

# **Magnetic Resonance Guided Focused Ultrasound Surgery For Treatment of Bone Metastases**

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**Safety and Performance Excellence**

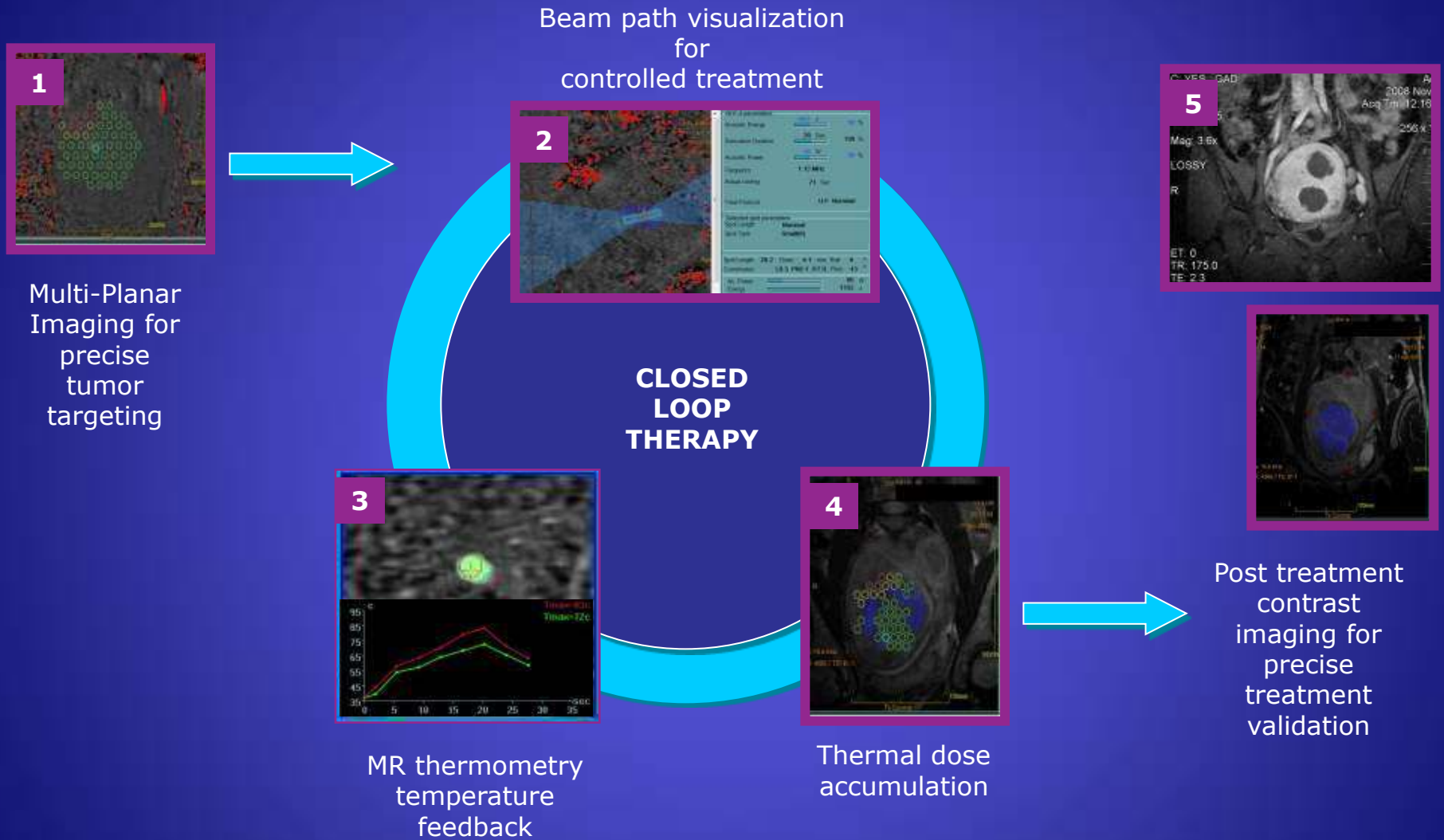
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# Background and Significance

# Advantages of MRgFUS at each step of treatment process



# Bone Metastases: The Problem

- Very common
- Debilitating pain
- Often primary factor impacting QOL
- Pain relief with current therapies has many limitations

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

### In Soft Tissue

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

### In Bone:

- Lower energy used
- Wide Beam Approach
  - Greater treatment area per sonication
  - Shorter treatment time

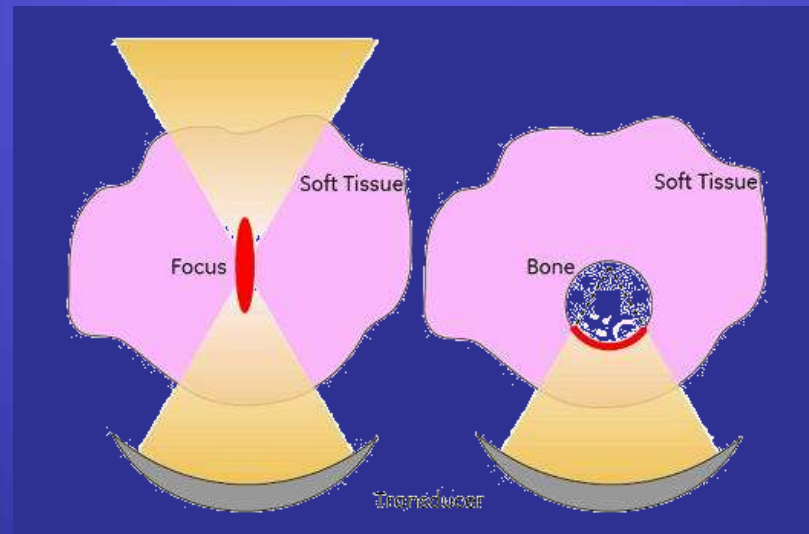
### UF Averages

**Energy: 2500 J**

**Sonications: 60**

**Tx time: 2:36**

Data from 279 commercial UF patients treated in the US



### BM Averages

**Energy: 1138 J**

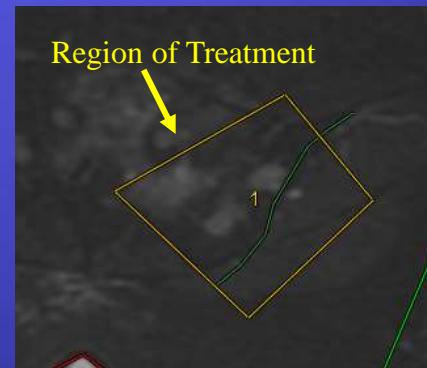
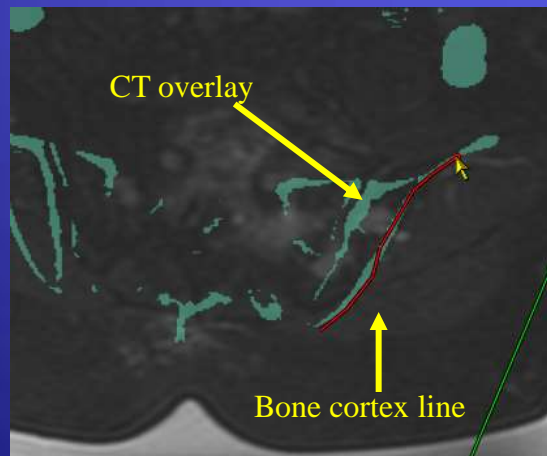
**Sonications: 17**

**Tx time: 1:07**

Data from 31 bone pts in feasibility study

# Treatment Description

- T2 and T1 planning images acquired to localize and plan treatment
  - Identify any potential obstacles (nerves, bowel, scars, etc.)
- Continue with treatment planning if:
  - Targeted tumor is visible on MR images
  - No obstacles obstruct treatment
  - Patient meets inclusion/exclusion criteria
- Use CT image registration to assist in defining the bone cortex contour
- Define the region of treatment around the targeted tumor



# Clinical Experience

# Summary of Phase I – II Bone Studies: Patient Demographics and Cancer Characteristics

<i>Patient characteristics</i>	
Number of patients treated	31
Female	16
Male	15
Age, median [range], years	61 [40–85]
<i>Primary tumor type</i>	
Renal CA	6
Colorectal CA	2
Lung CA	1
Breast CA	11
Prostate CA	5
Other	6
<i>Targeted lesion type</i>	
Osteolytic	20
Osteoblastic	10
Prior radiation to treated site	21/31
Concurrent opioid analgesics	10*
<i>Targeted lesion location</i>	
Iliac bone	18
Ischium bone	4
Sacrum	4
Femur	1
Scapula	2
Humerus	1
Clavicle	1

\* Excluding patients lost to follow-up.



# Summary of Phase I – II Bone Studies: Results

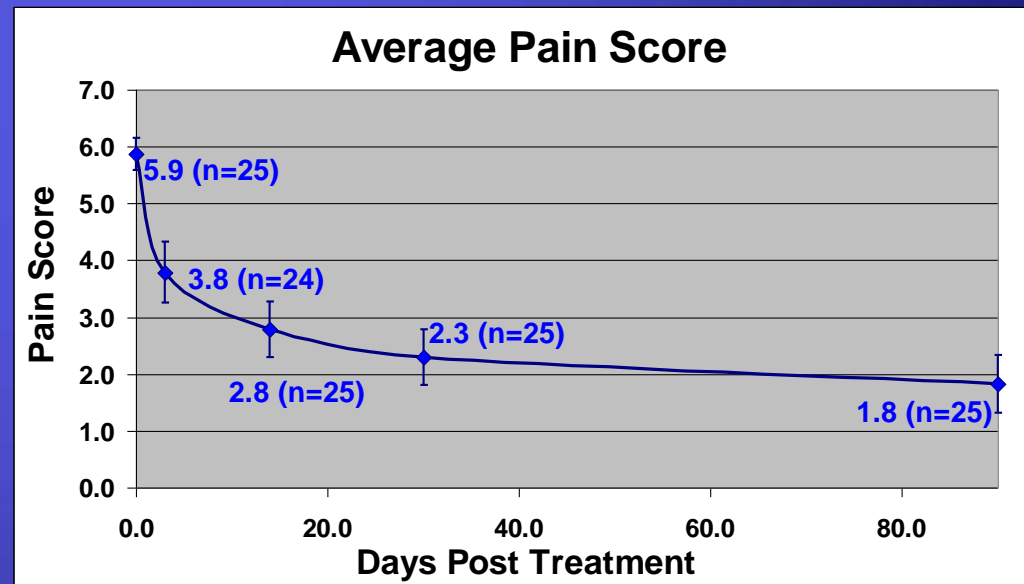
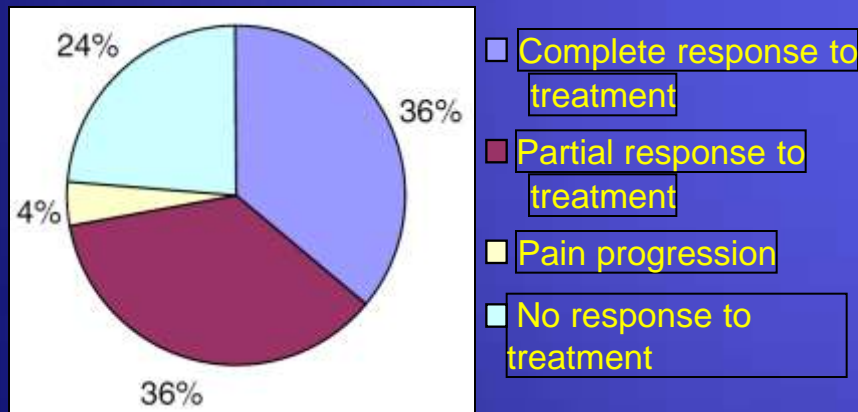
Criteria for treatment response as defined by the international consensus on palliative radiotherapy\*:

## Partial response:

- 1) Pain reduction of 2 or more at the treated site on a 0–10 scale without analgesic increase.
- 2) 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



\*Chow E, Wu JS, Hoskin P, et al. International consensus on palliative radiotherapy endpoints for future clinical trials in bone metastases. Radiotherapy Oncol 2002; 64(3):275–80.

# Magnetic Resonance Guided Focused Ultrasound Surgery for Palliation of Painful Bone Metastasis: Results of a Multicenter Phase III Trial

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# Study Overview

**Phase III multi-center single-blind two-arm study**

**The primary efficacy endpoint was two-fold:**

**1)  $\geq 2$  improvement in NRS worst pain score by 3 months in  $\geq 50\%$  of MRgFUS subjects**

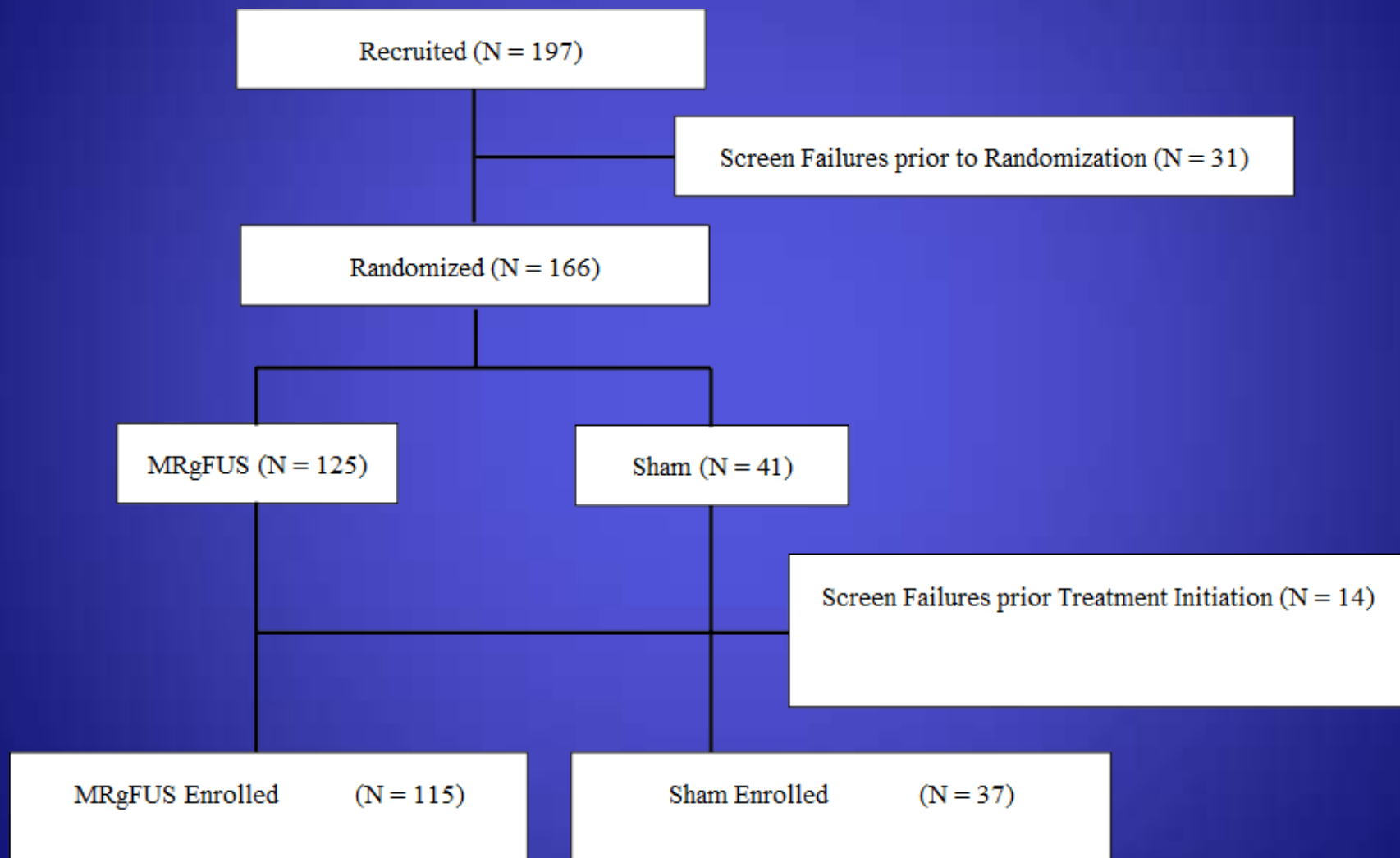
**2) The response rate in the MRgFUS arm would be significantly greater than in the placebo arm**

**Additional endpoints included assessment of quality of life and toxicity**

# Key Eligibility Criteria

- RT not a primary treatment option (e.g. prior RT to site)
- NRS pain score  $\geq 4$  irrespective of medication
- Only most painful lesion treated – pain from additional sites  $\geq 2$  NRS points less compared to treated site
- Targeted tumor in bone  $> 10$  mm from the skin and other critical normal organs/tissues
- No impending fracture sites ( $\leq 7$  Mirel's fracture risk score)
- KPS  $\geq 60$

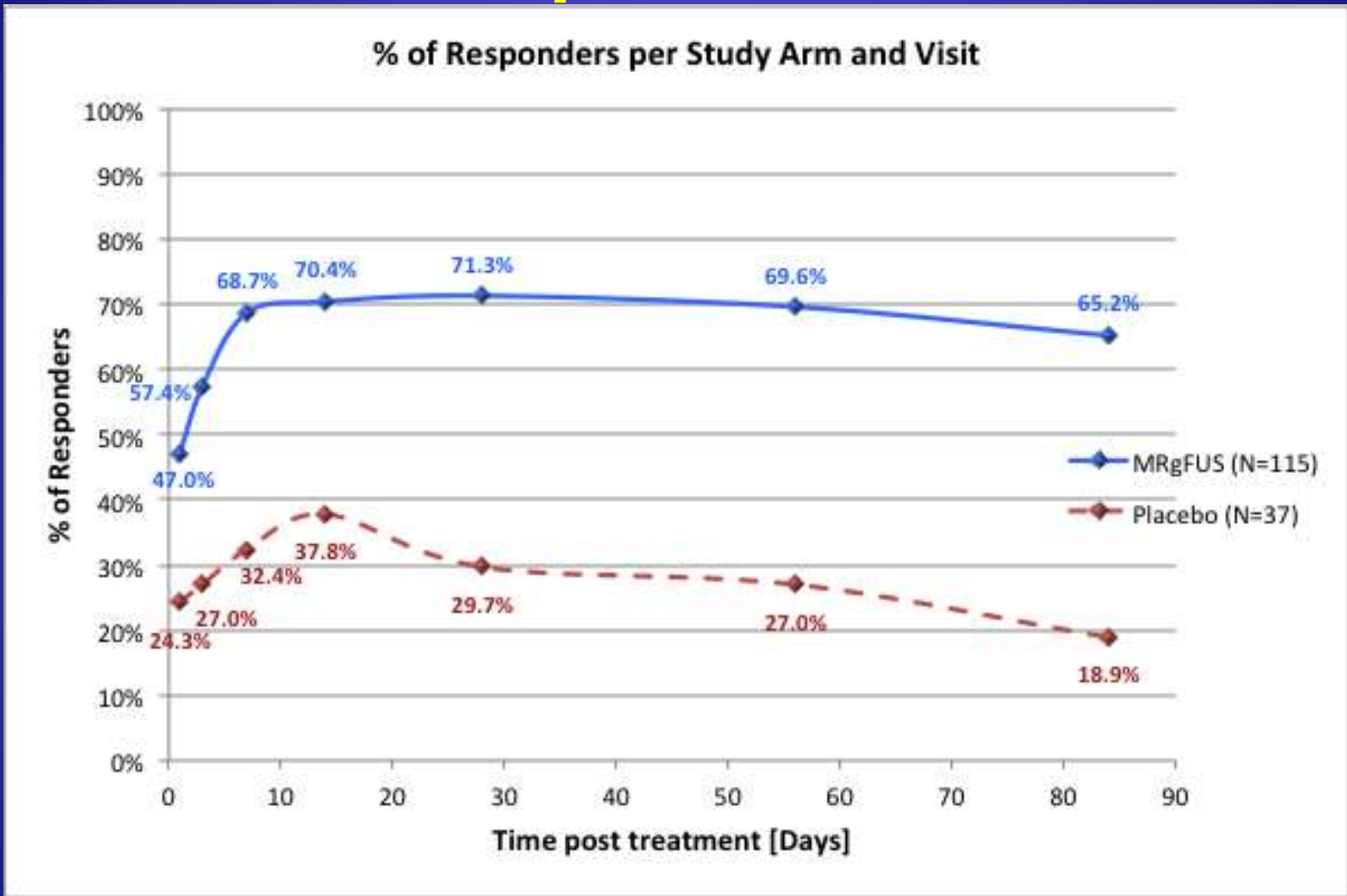
# Patient Disposition by Treatment Arm



# Baseline Patient Characteristics

Parameter	Description / Category	MRgFUS N=115 (76%)	Placebo N=37 (24%)
Age [years]	Median (Range)	61.1 (19.1-83.6)	59.7 (29.7-83.2)
Gender [n (%)]	Male	51 (44%)	7 (19%)
	Female	64 (56%)	30 (81%)
Target Lesion Volume [cm <sup>3</sup> ]	Median (Range)	75.4 (0.4-1341.2)	66.0 (1.8-2345.8)
Primary Cancer Type [n (%)]	Breast	37 (32%)	21 (57%)
	Prostate	15 (13%)	2 (5%)
	Lung	17 (15%)	4 (11%)
	Other	36 (33%)	8 (22%)
Target Lesion Type [n (%)]	Osteoblastic	25 (22%)	6 (16%)
	Osteolytic	60 (52%)	21 (57%)
	Mixed	29 (25%)	10 (27%)
	Unknown	1 (1%)	0 (0%)
Target Lesion Location [n (%)]	Pelvis	71 (62%)	20 (54%)
	Sacrum and Coccyx	12 (10%)	6 (16%)
	Rib and Sternum	18 (16%)	6 (16%)
	Extremities	7 (6%)	3 (8%)
	Scapula	7 (6%)	2 (5%)

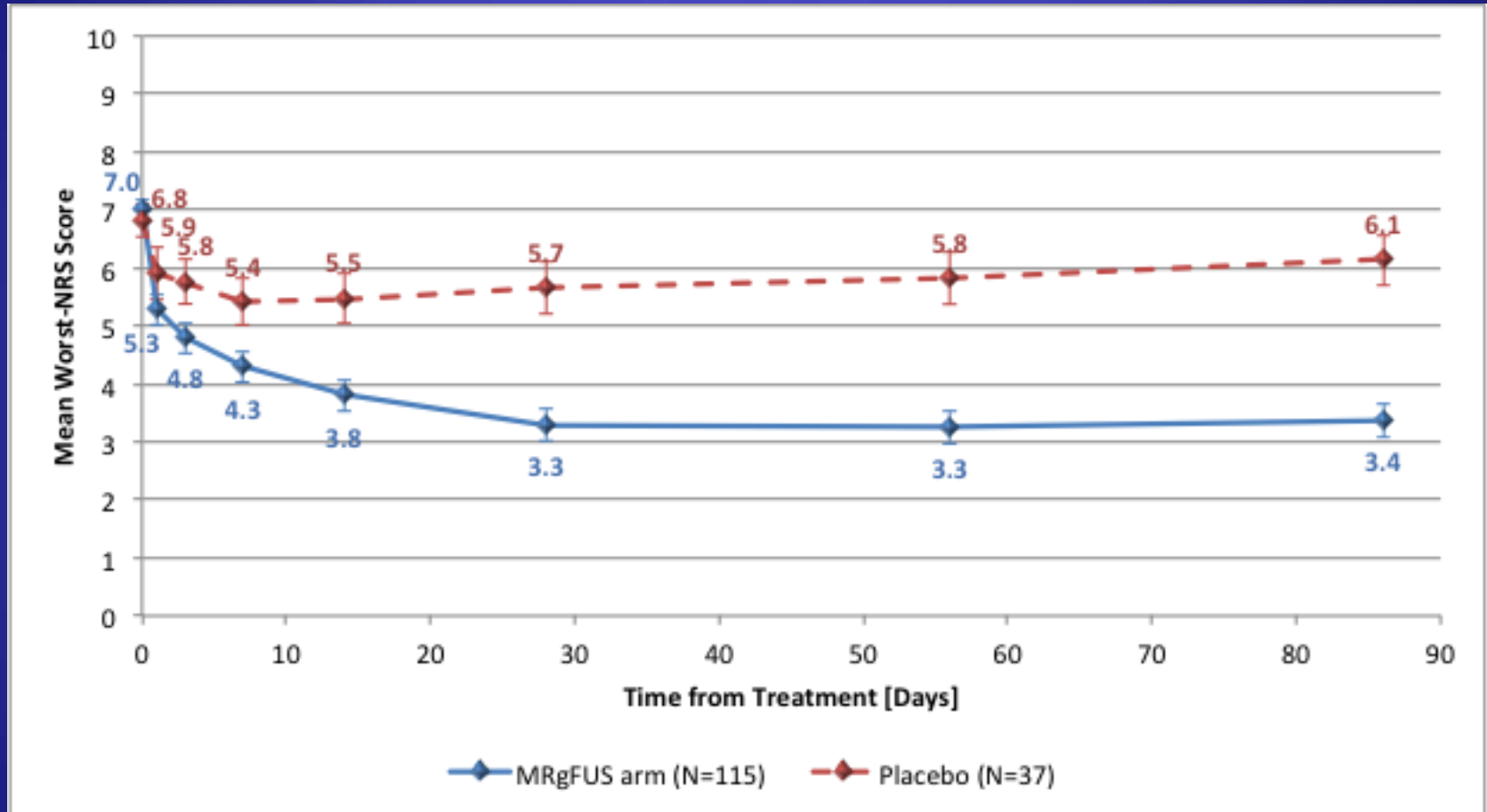
# Percent Responders Over Time



Note: responders= patients who had  $\geq 2$  pt improvement in score with decrease, no, or  $\leq 25\%$  increase in opiates intake

$p = 0.011$

# Worst-NRS Pain Scores Over Time

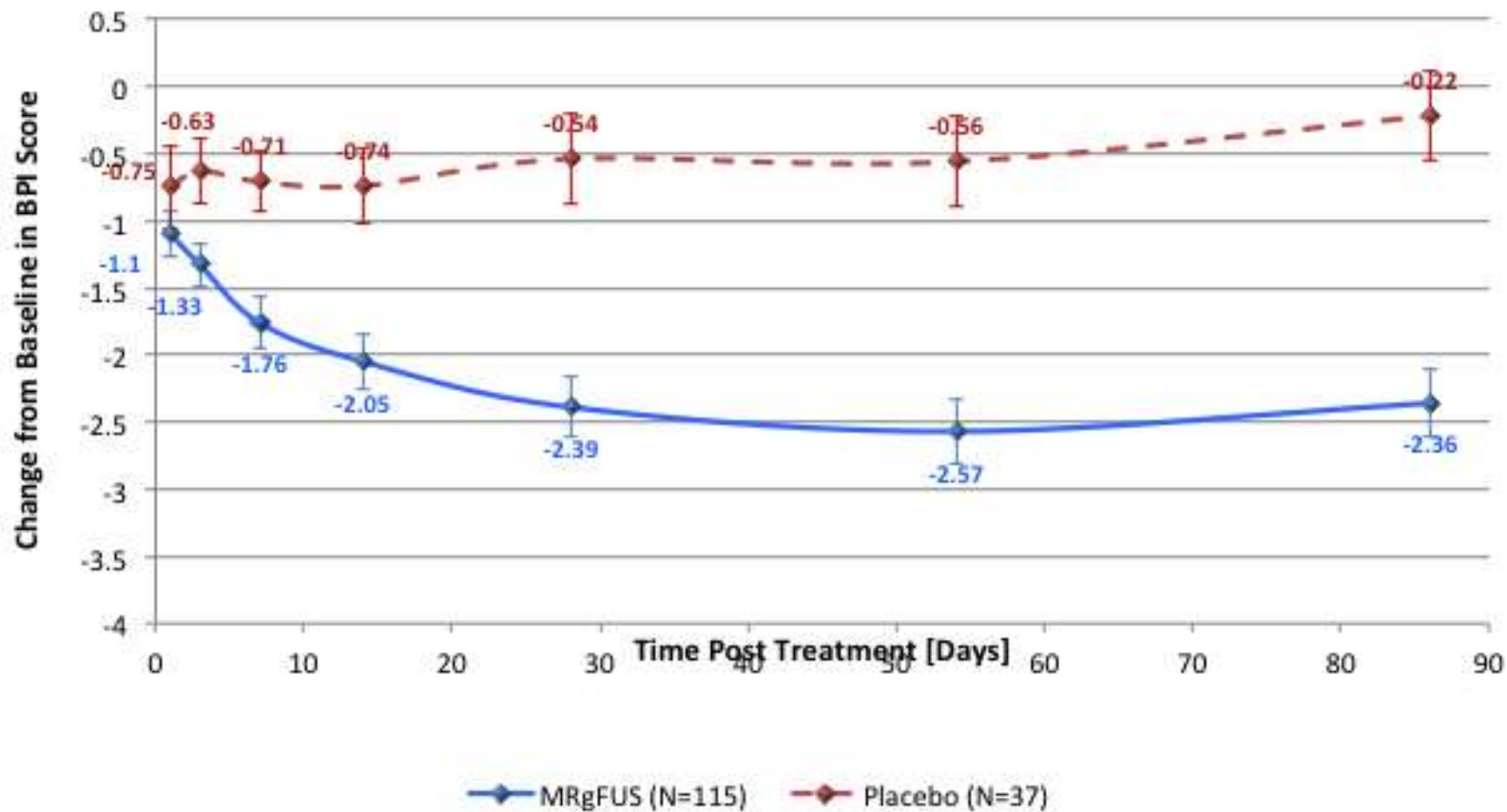


Note: A change of 2 points on NRS is clinically significant

$p < 0.001$



# Quality of Life Improvement was Clinically Significant



p < 0.001

# Frequency of Adverse Events

Adverse Event	MRgFUS (N=115)		Placebo (N=37)	
	N	%	N	%
Any Adverse Events	51	44.3	1	2.7
Sonication Pain	36	31.3	0	0
Position Pain	9	7.8	1	2.7
Post-Procedure Pain	5	4.3	0	0
Fatigue	2	1.7	0	0
Neuropathy - Leg	2	1.7	0	0
Fracture	2	1.7	0	0
Skin Burn	2	1.7	0	0
Blood In Urine	1	0.9	0	0
Fever	1	0.9	0	0
Myositis	1	0.9	0	0
Numbness	1	0.9	0	0
Skin Rash	1	0.9	0	0

# Phase III Trial: Conclusions

For patients with metastatic bone pain MRgFUS:

- results in high rates of rapid and durable pain relief
- provides improvement in quality of life
- should be a primary treatment choice for patients with otherwise limited treatment options

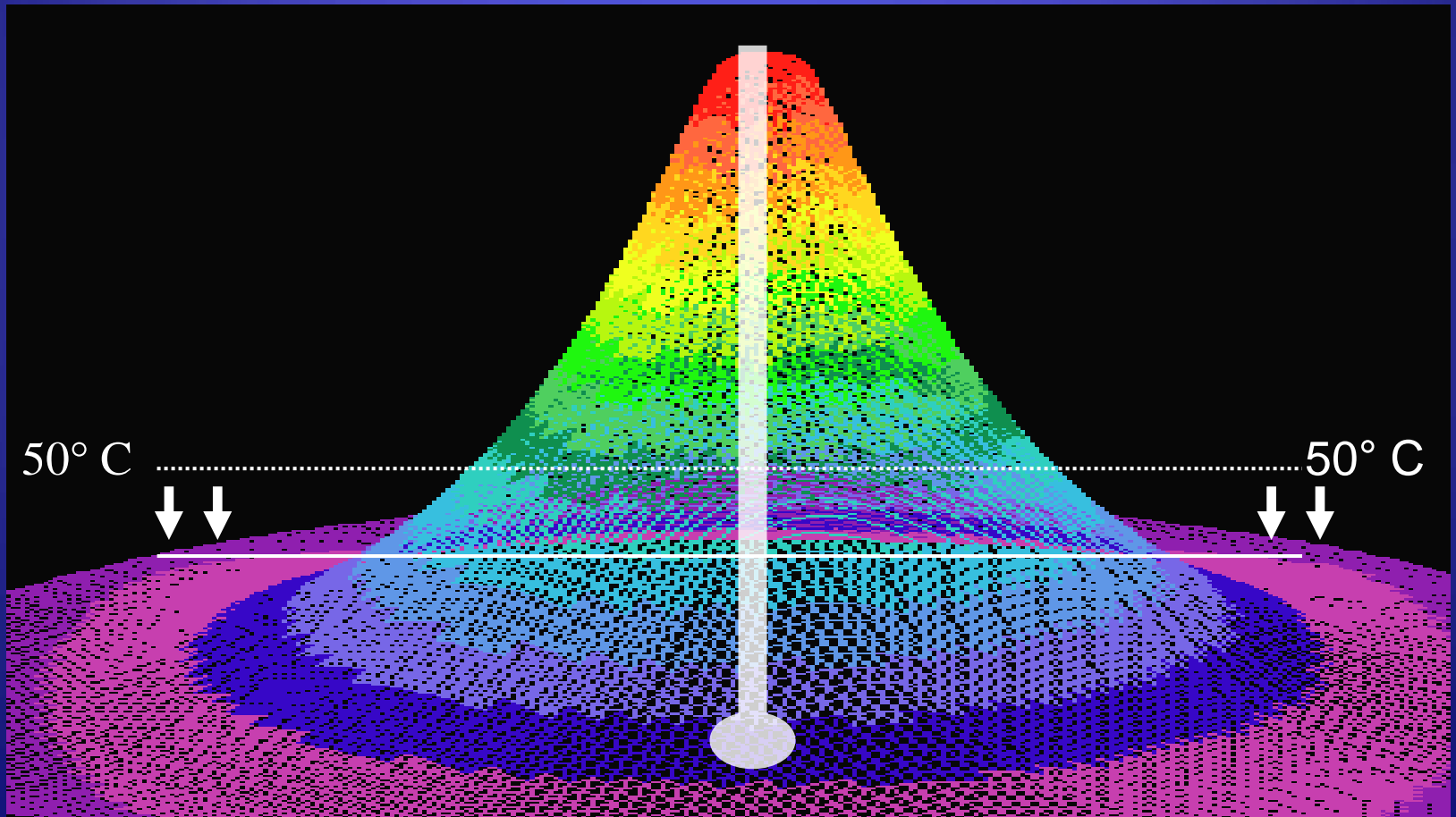
# Future Directions

# Conformal Bone Applicator System

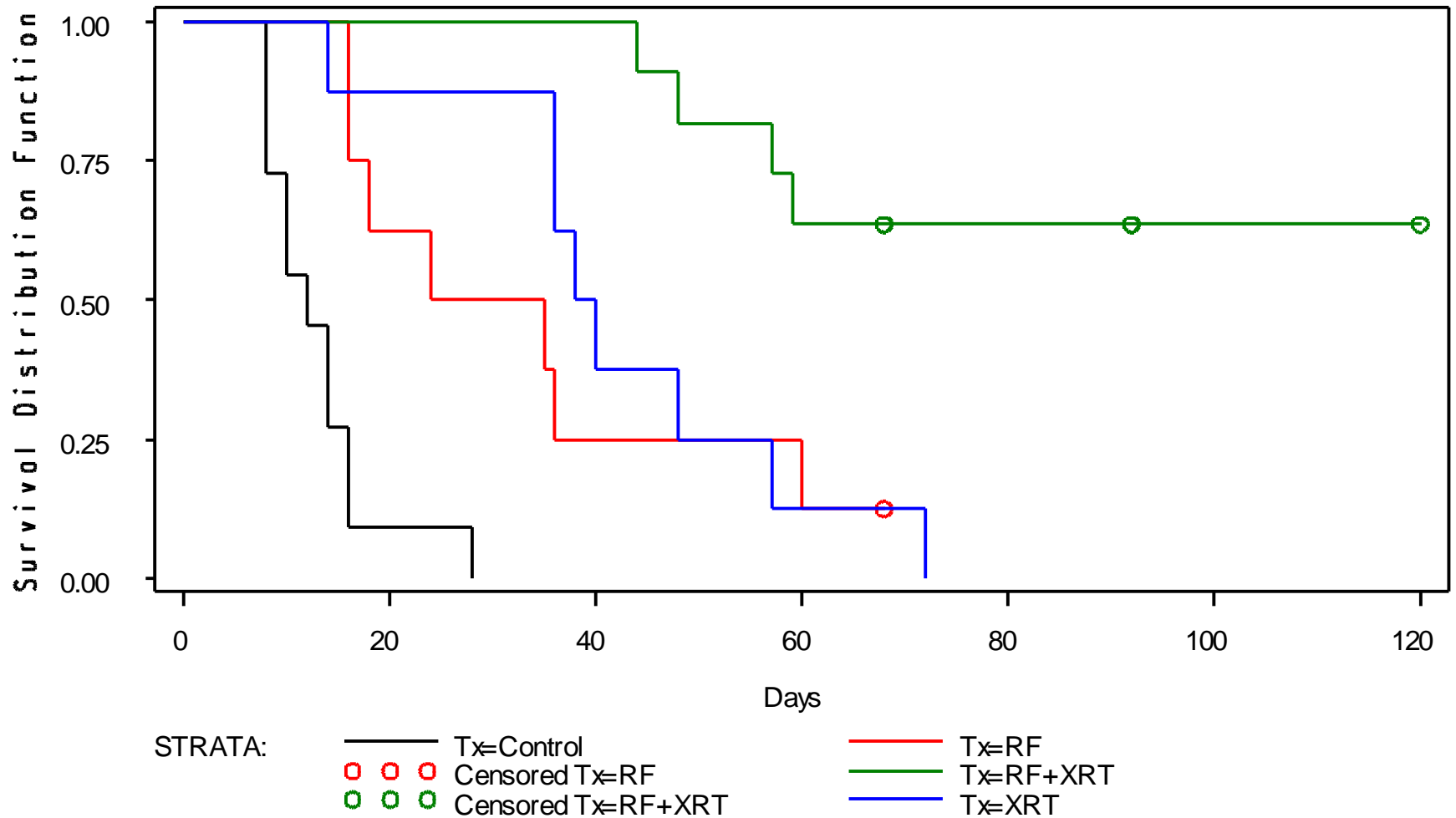
- Access to more anatomical locations
- Improved patient comfort, integrated skin cooling
- High density electronically steerable transducer
- Water-permeable membrane to provide acoustic coupling
- Automatic transducer position tracking



# Thermal Ablation In Multimodality Oncologic Care

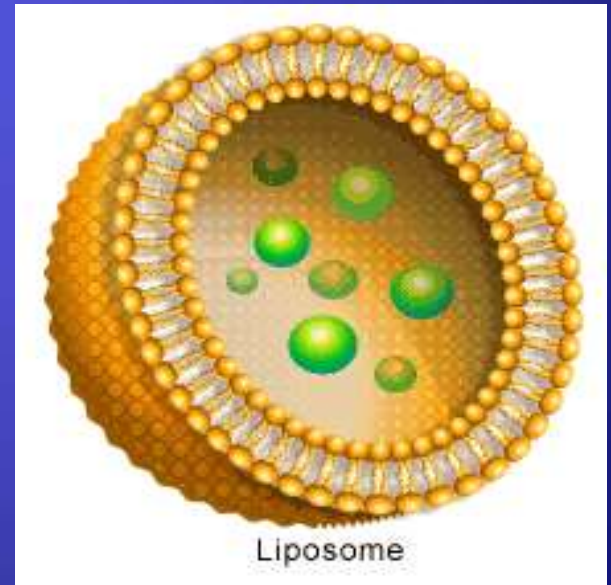


# RF with XRT: Survival



# Targeted Drug Delivery

- Deliver drugs in high concentrations
  - Precisely where needed
  - Minimizing systemic toxicity
- Delivery vehicles
  - Sonically activated: Microbubbles
  - Thermally activated: Liposomes
  - Nanoparticles





# CONCLUSIONS

- **MRgFUS has many properties that make it an attractive treatment modality for bone metastases**
- **MRgFUS is a safe and effective treatment for bone metastases**
- **Combining MRgFUS with other oncologic therapies may optimize clinical results and minimize risks**