THz Imaging: Biomedical Applications

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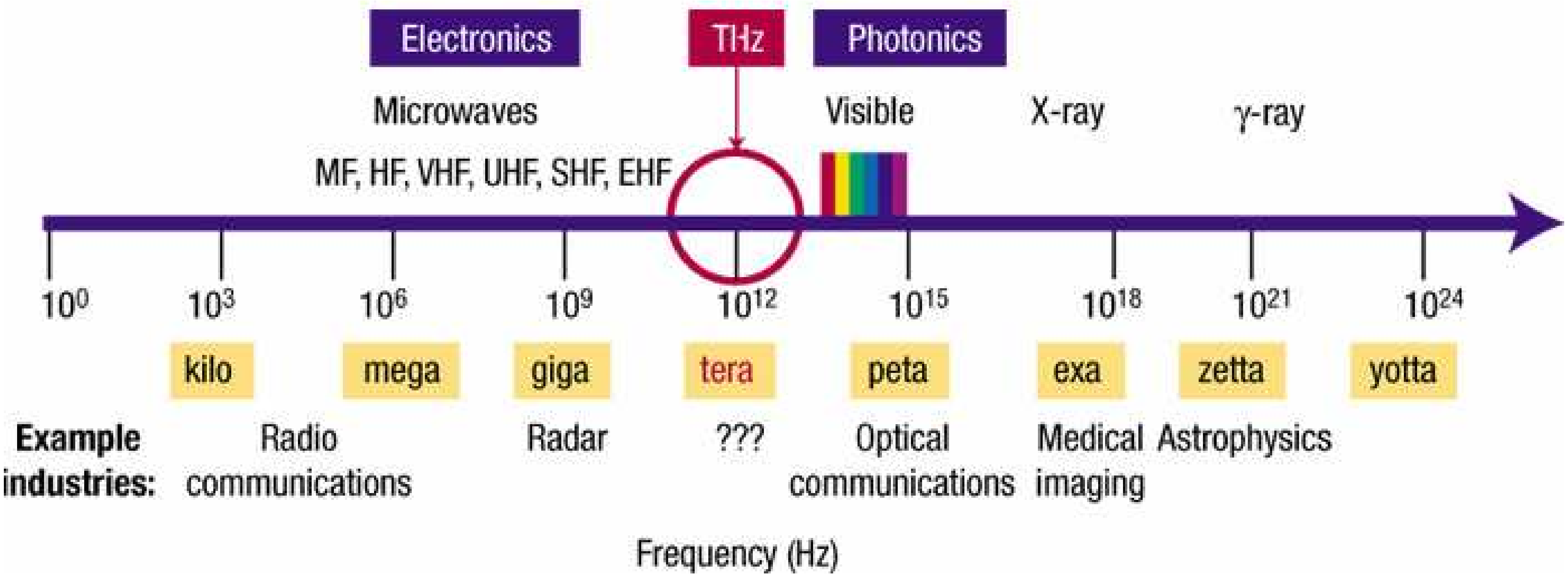
The "TeraHertz Gap"



Technology Review (MIT) 2004: THz selected as one of "10 emerging technologies that will change your world"

THz radiation

- Frequency: 0.1 – 10 THz
- Wavelength: 3 mm – 30 μm
- Wavenumber: 3.3 – 333 cm^{-1}
- Energy: 0.41 – 41 meV
- Colour Temperature: 1 – 100 K

THz interactions

- Changes in high-energy rotational states
- Changes in low-energy vibrational states
- Classical electromagnetic wave description for interaction with collections of molecules, in terms of:

Polarization and conductivity (complex permittivity)

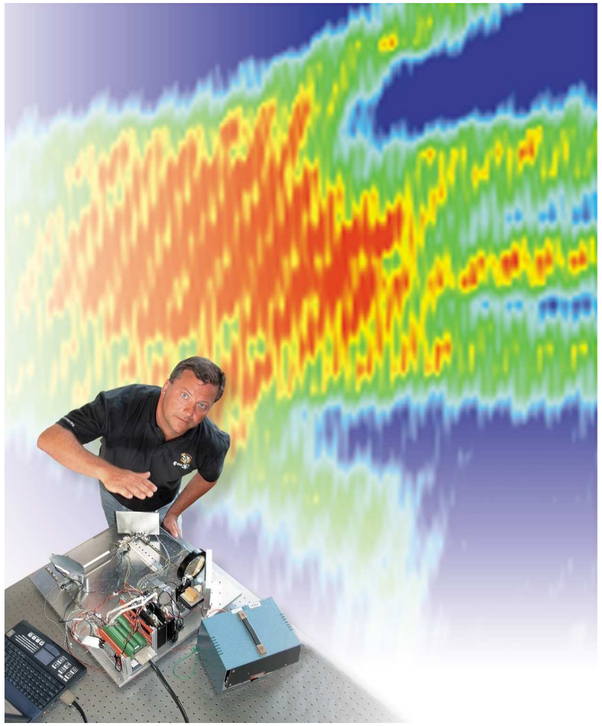
Refractive index and absorption coefficient (complex R.I)

Types of THz instrument

- Passive
  - Incoherent
- Active
  - Spectroscopy or Imaging
    - Pulsed (coherent)
    - Continuous wave (coherent)

Passive imaging

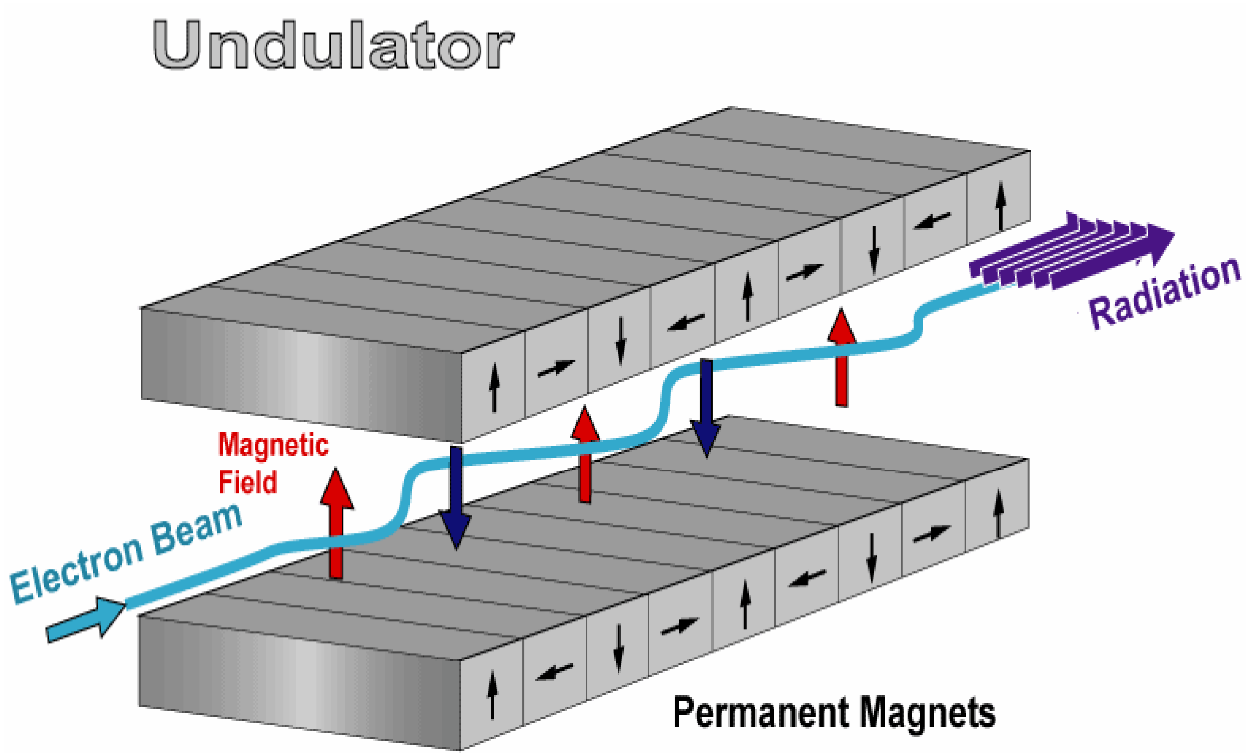
Dr Chris Mann (RAL) imaging his hand at ~250 GHz, using a passive system. (*StarTiger* ESA project)



Spin-off company *ThruVision* start airport trials

Active imaging (I)

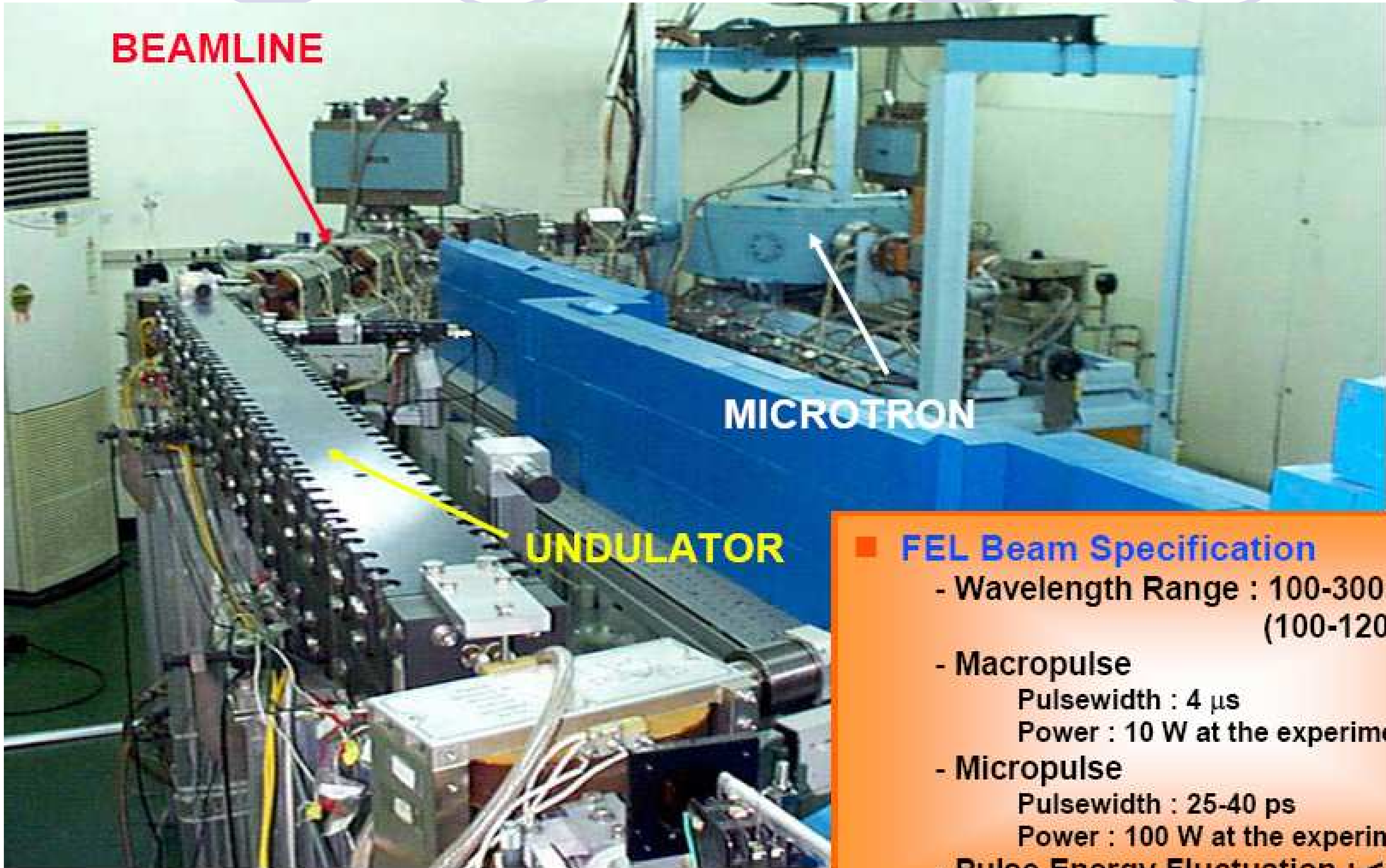
- Free Electron laser



Wide frequency range, high power coherent output

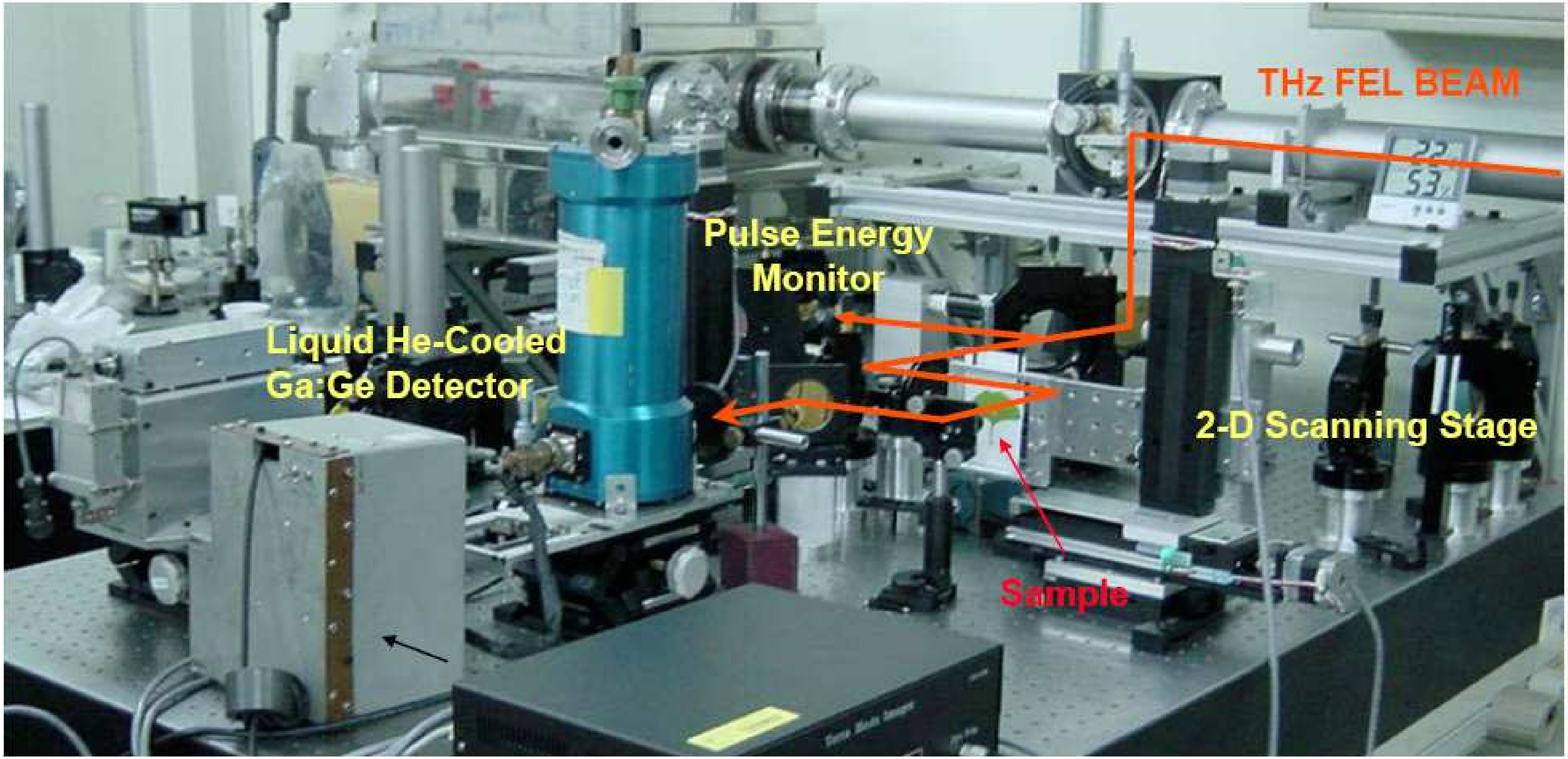
But - large, complex and very expensive

THz FEL: KAERI, Daejon, Korea

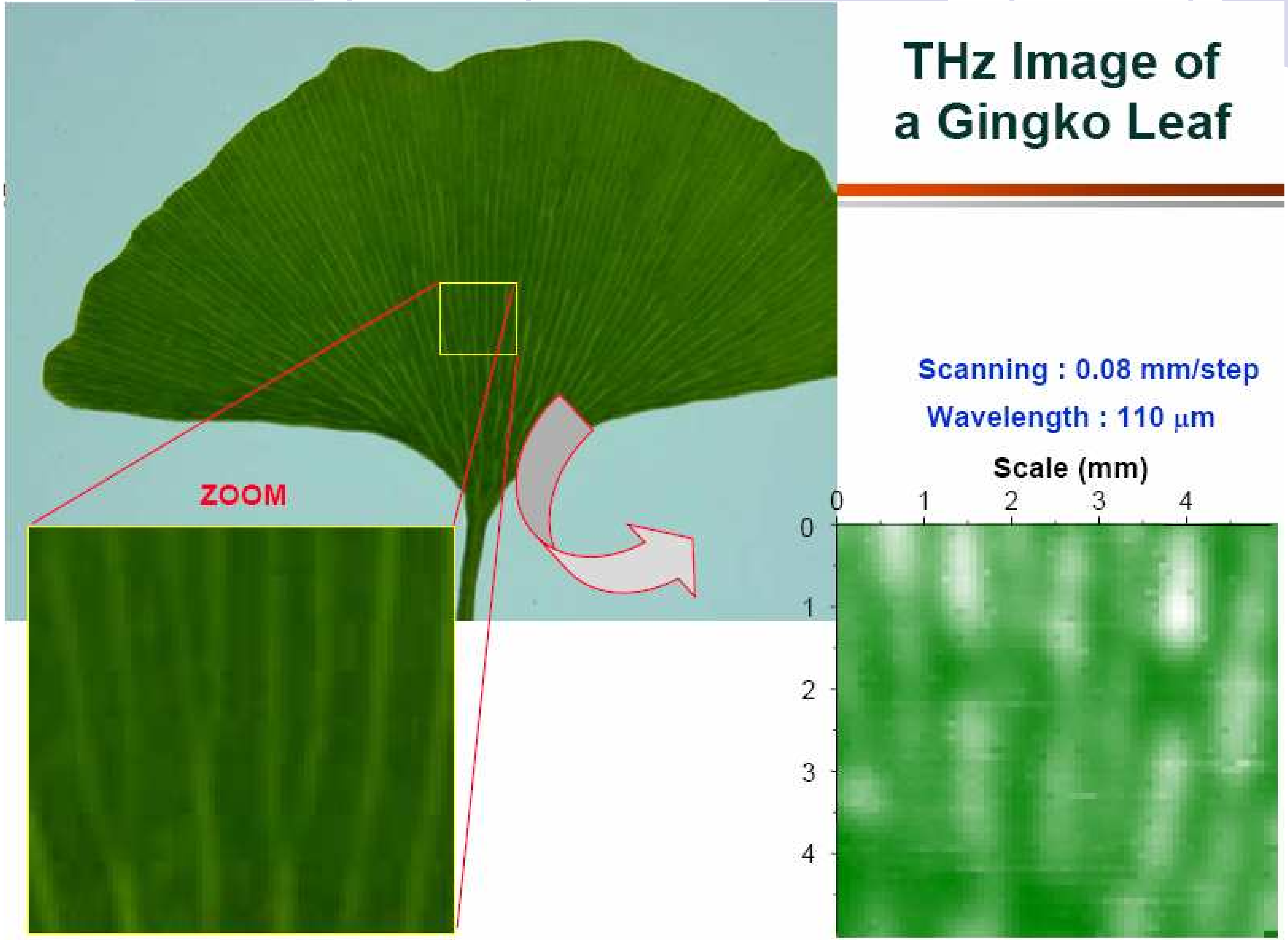


- **FEL Beam Specification**
  - Wavelength Range : 100-300 μm (100-1200 μm)
  - Macropulse
    - Pulsewidth : 4 μs
    - Power : 10 W at the experimental stage
  - Micropulse
    - Pulsewidth : 25-40 ps
    - Power : 100 W at the experimental stage
  - Pulse Energy Fluctuation : <10% rms

THz imaging stage

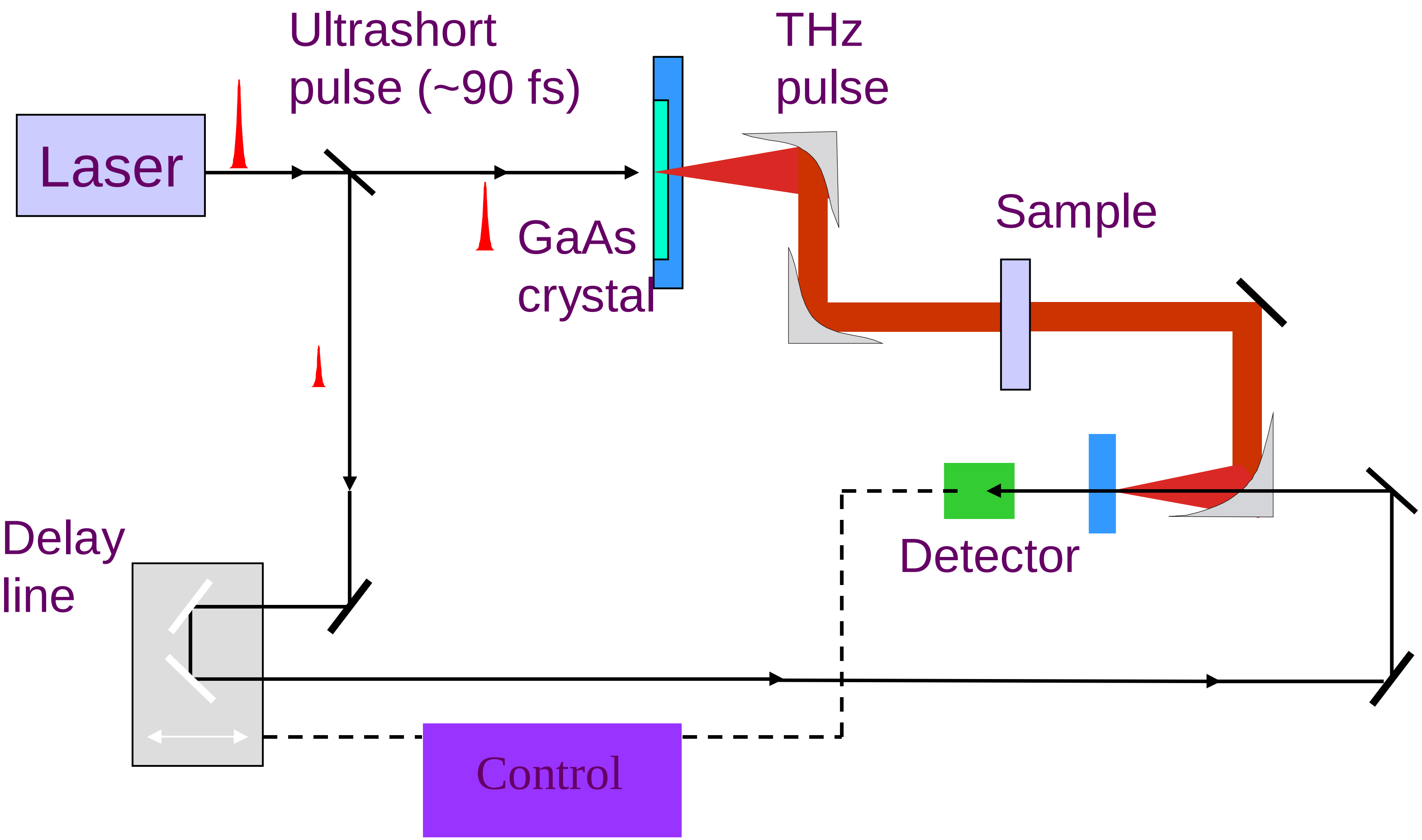


THz Image of a Gingko Leaf

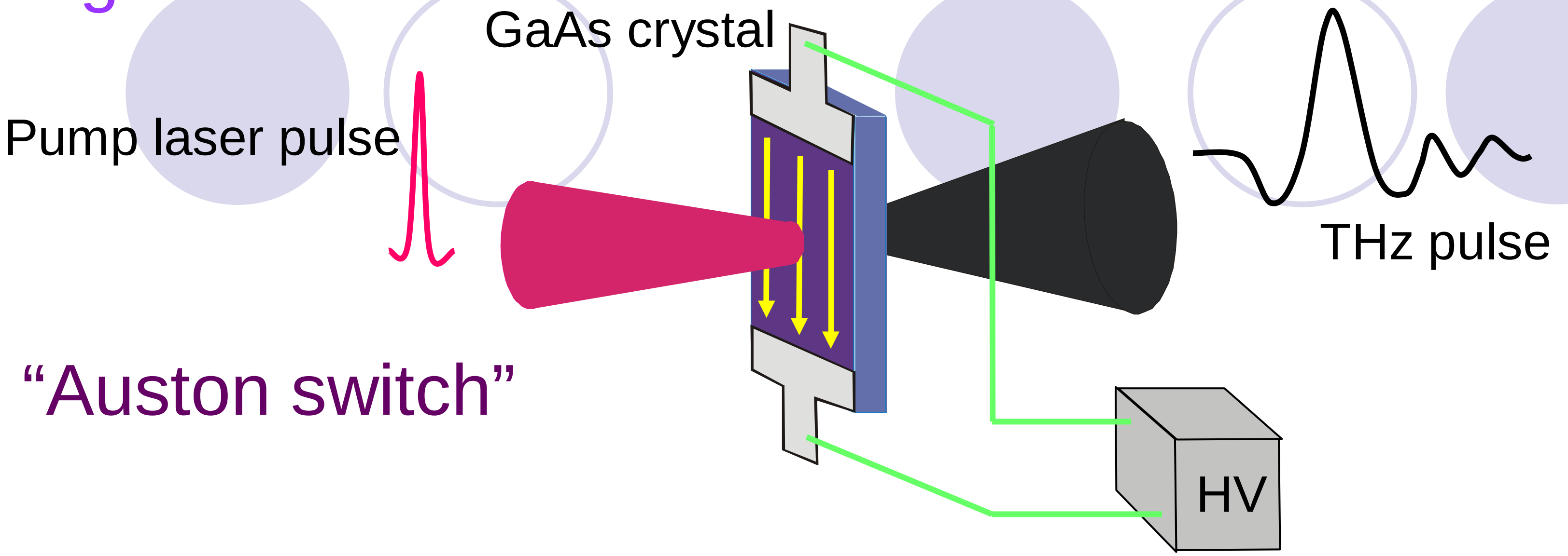


Active imaging (II)

- Time-domain spectroscopy

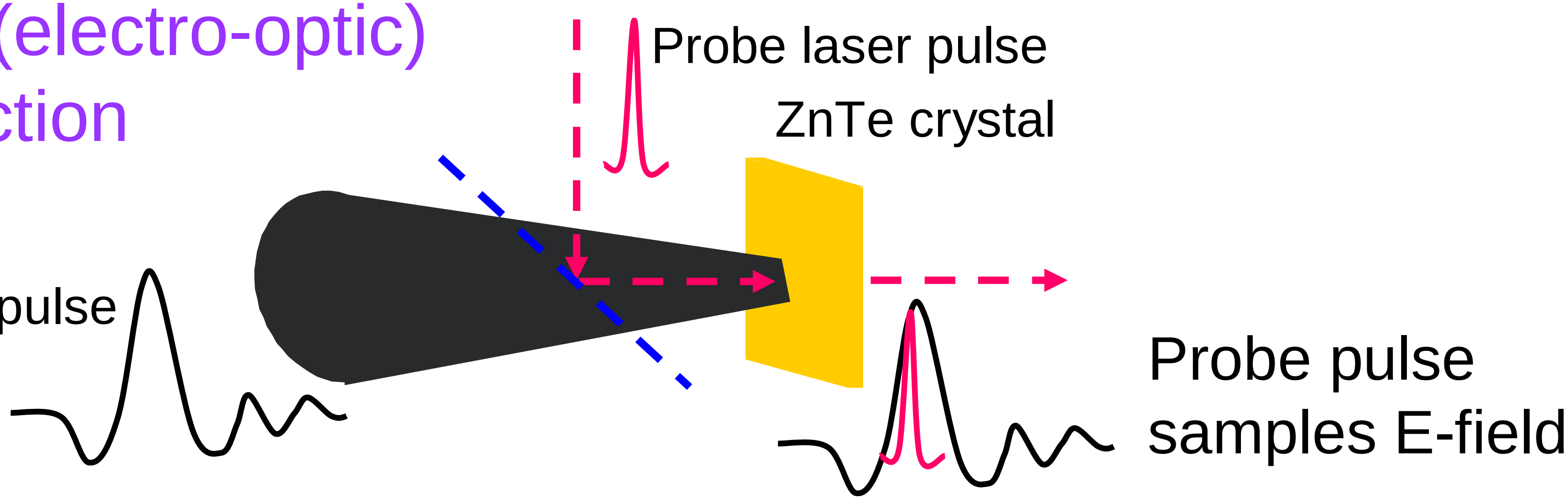


THz generation



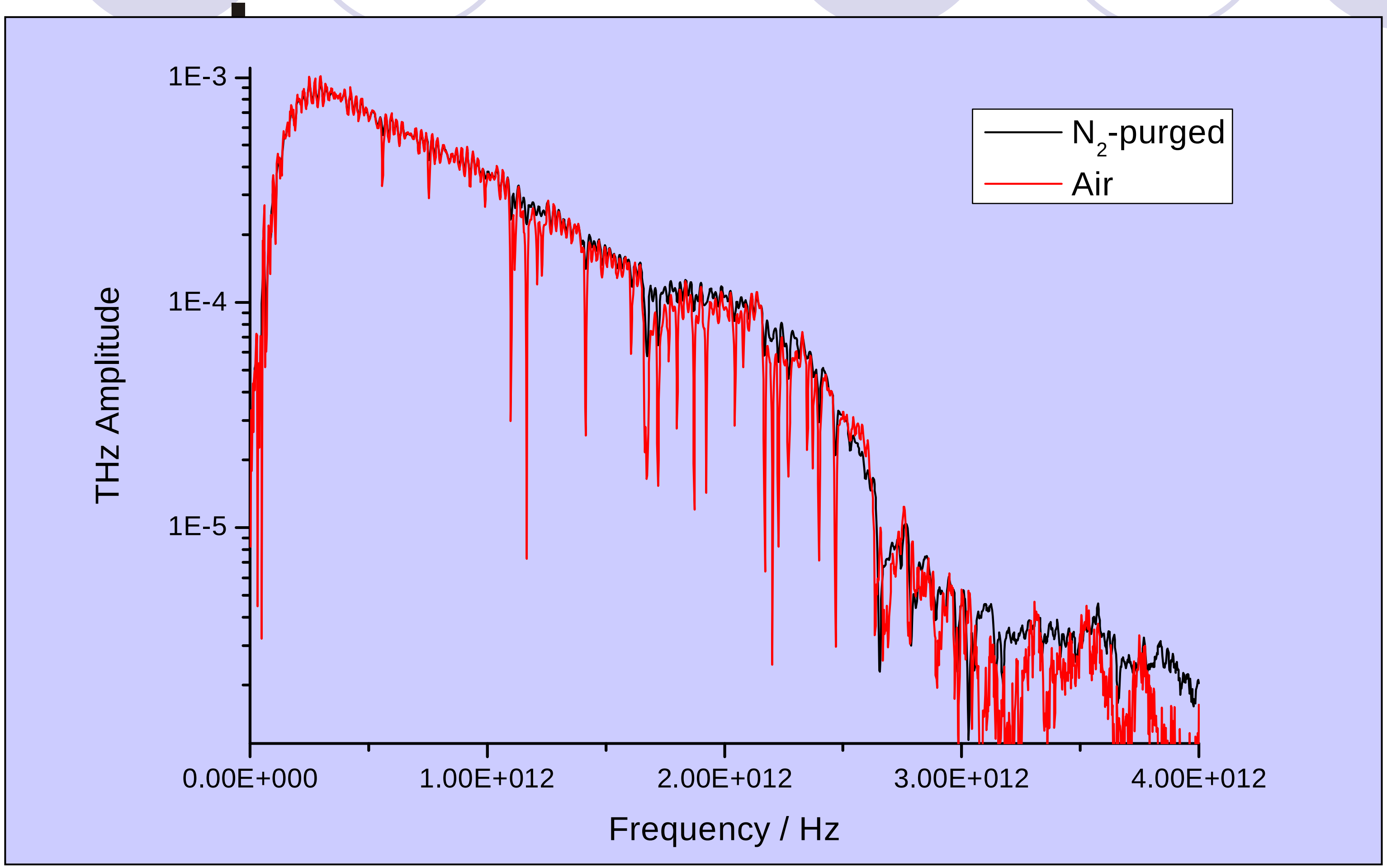
"Auston switch"

THz (electro-optic) detection

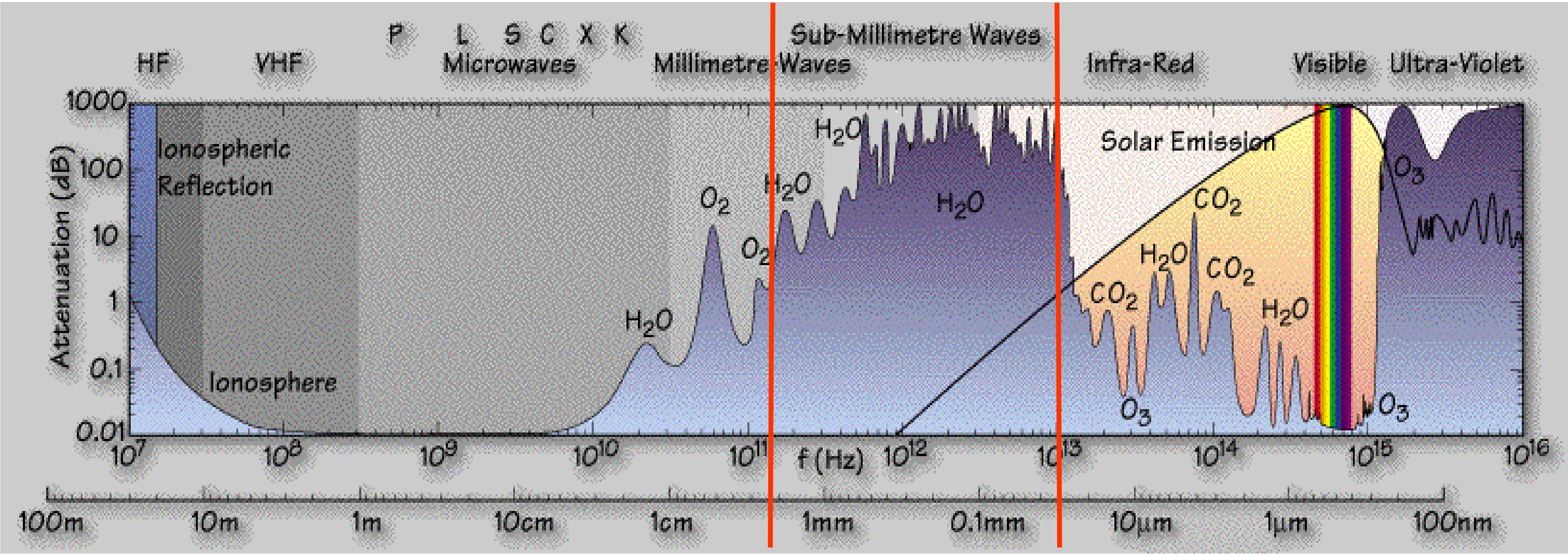


Change in polarization $\propto$ E

THz frequency spectrum



Bandwidth dictated laser pulse duration, electro-optic detection material, etc.



HF
VHF
P L S C X K
Microwaves
Millimetre Waves
Sub-Millimetre Waves
Infra-Red
Visible
Ultra-Violet
Attenuation (dB)
1000
100
10
1
0.1
0.01
Ionospheric Reflection
Ionosphere
Solar Emission
H_2O
O_2
CO_2
O_3
10^7
10^8
10^9
10^{10}
10^{11}
f (Hz)
10^{12}
10^{13}
10^{14}
10^{15}
10^{16}
100m
10m
1m
10cm
1cm
1mm
0.1mm
10µm
1µm
100nm

Bio-medical areas of investigation

- Biological effects of THz radiation
- Molecular spectroscopy
- *Ex-vivo* tissue spectroscopy/imaging
- *In-vivo* tissue spectroscopy/imaging

Examples (Journal of Biological Physics, 29, 2003)

Exposure of human keratinocytes up to 0.45 Jcm^{-2}:

(a) 0.2-3 THz @ 1 μW (Leeds system)

(b) 0.1-2.7 THz @ 10 μW (TeraView system)

- *No significant effect* ***Clothier and Bourne -Nottingham***

Exposure of human lymphocytes to 1.2 Jcm^{-2}:

0.12-0.14 THz @ 1mW (Frascati FEL system)

- *No significant effect* ***Scarfi et al - Napoli***

Spectroscopy: intrinsic resonances

Low-frequency vibrational modes (stretching, twisting)

Isomeric configurations

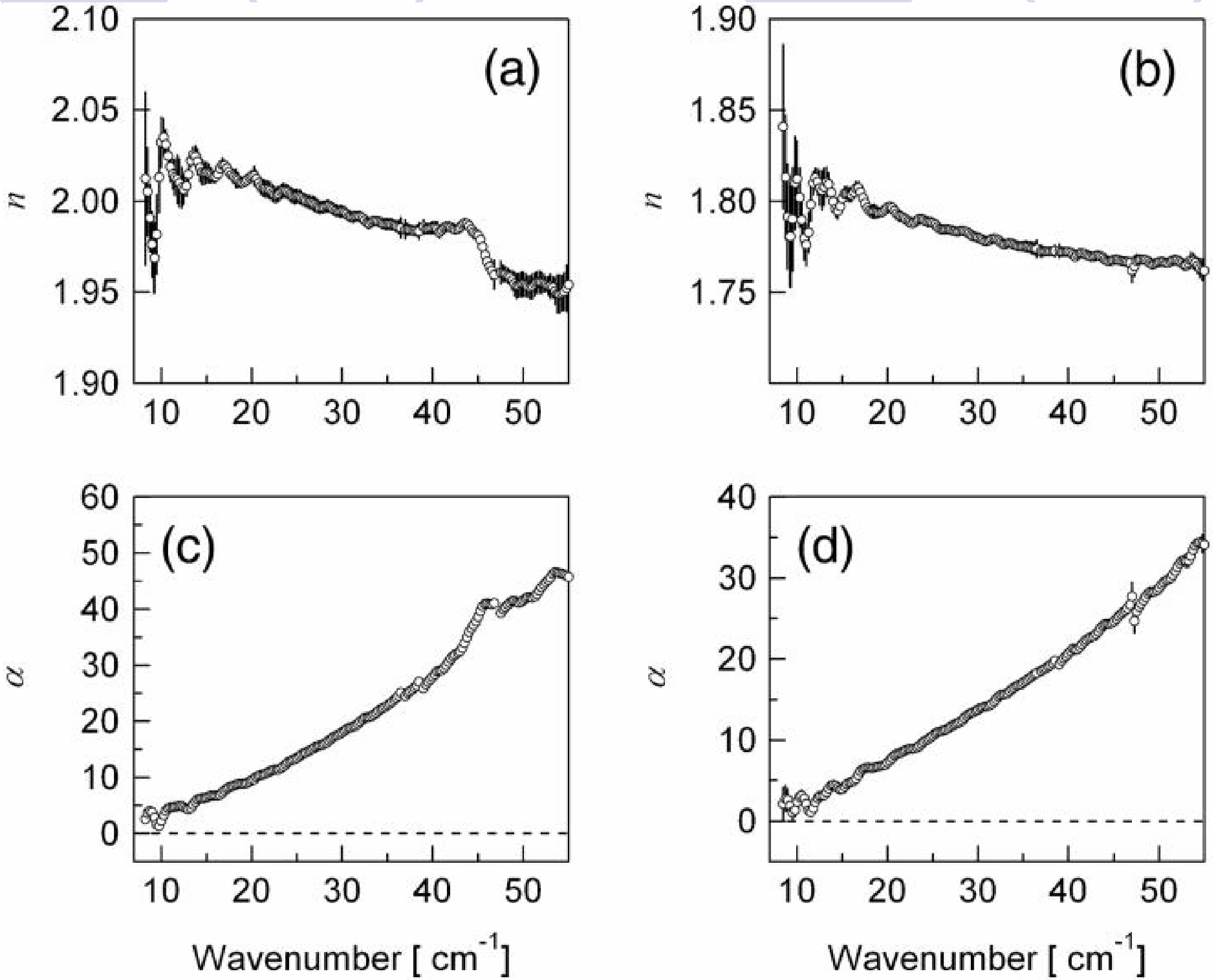
Intermolecular interactions

Kinetic measurements (excited state modes)

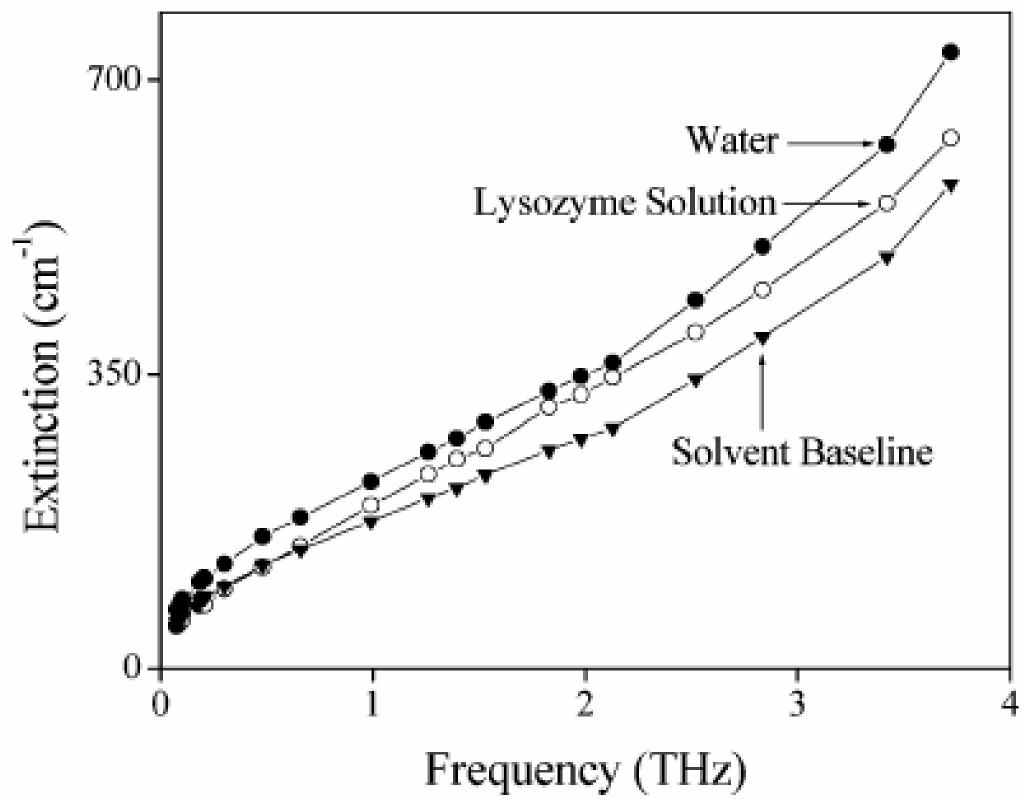
Bio-molecules (amino acids, proteins,
blood analytes, etc)

Pharmaceuticals, Pathogens, Cosmetics

Protein dynamics



polyglycine poly-L-alanine



Water
Lysozyme Solution
Solvent Baseline
700
350
0
0
1
2
3
4
Extinction (cm-1)
Frequency (THz)

Ex vivo tissue studies

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Systematic measurement of tissue optical properties

→ Tissue catalogue

Defining contrast - investigation of imaging parameters

Development of THz tissue phantom(s)

Identification of candidate disease states

Tissue properties

Material	N_n	<n>	N_μ	$\langle\mu\rangle/cm^{-1}$
Deionized water	16	2.04 ± 0.07	13	225 ± 21
Tooth enamel	44	3.06 ± 0.09	44	62 ± 7
Tooth dentine	72	2.57 ± 0.05	72	70 ± 7
Skin	36	1.73 ± 0.29	36	121 ± 18
Adipose tissue	37	1.50 ± 0.47	37	89 ± 23
Striated muscle	37	2.00 ± 0.35	37	164 ± 17
Cortical bone	59	2.49 ± 0.07	59	61 ± 3
Vein	33	1.58 ± 0.49	33	110 ± 43
Artery	12	1.86 ± 0.40	24	151 ± 25
Nerve	12	1.95 ± 0.46	12	246 ± 27

N_n = broadband refractive index N_μ = broadband attenuation coefficient

E. Berry et al. Proc. SPIE: Medical Imaging 2003

Contrast mechanisms

At each pixel in the image, one can plot:

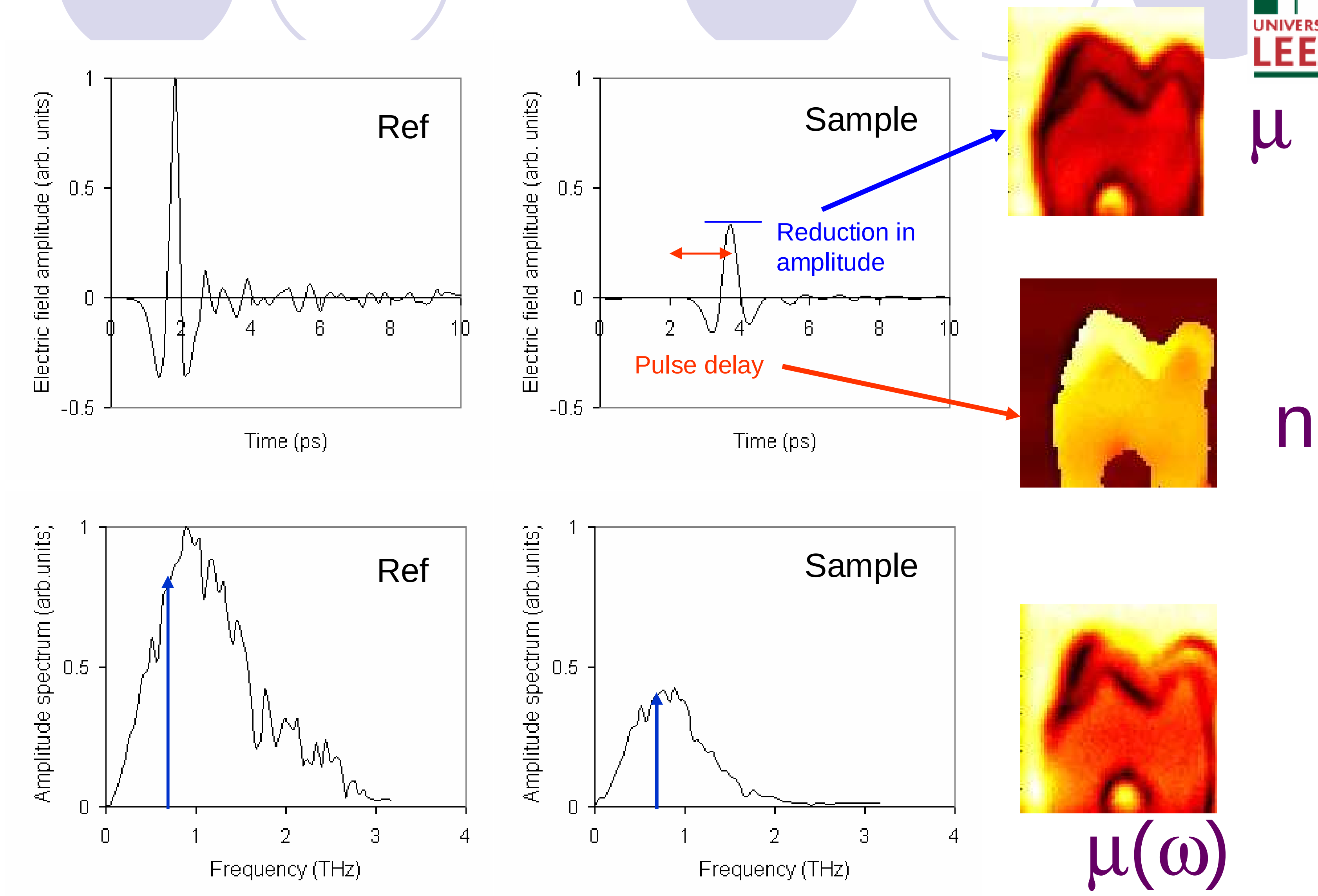
1. Absorption coefficient [$\alpha(\omega)$] over the whole bandwidth: *panchromatic absorption image*

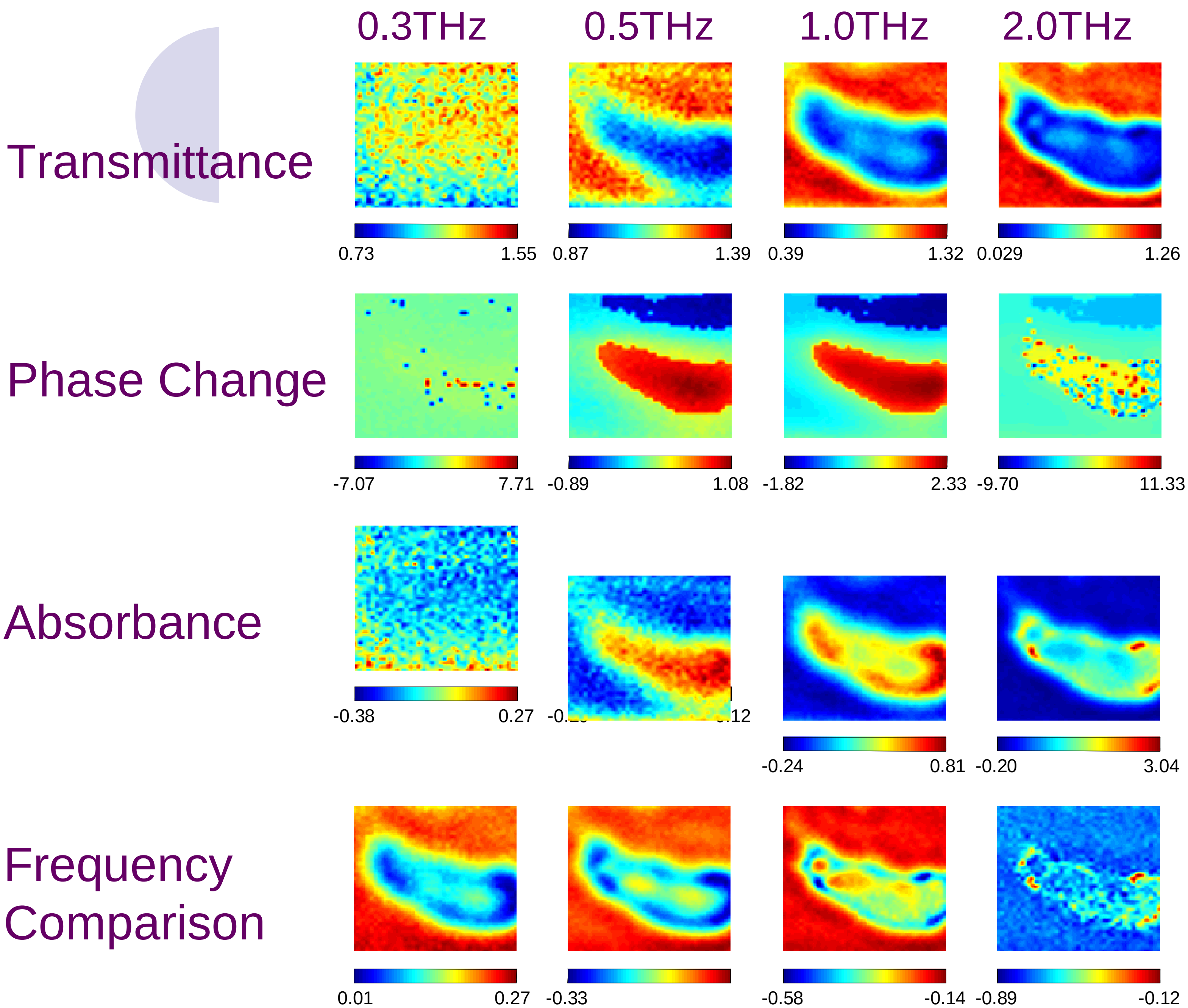
2. $\alpha(\omega)$ at a fixed frequency or narrow band of frequencies *monochromatic absorption image*

3. Thickness of object**:** *time-of-flight image*

4. Refractive index $n(\omega)$ at a fixed frequency, or over whole bandwidth: *refractive index image*

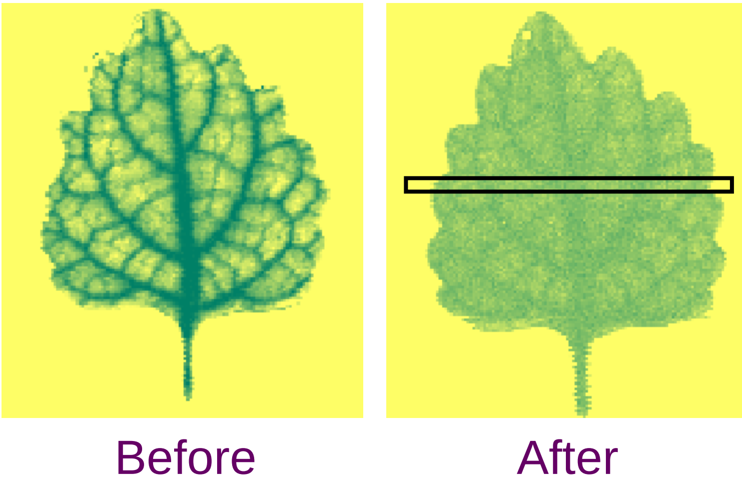
THz pulsed imaging

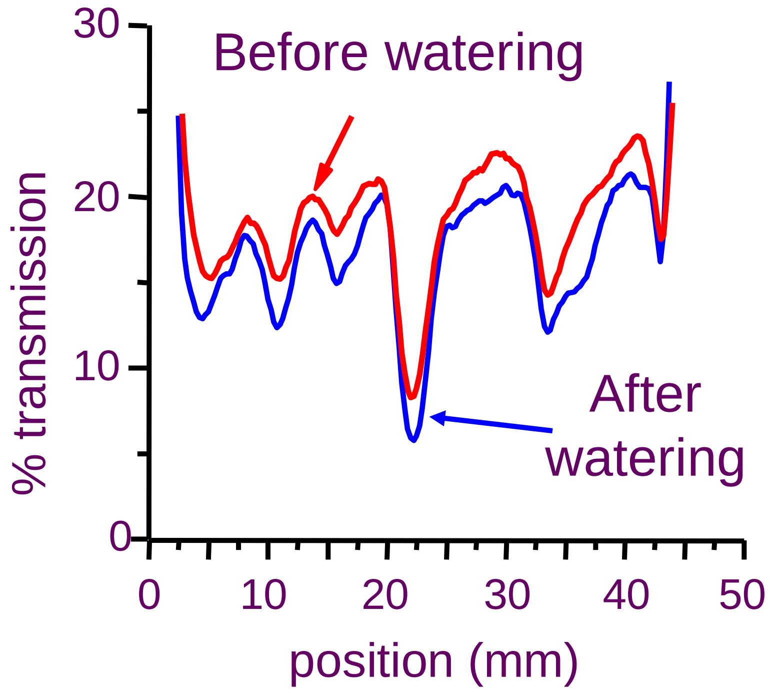




Paraffin – embedded melanoma

Water content in a living leaf





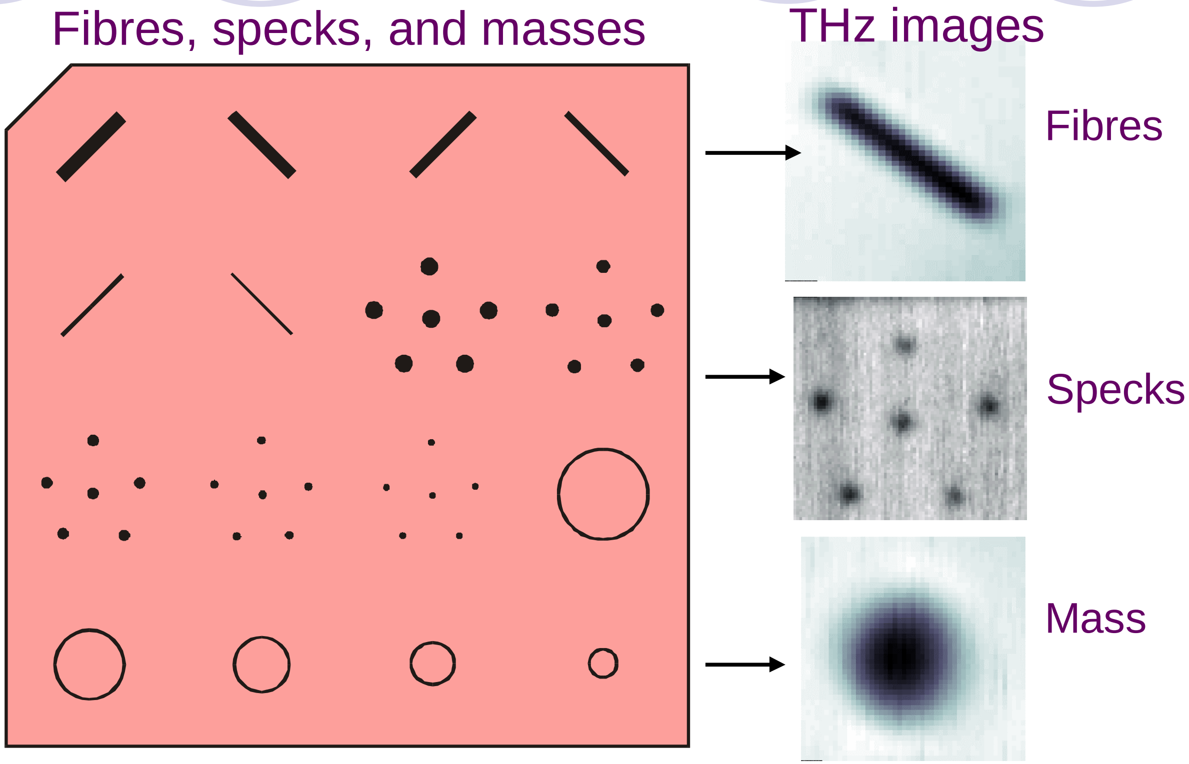
Proof of principle experiment:

Plant allowed to dry, and then watered

As the leaf re-hydrates, THz transmission decreases

Changes smaller than 1% are detectable

Mammographic phantom



Phantom is designed to perform a quantitative evaluation of the system's ability to image small structures similar to those found clinically. THz system resolved 0.4 mm fibre, 0.25 mm mass and 0.24 mm speck.

X-C Zhang et al. Rensselaer Polytechnic Institute, Troy, USA

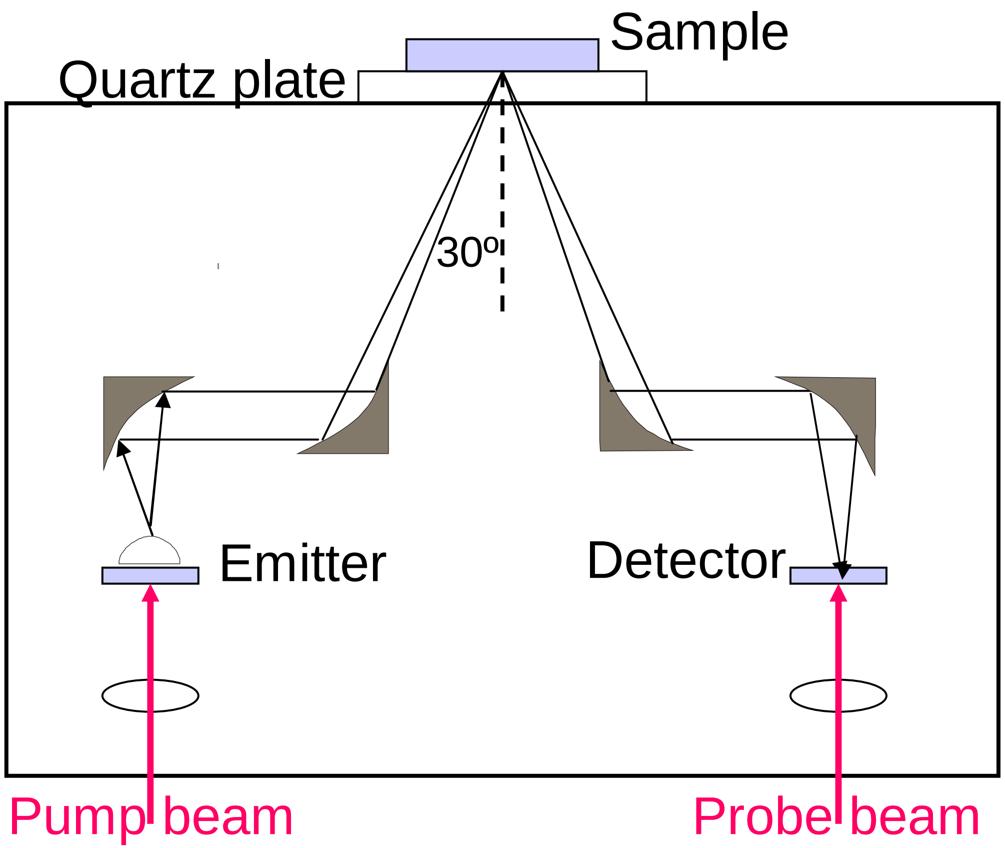
Commercial development

Transmission / reflection spectroscopy

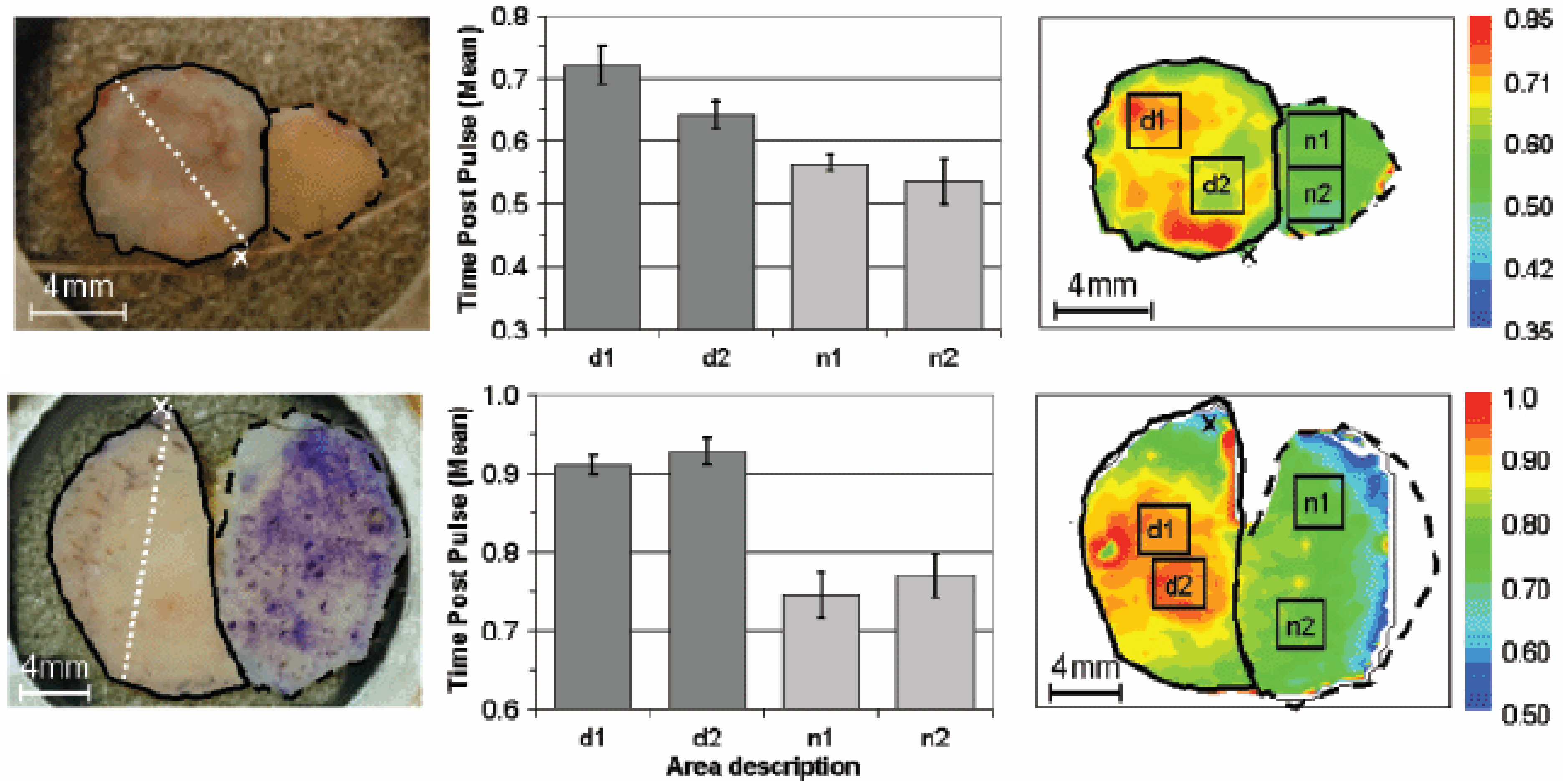
Reflection imaging system

Remote probe imaging

THz reflection imaging

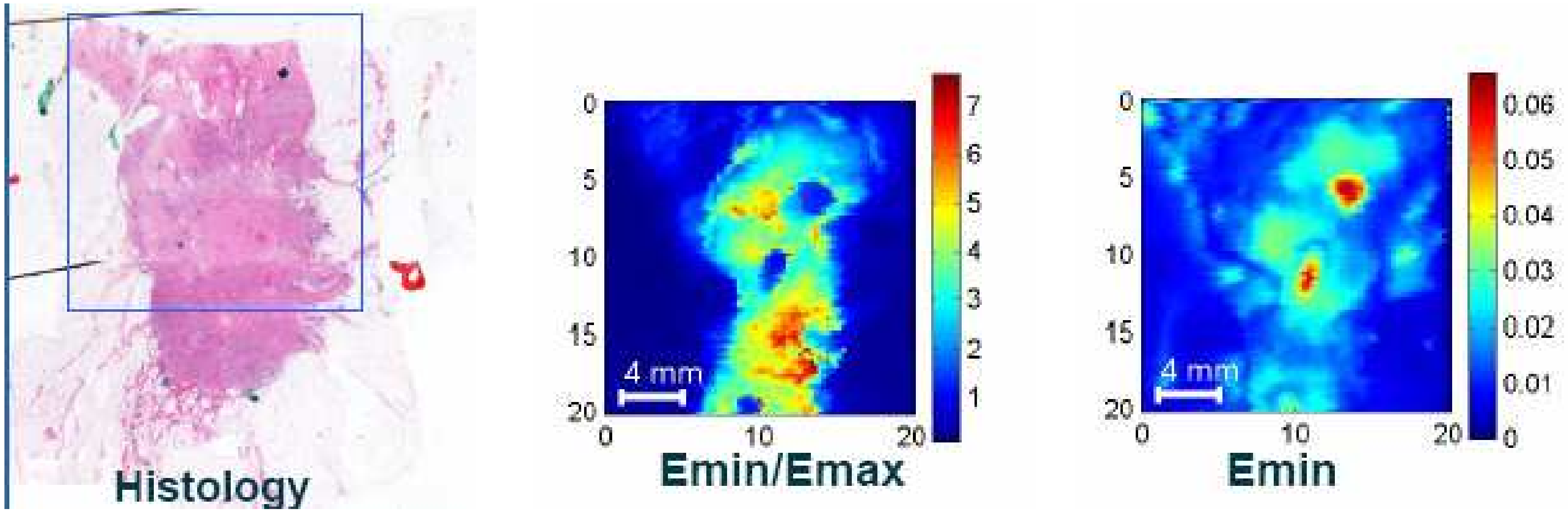


Ex vivo BCC



Woodward et al. JID 2003

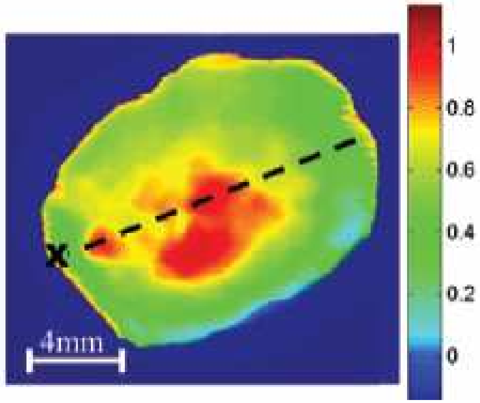
TPI of breast cancer *(ex vivo)*



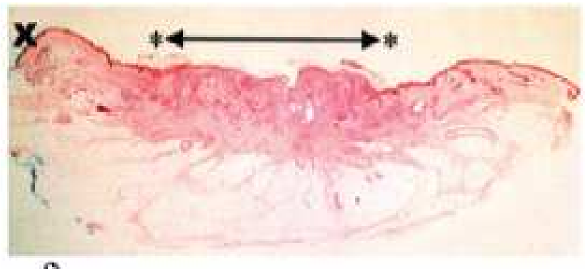
Fitzgerald et al. 2004

In vivo BCC

Clinical image



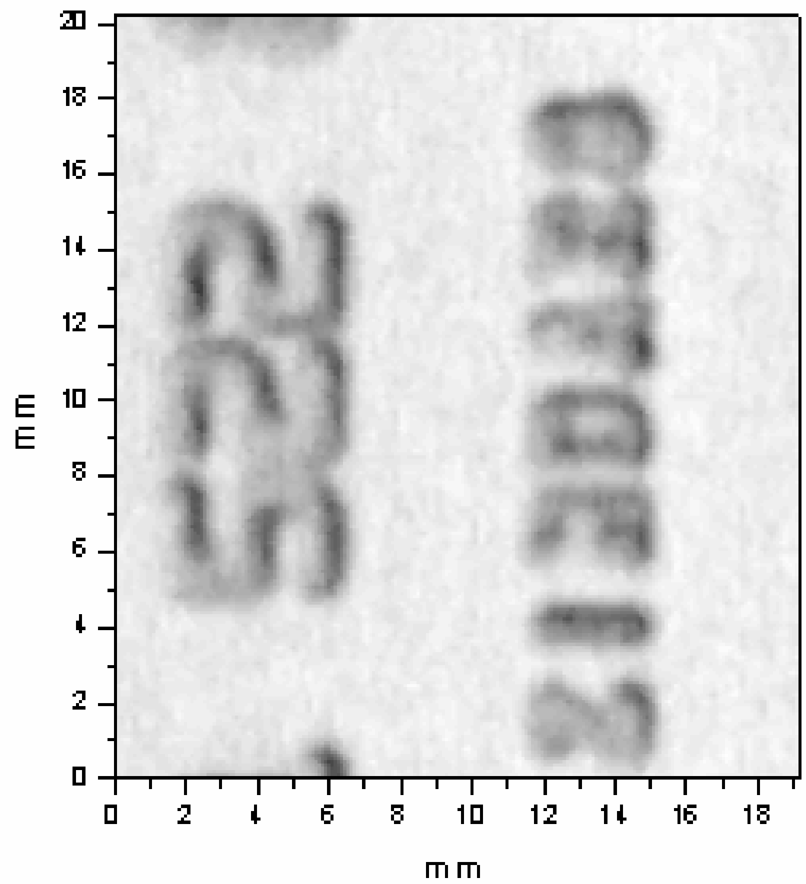
THz image



Histology section

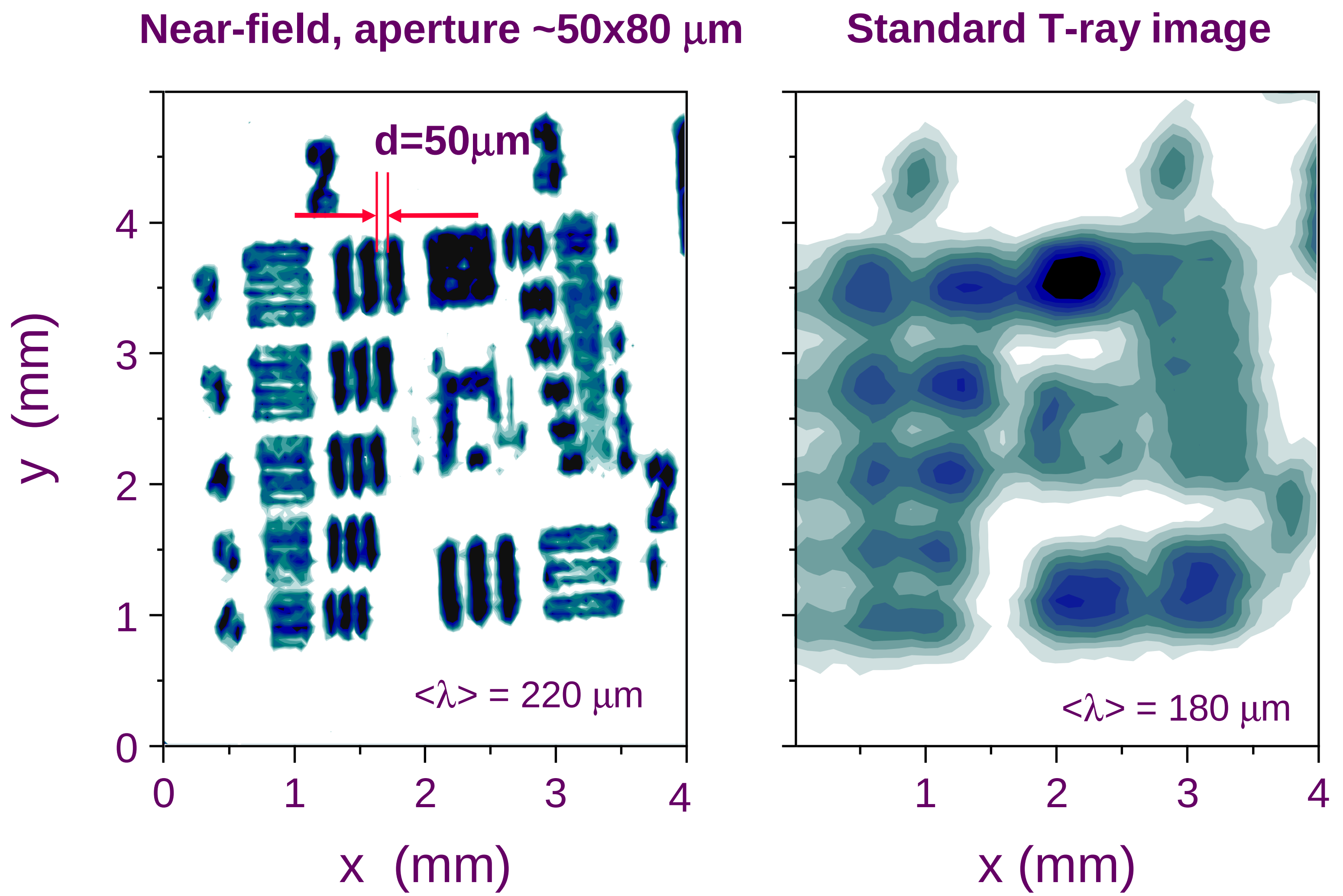
Wallace et al. BJD 2004

Limits of resolution (~100 μm)

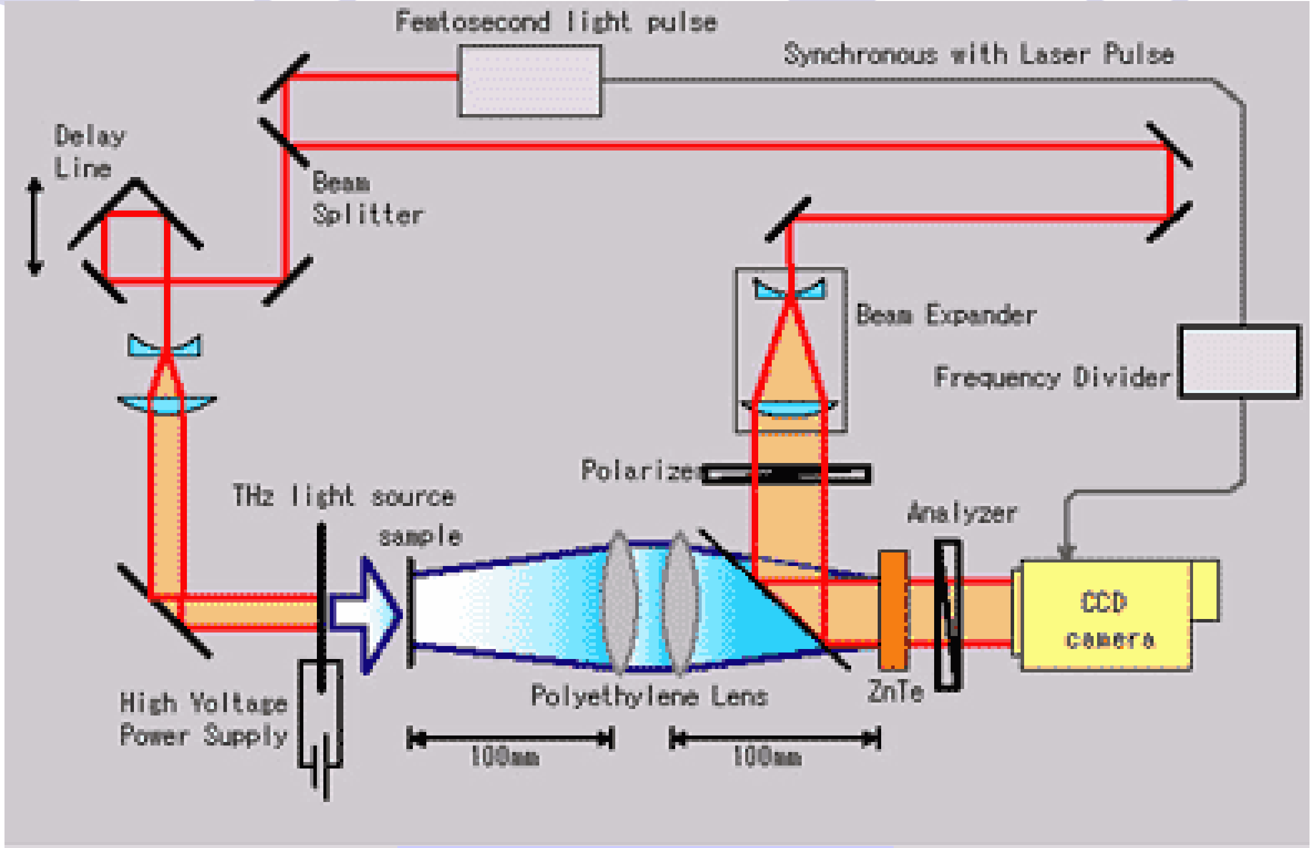


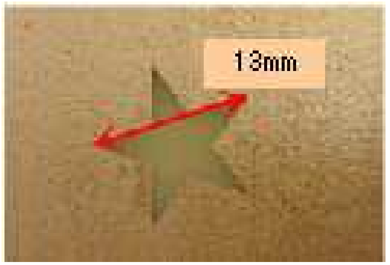
Courtesy: Dave Zimdars, Picometrix, Inc, Ann Arbor, USA

Near-field imaging (aperture at the sample) can enhance spatial resolution.



Real-time imaging

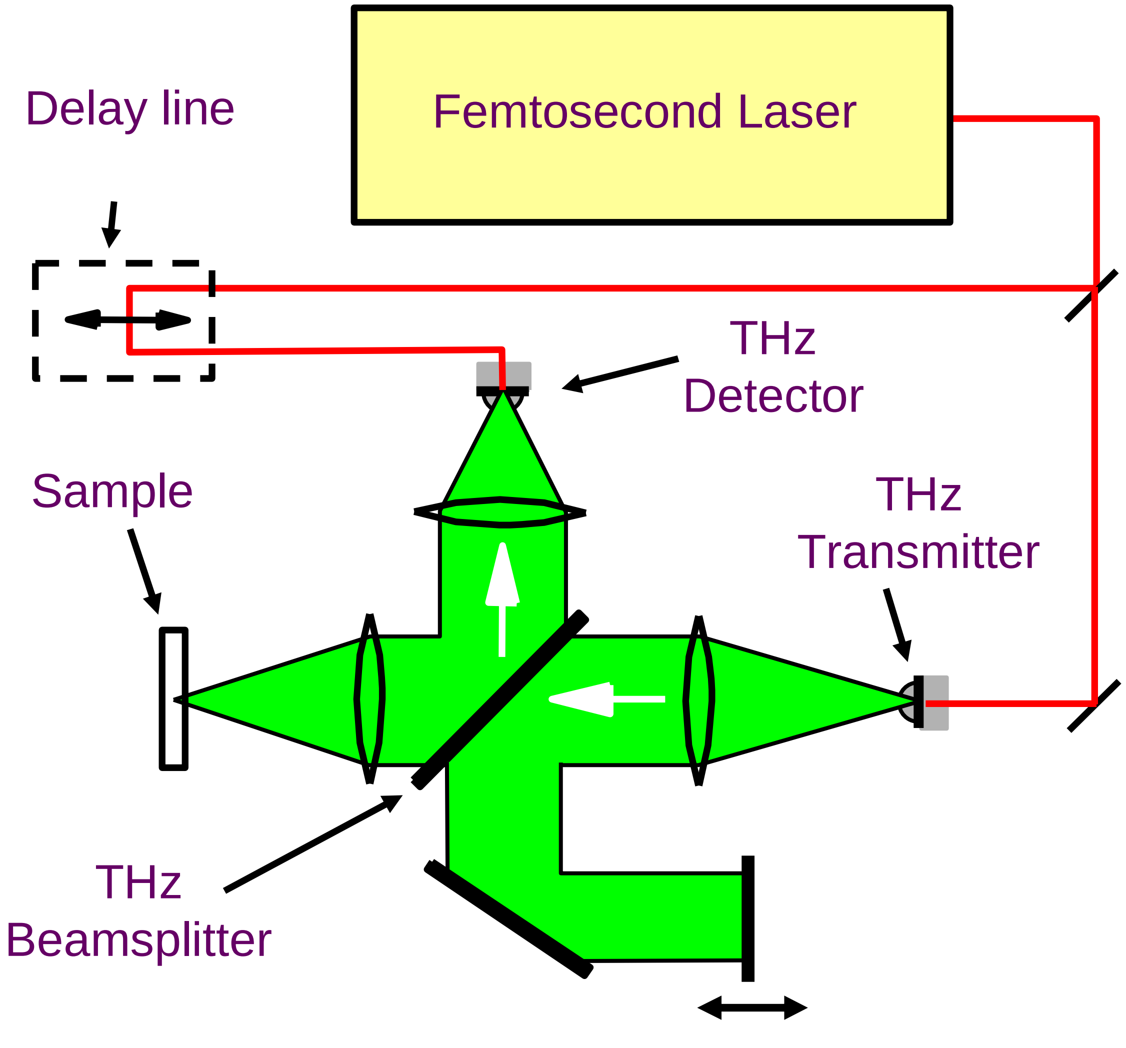




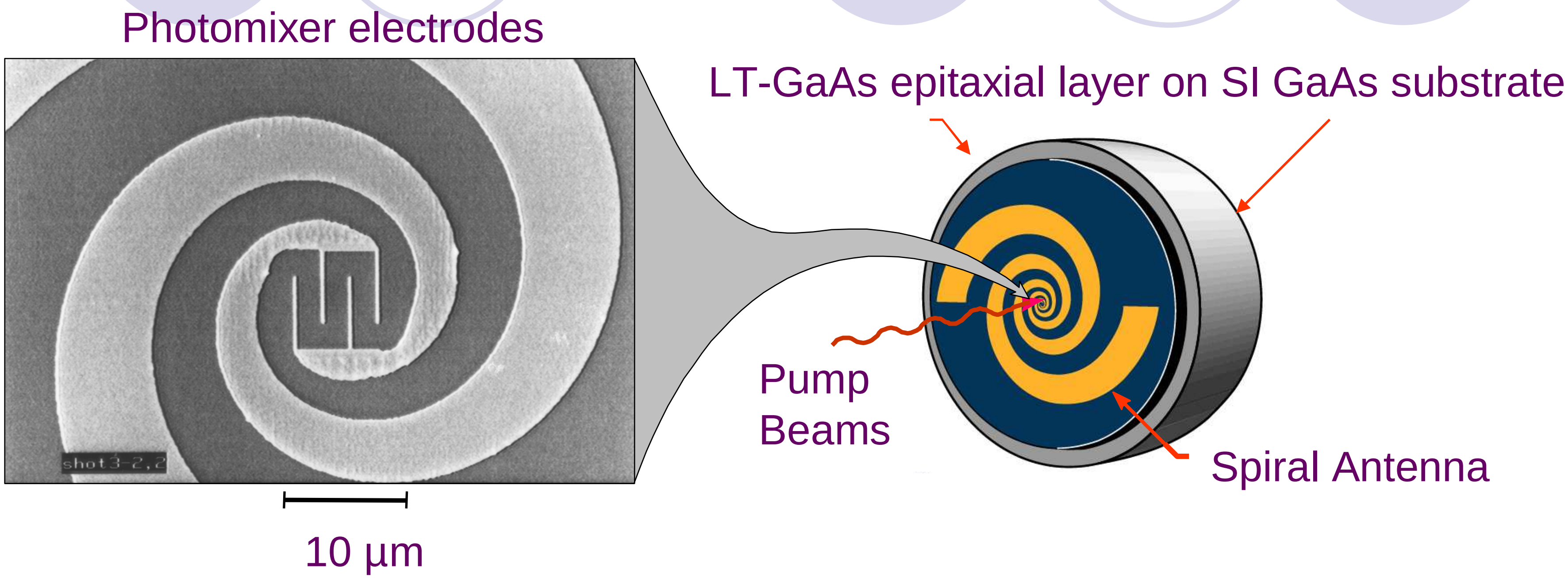
Resolution ~1.3mm

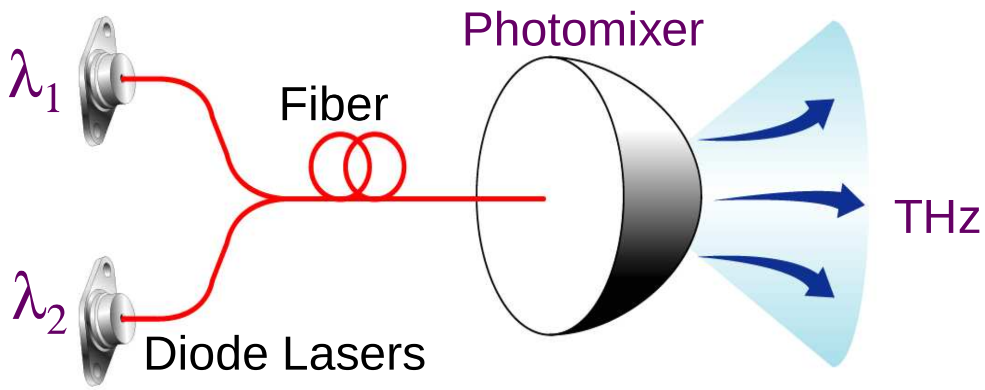
Tochigi-Nikon Corp.

Interferometry improves the depth resolution

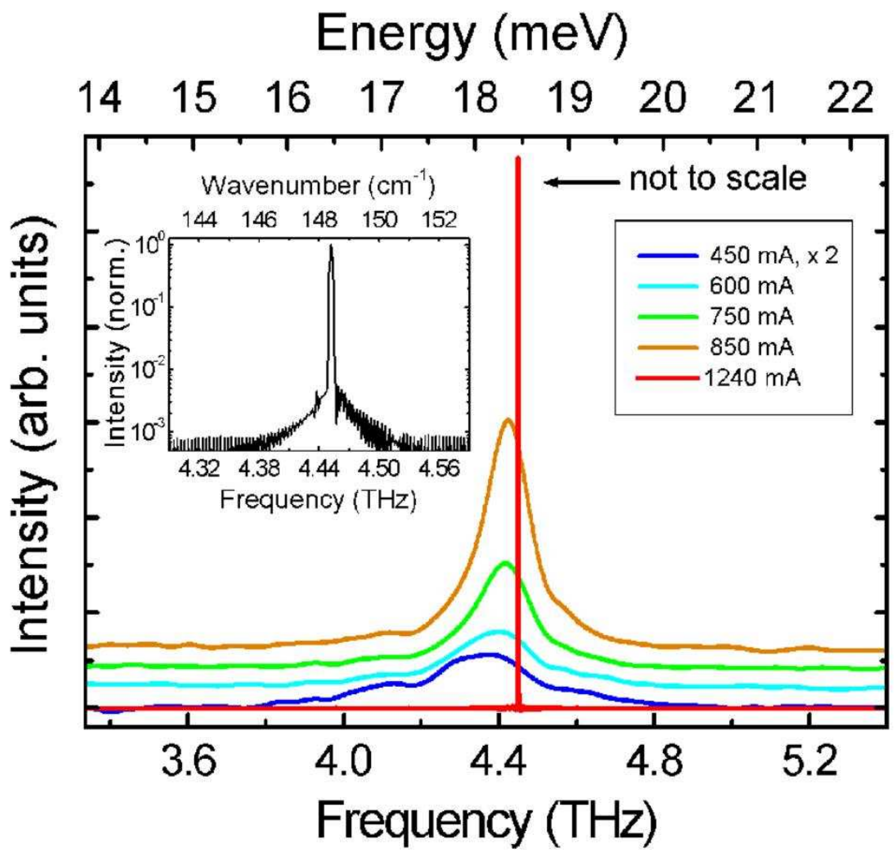


Photomixing (difference frequency generation)





cw THz : Quantum Cascade Lasers



Köhler_fig3

- Terahertz semiconductor-heterostructure laser. R Kohler, A Tredicucci, F Beltram, HE Beere, EH Linfield, AG Davies, DA Ritchie, RC Iotti and F Rossi. *Nature* 2002; 417: 156-159.

(Collaboration between INFM (Italy) and University of Cambridge, performed under the EC FP5 programme)

Medical imaging techniques

- Standard X-rays
- X-ray CT
- Radioisotope
- PET
- MRI / MRS / fMRI
- Ultrasound
- Applied potential tomography
- MEG
- Optical coherence tomography
- Confocal microscopy
- Infrared FT spectroscopy
- Fluorescence (UV)
- Raman spectroscopy
- mm wave / microwave

Future work

- Availability of stable terahertz systems
- Control of experimental variables
- Need to balance discovery-driven with hypothesis-driven studies
- Opportunities in data analysis
- More work on safety
- Exploitation of linear frequency dependence (analogy to broadband ultrasound attenuation, dual energy absorptiometry)
- Phase contrast methods (detection of anomalies, range finding, phase contrast analogues)
- Hybrid or synergistic technologies

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