Ultrasound Assisted Micro-Endoscopy for Medical Applications

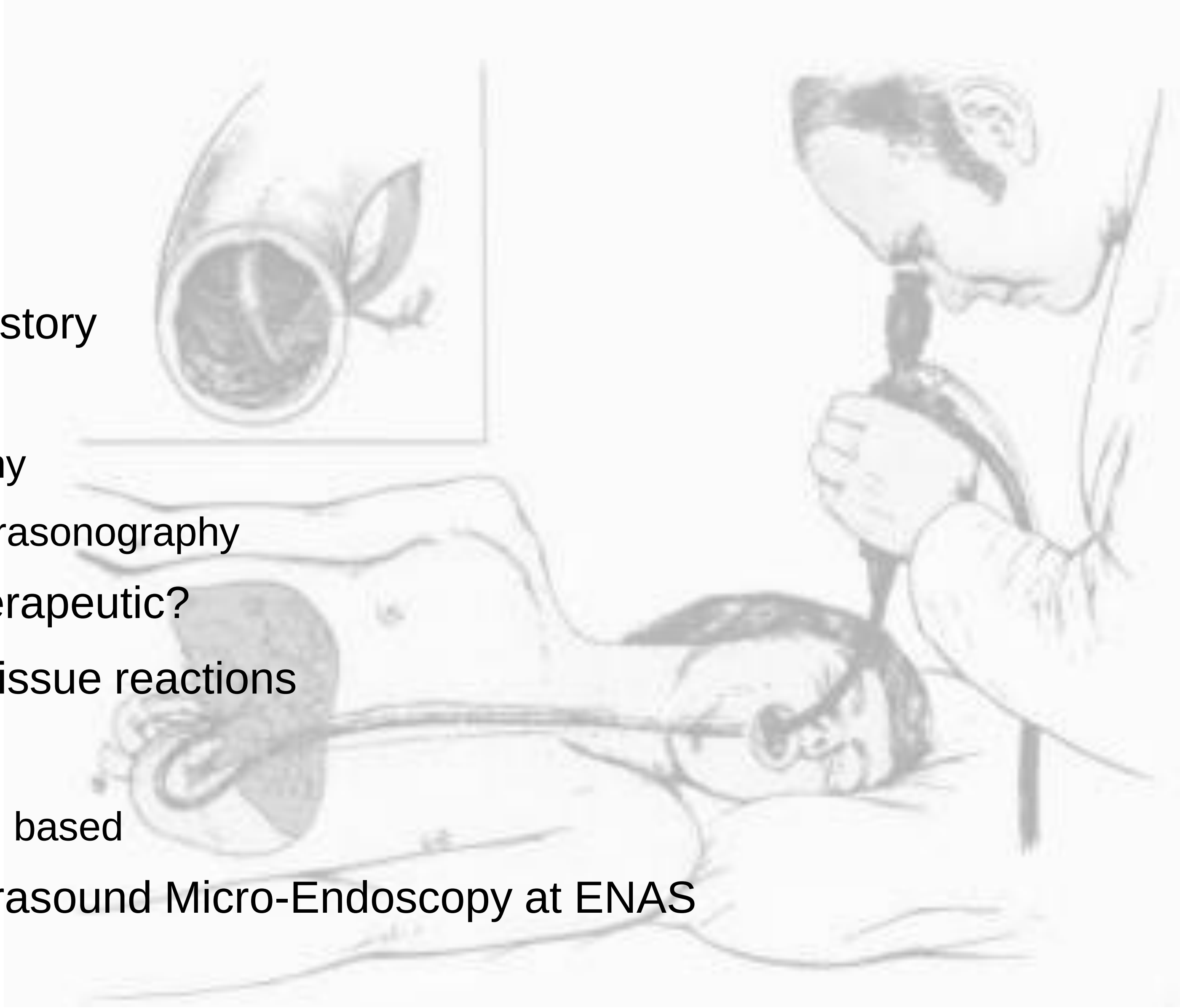
N. Saeidi, M. Baum

Fraunhofer ENAS

Department System Packaging

Chemnitzer Seminar „System Integration Technologies“ , 13 & 14 June 2017

Outline



- Introduction & History
  - Endoscopy
  - Ultrasonography
  - Endoscopic ultrasonography
- Diagnostic or therapeutic?
- Ultrasound and tissue reactions
- Technology
  - Piezo or silicon based
- Research on Ultrasound Micro-Endoscopy at ENAS
    - DeNeCoR
    - Endostim

Source: http://www.radtechonduty.com/2015/01/endoscopy-ercp-procedure.html

Enodscopy

1806 - Phillipp Bozzini

1853 - Antonin Jean Desormeaux

1865 - Sir Francis Cruise

1865 - Alexander Ebermann

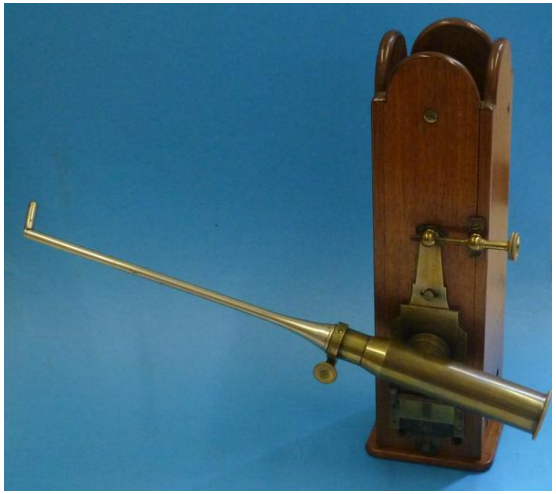
1883 . David Newman

Bozzini's endoscope

Source: Website of American College of Surgeons

Desormeaux's endoscope

Source: Website of European Association of Urology



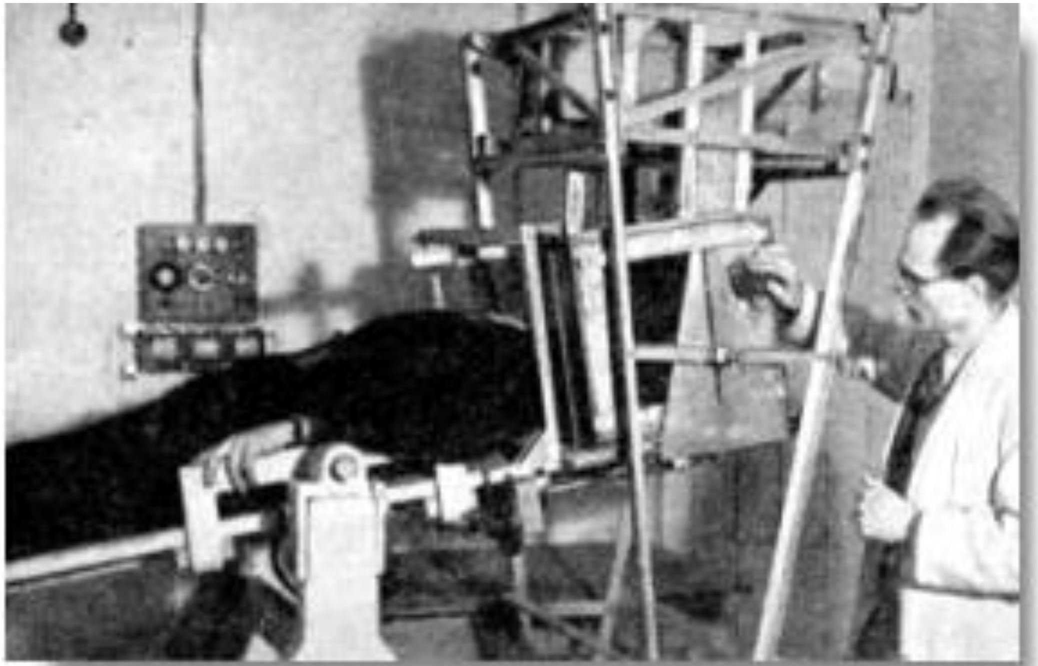
Cruise's endoscope

Source: Website of British Association of Urological Surgeon

Ultrasonography (medical ultrasound)

1940s - Karl Dussik

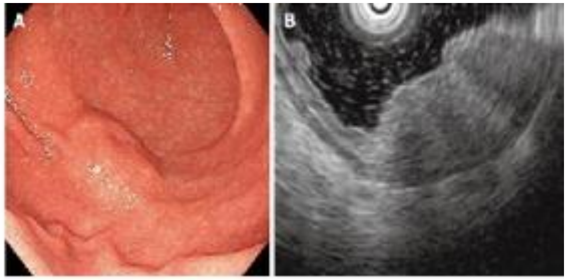
1950s – First practical (diagnostic) ultrasound devices



Source: http://www.ob-ultrasound.net/dussikbio.html

Endoscopic ultrasonography (EUS)

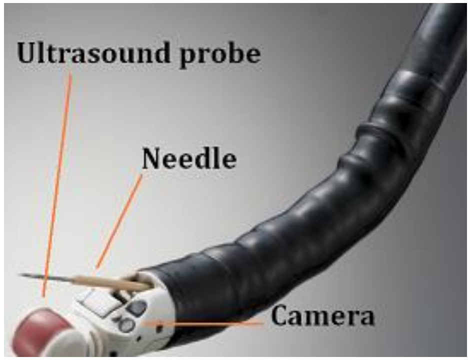
- Combining medical ultrasound and endoscopy
- Endoscopy images are captured from the surface of tissue while ultrasound can capture profile of the tissue to some depth
  - e.g. while an abnormality or suspicions area are detected by endoscopy, ultrasound comes to provide a more precise image
- Primarily used for examining gastrointestinal or lung tracts



Source:
http://www.grupuge.com.pt/information-to-pacients/endoscopic-ultrasound.html

Diagnostic or Therapeutic ?

- Endoscopy
  - A diagnostic procedure
- Ultrasound
  - Mainly imaging but also in use for therapy as non-surgical technique
    - Thermal:
      - Low power ultrasound to treat of joint or tendon inflammation
      - Lesion ablation (e.g. fibroid)
    - Non-thermal
      - lithotripsy
      - Cataract removal
- Endoscopic ultrasonography
  - currently considered as a diagnostic modality
    - Some tissue sampling or removal capability



Source: http://health.usf.edu/medicine/internalmedicine/digestive/eus

FDA approved modes of ultrasound therapy

Therapy Method	Therapeutic Outcome	Bioeffect Mechanism	Device Characteristics		
			Applicator	Frequency	Delivery
Unfocused beam	Tissue warming	Heating	Portable handheld	1–3 MHz	Continuous or repeated bursts
Hyperthermia	Cancer therapy	Regional heating	Multielement applicator	1–3.4 MHz	1 h
High-intensity focused ultrasound	Uterine fibroid ablation	Thermal lesion	Computer directed	0.5–2 MHz	Long bursts
High-intensity focused ultrasound	Glaucoma relief	Permeabilization	Fixed probe with water bath	4.6 MHz	1–3 s
High-intensity focused ultrasound	Laparoscopic tissue ablation	Thermal lesion	Handheld	4 MHz	Long bursts
High-intensity focused ultrasound	Laparoscopic or open surgery	Thermal lesion	Handheld	3.8–6.4 MHz	Long bursts
Focused ultrasound	Skin tissue tightening	Thermal lesion	Handheld, imaging and treatment	4.4–7.5 MHz	20-to 50-ms bursts
Extracorporeal lithotripsy	Kidney stone comminution	Mechanical stress, cavitation	Mainframe with image guidance	≈150 kHz	Shock waves

Miller et al., Overview of Therapeutic Ultrasound Applications and Safety Considerations. Journal of Ultrasound in Medicine (2012), 31: 623–634.

FDA approved modes of ultrasound therapy

Therapy Method	Therapeutic Outcome	Bioeffect Mechanism	Device Characteristics		
			Applicator	Frequency	Delivery
Intracorporeal lithotripsy	Kidney stone comminution	Mechanical stress, cavitation	Percutaneous probes	25 kHz	Continuous
Extracorporeal shock wave therapy	Plantar fasciitis, epicondylitis	Unknown	Mainframe with applicator head	≈150 kHz	Shock waves
Phacoemulsificatio n	Lens removal	Vibration, cavitation	Generator with probe	40 kHz	Continuous
Ultrasound-assisted liposuction	Adipose tissue removal	Fat liquefaction, cavitation	Generator with probe	20–30 kHz	Continuous
Tissue cutting and vessel sealing	Laparoscopic or open surgery	Thermal lesion, vibration	Handheld	55.5 kHz	Continuous
Intravascular ultrasound	Thrombus dissolution	Unknown, gas body activation	Intravascular catheter	2.2 MHz	Continuous
Skin perm-eabilization	Transdermal drug delivery	Unknown	Handheld	55 kHz	Continuous
Low-intensity pulsed ultrasound	Bone fracture healing	Unknown	Attached transducer	1.5 MHz	Pulsed, long duration

Miller et al., Overview of Therapeutic Ultrasound Applications and Safety Considerations. Journal of Ultrasound in Medicine (2012), 31: 623–634.

Interaction of ultrasound and tissue from a device developer perspective

Diagnostic/therapeutic ultrasound

- Different tissues have different acoustic impedances

Material	Velocity (m/s)	Density (kg/m^3)	Attenuation (dB/cm MHz)	Acoustic Impedence (MRayl)	Source
Air	330	1.2	–	0.0004	–
Blood	1584	1060	0.2	1.68	ICRU 1998
Bone, Cortical	3476	1975	6.9	7.38	Hoffmeister et al. 2000
Bone, Trabecular	1886	1055	9.94	1.45	Wear 1999
Brain	1560	1040	0.6	1.62	ICRU 1998
Breast	1510	1020	0.75	1.54	ICRU 1998
Cardiac	1576	1060	0.52	1.67	ICRU 1998
Connective Tissue	1613	1120	1.57	1.81	Mast 2000
Cornea	1586	1076	–	1.71	Mast 2000
Dentin	3800	2900	80	8.0	Kossoff and Sharpe 1966
Enamel	5700	2100	120	16.5	Xu et al. 2000
Fat	1478	950	0.48	1.40	Mast 2000
Liver	1595	1060	0.5	1.69	ICRU 1998
Marrow	1435	–	0.5	–	Clarke et al. 1994
Muscle	1547	1050	1.09	1.62	Mast 2000
Tendon	1670	1100	4.7	1.84	Hoffmeister et al. 1994
Soft tissue (Average)	1561	1043	0.54	1.63	Mast 2000
Water	1480	1000	0.0022	1.48	–

Culjat et al., A Review of Tissue Substitutes for Ultrasound Imaging, Ultrasound in Medicine & Biology, Volume 36, Issue 6, June 2010, Pages 861-873

Interaction of ultrasound and tissue from a device developer perspective

Therapeutic ultrasound (ablation)

- Thermal dose
  - CEM43 is a measure to evaluate thermal dose (a model introduced by Sapareto et al.)

$$CEM43°C = \sum_{i=1}^{n} t_i \, R^{43-T_i}$$

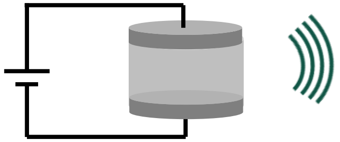
$CEM43°C$	Cumulative number of Equivalent Minutes at 43 °C
t_i	Time interval
T	Average temperature during time interval
R	Temperature dependence of cell death rate
	$T < 43°C$ -> $R = 0.25$ $T \geq 43°C$ -> $R = 0.5$

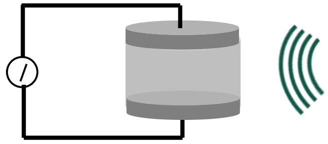
Sapareto SA, Dewey WC. Thermal dose determination in cancer therapy. Int J Radiat Oncol Biol Phys. 1984; 10:787–800.

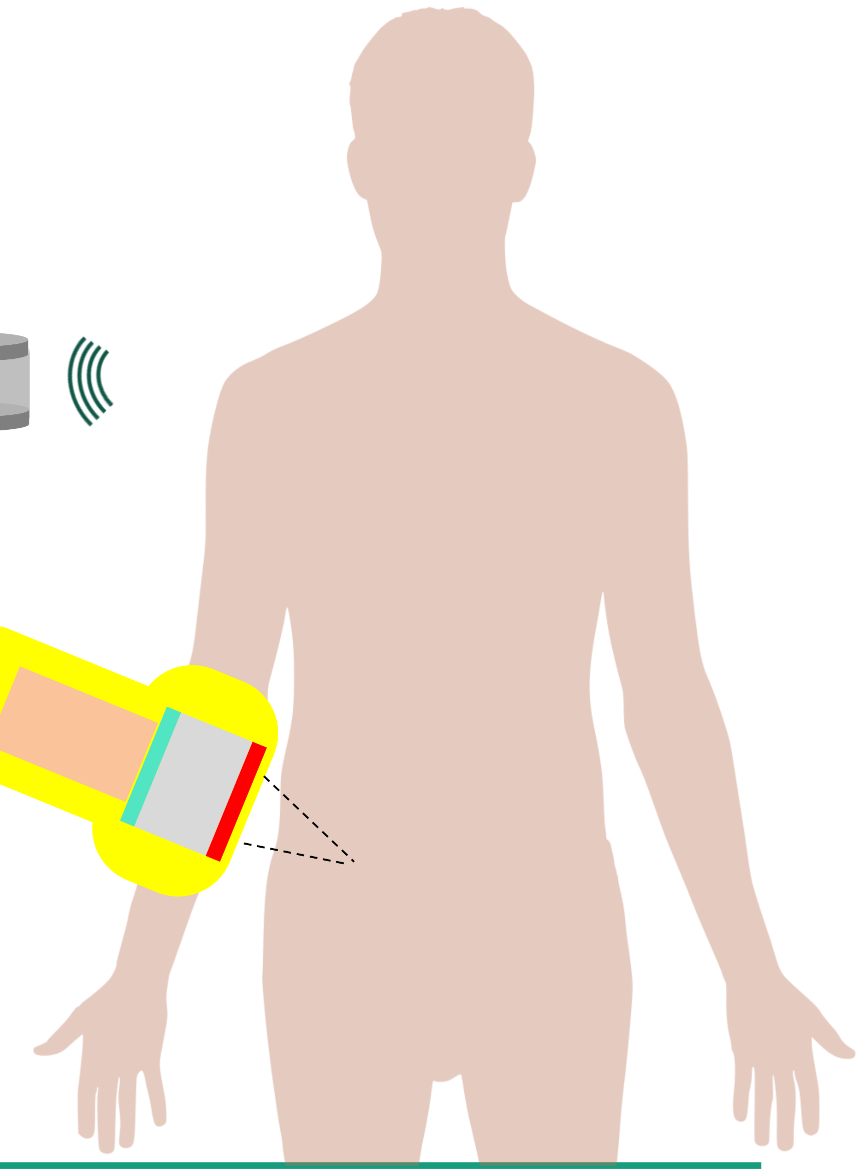
Fraunhofer ENAS

A closer look at the technology
Generating Ultrasound

- Piezoelectric based transducers







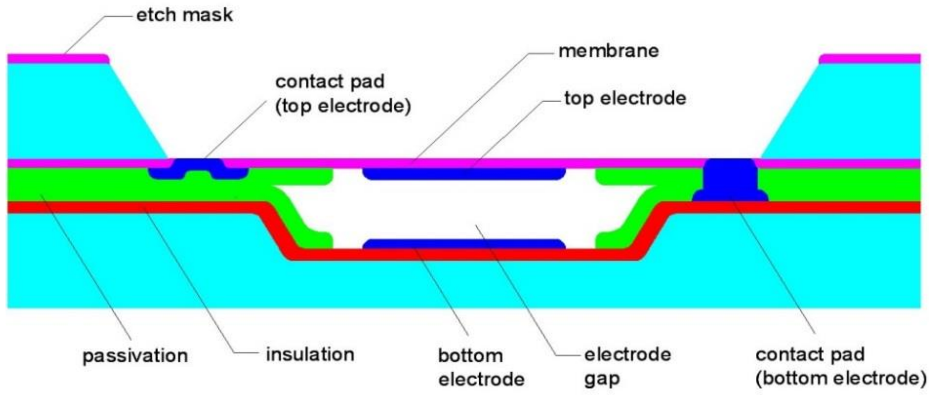
  - Market dominant
  - Established manufacturing techniques

Fraunhofer ENAS

A close look the technology
Generating Ultrasound

- Capacitive Micromachined Ultrasound Transducer (CMUT)
  - Advantages
    - Wide bandwidth
    - Possibility to integrate with the driving electronics
    - Batch processing
    - Various configurations, geometries
    - Miniaturized
    - Wider temperature range operation

CMUT design - ENAS



Fraunhofer ENAS

Research on Ultrasound Micro-Endoscopy @ ENAS

DeNeCoR --- Devices for NeuroControl and NeuroRehabilitation
EU funded

Goals:

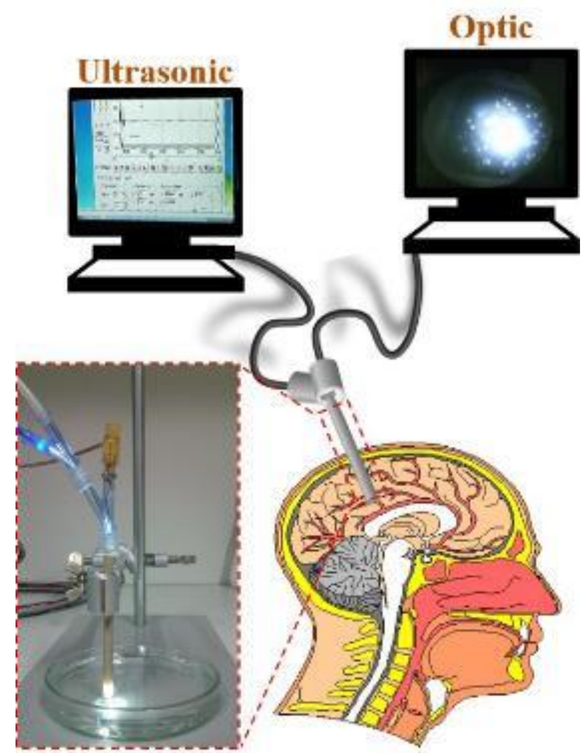
- Resolve the incompatibility between electronic neuromodulation and key neurological diagnostic systems such as EEG and MRI
- Demonstrate compatibility between therapeutic and diagnostic systems.
- Demonstration of an MRI compatible Transcranial Magnetic Stimulator (TMS)
- Development of new sensor and packaging technology for invasive and non-invasive neural sensing (e.g. EEG), compatible with the MRI and TMS environment.
- Demonstration of an MRI-guided endoscopic system with integrated ultrasound system, miniaturization of electronics and 3D packaging

Partners: Philips Medical Systems Nederland, Medtronic, Universitair Medisch Centrum Utrecht, Stichting Kempenhaeghe, Technische Universiteit Eindhoven, ST microelectronics, Politecnico di Torino, Universita Degli Studi di Pavia, Universita Degli Studi Roma Tre, Universita Degli Studi di Firenze, AIT Austrian Institute of Technology Gmbh, Guger Technologies Austria GTEC-A, Guger Technologies Spain GTEC-S, Plessey Semiconductors Limited, University of Sussex, Institut Mikroelektronickych Aplikaci s.r.o., Vysoké Učení Technické v Brne, Acondicionamiento

Fraunhofer ENAS

ENAS contributions

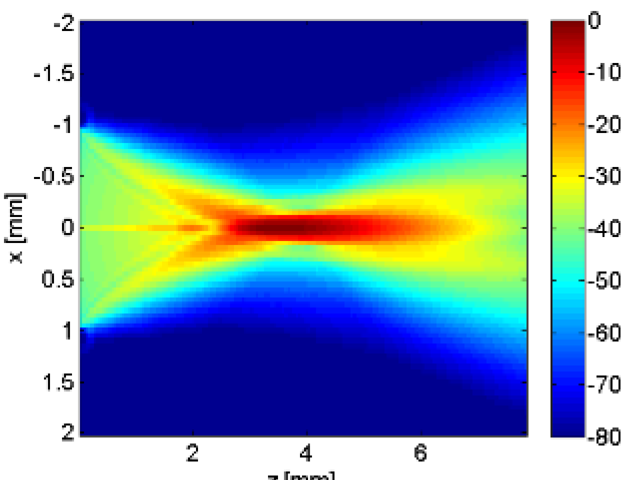
- MR conditionally safe µendoscope
  - Integration & evaluation of a µendoscope with optical and ultrasound functionalities
- Thin film encapsulation
  - Investigating multilayer thin film encapsulation
  - Parylene coating



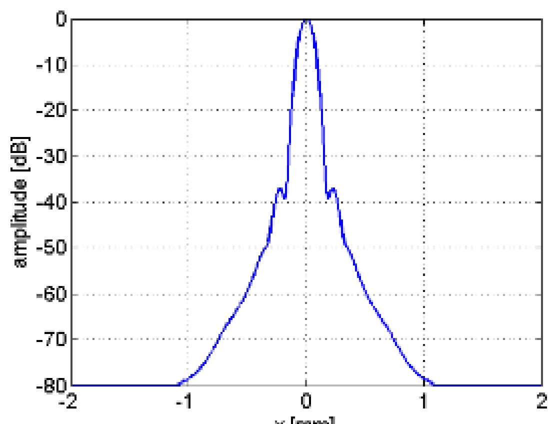
µendoscope

Prototypes of ultrasound transducer were fabricated (in collaboration with PVA TePla)

- Lens:
  - Material: quartz
  - Diameter: 2mm (-0.2 mm)
  - Length: 5.0 mm (+/- 0.2 mm)
  - Radius of curvature: 3 mm
    - Focal length: 3.8 to 4 mm in water
- Piezo-material: PZT ceramic
- Frequency range (15-20MHz)



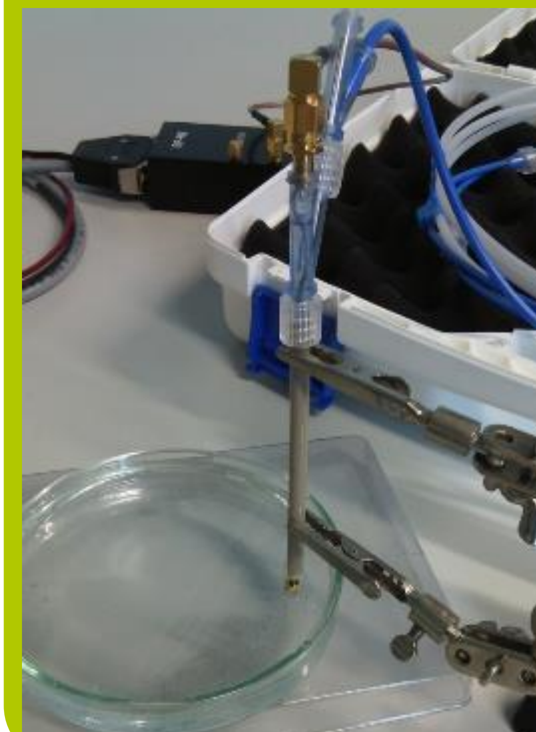
beam pattern at 20 MHz → Focal length: 3.8 to 4 mm



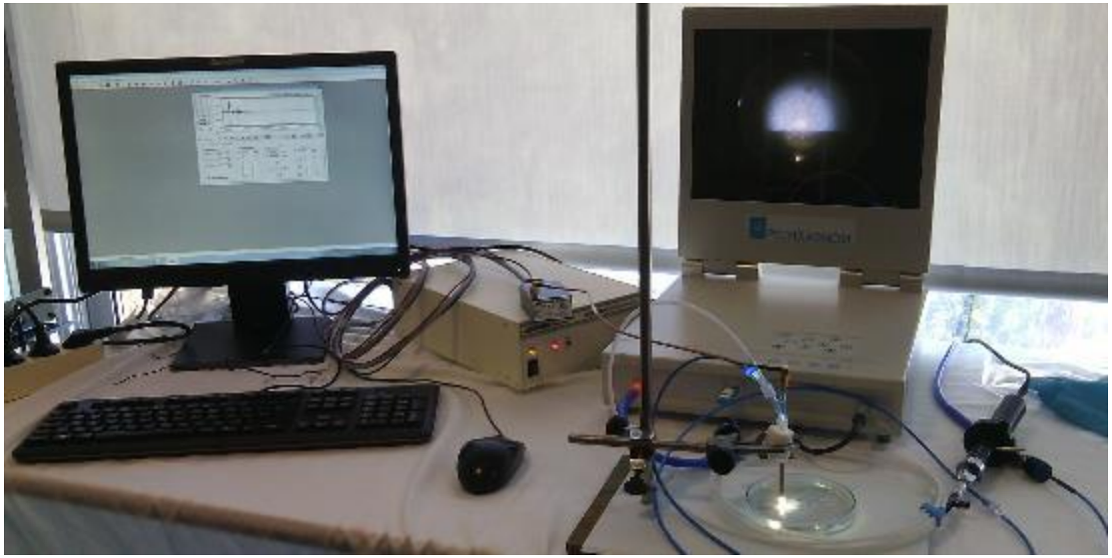
Beam profiles at 3.8 mm distance from the lens → lateral resolution: 0.2 mm

Integration of ultrasound & optical functionalities in a single probe

(in collaboration with PolyDiagnost)



µendoscope

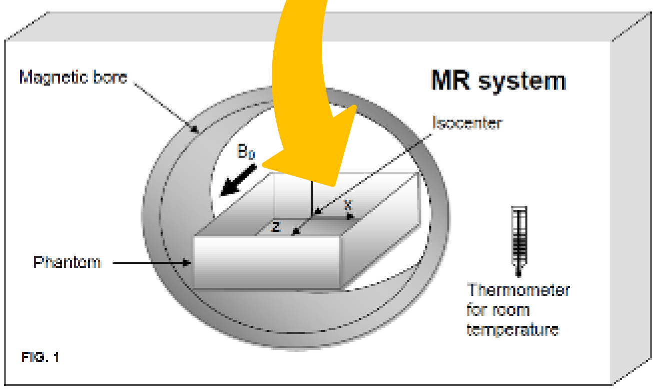


Workstations:

Two workstations, in laboratory setup, are used to display the acquired ultrasound signals and optical images.

MR Safety:

MR Safety test was performed (in collaboration with MR:comp)



- Conditions:
  - Combined Field Testing according to ISO/TS 10974
  - MR system: 3 Tesla
- Objective:
  - Function test after the exposure
- Results:
  - MR exposure has not affected the functionality

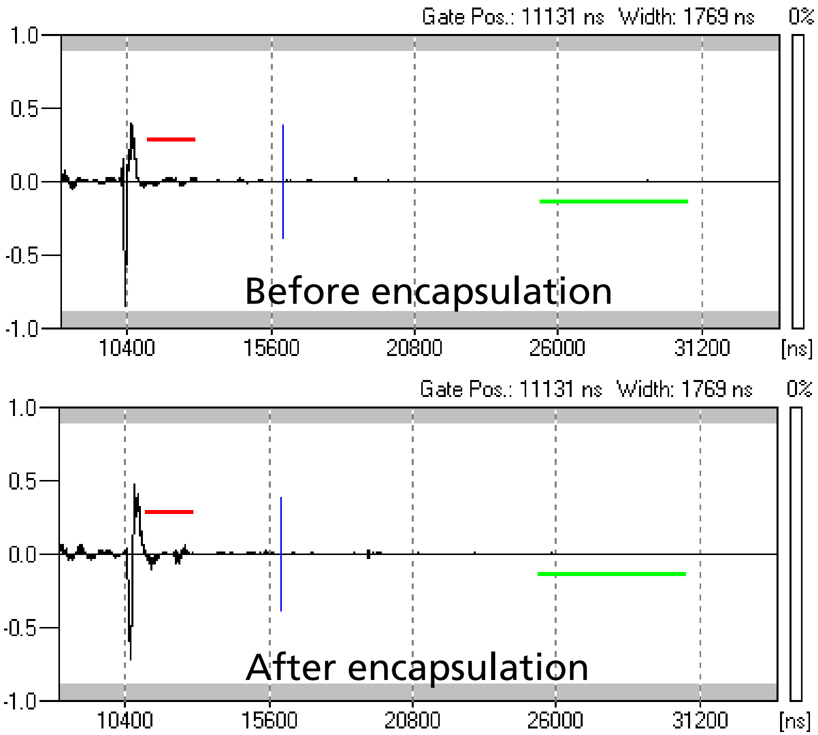
Thin film encapsulation

- Two approaches were investigated:
  - Multi-layer stack of thin films
  - Parylene thin film deposition
    - More suitable for the µendoscope due to its shape and geometry

Parylene deposition (~2µm) on the µendoscope

No change in optical/ultrasonic performance was observed

Examples of the performance tests



Fraunhofer ENAS

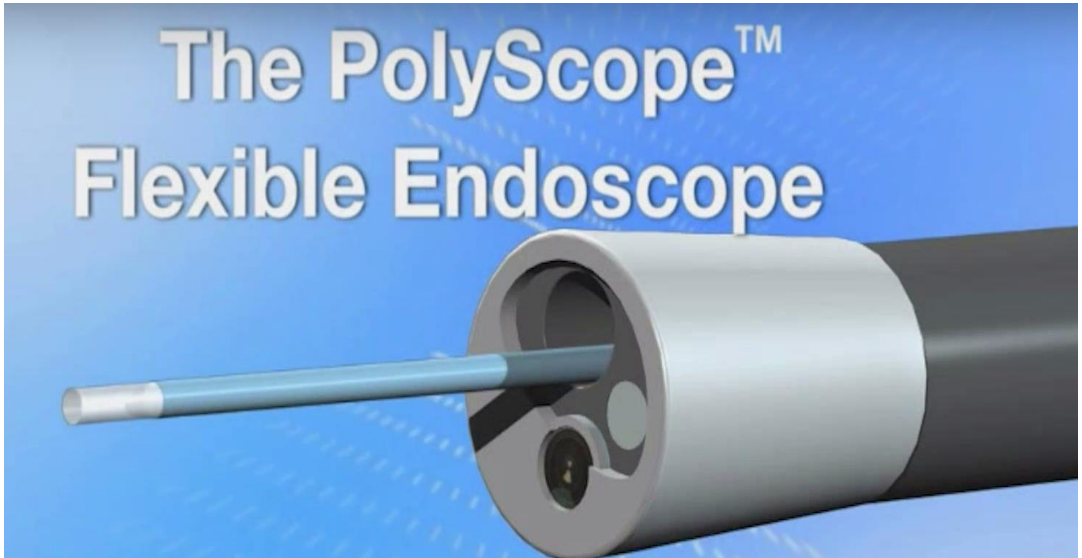
DENECOR

Video: http://www.denecor.info/en/dissemination/

Endostim
BMBF funded

Goal:

- Development of a miniaturized endoscope with integrated ultrasound transducer and CMOS camera
  - CMUT based
  - Diagnostics therapy



Target concept for EndoStim demonstrator

Acknowledgements

- European Commission (grant agreement No. 324257)
- German Federal Ministry of Education and Research (BMBF)
- Colleagues at System Packaging department and at ENAS,
- DeNeCoR & Endostim collaborators

Thank you!