IMAGING STRATEGIES FOR MR GUIDED THERMAL THERAPY

John D. Hazle, Ph.D.

Associate Professor and Chair *ad interim*

Department of Imaging Physics

UT M. D. Anderson Cancer Center

Houston, TX

Overview

- Minimally invasive therapies have the potential to replace conventional surgery for the treatment of some solid tumors.
- Many approaches to thermal therapy have been considered and tried, but they have largely met with limited clinical success due to tumor recurrence and normal tissue effects.
- Imaging can guide the delivery of the therapeutic energy to the target volume and assess the damage to tumor, and adjacent normal tissues.
- Real-time, interactive guidance is the goal.

Key concepts

- Image guided therapies offer cost effective, patient friendly approaches to some surgical procedures
- MR imaging is uniquely capable of excellent soft tissue contrast (planning), temperature sensitive imaging (monitoring), and perfusion sensitive imaging (post-therapy evaluation).
- Performing imaging guided therapies in conventional cylindrical MR scanners results in the largest possible base of available equipment.

Lecture outline

- Review of MR temperature imaging technique development
  - Imaging strategies
  - Fast(er) imaging techniques
- Review of thermal therapy strategies
  - Focused ultrasound for breast cancer
  - Interstitial ultrasound for brain cancer
  - Transurethral ultrasound for prostate cancer
- Summary and future directions

Therapy delivery drives imaging strategies

- Fast delivery – focused ultrasound
  - Small focal spot - focus <10 mm diameter and <20 mm length
  - Rapidly evolving - pulse duration <20 seconds
  - Less prone to motion during application
- Slow delivery – interstitial ultrasound and lasers
  - Larger treatment area - usually >10 mm diameter and >20 mm long
  - Slower to evolve - treatments last many minutes (~10-15 minutes)
  - Can be very susceptible to organ motion during therapy
    - Brain not such a problem
    - Prostate motion during therapy must be considered

Temperature sensitive MR imaging

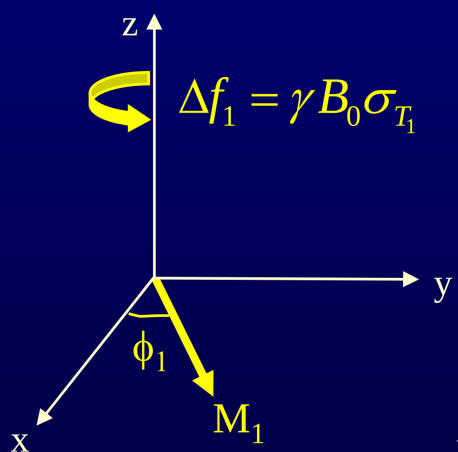
- T1-weighted imaging
  - Good temperature sensitivity
  - Tissue dependent and non-linear
- Diffusion weighted imaging
  - Highest temperature sensitivity
  - Sensitive to motion
- Proton resonance frequency
  - Good temperature sensitivity
  - Some motion sensitivity
  - Most robust

Temperature measurement using PRF

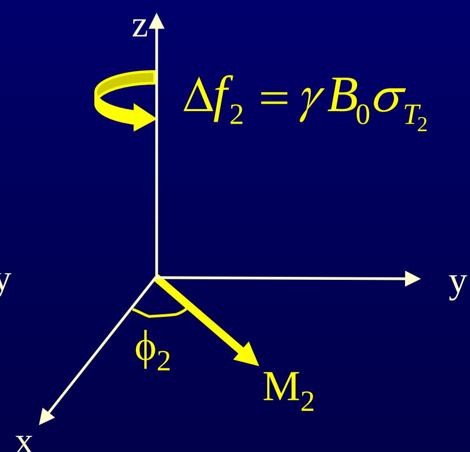
- Chemical shift imaging (CSI)
  - Methods are slow, but accurate
  - Insensitive to motion
  - Less prone to artifacts.
- Phase sensitive imaging
  - Methods are fast and accurate
  - More prone to artifacts
    - susceptibility, field inhomogeneity, motion

MRTI using the PRF

- Proton resonance frequency shift
  - Temperature goes up: H-bonds bend, stretch and break
  - Result: Protons better shielded by oxygen on average
  - Result: Linear increase in chemical shift
  - Indirectly measurable using MR signal phase



$$\Delta f_1 = \gamma B_0 \sigma_{T_1}$$



$$\Delta f_2 = \gamma B_0 \sigma_{T_2}$$

$$\Delta\phi_{2\to1} = 2\pi \cdot \gamma B_0 \cdot \Delta\sigma_{T_2 \to T_1} \cdot TE$$
$$= 2\pi \cdot \gamma B_0 \cdot \alpha \, \Delta T_{2\to1} \cdot TE$$

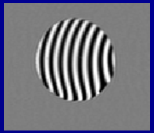
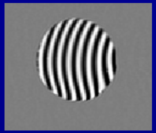
α = temperature sensitivity coefficient

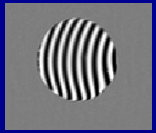
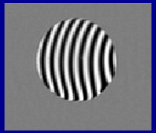
Phase-difference fundamentals

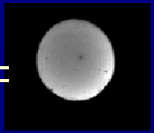
Temperature changes can be extrapolated from phase changes in the MR signal:

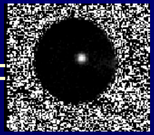
$$\Delta\phi \cong \Delta T \cdot \left(\gamma B_0 \cdot TE \cdot \alpha\right)$$

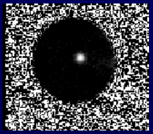
Processing CPD images for MRTI

$S_0 =$  $+ i*$  $= |S_0| \cdot e^{i\phi_0}$

$S_1 =$  $+ i*$  $= |S_1| \cdot e^{i\phi_1}$

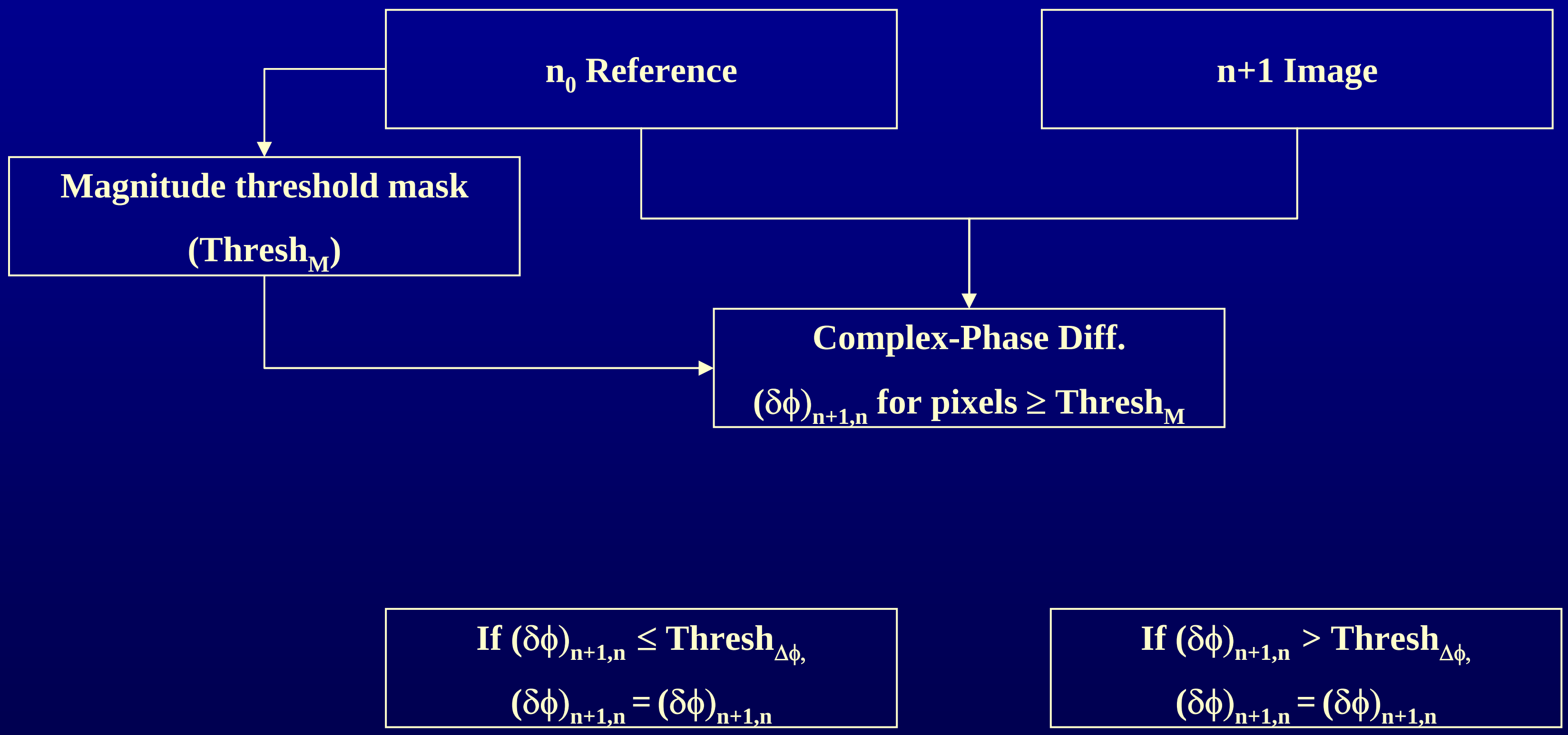
$S_1{}^* S_0 =$  $+ i*$  $= |S_0||S_1| \cdot e^{i(\phi_0 - \phi_1)}$

$\arg(S_1{}^* S_0) =$  $= -\Delta\phi$ *(CPD Image)*

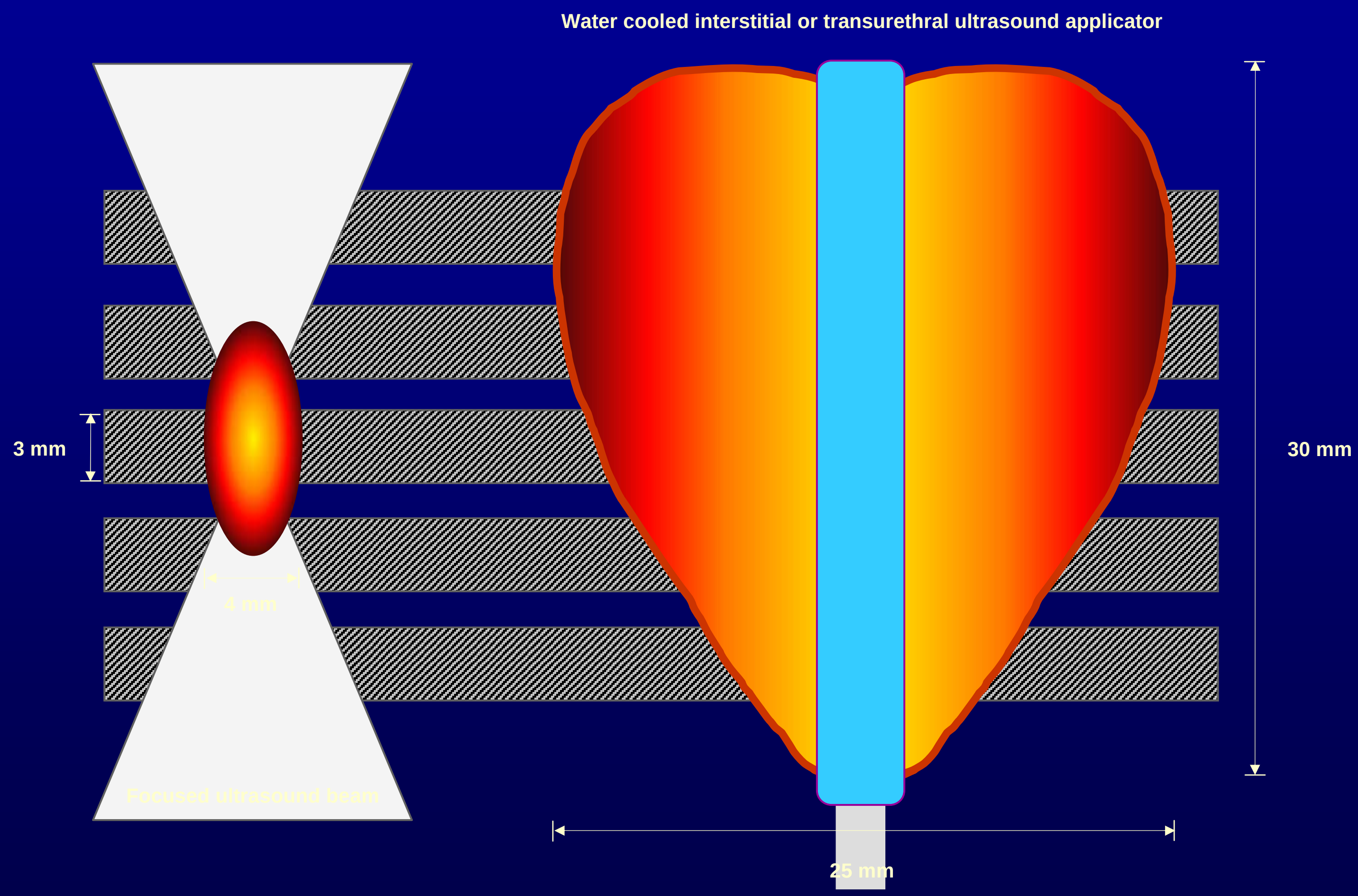
$\frac{-\Delta\phi}{2\pi \cdot \gamma B_0 \cdot TE \cdot |\alpha|} =$  $= \Delta T$ *(Temperature Image)*

(Thermal Dose)

Phase-difference recon flow chart



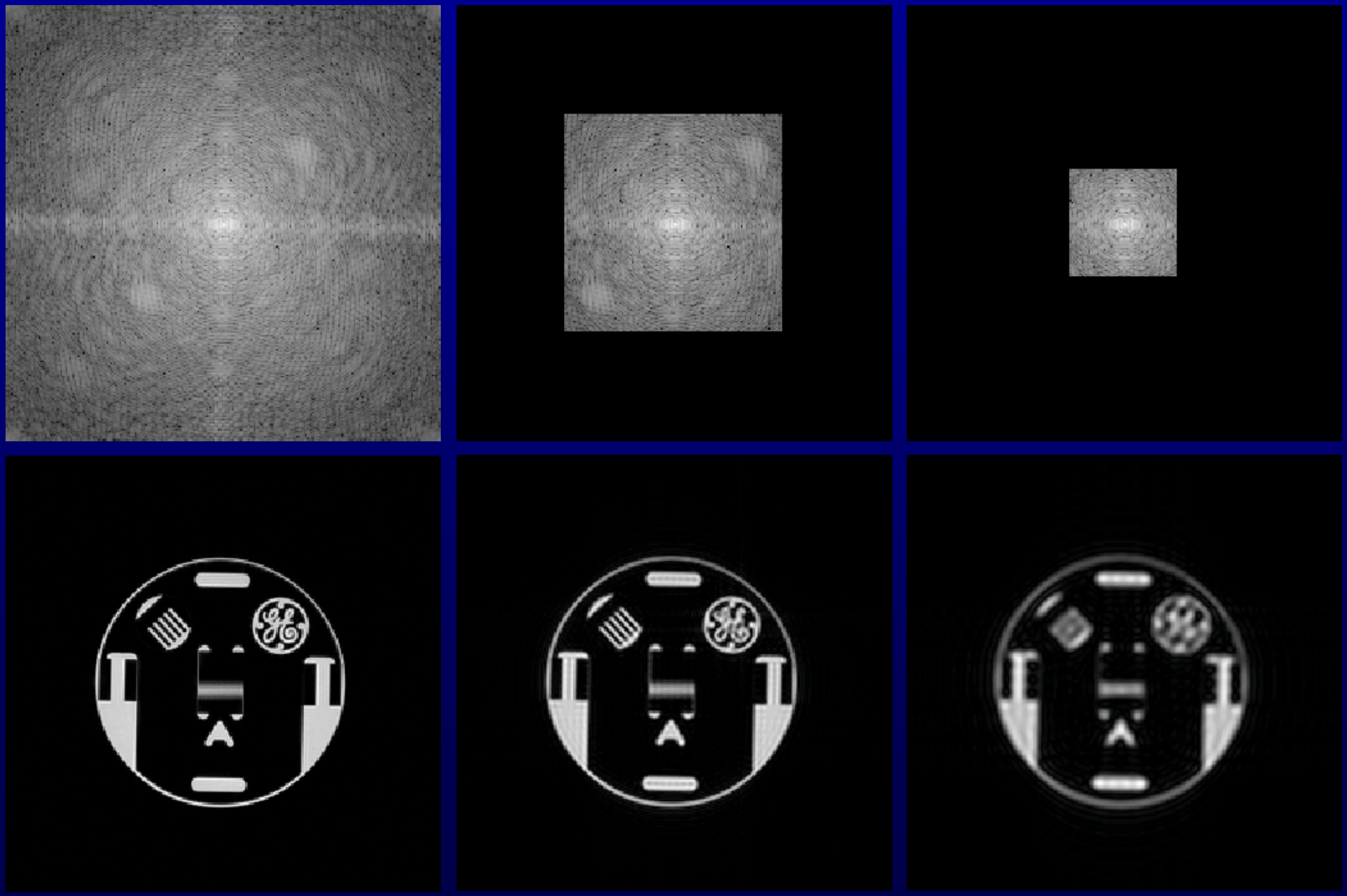
Imaging issues in MRgTT



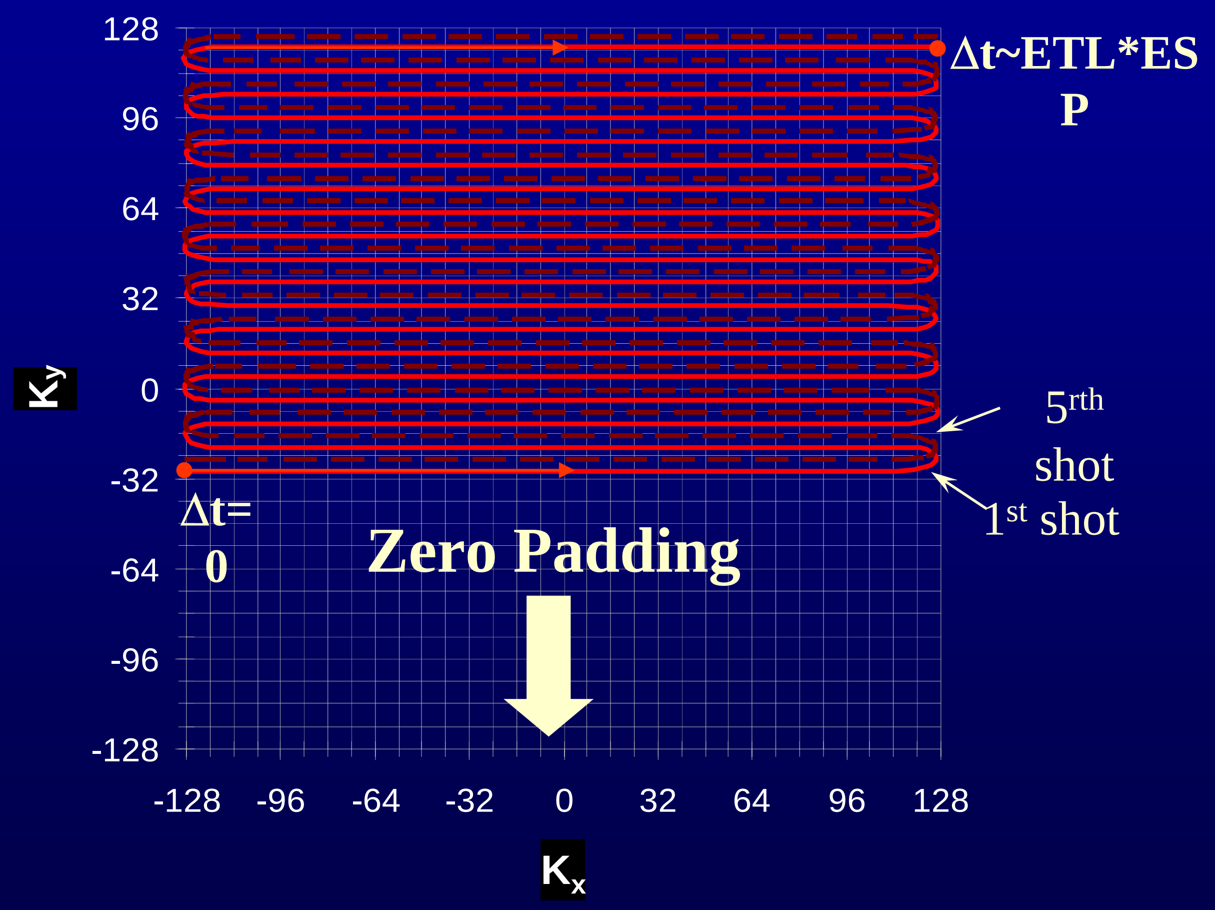
Goals for new sequences

- Increase slice coverage
- Improved temperature sensitivity
- Lipid suppression
  - Without decreasing current temporal resolution (~ 3 sec/update)
  - Without decreasing current in-plane spatial resolution (~ 0.8 mm)
  - Maintain adequate image SNR for MRTI.

Keyhole limitations



iGE-EPI k-space trajectory



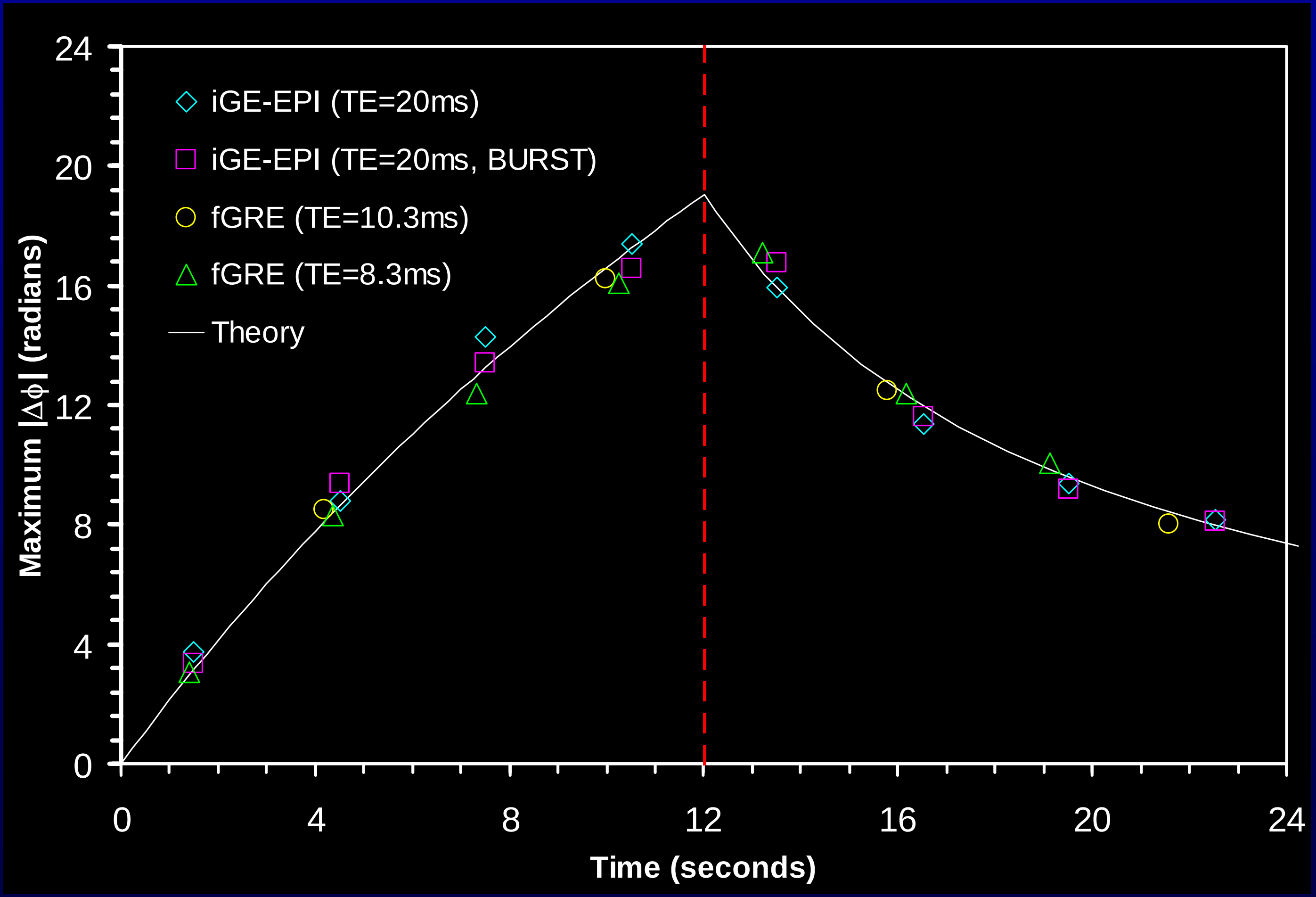
iGE-EPI for MRTI

- Advantages:
  - Increased slice efficiency (long TR).
  - Use of larger TE.
  - Use of water selective spatial spectral pulse.
- Limitations
  - High Bandwidth => lower SNR.
  - More sensitive to off-resonance and chemical shift.
  - Possible compromise in spatial resolution.
  - Use of special hardware (?).

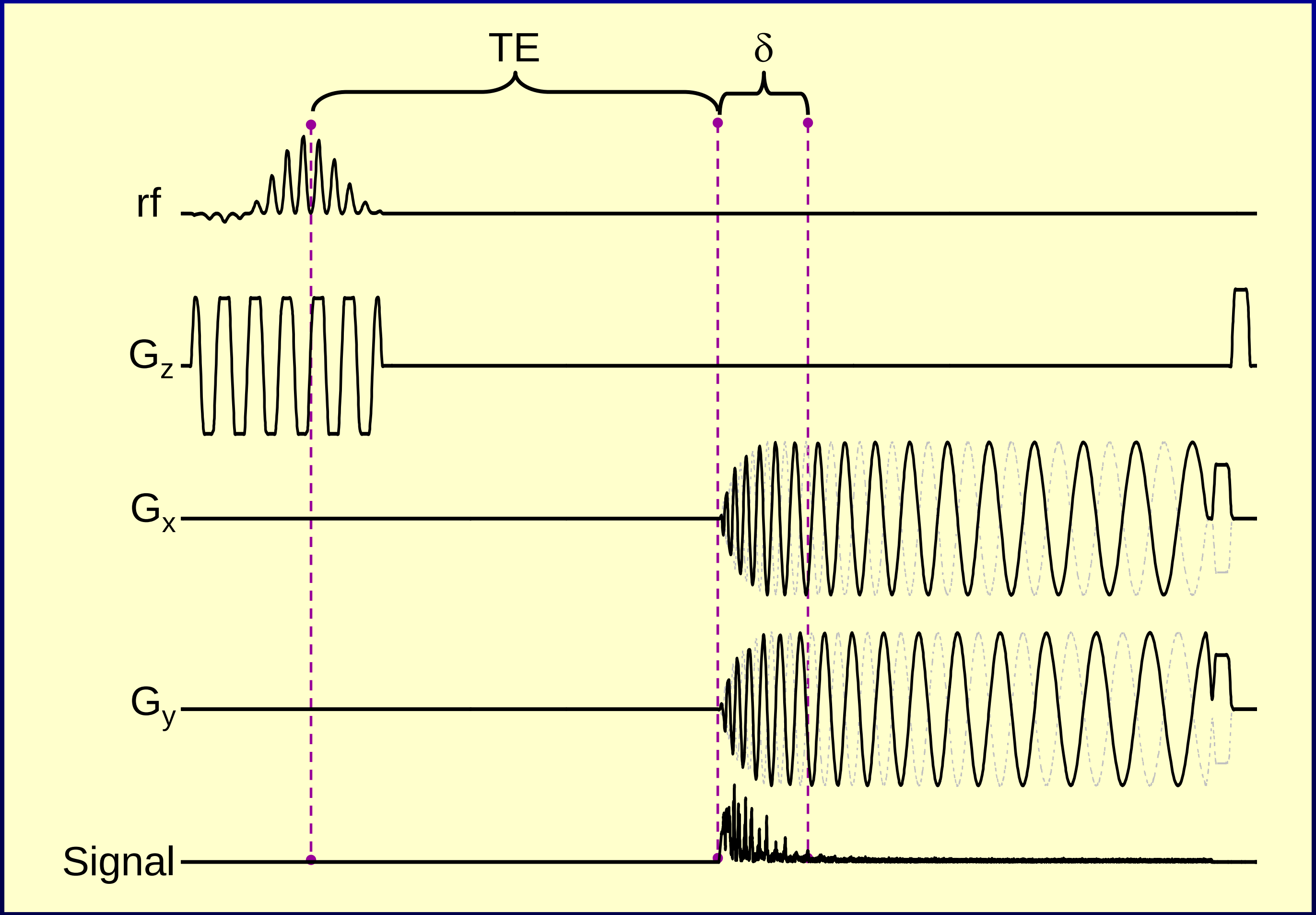
iGE-EPI for MRTI

- Optimizing TE (15 - 20 ms)
  - Ramp sampling
  - Fractional k_y sampling
  - 4-8 interleaves
- 4-8 interleaves to minimize ESP_{eff}.
- Multi-slice acquisition
  - Interleaved slice acquisition
  - “BURST” imaging

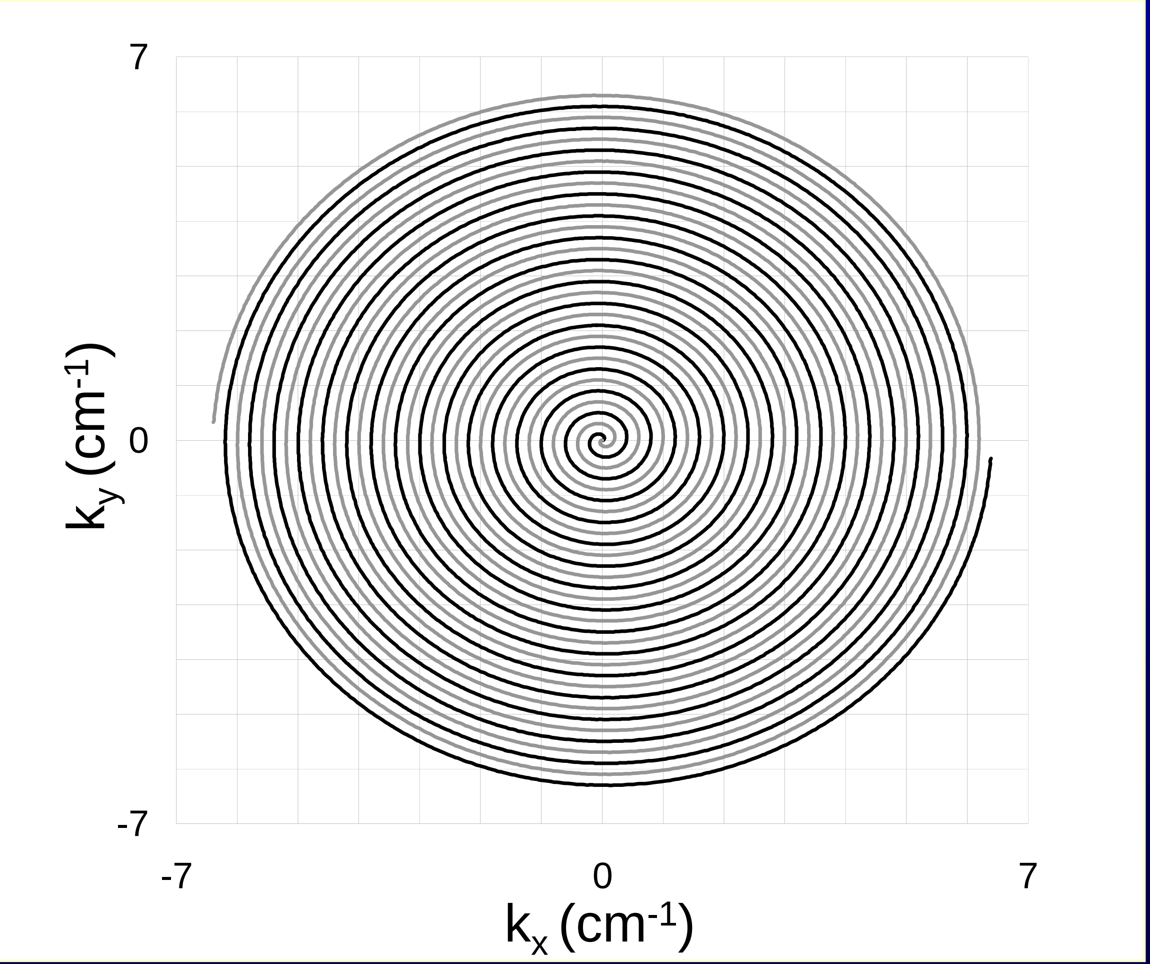
Maximum |Df| at focus



Spiral sequence



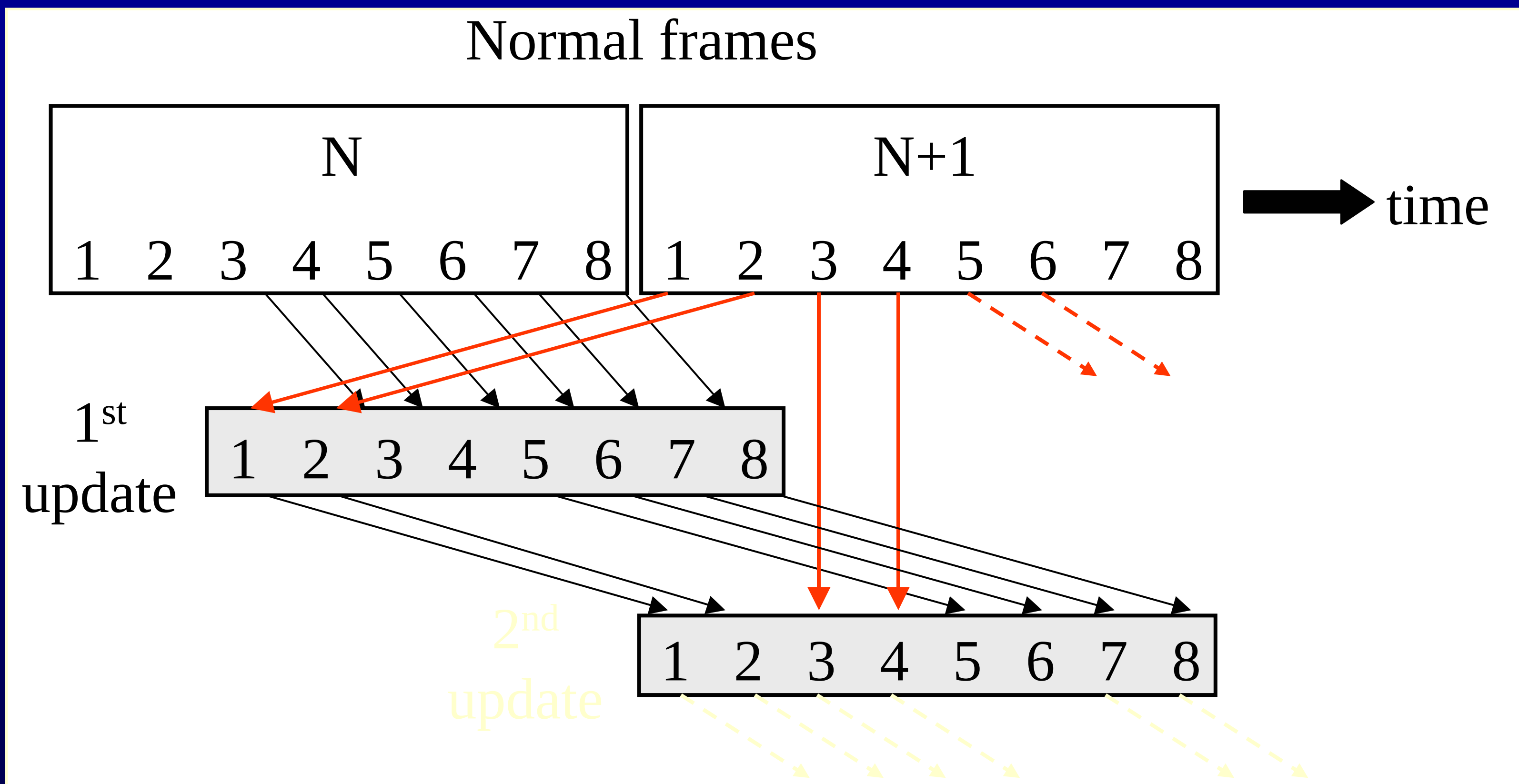
Spiral k-space trajectory



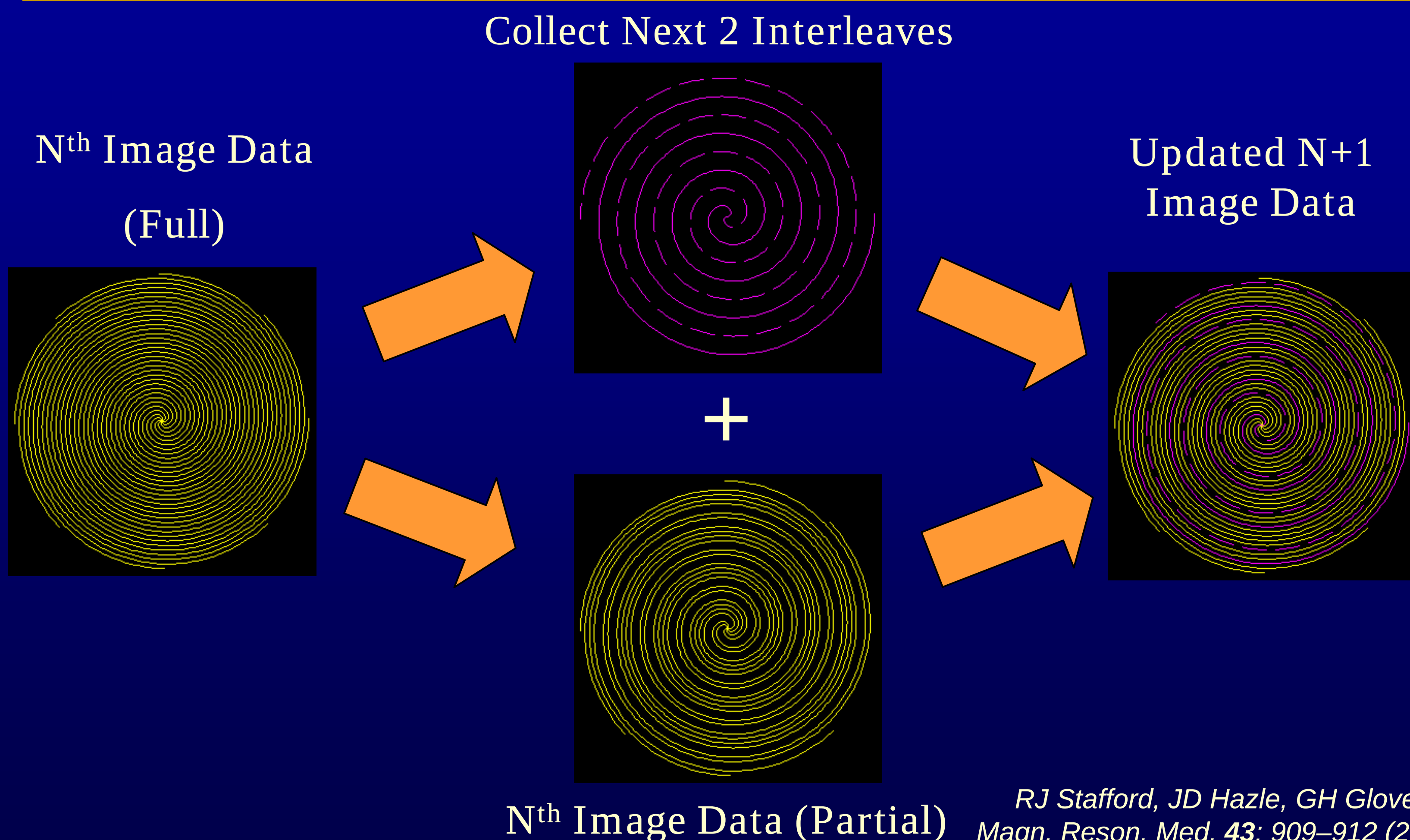
Why "dynamic updating"?

- Increase temporal resolution.
- Existing sequences adapt easily.
- "Normal" and "dynamic" acquisitions are *not* mutually exclusive.

Dynamic updating of iGE-spiral

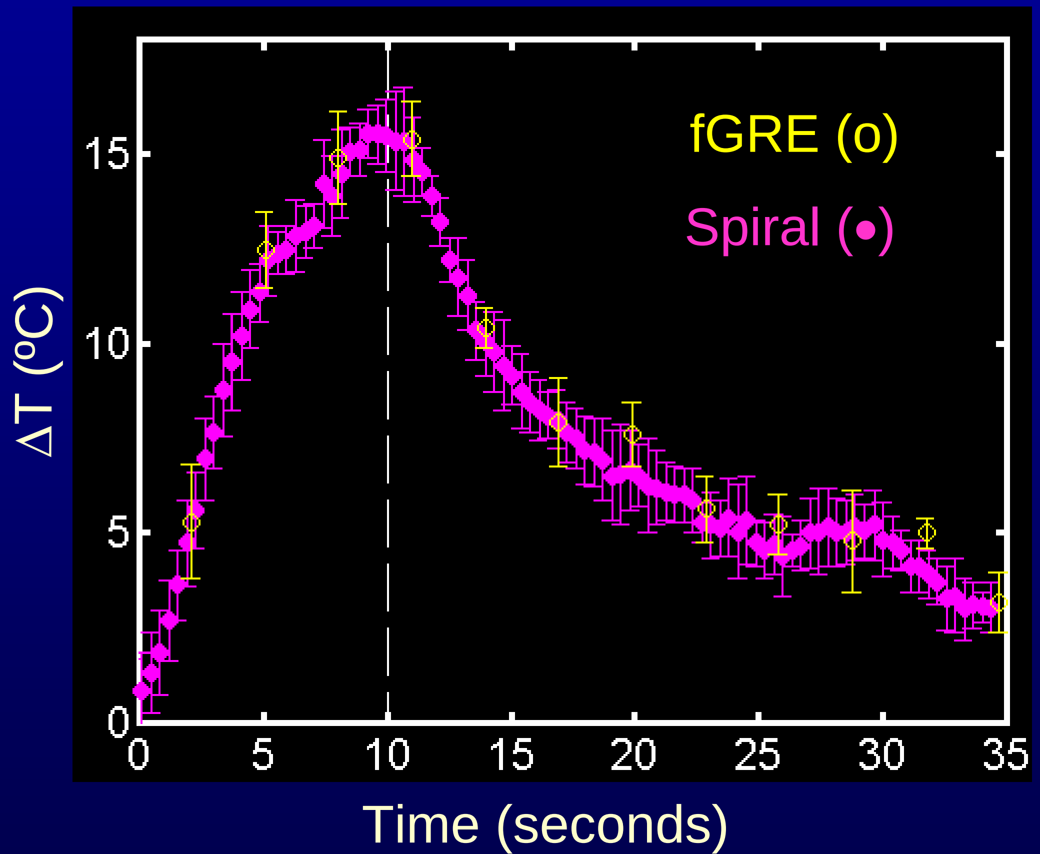


Dynamic updating of interleaves



RJ Stafford, JD Hazle, GH Glover
Magn. Reson. Med. ***43****: 909–912 (2000)*

Dynamic updating of spiral data

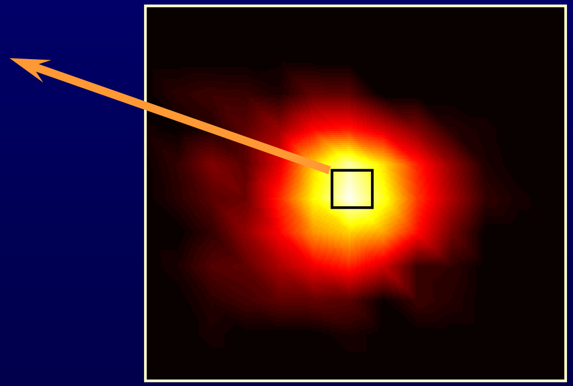


Spiral (0.375 s/image) (1.5 s/image)

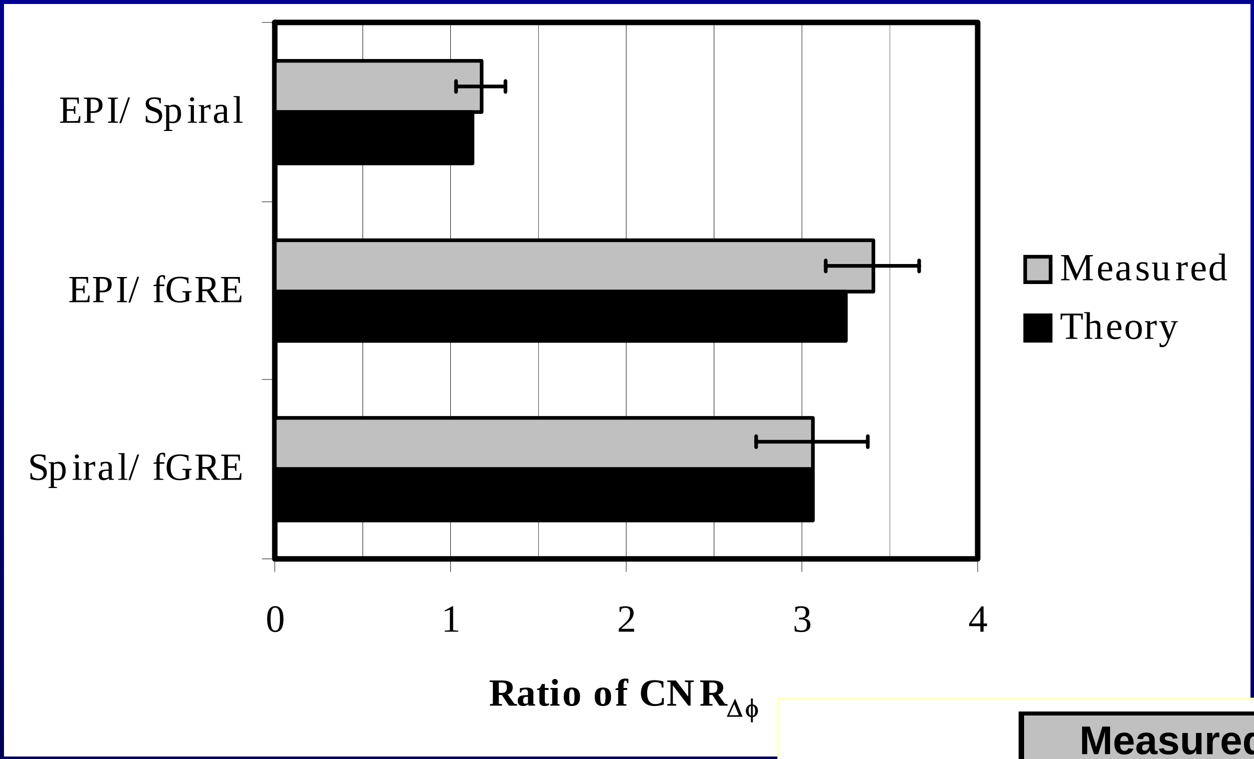
$\sigma_{\Delta T}$ = 0.93 ± 0.23 ºC

fGRE (3 s/image)

$\sigma_{\Delta T}$ = 1.06 ± 0.32 ºC



fGRE versus spiral and EPI (0.5 NEX)



	Measured		Theory	
Sequence	***Ratio***	σ	***Ratio***	***% Error***
EPI/Spiral	1.17	0.14	1.12	***4.67***
EPI/fGRE	3.40	0.26	3.25	***4.68***
Spiral/fGRE	3.06	0.32	3.06	***0.01***

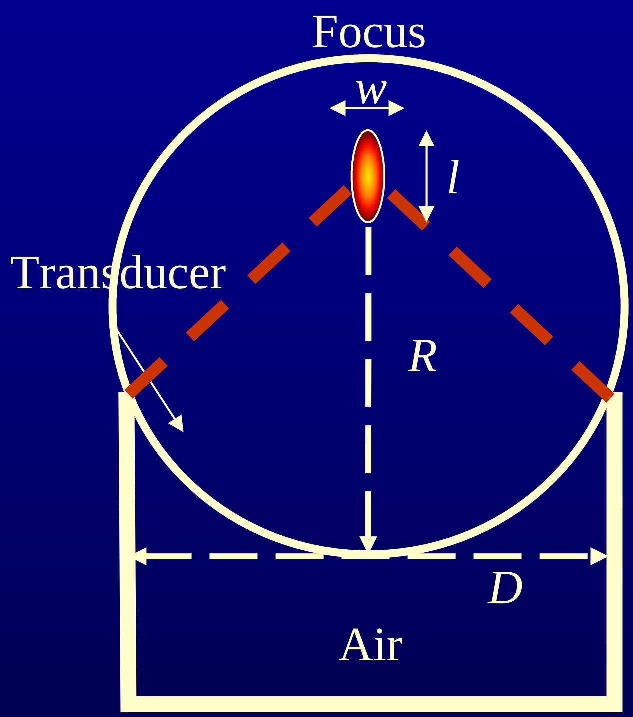
fGRE versus spiral and EPI

RATIO $(CNR_{\Delta\phi})_A/(CNR_{\Delta\phi})_B$	THEORY	MEASURED Mean (SD)	ERROR (%)
EPI/Spiral	1.12	1.17 (0.14)	4.67
EPI/fGRE			
0.50 NEX	3.25	3.40 (0.26)	4.68
0.75 NEX	2.25	2.21 (0.34)	1.70
Spiral/fGRE			
0.50 NEX	3.06	3.06 (0.32)	0.01
0.75 NEX	2.12	1.99 (0.38)	6.08

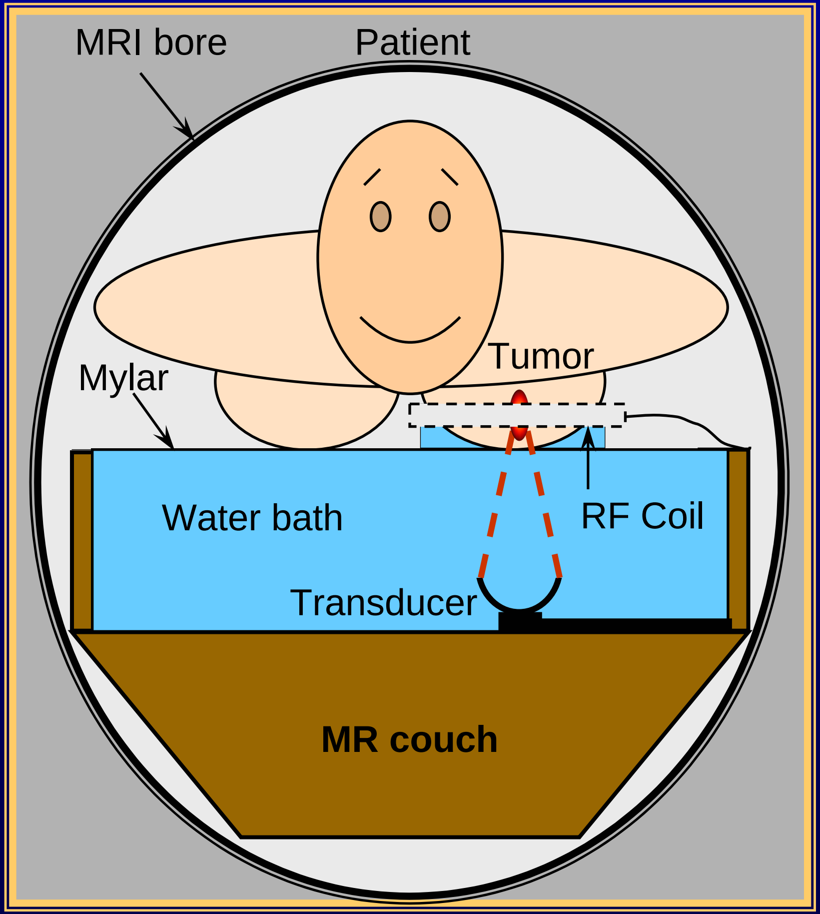
Ultra-fast imaging summary

- Advantages of fast acquisition (EPI, Spiral)
  - Increased $CNR_{\Delta T}$,
  - increased slice efficiency,
  - suppressed lipid signal, and
  - potential for greatly improved temporal resolution.
- Limitations
  - Longer readout times.
  - Ambiguity in definition of TE.
  - Increased image reconstruction complexity.

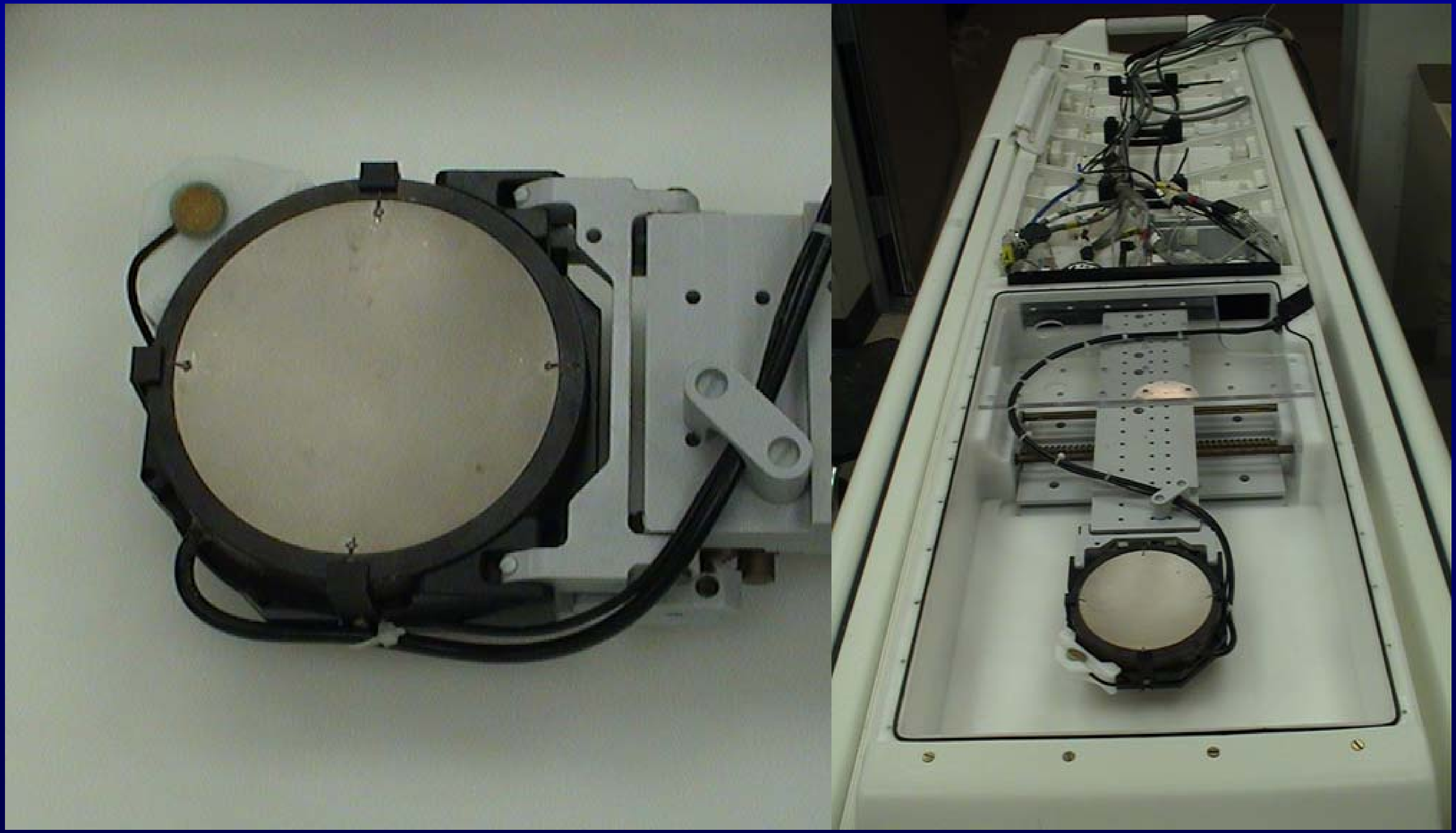
FUS thermal therapy for breast ca



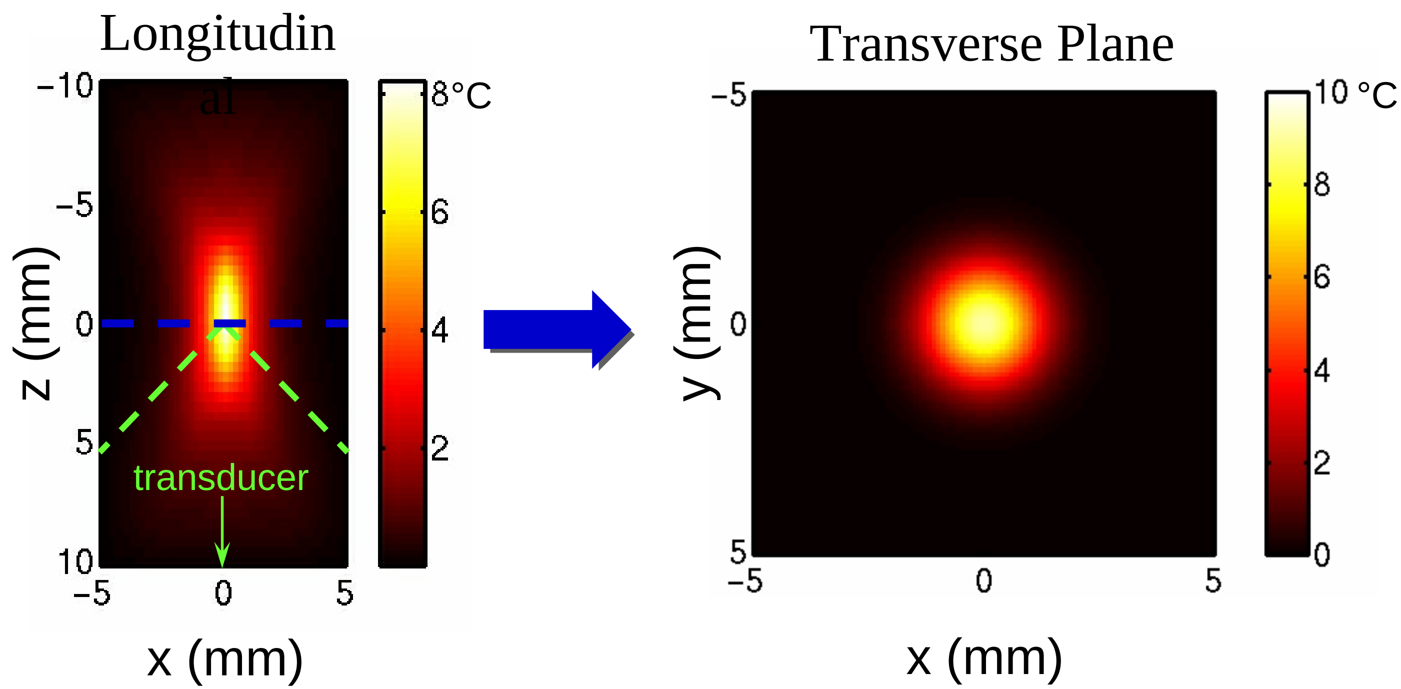
$$w = 2.44 \frac{c}{f} \frac{R}{D} \text{ and } l = 9.9 \frac{c}{f} \left(\frac{R}{D} \right)^2$$



Focused ultrasound system



Numerical solution of bioheat equation



Transverse temperature distribution is approximately Gaussian:

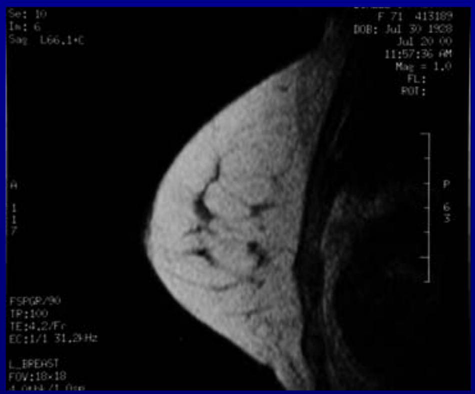
$$T\left(r, z=0, t\right) = T_0 \cdot f\left(t\right) \cdot \exp\left[-\left(r-r_0\right)^2 / 2 \cdot \left(\sigma^2 + 2\kappa t\right)\right]$$

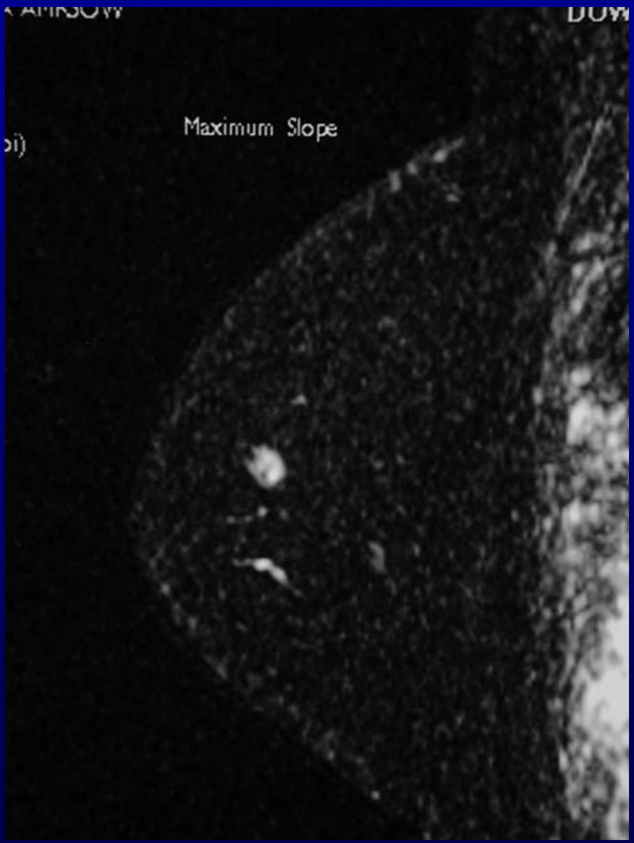
MRgFUS VX-2 tumor ablation in rabbit

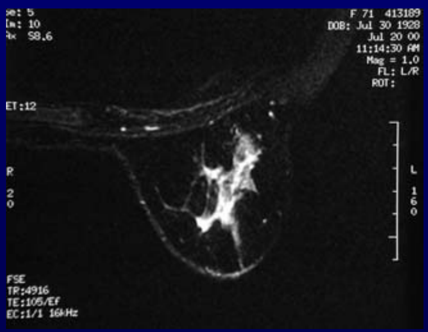
- Treatment Planning
- Treatment Localization
- Treatment Monitoring
- Treatment Verification

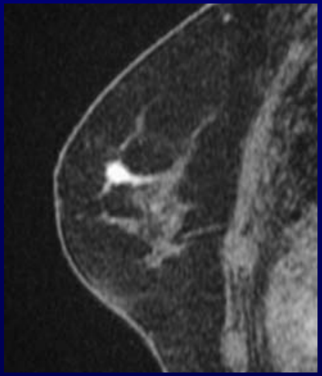
— Treatment prescription
○ Prescribed sonication point
● Thermal dose (point)
— Thermal dose (total)

Patient #1 - Pre-therapy MR



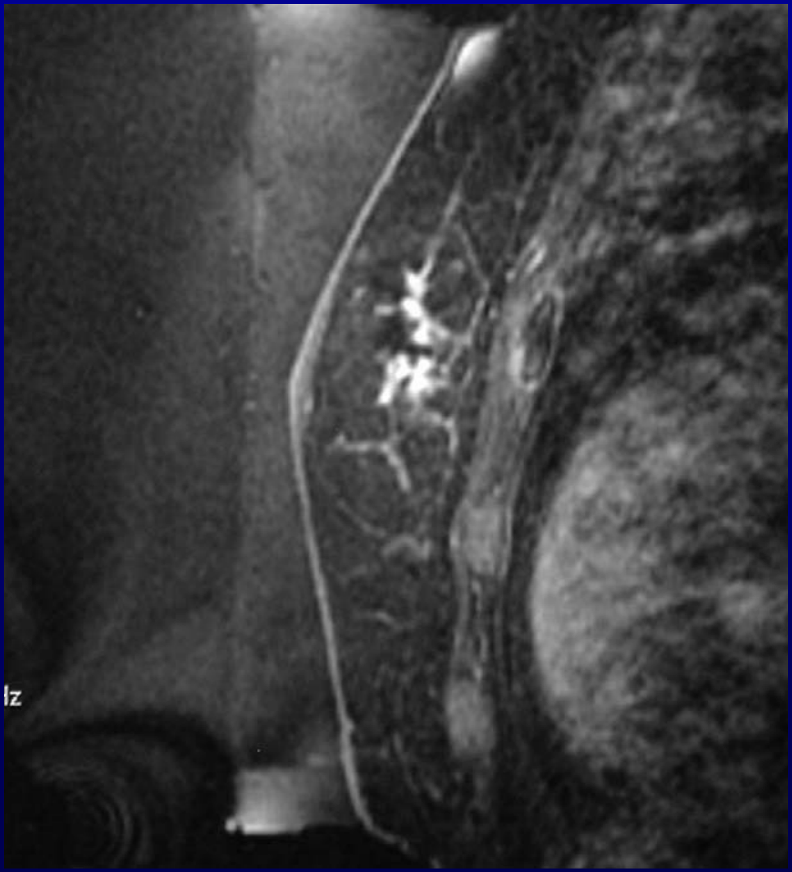






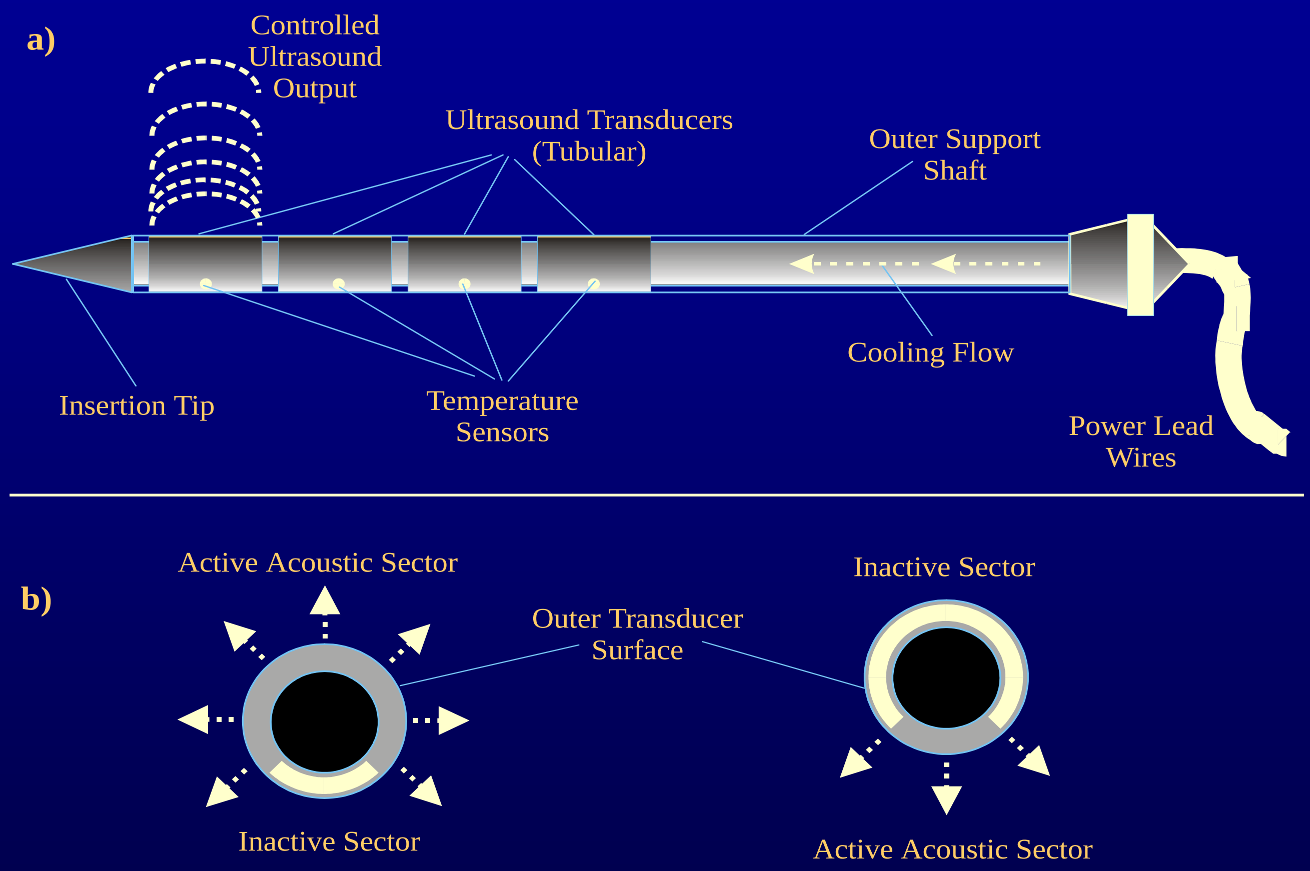
Patient #1 - Immediate post-Rx pre/post Gd

T1-weighted



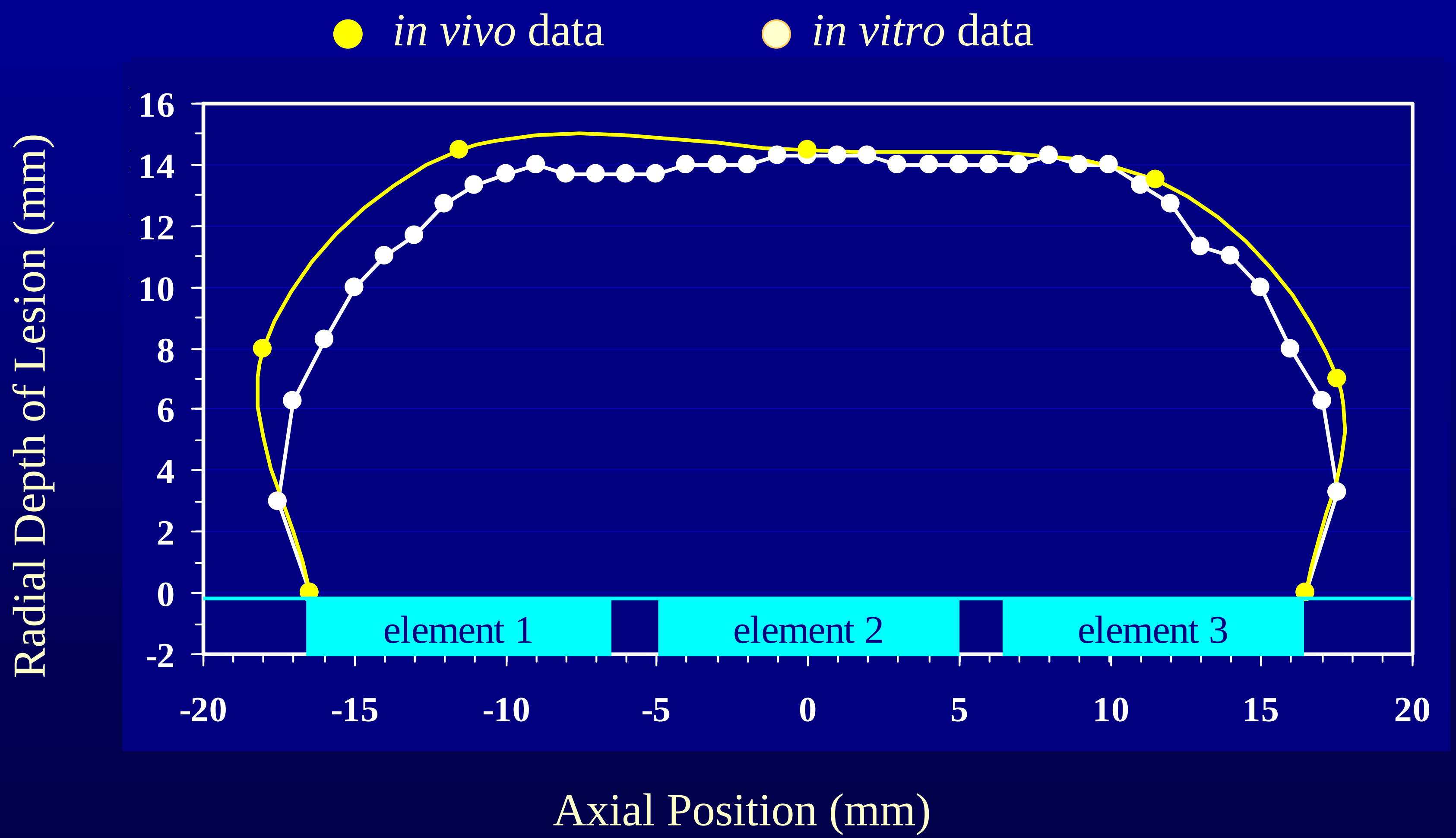
T1-weighted + Gd-DTPA

ACOUSTTiC™ applicator

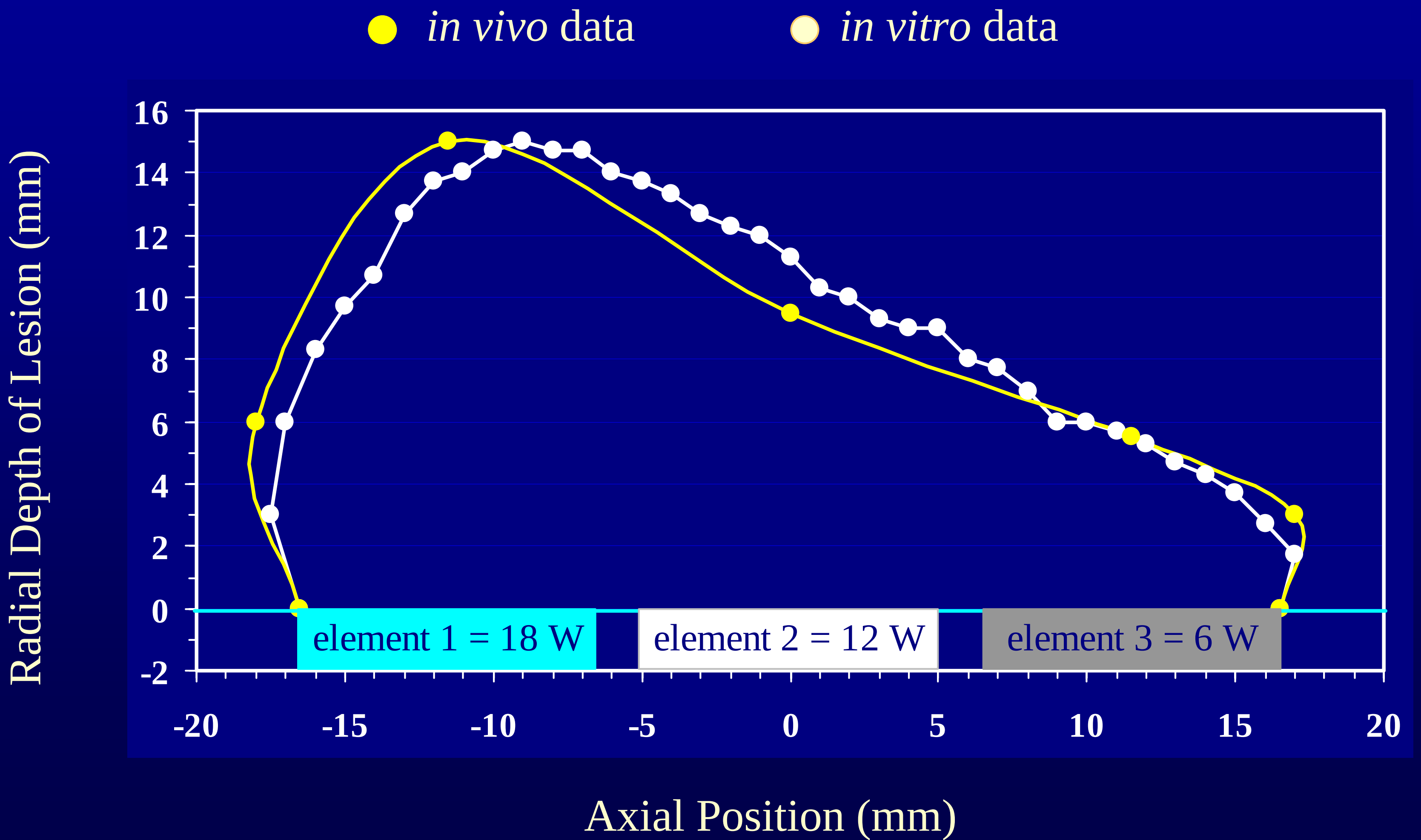


From Chris Diederich, Ph.D. at UCSF.

Independent element heating

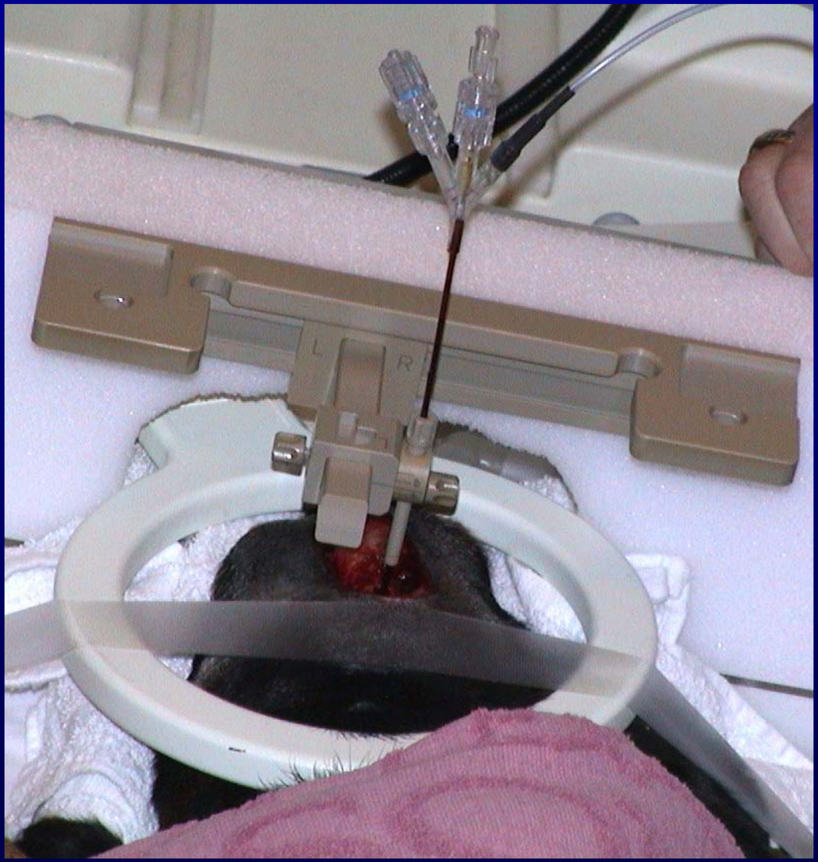


Multi-element heating



Stereotactic placement of the applicator

- A 5 mm diameter craniotomy was created directly over the site of the craniotomy used for the original inoculation of the tumor.
- An MR-compatible system is used to stereotactically position and guide the applicator placement.
- MR images are used to verify the positioning of the applicator prior to therapy.



Heating in central planes: Canine Brain

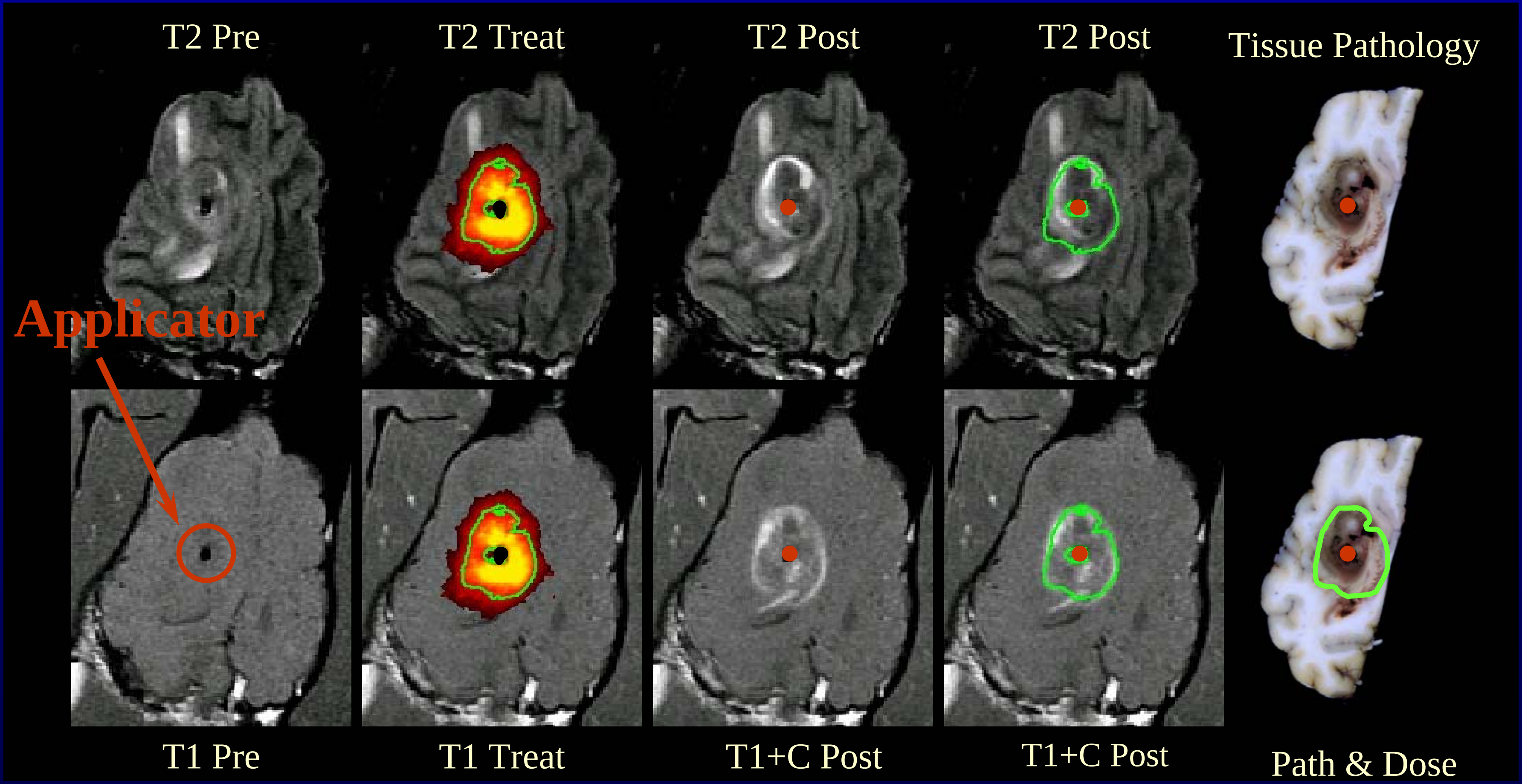
-4 mm　　　　0 mm　　　　4 mm

45°C　　　　80°C

Isodose: t_{43} = 50 min.

Treatment Time: 15 min.

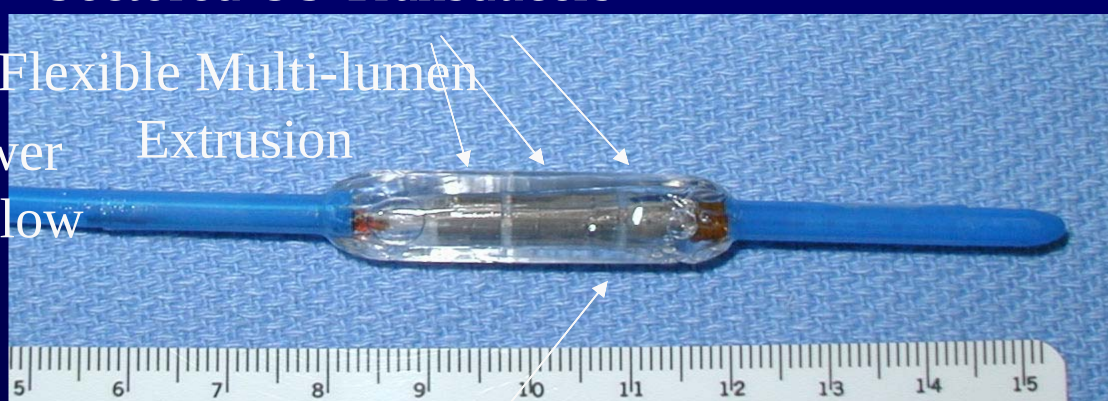
Isodose in Brain



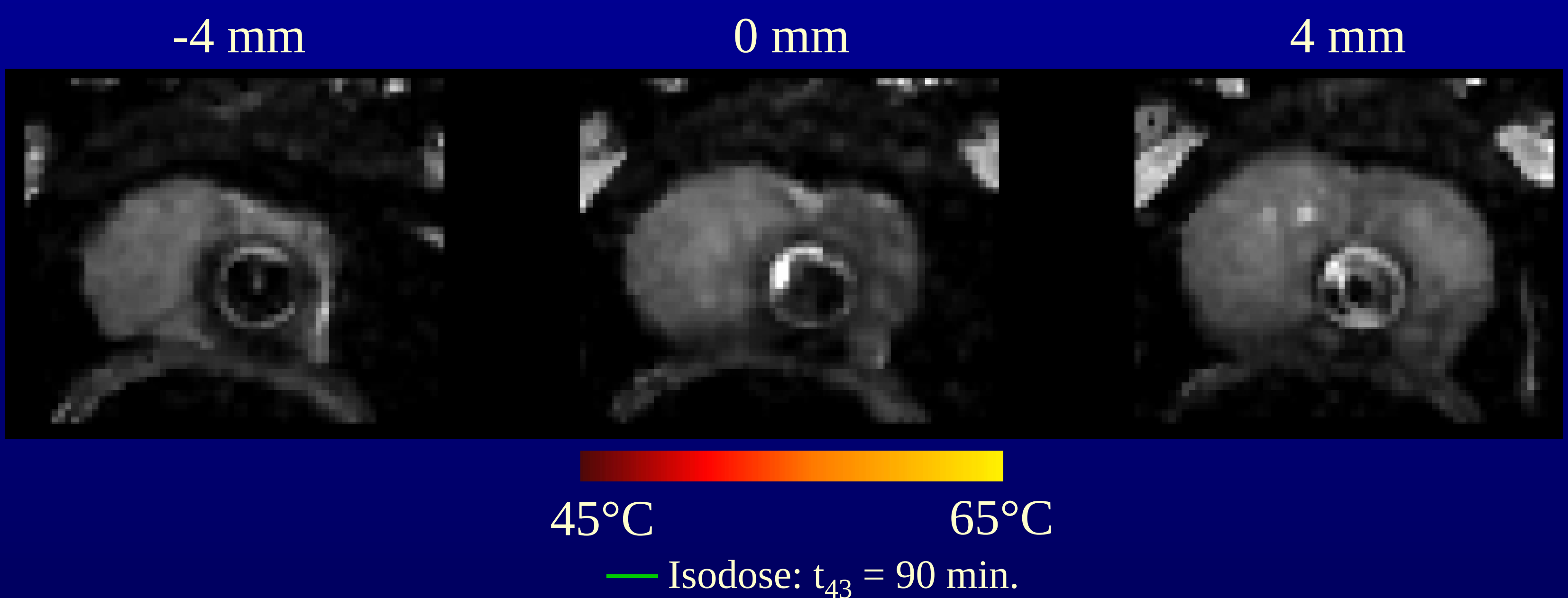
Isodose: t_{43} = 50 min.

Transurethral prostate application

>180,000 new prostate cancer cases per year in U.S.



Heating in central planes: canine prostate



3 element, water cooled, transurethral ultrasound applicator

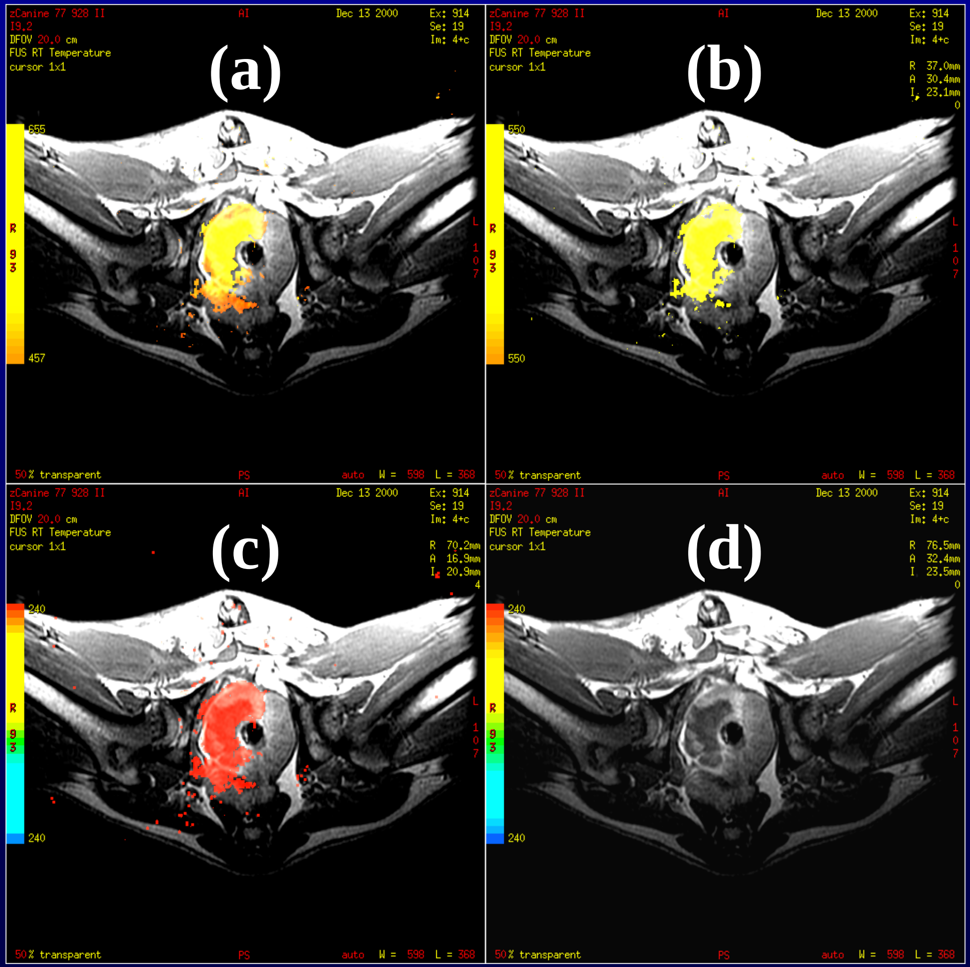
180° directivity, treatment of right lobe

2.5 cm effective treatment length

Treatment time: 15 minutes

Power varied: 4-12 W over treatment time

Real-time MRTI guidance: canine prostate



(a) Maximum Temperature

- $45 \leq T \leq 65$

(b) Threshold Temperature

- $T \geq 55°C$

(c) Integral Dose (Arrhenius)

- $t_{43} \geq 240$ min

(d) Contrast-enhanced T1 MRI

n=4 canines treated, n=2 with TVT lesions in lobe

3 element, water cooled, transurethral ultrasound applicator

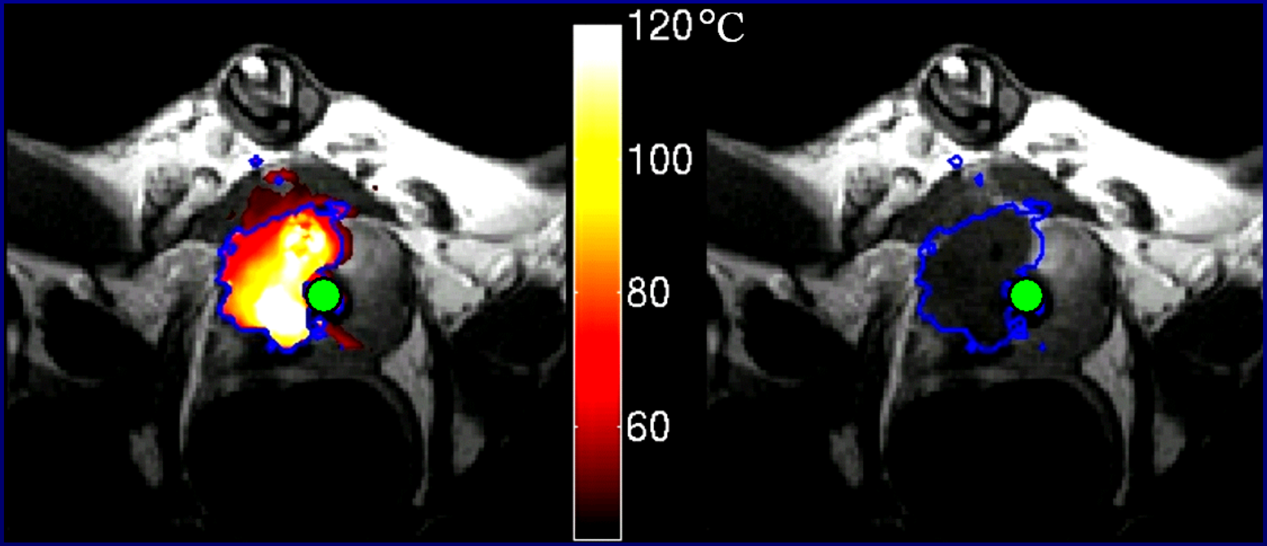
180° directivity, treatment of right lobe

2.5 cm effective treatment length

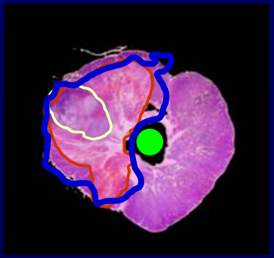
Treatment time: 11 minutes

Power varied: 4-12 W over treatment time

Thermal isodose verification: canine prostate



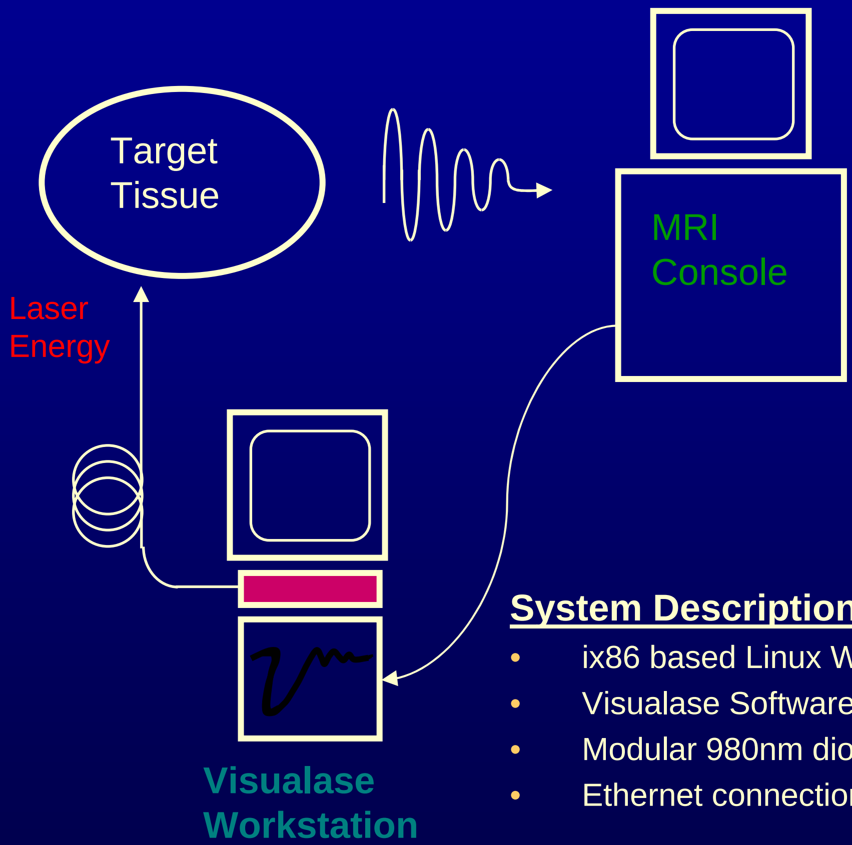
(a) **Temperature** (b) **Contrast enhanced T1**



Isodose (t_{43} = 90 min.)
Necrosis
Tumor

(c) **Tissue pathology** (d) **Tissue histology**

Visualase® system from BioTex



System Description

- ix86 based Linux Workstation
- Visualase Software/Hardware
- Modular 980nm diode laser
- Ethernet connection to MRI host

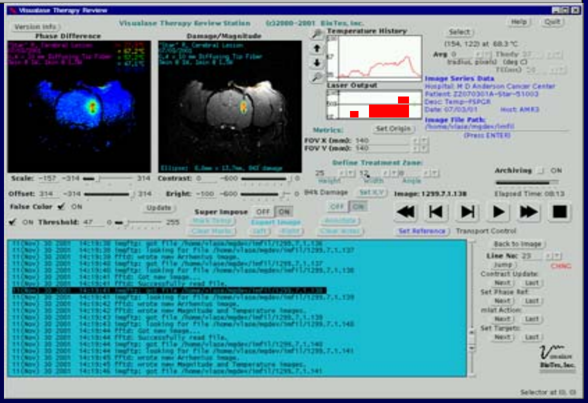
Visualase ® system interface

Software Features

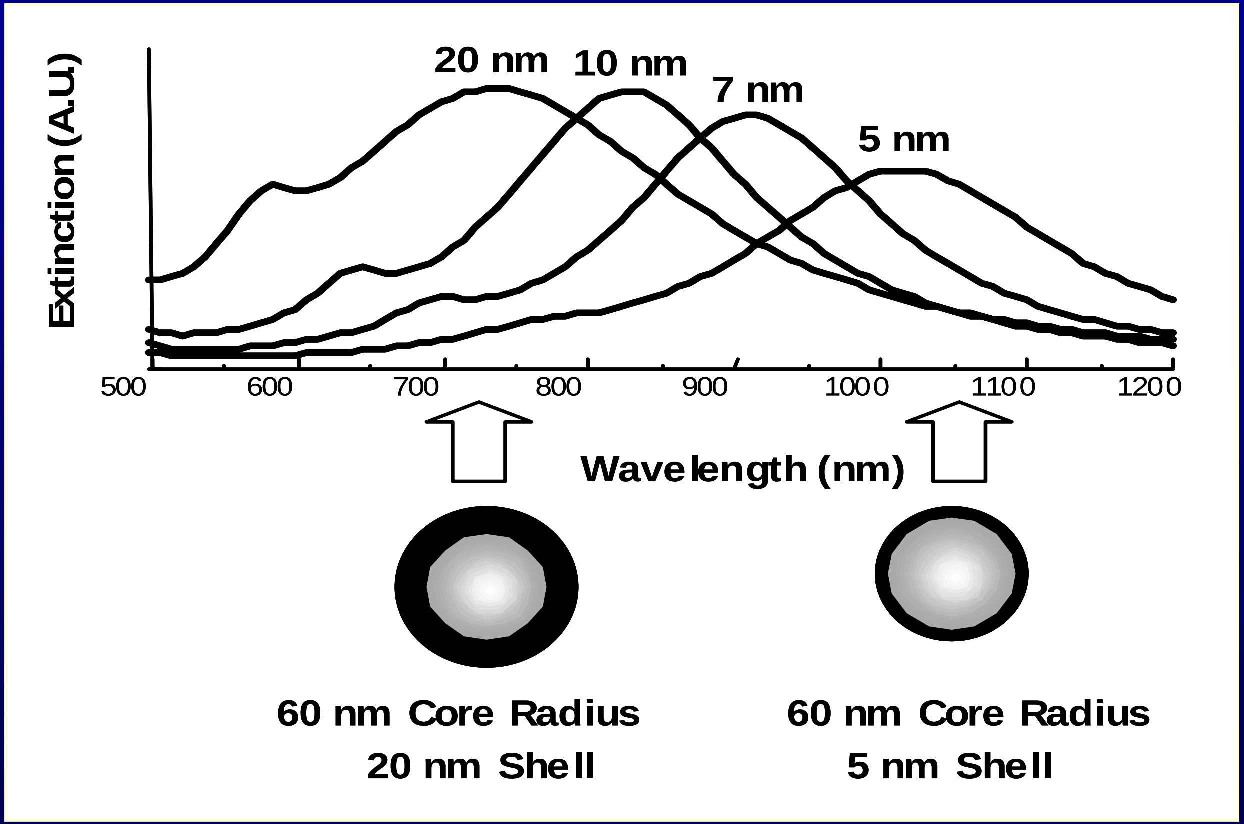
- Real Time Visualization of Thermal Profiles
- Continually Updated Estimate of Thermal Damage
- Set/Select/Move Control Points in Real Time
- Manual Laser Control Interface
- Alarm and Laser Deactiviation on Overheating
- Fully-Automated Fuzzy Logic Control of Laser Available
- Measurement and Targeting Tools

Extensive logging during treatment allows complete Review/Replay of any therapy.

Allows for validation, review, training.

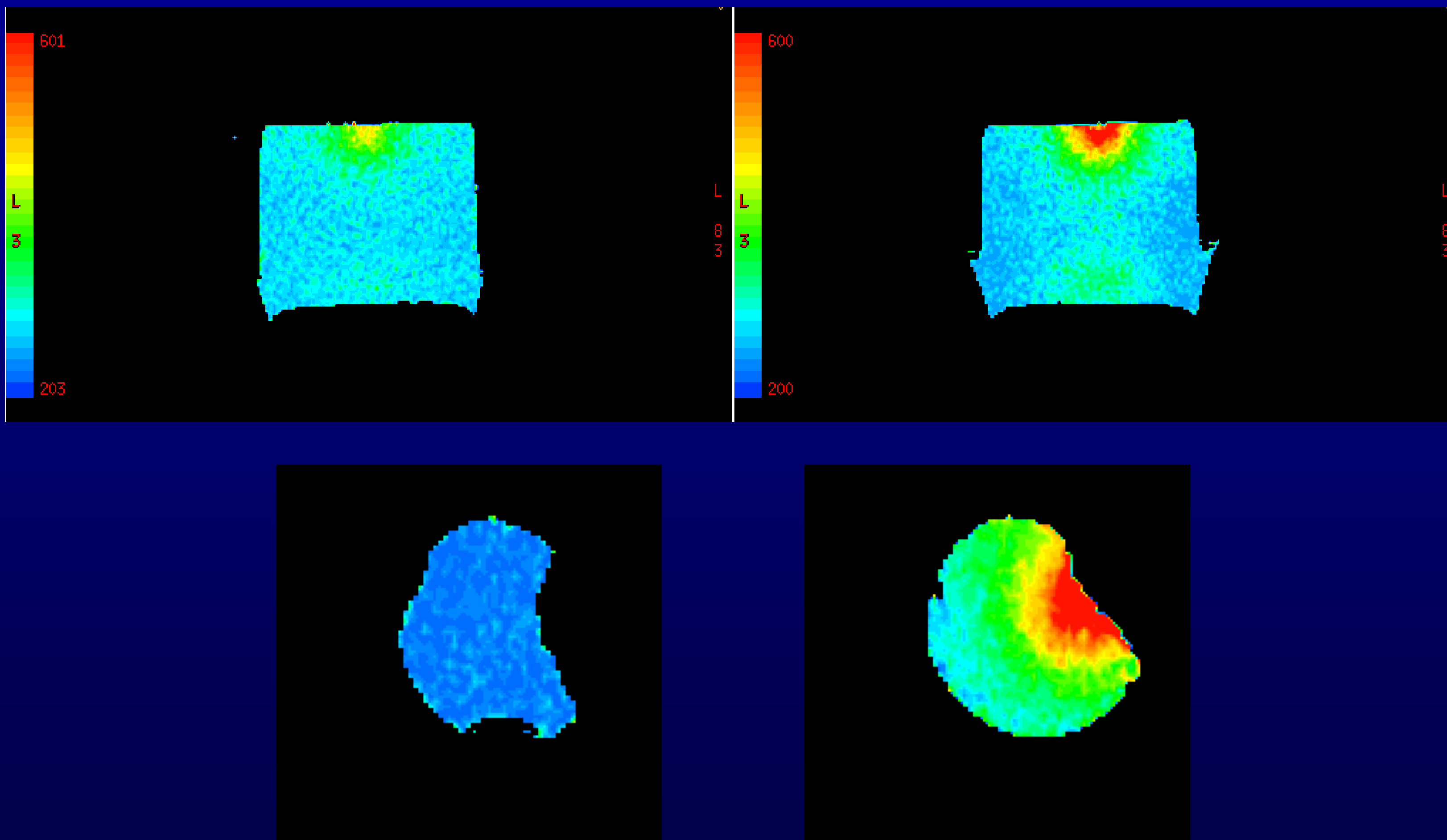


Tunable gold nanoshells



Courtesy of Drs. Jennifer West and Naomi Halas at Rice University.

Differential heating with nanoshells



Applications for targeted therapy

- Cancer applications
  - Prostate cancer using transurethral or transrectal approachs
  - Brain using percutaneous or transarterial approach
  - Bladder using transurethral approach
  - Breast using compression
- Other applications
  - Vulnerable vascular plaques
  - MS plaques

Summary and future directions

- Many MR compatible options for thermal therapy
- Imaging approach must meet demands of therapy delivery system (consider temporal & spatial resolution, temperature sensitivity, artifacts)
- Volumetric temperature imaging is the goal for real-time feedback control of therapy delivery
- Approaches with minimal artifacts and motion sensitivity will be needed for longer applications
- Targeted thermally enhancing nanotechnology is promising for treating with tissue selection