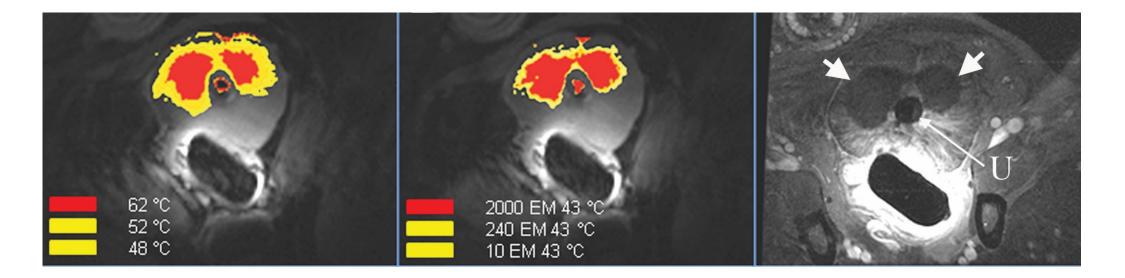
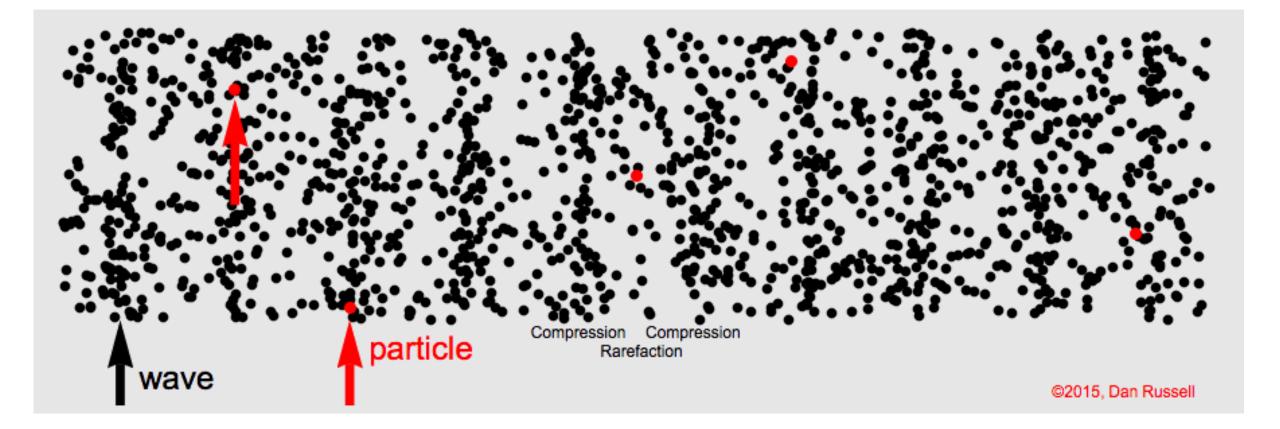
ESHO 2022 School on Clinical Hyperthermia Goteborg, Sweden September 12, 2022

Physics of Ultrasound Thermal Therapy



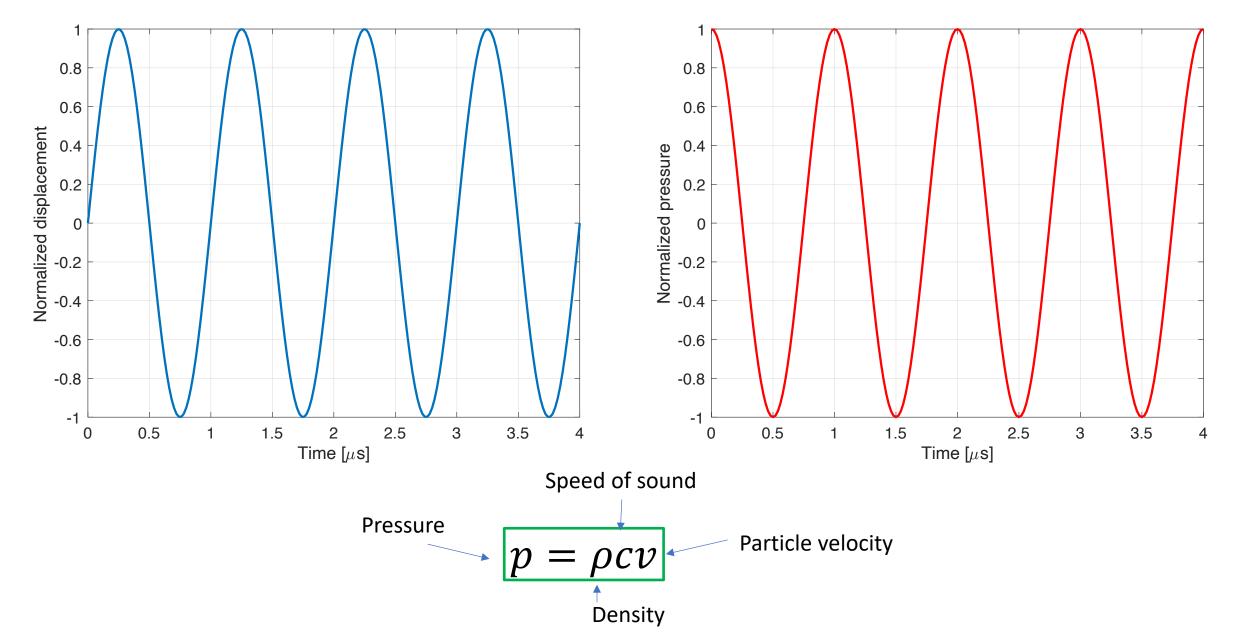
Punit Prakash Dept. of Electrical and Computer Engineering Kansas State University prakashp@ksu.edu

Particle displacement and wave propagation



2

Particle displacement, velocity, and pressure



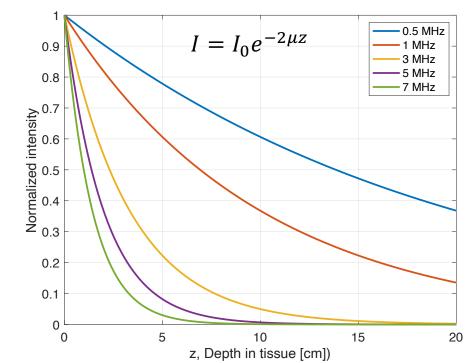
Acoustic properties of tissue

Selected tissues	Attenuation coefficient [Np m ⁻¹ MHz]	Penetration depth @ 1 MHz [cm]	Wavelength @ 1 MHz [mm]	Speed of sound [m/s]	Density [kg/m ³]	Acoustic impedance [M Rayl]
Liver	6.9	14.5	1.6	1586	1079	1.71
Muscle	7.1	14.1	1.6	1588	1090	1.73
Cortical bone	54.5	1.8	3.5	3515	1908	6.71

Time-averaged power absorption:

$$q = 2\alpha I$$

Absorption coefficient (~attenuation coefficient)

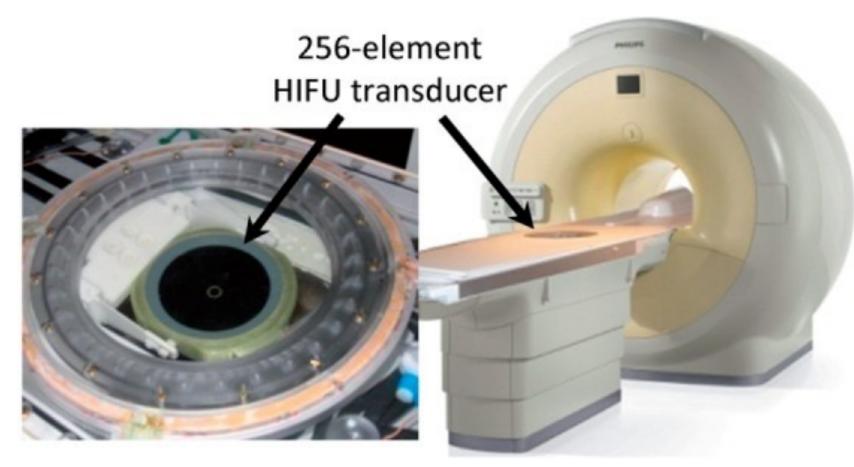


 $\frac{\text{Acoustic intensity:}}{I \propto p^2}$

Reflection at interfaces:

$$\Gamma = \frac{Z_2 - Z_1}{Z_2 + Z_1}$$

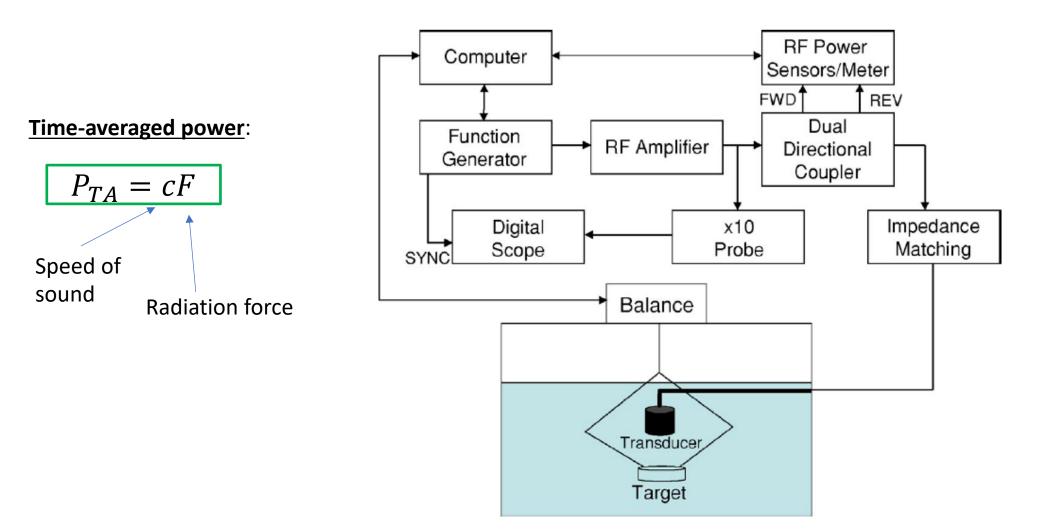
Ultrasound thermal therapy systems



From: Wiljemans et al, *Cancer Imaging*, 12(2), 2012

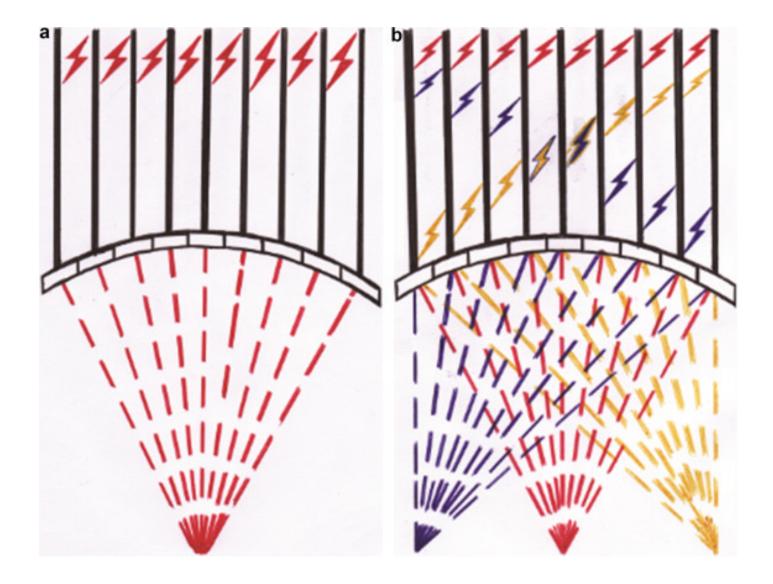
- 1-1.5 MHz operating frequency for most non-invasive ultrasound thermal therapy systems
 - \odot Deep penetration in to issue & short wavelengths for small focal spots
 - $_{\odot}$ Considerably separated in frequency from 1.5 T (64 MHz) and 3 T (128 MHz) MRI scanners

Electro-acoustic efficiency assessment

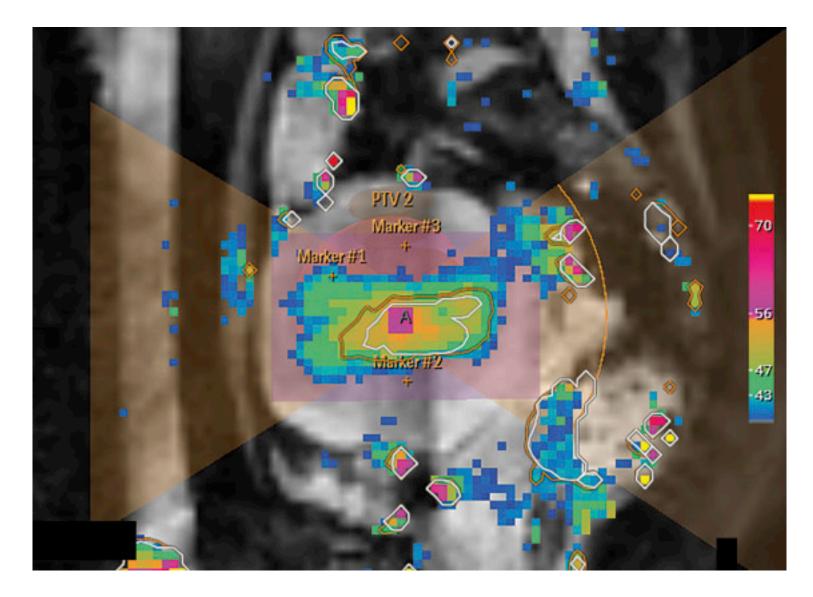


From: Maruvada et al, J Acoust Soc Am, 121(3), 2007

Electronic beam steering with phased array transducers

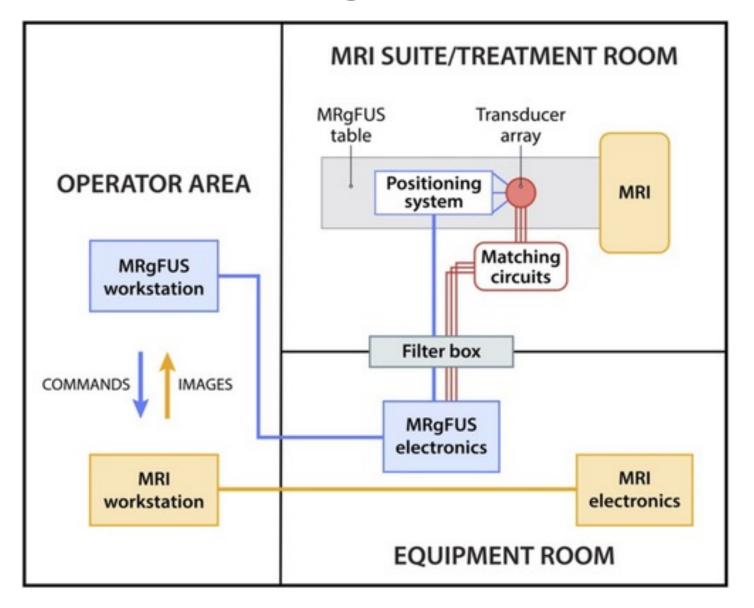


Integration with MRI thermometry



From: Shehata et al, *Diagn Interv Imaging*, 99(6), 2018 8

Treatment room setup for MRgFUS system



Treatment sites under investigation for ultrasound based therapy

FIELD OVERVIEW

State of Research and Regulatory Approvals by Body System

Preclinical	Pilot trials	Pivotal trials	Outside US approvals	FDA approvals	US reimbursement				
\rightarrow		\rightarrow	\rightarrow	\geq	\rightarrow				
		Gastrointes	tinal						
		Liver metastases							
		Liver tumors							
		Pancreatic tumors, malignant							
		Biliary tract can							
		Colorectal tumo							
-		Esophageal tumors							
		Gastric tumors							
		Malignant obstructive jaundice							
		Pancreatic tumors, benign							
Cardiac hypertrophy Cardiac pacing				Root canal endodontia					
Coarctation of the aorta				Inflammatory bowel disease 1					
		Irritable bowel	Irritable bowel syndromet						
Congestive heart failure Deep vein thrombosis			osis						
		Miscellaneo	us						
		Actinic keratosi	s 🚬						
		Basal cell carcinoma							
		Dercum's disea	se 🔪 🔪						
		Head & neck tu	mors 📃 🚬						
Ventricular tachycardia				Hypersplenism					
		Kaposi's sarcon	nat 📃 🚬	\rightarrow					
		Lipoma							
Thyroid nodules			Melanoma						
Graves' disease			Multiple tumors ¹						
		Obesity							
		Heterotopic oss	ification† 📃 🚬						
		Infection†							
		Wound healing							
			Heterotopic oss	Heterotopic ossification †	Heterotopic assification †				

FIELD OVERVIEW

State of Research and Regulatory Approvals by Body System continued

	Conceptual	Preclinical	Pilot trials	Pivotal trials	Outside US approval	s FDA approvals	US reimbursement
Development stage		\rightarrow	\rightarrow	\rightarrow	\rightarrow	\rightarrow	\rightarrow
Musculoskeletal				Neurologica	al		
Bone metastases				Essential tremo			
Osteoid osteoma				Parkinson's dis	ease, tremor	555	->>>
Arthritis, facetogenic			•	Depression	X	> > >	
Bone cancer			•	Neuropathic pa	in 🔰	555	
Bone tumors, benign			•	Obsessive-com	pulsive disorder 📃 🚬		
Epicondylitis			•		ease, dyskinesia 🔰	555	
Multiple myeloma ²			•	Alzheimer's dis	ease		
Plantar fasciitis			•	Amyotrophic lat	teral sclerosis		
Soft tissue cancer			•	Astrocytoma			
Soft tissue injury			•	Brain tumors, g	eneral 📃 🔰		
Soft tissue tumors, benign			•	Cancer pain			
Arthritis				Dementia			
Arthritis, ankle				Dystonia			
Arthritis, hand		-		Dystonia, hand			
Arthritis, hip		_		Epilepsy			
Arthritis, knee		-		Glioblastoma			
Arthritis, sacroiliac				Holmes tremor			
Desmoid tumors				Huntington's d	sease		
Disc degeneration				Migraine			
Sacral chordoma				Mood disorder	F 🔰 🔰		
Muscle atrophy				Multiple sclerosis			
Osteomyelitis				Neuroblastoma			
Osteopenia†			Neuropathy	opathy			
Rotator cuff injury				Opioid and oth	er addictions		
Tendon contracture				Painful amputa	tion neuromas 📃 🔰		
				Parkinson's dis	ease, other ^a		
				Pontine glioma	2		
				Traumatic brain	injury 🔰 🔰		
				Cavernomas	X		
				Hydrocephalus			
				Neuromyelitis o	optica 📃 🔪		
				Rett syndrome			
				Spinal cord inju	ry 🛛 🛛		
					bral hemorrhage 🔰		
				Stroke, thrombo	embolic 💦 🔪		
				Trigeminal neu	ralgia 📃 🔪		

Anorexia

State of Research and Regulatory Approvals by Body System continued

	Conceptual	Preclinical	Pilot trials	Pivotal trials	Outside US approvals	FDA approvals	US reimbursement		
Development stage		\rightarrow		\rightarrow	\rightarrow	\geq	\rightarrow		
Ophthalmological				Women's he	alth				
Glaucoma				Uterine fibroids					
Keratoplasty				Breast tumors,	Breast tumors, benign				
Macular degeneration		•		Breast tumors,		555			
Retinal impairment†				Cervicitis					
Retinal injury†		•		Lichen sclerosis	†	55			
				Uterine adenon	wosis	555			
Pulmonary				Brain metastases, breast cancer					
Rhinitis				Cervical tumors					
Lung cancer				Ectopic pregnar	icy 🗧	55			
Lung metastases				Endometrial tu	nors	55			
Tuberculosis		•		Endometriosis					
				Endometriosis,	colorectal				
Irological		Hyperplasia of	the vulvat						
Prostate cancer ^{4, 5}				Ovarian tumors					
Benign prostatic hyperplasia ⁴	ign prostatic hyperplasia ⁴		Retained place	nta 📃 🚬					
Kidney tumors	ney tumors		Vaginal tumors						
Bladder tumors	adder tumors		Vulvar dystrophy						
Chyluria			Polycystic ovary	syndrome 📃					
Kidney stones		>>>							
Acute kidney injury		•							
Acute tubular necrosis		•							
Fetal bladder obstruction		•							
Ureterocele		•							
Urinary tract infection		•							
Vasectomy		•							

There are 152 distinct indications for 2020

1 Protocols inclusive of more than one indication † New in 2020

There are 152 distinct indications for 2020.

2 Multiple myeloma approval is based on bone metastases. 3 Treatment of the underlying cause of the disease † New in 2020

There are 152 distinct indications for 2020.

4 FDA approval is for prostate tissue ablation. 5 Reimbursement is for salvage therapy in radiorecurrent prostate cancer. † New in 2020

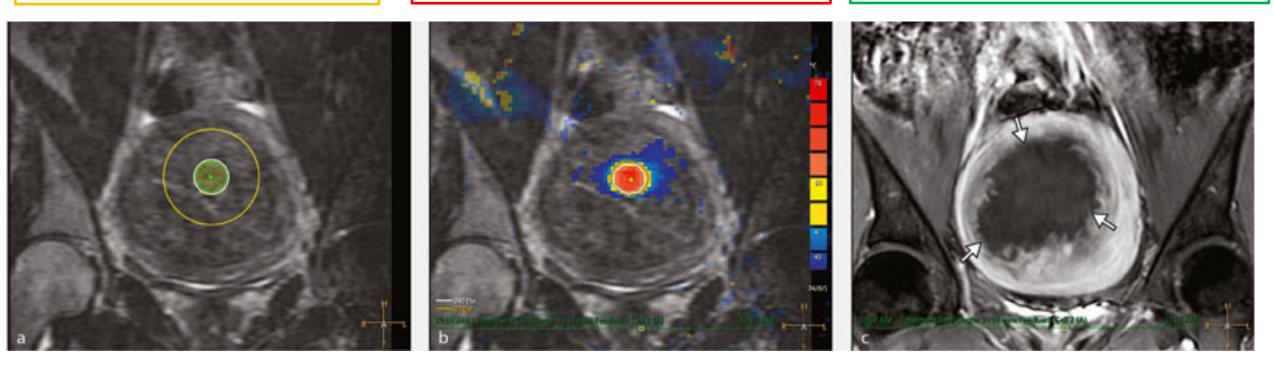
Focused Ultrasound Foundation | 2021 State of the Field | 1.11 1.12 Focused Ultrasound Foundation | 2021 State of the Field

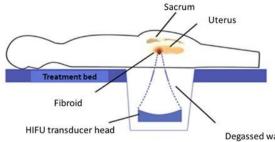
Focused ultrasound ablation: uterine fibroids

MR-imaging based pre-treatment planning

Real-time MR thermometry feedback to monitor ablation progress

Non-perfused volume (NPV) provides a means for assessing ablation effect

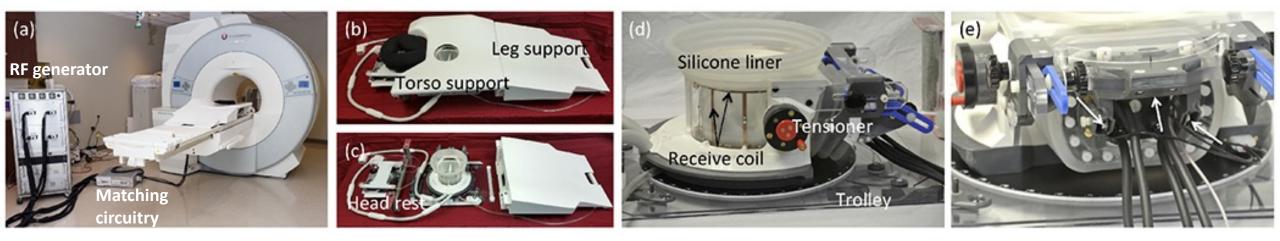


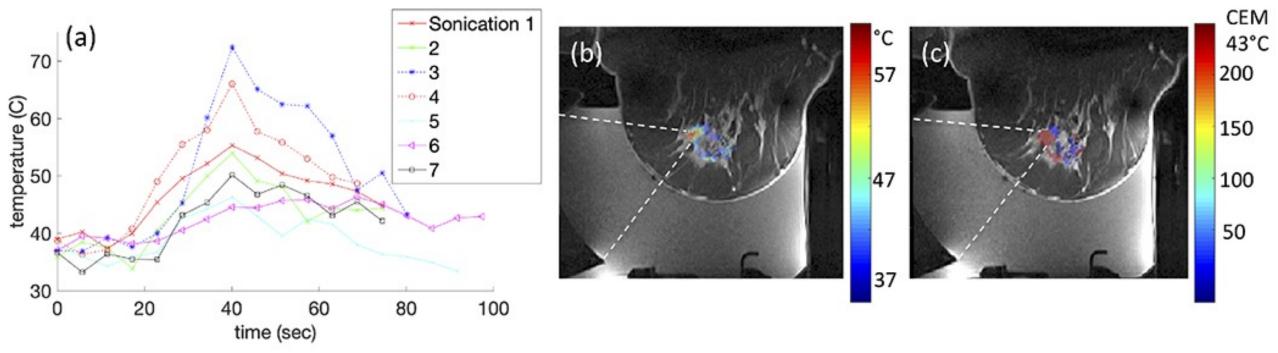


Degassed water

From: Wong, WJARR, 2021

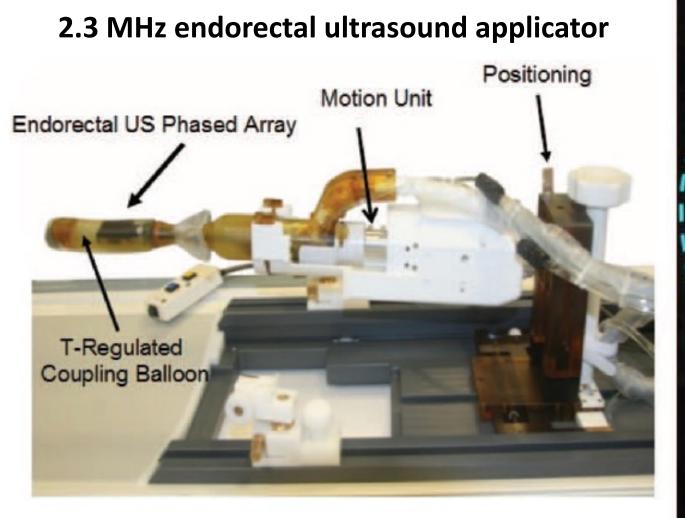
MRgHIFU system for breast ablation



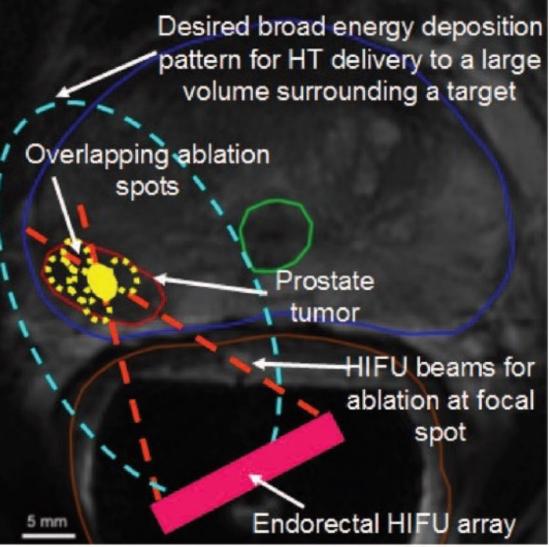


Adapted from: Payne et al, IEEE Trans Biomed Eng, 68(3), 2021

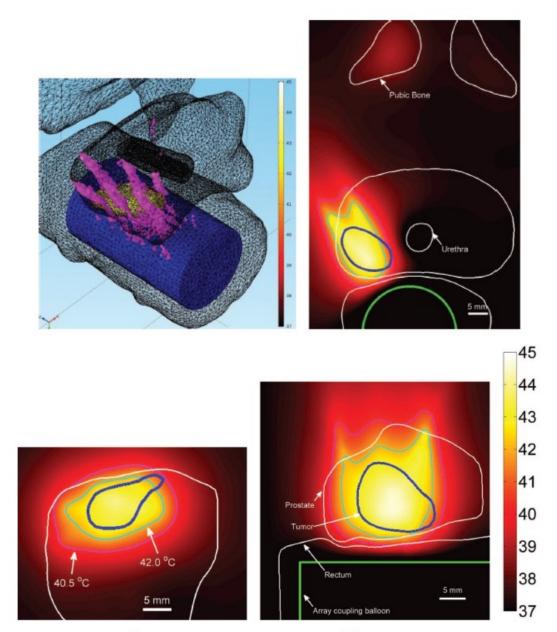
Adapting HIFU ablation systems for large volume hyperthermia

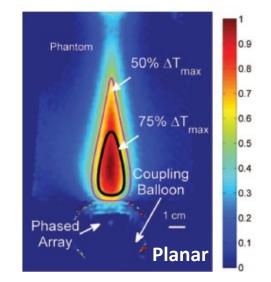


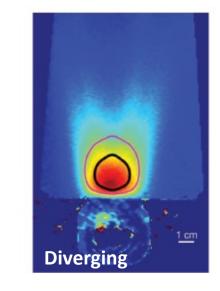
From: Salgaonkar et al, Med Phys, 41(3), 2014

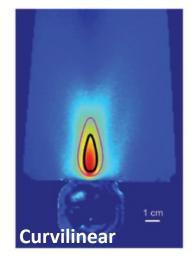


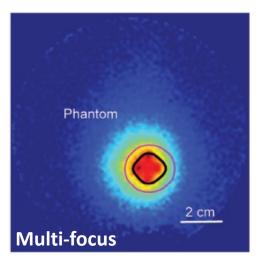
Adapting HIFU ablation systems for large volume hyperthermia





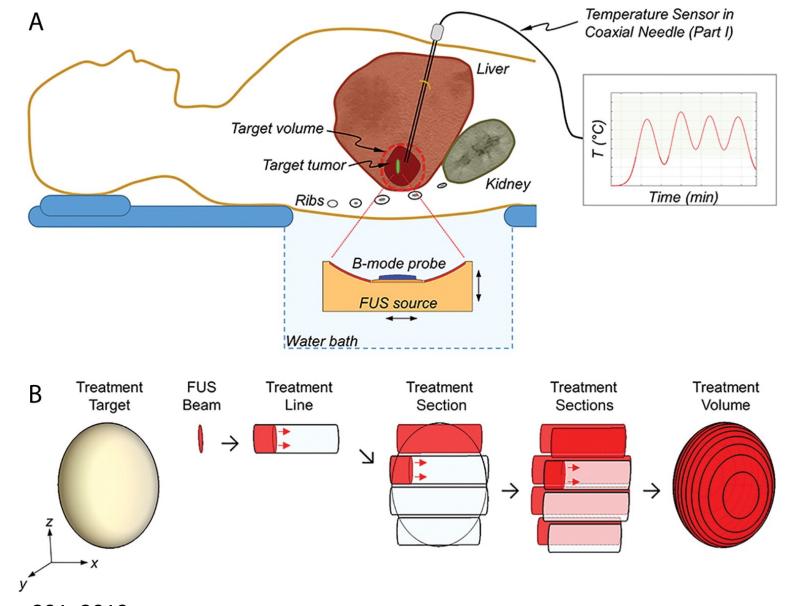






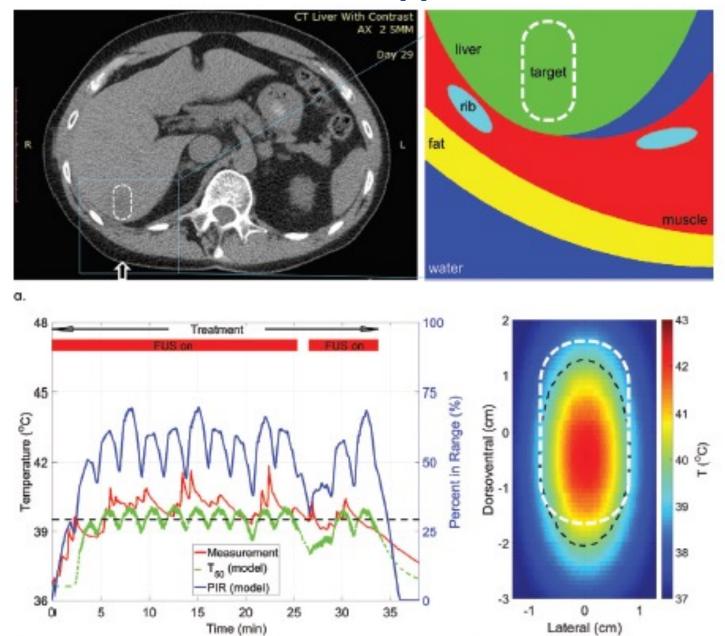
From: Salgaonkar et al, Med Phys, 41(3), 2014

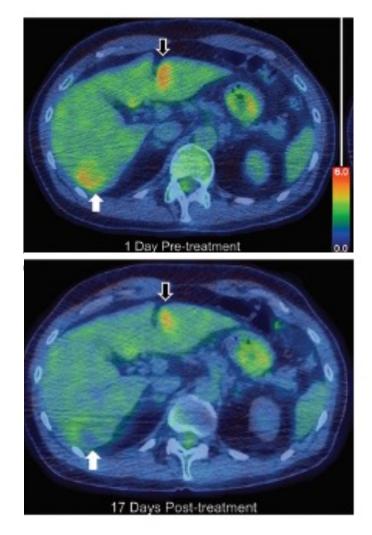
Focused ultrasound hyperthermia



From: Gray et al, Radiology, 291, 2019

Focused ultrasound hyperthermia

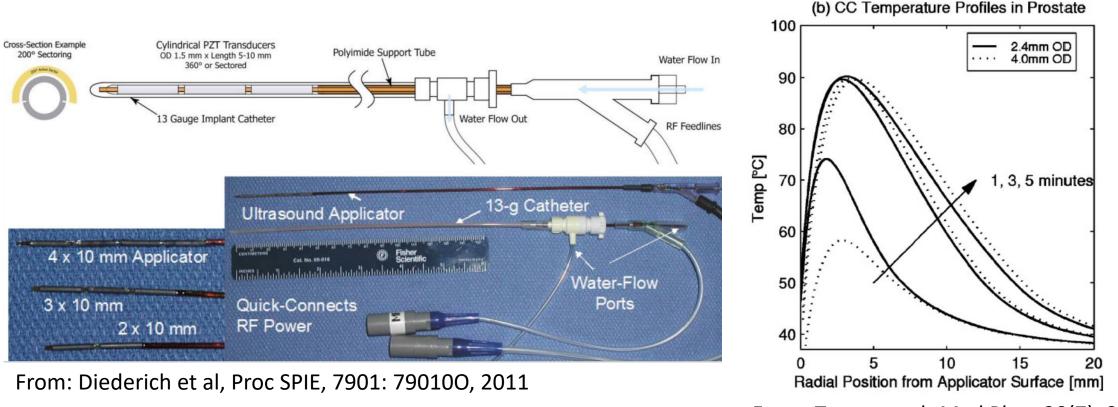




From: Gray et al, Radiology, 291, 2019

16

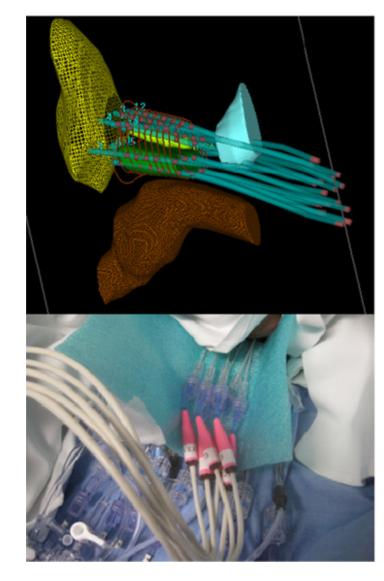
Interstitial ultrasound thermal therapy devices

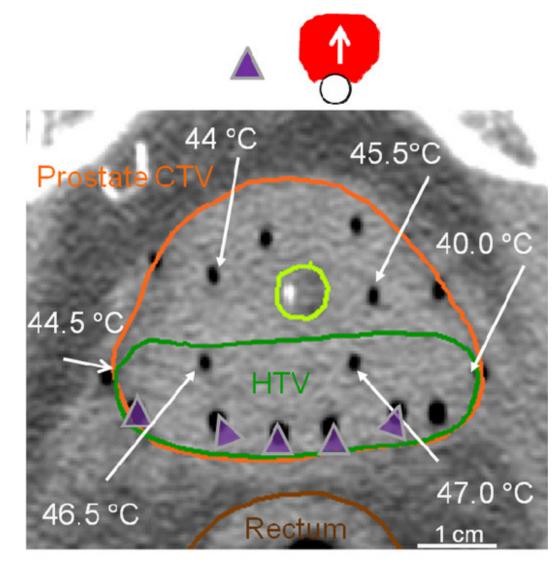


From: Tyreus et al, Med Phys, 30(7), 2003

- Linear arrays of independently powered ultrasound transducers
 - Typical operating frequencies: ~6 9 MHz
 - Angular control of power absorption feasible with sectored transducers

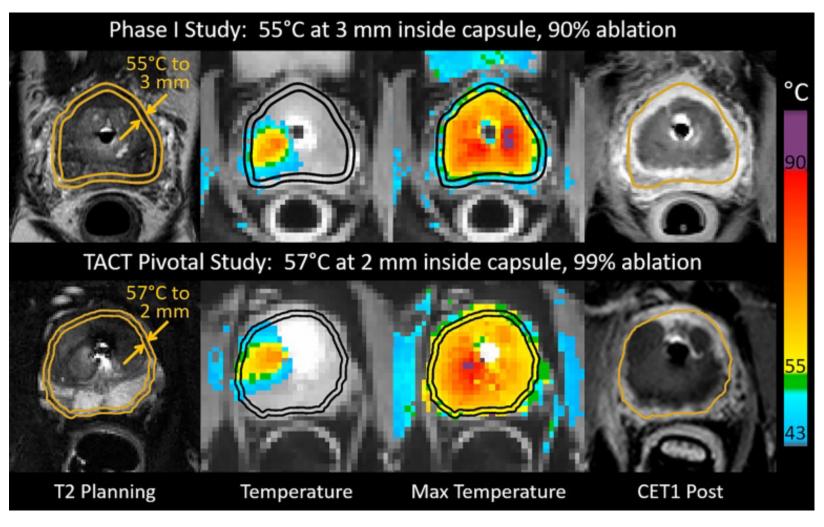
Interstitial ultrasound thermal therapy: prostate

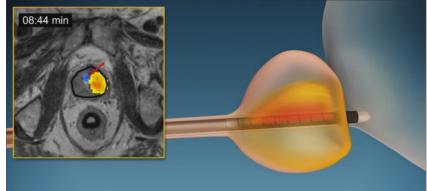




From: Diederich et al, Proc SPIE, 7901: 790100, 2011 18

Transurethral ultrasound prostate ablation





• Multi-element linear array of planar transducers with rotary control

Summary

- Ultrasound offers deep penetration and short wavelengths for conformal thermal therapy of targets in diverse anatomic sites
- Ultrasound thermal therapy systems have been integrated with magnetic resonance and ultrasound imaging for thermometry and guidance of clinical delivery
- Non-invasive and catheter-based ultrasound systems are in clinical use for thermal treatment of uterine fibroids, painful bone metastases, prostate disease, and other conditions



Thank you!

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