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IMSAT INSTITUTE OF MEDICAL SCIENCE & TECHNOLOGY

UNIVERSITY OF DUNDEE

AAMP 2020

„Molecular Imaging (PET and MRI) guided Focused Ultrasound, a potential future application?“

Andreas Melzer

ICCAS University Leipzig, DE
IMSaT University Dundee, UK
visiting Professor AMIGO Project @ BHW Harvard Medical School
1000 Expert Plan Professor @ Chongqing University of Technology, China
General Secretary and Chairman of the Board www.iSMIT.org and www.EUFUS.org

presenting results from NANOPORATION, IIIOS, FUTURA & TRANS-FUSIMO FP7 and SONO-RAY BMBF Consortia

MARIE CURIE ACTIONS

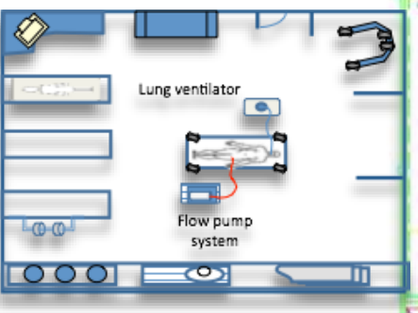
SEVENTH FRAMEWORK PROGRAMME

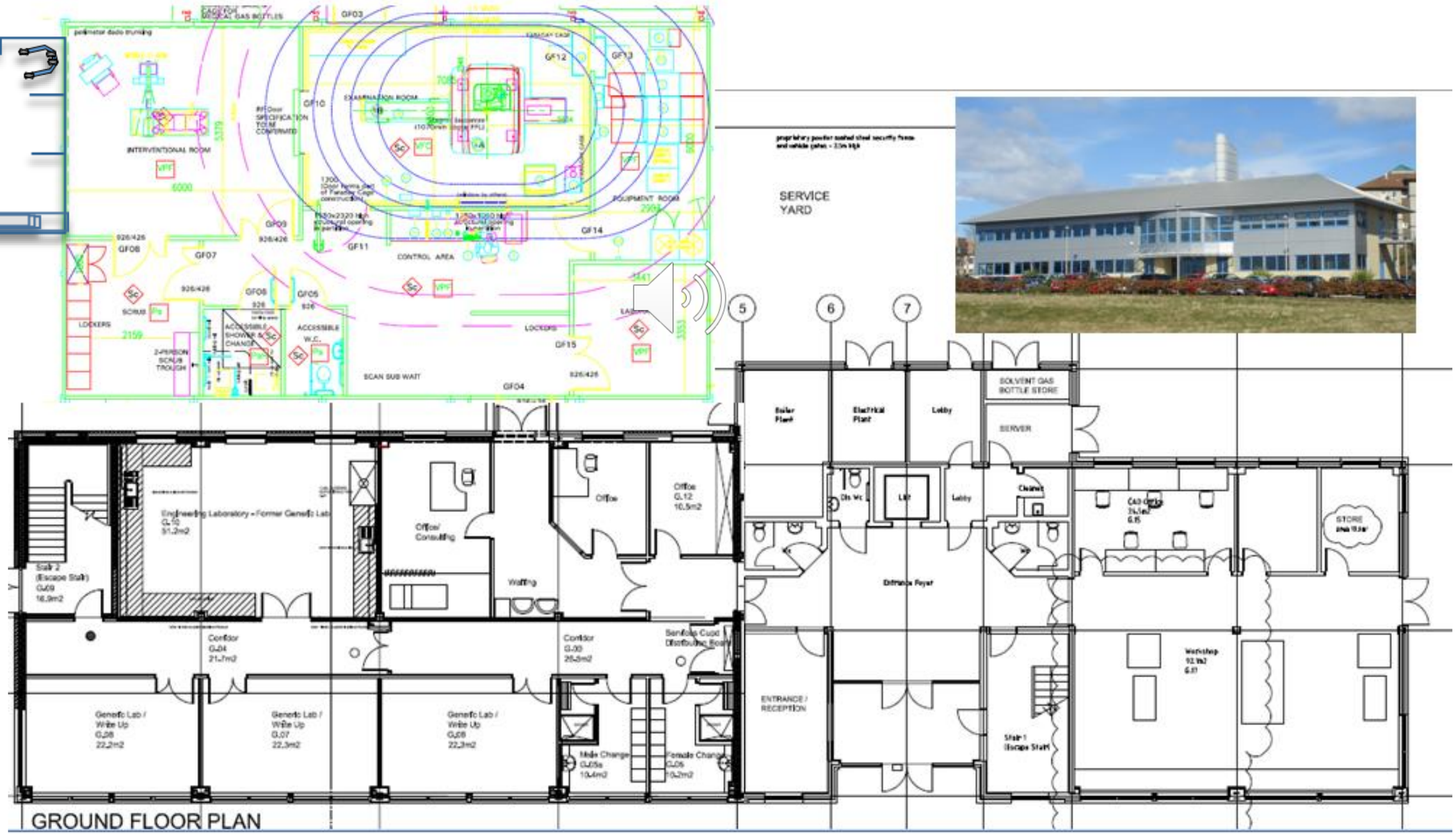
Nanoporation

I3OS

FUSIMO

IMSaT GE's first European Center of Excellence for MRI guided Interventions and Surgery 2008





Thiel Lab

IMSaT GE's first European Center of Excellence for MRI guided Interventions and Surgery 2008

One MR with numerous Diagnostic and Interventional applications

Multi-use capability workflow
HD Image Quality

Diagnosis & Screening

Biopsy Guidance

Surgical Oncology

Radiation Oncology

Non-radiation Based treatment (UF & WIP)

imagination at work

IMSaT GE's first European Center of Excellence for MRI guided Interventions and Surgery 2008

One MR with numerous Diagnostic and

Multi-u
HD Im

Non-radiation
Based treatment
(UF & WIP)

MR guided FUS

Screening

imagination at work

MRI Cleaner's Store 5.039

MRI Control Room 5.036

MRI Patient Waiting 5.035

Equipment Store 5.034

PET/CT Control Room 5.029

Pass Door To Be Locked Unless Emergency

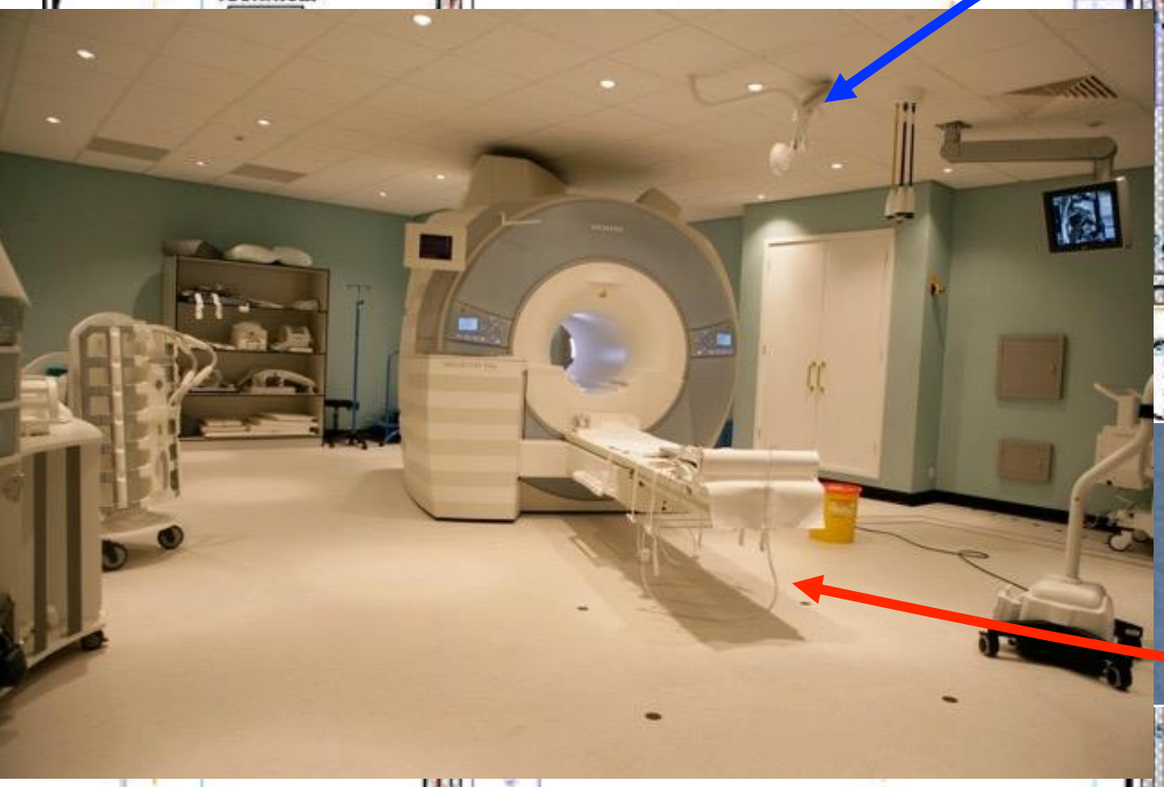
3Tesla MRI

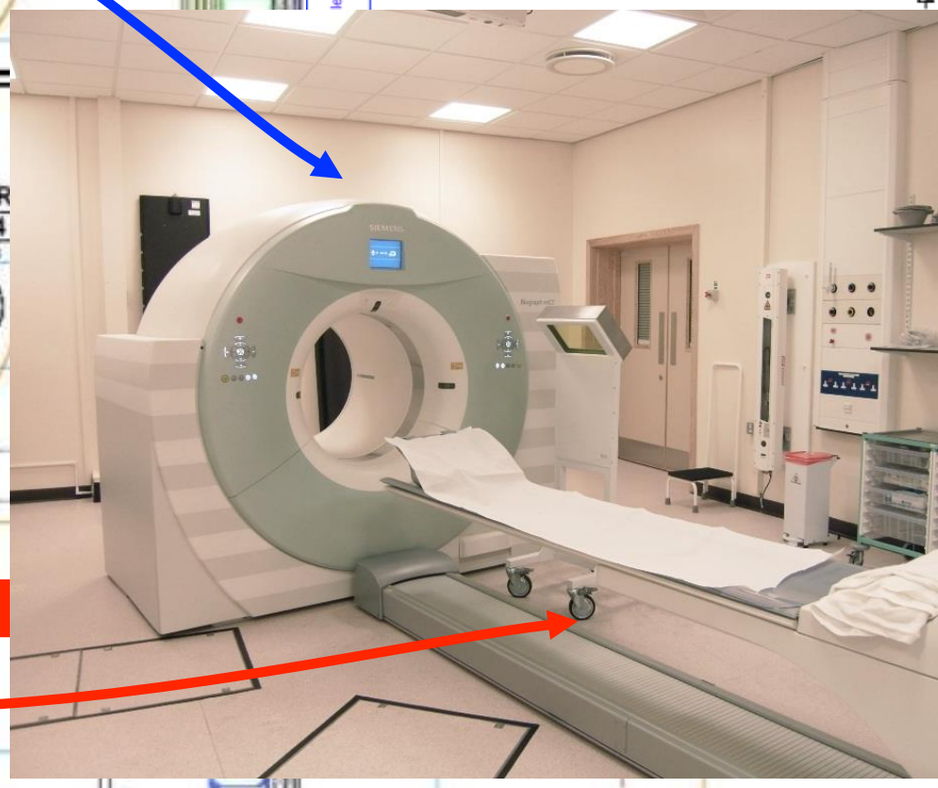
MRI Technical

Anaesth. & Resuscit Bay 5.033

Disposal R 5.044

Intervention S 5.032





Diagnostic Work Flow

Interventional Suite Angio, Ultrasound Endoscopy, Navigation & Robotics

Image guided Therapy Work Flow

Dundee MITOS Multimodalitiy Imgaging Operating System, 2005-8

from t
'/200

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Non invasive US/MRI guided Focused Ultrasound

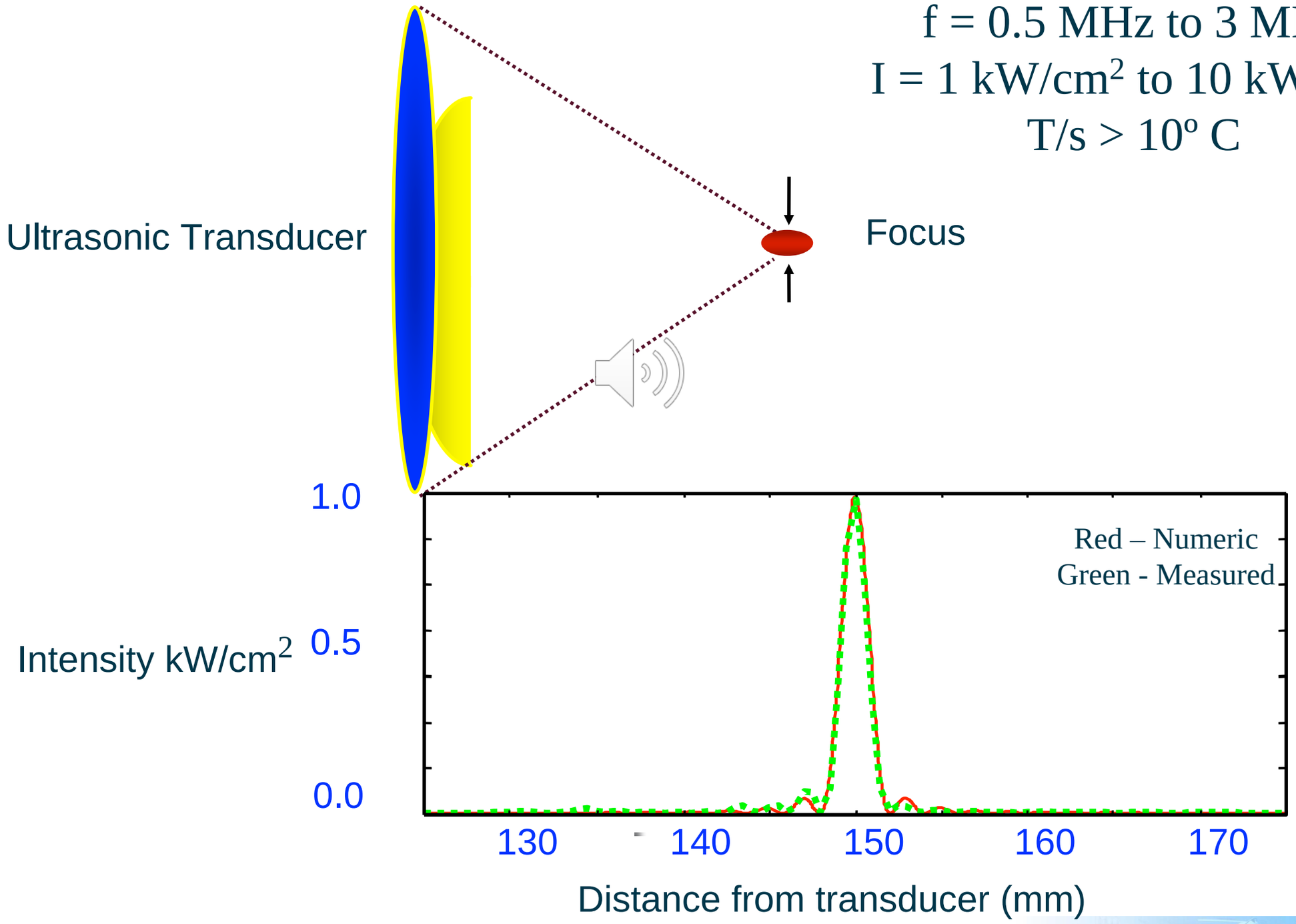
Thermal and non Thermal therapeutic effects

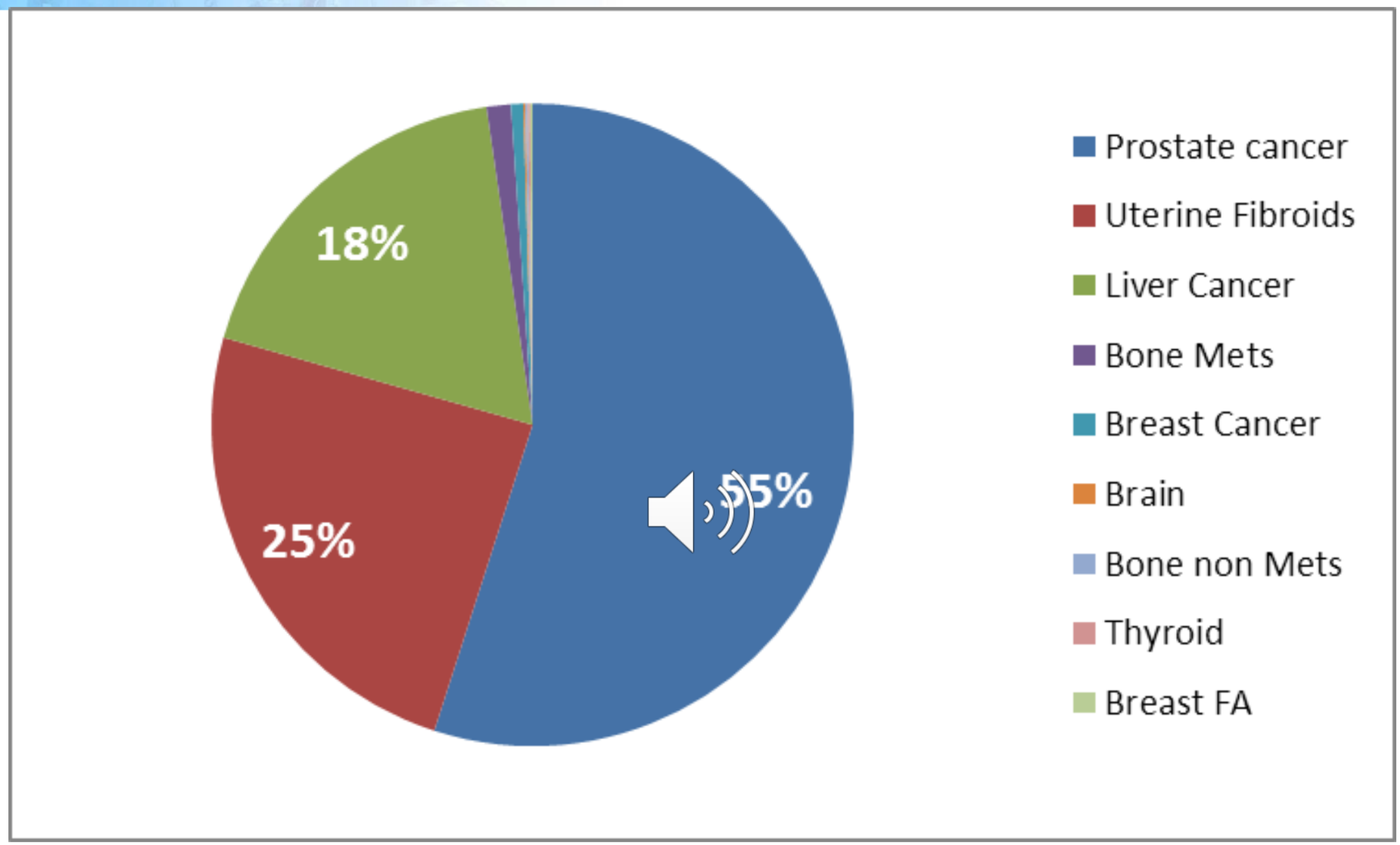
Fundamentals of High Intensity Focused Ultrasound

f = 0.5 MHz to 3 MHz

I = 1 kW/cm^2 to 10 kW/cm^2

T/s > 10º C





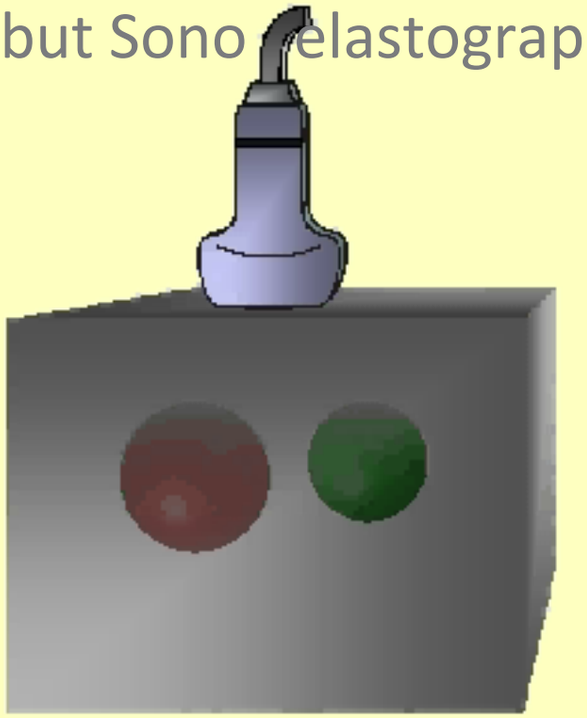
Overall, more than 100,000 patients have been treated using HiFU/FUS
among those are <20,000 MR guided FUS/HiFU
ONLY 200 MR guided Ablation of Prostate

USgFUS/HiFU

Ultrasound guided Focused Ultrasound/HiFU, Fibroadenoma

- Lack of Monitoring during Sonication
- Lack of Temperature Mapping
- Lack of MR Imaging features

but Sono elastography



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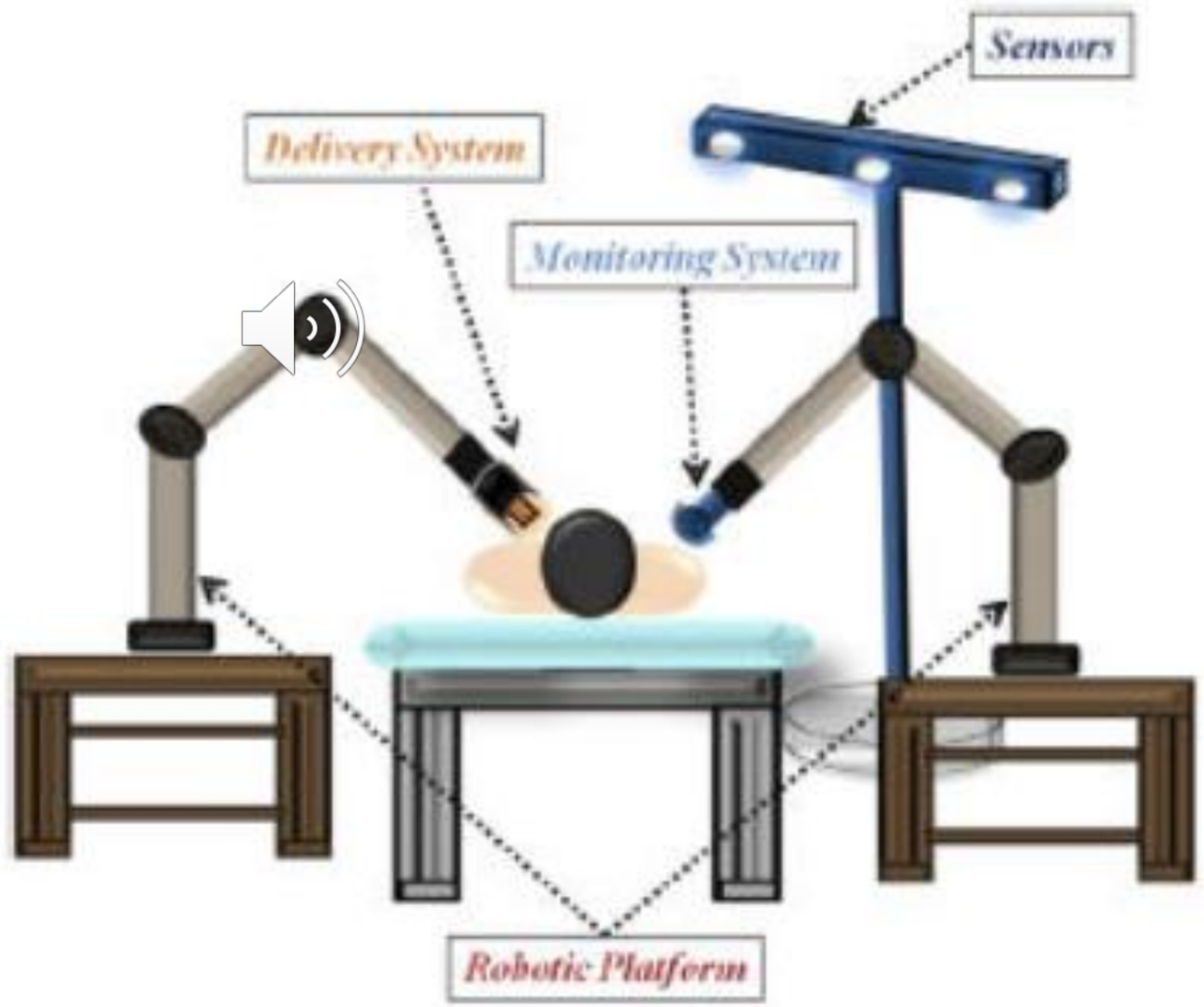
Robotic positioning of Focused and Diagnostic Ultrasound

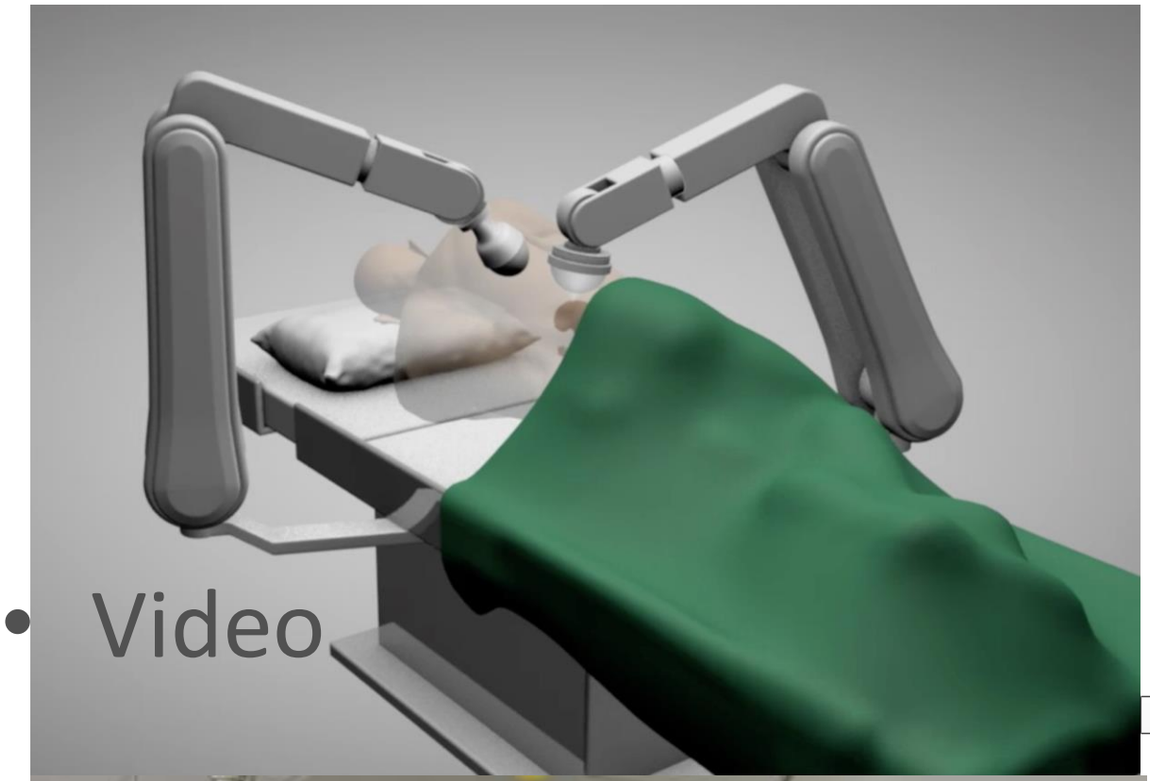
EU F7 project 3.6m€ SUCCESS Story

Grant Agreement no: 611963

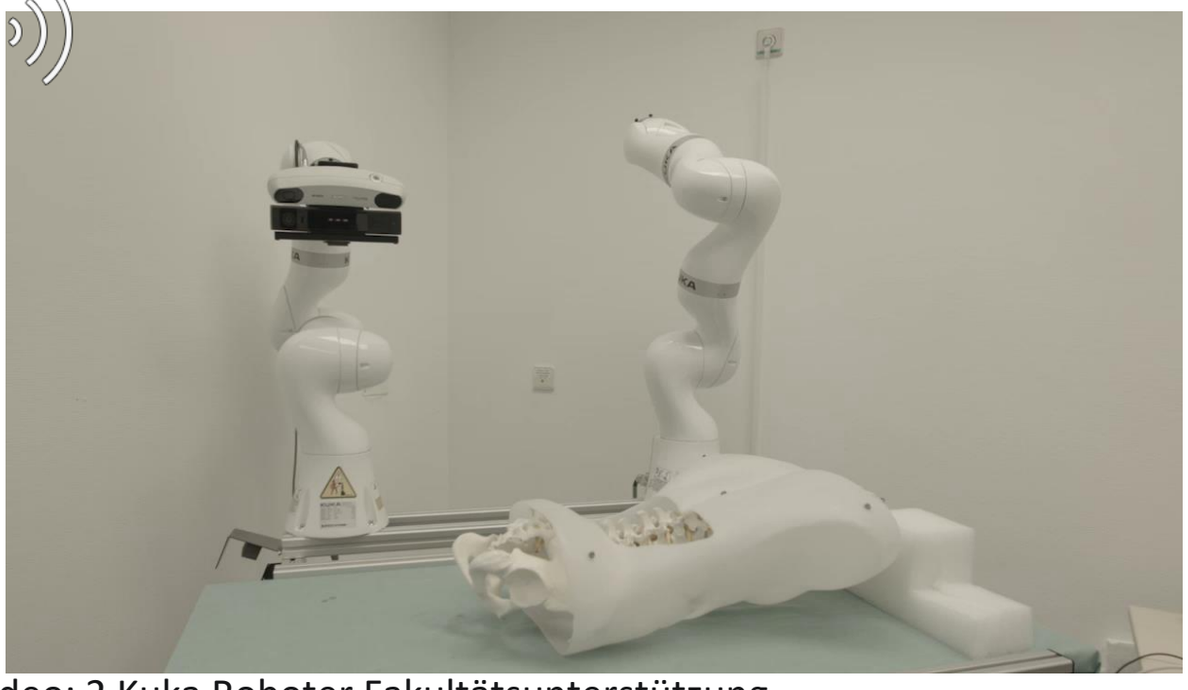


META ZIK SONO-RAY ICCAS UND ONCORAY UNI

- Video



Focused Ultrasound enhanced Radiation Therapy
BMBF MetaZIK
6.2mio Euro



Video: 2 Kuka Roboter Fakultätsunterstützung
für Projekt OncoCockpit: 333T€

https://1drv.ms/v/s!AlXw5LElYS5ciboS6WUs1u9ivVnegA

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Profound (Philips) Sonalleve MRI HiFU

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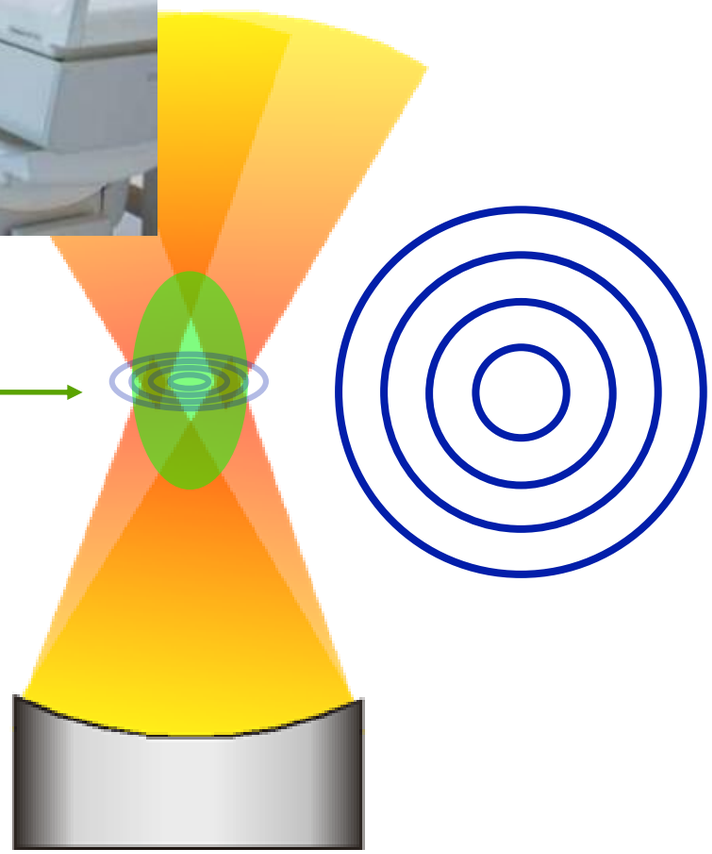
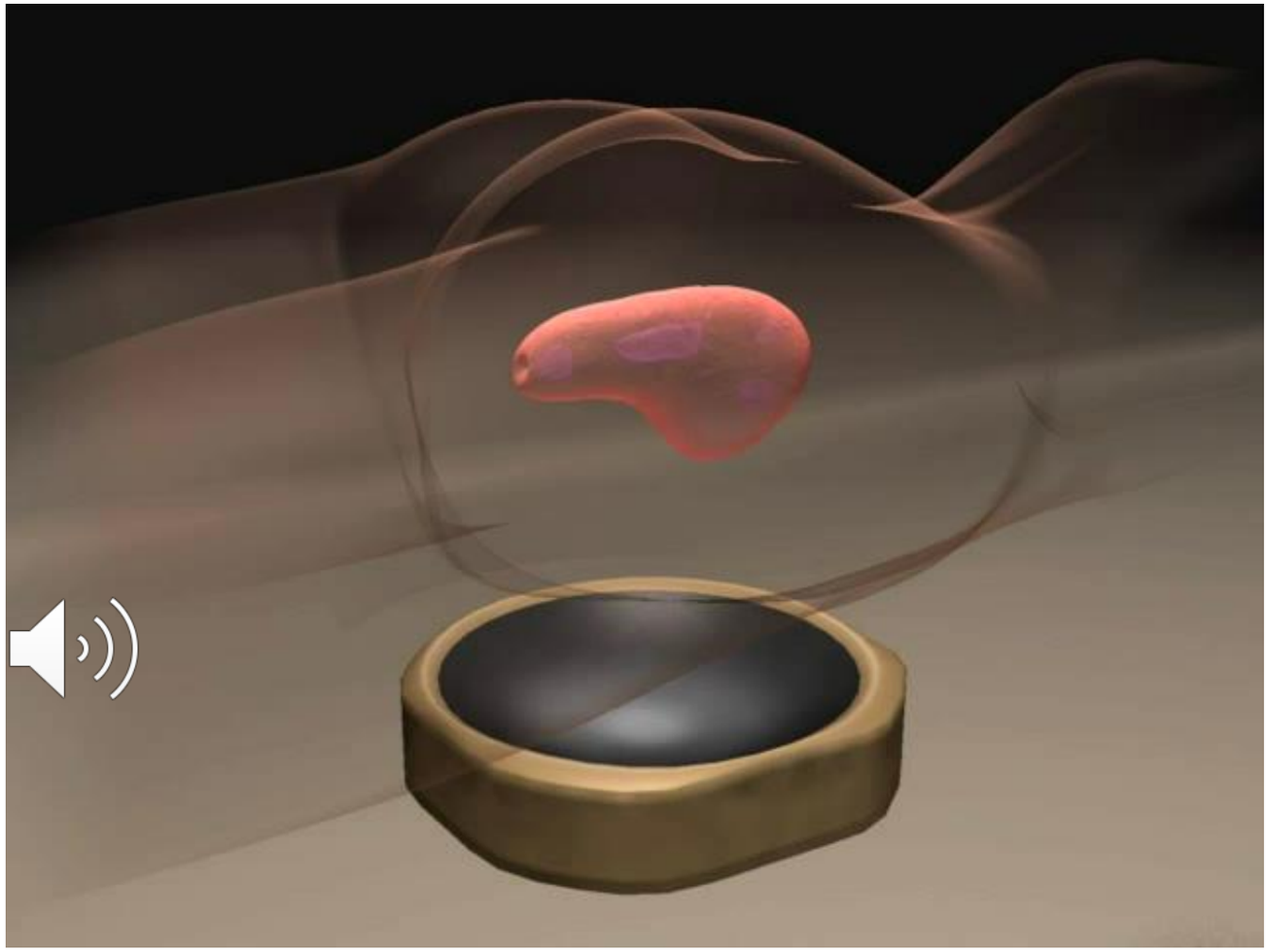


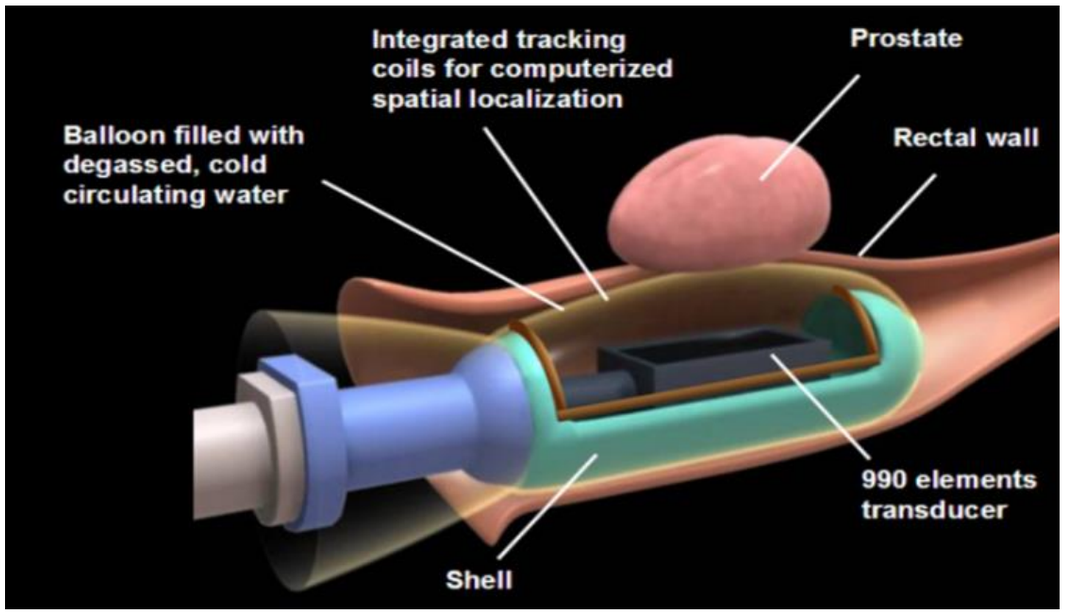


Electronic beam steering:
Outwards-moving concentric circles 4 – 16 mm Ø
42° C Hyperthermia WiP for drug delivery

Diameter (mm)	Length (mm)	Volume (ml)
4	10	0.1
8	20	0.6
12	30	2.3
16	40	5.4

For details see:
M. Köhler et al., Med.Phys. 36 (8),3521, August 2009

THE EXABLATE SYSTEM - ENDORECTAL THERAPEUTIC APPROACH

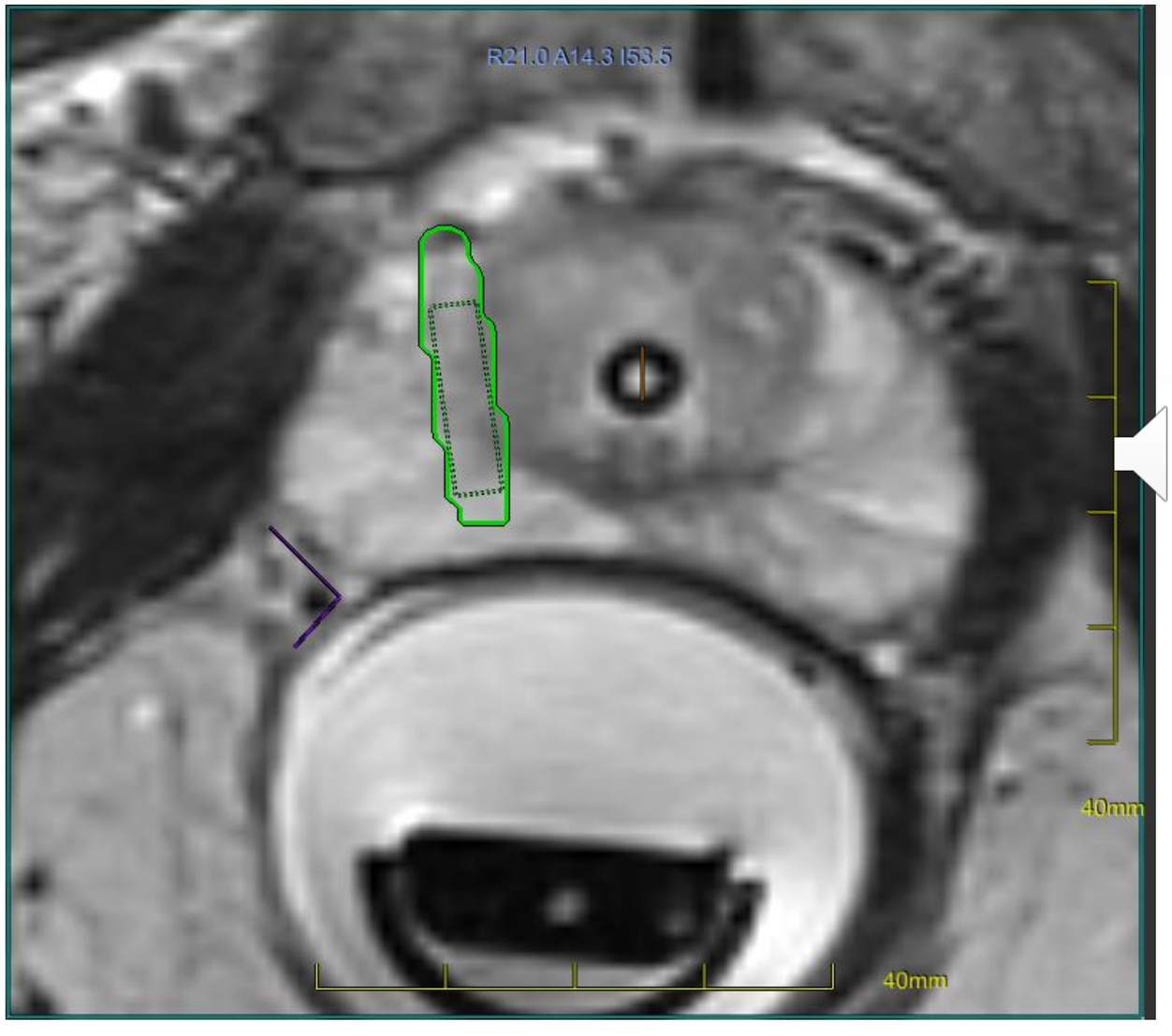


CE Mark 2016

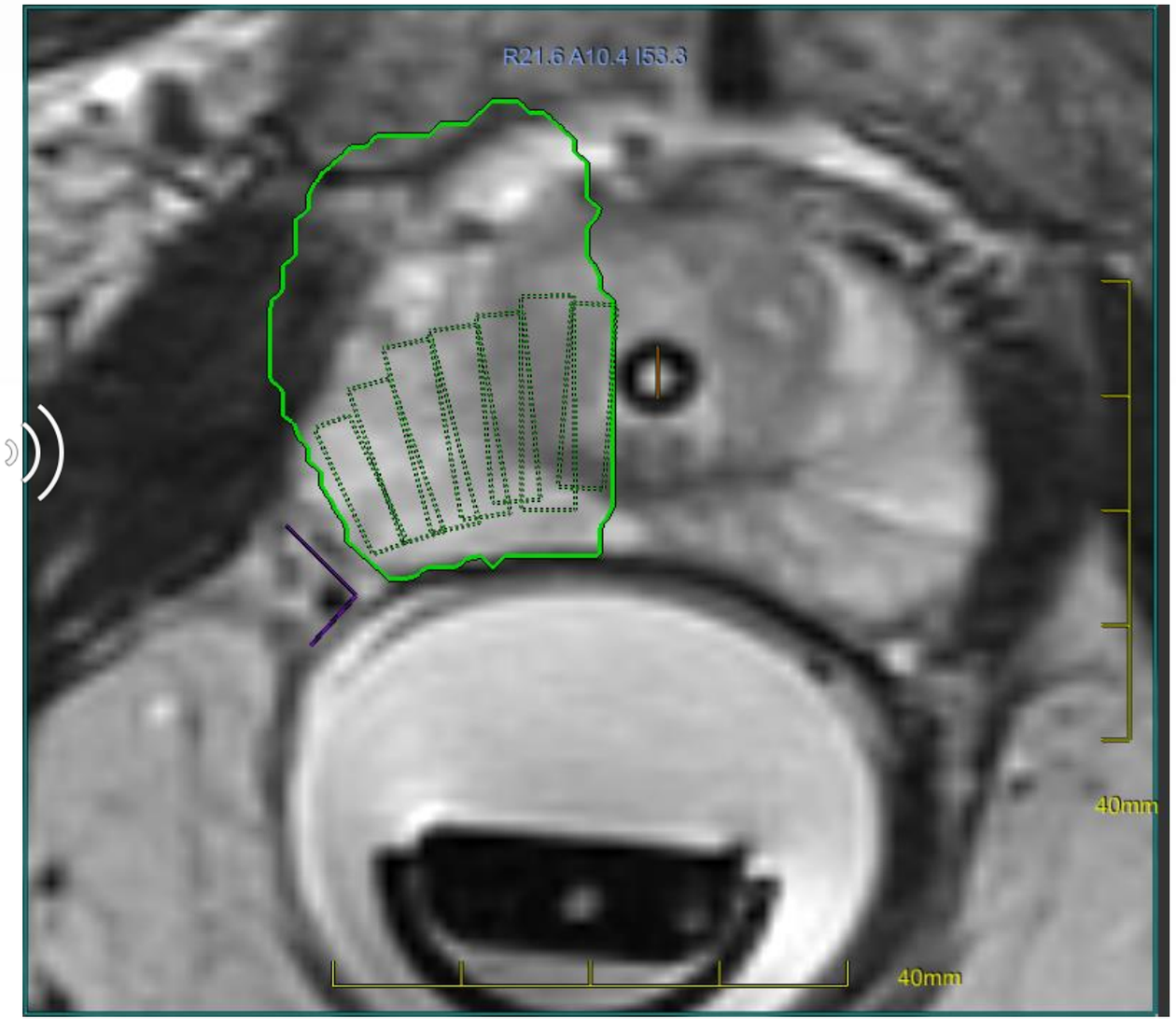
Robotic positioning of a transducer with <900!! elements

FUS Spot Types

Single Spot



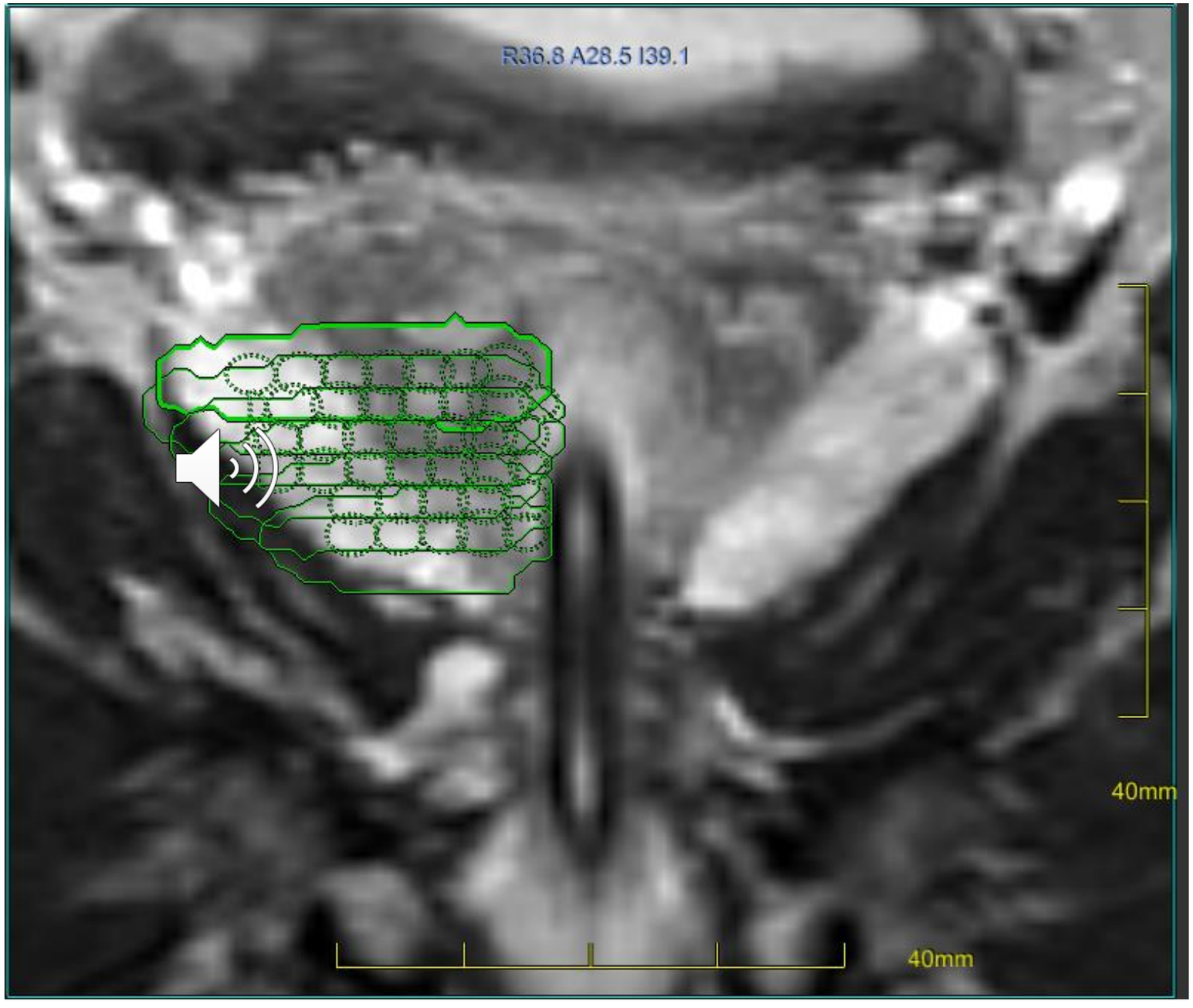
Multiple Spots



Axial T2w images

Macro FUS Spots Overlap

- Multiple spots are added and performed slice by slice of the MR Image
- Distance between Axial slices is 3mm
- Multiple spot “thickness” can reach 10mm
- The overlap is established for complete ablation



Coronal T2w image

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Trans Urethral MR guided Ultrasound Ablation

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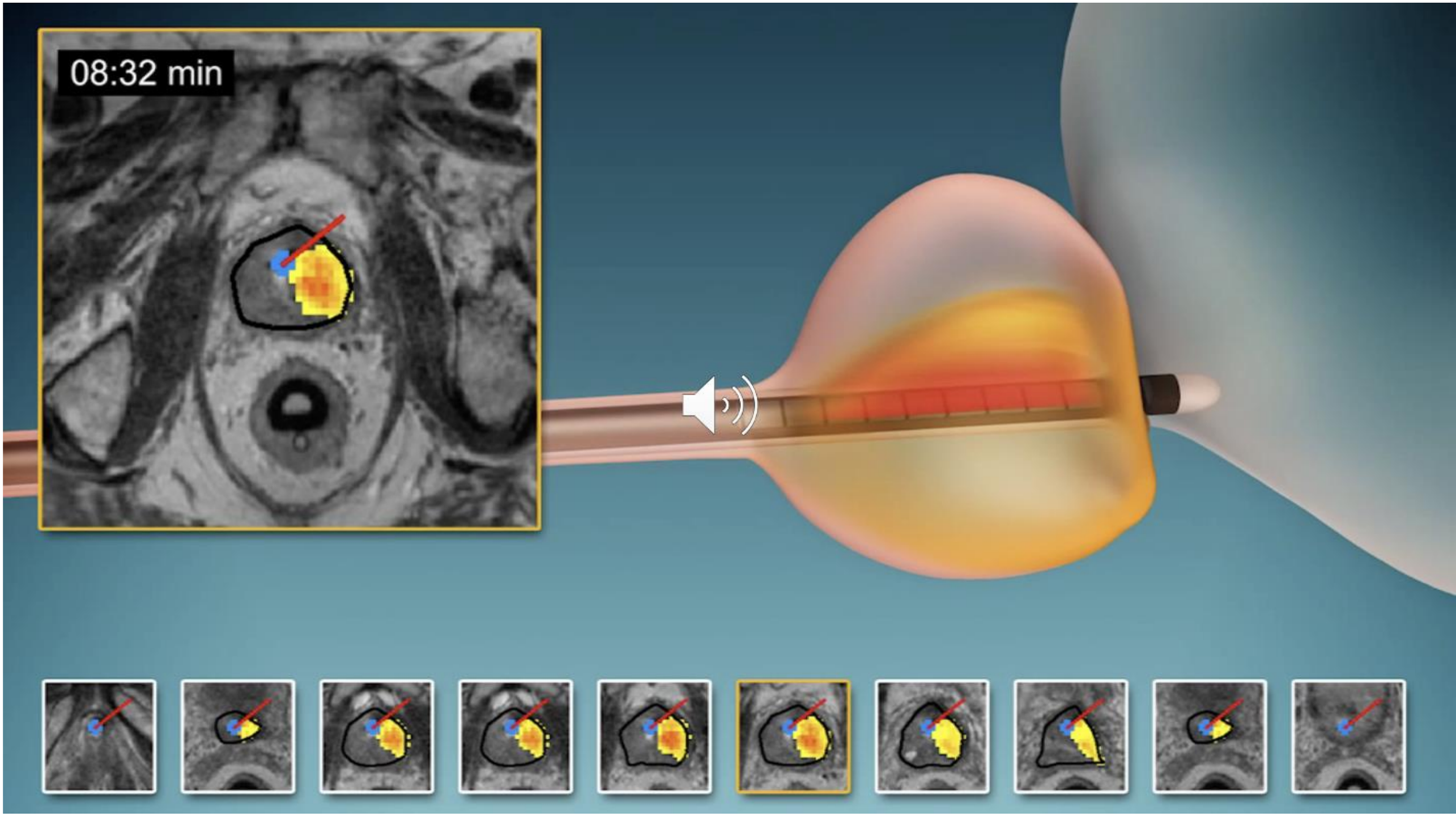
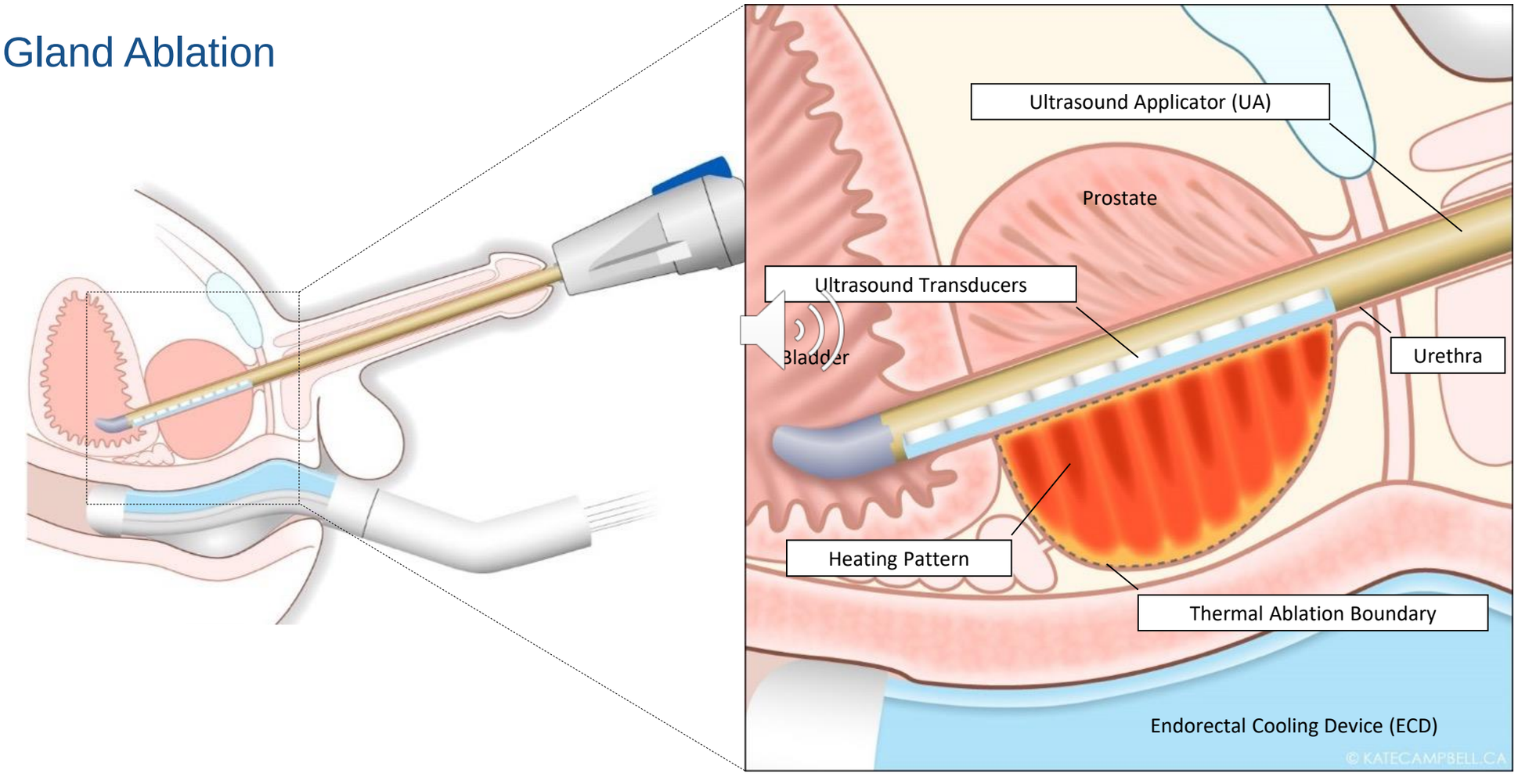


https://www.youtube.com/watch?v=Wyy5jLOi8ac

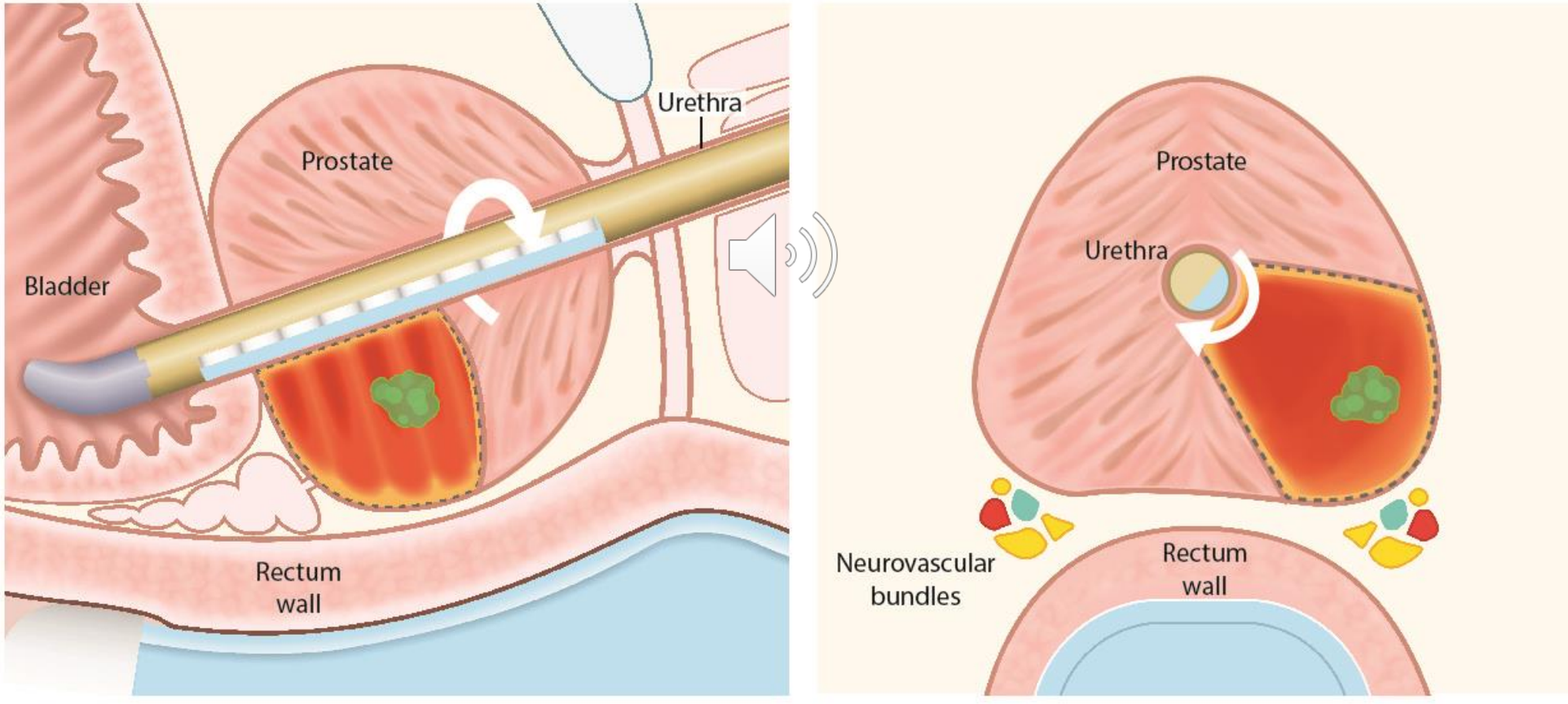
ULTRASOUND – PROSTATE ABLATION FROM THE INSIDE OUT

Whole Gland Ablation



ULTRASOUND – TARGETED ABLATION

Partial Gland Ablation

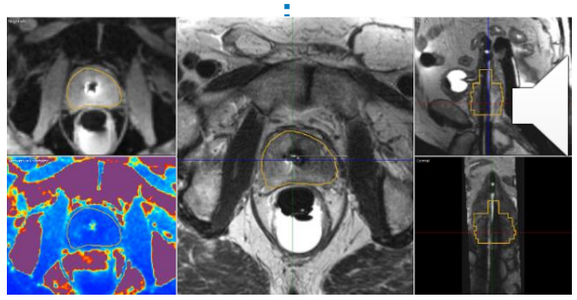


MRI-Guided HiFU Treatment Work Flow 60-90 min

1

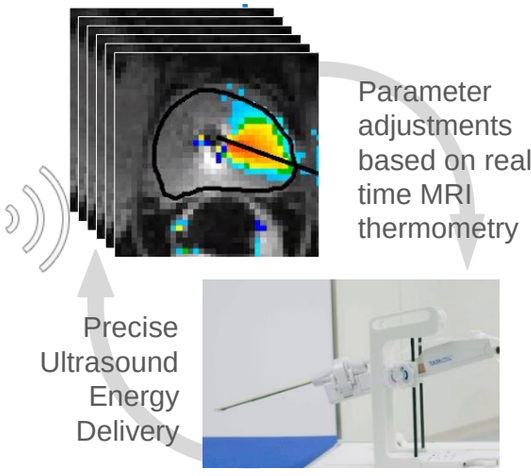
MRI Guided Device Positioning

2



MRI Treatment Planning

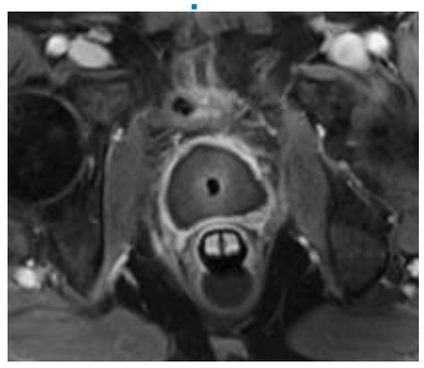
3



Automated, Robotically driven, Adaptive Therapy Delivery

1. Controlled algorithm
2. Target temp 57^0 C
3. Ablation in 1-2 cc/min

4



Confirmation of Ablation Margin with MRI

TRANSURETHRAL MR GUIDED US ABLATION

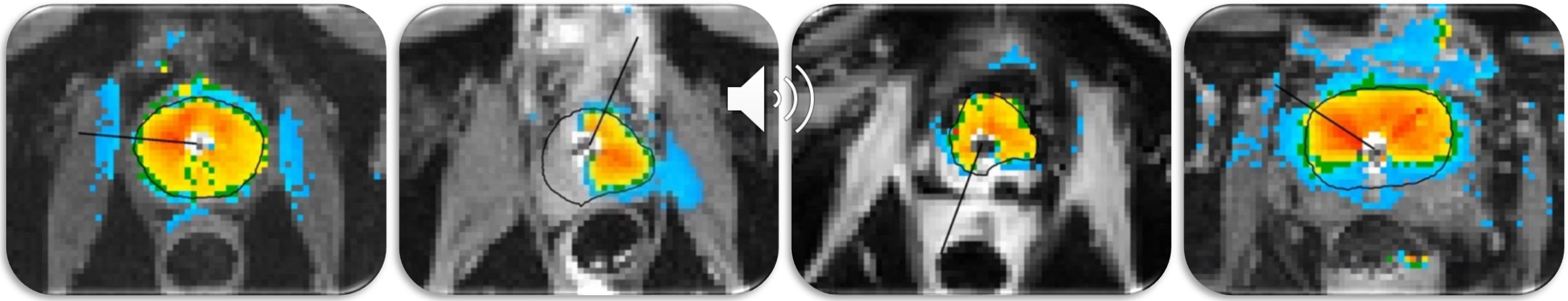
Magnetic Resonance Thermal Mapping

Whole Gland Ablation

Targeted Ablation

Salvage Therapy Post Radiation Therapy Failure

Benign Prostate Hyperplasia (BPH)



3 PATIENT TREATED IN OPHILISP PET MR AT ONCORAY IN DRESDEN PARTNER OF SONO-RAY PROJERCT

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TRANS FUSIMO

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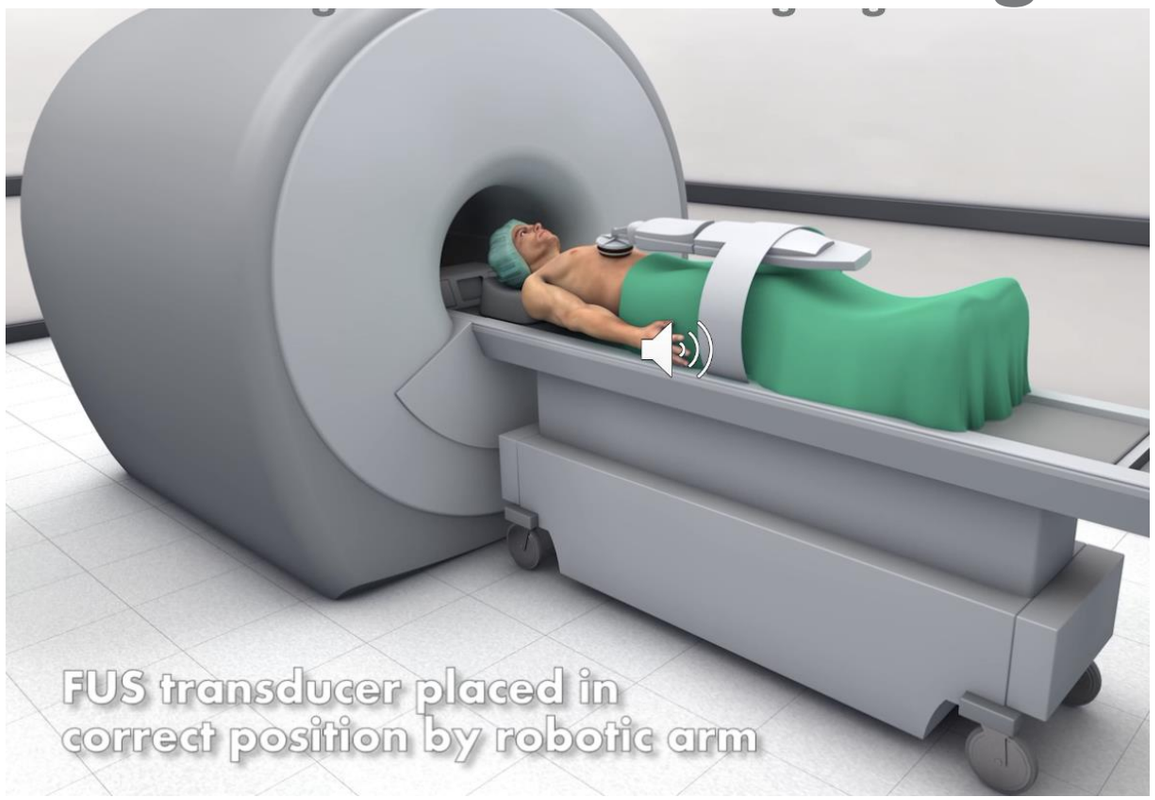
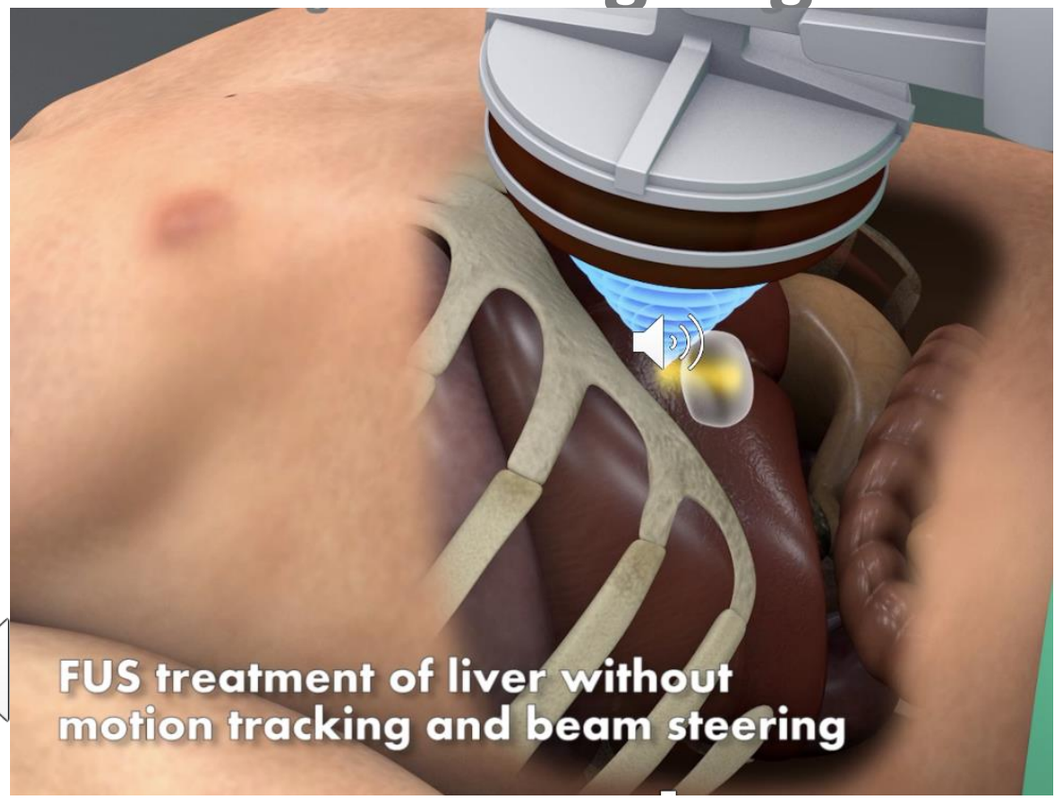
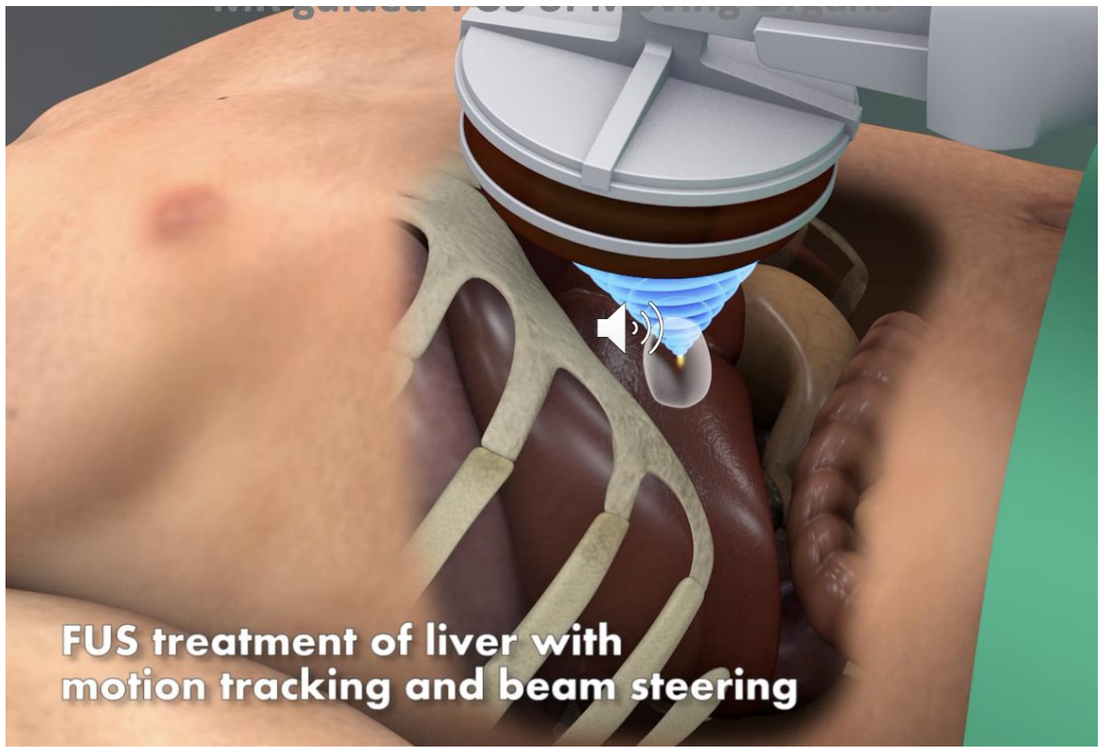
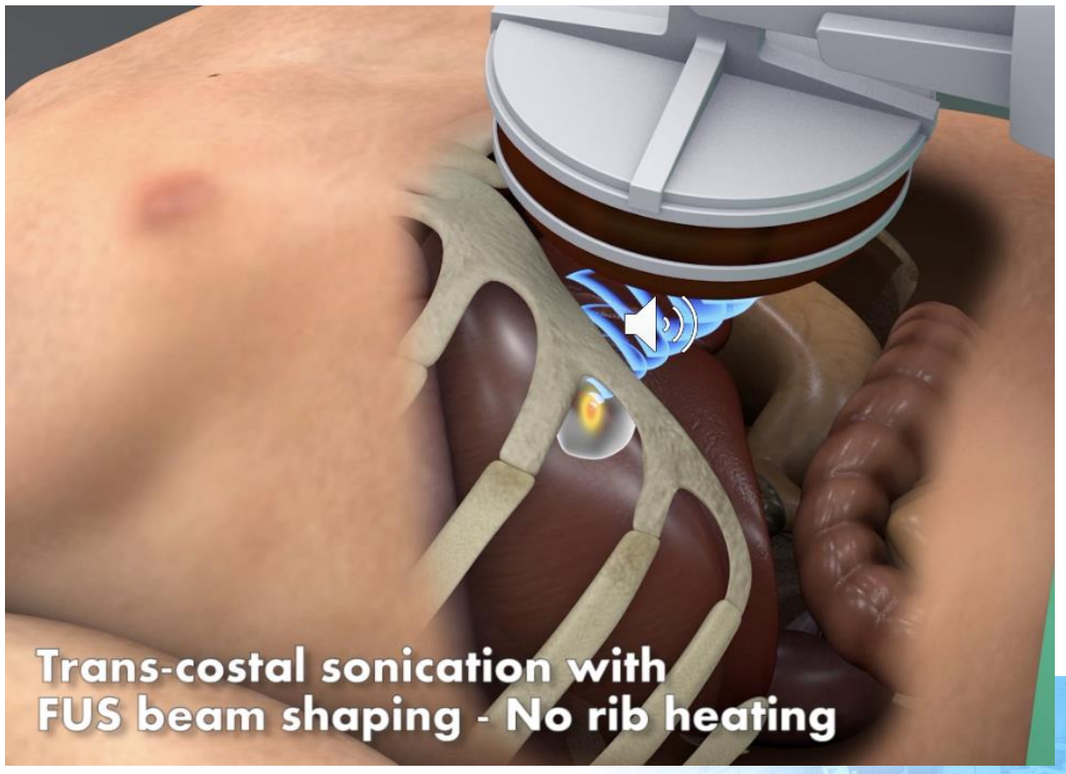
MR guided FUS of Moving Organs

8m€ EU FP 7









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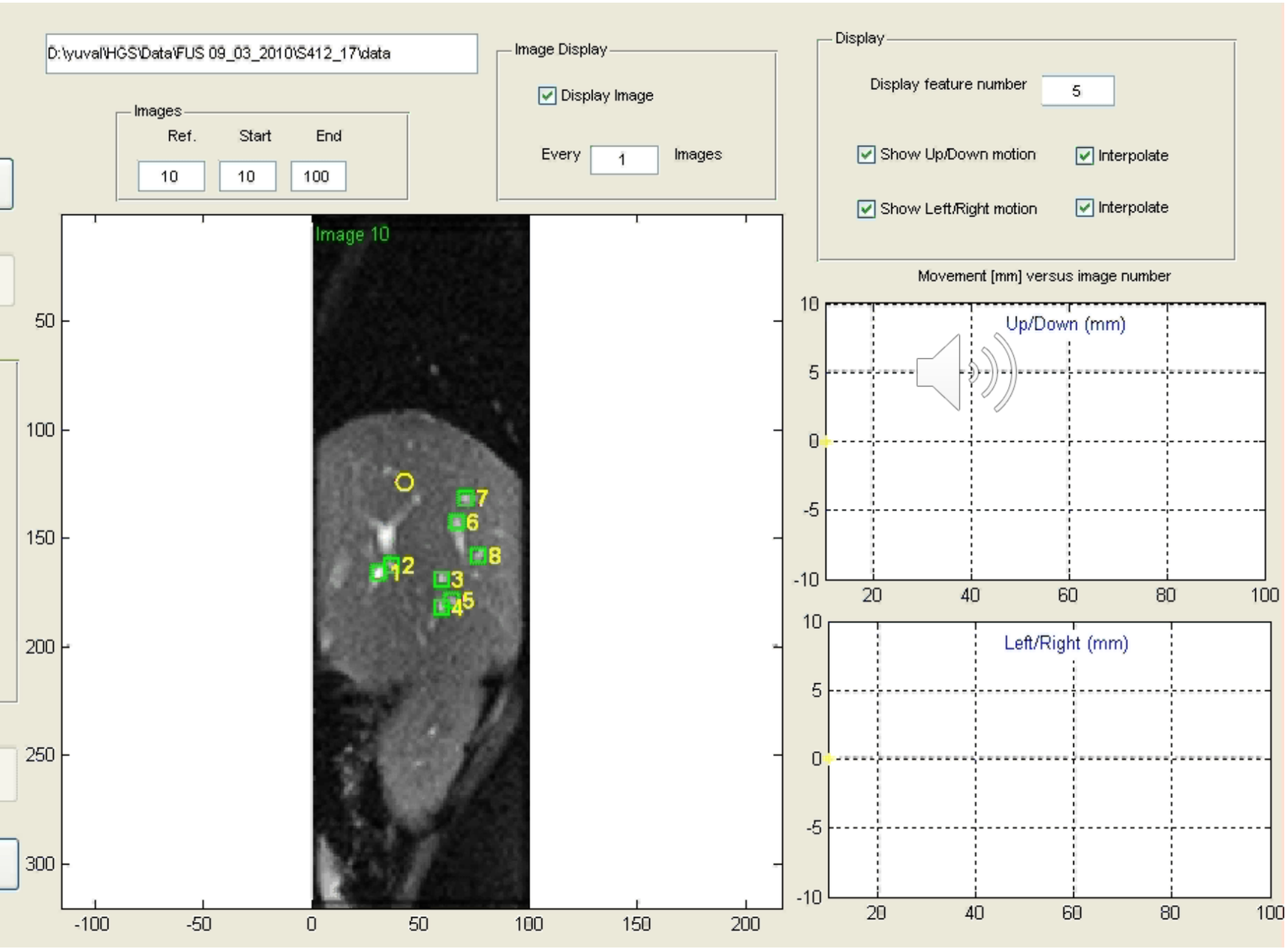
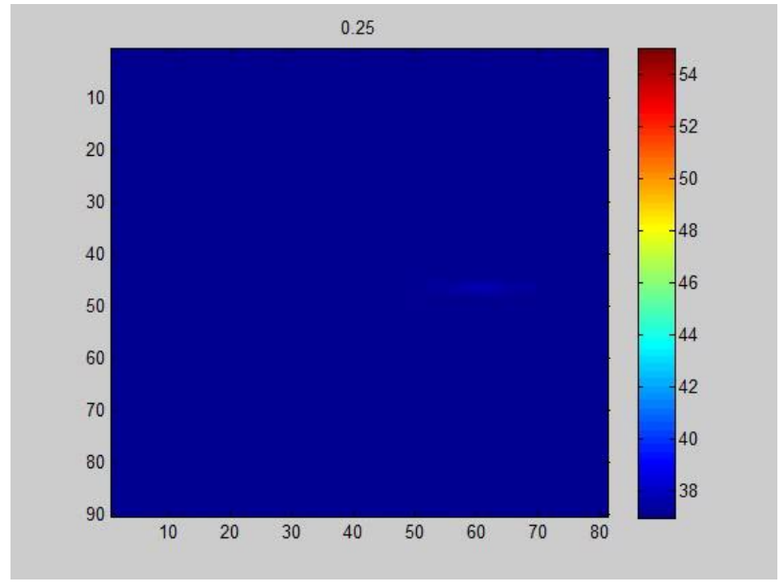
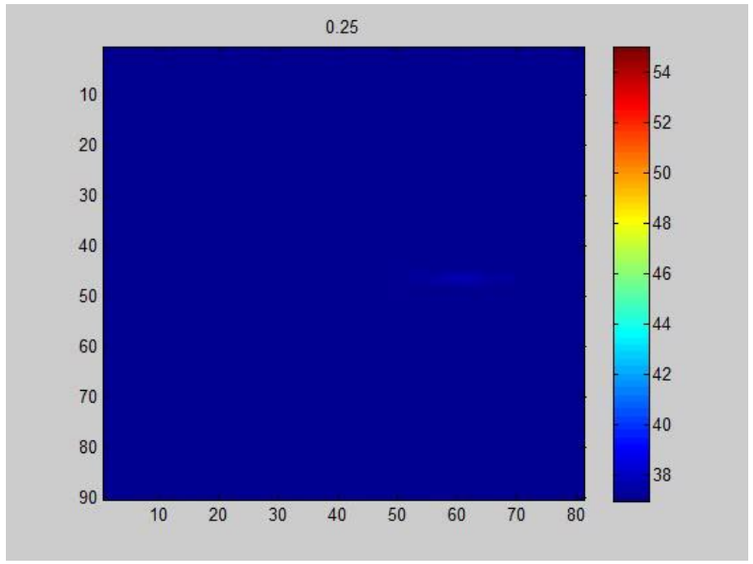
4D MR organ tracking FUS Beam Forming





Following sharp focus

- high temp&pressure



soft focus

- low temperature&pressure

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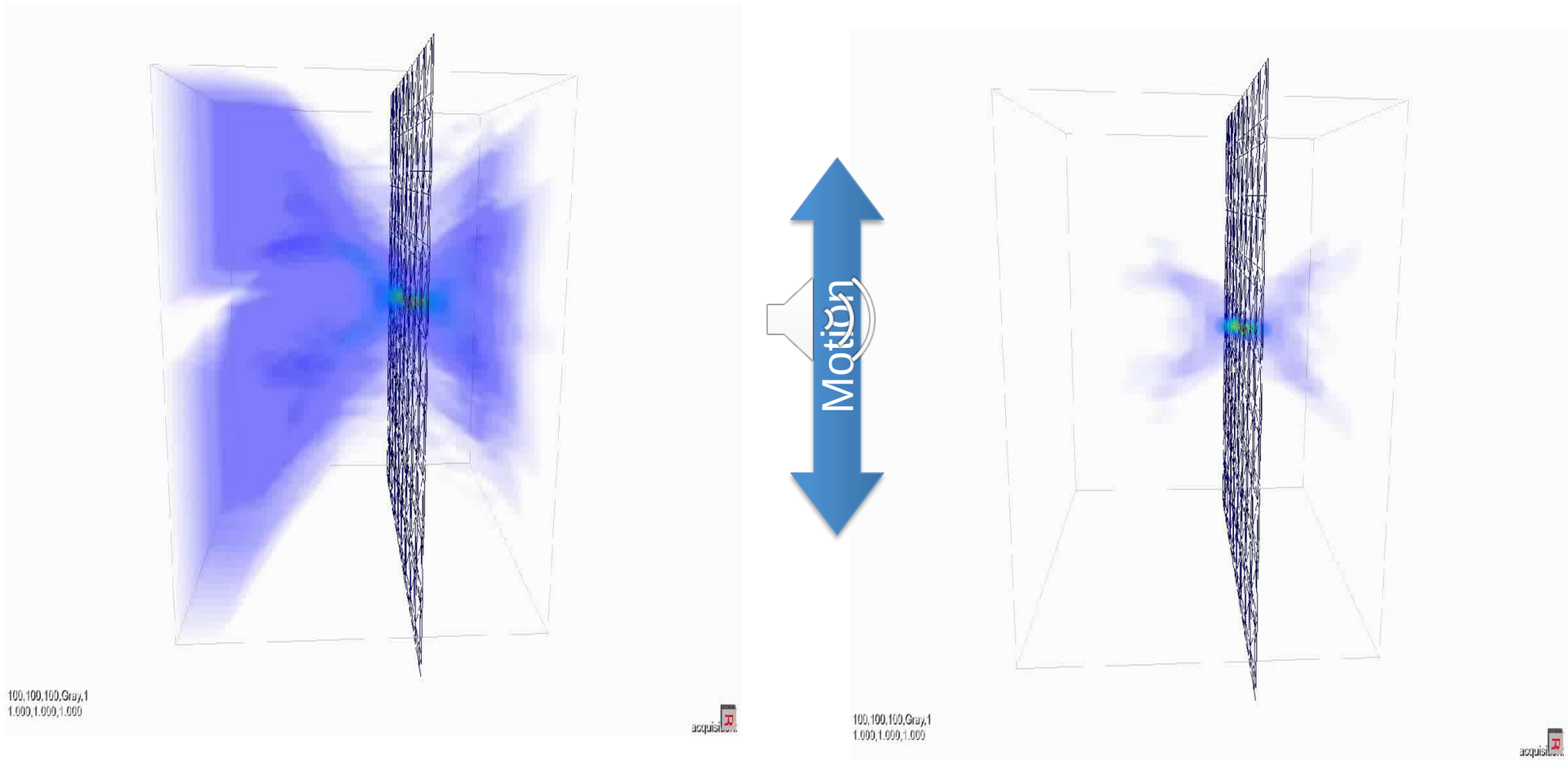
FUSIMO MRI-FUS Model in Moving Organs



Ultrasound pressure

Temperature

MRgFUS mediated targeted drug delivery

Nanoporation, 2.5m €, ranked first out of 148, Success Story
FP7 IAPP EU Project, University Dundee, InSightec and Capsutec (Israel)

Liposomes, Cyclodextrine polymer carriers, micro-bubbles

Journal of Controlled Release 170 (2013) 316-324

Contents lists available at SciVerse ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel

Ultrasound-mediated targeted drug delivery with a novel cyclodextrin-based drug carrier by mechanical and thermal mechanisms

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[a] InSightec Ltd, 5 Nahum Heth St, Tirat Carmel 39120, Israel
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[c] Institute for Medical Science and Technology, University of Dundee, 1 Wurzburg Loan, Dundee DD2 1FD, UK

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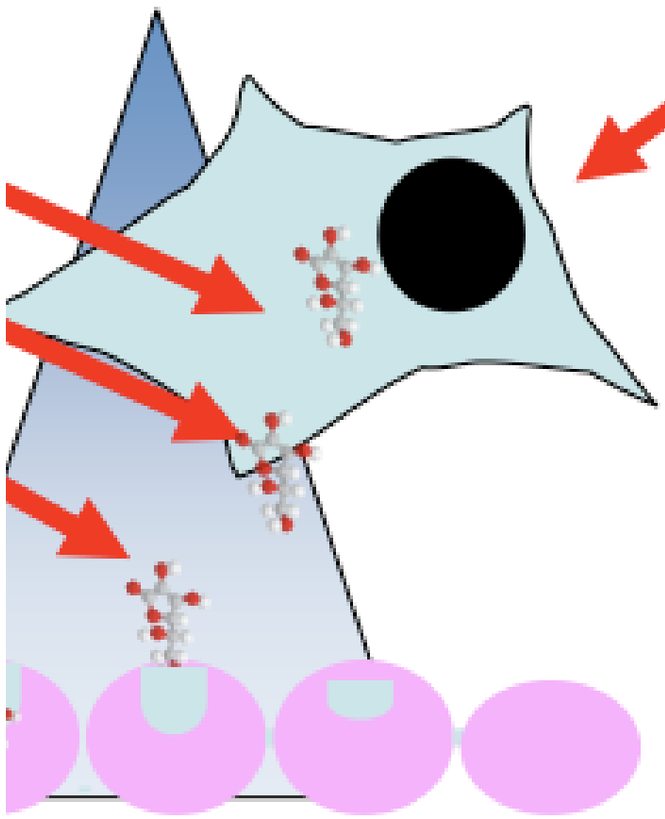
Sonoporation

ABSTRACT

Various mechanisms for ultrasound-mediated targeted drug delivery have been investigated in the past several decades. Cyclodextrins are already known for their ability to encapsulate various drugs in their lipophilic cavity; this paper reports evaluation of the potential of a cyclodextrin-based nanocarrier as a drug delivery vehicle, using cell monolayers *in vitro* in conjunction with ultrasound as the release mechanism. The application of ultrasound to the cell monolayers results in both thermal and mechanical effects; a current challenge is to differentiate between these effects. In this study, the cell uptake routes of doxorubicin encapsulated in the cyclodextrin-based carrier were investigated, examining individually the thermal and the mechanical effects of focused ultrasound for drug release. Exploiting mechanical effects, the uptake of encapsulated doxorubicin into cancer cells was increased by a factor of up to 5.5 when ultrasound was applied. Thermal application of FUS increased the cellular uptake of encapsulated doxorubicin by a factor of up to 9.6. Hyperthermia without focused ultrasound resulted in an increase by a factor of up to 5.7.



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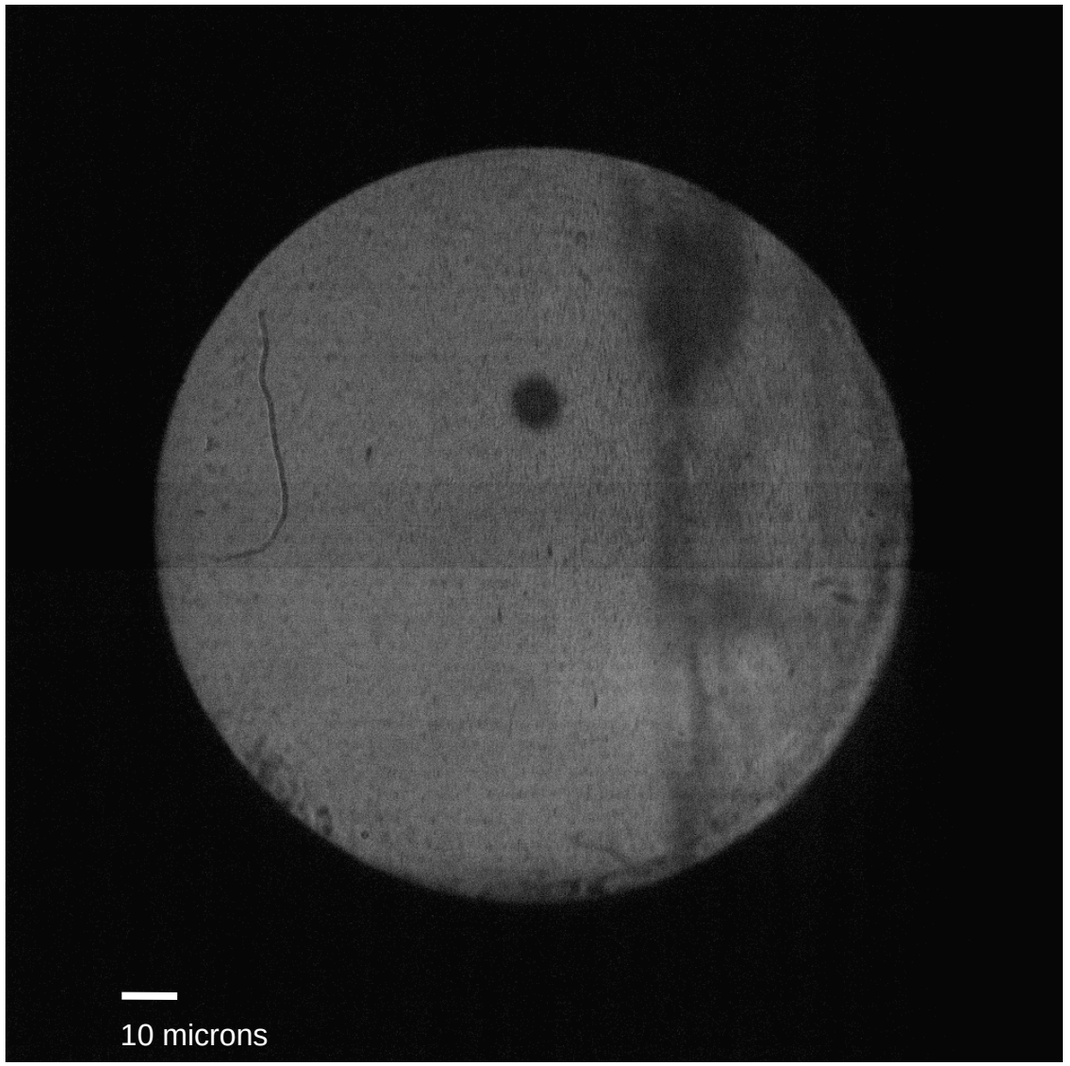
Micro-bubbles for enhanced drug delivery

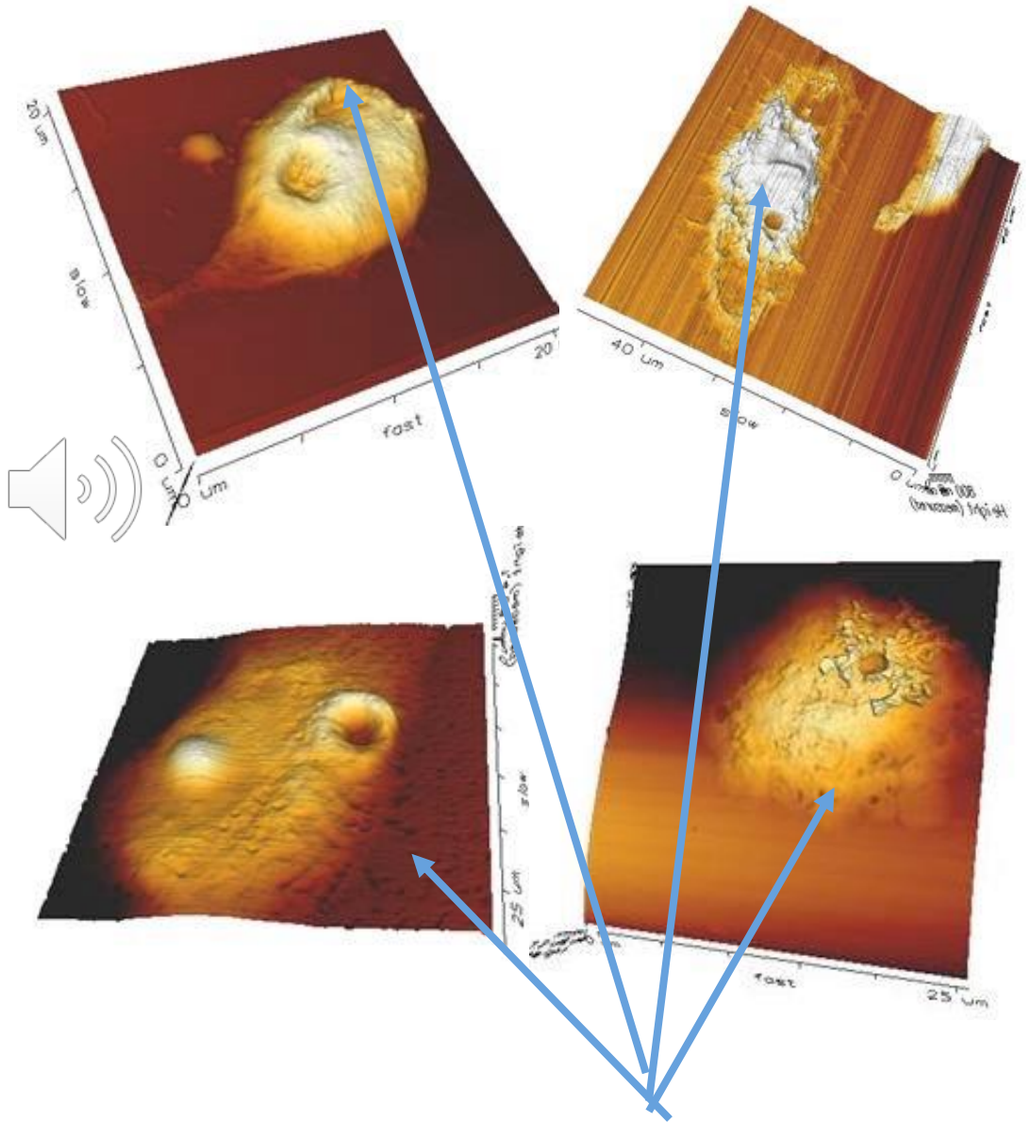
(P.Prentice & B.Gerold: IMSaT Dundee)



optically trapped SonoVue micro-bubble demonstrating ovarian cell membrane perforation in 1 Mhz focused Ultrasound beam

movie at 1.7 million fps , 400x

Sonoporation
FUS mediated Drug delivery



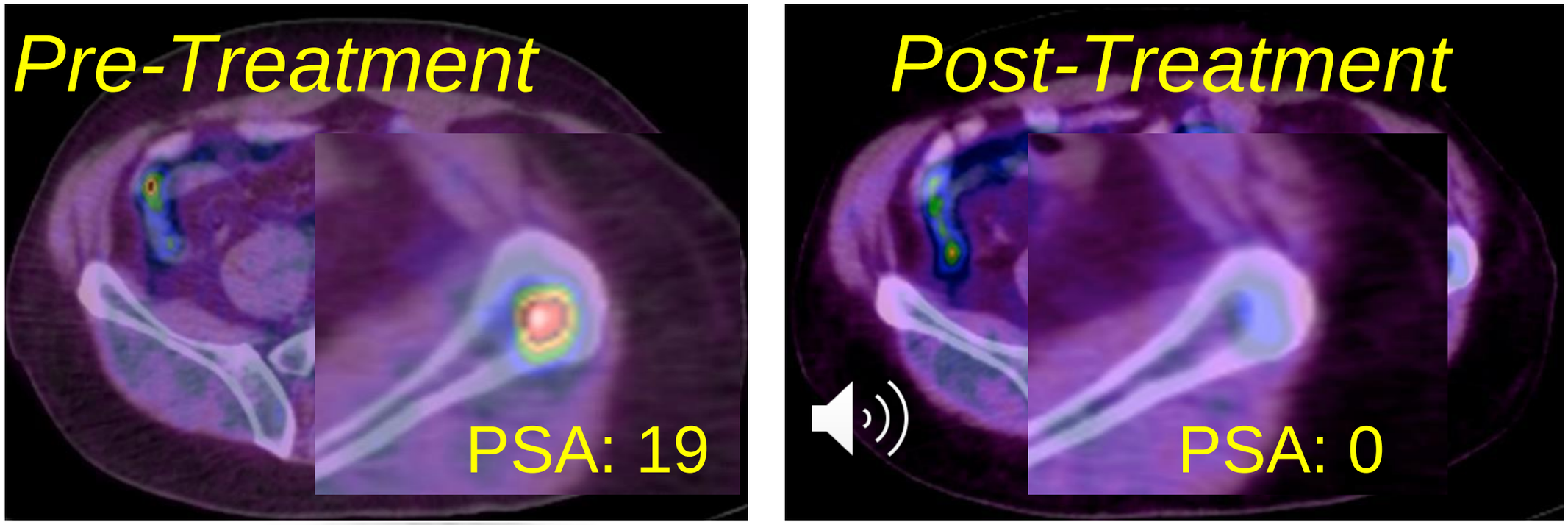
Cells ‘micro-syringed’ by jets from collapsing bubbles, AFM Brucker “life scan”

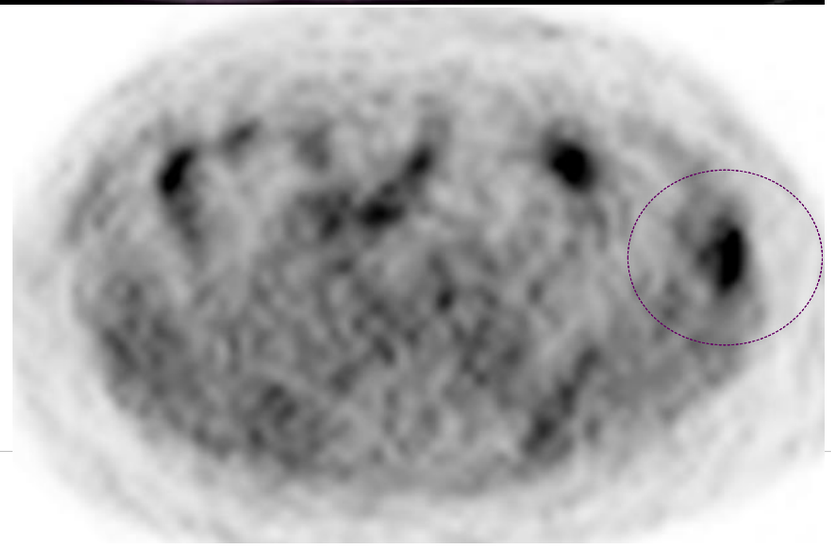
Nature Science 2005 & APL 2012

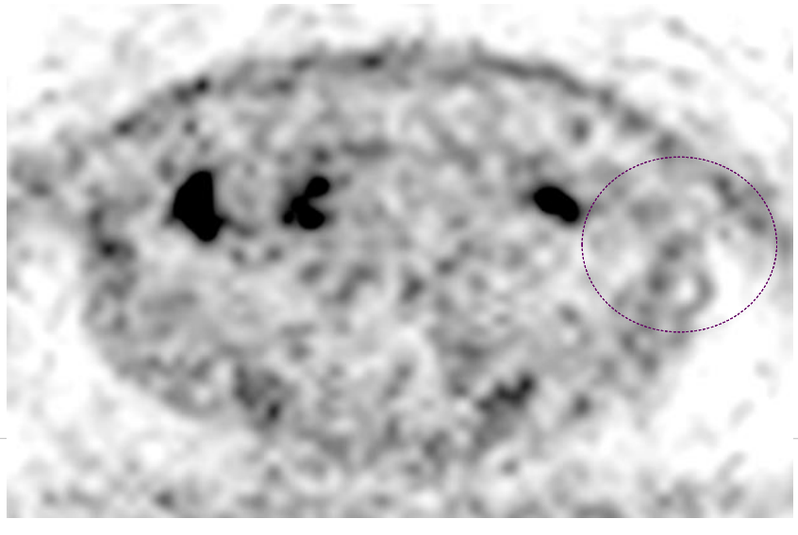
Monitoring FUS Effects

LOCAL TUMOR CONTROL by MRgFUS & PET monitoring

Investigative Radiology • Volume 48, Number 6, June 2013





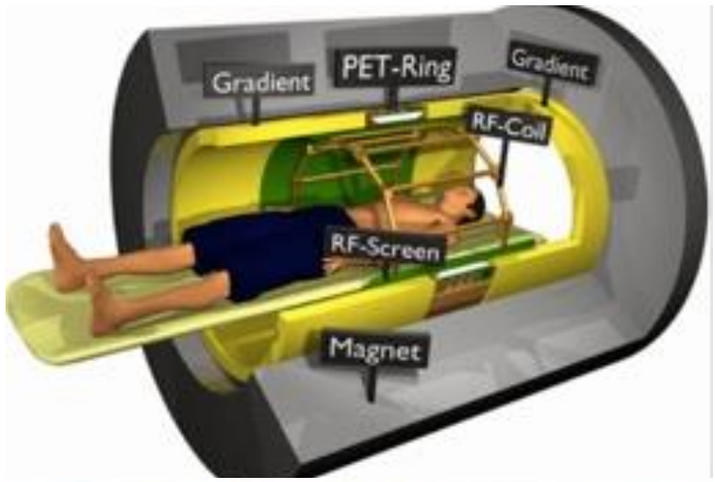


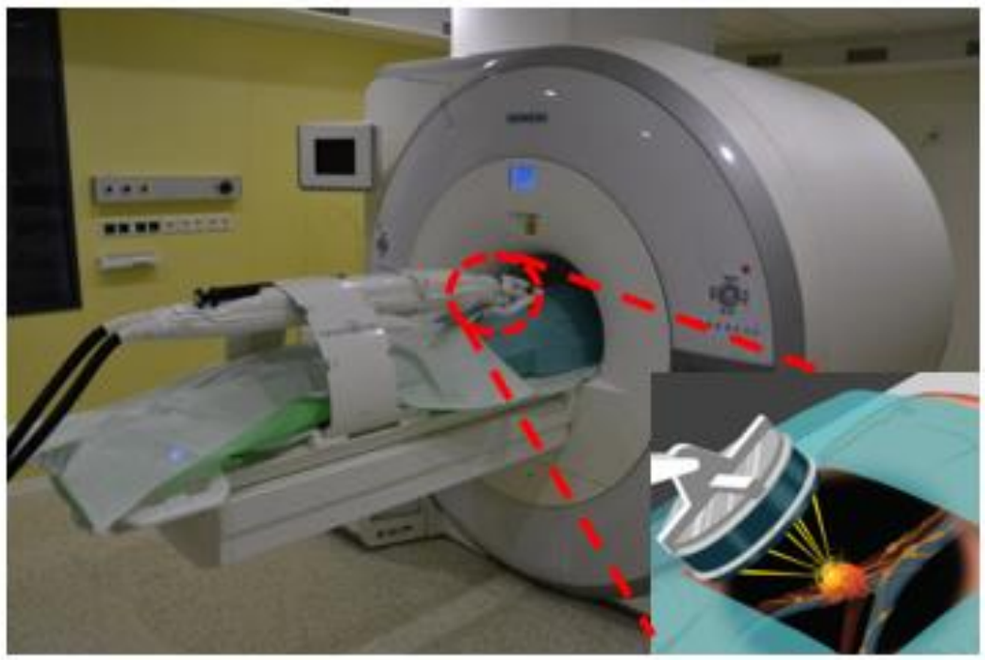
M, 53 yr.
Metastatic
Prostate Ca

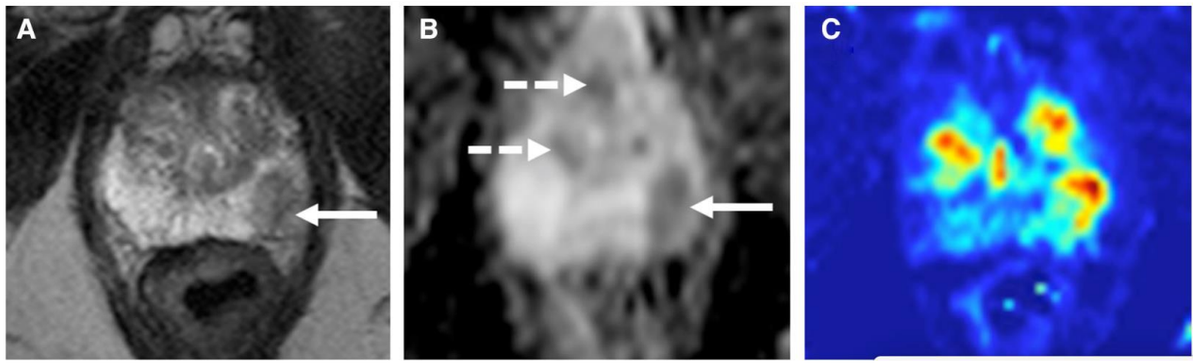
court. Alessandro Napoli

Future development: PET& Multiparametric MR guided Biopsy and FUS

PSMA Localising and monitoring Tumor Metabolism for MRgFUS Ablation, RT and Drug delivery
Dept NUK B Sattler, Purz, Barthel, O Sabri, Jochimsen - Urology JU Stolzenburg, Dept Radiology, JO Petersen, Bailis, T Denecke





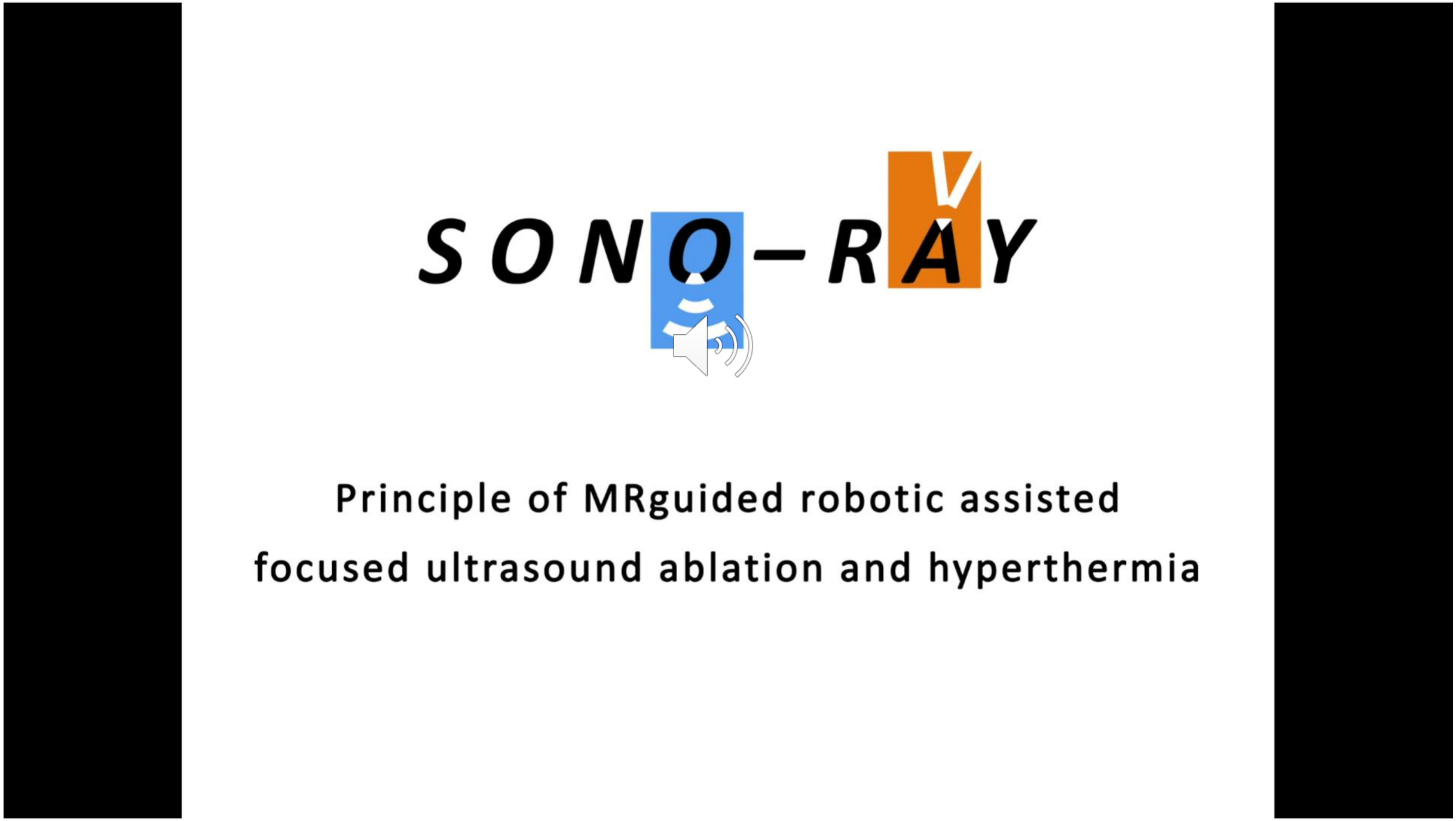


Multiparametric imaging and analysis of primary prostate cancer using 68 Ga-PSMA PET/MR Eiber et al Abdom Imaging 2014

INNOMOTION MR Robot in Siemens Biograph 3Tesla PET MR Concept of PET MR guided tumor ablation

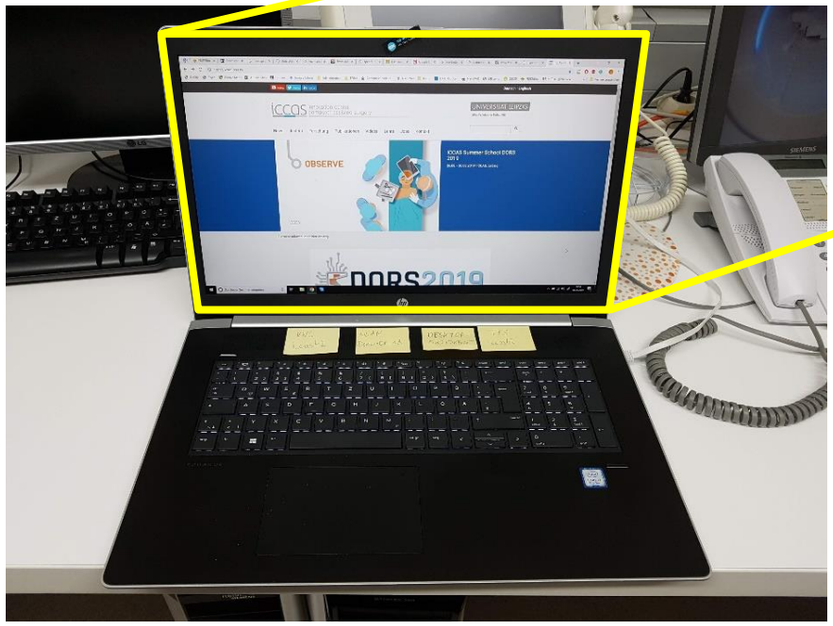
SONO-RAY 6.3 m Euro BMF Project ICCAS Leipzig and OncoRay Dresden

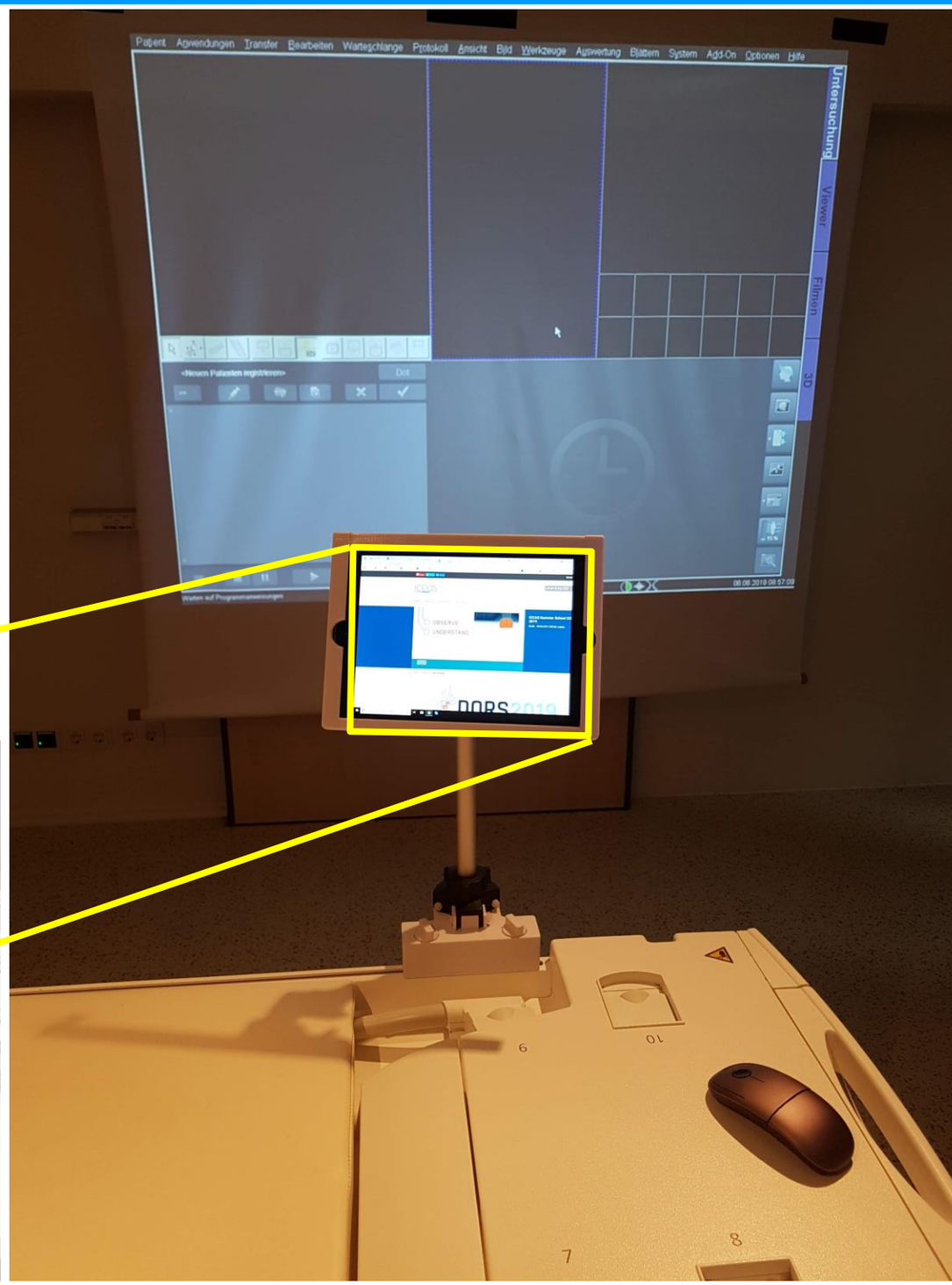
✦ Support Radiation Therapy by Focused Ultrasound FUS RT



https://www.youtube.com/watch?v=GSegl5MIySs#action=share

PET MR Intervention Setup, NUK UKL Leipzig





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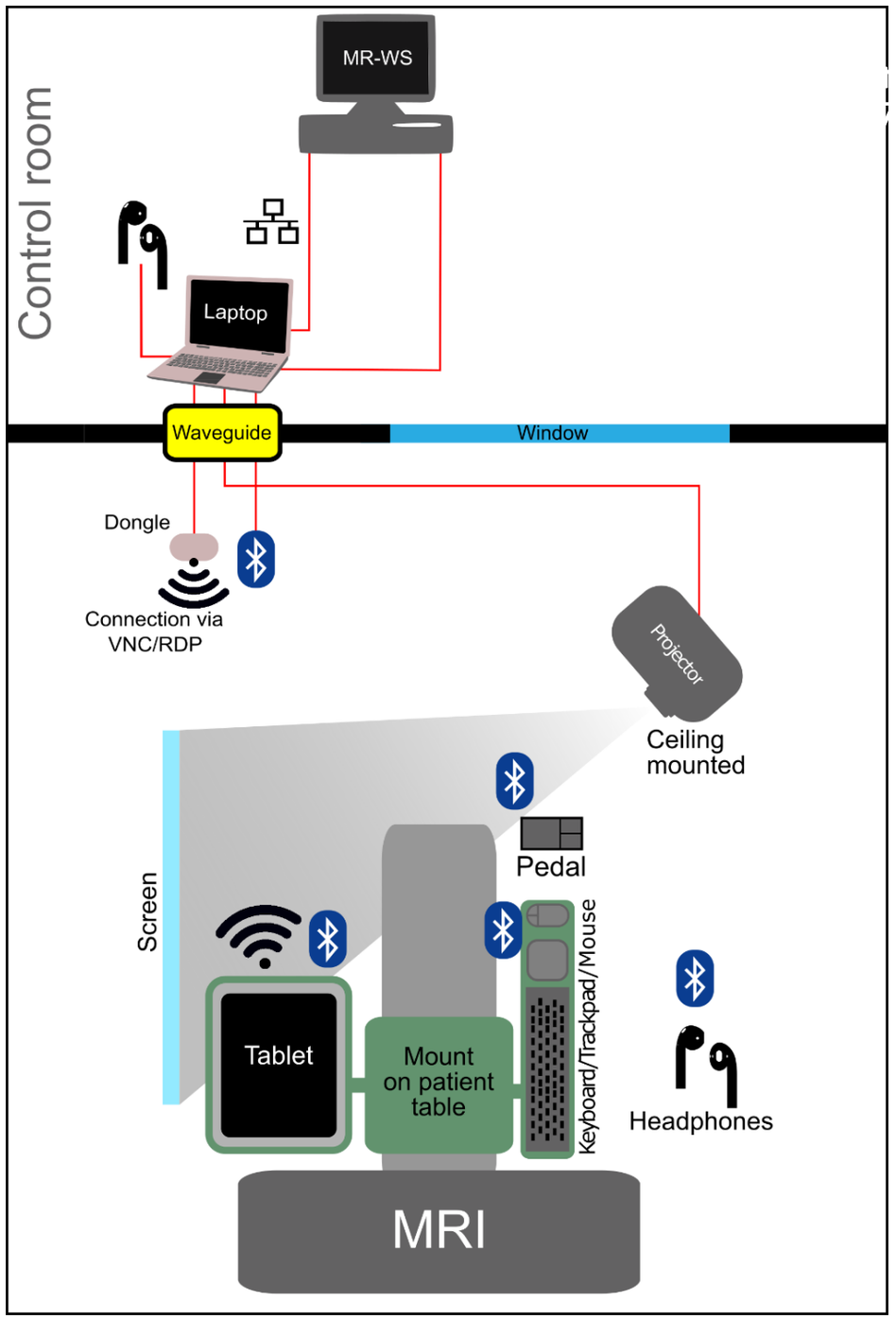
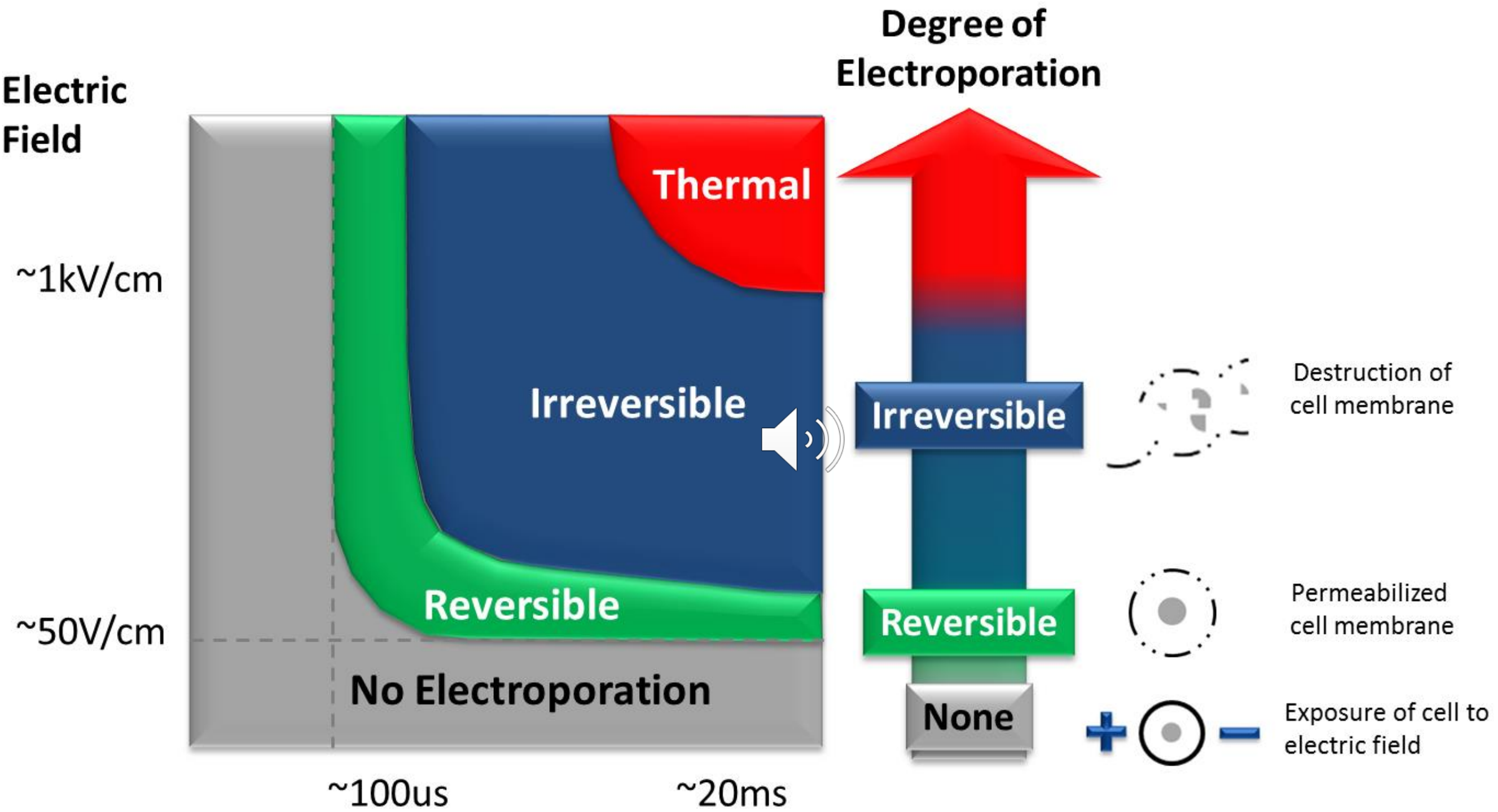
PET MR Intervention Setup, NUK UKL Leipzig

- Wired/wireless **network** connection in MR room
- **Output** devices in MR room
  - Projector/Screen
  - Tablet
  - (Monitor)
- **Input** devices in MR room
  - Keyboard
  - Mouse
  - Pedal
  - Tablet
  - Headphones

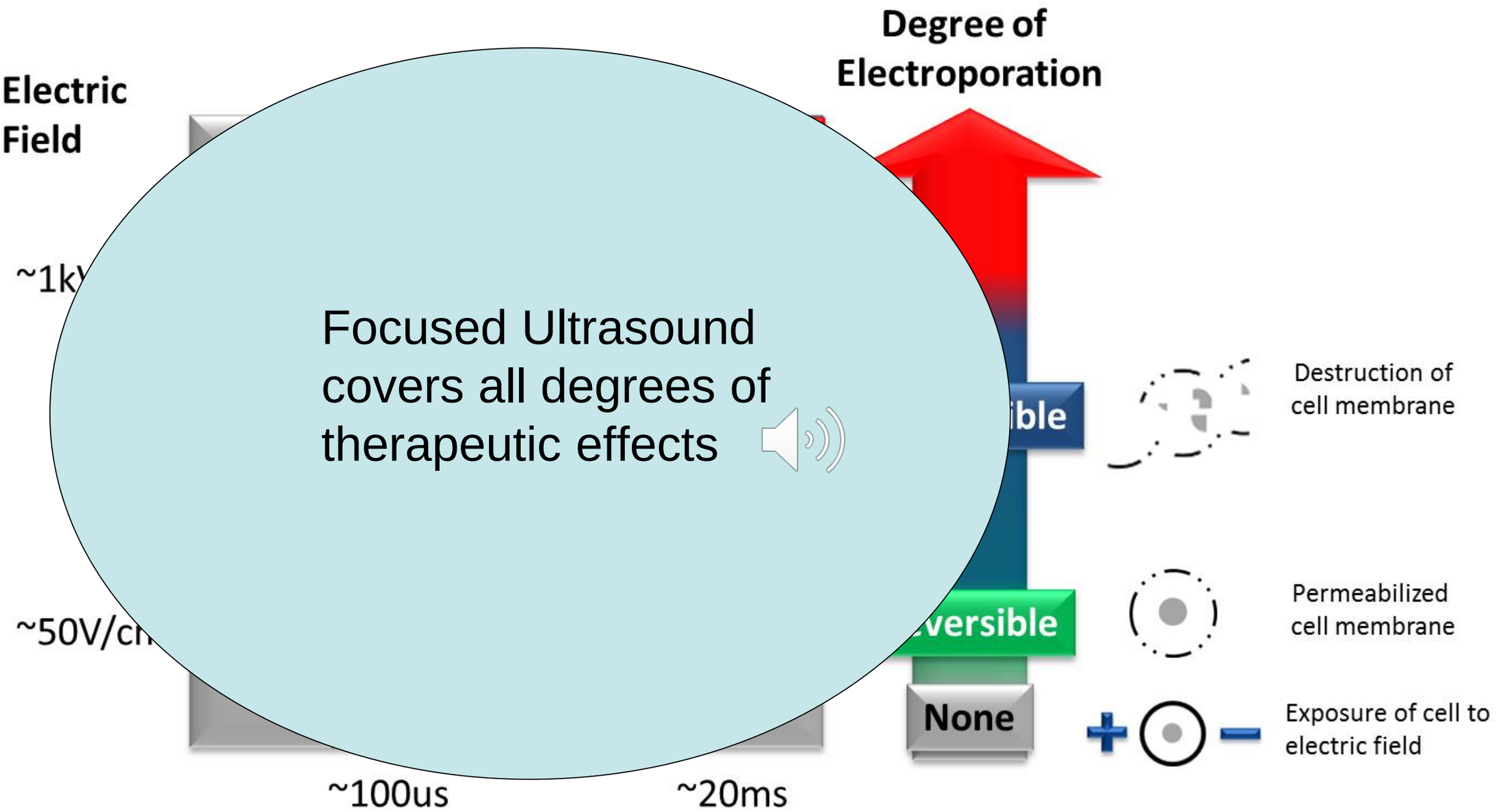
→ **Enabeling MR control from inside MR room**



Conclusion: Effect on Cells/tissue by FUS Application



Conclusion: Effect on Cells/tissue by FUS Application



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