MR GUIDED FOCUSSED ULTRASOUND CURRENT STATE AND FUTURE DIRECTIONS

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WHAT IS FUS

- Uses ultrasonic power approximately 5000 to 10,000 times that of diagnostic ultrasound
- Produces intense local heating at focus which is relatively small
- No intervention is required
- Can be guided by MR to target and controlled with online MR thermal map

MRgFUS

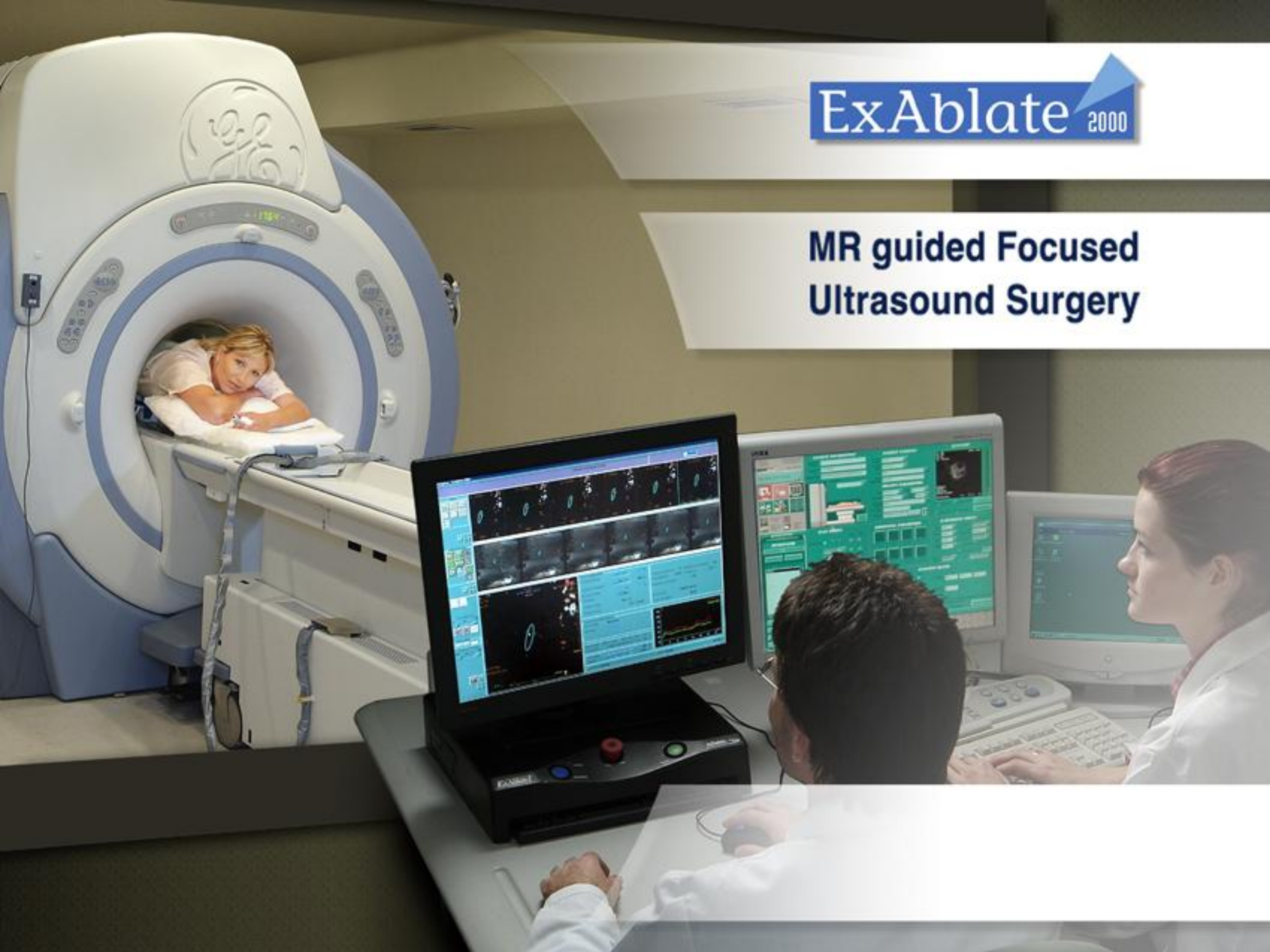
- Previous talk should have explained nature of technology
- What MR brings to the procedure
- Utility of thermal mapping
- Therefore I will say no more about these areas

MRgFUS

- St Marys have treated 430 patients mostly fibroids with a few other areas
- We have been working in this field for 8 years
- All work undertaken by appropriate multidisciplinary teams with all involved specialties involved in all aspects of the work

MRgFUS

- Our fibroid work will be discussed in detail later on in the conference
- I am going to try to give you glimpses of the potential breadth of this technology and how it could impact many areas of treatment
- This is just a limited personal vision and many more able investigators will develop many other areas

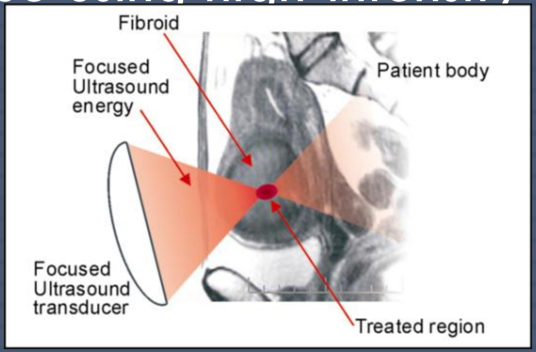

ExAblate 2000
MR guided Focused
Ultrasound Surgery

What is MR guided Focused Ultrasound (MRgFUS)?

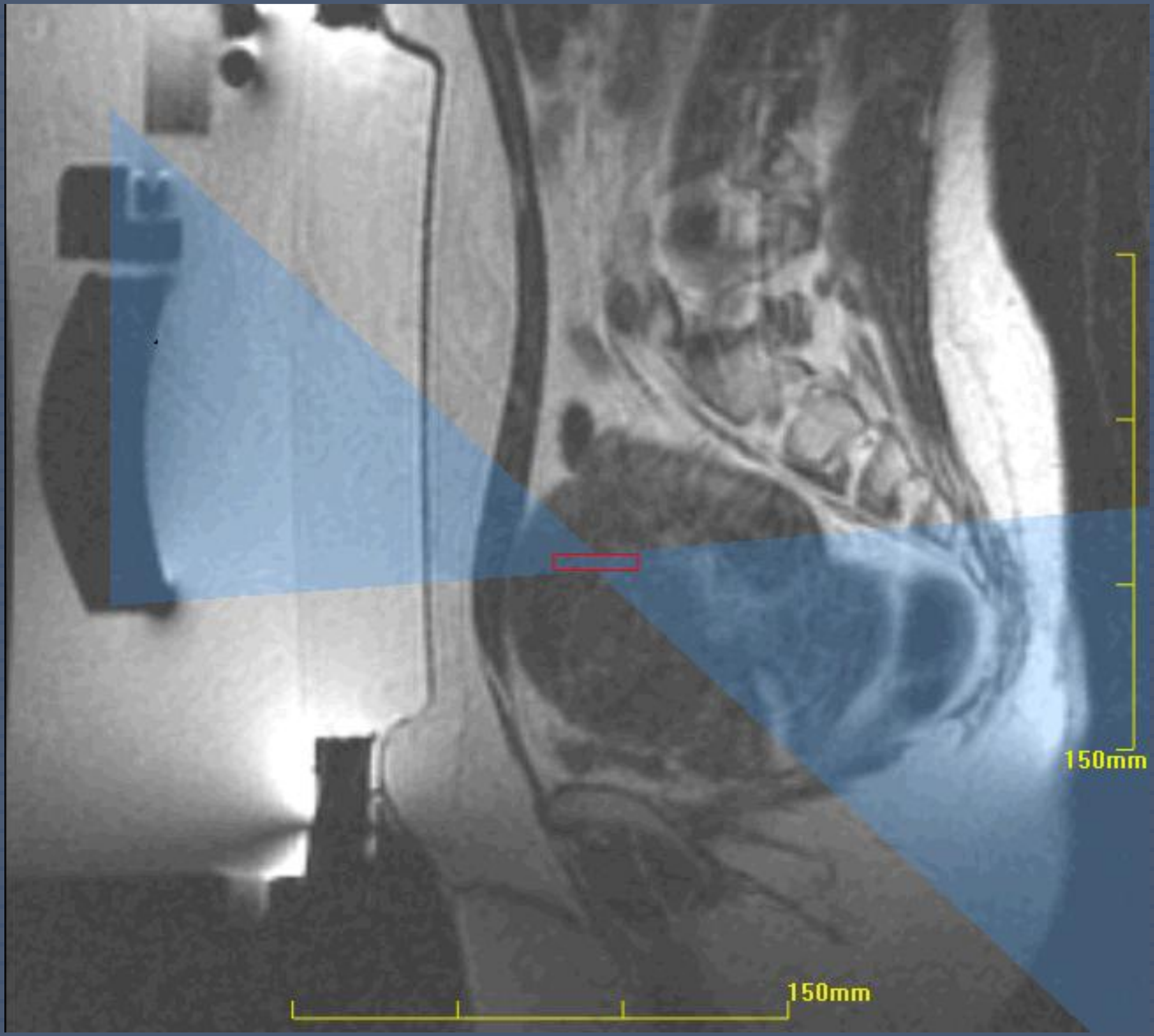
- MRgFUS combines two systems:

1) Magnetic resonance imaging (MRI) scanner to visualize patient anatomy, map the volume of tissue to be treated, and control the treatment by monitoring the temperature of the tissue after heating

- 2) Focused beam of ultrasound energy that heats and destroys the tissue using high-intensity sound waves

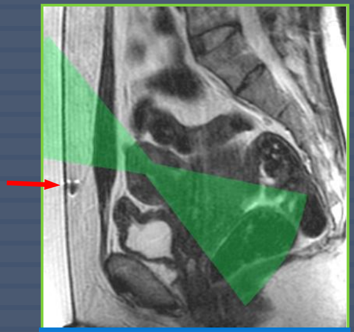


First time the two systems have been combined in one product and the first time MR has been used to monitor tissue temperature.

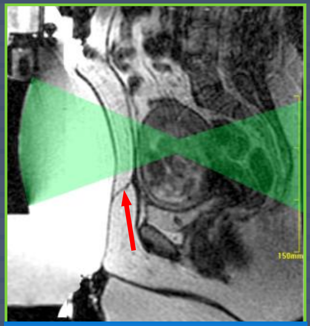

150mm
150mm

3D beam path visualization

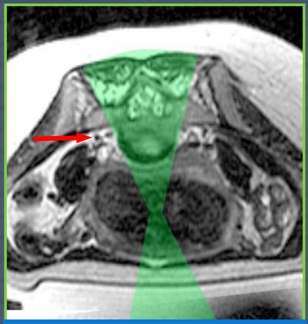
Positioning transducer to avoid complications



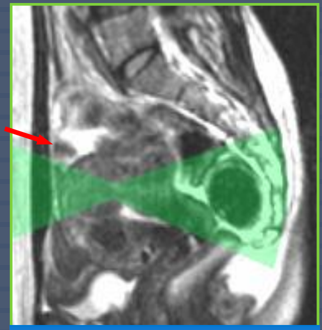
Surgical Clips



Scars

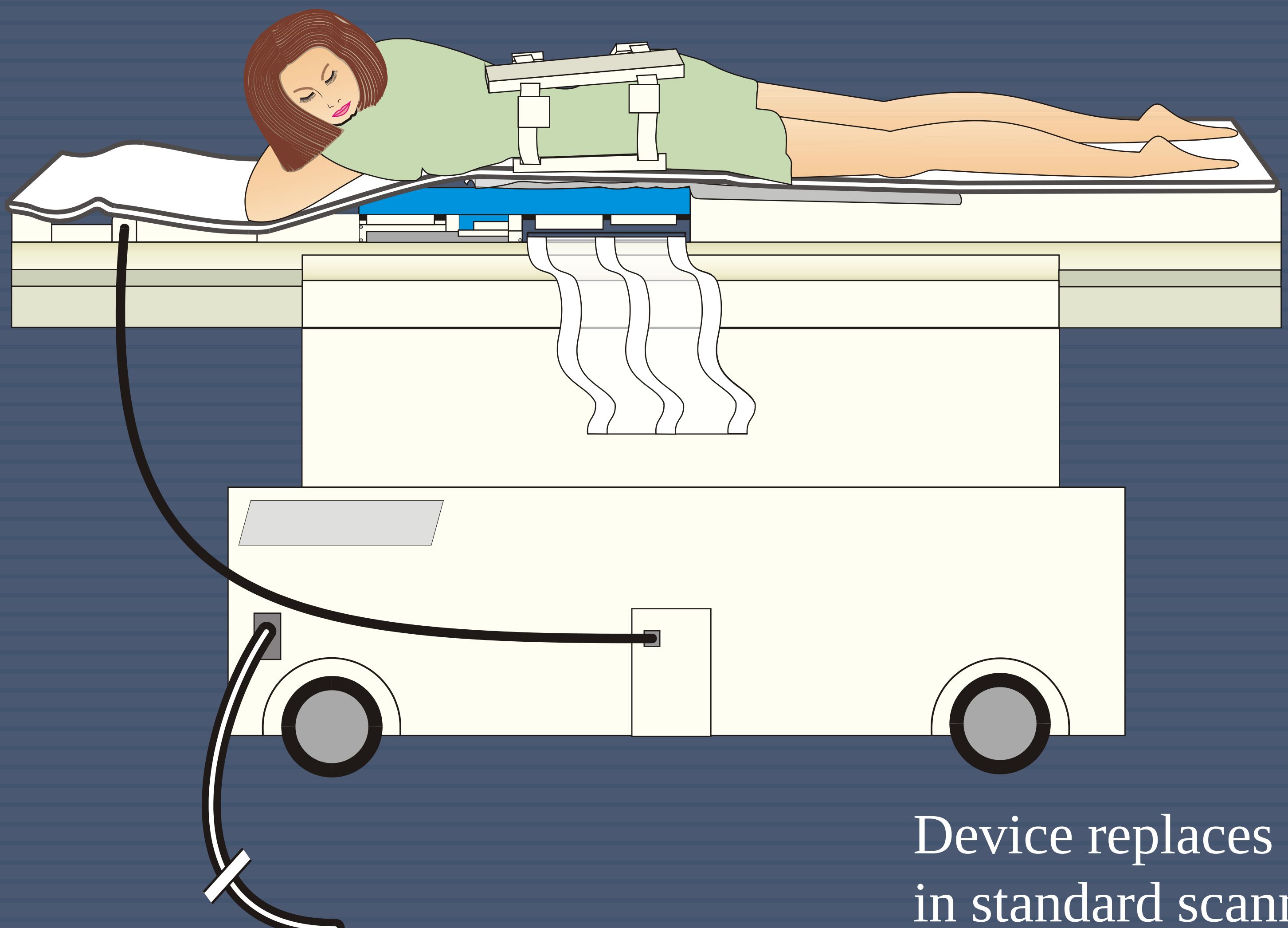


Sciatic Nerve



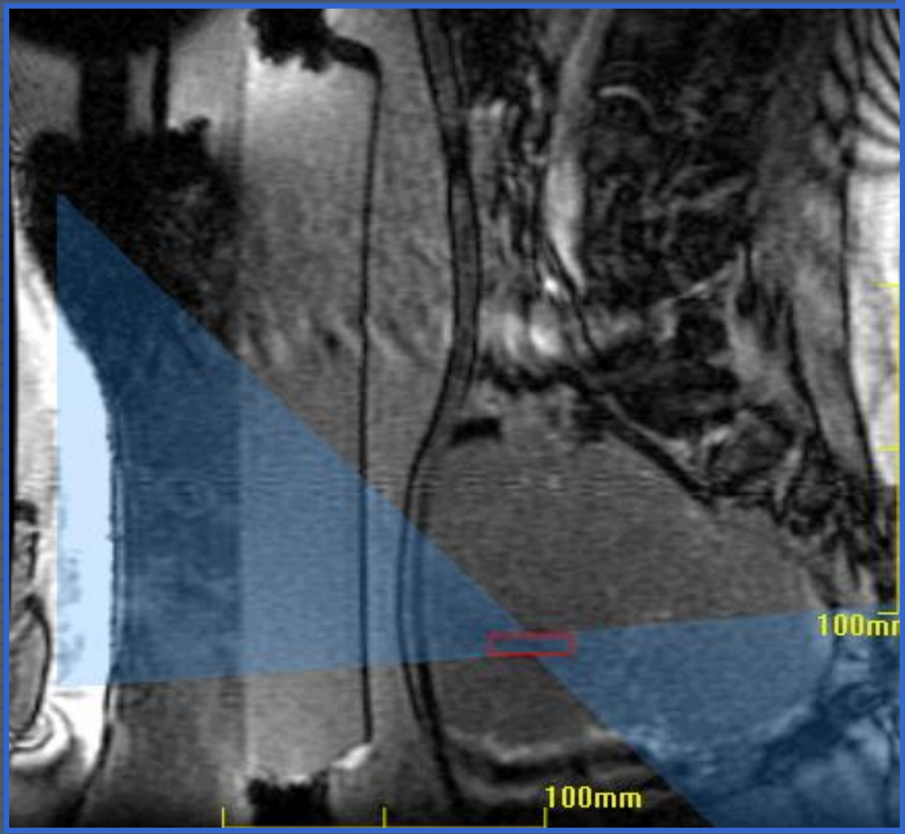
Bowel

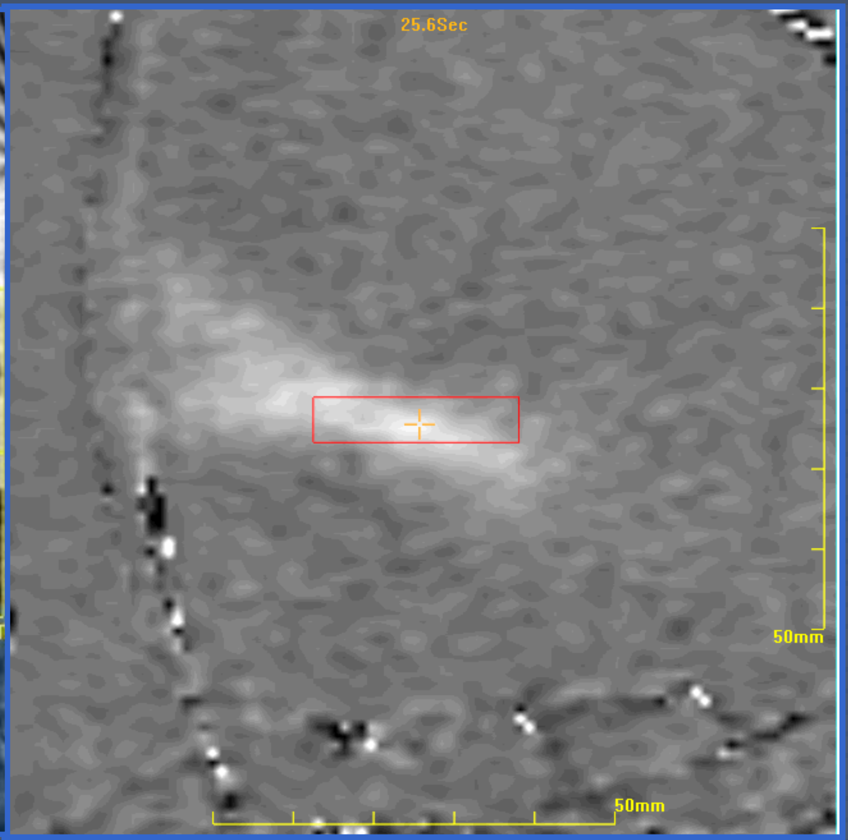
Patient positioned on ExAblate FUS device.

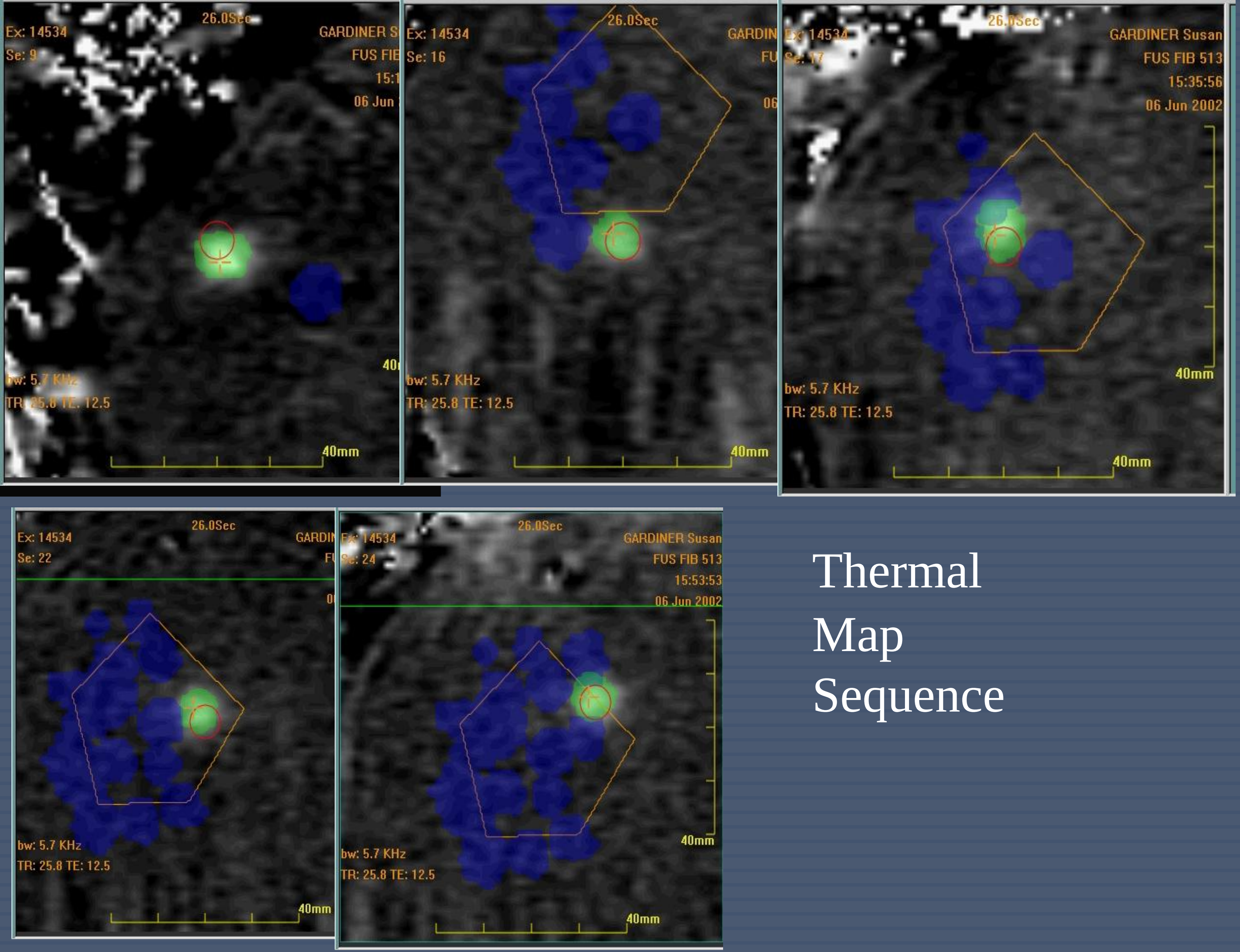


Device replaces MR bed in standard scanner.

Thermal Mapping







Thermal Map Sequence

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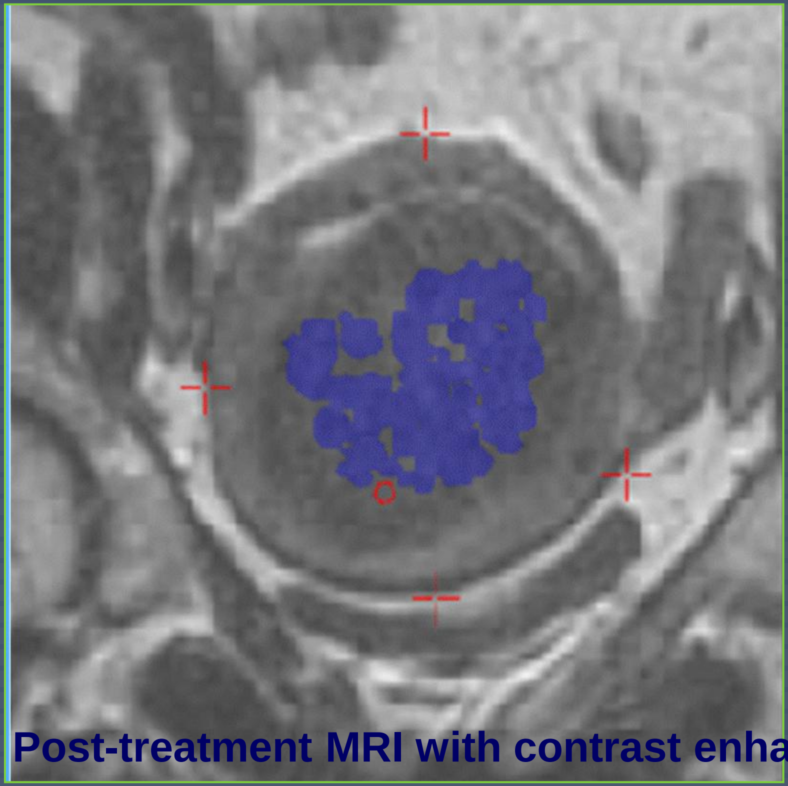
Outcome assessment



Post-treatment MRI with contrast enhancement to evaluate outcome

Accumulated thermal dose

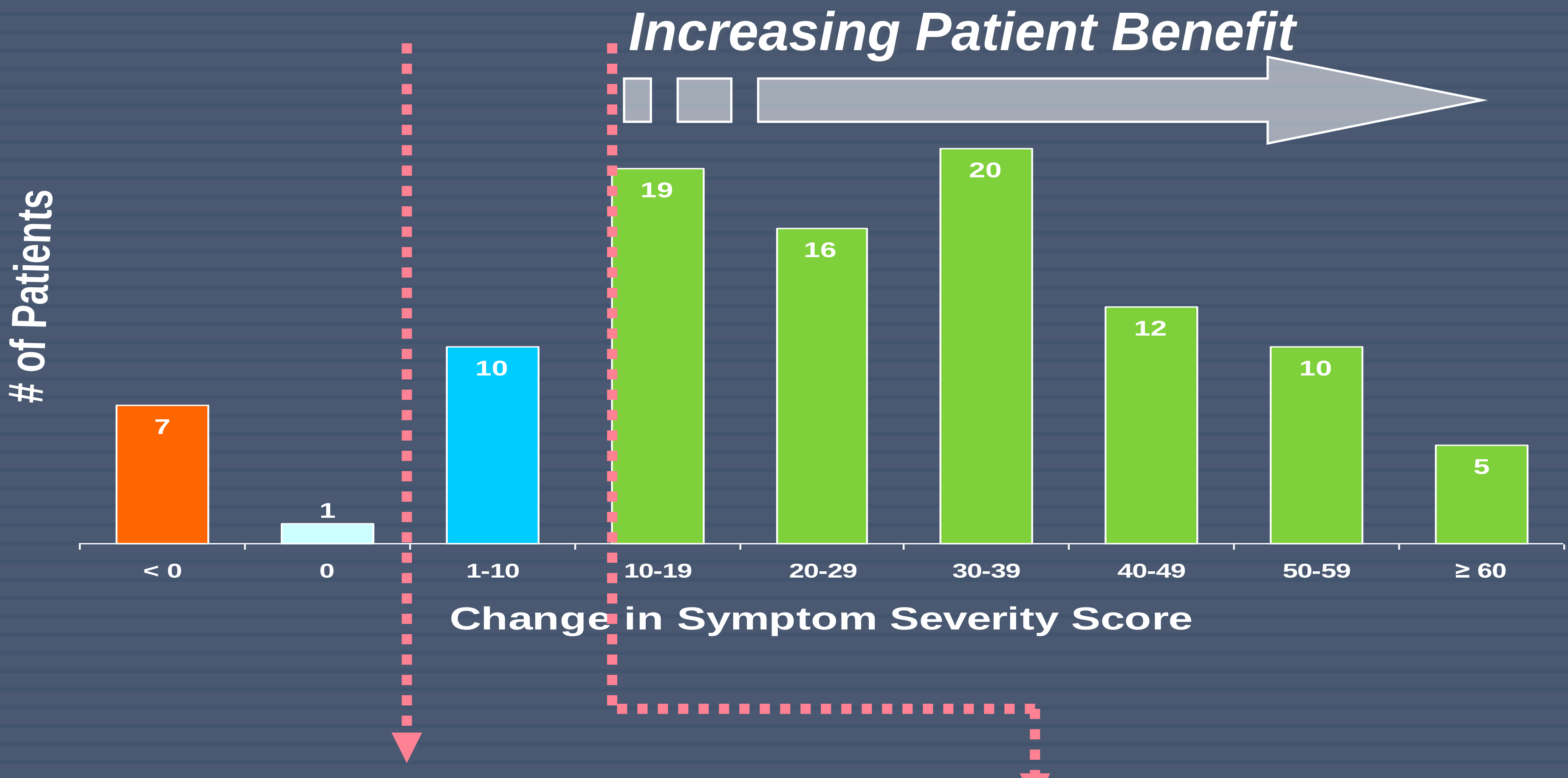
Non-perfused region

Contrast enhanced MR images showing that individual fibroids have been damaged (not enhanced) leaving the myometrium intact.

Study Hypothesis

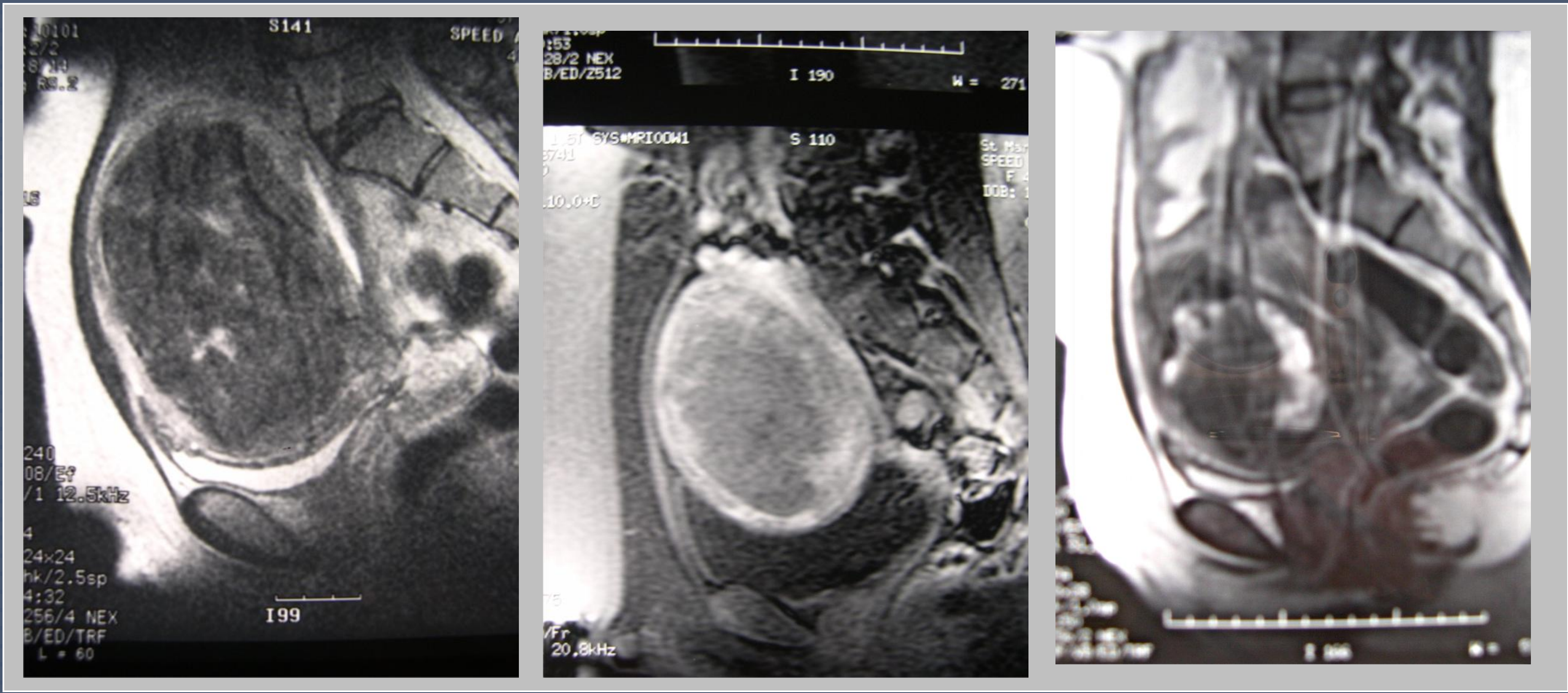
Focused Ultrasound will result in a 10 point improvement in
Symptom Severity scores
at 6 months post-treatment
for ≥50% of symptomatic patients.

Frequency Distribution
Symptom Severity Score at 6 Months

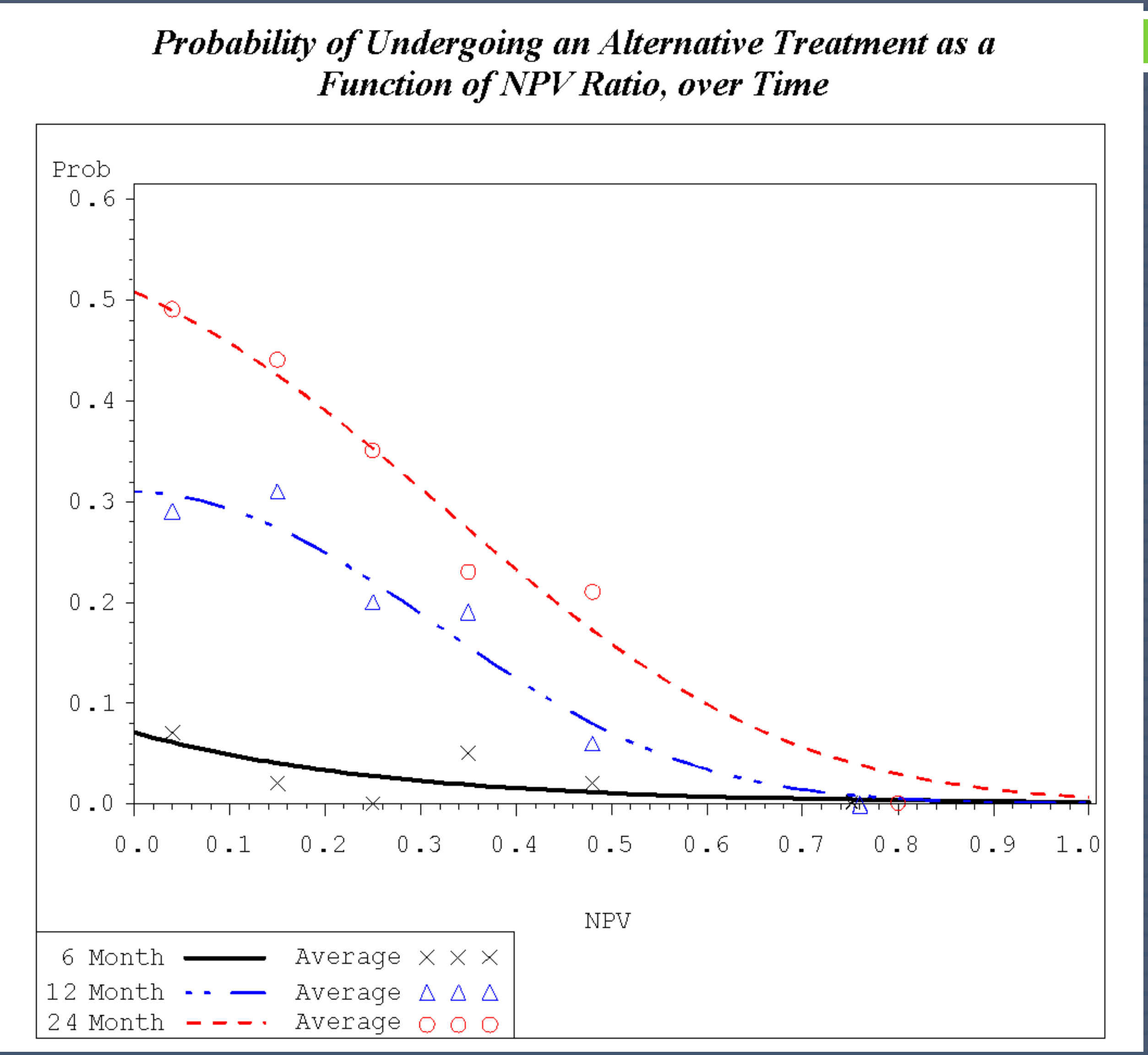


92% SOME improvement. ***82% SIGNIFICANT improvement***

Reduction in Fibroid Volume



Alternative Treatments



A significant relationship between the NPV ratio and the percentage of patients who went on to alternative treatments at 12 and 24 months

Magnetic Resonance Guided Focused Ultrasound (MRgFUS) of Liver Tumours – our early experience

Current limitations - access

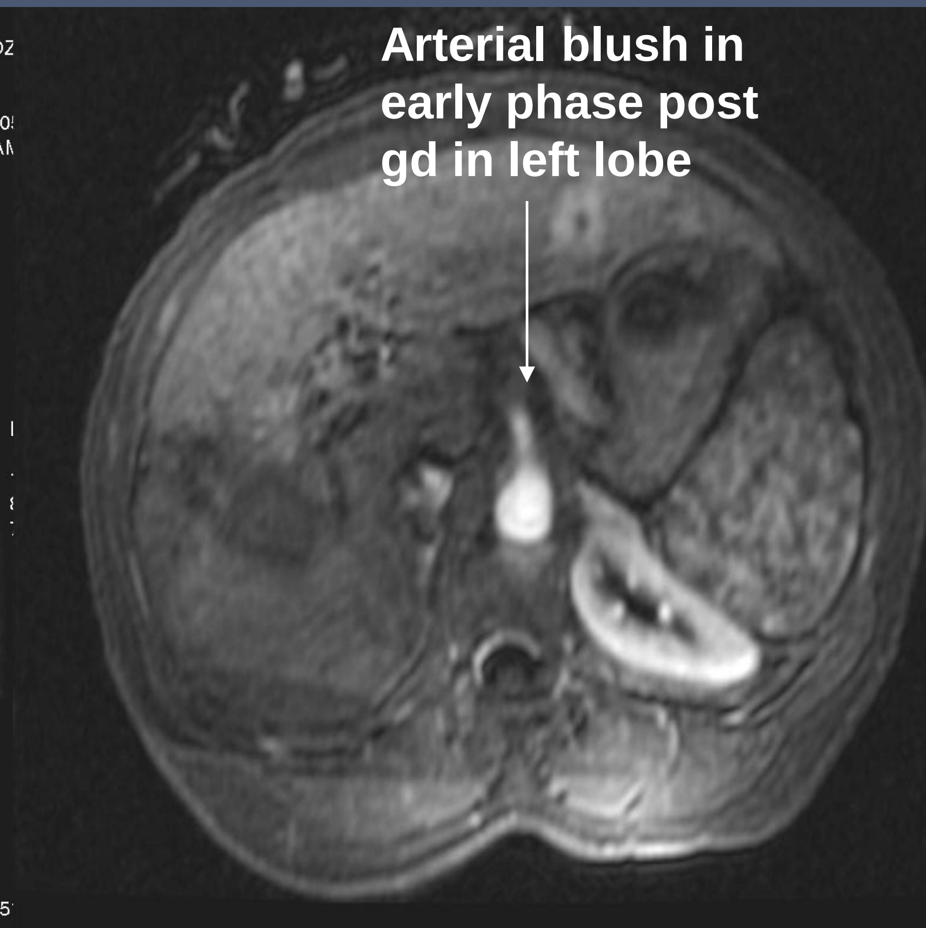
- Currently cannot get FUS effectively across ribs
  - Footprint of present array is large
  - Ribs absorb energy and destroy focus
- Lesion below rib line can be easily reached
- Left lobe masses are easiest at the moment
- Anticipated that this problem will be largely overcome within 12-18 months

Current limitations - respiration

- Respiratory movement raises problems with exact positioning of each sonication
- We currently use GA where ventilator and respiratory excursion are controlled by FUS machine (not by anaesthetist) to overcome this problem
- This recaptures exact 3D spatial control so that sonication site can be precisely controlled

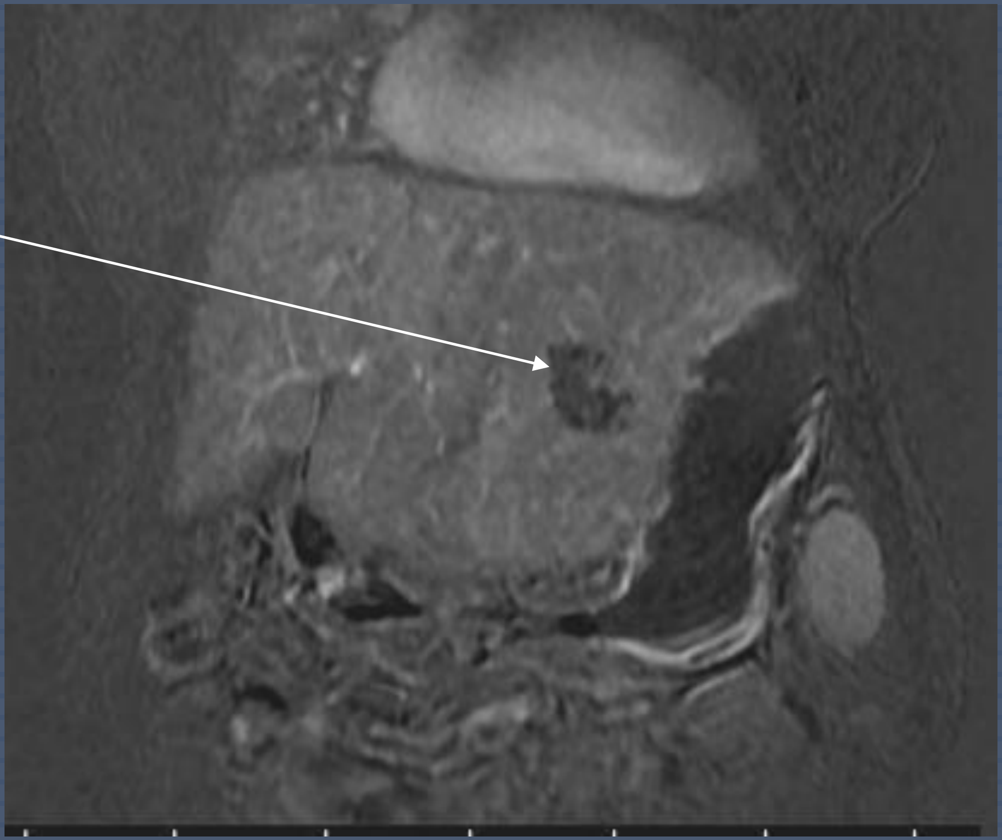
Liver MRgFUS animation

Case 2 – pre treatment imaging



Case 2 – Post treatment subtracted post contrast image

Note area of decreased perfusion post ablation in the target (site of HCC) with margin



Treatment Follow-Up

T2w FSE

1 week

T2w FSE

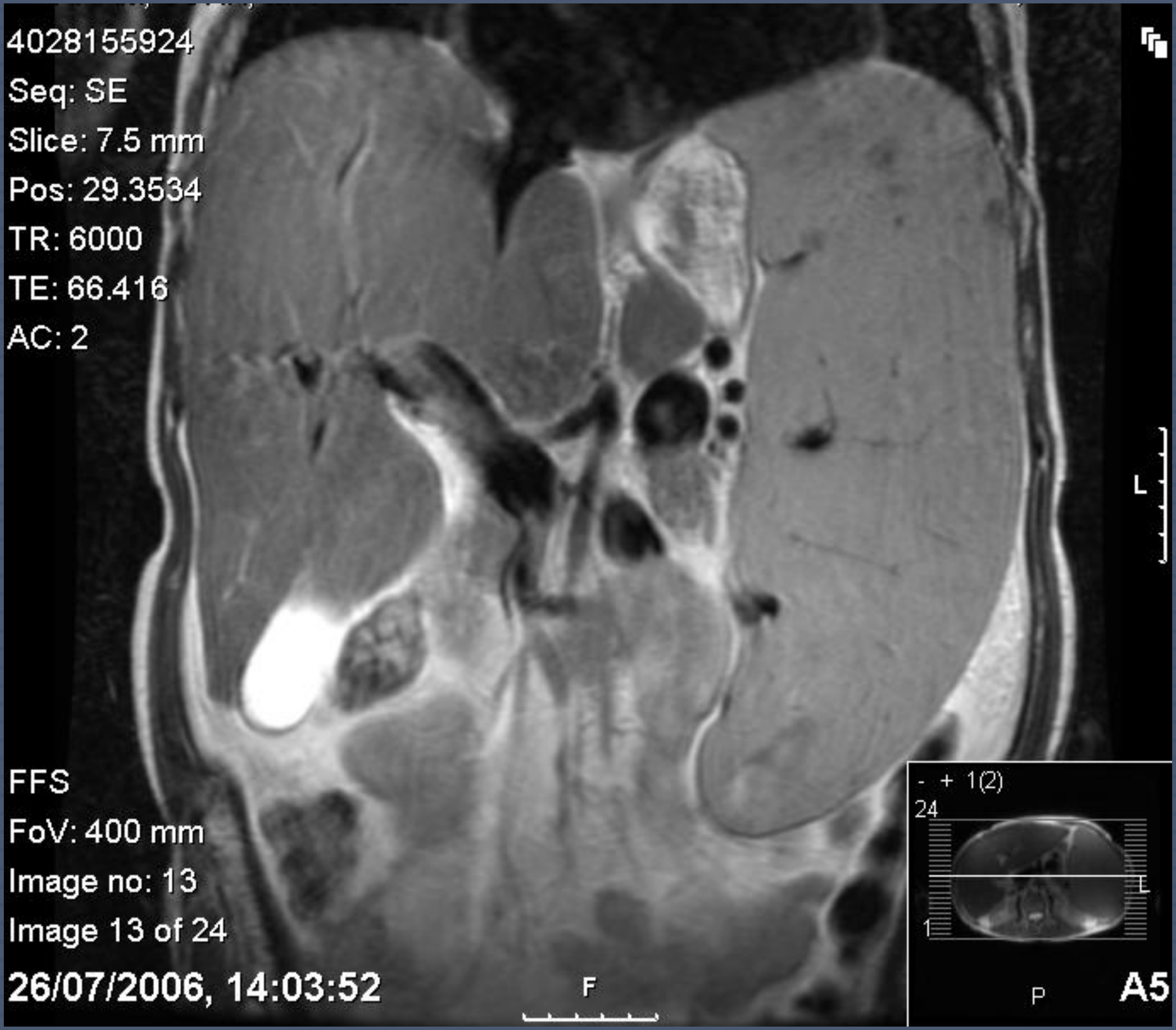
1 month

T2w FSE

2 months

MRgFUS: Spleen

- 70 yr old male
- Myelofibrosis v slowly progressive leading to immense splenomegaly plus added hyperslenism
- Physicians asked if we could carry out some non invasive debulking of spleen in this patient who was not fit for any other procedure



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TE: 66.416
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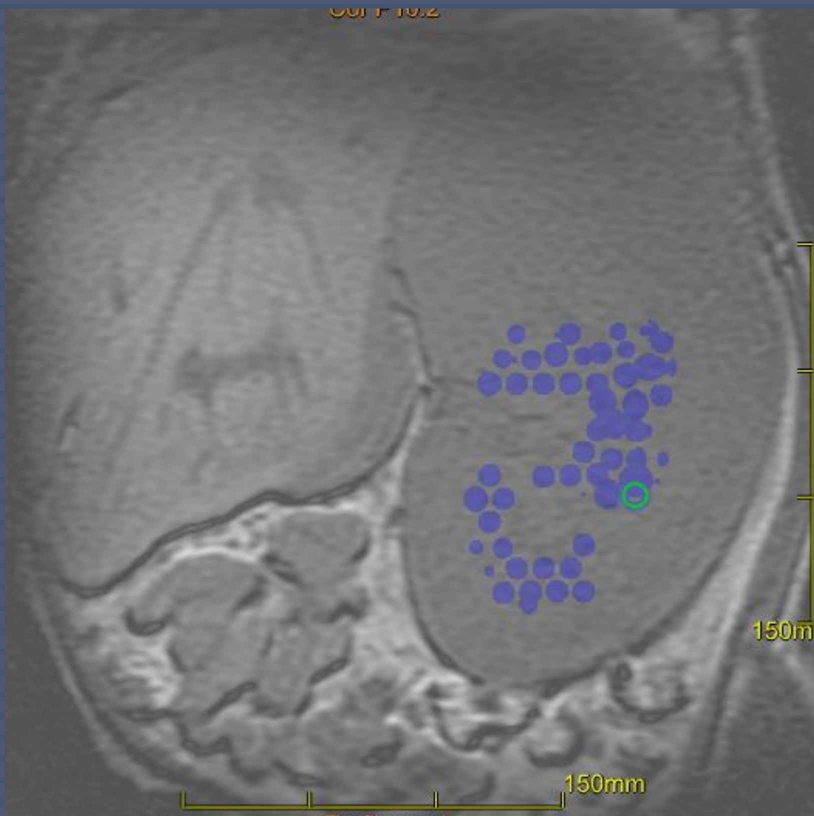
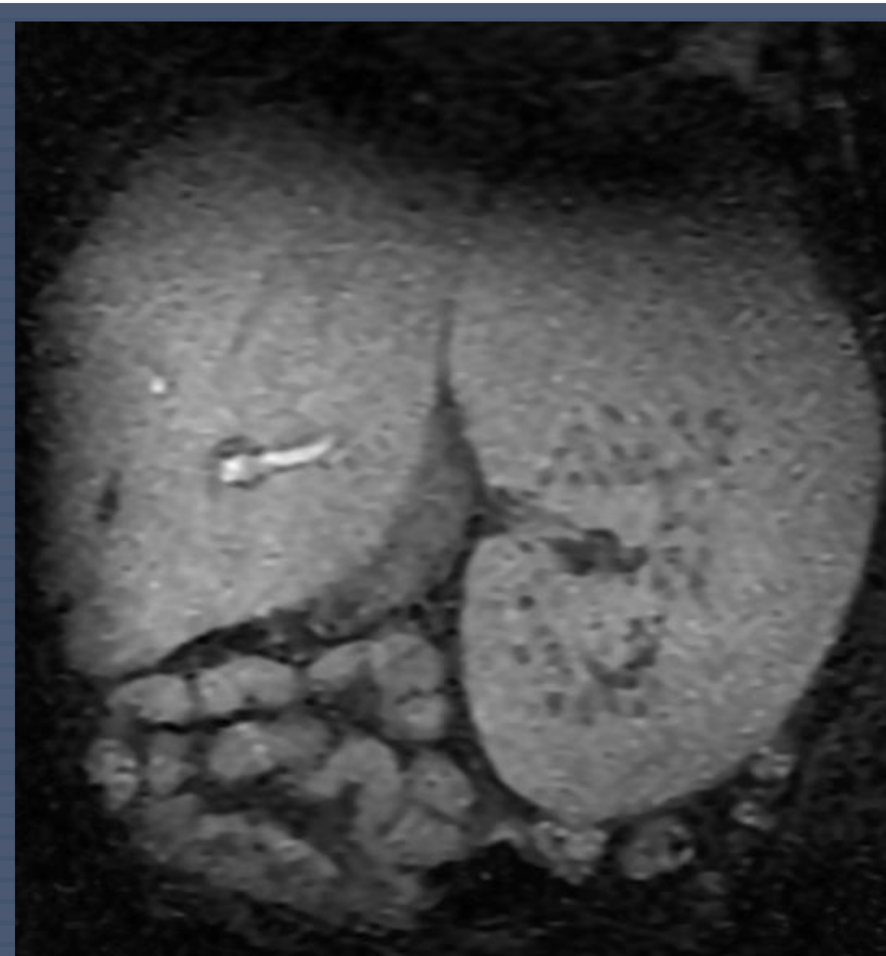
2nd treatment results





Soft tissue secondary

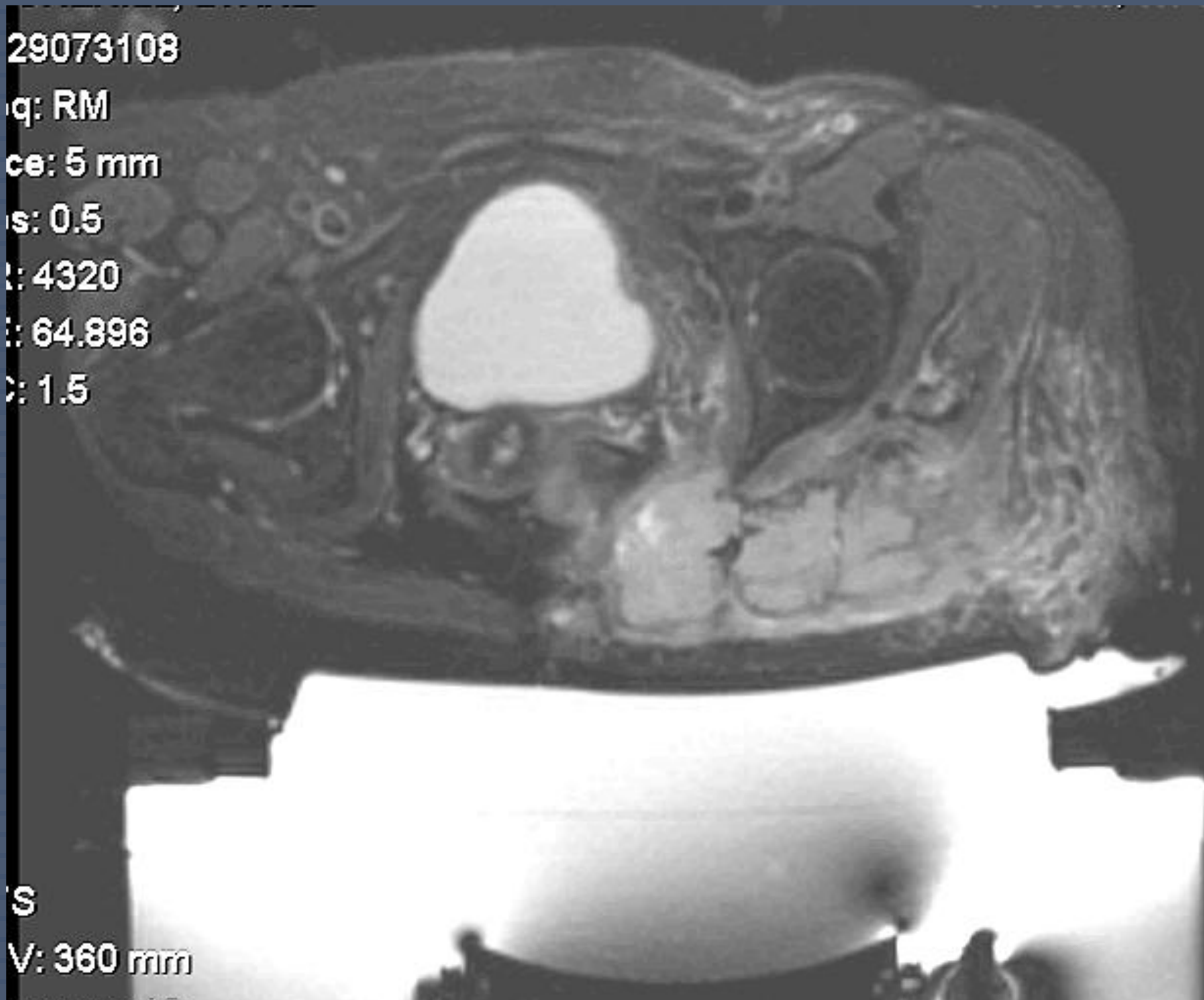
72 yr old female

NSC lung Ca pneumonectomy, no chest disease now

Left buttock metastatic deposit

Has had DXT, only temp improvement

Can FUS improve substantial pain symptomatology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: 64.896
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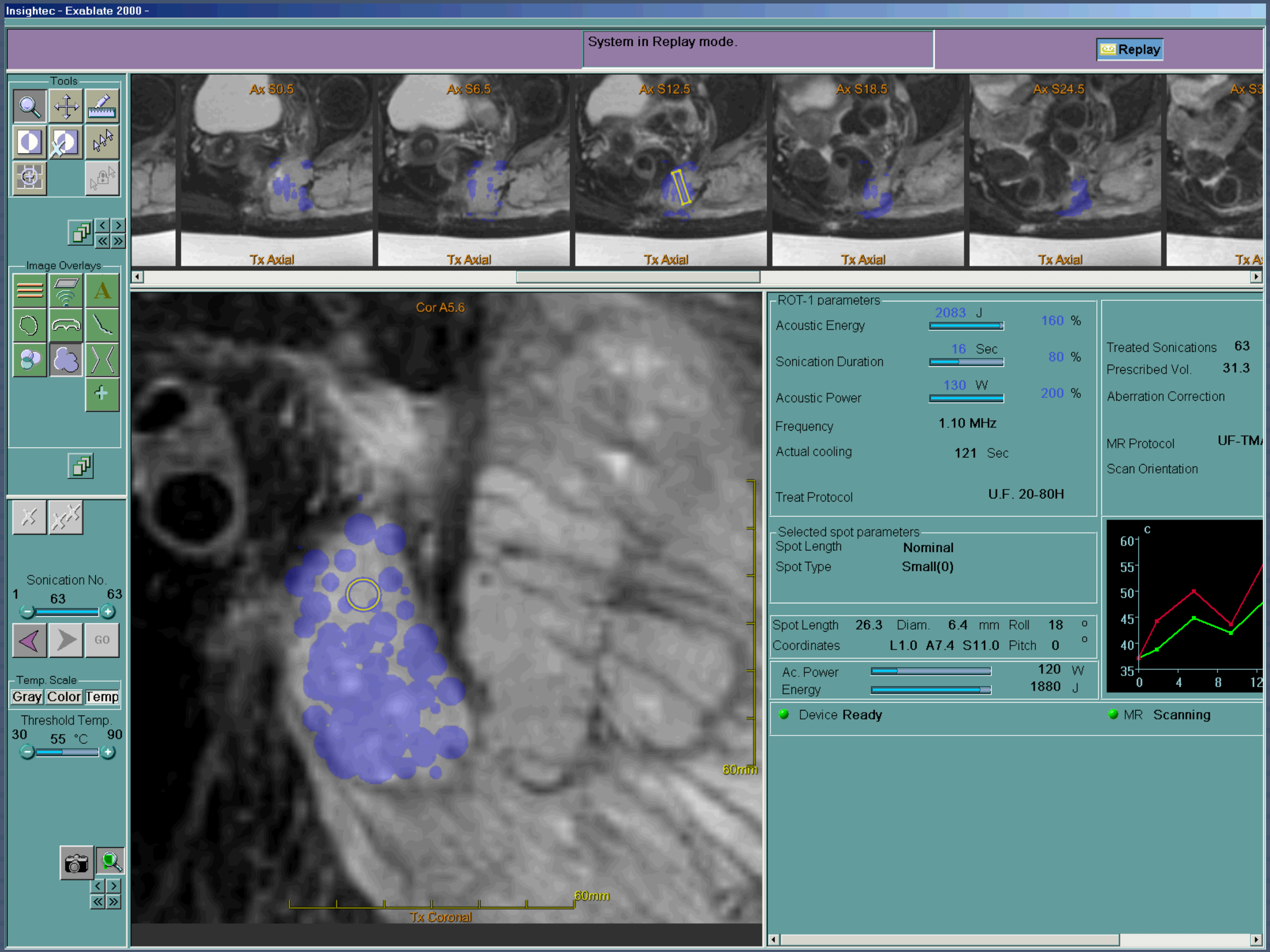
V: 360 mm

Soft tissue met: cumulative thermal map



Subtraction post gd image
No perfusion in treated area

Coronal post gd
Post treatent

MRgFUS for Palliation of Bone Metastasis

Bone Mets

- Intention is to create an effective palliative treatment which is independent of tumour histology
- Requires one outpatient procedure only
- Avoids multiple attendances of DXT and its associated problems

MRgFUS for Palliation of Bone Metastasis

- Treatment principles
  - Bone heating is used to ablate the adjacent periosteum
  - Palliation achieved by the ablation of the bone periosteum

Ultrasound absorption in bone vs. tissue

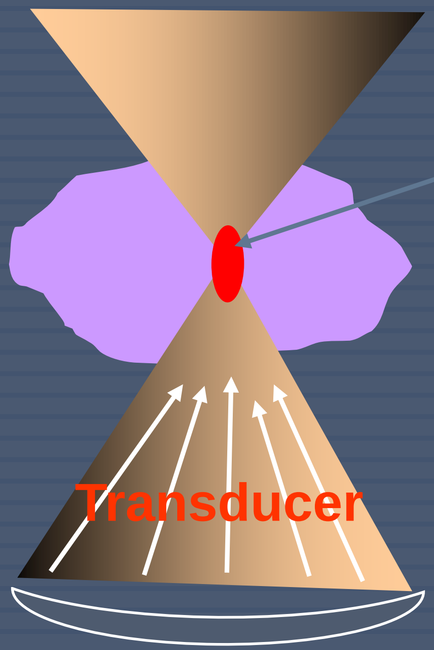
Absorption of FUS energy by bone is **~50 times greater** than that of soft tissue.

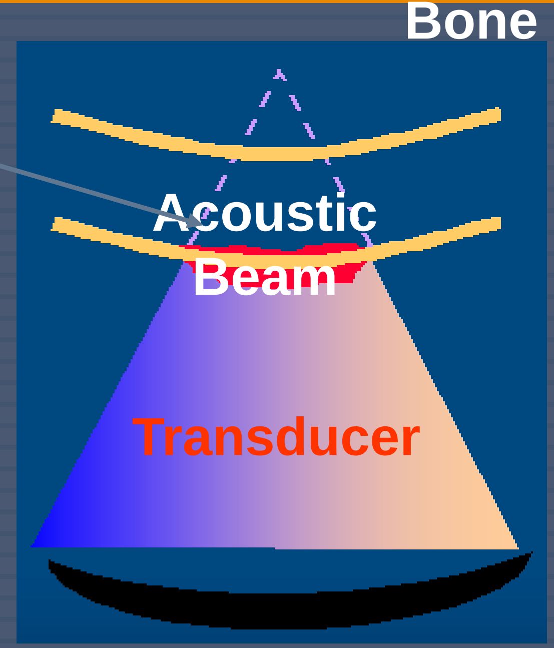
Soft tissue:

- Narrow, point-shaped focus is required
- High energy density at focal point

Bone :

- Wide beam approach
- Low energy usage
- Shorter treatment time





Typical Sonication Energy – 2500J

Typical Sonication Energy – 1000J

ExAblate for pain palliation of bone metastases

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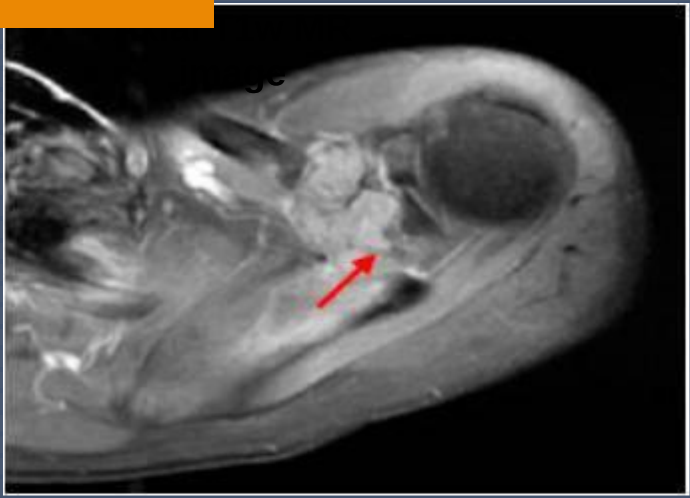
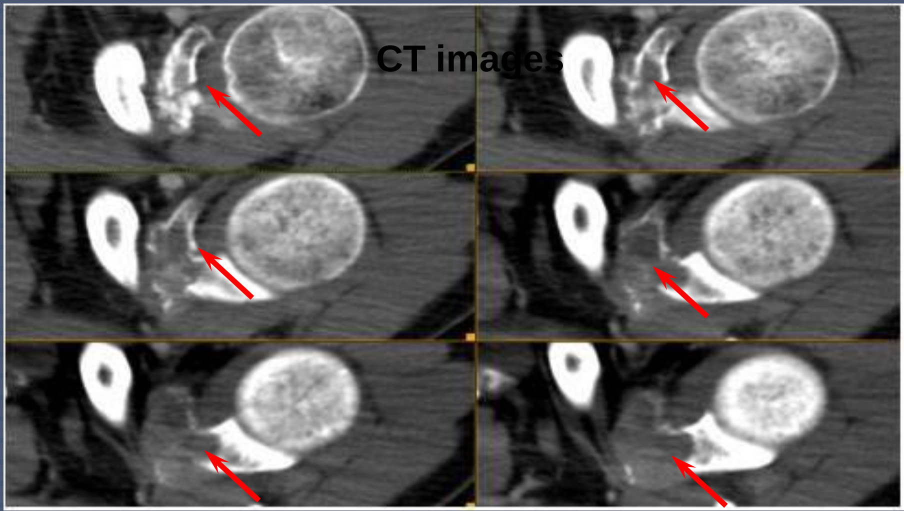
Case review – pain palliation of bone metastases

- 40 year old male patient
- Primary tumor: Renal cell carcinoma
- Targeted lesion in the **left scapula**, close to the humerus
- Total of 11 sonications
- 50 min. procedure duration





Clinical results: Patient VAS pain score dropped from 7 (severe) to 0 (no pain)

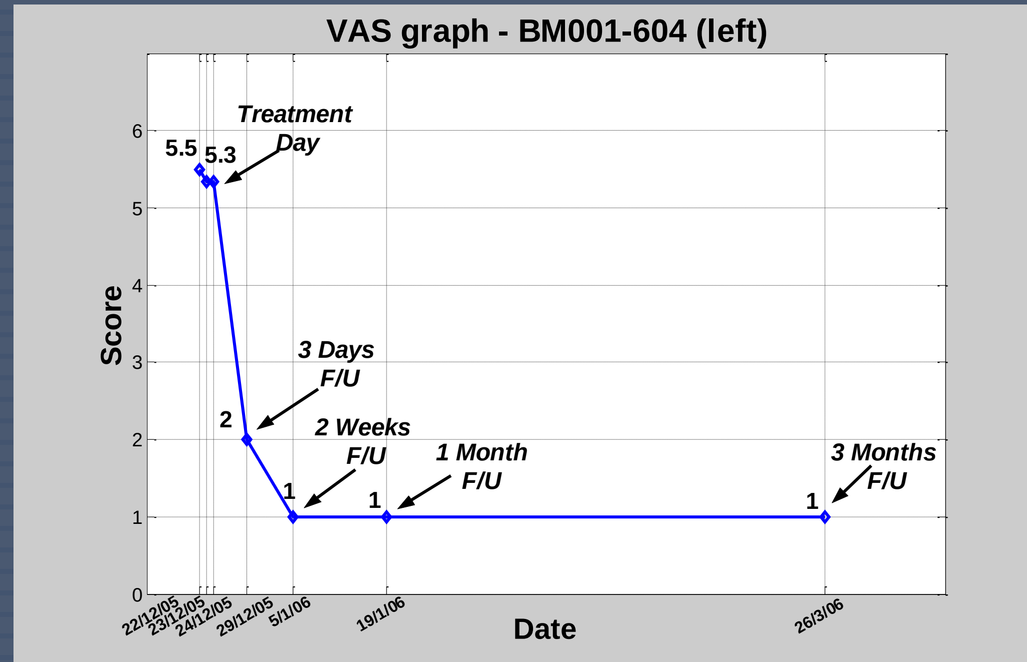
Courtesy of Mt. Sinai Hospital, Toronto

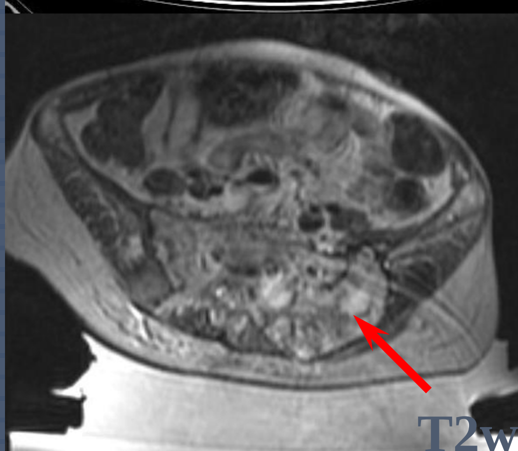
• 44 year old female patient

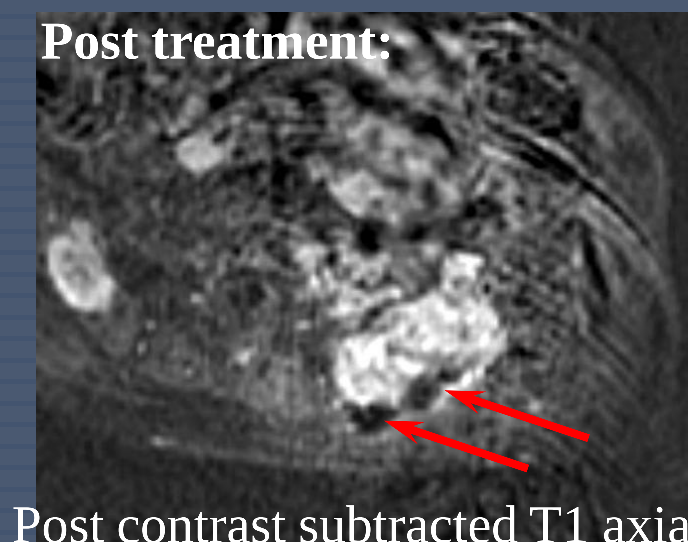
• Primary Tumor: Breast Ca

• Left iliac bone metastasis

• Procedure performed 26th Dec 05

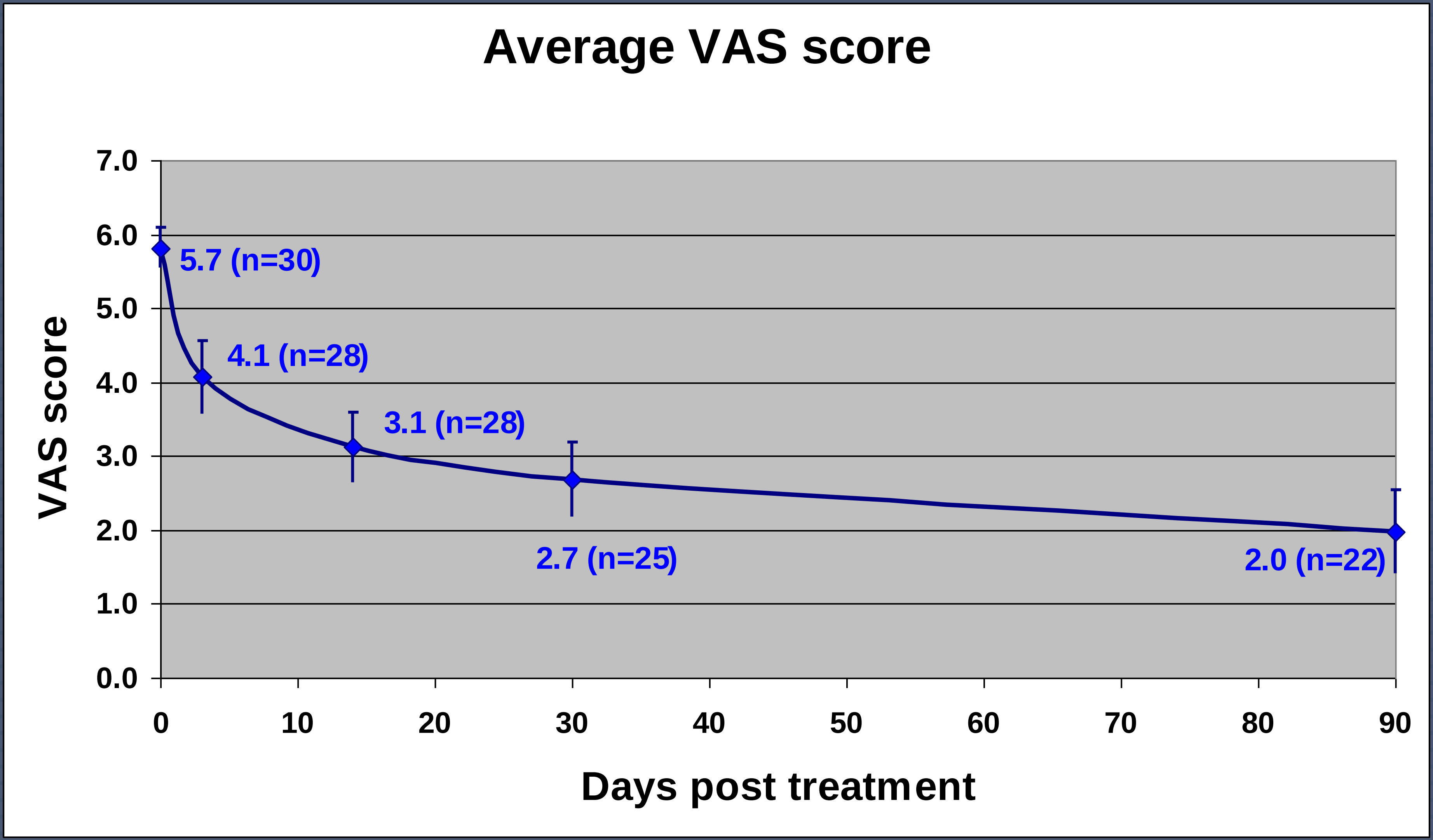






MRgFUS for Palliation of Bone Metastasis

- Clinical results



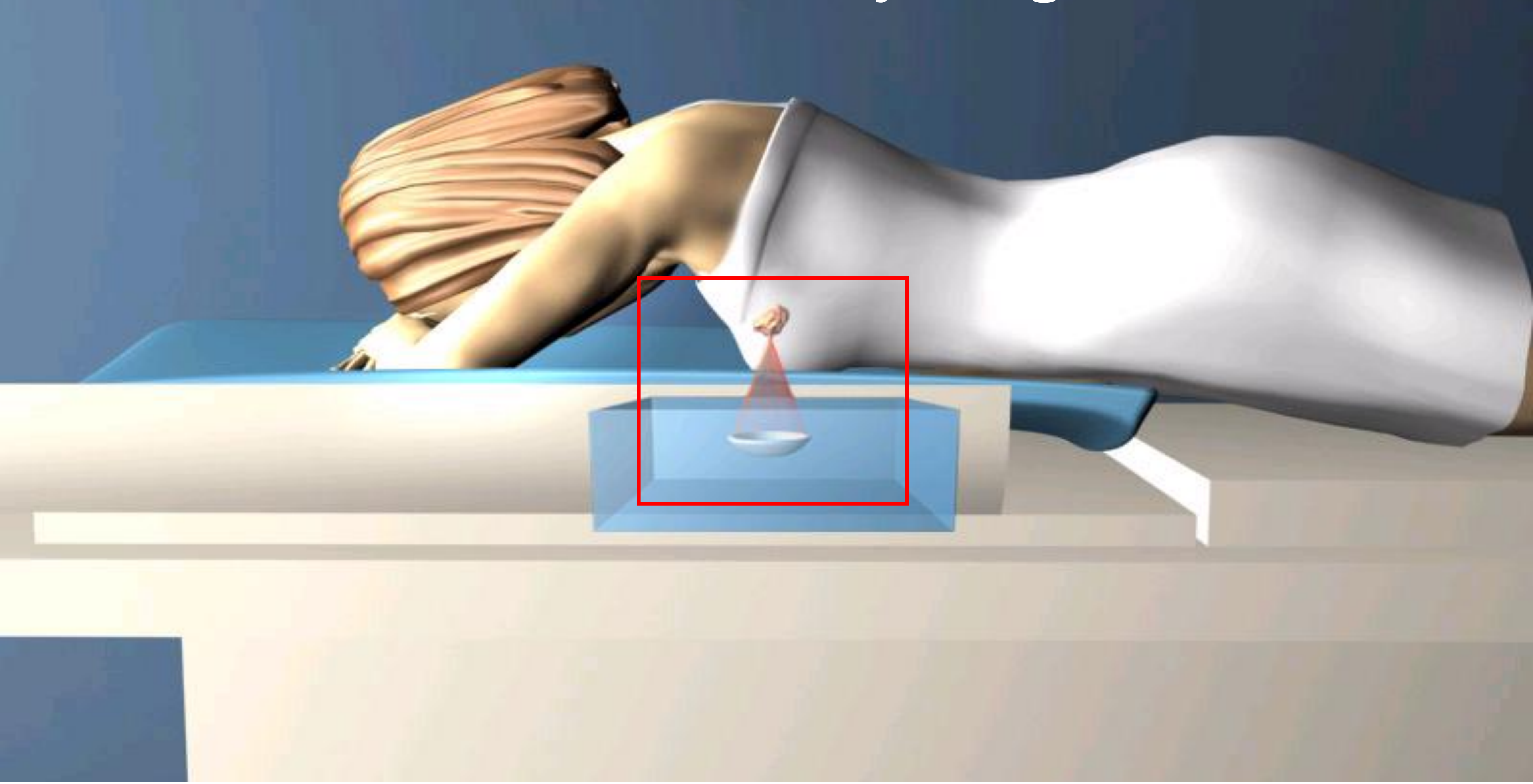
MRg FUS of Breast Cancer

Studies carried out at Breastopia Namba Hospital Japan

I will present some of their results which are leading the way for this application

Breast MRgFUS procedure

Treatment of Breast Tumors by MRgFUS



Focused Ultrasound: Non-invasive Thermal Ablation

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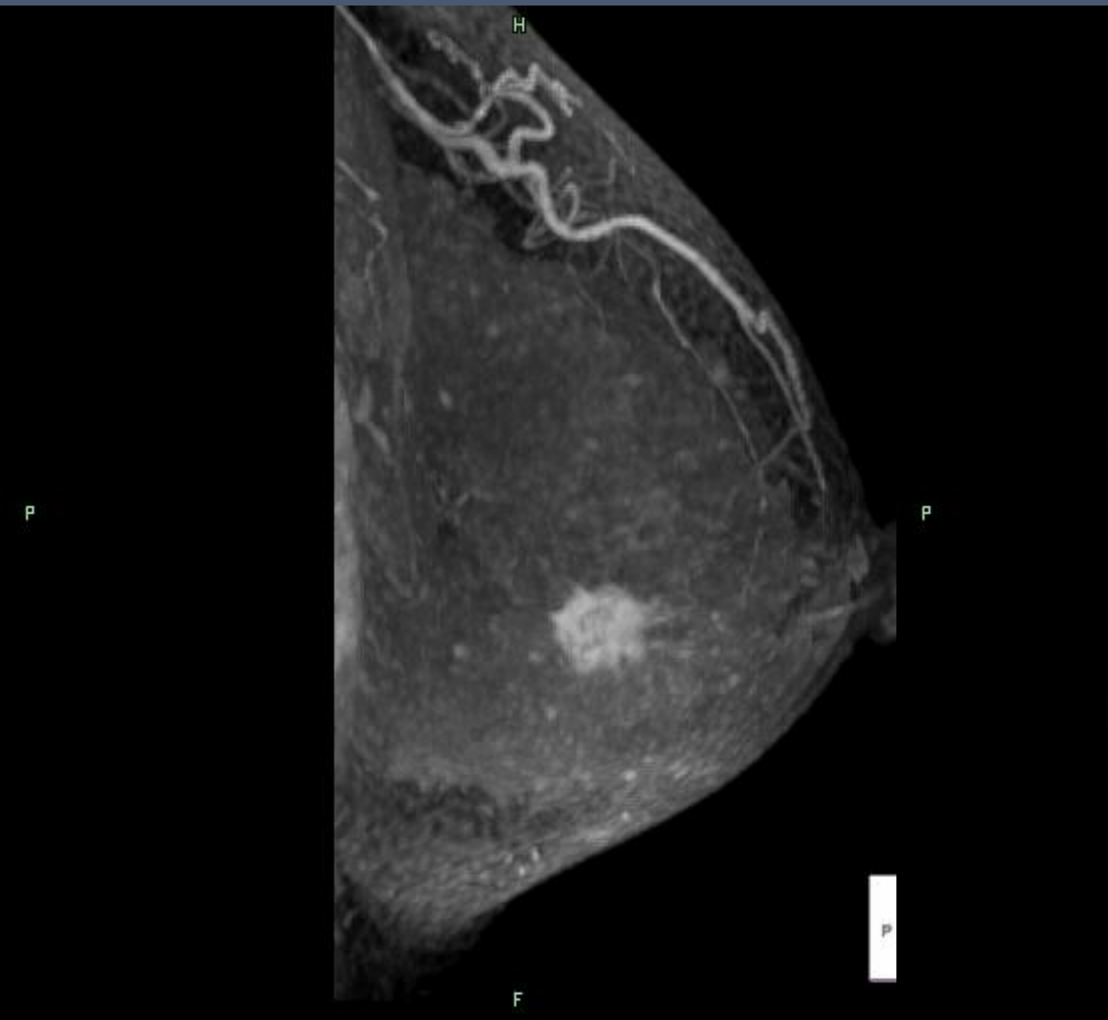
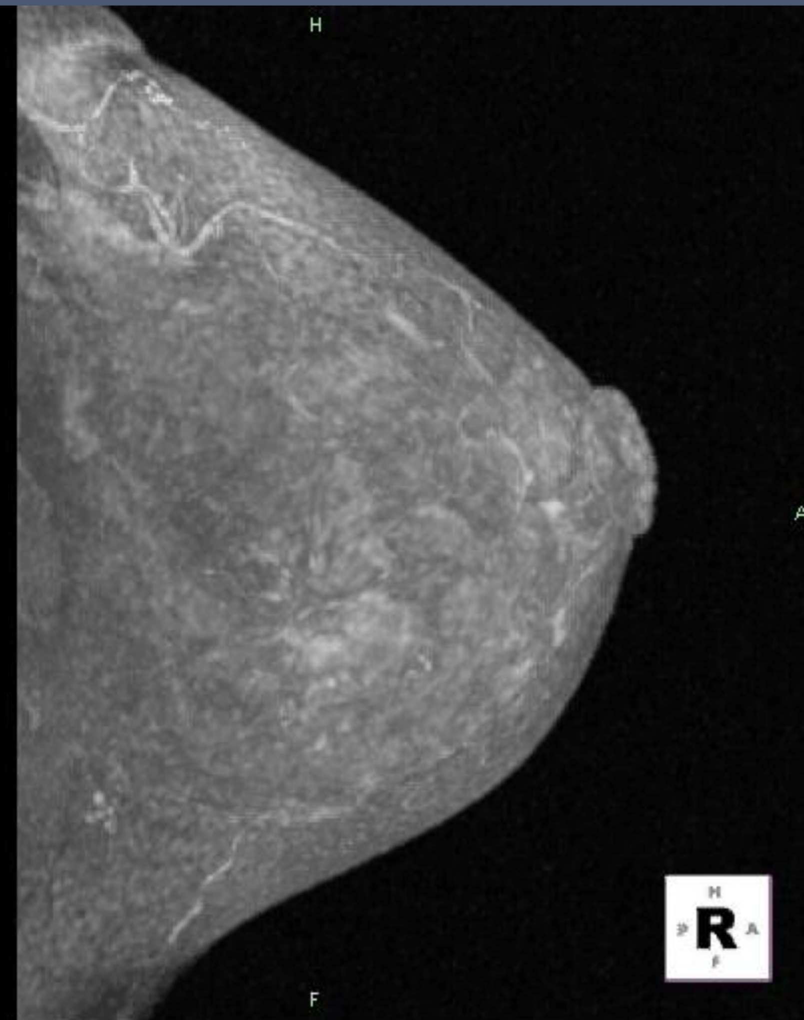
MR: Ability to Plan and Control Treatment

BREASTOPIA

Confirmation of Treatment by MRI

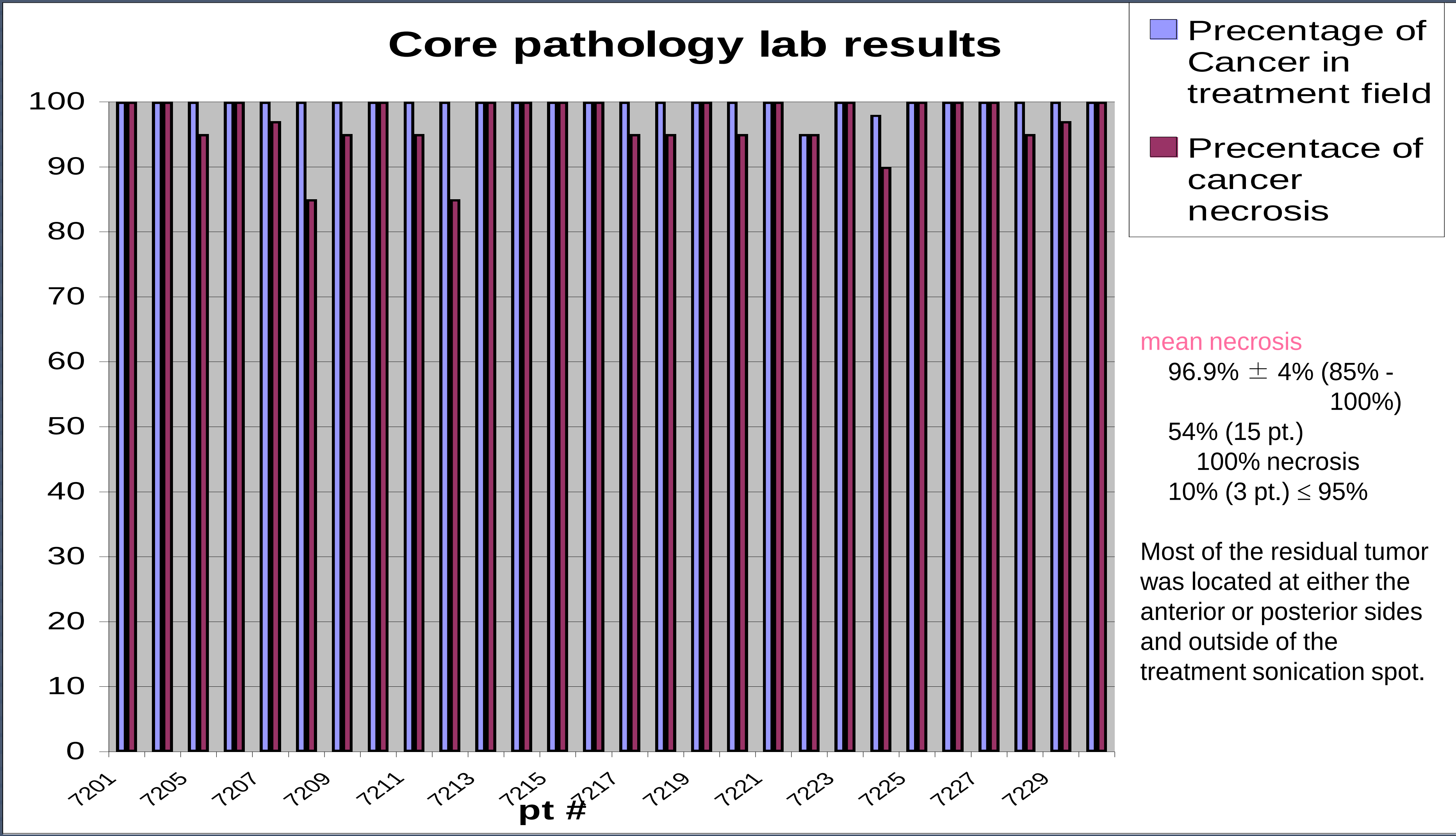




Pre-FUS

Immediate post-FUS

Results : Efficacy BC003



mean necrosis

96.9% ± 4% (85% - 100%)

54% (15 pt.) 100% necrosis

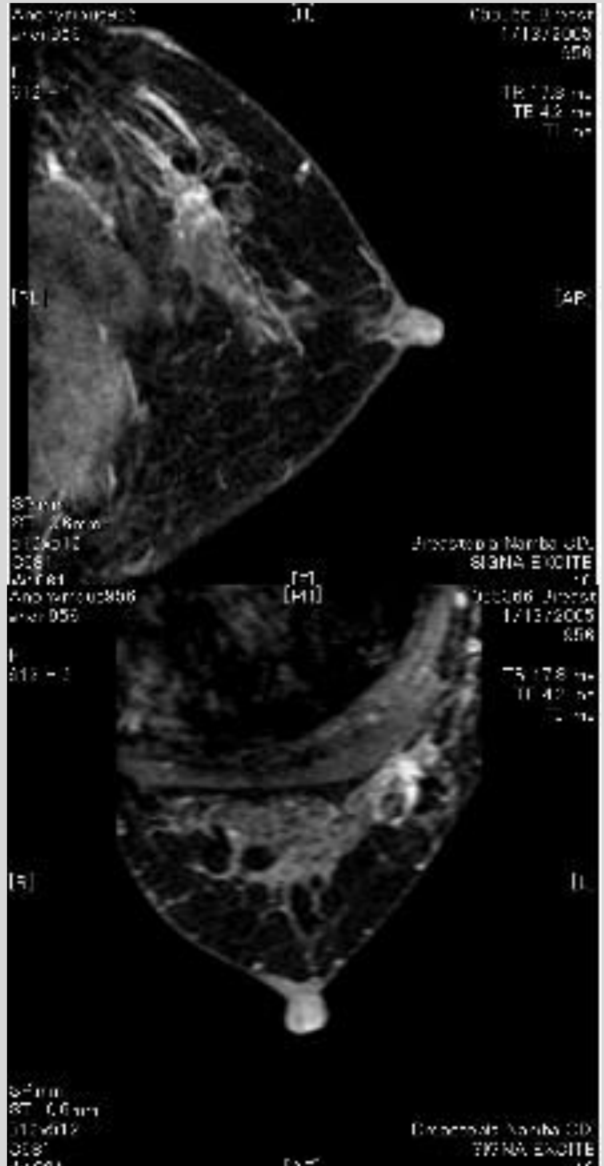
10% (3 pt.) ≤ 95%

Most of the residual tumor was located at either the anterior or posterior sides and outside of the treatment sonication spot.

BREASTOPIA

A Case of MRgFUS alone

pre-MRgFUS



post-3 month

post-15 months

MRgFUS for Prostate Cancer

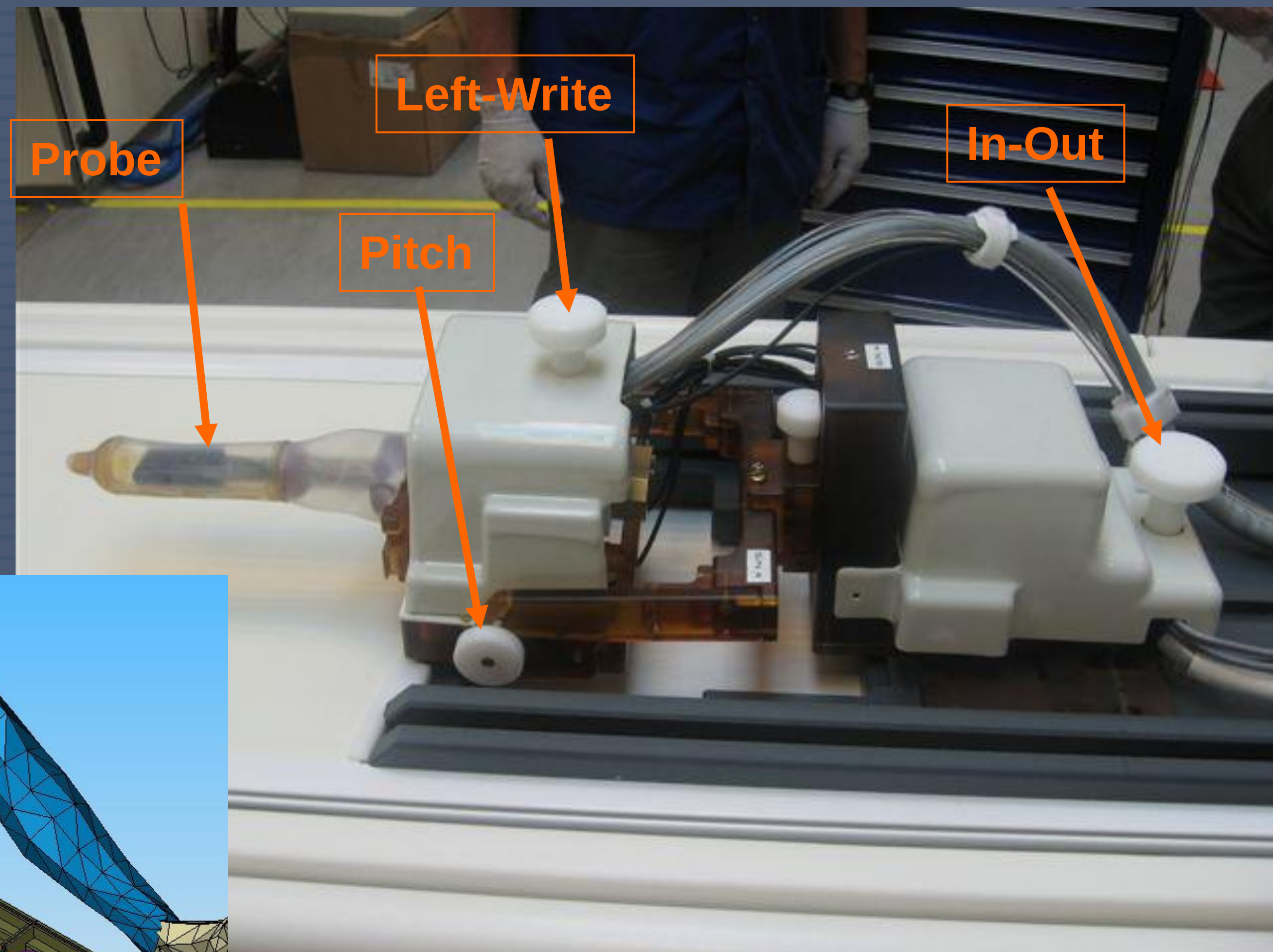
MRgFUS For Prostate Cancer

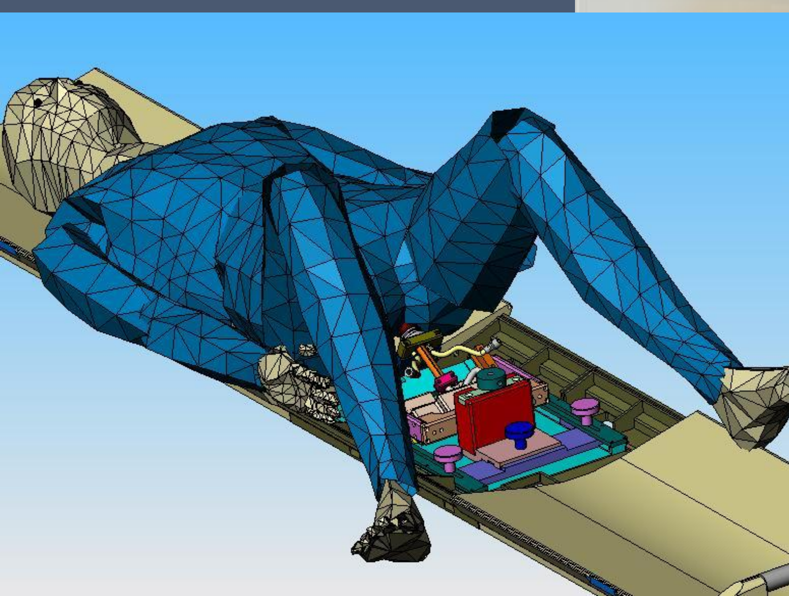
Principles of Prostate System and Treatment

1. Treatment done using a rectal probe containing a phased array transducer. The probe is integrated with the ExAblate 2000 Operator Console and GE MR (1.5T or 3T)
2. Procedure is planned to be done using epidural sedation.
3. Planned to do either
   (a) “localized ablation”
   (b) whole gland ablation
4. Accurate spots, prevent damage to nearby essential organs
5. MR closed loop thermal feedback and system design are expected to lead to high safety profile.
6. Combined pelvic and the integrated endorectal imaging coil for high resolution target definition

MRgFUS For Prostate Cancer

Positioner





•Company Confidential

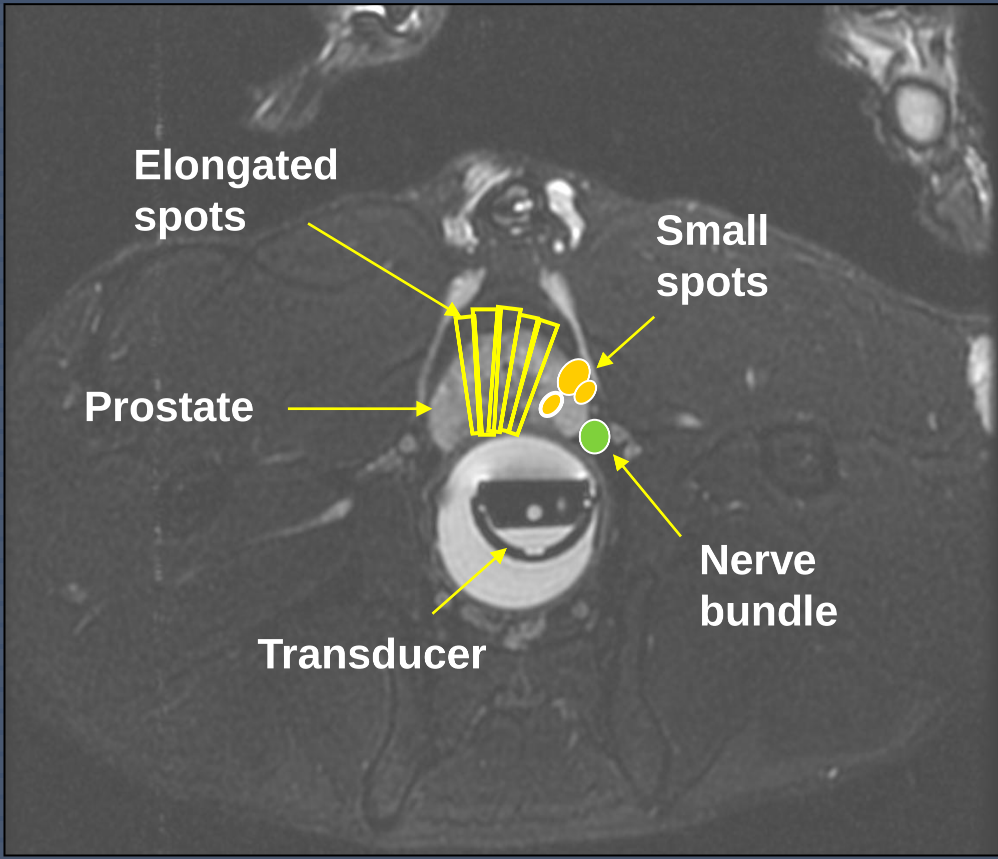
MRgFUS For Prostate Cancer

Simulation

MRgFUS For Prostate Cancer

Functional overview

- Steerable beam for focal spot size control (2 x 7mm to 10 x 30mm) for fast treatment and to prevent complications related to nerve bundle
- Combined pelvic and endorectal imaging coil for high resolution target definition



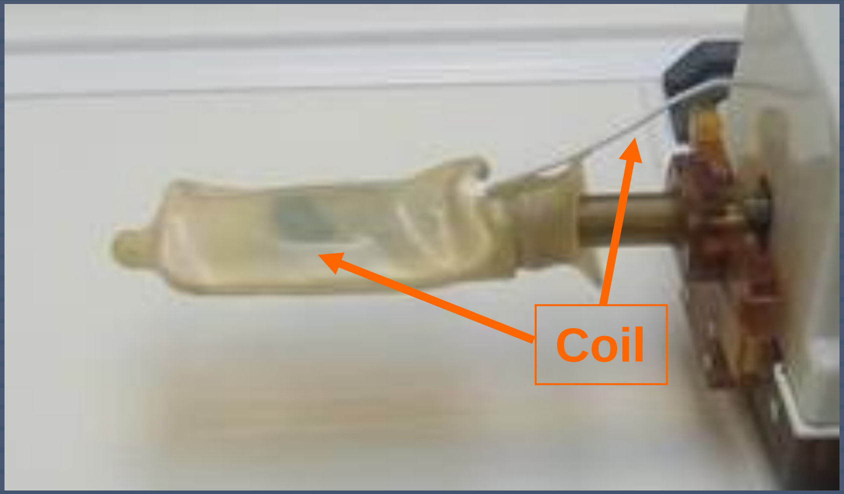
Steerable beam and spot size control

Courtesy of Sheba Hospital, Tel-Aviv, Israel

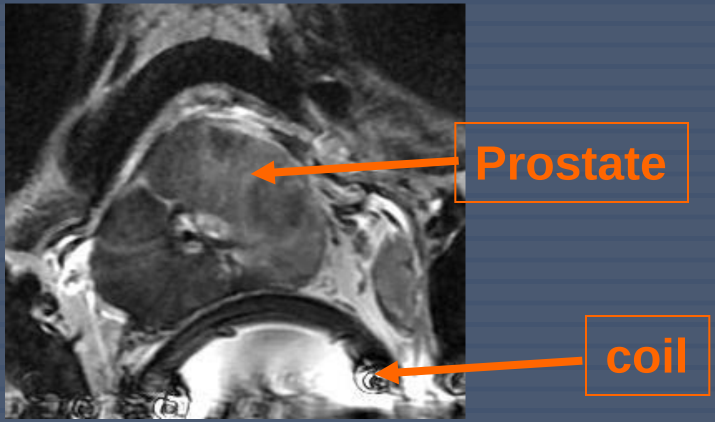
MRgFUS For Prostate Cancer

EndoRectal Imaging Coil

• Endorectal phased array coil:



• Imaging result (T2):



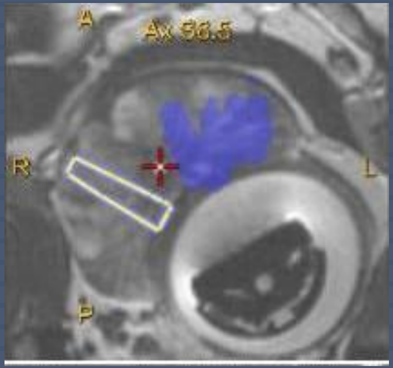
Courtesy of Sheba Hospital, Tel-Aviv, Israel

MRgFUS For Prostate Cancer

Animal studies status

- 23 experiments were conducted so far in the US and Israel
- The studies was done on a canine model, since its prostate anatomy is similar to the human prostate
- Largest percent of ablated prostate achieved: **~60%**
- Largest ablated volume achieved: **~40cc**

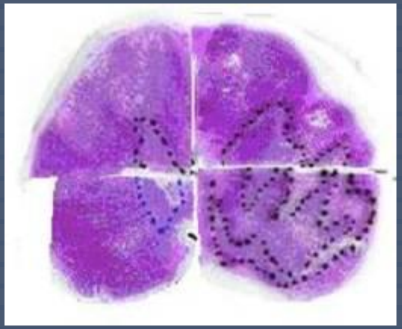
WS expected dose:



Non-perfused volume, T1w+contrast imaging:

TTC stained tissue:

Pathology results:



Courtesy of Sheba Hospital, Tel-Aviv, Israel

LOCAL DRUG ACTIVATION OF THERAPEUTIC NANOPARTICLES USING MR GUIDED FOCUSED ULTRASOUND

THE PROBLEM

- In vivo Drug toxicity limits many therapies curtailing their effectivness
- Therapeutic window in many cases is very narrow and varies between patients
- Chemotherapy is an easy example but this problem applies to many other therapeutic areas

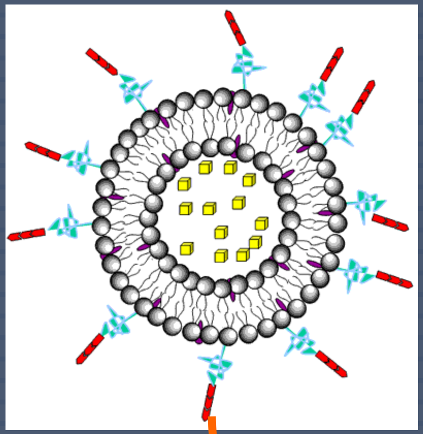
THE SOLUTION

- Local delivery of drugs would avoid systemic toxicity whilst providing high local therapeutic levels
- How to produce a safe and feasible system that allows easy drug administration and is only activated at the desired site of action and is not associated with intervention or other unpleasant methods of activation

THE SOLUTION: 3 EXISTING TECHNOLOGIES COMBINED(MR, FUS AND NANOPARTICLES)

- Many drugs can be coated with inert carrier compounds so that they are not toxic when given systemically
- These carriers can be engineered to be heat sensitive so that they release their contents at a specific temperature
- Highly controlled Local temperature elevation can be produced by using MR guided focussed ultrasound

Potential clinical applications



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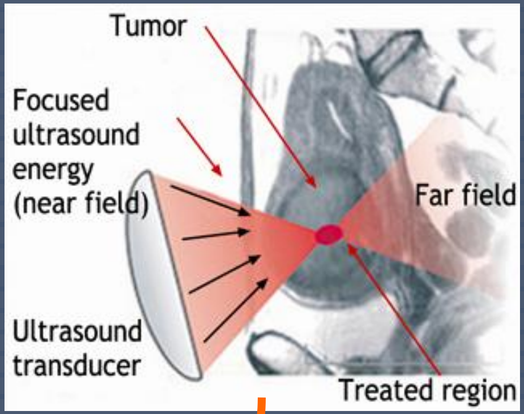


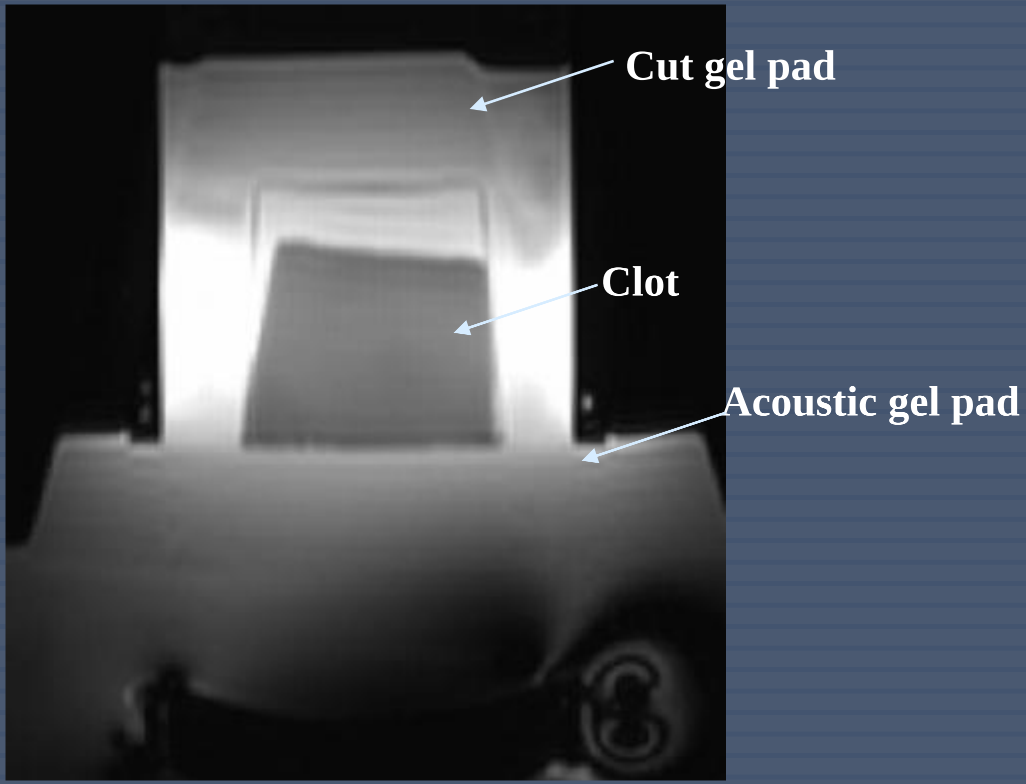
Focused U-S bursts nano-particles at target site
Drug contents released locally
Tissue access enhanced by heat effect

Cancer tumours *
Thrombus *
Arthritis
Focal infections
Atherosclerosis

* current project

Bulk Clot

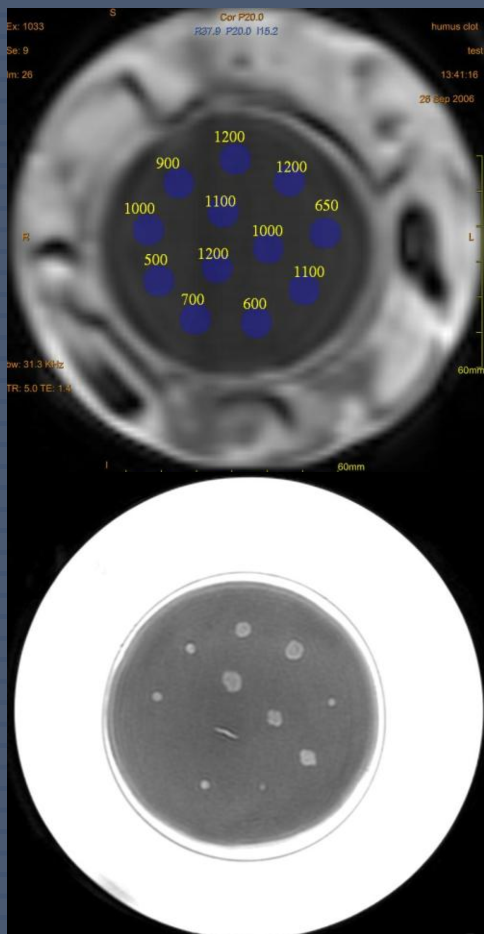
- The clot was made of ~400cc porcine blood that coagulate in a plastic cup, with and without thrombin

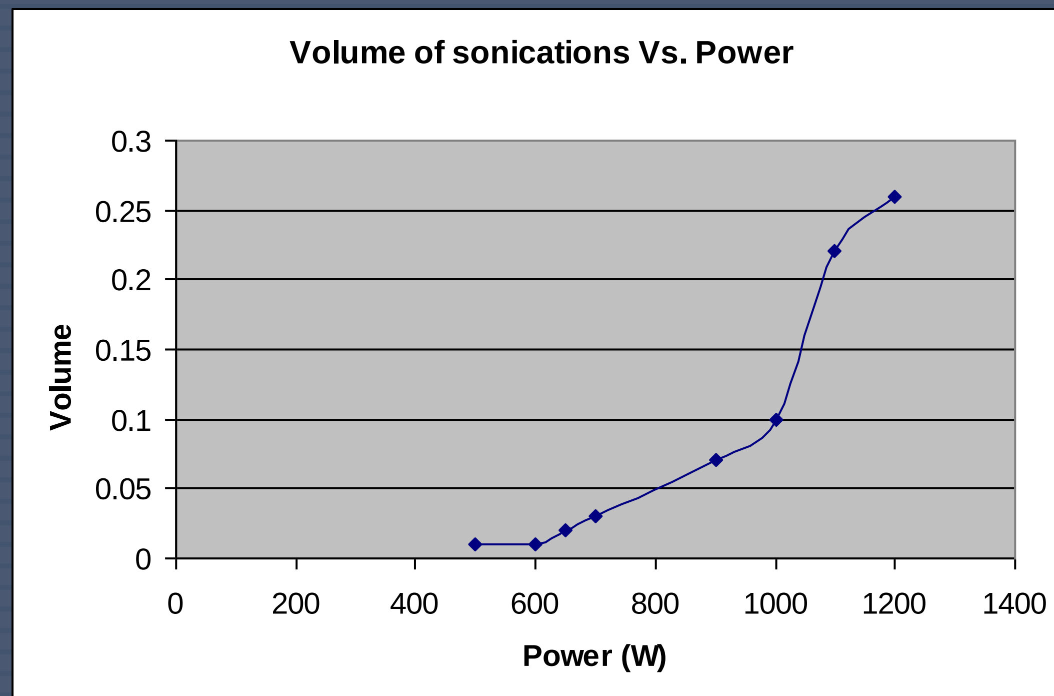


*Courtesy of Dr Harnof Sheba medical center

Bulk Clot – cont’

- Different Power – Different Size





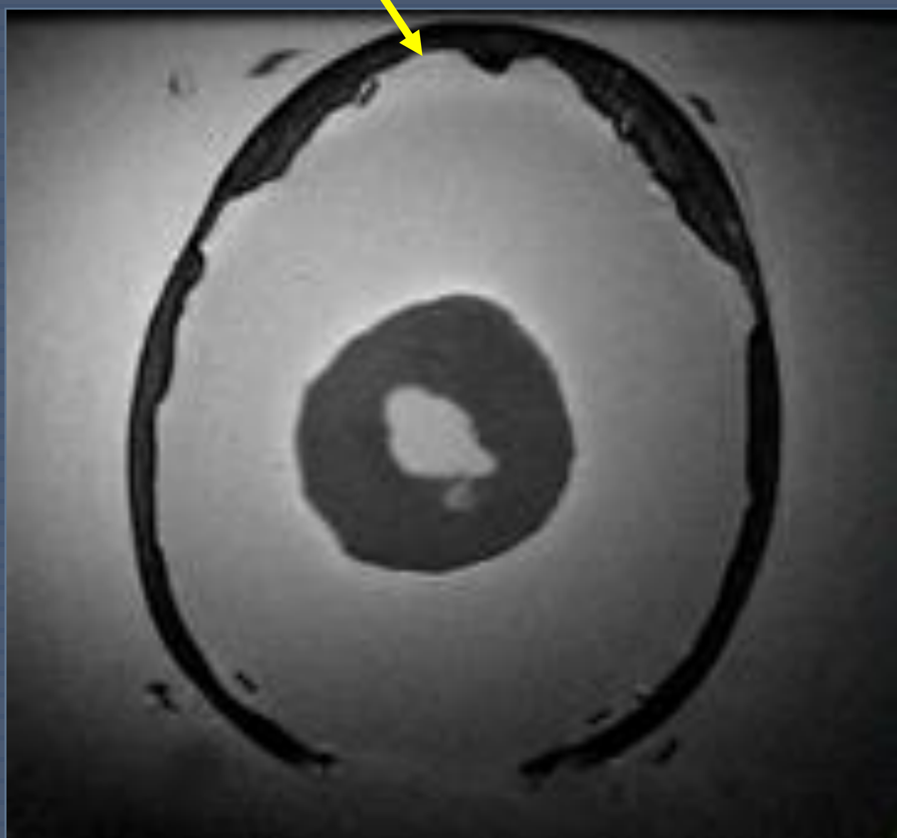
*Courtesy of Dr Harnof Sheba medical center

Clot Lysis

*Courtesy of Dr Harnof Sheba medical center

Trans Skull Clot lysis (1/2)

Skull

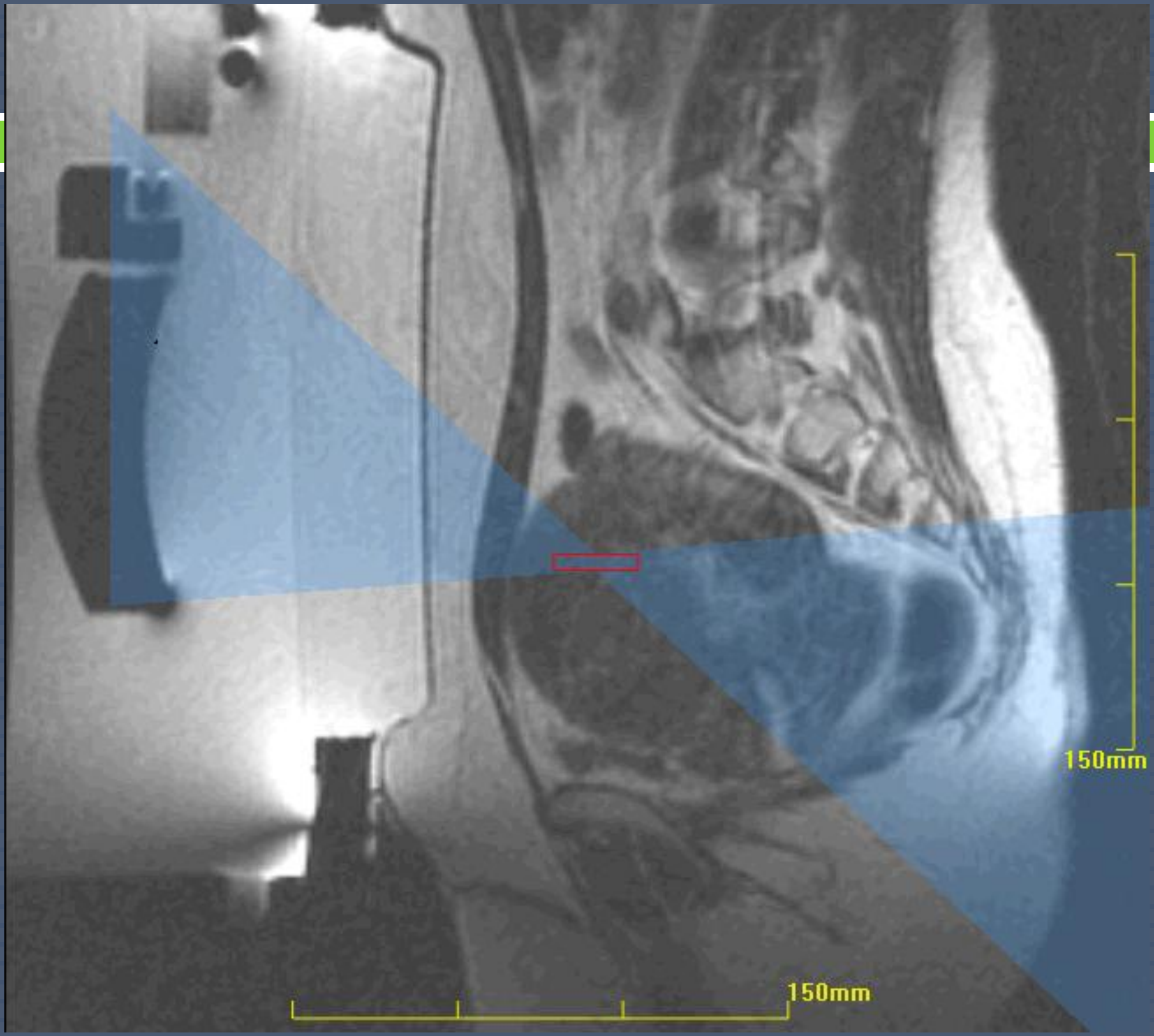


Transducer

*Courtesy of Dr Harnof Sheba medical center

MR guided FUS Huge Potential .

- Already very successful for uterine fibroids changing the way these tumours are treated
- Similar changes will happen in other areas of treatment as invasive procedures are converted into closed non invasive ones
- Acceptance in malignant conditions will take much longer plus controversy++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