



# MRgFUS for Bone Metastases

Rome, September 2011

update and future trends

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*Sheba Medical Center, Israel*

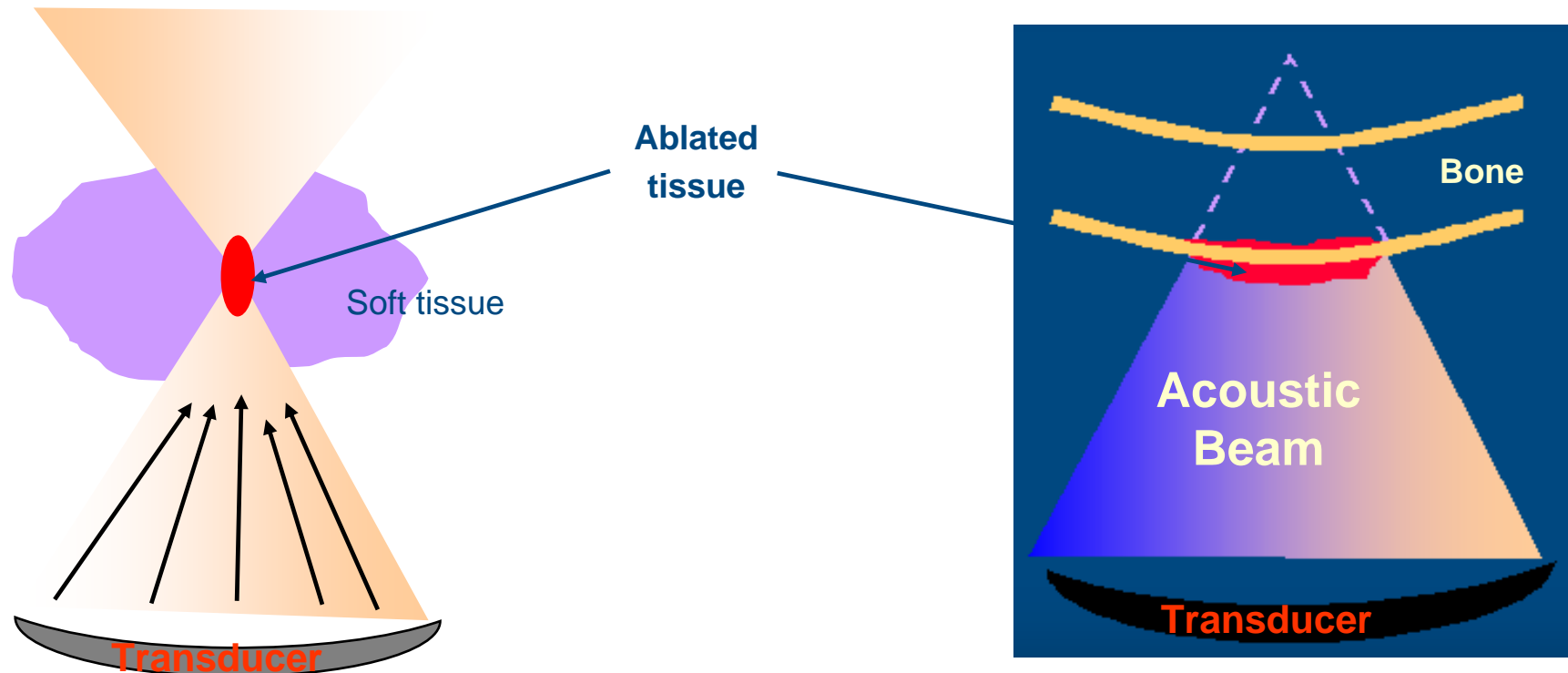
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# MRgFUS for Bone metastases treatment principles

*Bone heating is used to ablate the adjacent periosteum.*

*Palliation achieved by the ablation of the bone periosteum, which is the sensory origin of the pain*



# ExAblate for Bone: Treatment Technique



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

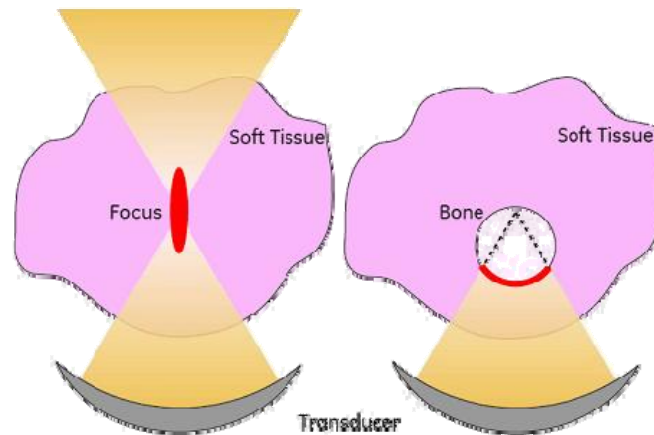
## **In soft tissue:**

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

## **In bone :**

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

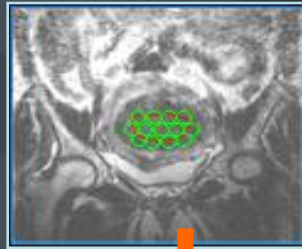
**Typical sonication energy 2500J**



**Typical sonication energy 1500J**

# Importance of MR Guidance and Control

**Planning:** 3D Imaging for precise tumor targeting

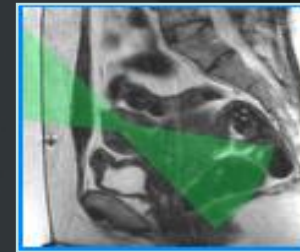


**CLOSED LOOP THERAPY**

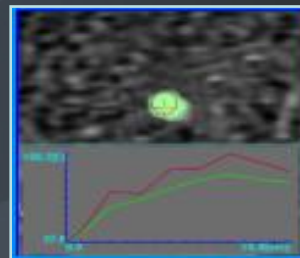
**Modify parameters** based on thermal feedback

-ROT-1 parameters-		
Acoustic Energy	2305 J	90 %
Sonication Duration	20 Sec	100 %
Acoustic Power	115 W	90 %
Frequency	1.05 MHz	
Actual cooling	160 Sec	
Treat Protocol	U.F. 20-80	

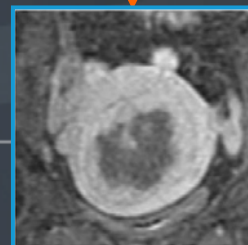
Beam path **visualization** for controlled treatment



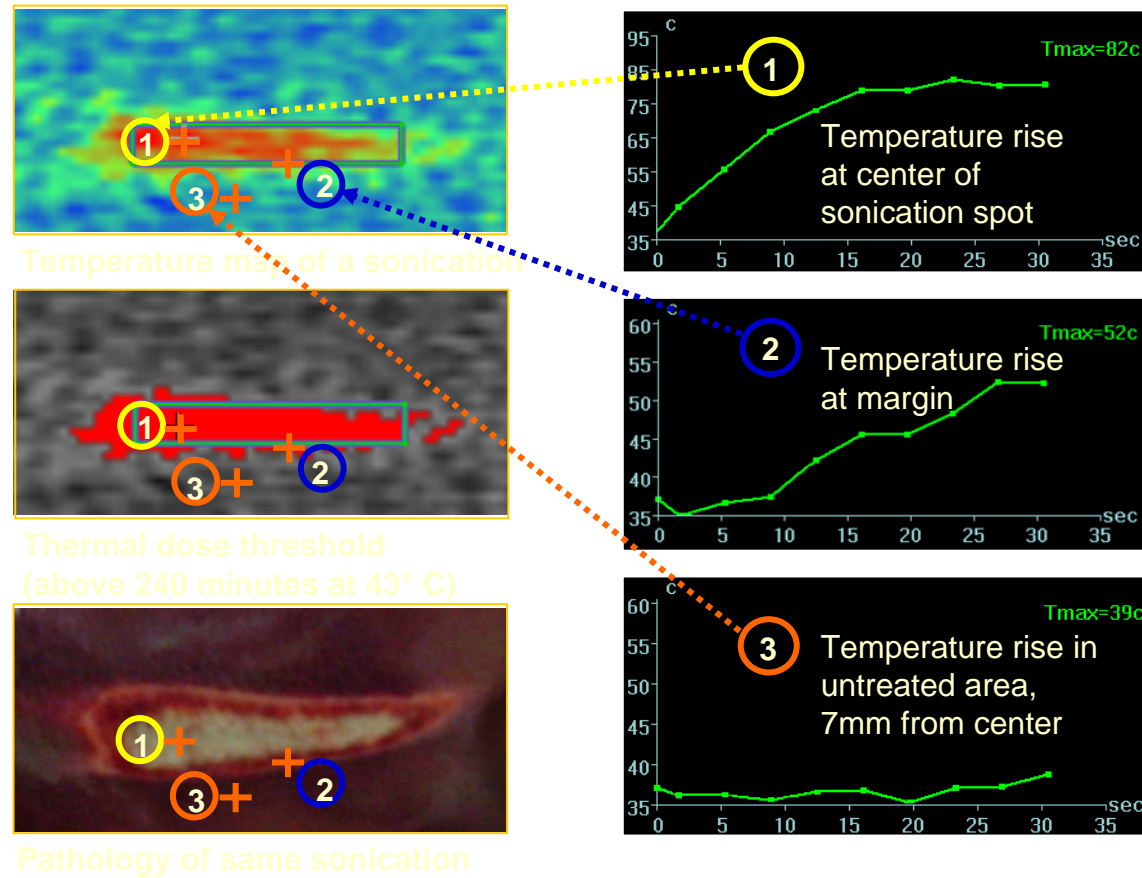
MR **thermometry** for real-time temperature feedback



**Post treatment** contrast imaging for precise treatment validation



# Real time MR thermometry and tissue ablation



**MR thermometry demonstrates clear correlation with tissue ablation and sharp edges of sonication**

# MRgFUS for Bone metastases treatment principles



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# Pain Palliation Feasibility Study



## Patient population:

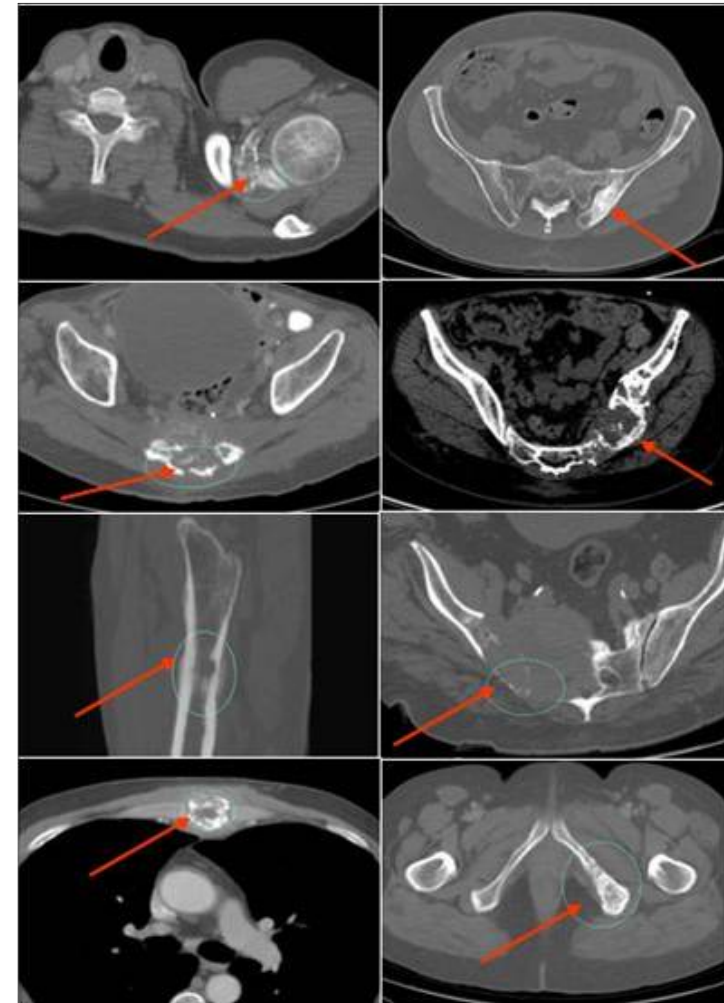
36 treatments in 31 patients were conducted, targeting 32 metastatic lesions

## Patient tumor characteristics:

- Treated bone mets from **primary tumor type**: renal, colorectal, lung, breast, prostate and other cancers
- Treated **lesion locations**: iliac bone, ischium, sacrum, femur, scapula, humerus, clavicle
- Treated **lesion type**: both osteolytic and osteoblastic
- Most were radiation failure patients

### *Published in Annals of Surgical Oncology*

*Liberman B, Gianfelice D, Inbar Y, Beck A, Rabin T, Shabshin N, Chander G, Hengst S, Pfeffer R, Chechick A, Hanannel A, Dogadkin O, Catane R. Pain Palliation in Patients with Bone Metastasis Using MR guided Focused Ultrasound Surgery, Preliminary Multicenter Clinical Experience,*



CT images of patients treated with MRgFUS. Red arrows shows the targeted bone metastases.

# Bone Metastases Pain Palliation Feasibility Study Results



## Criteria for treatment outcome

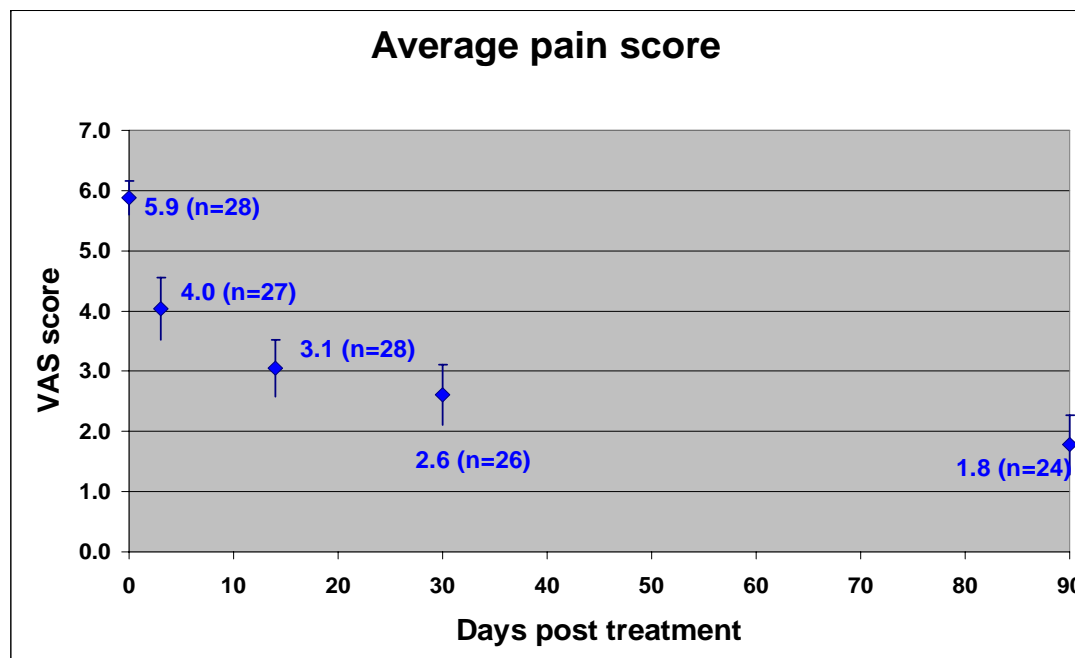
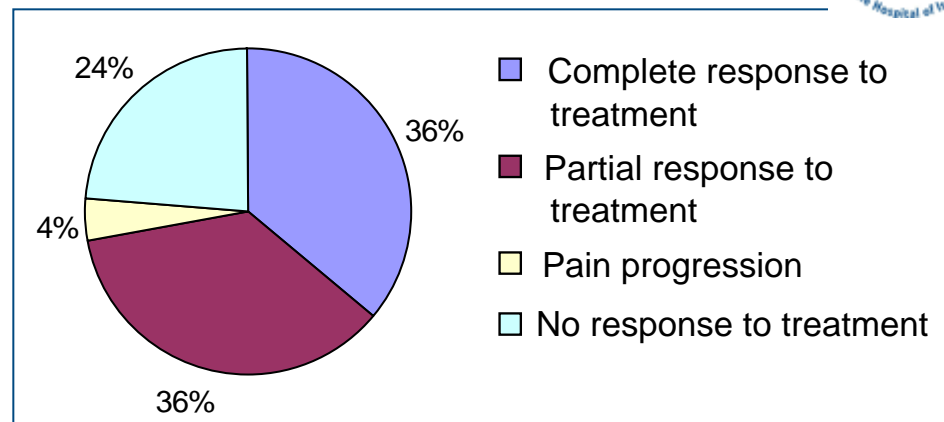
### Partial response:

- I. Pain reduction of 2 points or more of Visual Analog Score (VAS) at the treated site on a 0–10 scale without analgesic increase.
- II. Analgesic reduction of 25% or more from baseline without an increase in pain.

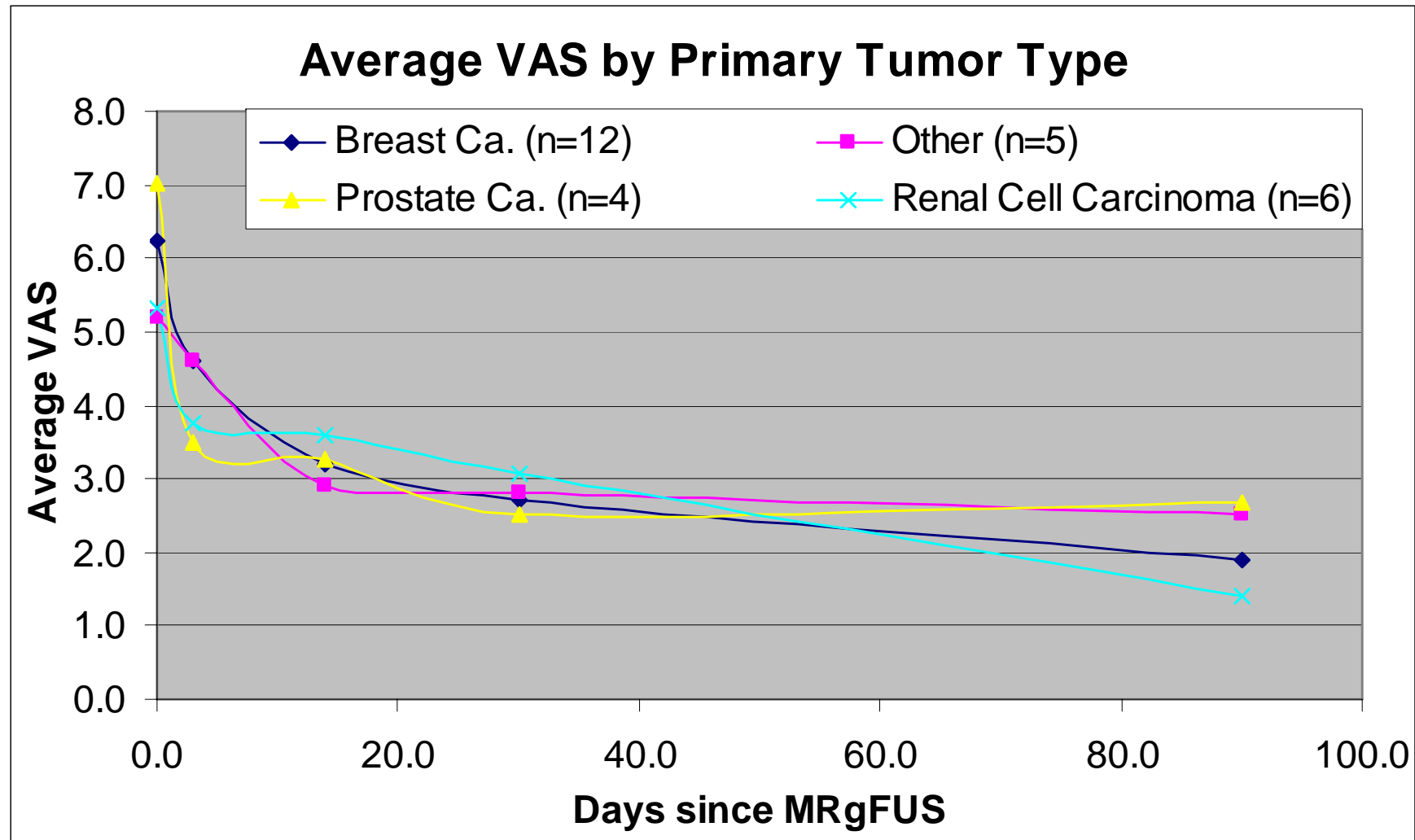
### Complete response:

Pain score of zero at the treated site with no concomitant increase in analgesic intake

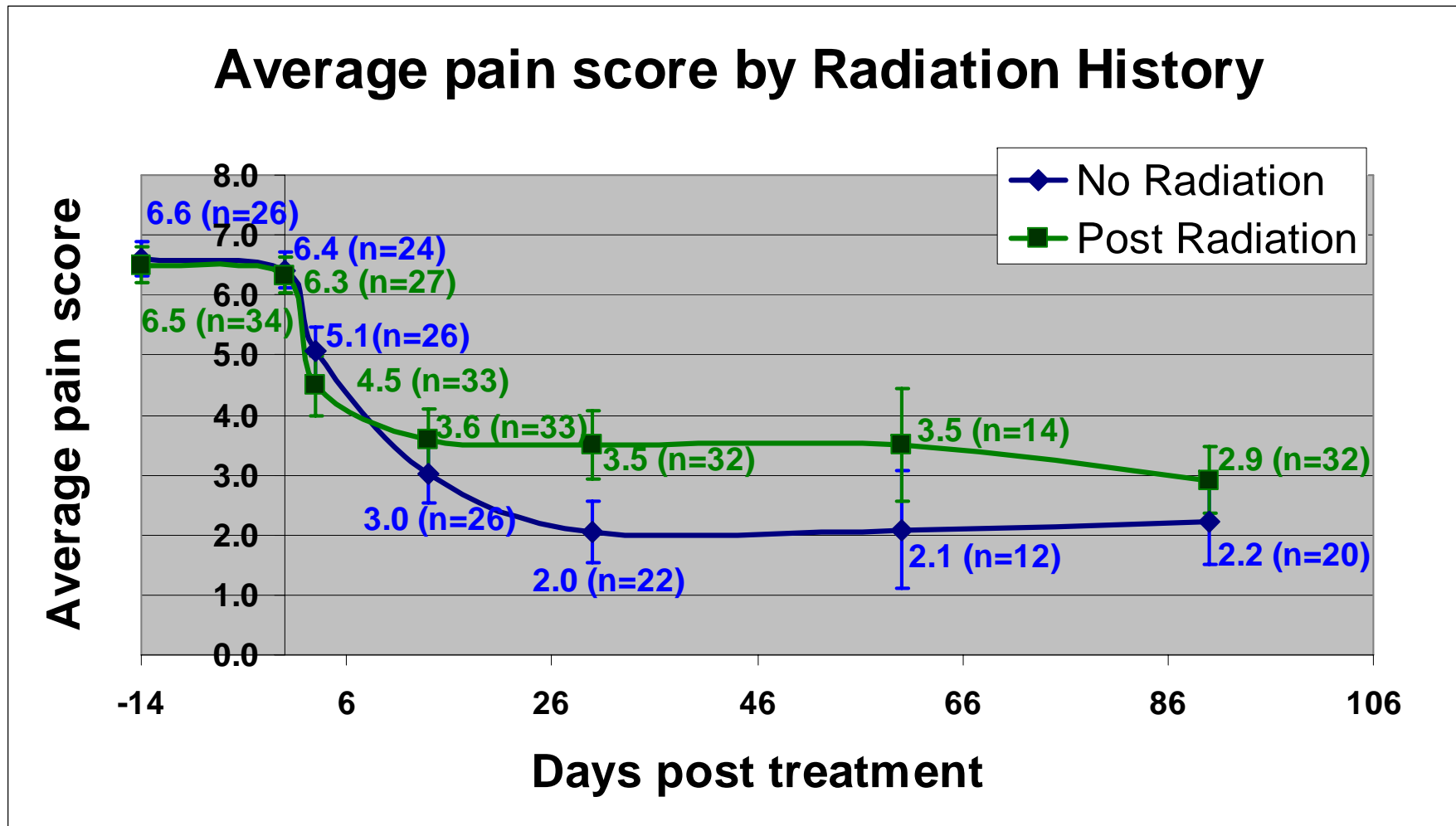
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 Liberman B, Gianfelice D, Inbar Y, Beck A, Rabin T, Shabshin N, Chander G, Hengst S, Pfeffer R, Chechick A, Hanannel A, Dogadkin O, Catane R. **Pain Palliation in Patients with Bone Metastasis Using MR guided Focused Ultrasound Surgery, Preliminary Multicenter Clinical Experience,**



# Phase I study – data analysis



# Summary of Three Studies

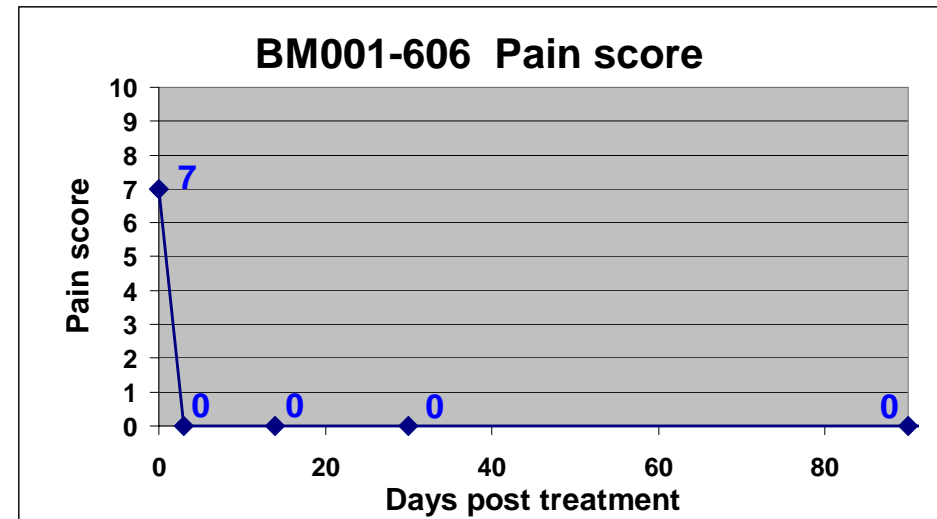
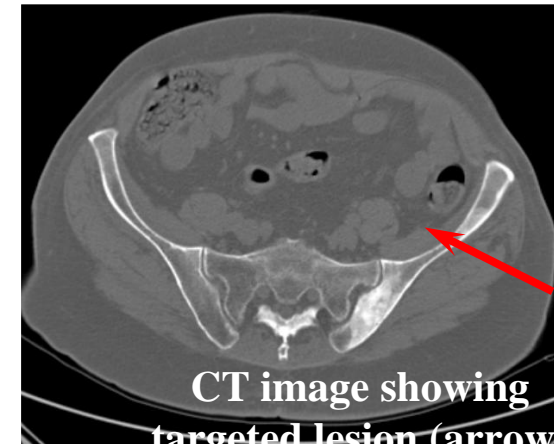


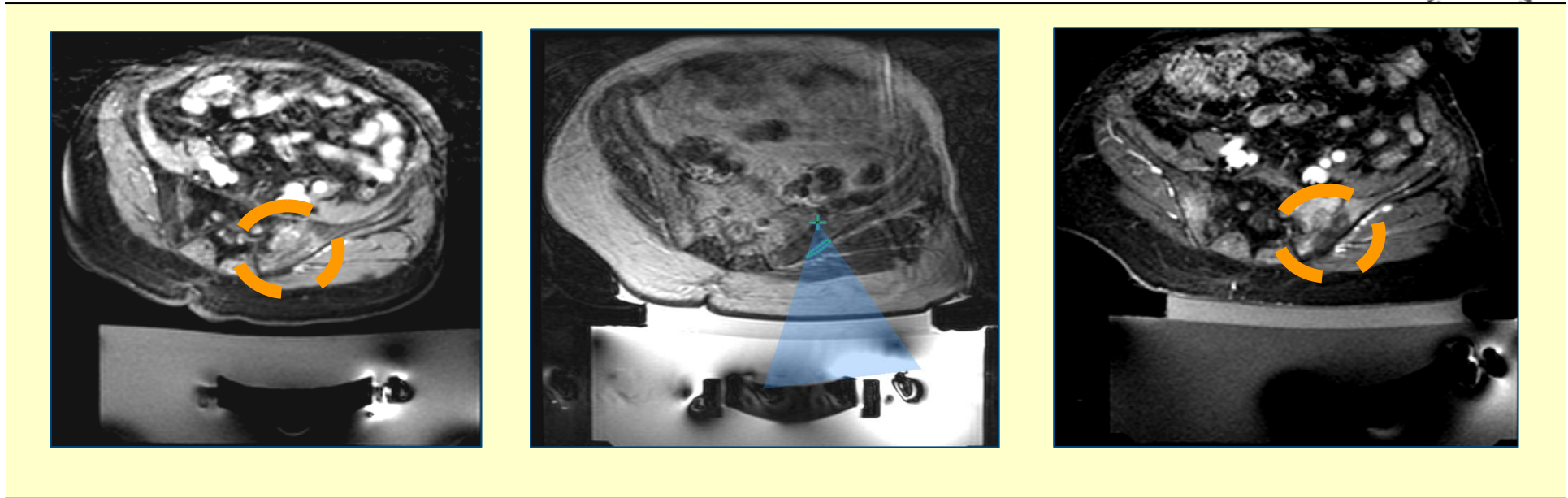
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# Clinical Case



- 70 year old male patient
- Primary tumor: Prostate Cancer
- Targeted lesion is osteoblastic and located in the left iliac bone
- MRgFUS procedure was performed on Jan 19th, 2006
- 26 sonications, Energy=1000J
- 48 min treatment time
- Pain in the treated area disappeared 3 days after treatment
- Patient stopped using walking cane shortly after treatment





### *MRgFUS bone metastasis treatment overview*

Left: Screening MR Axial T1w with contrast, showing enhancement of the bone metastasis in the left iliac bone (marked with orange dashed circle);

Middle: MR Axial T2w planning image with ultrasound beam overlay (blue);

Right: Post treatment MR axial T1w with contrast, showing non-enhancement in the treated area (marked with orange dashed circle).

# Clinical Trials – Three studies



## Objective:

To evaluate the effectiveness and safety of ExAblate in the treatment of palliation of pain from metastatic or primary bone tumors



## Study design:

1. BM 004 Prospective, randomized treatment vs. Sham  
Crossover allowed for non-responders
2. BM 011 Prospective, single arm, using conformal transducer
3. BM 016 Prospective, randomized treatment vs. EBRT  
Longterm tumor control, including imaging at 3 & 6 months

## Exclusion / Inclusion Criteria:

1. Target lesion should have a pain score of 4 or more
2. Targeted lesion is not in vertebra bodies or skull
3. Treatment area is more than 1cm from skin, major nerve or hollow viscera



# MRgFUS for Bone metastases Background



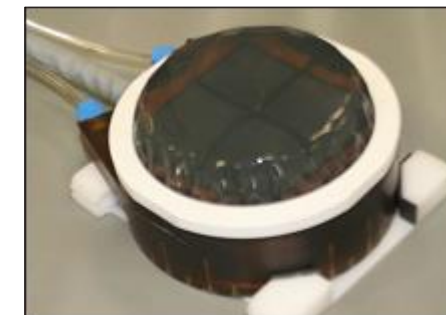
- Patients with a painful metastatic bone lesions.
- Conscious sedation by anesthesist during procedure.
- Procedure requires shaving of skin overlaying targeted painful tumor and placement of an IV-line.
- Treatment duration is 1 to 2 hours on the average.
- To date, known device related complications include three patients with small second degree skin burns and several cases of transient post treatment pain.

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# ExAblate Conformal Bone system

Access to more anatomical locations

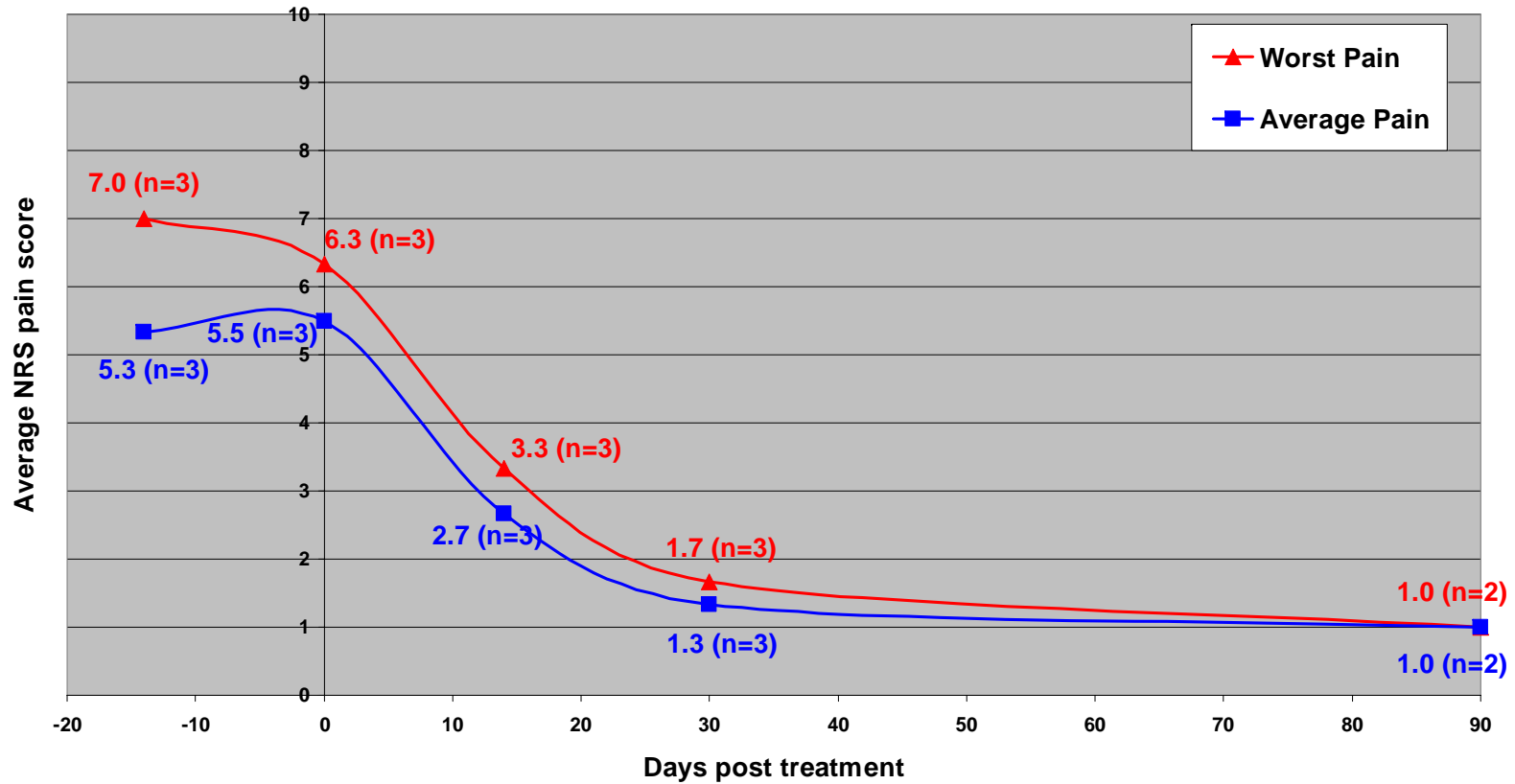
- *Improved patient comfort*
- High density electronically steerable transducer
- Leaking membrane to provide acoustic coupling
- Micro-coils for tracking transducer position
- Lower frequency (550kHz)



# Conformal Bone System – Initial Results



BM011 Conformal Bone System Sheba Results - Pain Score



# MRgFUS and tumor control

## Interaction of Focused Ultrasound with bone

**Ribs:**

**A- macro pathology showing lesion**

**B- CT images showing new bone formation.**

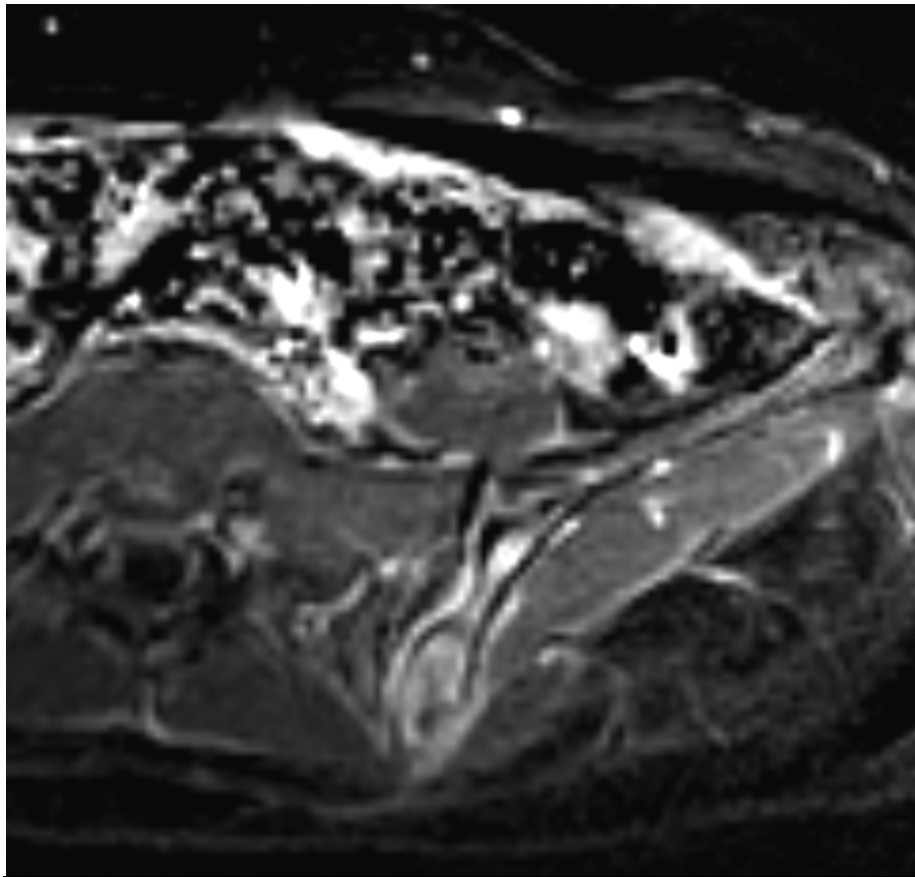
**Note: At 3M new bone formation & thickening of the cortical layer in the area of treatment**



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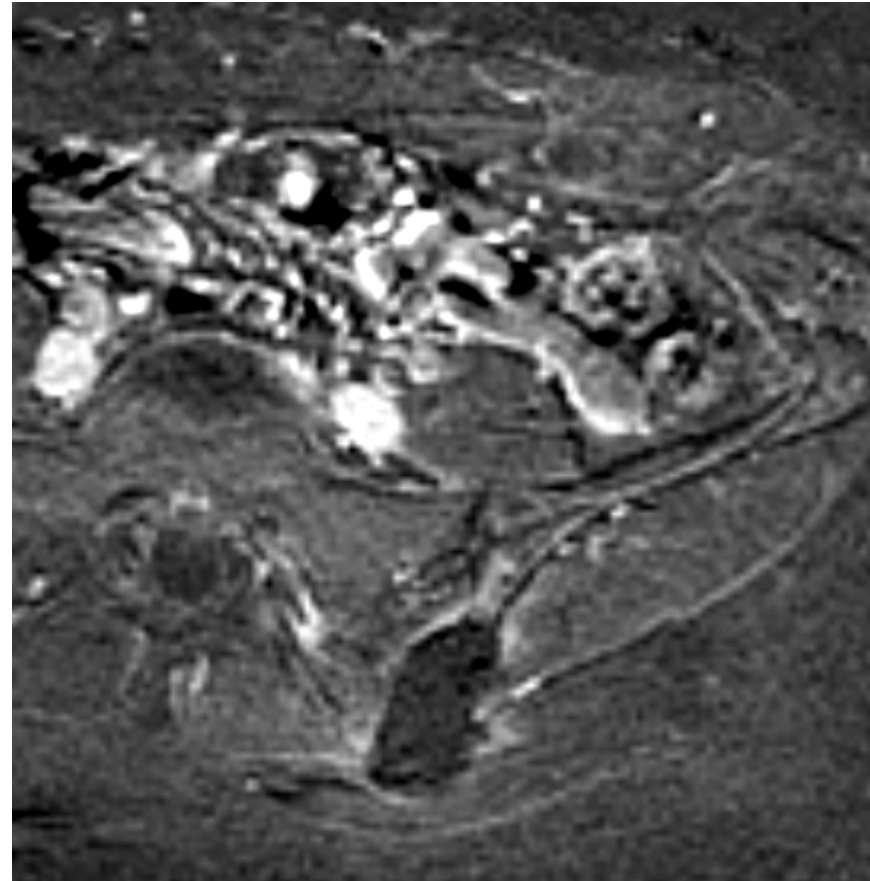


# Tumor Control – preliminary clinical data



**Pre-Treatment**

**T1w Contrast enhanced**



**Immediately Post treatment**

**T1w Contrast Enhanced subtraction**

\*courtesy of Sheba Medical Center Dr Yael Inbar

# BM 016

## Prospective, randomized study MRgFUS vs External Beam RadioTherapy

### Goal:

Pain control

local tumor ablation within the bone

### Endpoints:

1. Pain assessment
2. Follow up MR Imaging

# Pain Palliation of Bone Metastases or Primary Bone Tumors



## **Potential benefits of MRgFUS:**

- No ionizing radiation
  - Allows retreatment if needed
  - Allows treatment of patient not eligible for radiation
- Single treatment session
- Outpatient treatment
- Speedy reduction of pain
- Durable, (3 month study data)
- High Safety profile

# Pain relief comparison: EBRT and MRgFUS

	<i>MRgFUS</i>	<i>Radiation Therapy</i>
<i>Complete response</i>	<b>27%</b>	<b>14%</b>
<i>Partial response</i>	<b>71%</b>	<b>71-73%</b>
<i>No response</i>	<b>29%</b>	<b>30%</b>
<i>Speed of relief</i>	<b>1-3 days</b>	<b>2-3 weeks (after tx completion)</b>

## Criteria for treatment outcome

### Partial response:

- Pain reduction of 2 points or more of Visual Analog Score (VAS) at the treated site on a 0–10 scale without analgesic increase.
- Analgesic reduction of 25% or more from baseline without an increase in pain.

### Complete response:

Pain score of zero at the treated site with no concomitant increase in analgesic intake

*Sources: InSightec, Chow E. Palliative Radiotherapy Trails for Bone Metastases: A Systematic Review. Journal of Clinical Oncology, Vol 25, No 11, April 10, 2007*

# BM016 current results



Total number of patients: n=11

4 active sites:

- Cartuja (n=4 Pts)
- Sheba (n=3 Pts)
- Rome (n=3 Pts)
- Jaslok (n=1 Pts)

**MRgFUS (n=6 Pts, 7 lesions):** 5 patients reached 3 months FU, 1 patient crossed over to XRT arm after 2 months follow-up

**XRT (n=5 Pts, 5 lesions):** 1 patient left the study after 1 week and the rest of 4 died (not reaching 3M FU)



## BM 016

# MRgFUS vs External Beam RadioTherapy

Patient accrual slow – 3 patients in Sheba

### Analysis of poor accrual

Radiotherapy available within 24 hours in department

MRgFUS requires availability of open MRI & co-ordination with radiology (MR) and anesthesiology

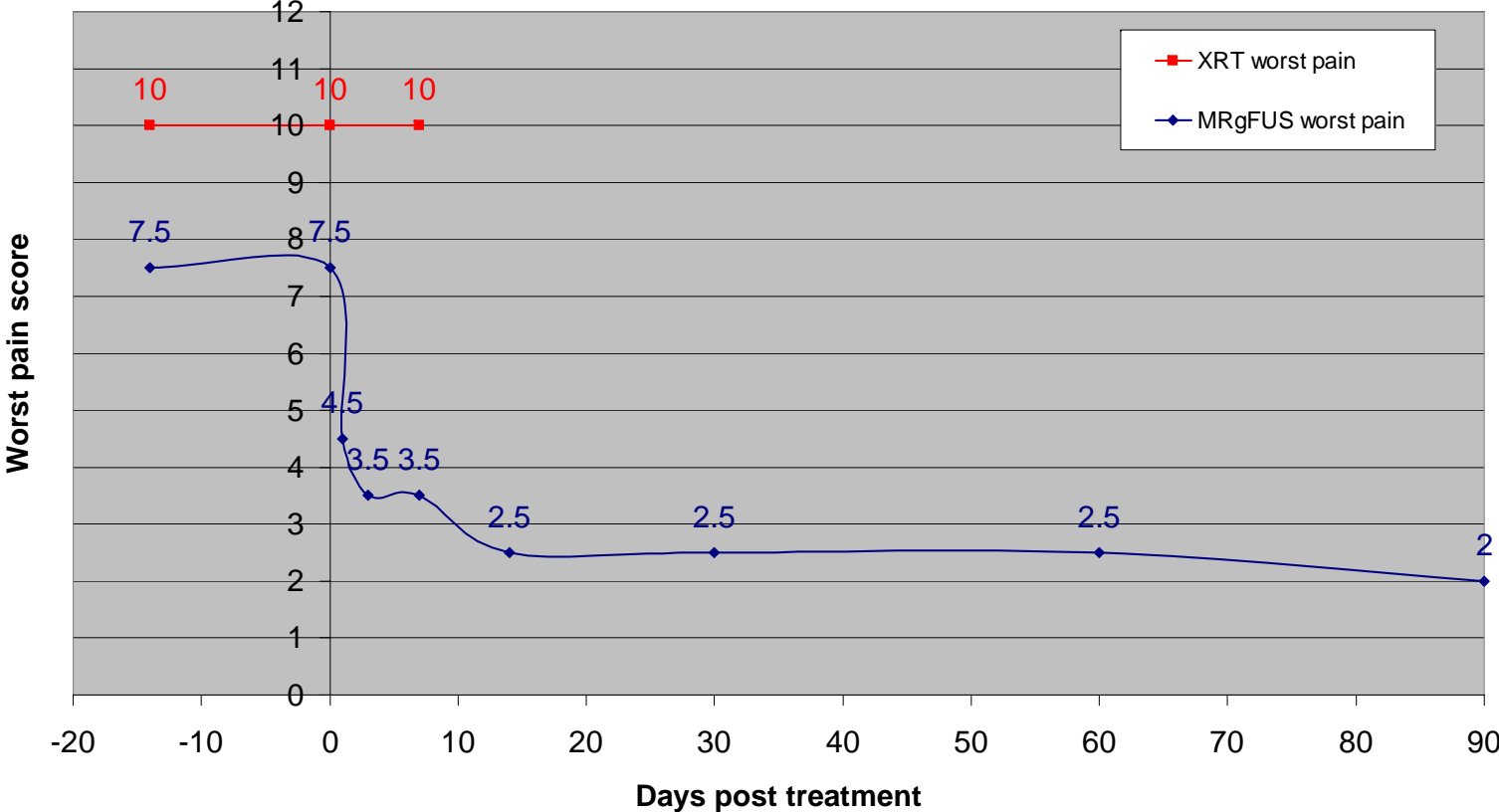
Therefore referring physicians reluctant to enter patients on study

Patients with acute pain do not wish to be subject to randomisation

# BM016 – Sheba results (n=3)



BM016 Sheba data - Worst pain score

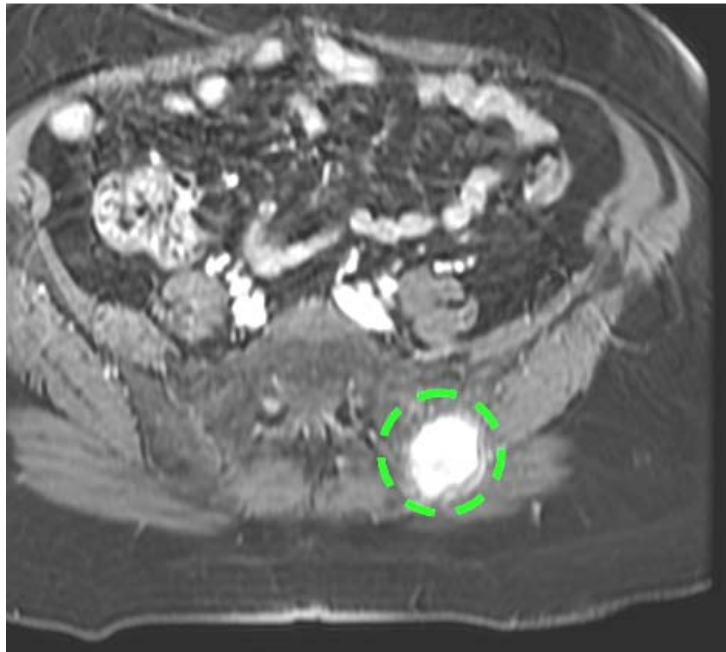


# BM016 – Evidence for Tumor control

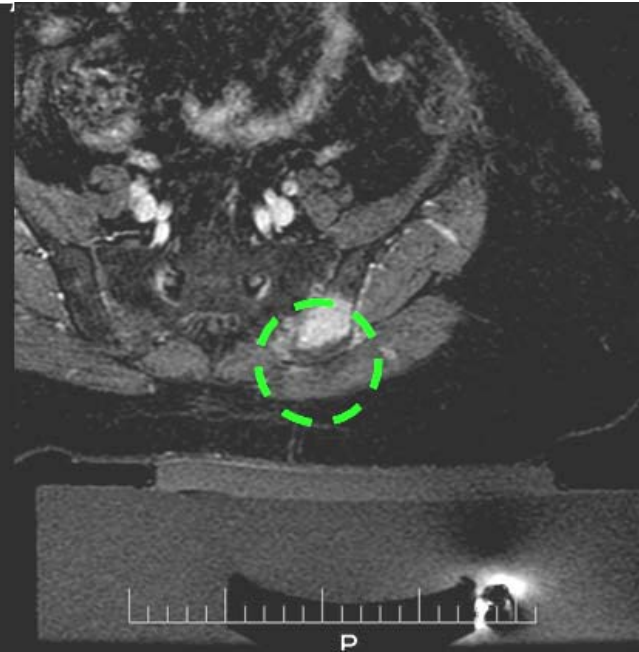


BM016-6003 (Sheba patient from MRgFUS arm)

**Pre-treatment**



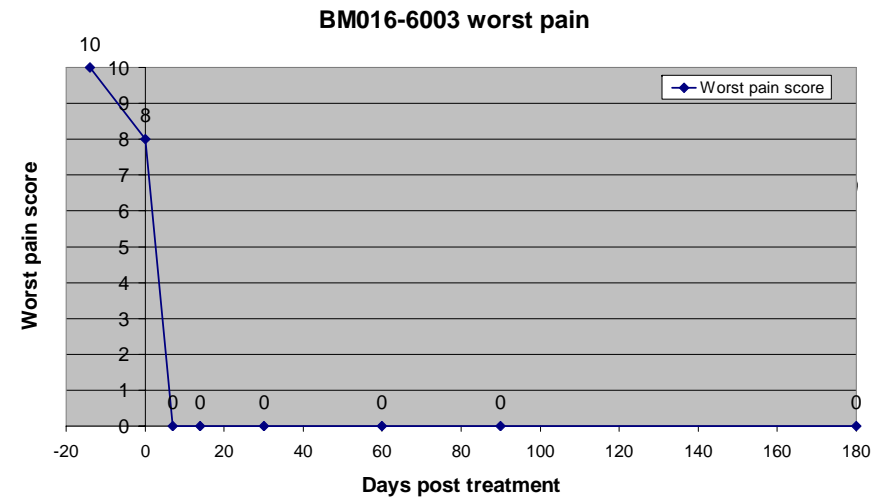
**Immediately post-treatment**



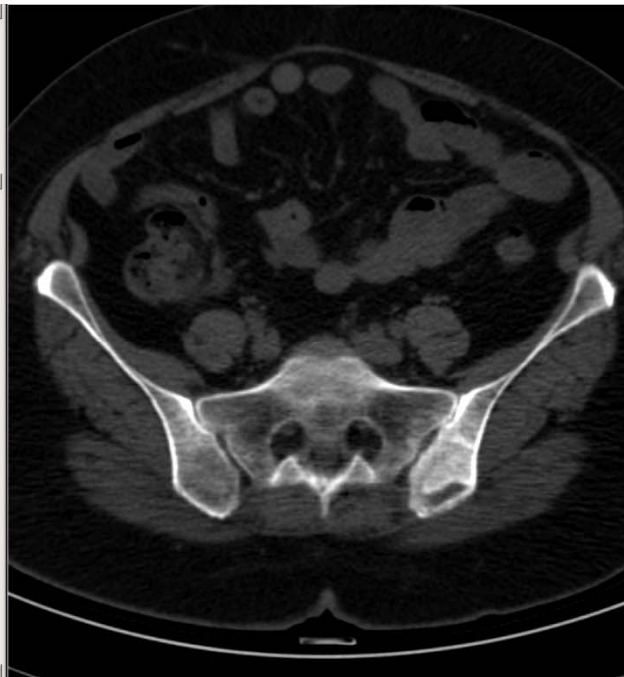
Axial T1w FS with contrast shows non-enhancement of the posterior aspect of the treated lesion

**Pain: VAS dropped from 10 at screening to 0 immediately after treatment**

# BM016-6003 Sheba



CT screening –  
osteolytic lesion in the left ilium

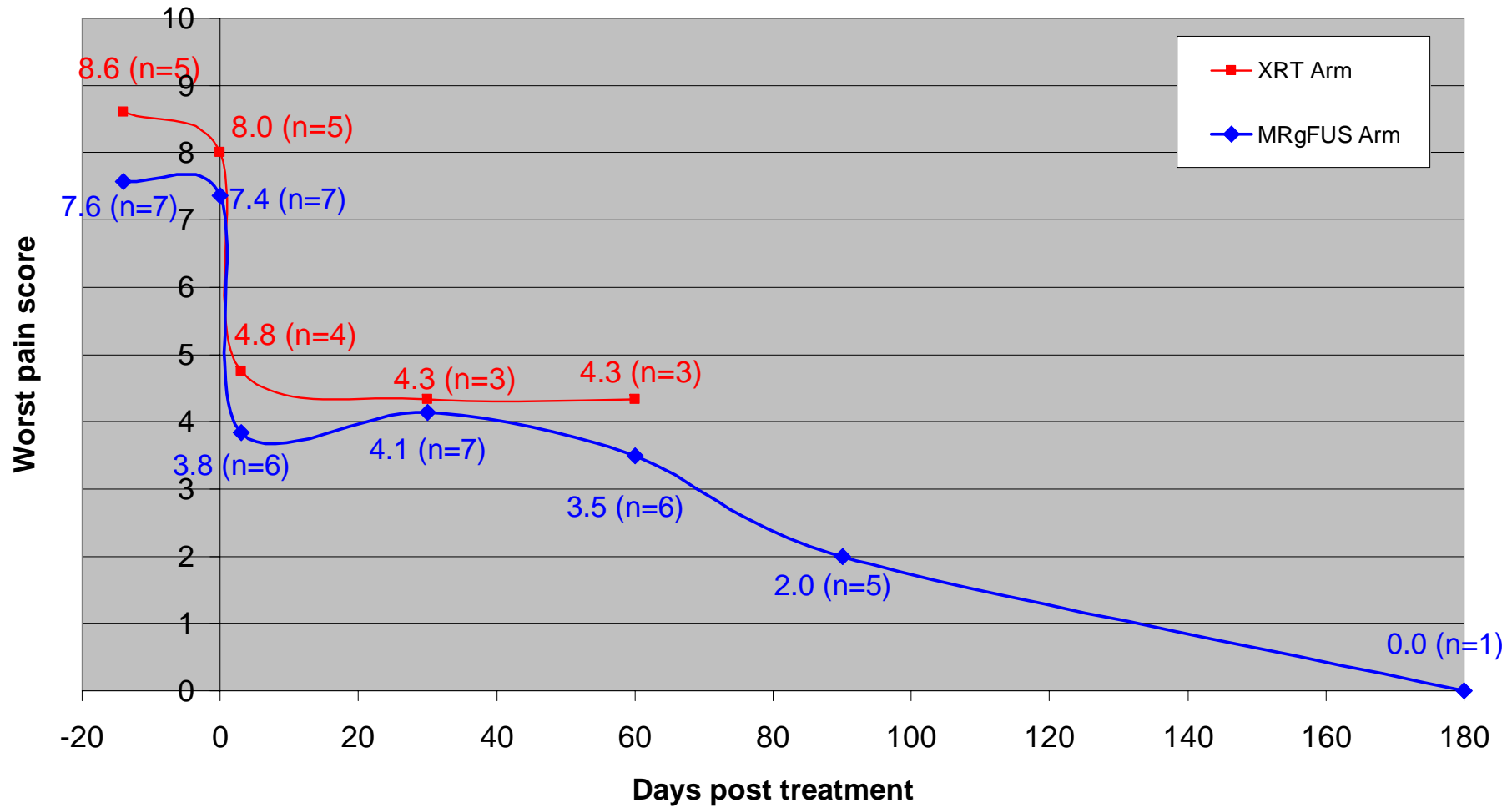


6 months follow-up CT after MRgFUS Tx shows  
evidence for new bone formation

# BM016 all results



Worst pain score - Current Status in all Sites



# Conclusions



MRgFUS is effective for treatment of painful bone metastases

Effective for recurrent pain post-XRT

Effective for radioresistant tumors e.g. renal cell ca

Initial data indicate that it should be as effective as XRT as initial therapy for painful bone metastases

Need to assess long term outcome

Treatment flow should be improved

# MRgFUS for bone metastases - the future



- MR imaging required for target delineation in radiotherapy
  - CNS, spine, sarcoma, (prostate)
- Image fusion has limitations
- Wide-bore MR simulators are being introduced to radiotherapy departments
  - Improved tumor targeting
  - No registration errors between MR and CT simulation
- MRgFUS should be an integral part of the Radiotherapy Department
  - Availability of MRI
  - Increasing number of oncological indications for MRgFUS

# MRgFUS for bone metastases - the future

Convergence of radiotherapy and interventional radiology

21<sup>st</sup> century Radiotherapy key themes– *conformality*

- *image guidance*

## **Holy grail of radiotherapy**

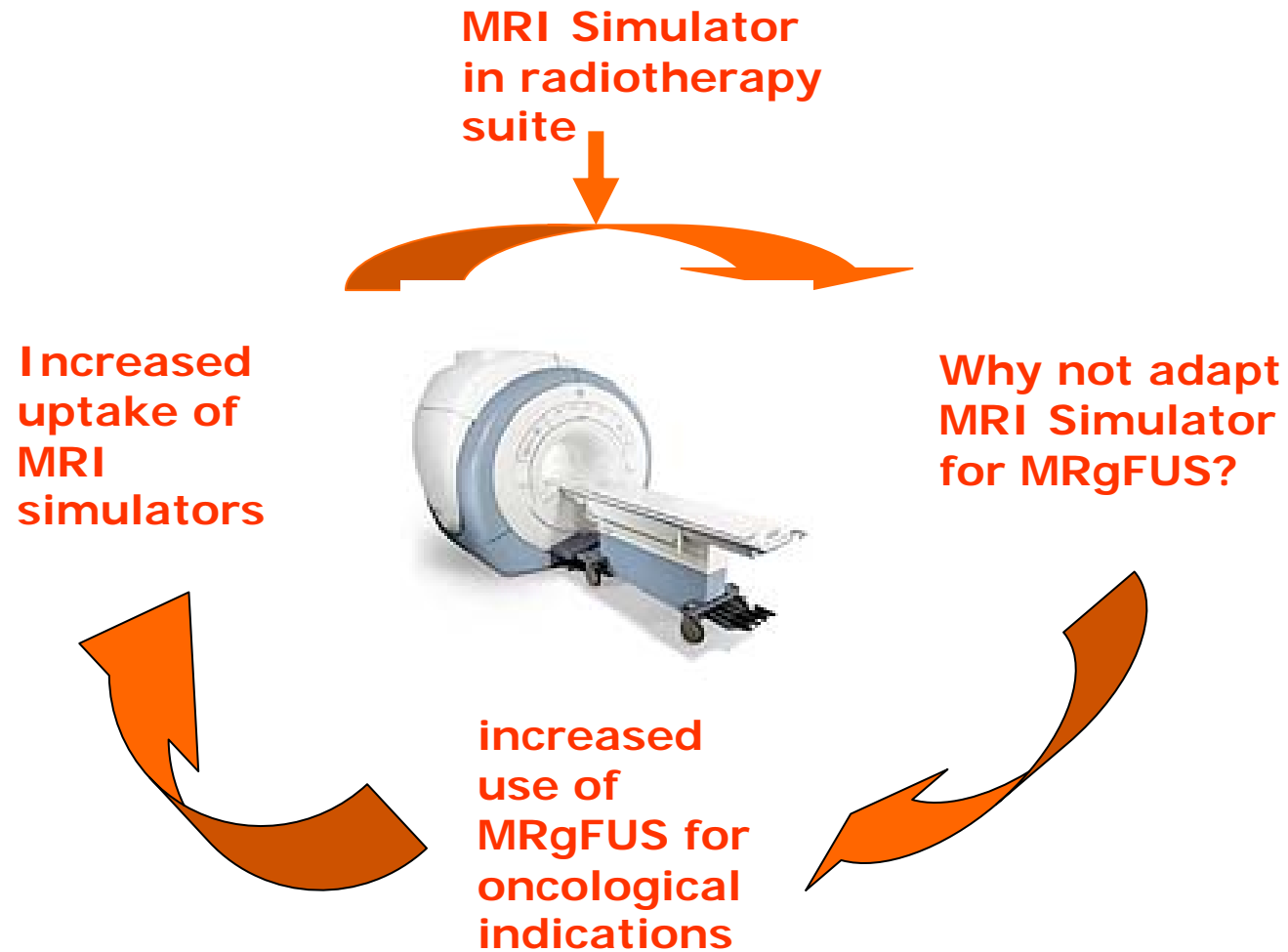
*know where you treat – imaging (MRI)*

*know how much energy is deposited in tissue*

*measure immediate effect on tumor*

*personalize dose planning for patient specific rx planning*

# Utilization of MRI in Radiation Oncology



# MRgFUS for bone metastases - the future

This is a team effort

Yael Inbar & interventional MR team

Radiation Oncology colleagues

Sheba Oncology clinical studies center

Insightec