MRI guided Therapies: seeing what you treat

Universitair Medisch Centrum
Utrecht

Chrit Moonen

Interventional radiology

University Medical Center Utrecht

- Vascular interventions
- Image guided biopsies
- Image guided drug infusion
- Tumor ablation
  - *Radiofrequency*
  - *Microwave*
  - *Laser*
  - *High Intensity Focused Ultrasound (HIFU)*
    - US guided HIFU
    - MRI guided HIFU

MRI guided
High Intensity Focused Ultrasound (HIFU)

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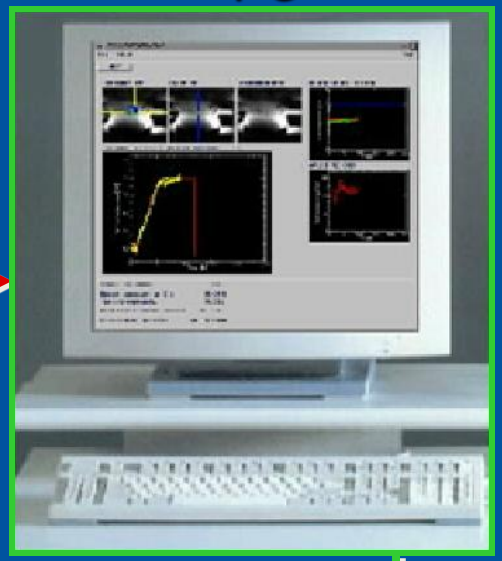
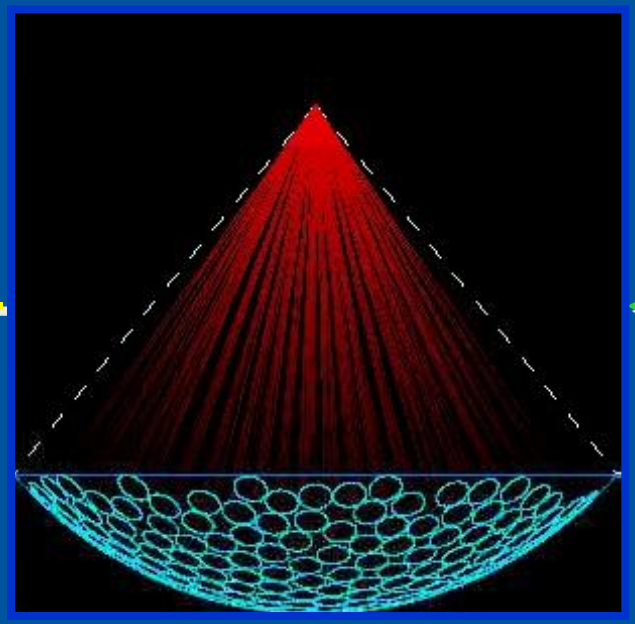
MRI with HIFU

anatomy and
temperature mapping

PC





TRANSDUCER

thermo-therapy

position and
power control

MRI guided Focused ultrasound: clinical applications

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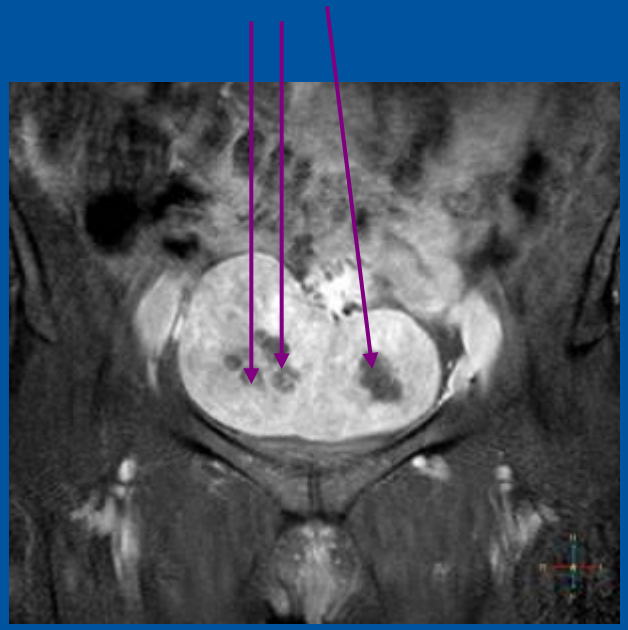
Patient 1 (Uterine Fibroid) 20/11/2008, Philips/CHU Bordeaux (Pr Trillaud)

Before

HIFU Ablation



After

Radiotherapy

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- Standard-of-Care for many types of cancer
- High-Precision Treatment (Gamma-knife, linear accelerator, proton beam)
- Pre-planning is image guided
  - *Definition of Gross Tumor Volume (GTV)*
  - *Definition of Clinical Target Volume (CTV)*
  - *Identification of Organ At Risk (OAR)*
- Until now, treatment itself is not (real-time) image guided
- Mobile organs are generally not treated with RadioTherapy
- Modern RadioTherapy moves towards real-time image guidance (US, X-ray, MRI)

MRI offers superb soft tissue visualization

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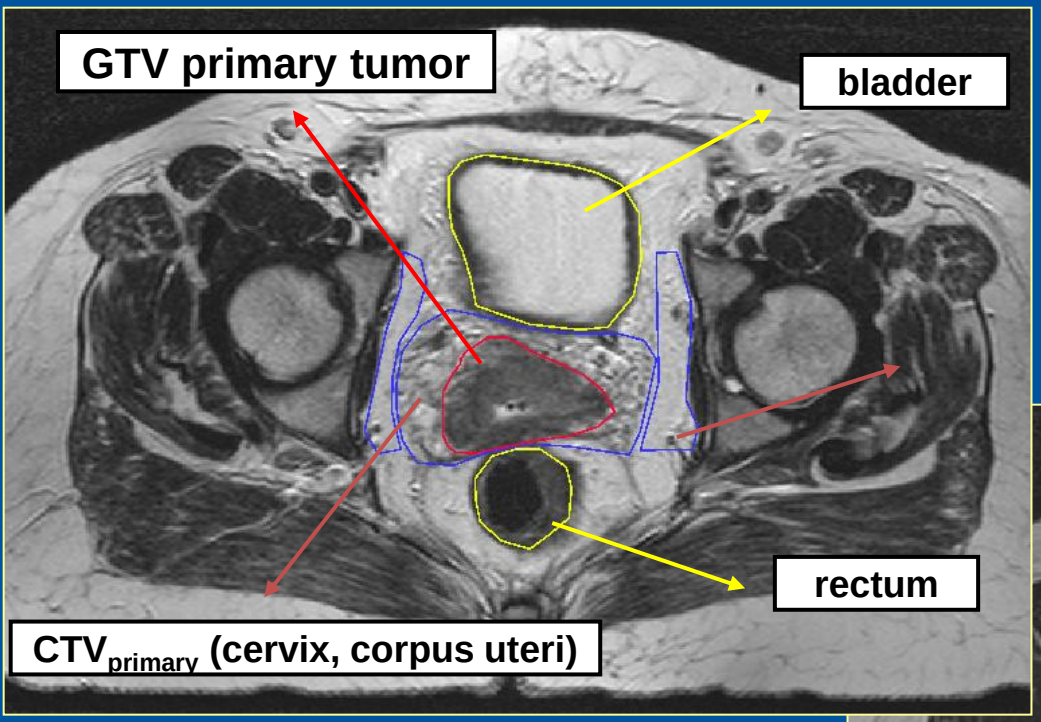
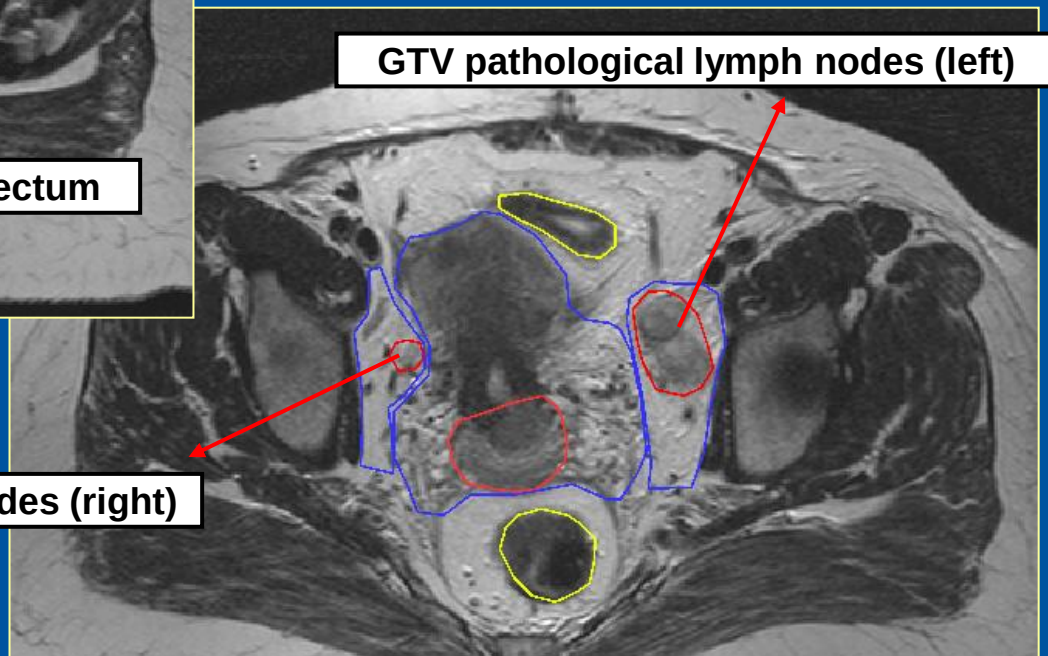


T2 weighted MRI sequence cervix



Real time breathing related motion

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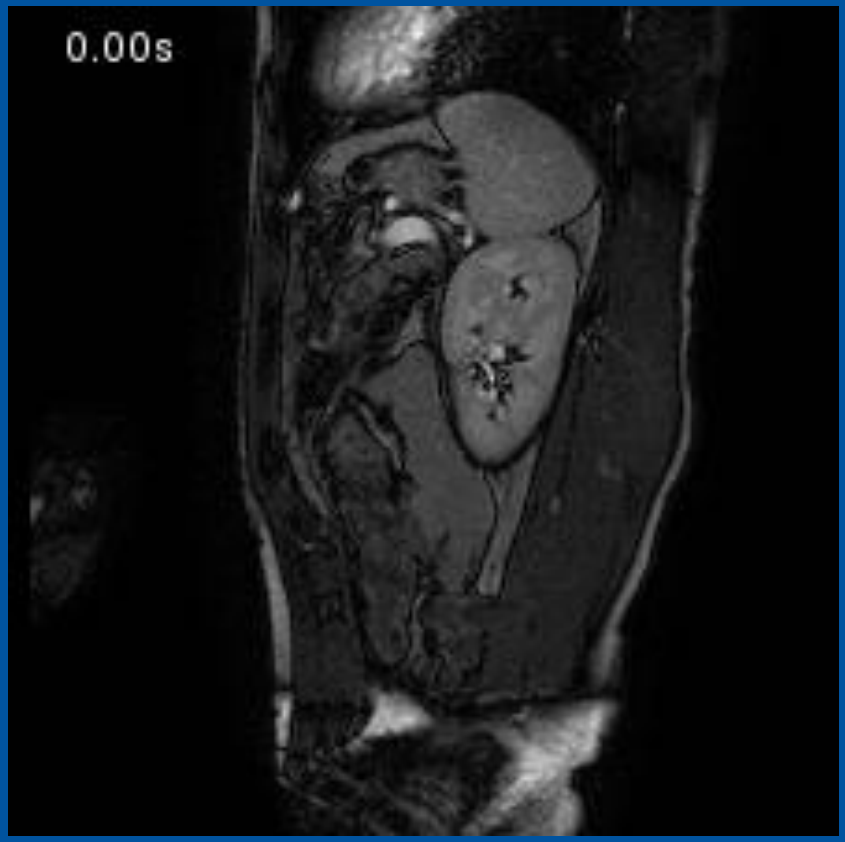

irregular breathing von Hippel Lindau kidney tumour

Breathing related motion

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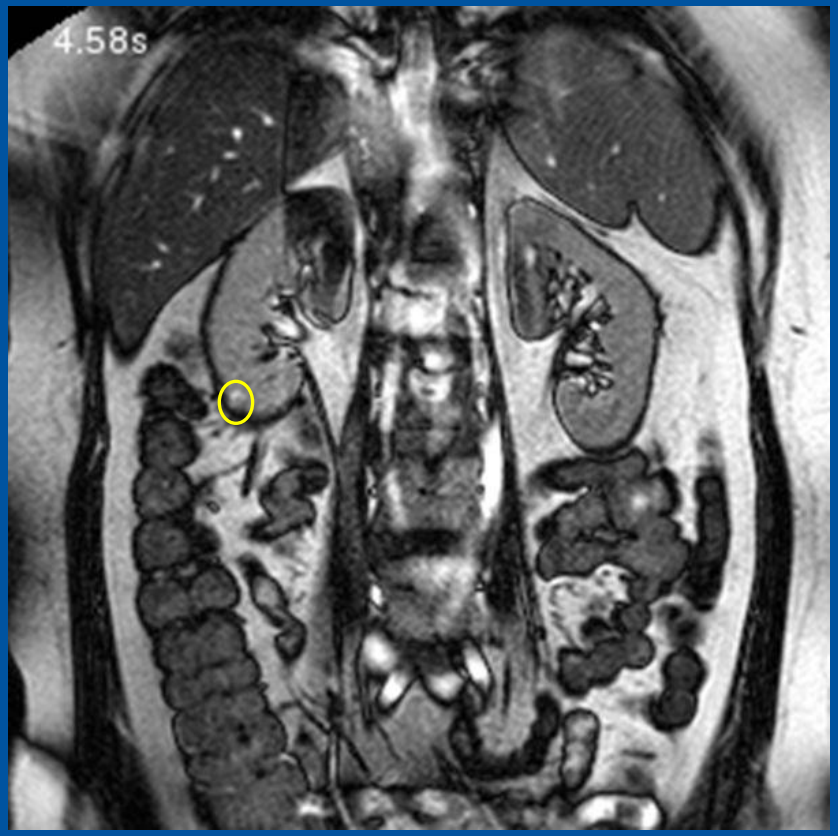
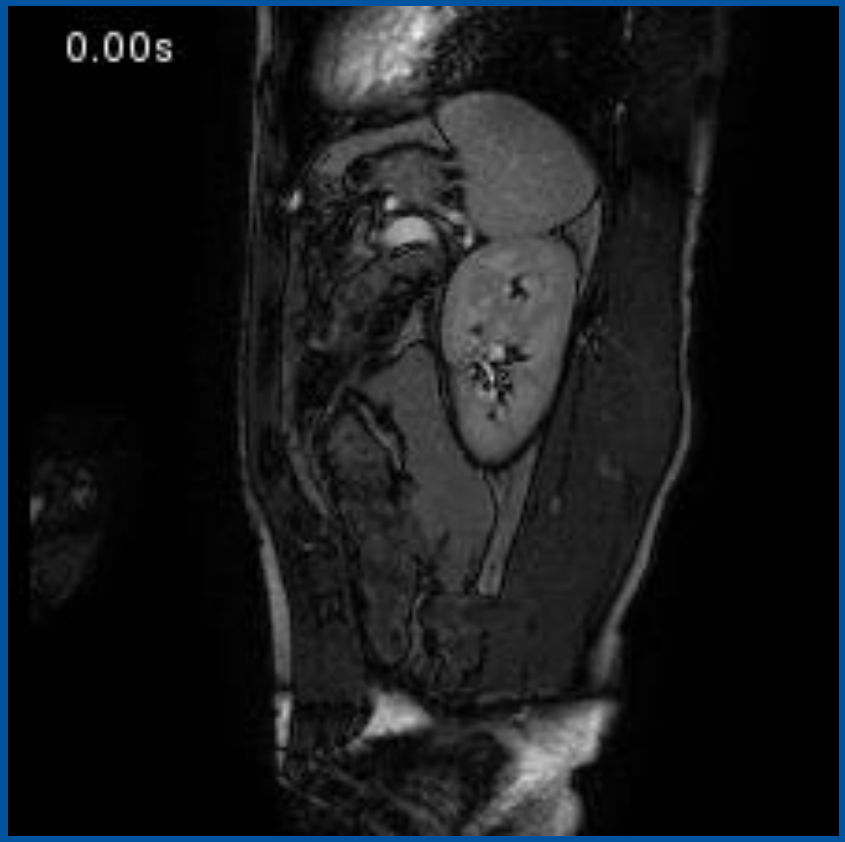


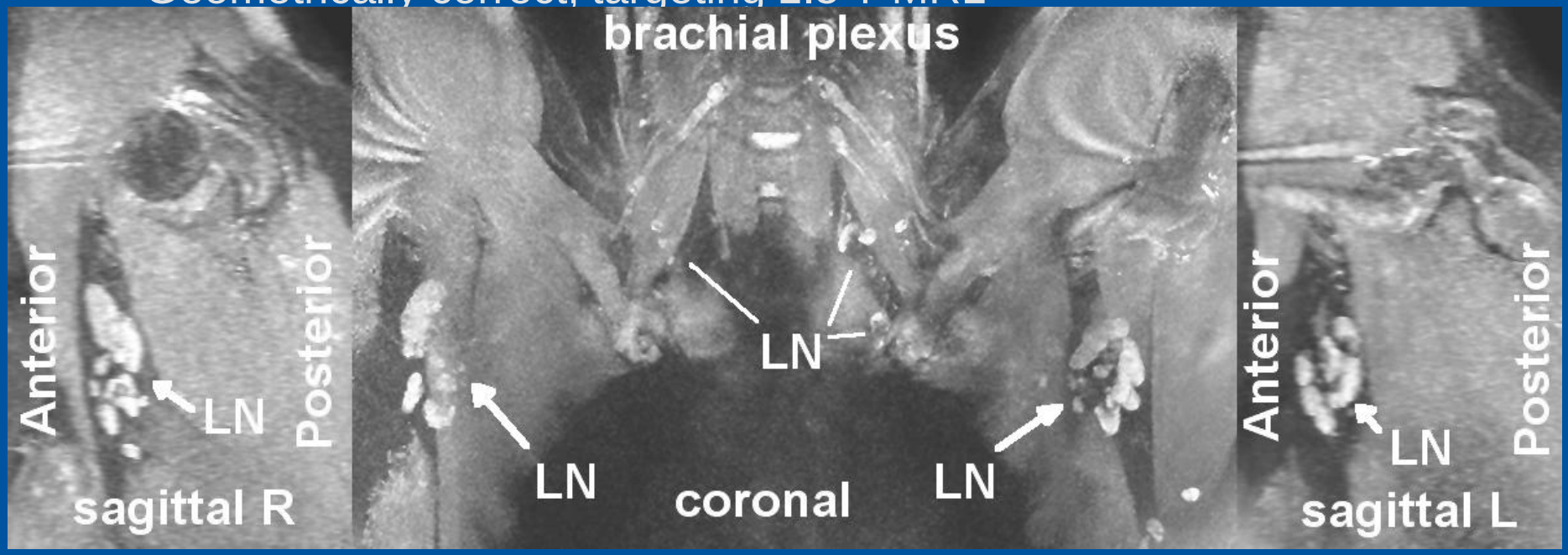


irregular breathing von Hippel Lindau kidney tumour

New 3D T2-FFE sequence with unique potential lymph nodes breast cancer patients

University Medical Center Utrecht

- 3D T2-FFE with some intrinsic diffusion weighting, fat suppression and black blood imaging
- Resolution 0.7x0.7x1 mm
- Geometrically correct, targeting 1.5 T MRL



T2-FFE MRI axillary lymph nodes

Vision: MRI guided Therapy

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- With MRI we see the GTV and we can follow/track tumours
- The GTV is hard to track with present day radiotherapy
- Tumour infiltrations are relatively well visualized
- We want to use the actual MRI to better track the GTV and spare OAR

Conclusion UMCU: MRI guided cancer treatment, **seeing what you treat**

Outline

University Medical Center Utrecht

- MRI guided RadioTherapy
- MRI guided Focused Ultrasound
- Image Guided Chemotherapy
- Center for Image Guided Oncological Interventions

Outline

University Medical Center Utrecht

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Volumetric MR-HIFU ablation of breast cancer using a dedicated breast platform

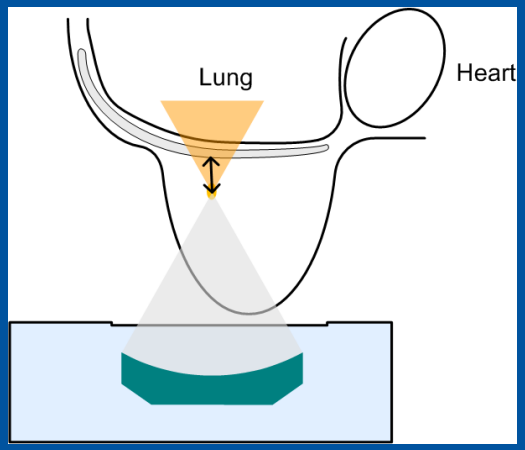
University Medical Center Utrecht

- Phase 1 study on patients with pathologically proven invasive breast cancer (n=10)
  - *Feasibility study to assess safety and treatment accuracy in patients with breast cancer*
- Treat-and-resect protocol
  - *Surgery between 48 hours and one week after HIFU treatment*
- Sentinel lymph node procedure
  - *Peritumoral injection of radioactive colloid just before surgery*
  - *Detection during surgery*

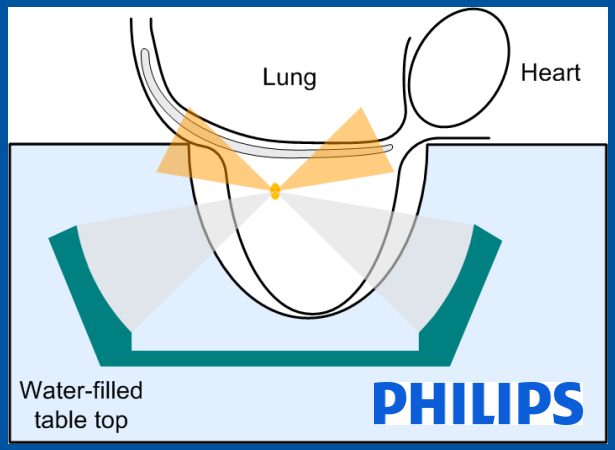
Dedicated breast MR-HIFU system

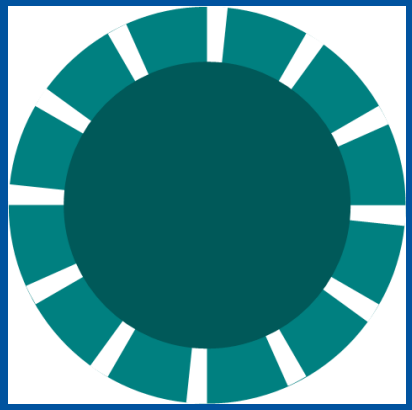
University Medical Center Utrecht

"Conventional" approach



Dedicated system with lateral sonication





transducer top view

Dedicated breast platform

Sonalleve Breast MR-HIFU

University Medical Center Utrecht

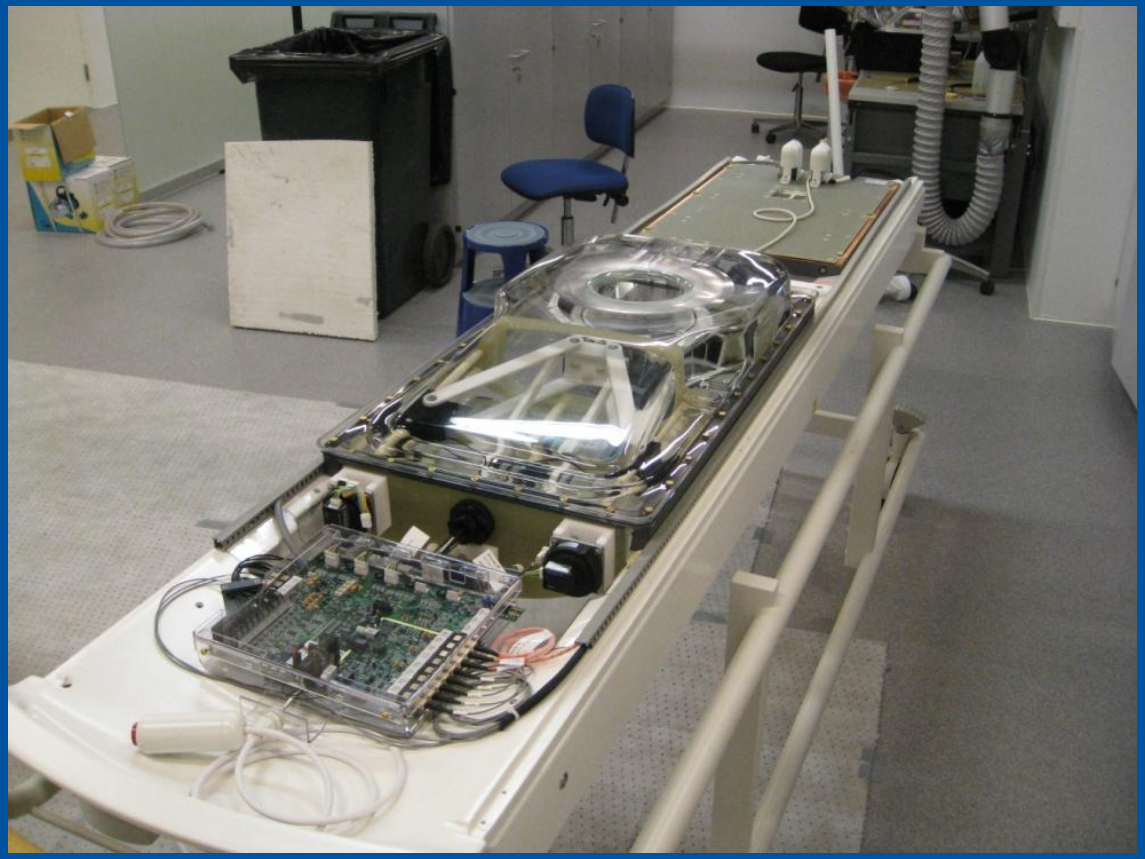
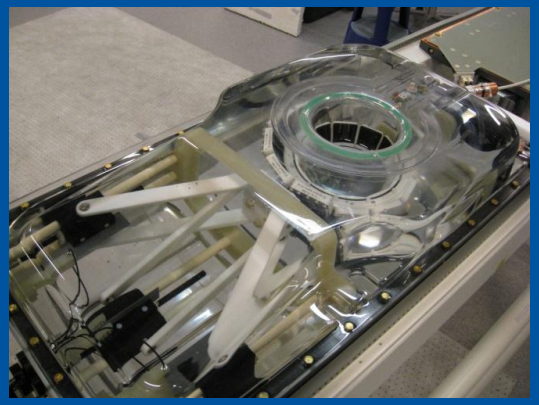
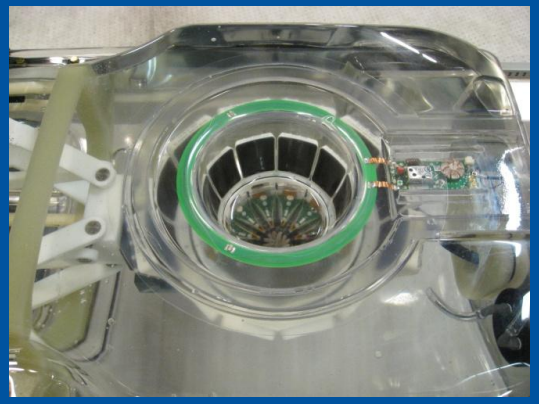


Table top without covers



Water box with transducer and motors



Close-up of breast cup, single-element RF coil, and transducer

Results: 3 Tesla MRI

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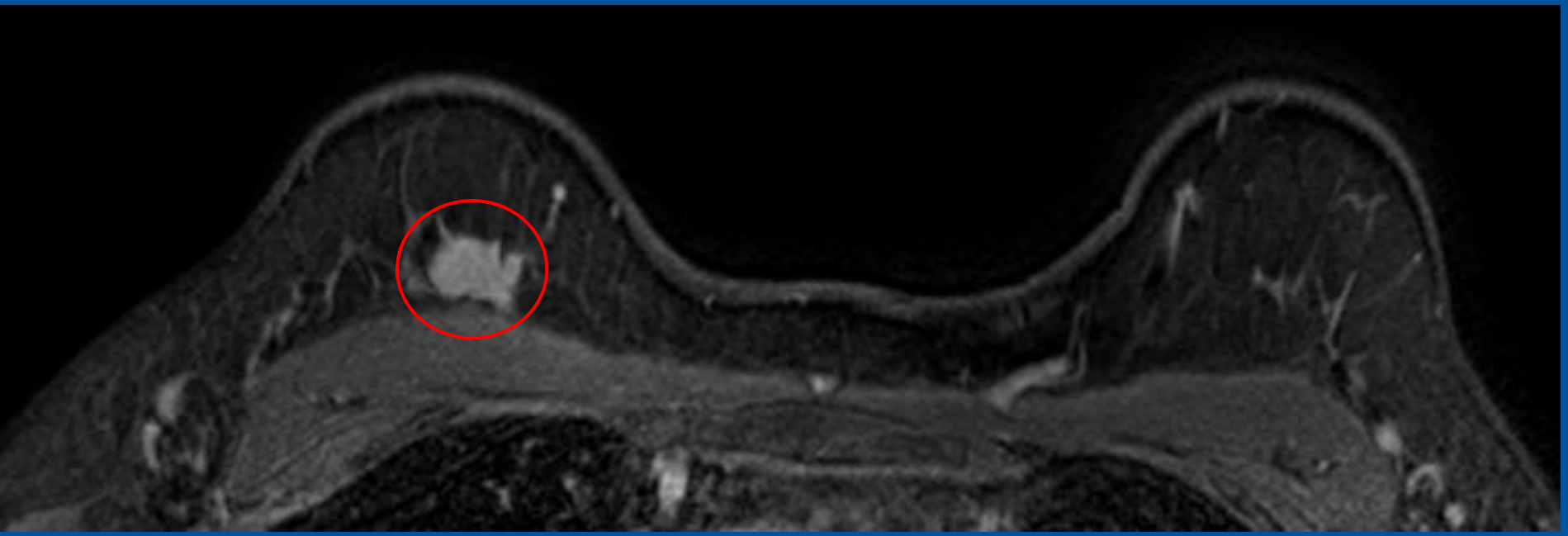

Results: MR-HIFU

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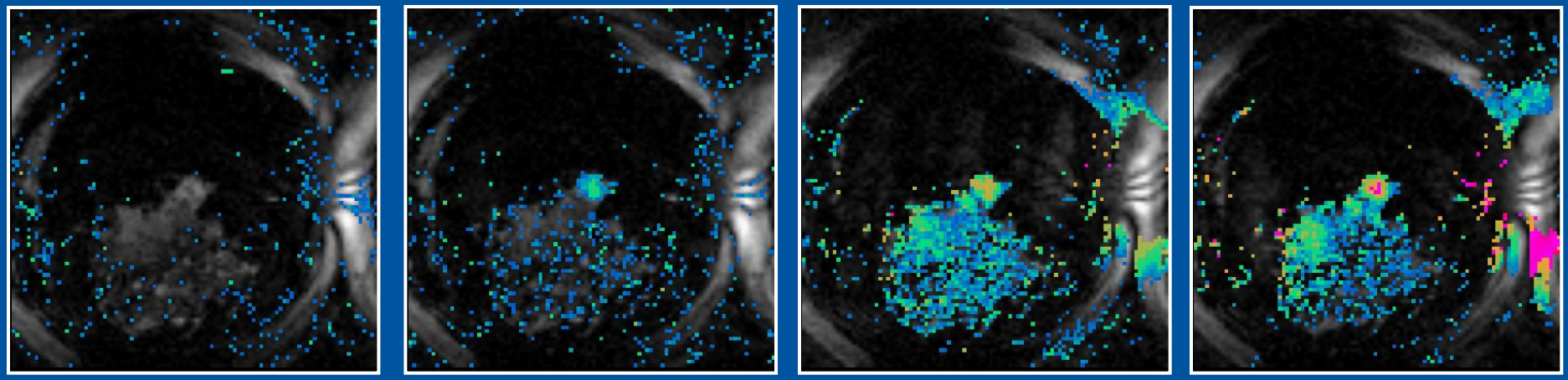

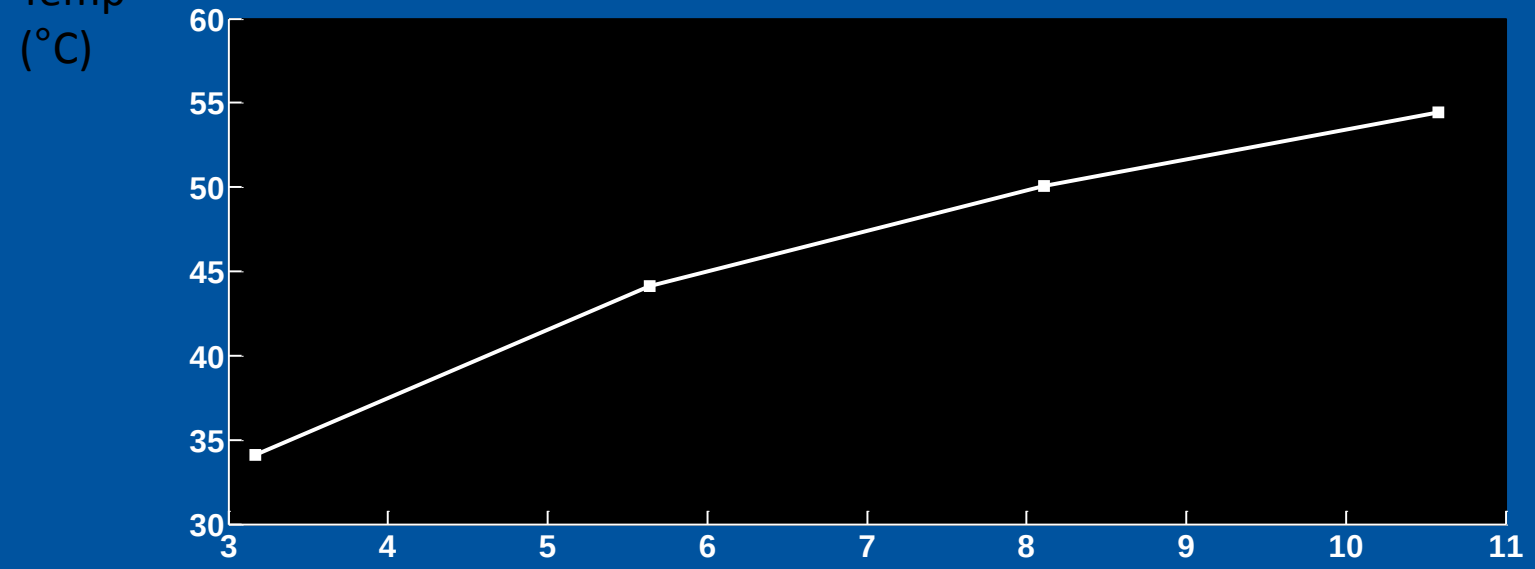

Results: after MR-HIFU ablation

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- Minimal pain after MR-HIFU ablation
- Lumpectomy three days after MR-HIFU ablation
  - *Detection of sentinel lymph node*
  - *No damage to pectoral muscle*
- Pathology
  - *No macroscopic or microscopic changes visible in tumor tissue (patient 1)*
  - *Macroscopic changes visible in tumor tissue (patient 2) with diameter corresponding with thermal dose threshold*

Outline

University Medical Center Utrecht

- MRI guided RadioTherapy
- MRI guided Focused Ultrasound
- Image Guided Chemotherapy
- Center for Image Guided Oncological Interventions

Development of the ultimate MRI targeting system for RadioTherapy

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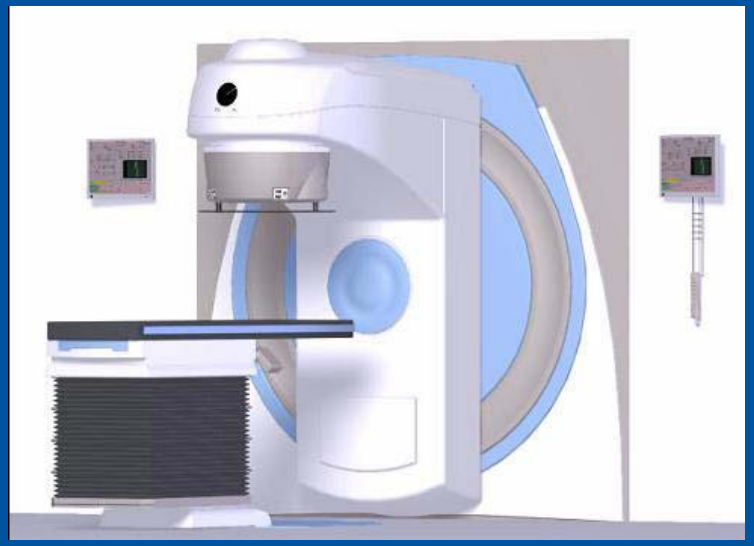
- Diagnostic quality MRI
- Targeting accuracy 0.5-1 mm
- On line/intrafraction/breathing
- Therapy plan update continuously
- Dose accumulation
- High dose rate
- Good IMRT properties (penumbra, scatter, transmission)
- Fast MLC



Concept of MRI accelerator

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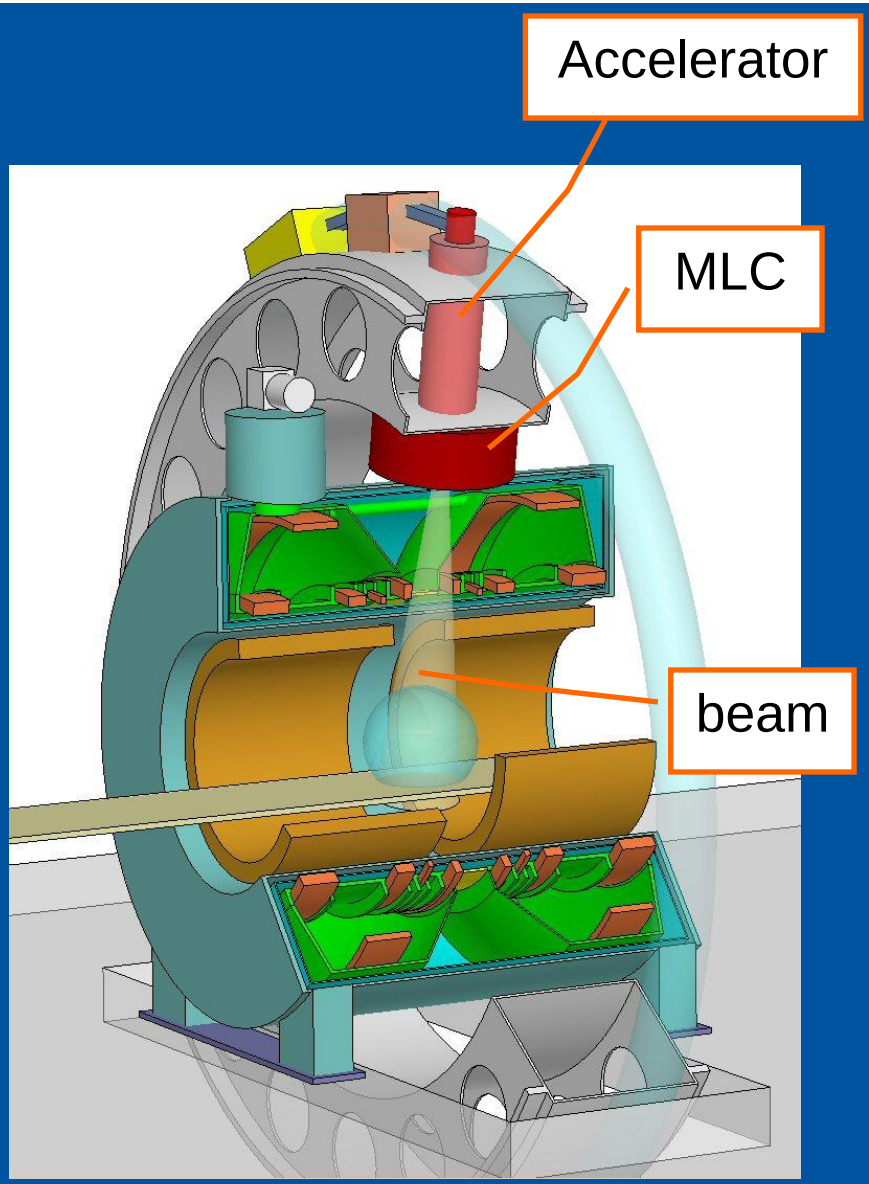

Principle of active B field shielding

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$B0_{out}=Bp_{out}-Bc_{out}=0$

0 T area

Bp_{out}

Bc_{out}

+

=

$B0=Bp_{in}-Bc_{in}$

0 T area

cross section through magnet

Radiation windows

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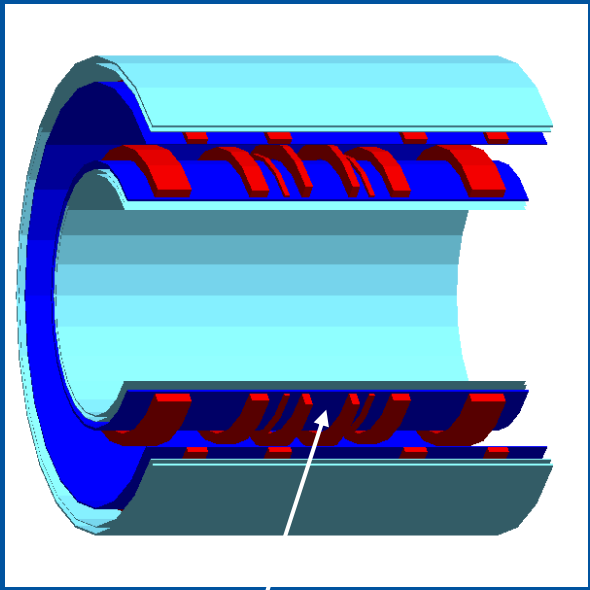
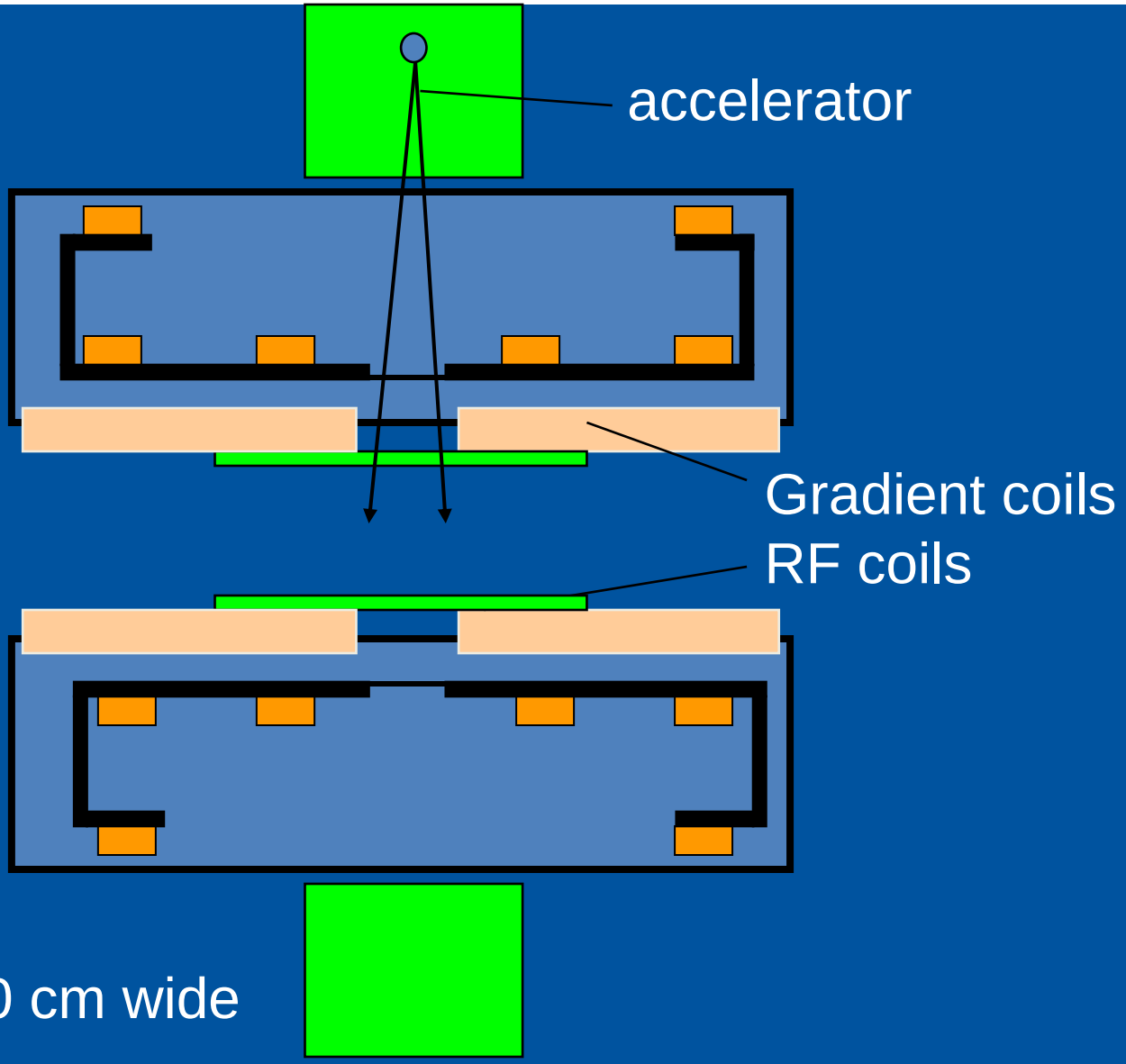


window for beam



Present design:
field 24 cm long x 40 cm wide

Specifications MRI accelerator

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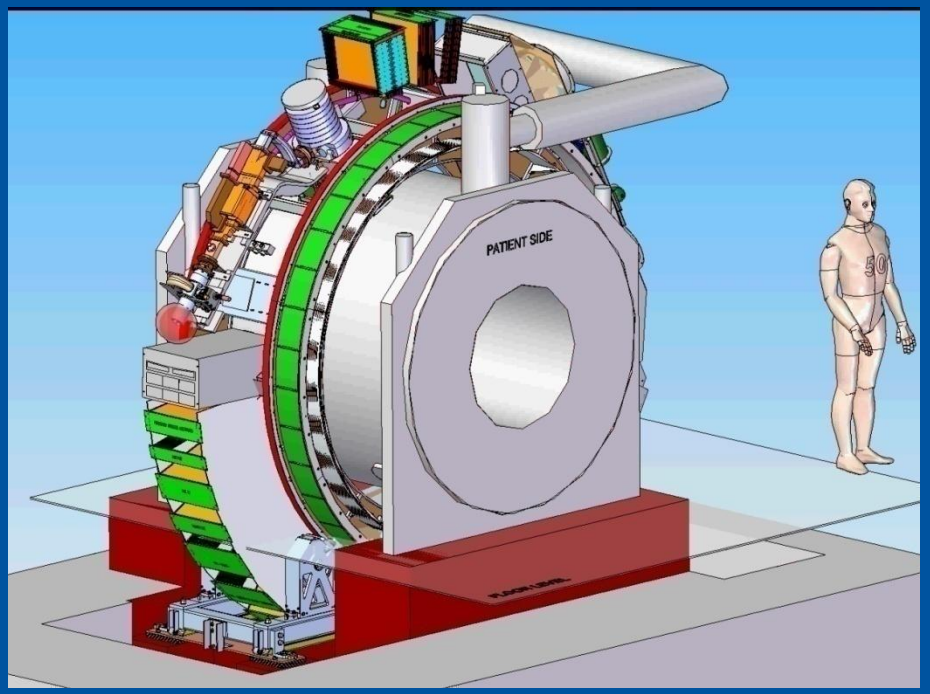
- 1.5 T diagnostic MRI
- 6 MV linac
- Simultaneous irradiation and MRI
- Continuously rotation
  - *Both directions*
  - *10 RPM*
  - *0.1 degree accuracy*
- 1 mm spherical volume as target
- MLC Field size 24x56 cm2
  - *7 mm leaves at isoc*



Philips and Elekta go MRI

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- Tumor characterization
- MRI simulation: delineation
- MRI guidance
  - *MRI treatment guidance external beam*
- MRI treatment response assessment

Outline

University Medical Center Utrecht

- MRI guided RadioTherapy
- MRI guided Focused Ultrasound
  - *Liver- preclinical (large animal)*
- Image Guided Chemotherapy
- Center for Image Guided Oncological Interventions

Magnetic Resonance guided HIFU of liver and kidney

University Medical Center Utrecht

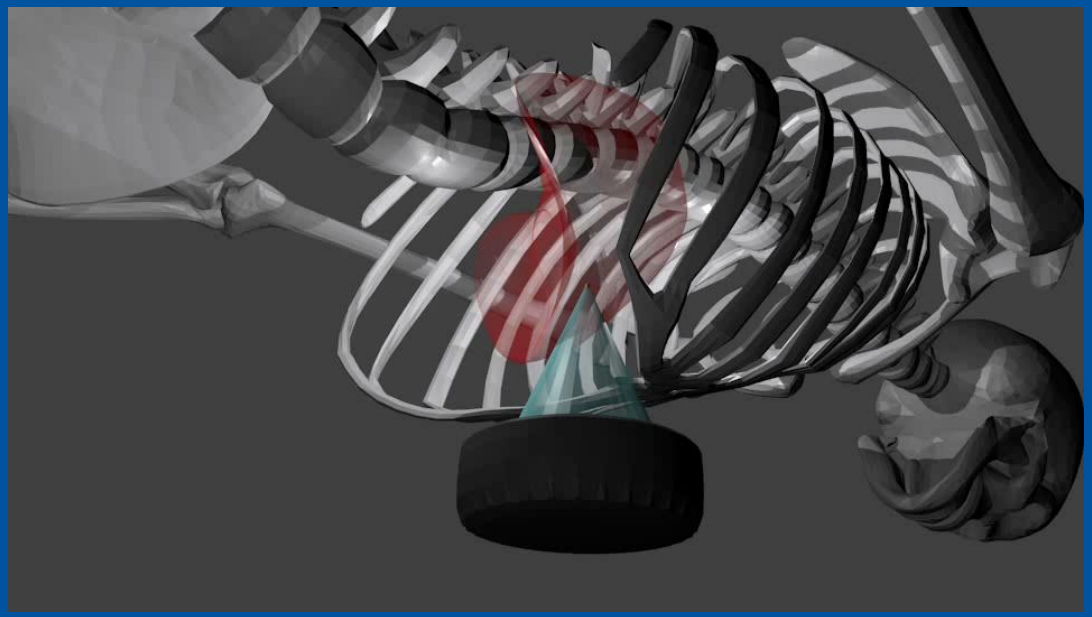
Challenges :

1. motion:
   - Artifacts in MRI thermometry
   - Target tracking/gated HIFU
2. Presence of ribs
   - Block propagation of HIFU
   - Burn risk in and around ribs
3. Highly perfused organs
   - Cooling due to flow/perfusion
   - High HIFU energy deposition
   - Burn risk in near and far field

MRgHIFU for cancer therapy: Challenges for HIFU in the liver

University Medical Center Utrecht

#1: Respiratory motion



- Motion Tracking:
  - MRI
  - Ultrasound
- HIFU guidance
  - Beam steering
  - Gated sonication

MRgHIFU for cancer therapy: Challenges for HIFU in the liver

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#1: Respiratory motion

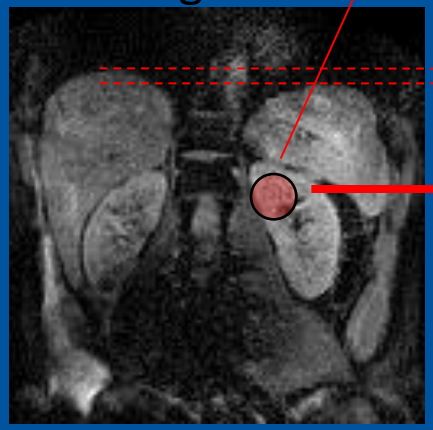
Abdomen of a free breathing volunteer

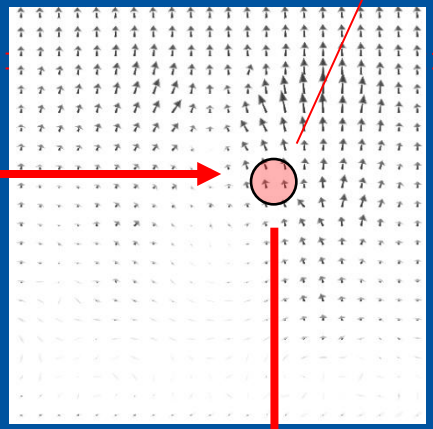
2) Optical flow based image registration image registration

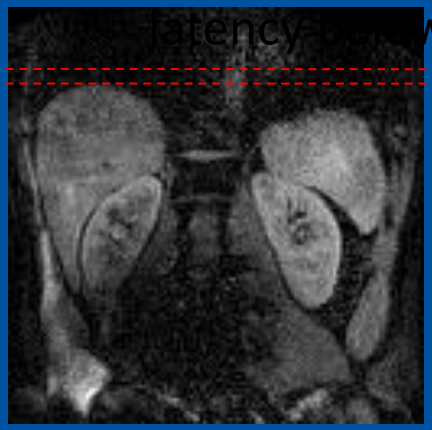
identify designated target position Look up the current target location

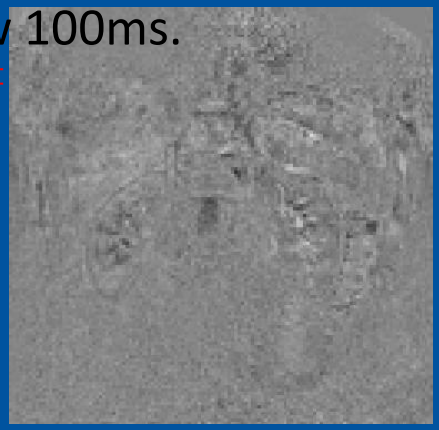
Global affine image registration

For respiratory motion this is done at a rate of 10Hz with a latency of ~ 100ms.



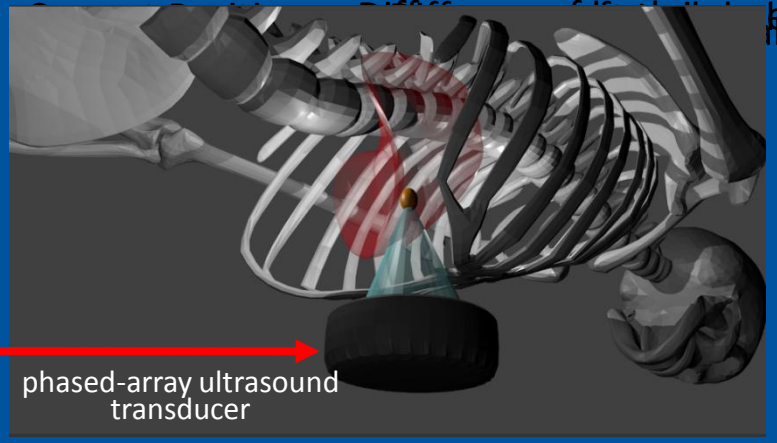






Reference Position

Update focal point position



Towards clinical MR-HIFU treatment in the liver

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Interventional Pre-Planning

- Preparatory scanning
- Evalute acoustic access
- Determine diffractive/refractive effects
- Estimate duty-cycle/volumetric ablation rate (treatment duration)

Treatment

- Inter-costal firing
- Respiratory motion compensation
- Feed-back control

Evaluation

- Comparison of Contrast-Enhanced MR images to thermal dose maps
- Correlation of histopathological Findings and thermal dose maps

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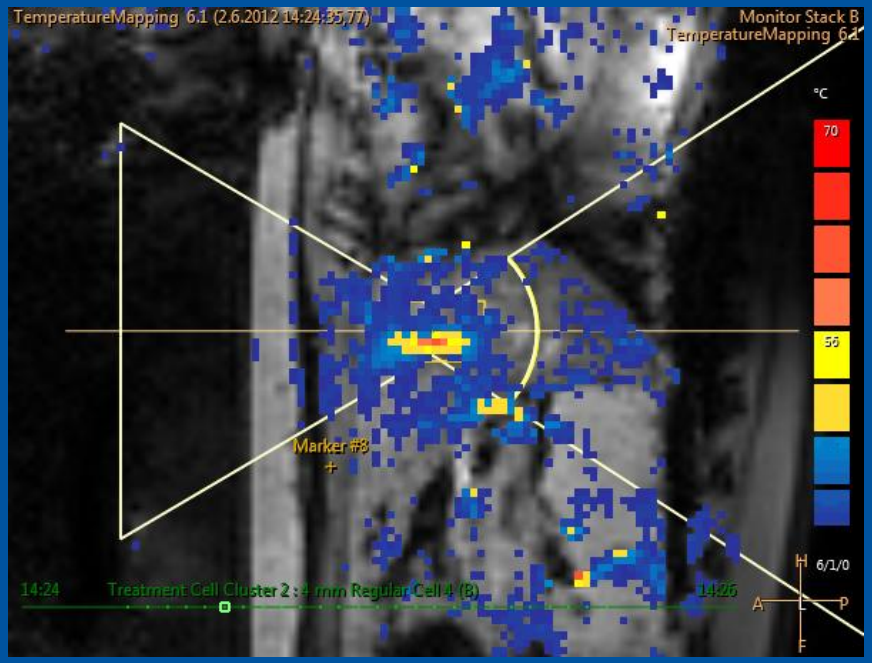
Treatment

- Inter-costal firing
- Respiratory motion compensation
- Temperature feed-back control



Liver ablations under clinical conditions

Continuous sonication with gated thermometry

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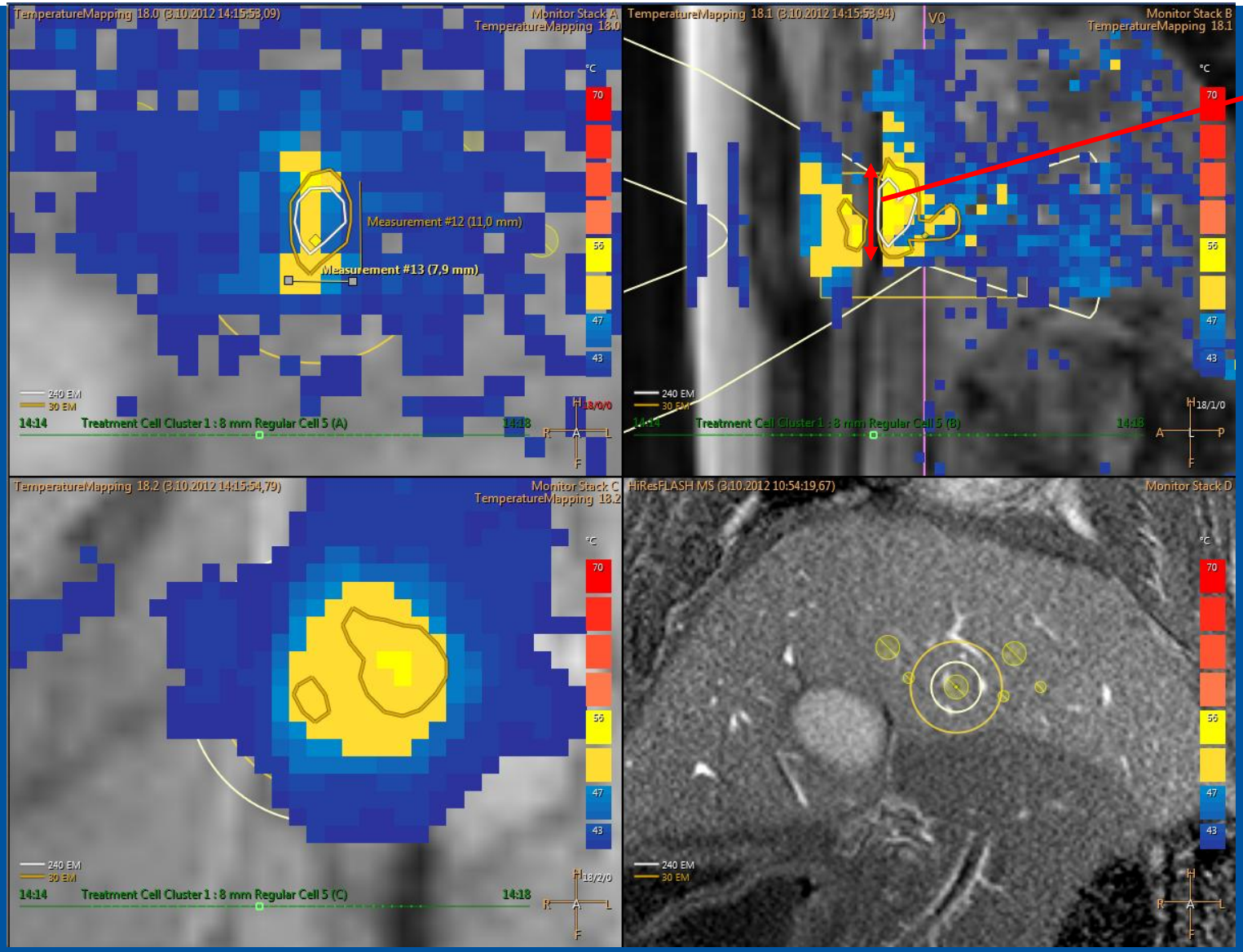

smearing of energy due to breathing motion

Reference: gated sonication

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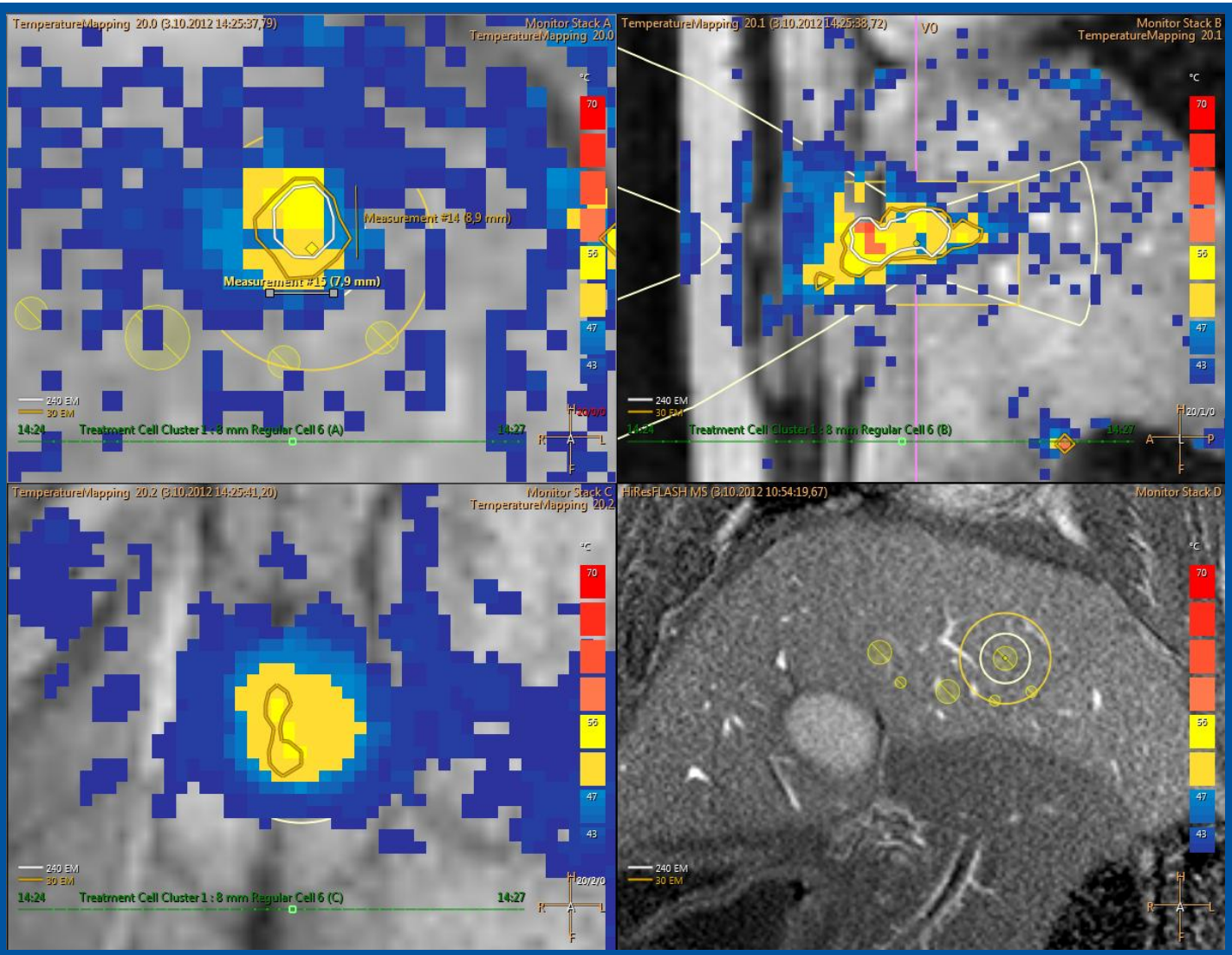
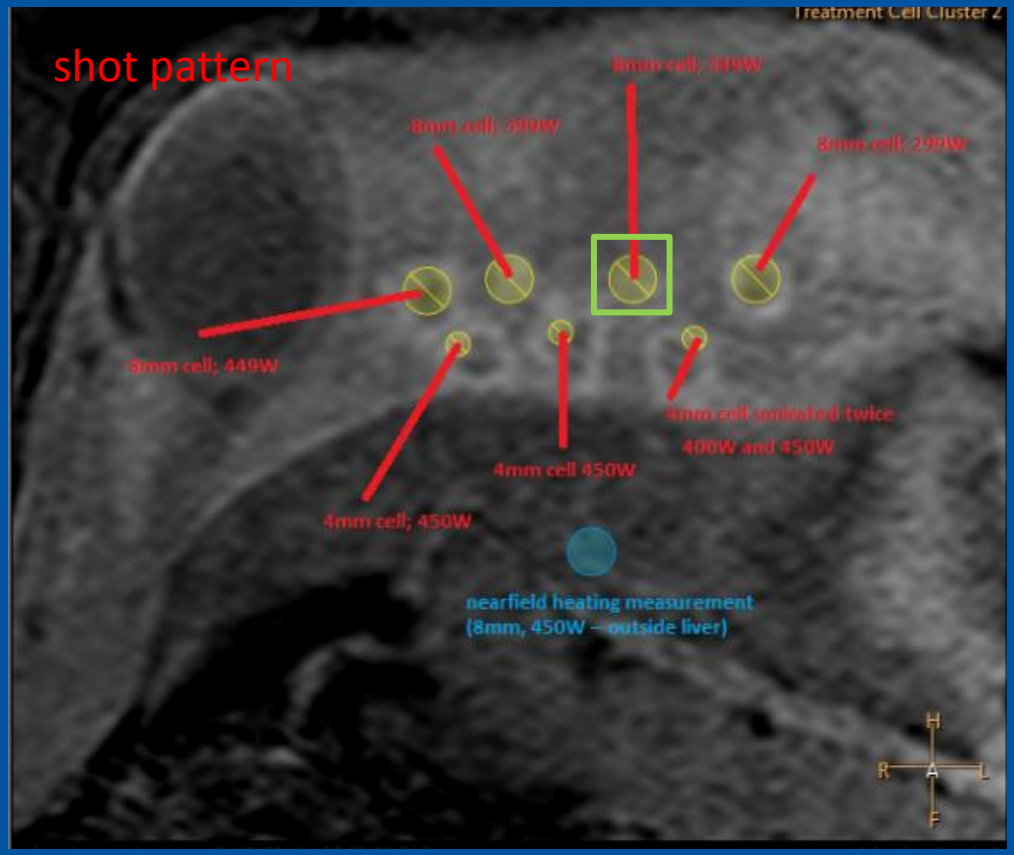
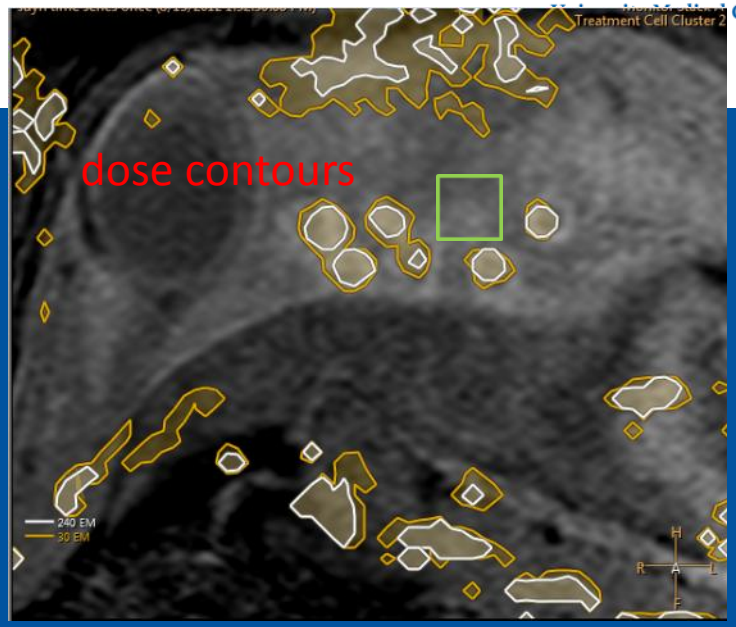


- adapted duration to duty-cycle
- isotropic shape

layered structures in beam-path strongly heated → oedema! (all sonications)

Power calibration animal 4





What about the 8mm 349W sonication?

Case study: Larger volume ablation

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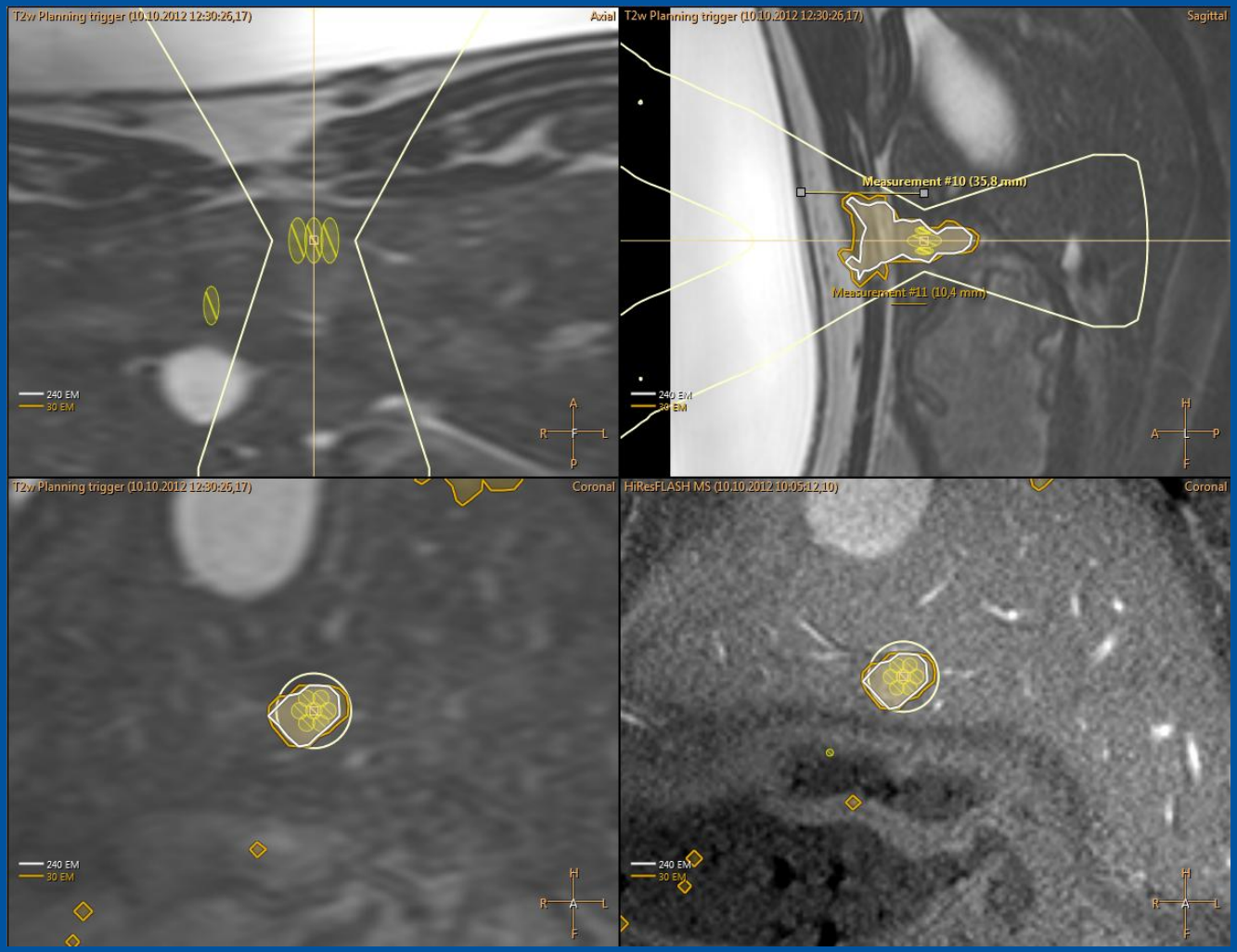

→ feasible for unobstructed, shallow shot

- ablation of region with 10mm diameter
- location:
  35mm from skin, 12mm inside liver
- 7 cells @ 4mm
- cooling time between shots > 10 min
- check for oedema with T2 while waiting

Larger volume ablation: pathology puzzle

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Intercostal-firing: The problem

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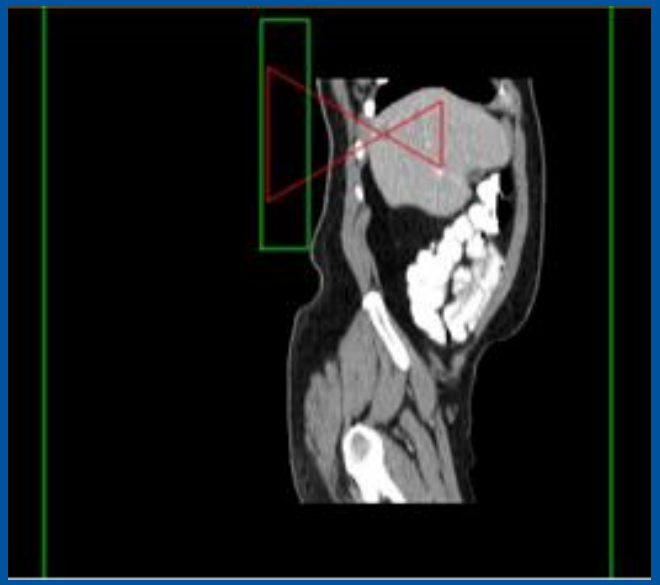
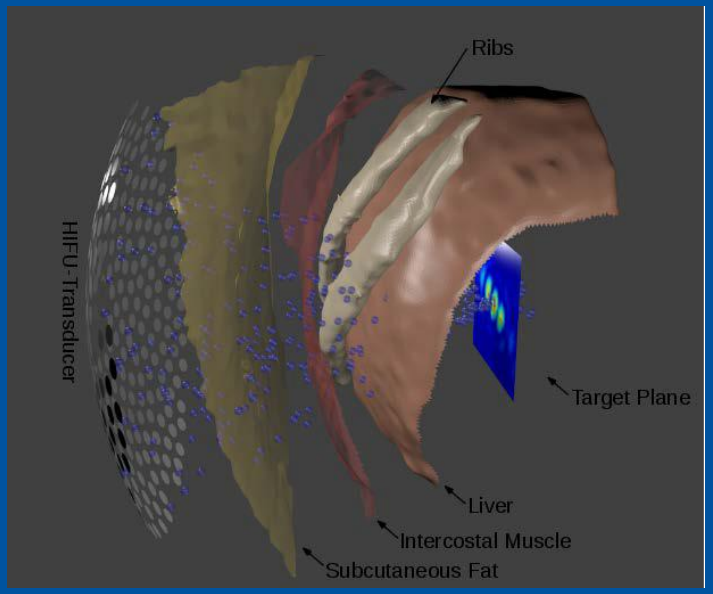


MRI / CT based preplanning tools



Treatment simulations for patient selection

Geometric Shadow

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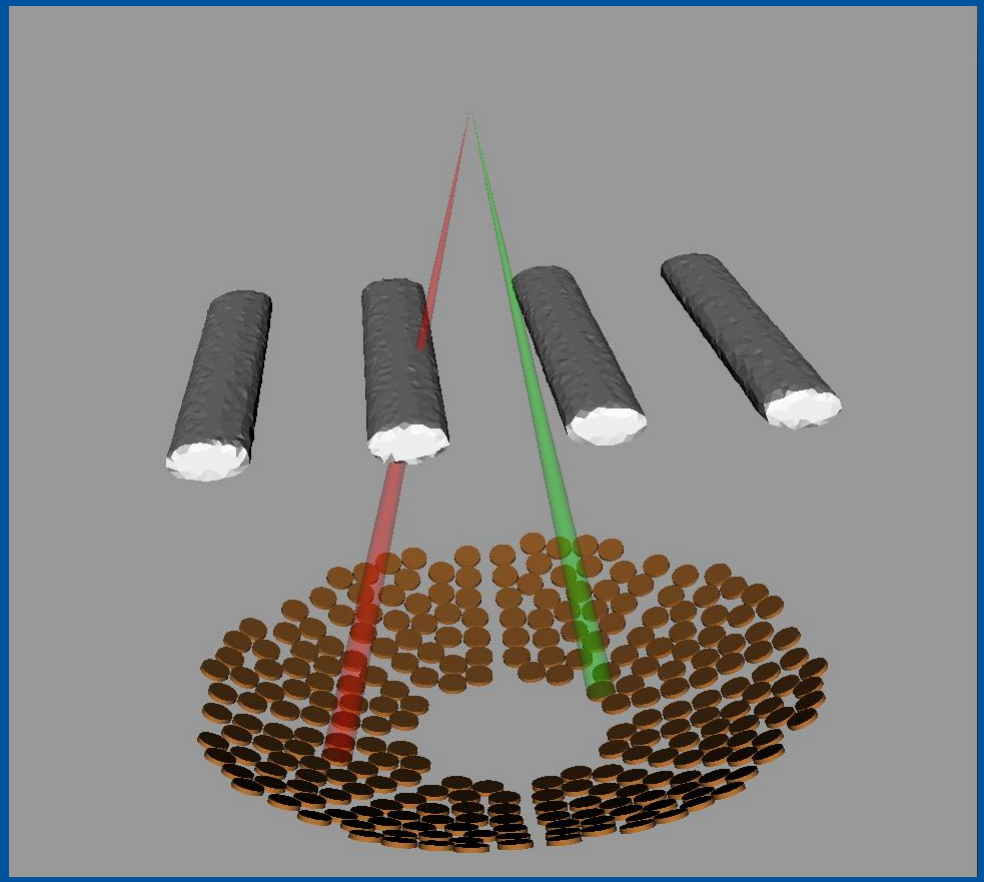

Determine shadowed fraction of area A_s

If A_s > threshold:

Switch Element OFF

$$P_{elem} \leftarrow P_{elem} \frac{n_{total}}{n_{active}}$$

Intensity-based thresholding

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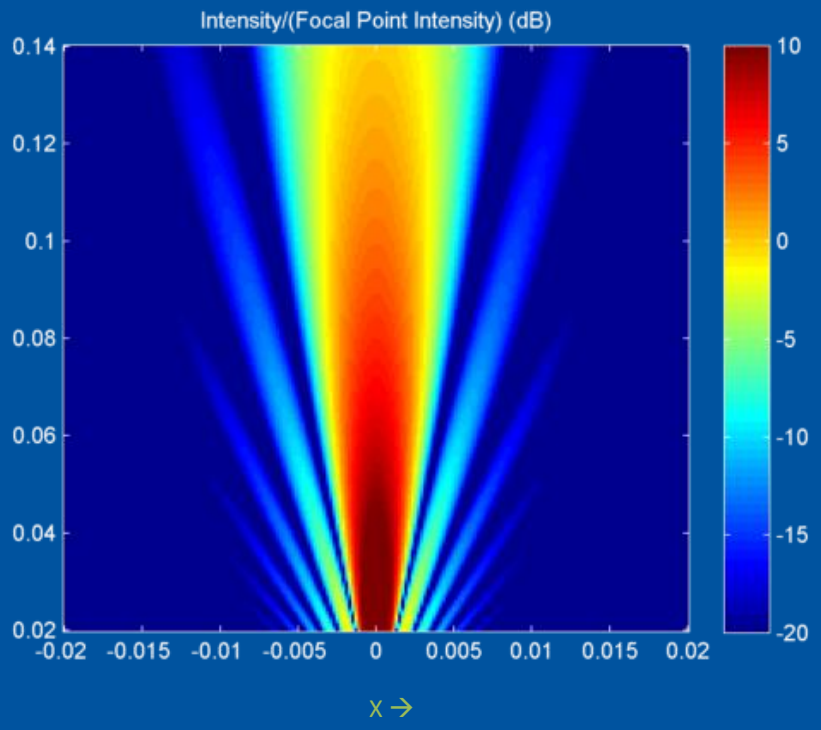
- Shadow casting ignores transmission characteristics
  - *'Blocked' elements can contribute to focus*
  - *'Unblocked' elements can expose the ribs*

Element Directivity Pattern



10% of focus intensity @ |x| = 6mm

Geometric Shadow

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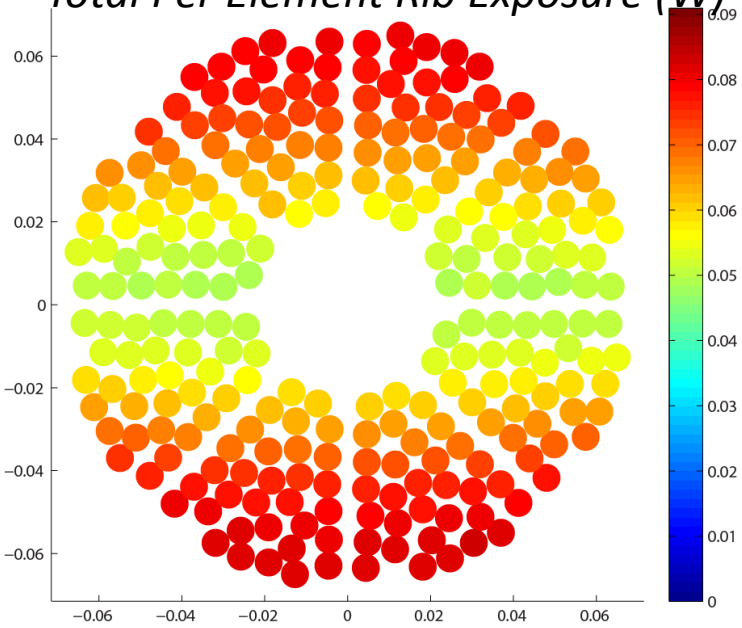
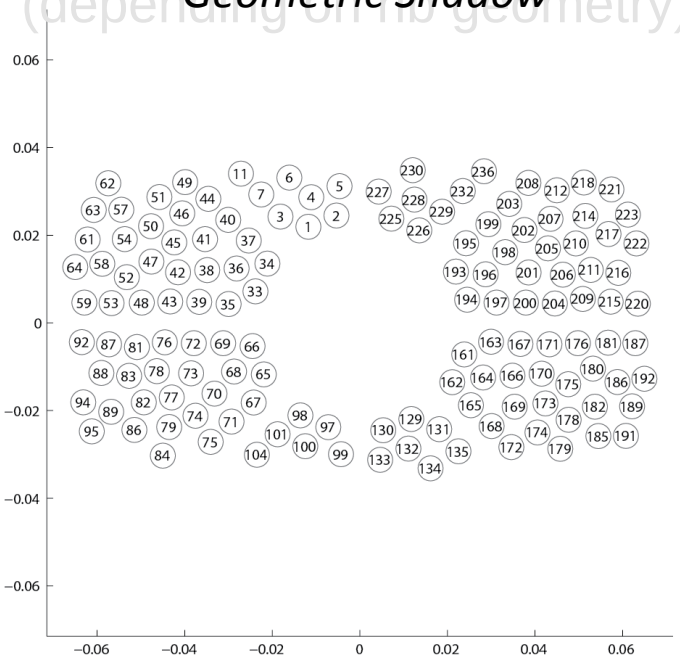
Pro

- Fast
- Relatively Simple

Contra

- Requires rib segmentation
- Weak correlation with exposure





Intensity-based switch-off

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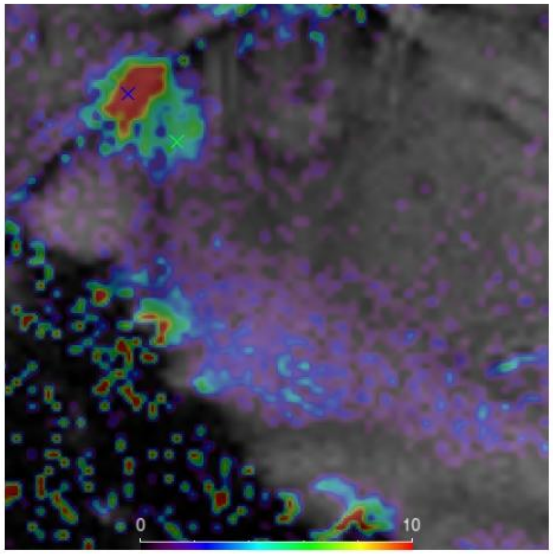
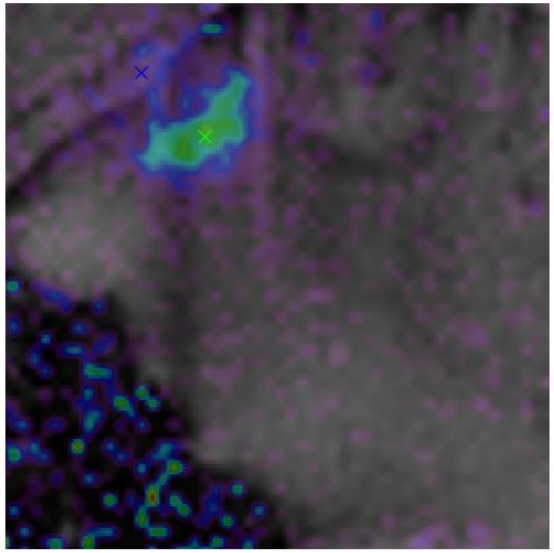
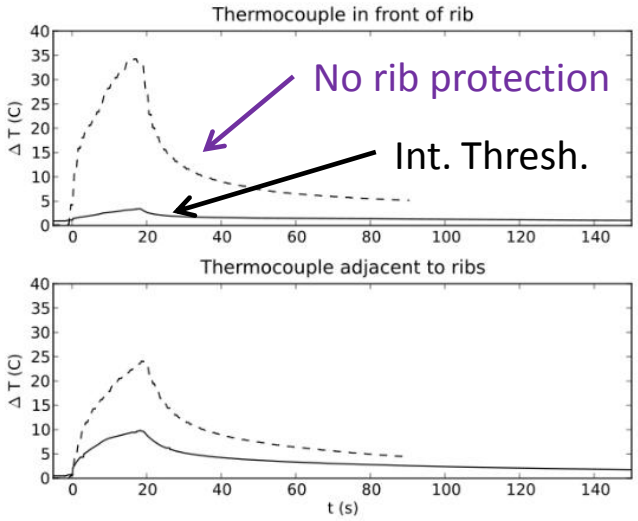
PRFS Thermometry @ rib level

Thermocouple measurements







No Rib Protection | Intensity Threshold

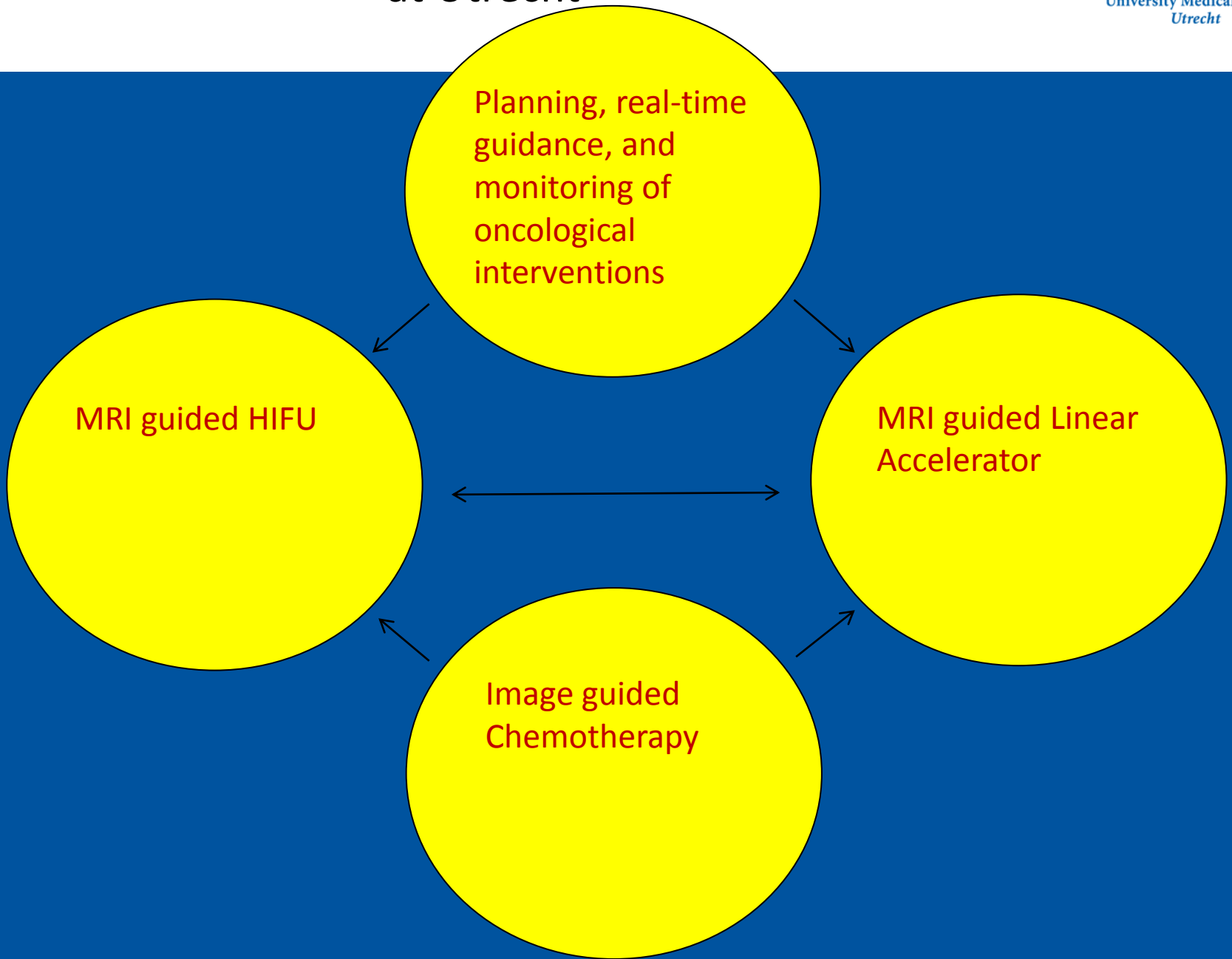
Outline

University Medical Center Utrecht

- MRI guided RadioTherapy
- MRI guided Focused Ultrasound
- Image Guided Chemotherapy
- Center for Image Guided Oncological Interventions

Center for Image Guided Oncological Interventions at Utrecht

University Medical Center Utrecht



Applications of Focused Ultrasound

University Medical Center Utrecht

- MR-HIFU for Image Guided, Local Drug Delivery
  - *Extravasation*
  - *Membrane permeabilization*
  - *Triggered drug release from nanocarriers*

Blood Brain Barrier (BBB)

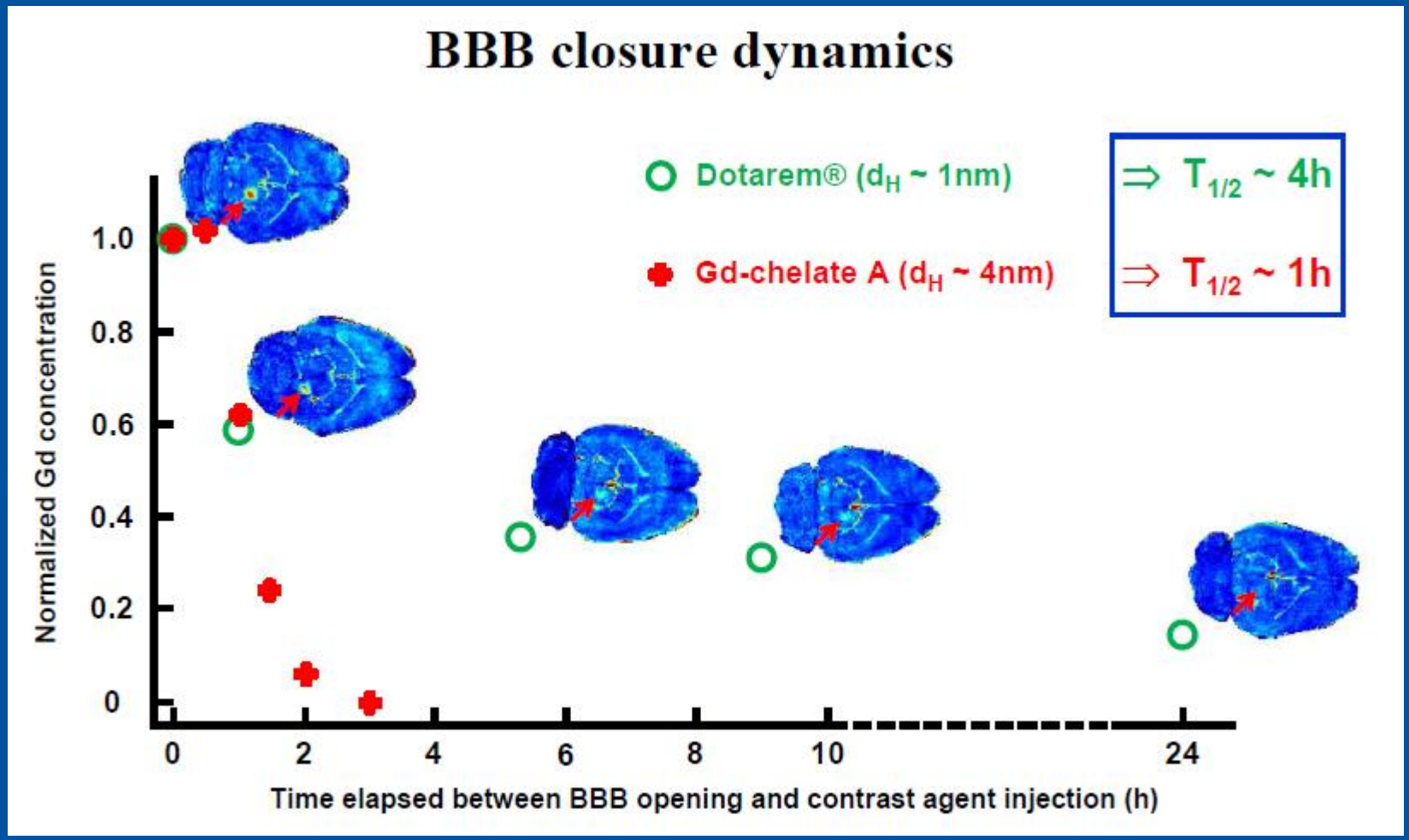
University Medical Center Utrecht

- **The primary hurdle to the use of drugs in the central nervous system for most small molecule agents and all large molecule agents**
- **Methods developed to bypass the BBB are invasive, non-targeted and/or require the development of new drugs**

Nathan McDannold, Harvard Univ

Focused Ultrasound and Microbubbles: BBB opening

University Medical Center Utrecht



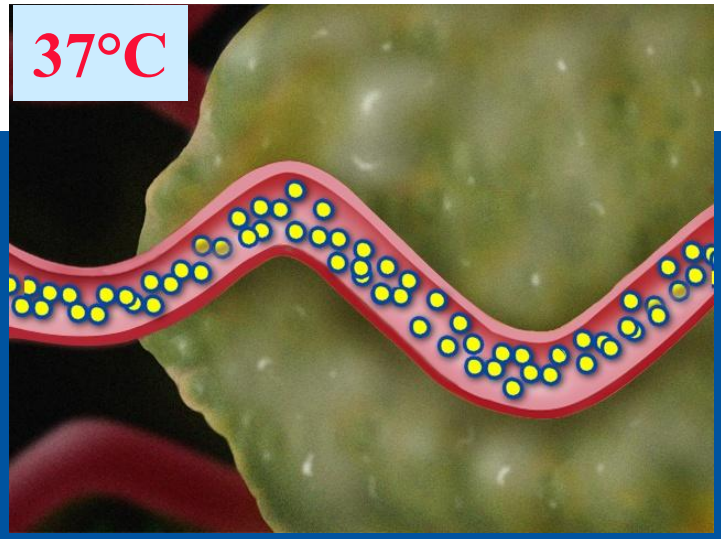
Benoit Larrat et al ISMRM 2011

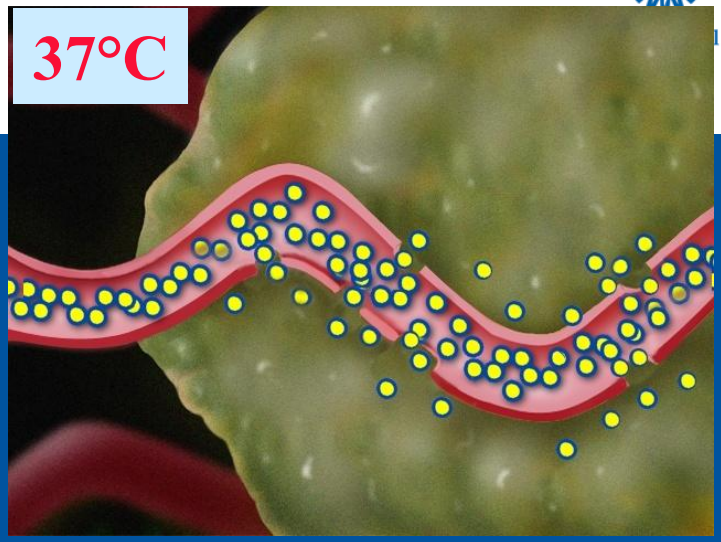
Applications of Focused Ultrasound

University Medical Center Utrecht

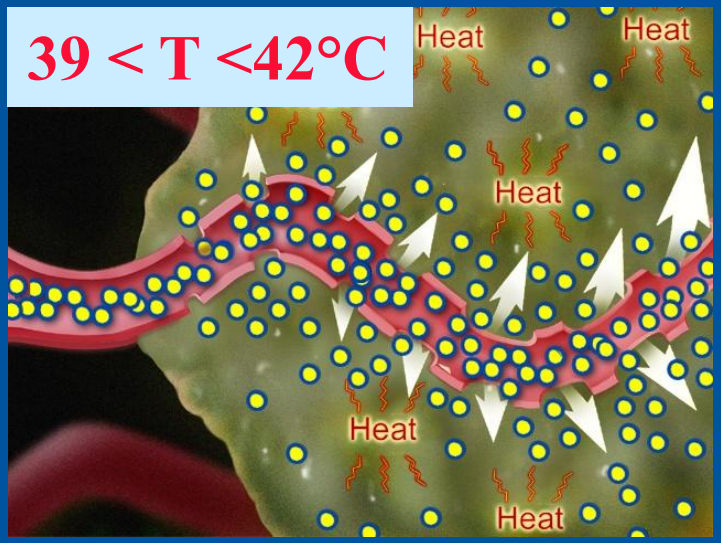
- MR-HIFU for Image Guided, Local Drug Delivery and Gene
  - *Extravasation*
  - *Membrane permeabilization*
  - *Triggered drug release from nanocarriers*

Low Temperature Heat Sensitive liposomes

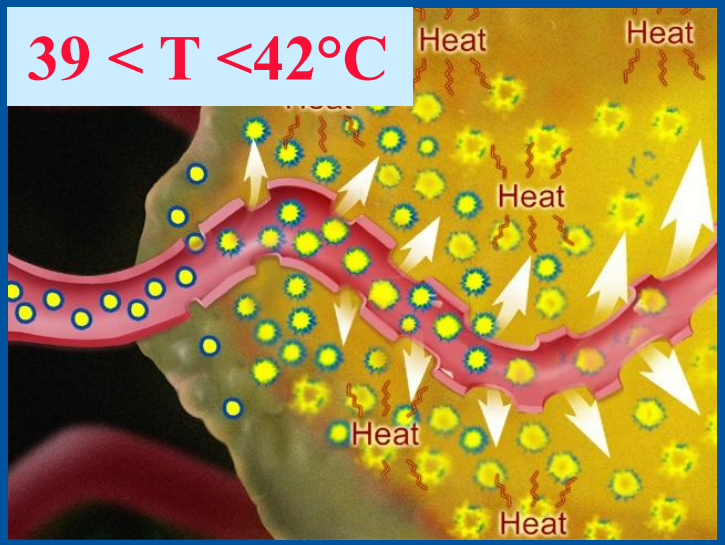




Leaky tumor vessels



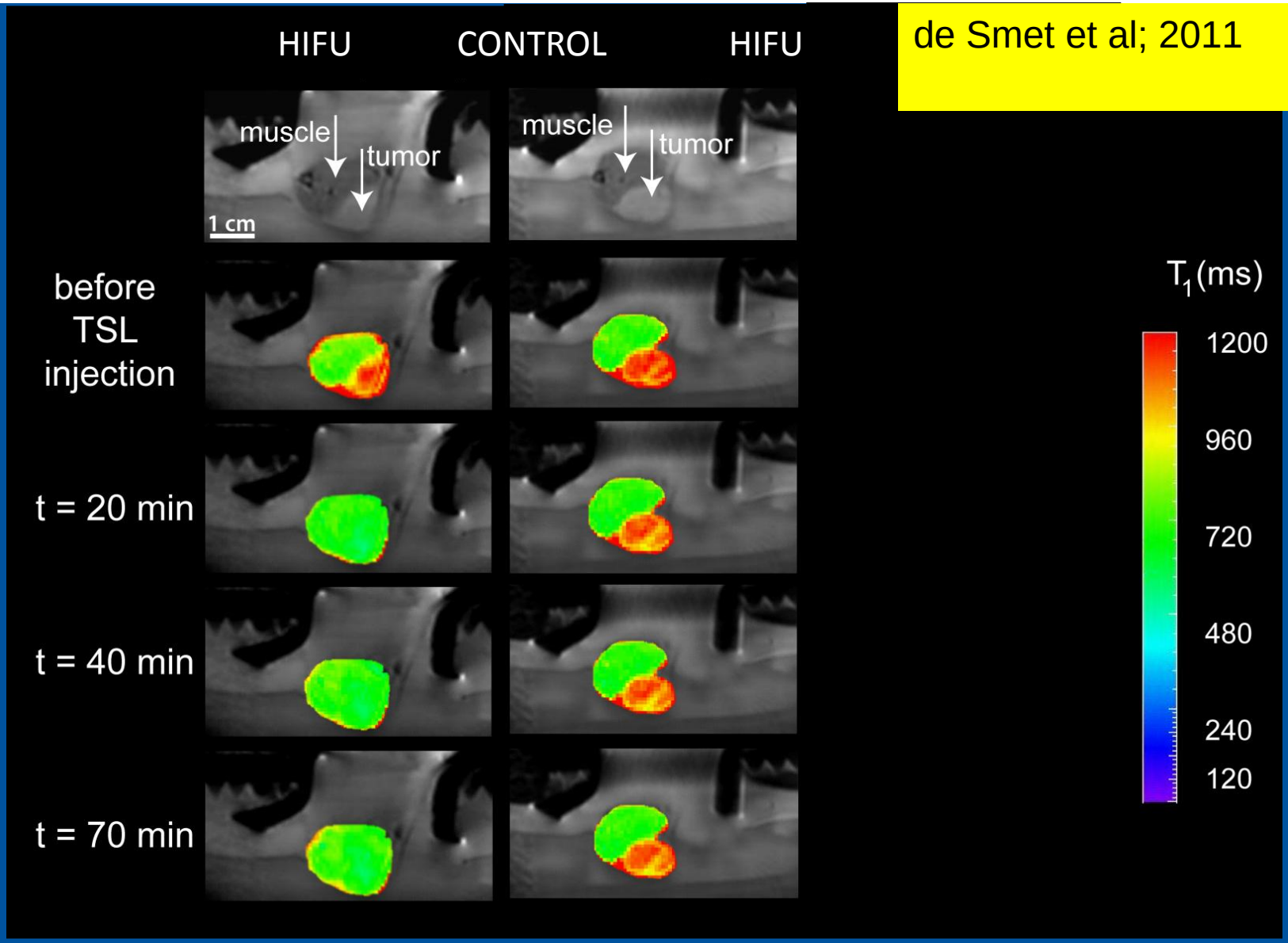
Heat adds permeability / extravasation



Cargo deployed @ 39-42 deg

Courtesy Mark Dewhirst, Duke University

Co-release of MRI contrast agents from liposomes visualized with T_1-maps

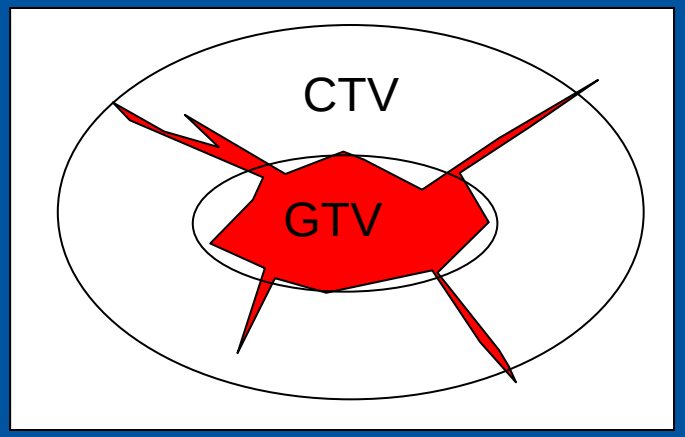


de Smet et al; 2011

Present indications Cancer Therapy

University Medical Center Utrecht

	distant	CTV	GTV
Chemo	+	+	-
RT	-	++	-/+
Surgery	--	-/+	+



Development MR-HIFU and MR-LINAC

University Medical Center Utrecht

	distant	CTV	GTV
Chemo	+	+	-
RT	-	++	++
Surgery	--	-/+	+
HIFU	-	+	++

MR-LINAC

MR-HIFU

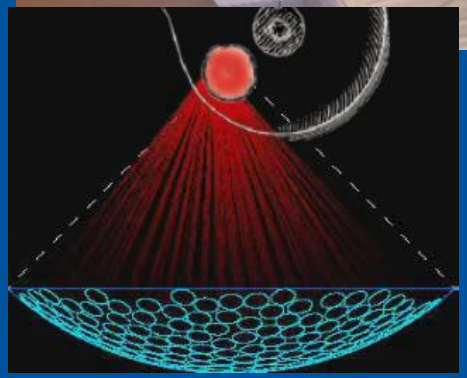
Centre for **I**mage **G**uided **O**ncological **I**nterventions (**CIGOI**)

University Medical Center Utrecht

MR-LINAC

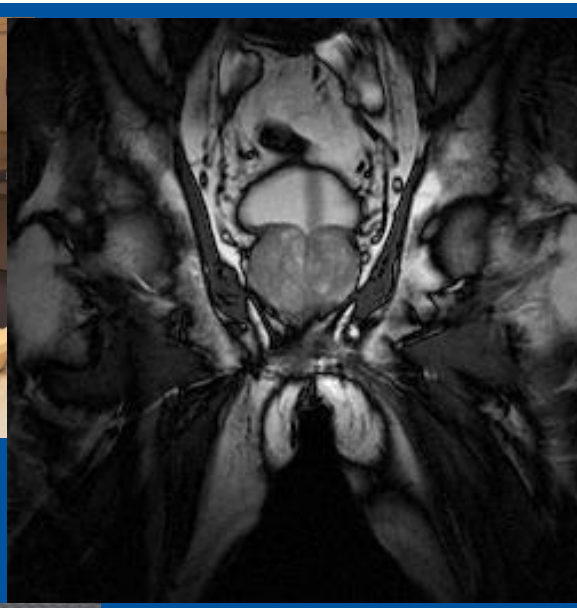
MRI guided brachytherapy

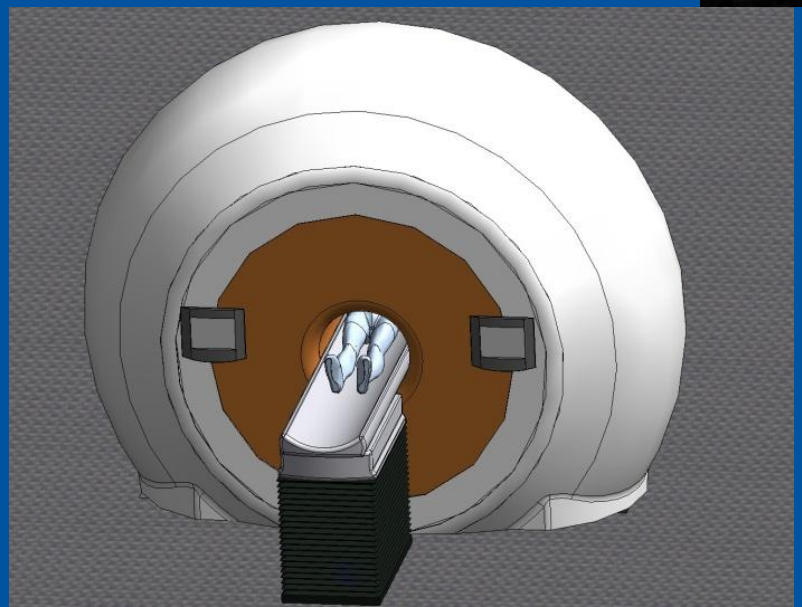
MR-HIFU



HIFU

HDR robotic brachytherapy





MRI linac

Summary

University Medical Center Utrecht

- *MRI guidance of RadioTherapy and MR guided HIFU will set the next stage in high-precision tumor therapy*
- *Synergy in development (motion descriptors, target tracking)*
- *MR-LINAC will be the next standard-of-care in RadioTherapy*
- *MR-HIFU offers many complementary features and may be added to the Surgical, RT and Chemo therapies*
- *MR-HIFU may lead to MR guided Drug Delivery*

University Medical Center Utrecht

Imaging Division, UMCU; Pharmaceutical Sciences UU

Jan Lagendijk, Marco van Vulpen, Bas Raaijmakers, Baudouin Denis de Senneville, Mario Ries, Clemens Bos, Anna Yudina, Wilbert Bartels, Gert Storm, Maurice van den Bosch, Willem Mali et al

Philips Healthcare

Charles Mougenot, Max Köhler, Sham Sokka and the Helsinki team

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SONODRUGS

ctmm

erc