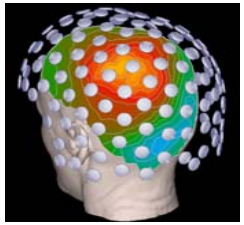
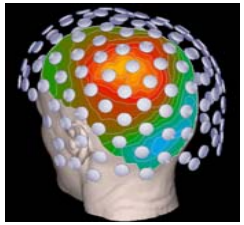


A Novel Minimally-invasive Method for Imaging and Treatment of Cancer

Presented to
NIH Workshop on Thermography
(2-3 December 2001)

Robert H. Kraus, Jr., Ph.D. (PI)
Biophysics Group, P-21
Los Alamos National Laboratory



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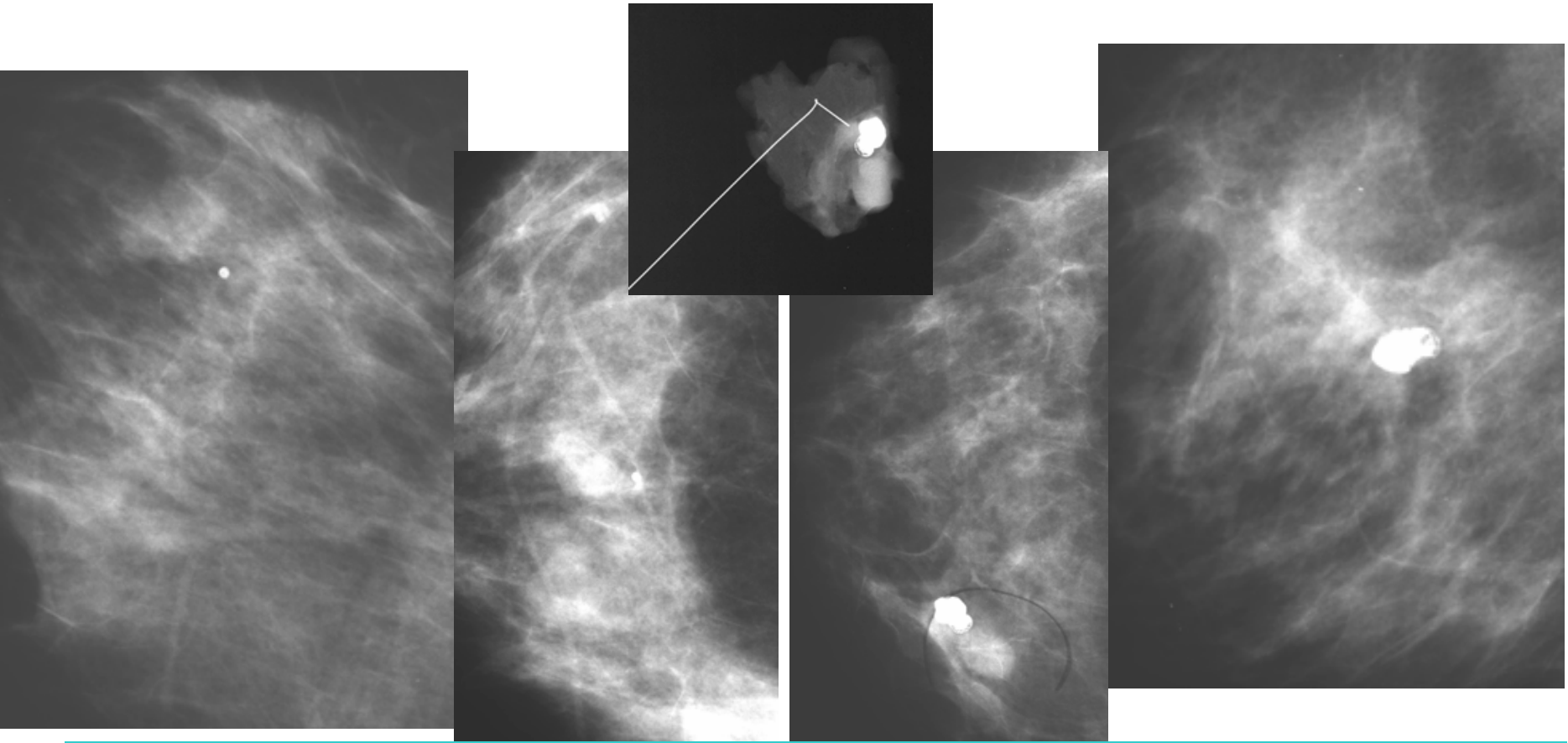
Magnetocarcinotherapy (MCT)

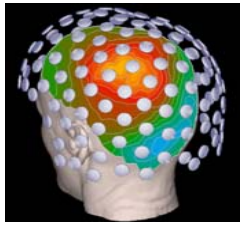
Biophysics Group in the Physics Division

Use Breast Cancer as a Paradigm to illustrate MCT



However, MCT is potentially applicable to any tumor type.

●Dr. R.H. Kraus, Jr., Ph.D. Biophysics Group, Los Alamos National Laboratory email: rkraus@lanl.gov



Detection Concept

Targeting

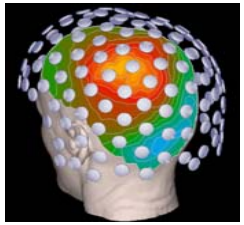
Selectively bind *supermagnetic nanoparticles* to tumor cells.

Detection

SQUID (Superconducting QUantum Interference Device) sensor technology used to detect magnetic nanoparticle concentrations that are bound to tumor cell receptor sites.

Imaging

Use methods commonly used in functional brain imaging methods to 'image' localized concentrations of magnetic nanoparticles



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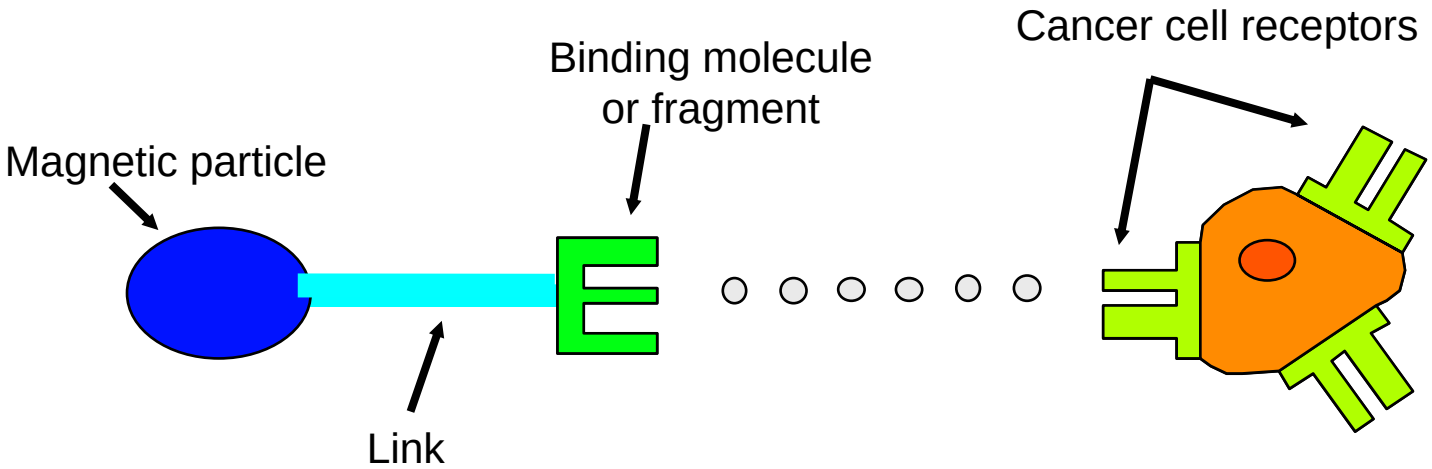
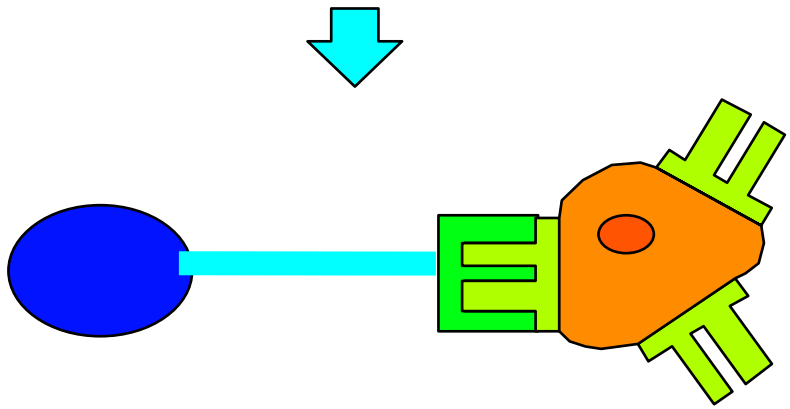
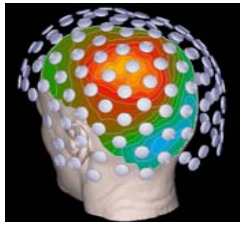


Targeting Chemistry Concept

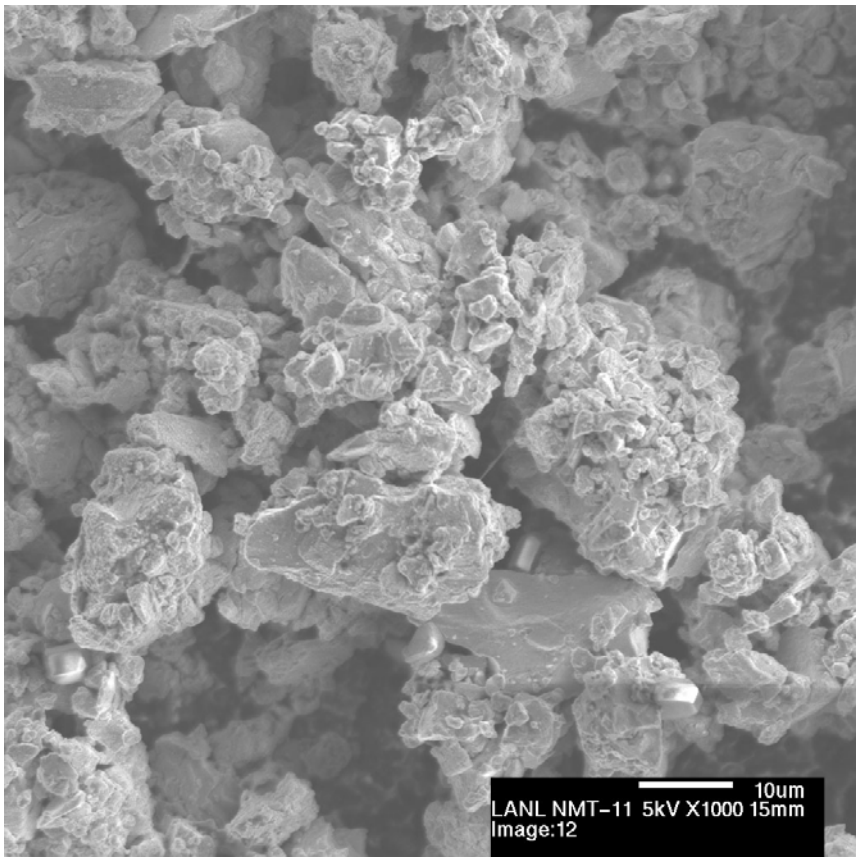


Magnetic particle bound to cell

●Dr. R.H. Kraus, Jr., Ph.D. Biophysics Group, Los Alamos National Laboratory email: rkraus@lanl.gov



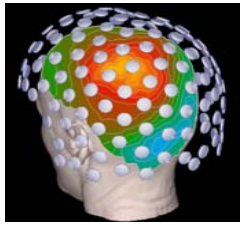
Magnetic nanoparticle technology developed



Methods to sort by particle size developed.

Process to produce material with uniform size distri-bution under development (UNL)

Methods to encapsulate particles or groups of particles available (LANL, UNMC)



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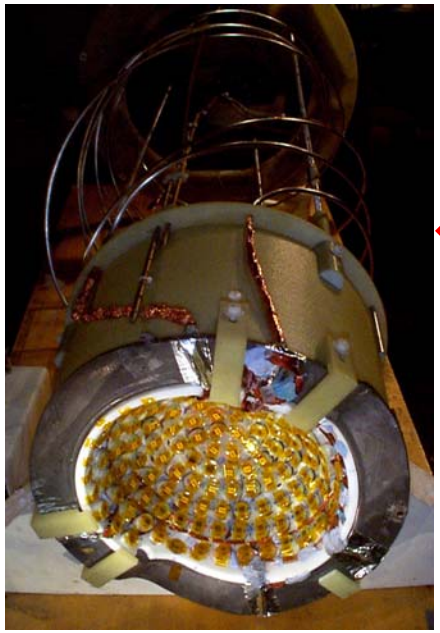
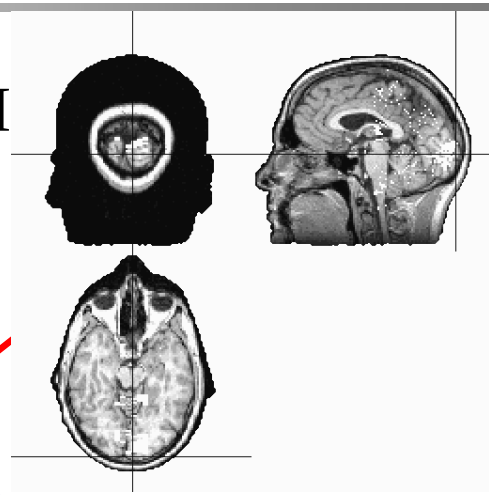
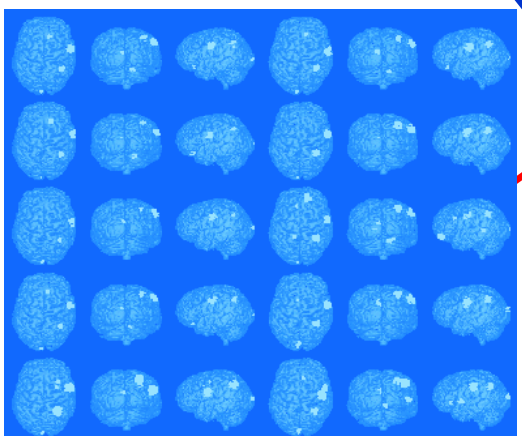


Instrumentation Research

Advanced MRI and fMRI Research

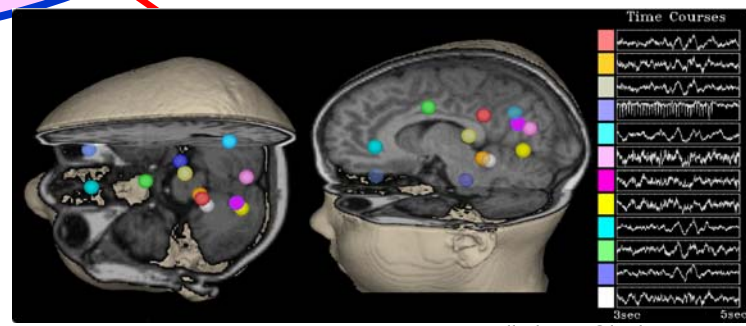


Imaging based on Functional Brain Imaging technology



Modeling & Computation

Visualization



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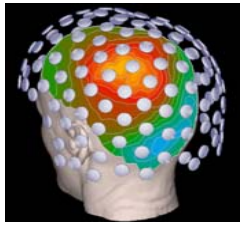
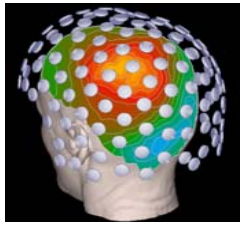


Particle/Field Requirements to 'Image'

Single Molecules	N atoms	Field @ 5cm	Moles	grams
L + Fe_2O_3	$3.5x10^{11}$	330fT*	$5.8x10^{-13}$	$9.3x10^{-11}$
L + $SmCo_5$	$3.5x10^{11}$	210pT*	$5.8x10^{-13}$	$2.6x10^{-10}$
nanoparticles (100nm radius)	N particles	Field @ 5cm		grams
L + n(Fe_2O_3)	$2.4x10^{3}$	1pT		$2.8x10^{-11}$
L + n($SmCo_5$)	<10	1pT		$8.3x10^{-13}$

L = Targeting agent (e.g. monoclonal antibody as per:
del Gratta, et al., Phys. Med. Bio. v40, p671-681 (1995))
Remnant magnetization: (Fe_2O_3) <10G (7-9 typical)
($SmCo_5$)>10,000G (11,000-12,000 typical)

* Magnetoencephalography detection limit ~10fT



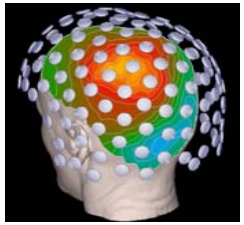
Treatment Approach

Thermal Energy Deposition – Rapid & Significant

Use 'shaped' RF magnetic field coupled to "supermagnets" to induce thermal energy deposition (*distinct* from traditional hyperthermia using magnetic materials)

Tumor necrosis, Collateral Damage

- >>15°C (27°F) temperature rise causes rapid cellular necrosis
- Rapid (<100 sec) thermal deposition minimizes thermal diffusion & associated collateral damage
- phagocytosis removes necrotic tissue over time obviating surgery



Mechanisms of Thermal Deposition
(Basic concepts)

Target: >>15^{o}C rapid temperature increase in <1 min.

Onset of cell necrosis ~10^{o}C above body norm.

Minimize collateral damage due to thermal diffusion.

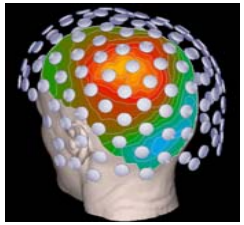
$$\dot{Q}_{visc} \sim 8\pi\eta a^3 \omega B_o M \qquad \dot{Q}_{hyst} \sim a^3 \omega B_o^2; \quad \dot{Q}_{ohmic} \sim R(\omega B_o)^2$$

B_o = external applied field ~ 100-1000G

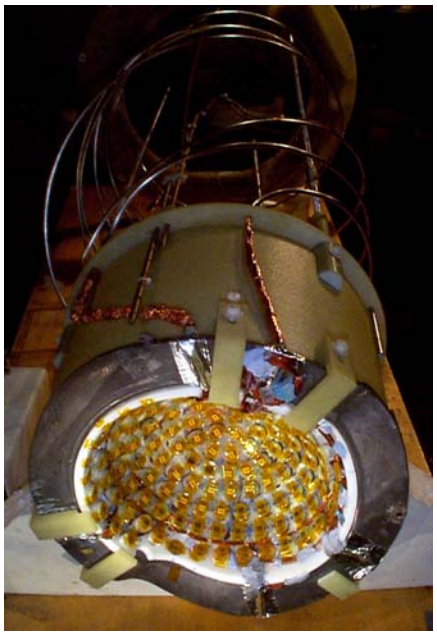
M = particle magnetization > 10kG

R = tissue resistivity; a = particle radius; η = viscosity.

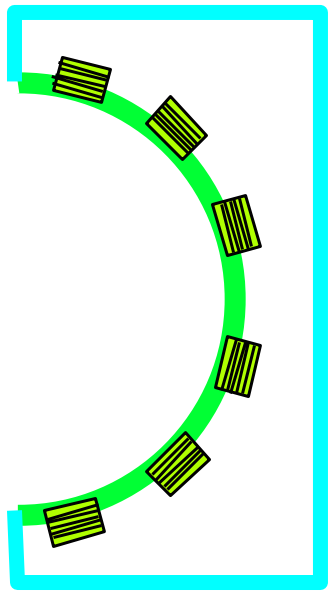
Balance heating in tumor against global tissue heating
And thermal diffusion.

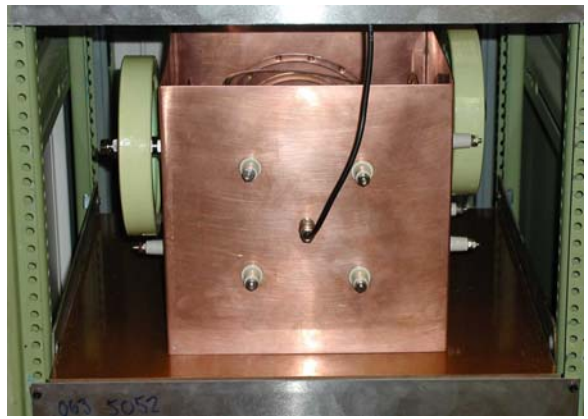


Diagnostic & Therapy Array Concept

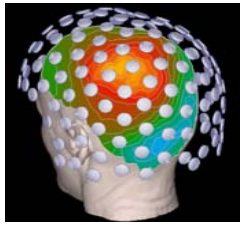


Detector SQUID array





Treatment coil array, (concept and first lab version)
Computer or phased Power Supply driven



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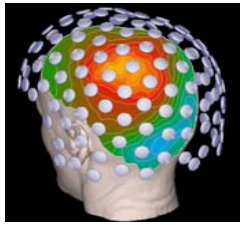
Biophysics Group in the Physics Division

Phase-coupled Power Supply and test 'magnet'

Capable of 1.8-3MHz >10kW power



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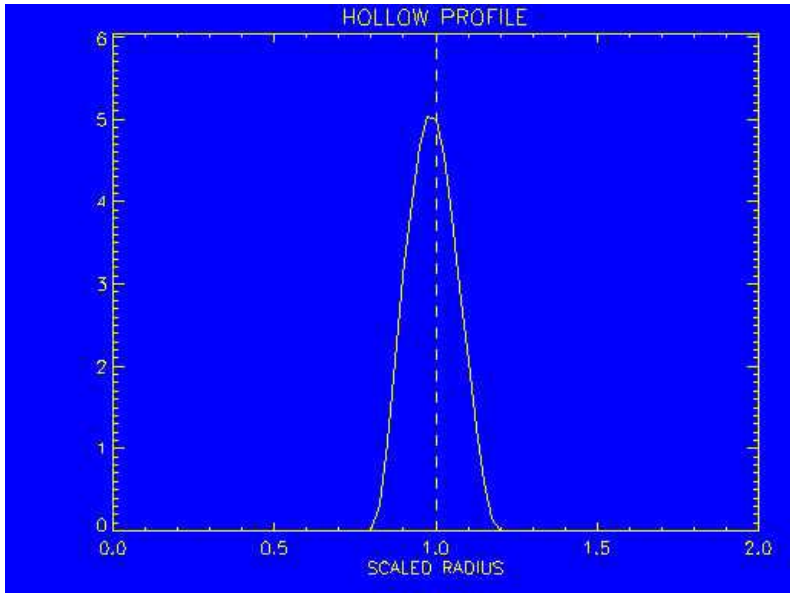
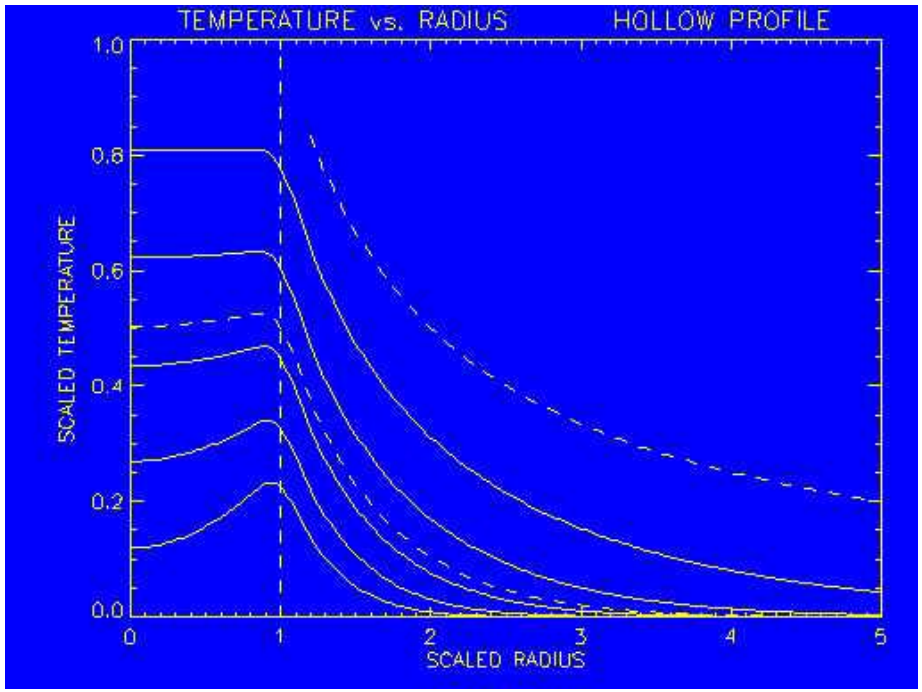
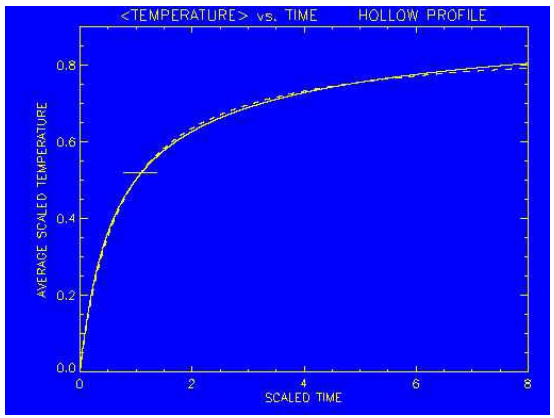


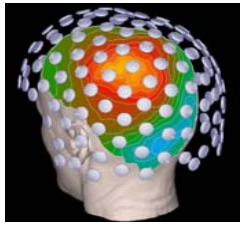
Temporal evolution of thermal energy deposition at tumor surface





Dashed line represents "optimal" pulse time

●Dr. R.H. Kraus, Jr., Ph.D. Biophysics Group, Los Alamos National Laboratory email: rkraus@lanl.gov



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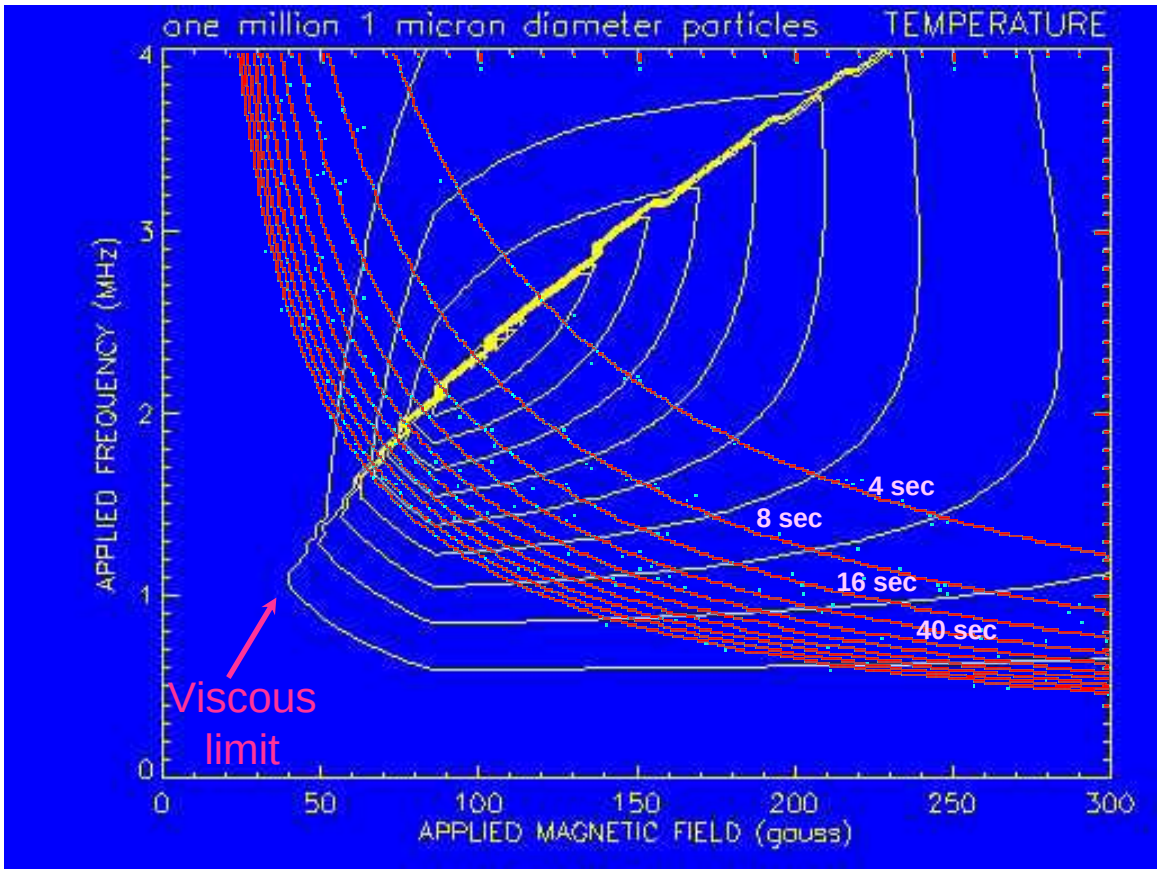
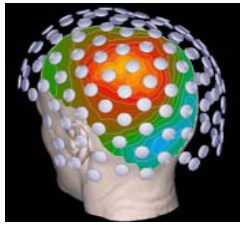


RF Magnetic field "Pulse time" comparison with RF field parameters.



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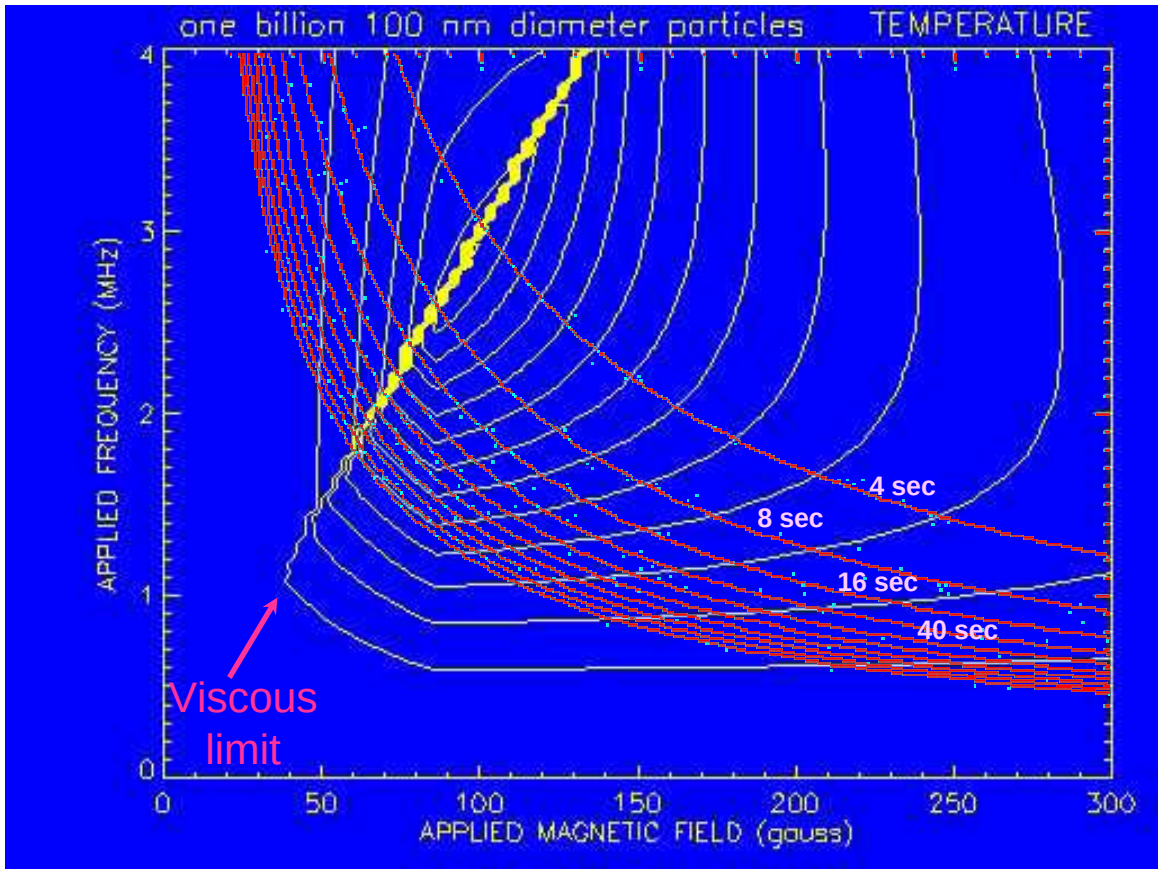

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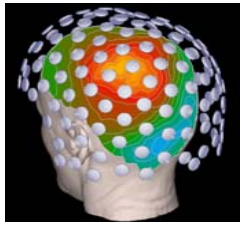


MCT Status

Broad patent allowed

Magnetic material technology in hand

- nanoparticle SmCo

Detection method & imaging methods in hand

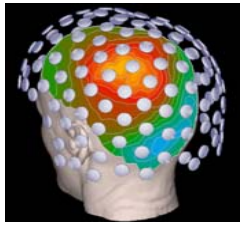
- SQUID array and source localization codes at LANL

RF PS and magnet in fabrication (complete ~Dec. '01)

Thermal imaging experimental hardware in hand

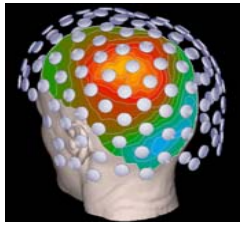
Target-binding chemistry options developed

- Atcher, et al. at LANL



Technology Advantages:

- Envisioned to be minimally invasive (no ionizing radiation)
- Potential for use with inoperable tumors (eg. Brain)
- Detection of tumors can be conclusive and unambiguous
- Extension to molecular imaging possible
- Diagnoses and treats all tumor cells in treatment envelope (e.g. multi-focal tumors)
- Believed to be superior to surgical procedures.
- Minimal collateral damage to healthy tissue (rapid heating)
- Combined diagnostic and treatment modality



Collaborators

LANL (R. Atcher, D. Berning, W. Reass, B. Wright, et al.)
Univ. Nebraska (Diandra Leslie-Pelecky (UNL), and V. Labhasetwar (UNMC))

END