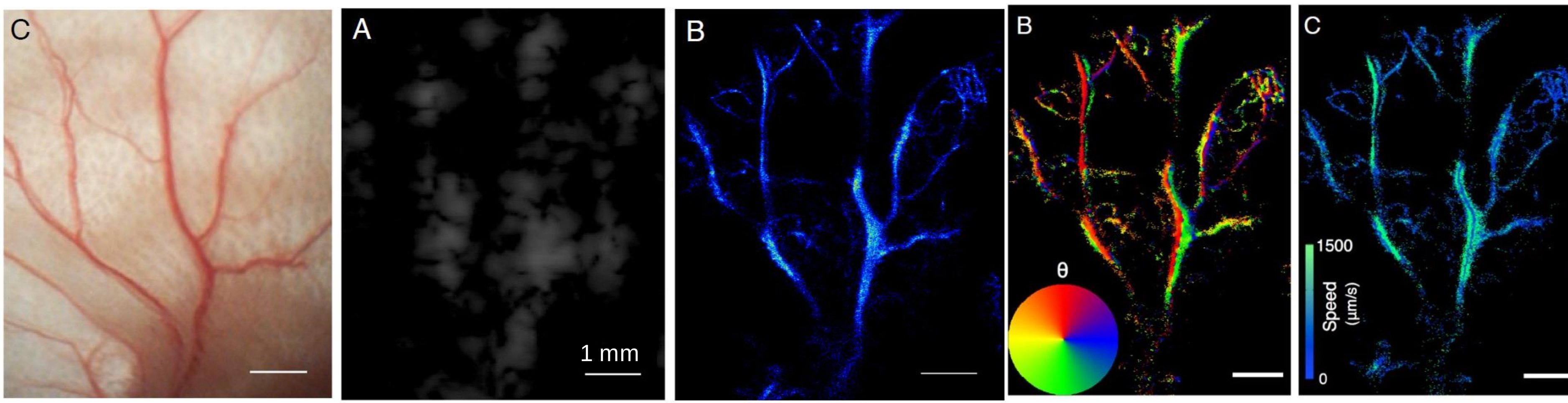


Chee Hau Leow, Nigel Bush, Anant Shah, Jeff Bamber, Mengxing Tang

Super-resolution imaging by integrating microbubble localisations

Robert Eckersley (KCL), Kirsten Christensen-Jeffries (KCL) , Mengxing Tang (ICL) and Chris Dunsby (ICL)

Images of vasculature at 6.5 MHz, in a mouse ear, using a clinical US system



Optical

Commercial mode (“Cadence™ CPS”)

With super-resolution processing

Super-resolved direction of flow

Super-resolved speed of flow

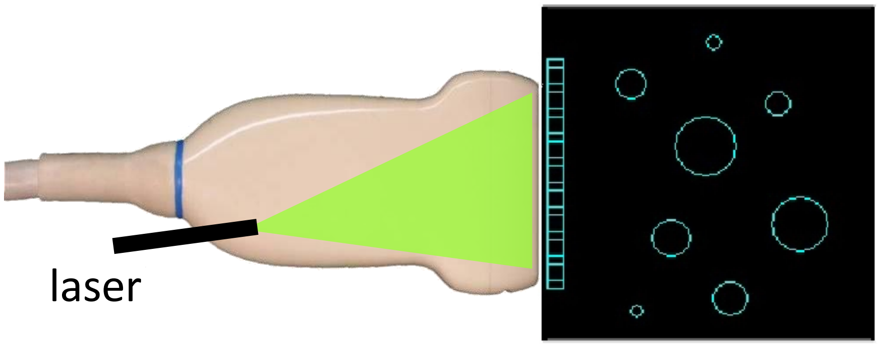
- **Vessels of diameter 19 µm visualised** with a clinical ultrasound scanner; smaller than 1/5th the diffraction limited resolution.
- **Potentially achievable clinically at large depth** - needs 3D and motion correction
- Applications in tumour hypoxia estimation

Photoacoustic imaging

Replace the ultrasound pulse with a short (ns) light pulse

Absorption of light by tissue → heating → pressure → **acoustic emission**

Ultrasound emissions are recorded by multiple transducer elements and used to reconstruct images of the **location and strength of optical absorption**



Varying the wavelength of light brings **absorption spectroscopy** to ultrasound imaging

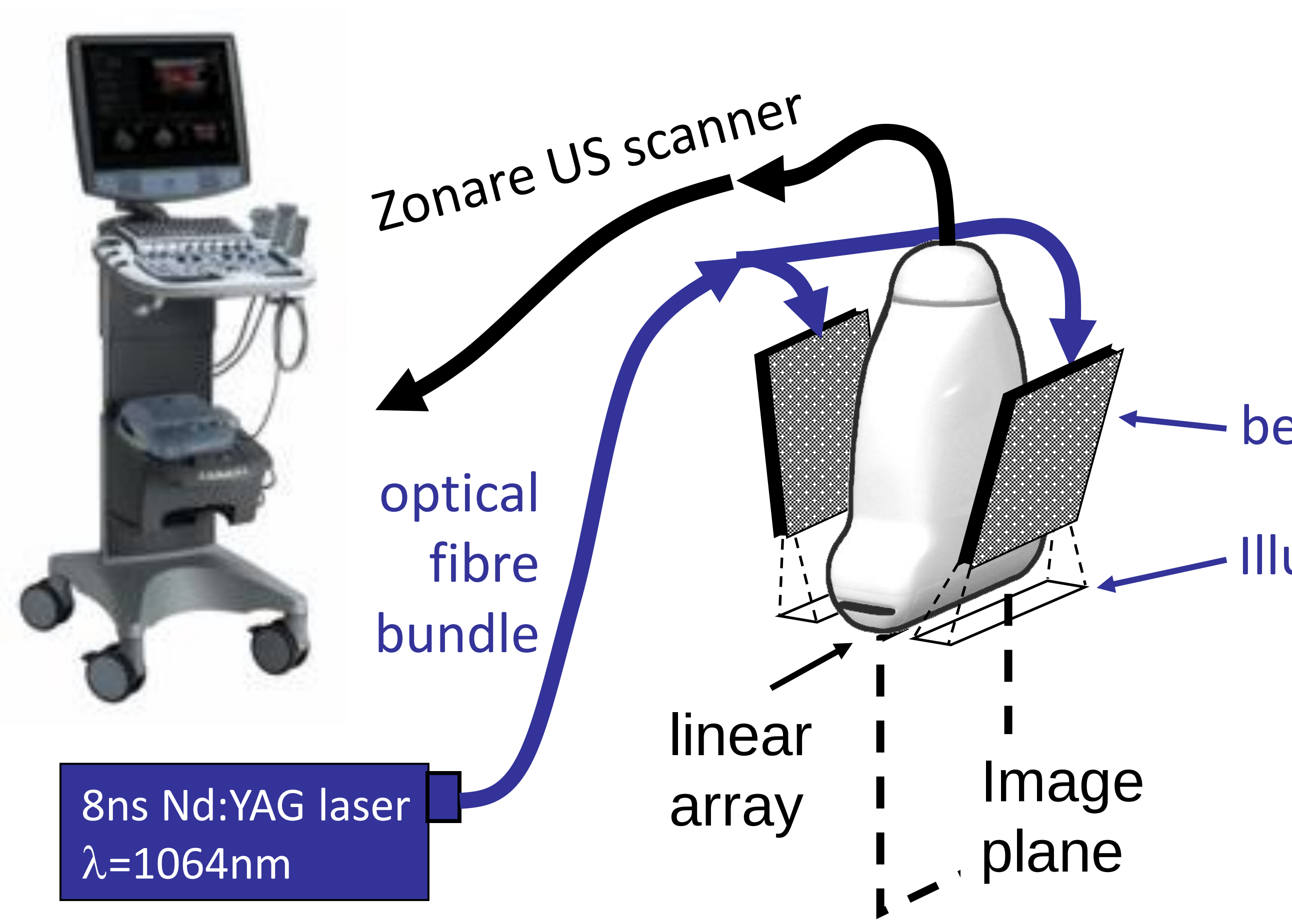
Endogenous contrast: melanin, Hb, HbO_2, saO2, lipid, …

Exogenous contrast: ICG, meth blue, nanoparticles, …

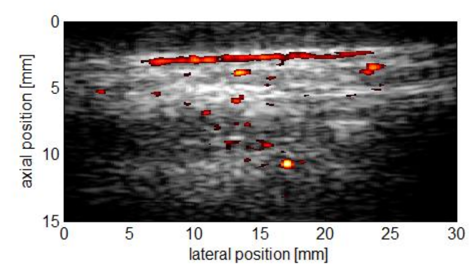
Thanks to Michael Jaeger, University of Bern, for the simulation

Epiphotoacoustic (EPA) imaging

combined reflection-mode PA and pulse-echo imaging for clinical application

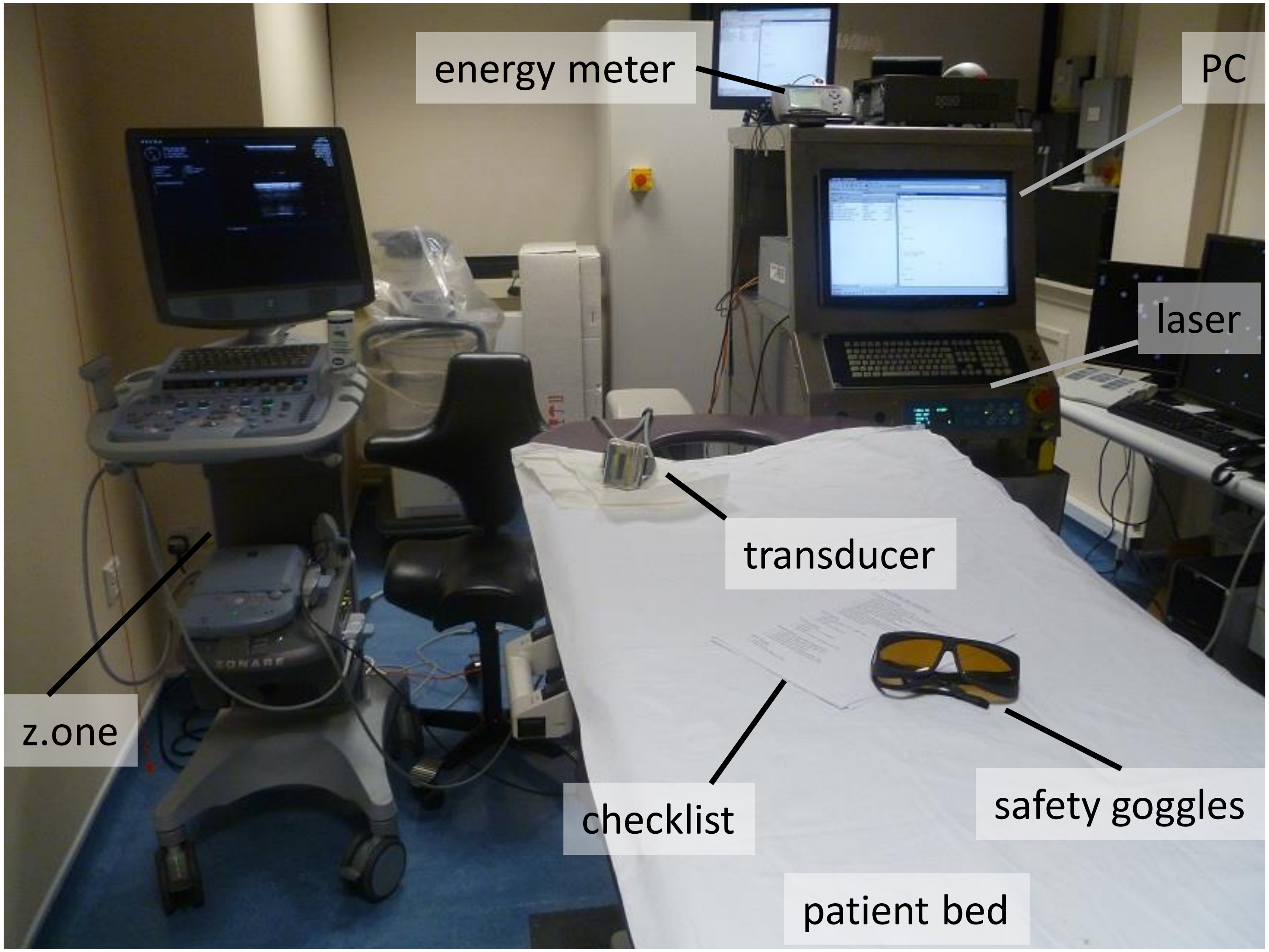


Freehand scanning



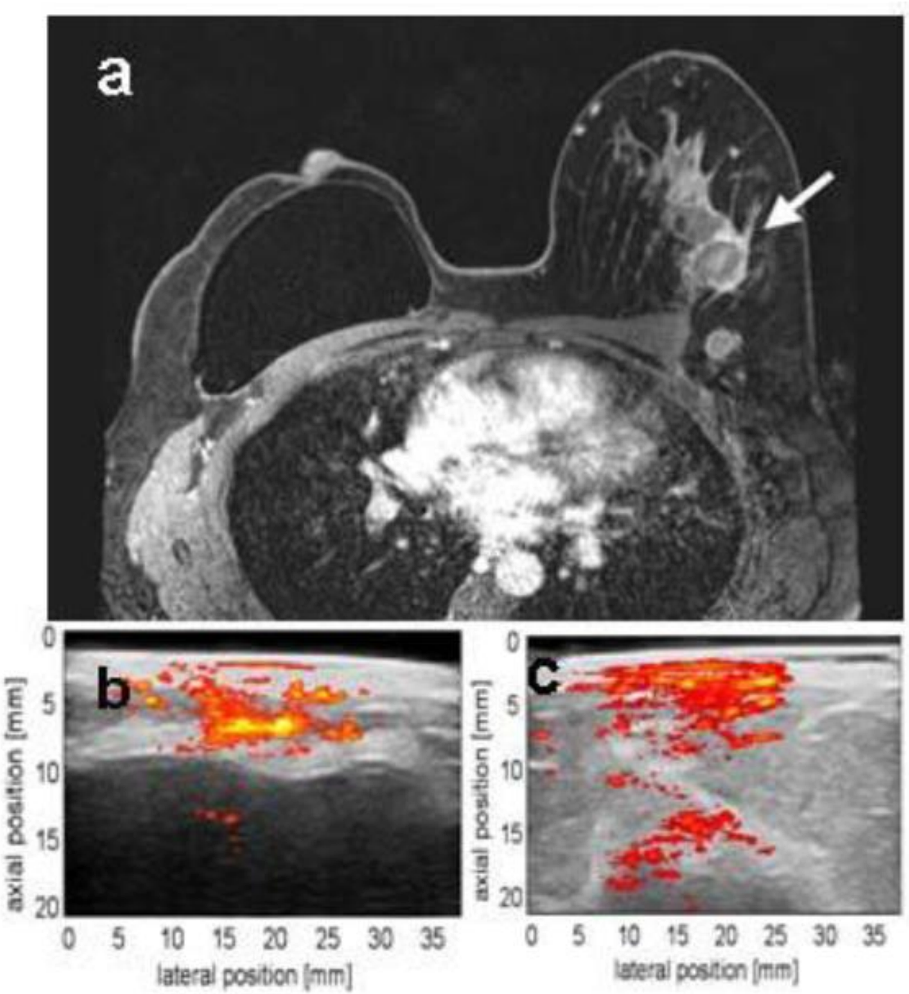
Bush N, Jaeger M, Gertsch A, Birtill D, Shah A, Alles E, Bamber J ….

First clinical photoacoustic breast scanning



Jaeger , Gertsch, Birtill, Bamber

Preliminary clinical experience with ICR epiphotoacoustic imaging system (1100 nm)



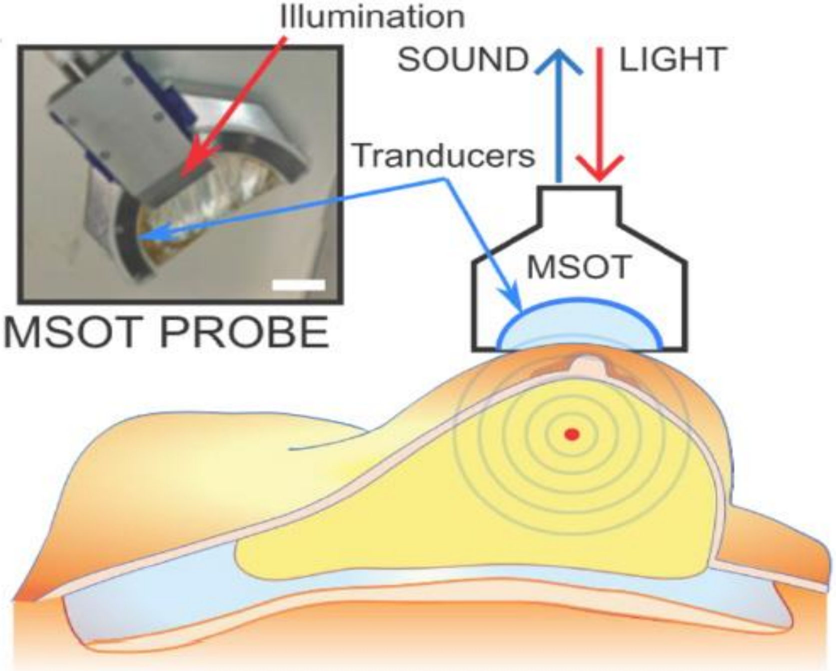
- Strong signal in skin and peritumour regions, presumed vascularity
- Correlation of signals present with breast architectural features
- Evidence of clutter signals producing below 15-20 mm
- Stronger skin signal and clutter signal for dark skin relative to light skin

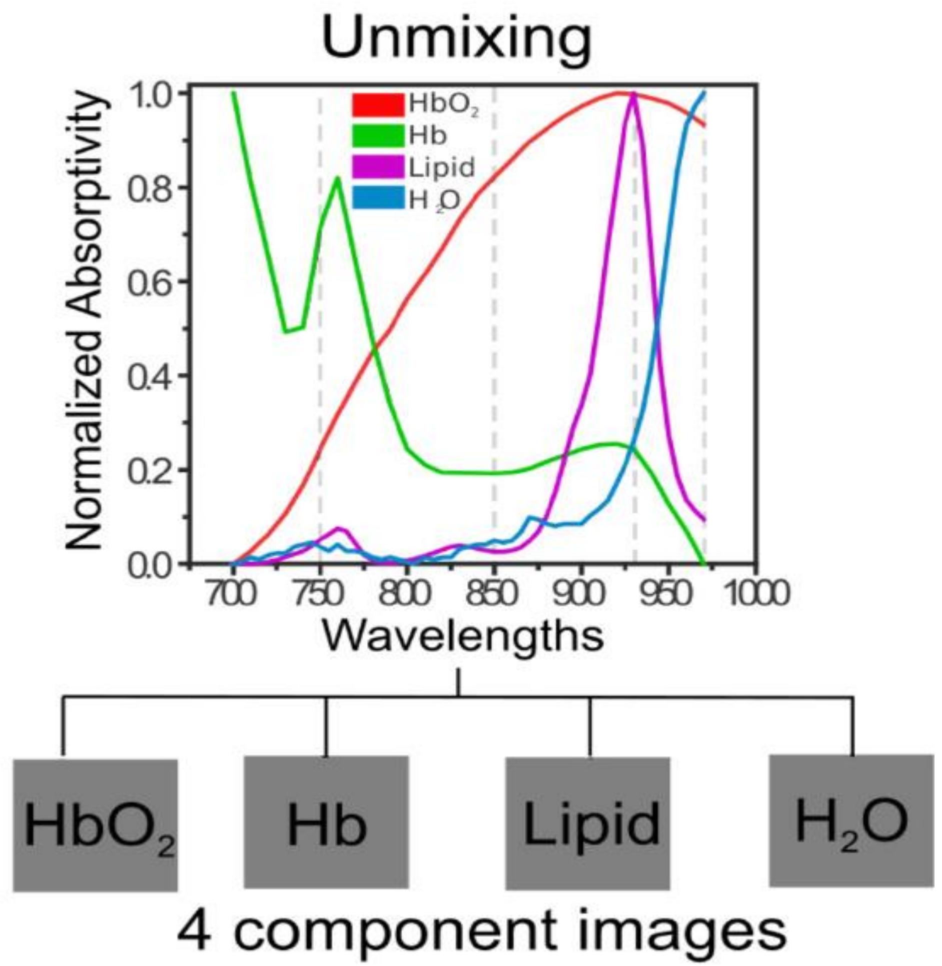
➡ Need to reduce clutter

D Birtill, M Jeager, E O'Flynn, A Gertsch, E Alles, N de Souza, J Bamber

MSOT™ (iThera) multispectral photoacoustic imaging

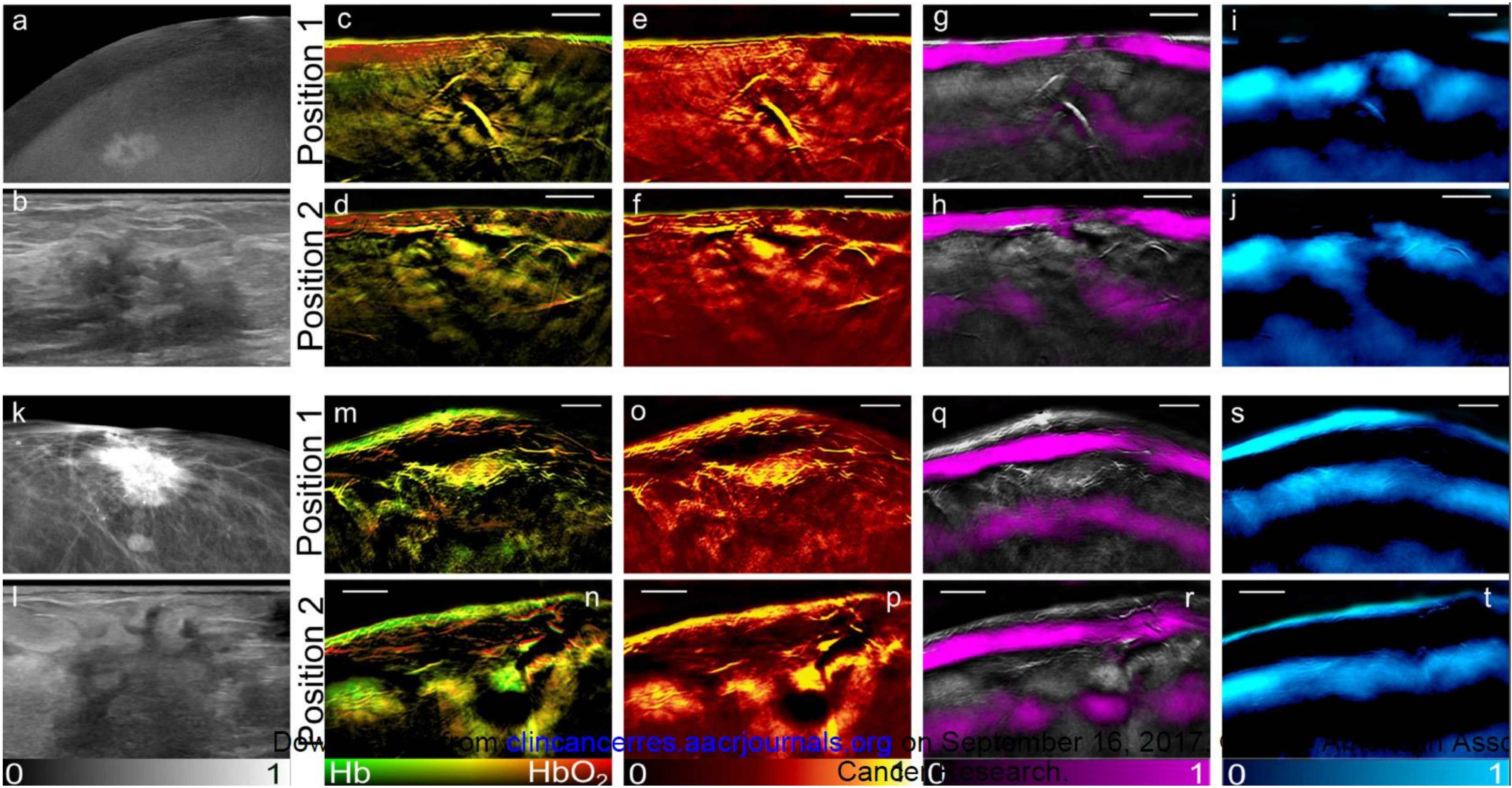
28 wavelengths, frame rate 2 Hz





Diot G et al, (Vasilis Ntziachristos) Clin Cancer Res. 2017 Sep 15;23(18):5658

iThera clinical multispectral photoacoustic imaging – breast cancers



Diot G et al, (Vasilis Ntziachristos) Clin Cancer Res. 2017 Sep 15;23(18):5658

Ultrasound Tomography

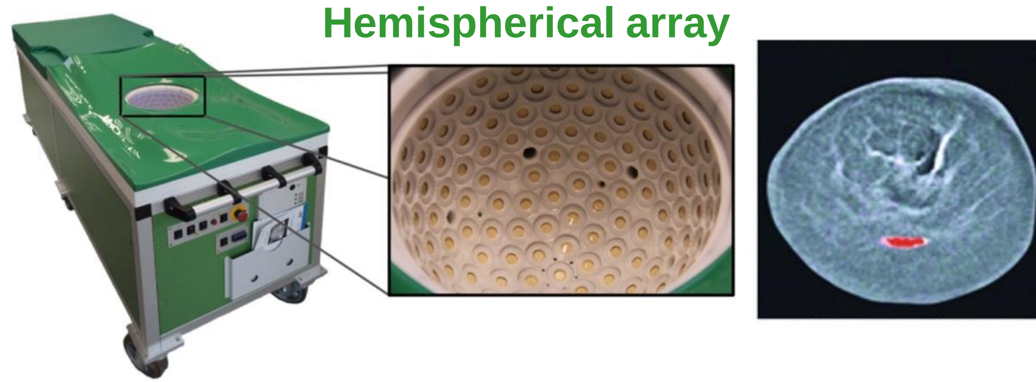
Ring array ultrasound CT
Karmanos Cancer Institute

2048 element **ring array**, 2.5 MHz
Whole breast 3D by moving the ring (2.5 mm steps)
~ 45 seconds per breast
~ 15 minutes total examination time

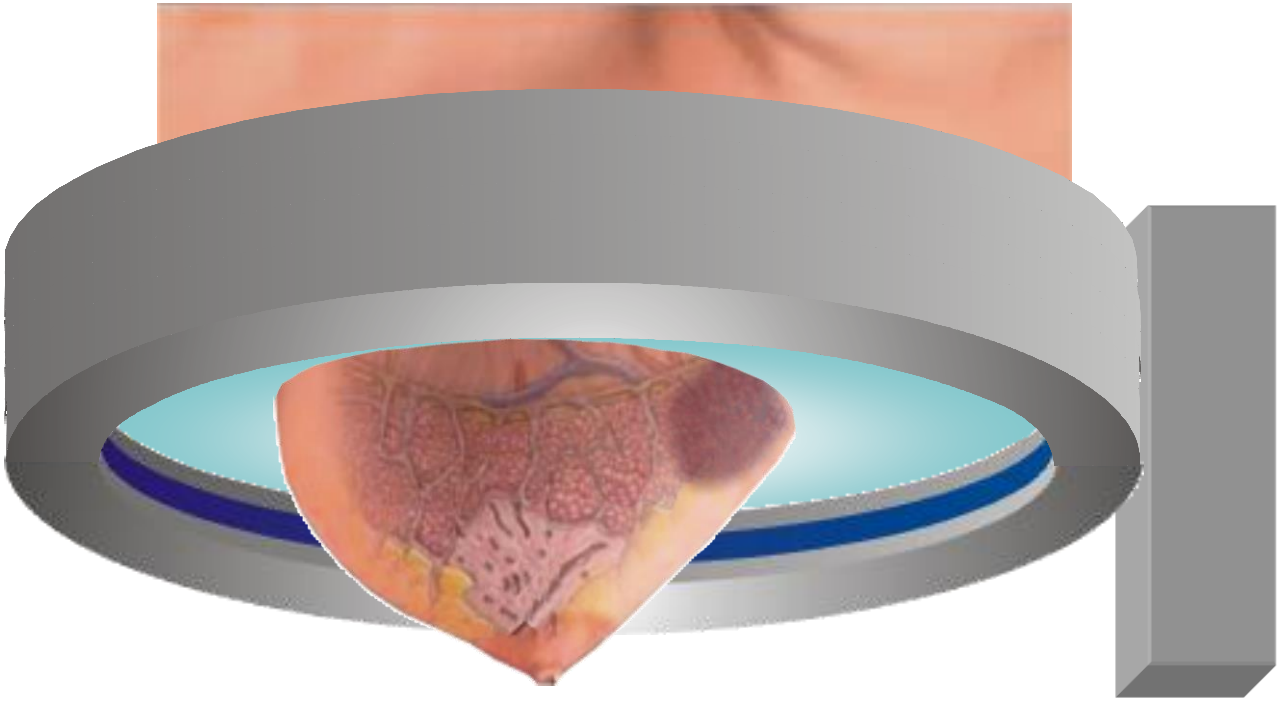
Commercially translated
Delphinus Medical Technologies Inc.

Other systems exist, e.g., 3D Ultrasound Tomography at Karlsruhe Institute of Technology, N. Ruiter et al. 2017

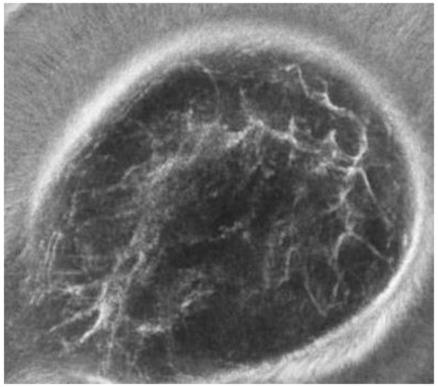
Hemispherical array



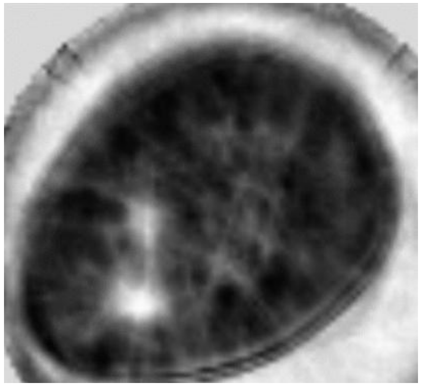
UST scanning (Karmanos Cancer Institute)



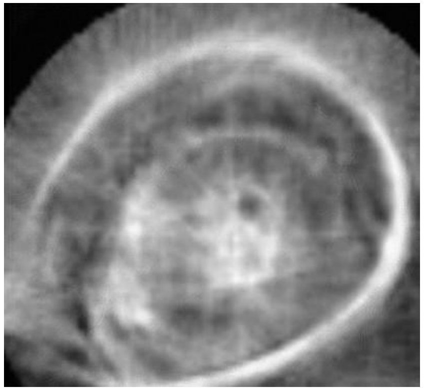
Reflection



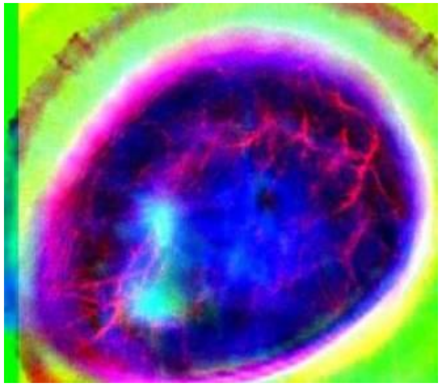
Sound Speed



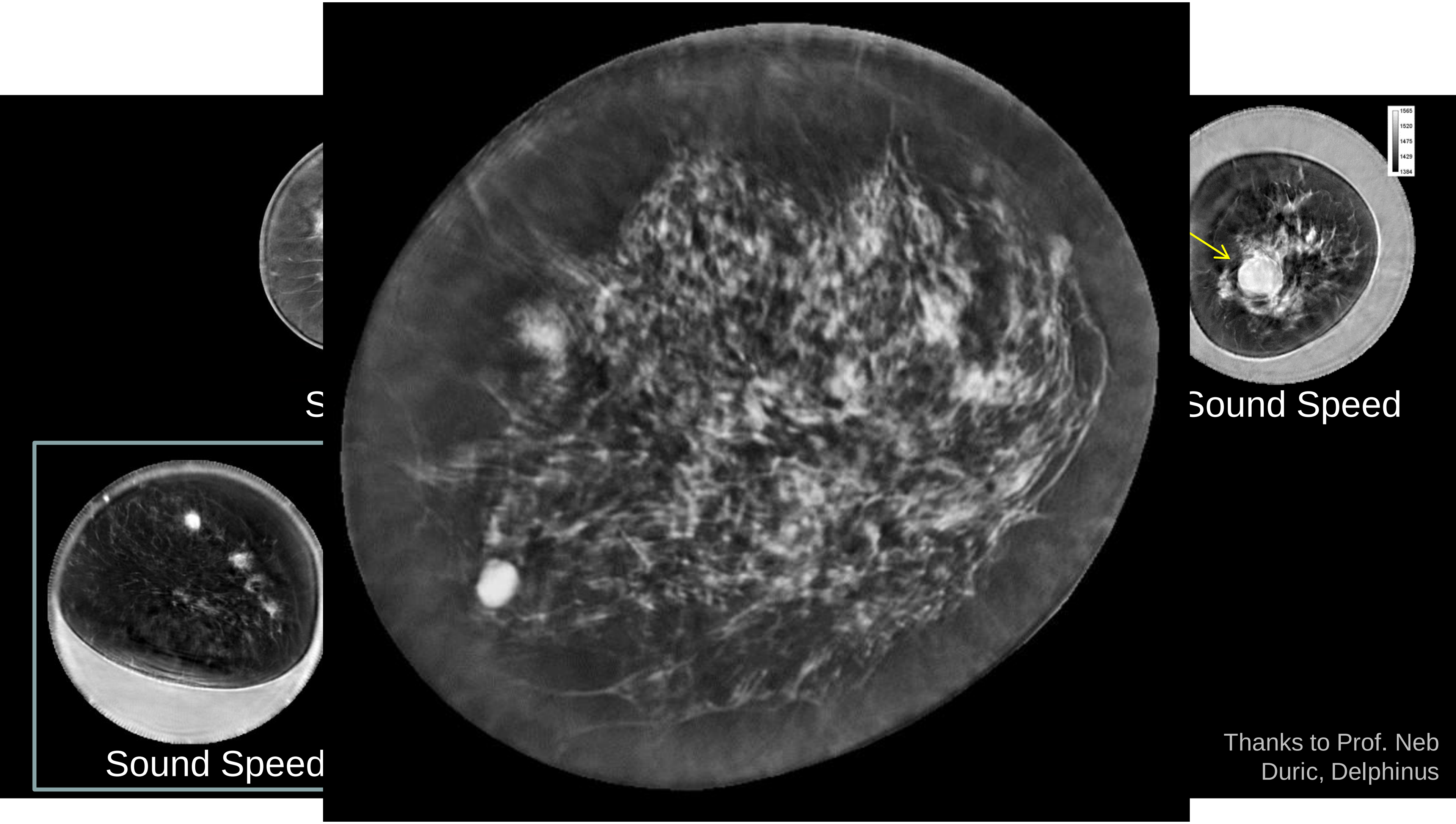
Attenuation



Fusion

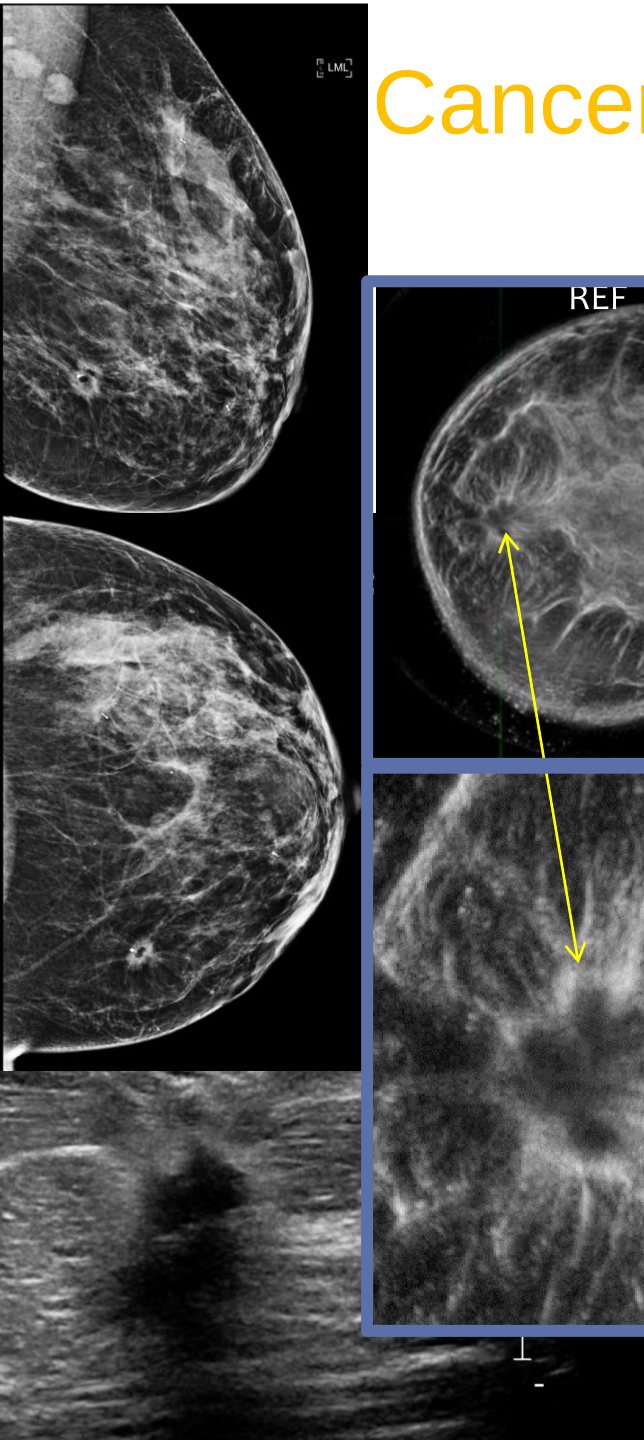


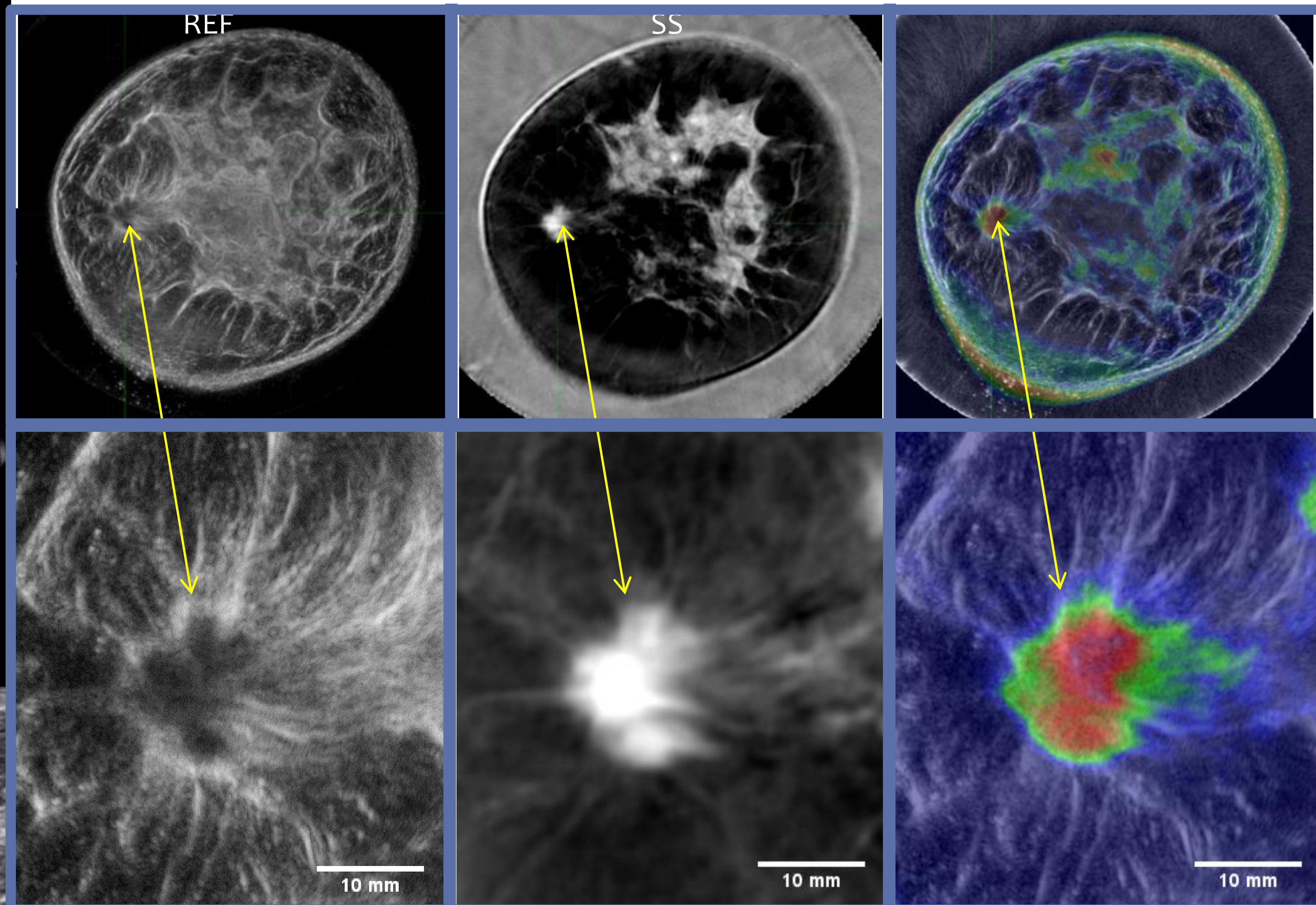
Recent Ultrasound Tomography using wave inversion from geophysics



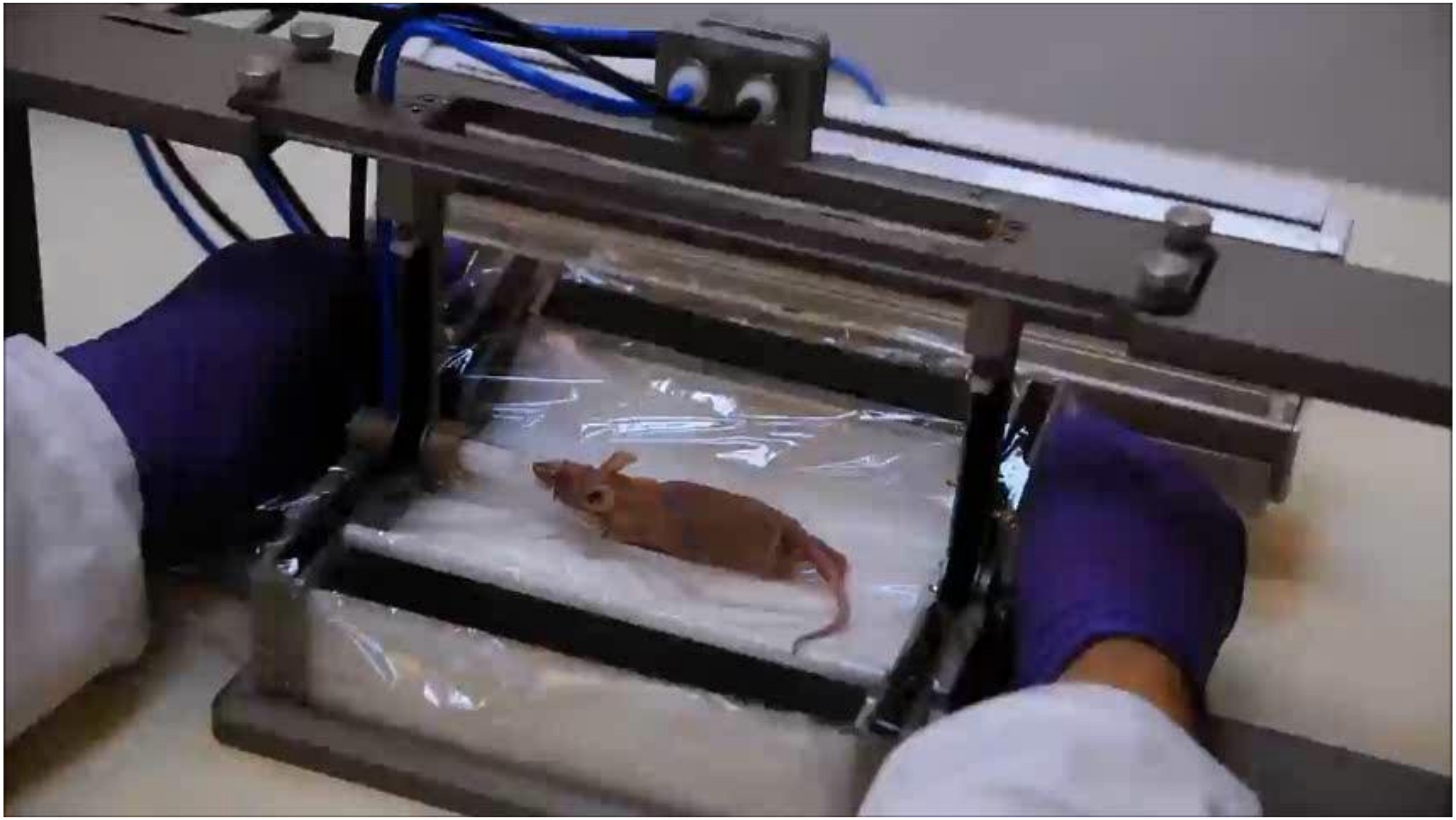
Thanks to Prof. Neb Duric, Delphinus

Cancer example on UST





Preclinical photoacoustic imaging



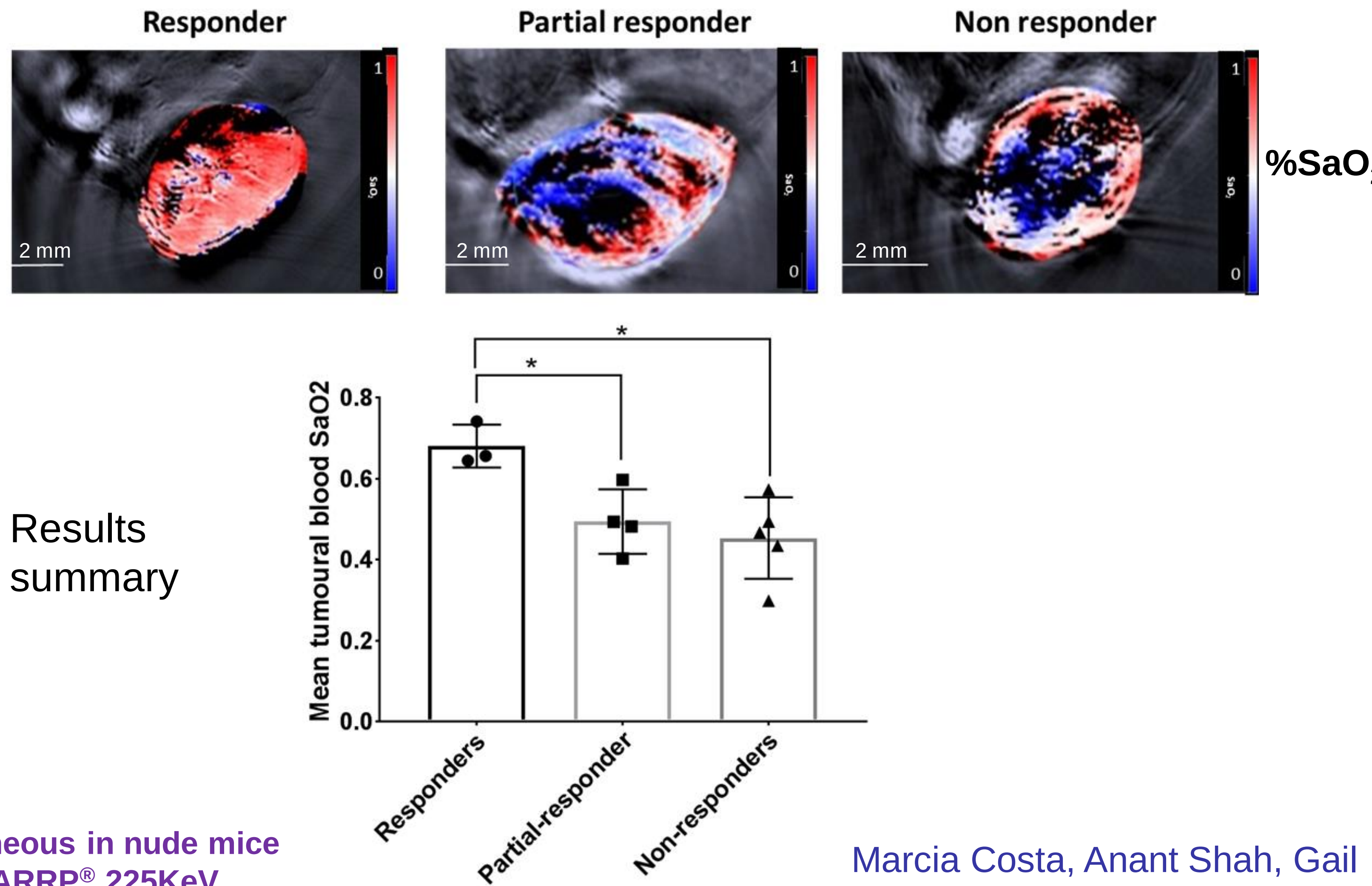
- **MSOT inVision 256^{TF}** iThera GmbH

Relationship between tumour blood %SaO_2 and the level of response to radiotherapy

17

Example cases. MSOT imaging before RT

Results summary



CAL[R] subcutaneous in nude mice
10 Gy, using SARRP® 225KeV
25% complete response in 60 days

Marcia Costa, Anant Shah, Gail ter Haar, Jeff Bamber …….

Proton/Ion-acoustic imaging

- Works in a similar way to photoacoustic imaging.
- LhARA Ambition: in-vivo real-time 3D dose localisation and quantitative imaging, for real-time pulse-to-pulse adaptive treatment as the beam is moved around.
    - Localise the Bragg peak (submillimetre accuracy possible), to avoid damage to healthy tissue and under-dosing of the tumour
    - Measure the deposited-energy distribution in the tissue, preferably on a pulse-by-pulse basis.
    - Simultaneous multimodality ultrasound and photoacoustic images registered to planning CT/MRI - track tissue motion, image anatomy, perfusion, microvasculature, hypoxia, elastography, speed of sound, molecular biomarkers and dose enhancement distribution from molecularly targeted dose enhancers.
    - Suitable for organs where acoustic access is possible: breast, prostate, liver, pancreas, pelvic, head and neck, etc.
    - Enable preclinical research to provide the radiobiology knowledge needed to take full advantage of the new accelerator, and for its optimal clinical use.
    - Especially applicable to mini/micro-beam and FLASH irradiation.

Proton/Ion-acoustic imaging

Work needed:

- Review proton/ion-acoustics work to date, options and potential.
- Define key radiobiological questions.
- Define preliminary required performance specification.
- Monte Carlo, thermoacoustic generation and acoustic propagation modelling, with varied PB properties such as beam size, pulse length, particle energy, particle type and dose per pulse, and varied ultrasound detector characteristics
  => predicted dose imaging capabilities for the expected accelerator
  => ultrasound system requirements
- Early experiments to validate the modelling – needs a source
- Build protoype preclinical demonstrator system – industry collaboration
- Bring together with LhARA prototype
- Conduct preclinical experiments to generate radiobiological knowledge
- Refine and repeat, translate to clinical scale, …