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STITUTES

OF

HEAL

National Institute of Biomedical Imaging And Bioengineering



Basics:

-The institute's mission is to develop <u>new technology</u> that is health- related

-The Institute is committed to integrating the physical and engineering sciences with the life sciences to profoundly advance basic research and medical care.



NIBIB Usnd Therapy Program

- Opening of BBB (2)
- Therapy through intact skull
- Wound Healing (2)
- Non-invasive drug delivery(2)
- HIFU-enhanced tumor vaccines
- Quantitative US and Image guidance of HIFU treatments (3)
- Cardiovascular projects (discuss today):
 - Non-invasive Coronary thrombosis treatment
 - Non-invasive Deep vein thrombosis treatment
 - Non-invasive Anti-fibrillation treatment
 - Non-invasive cerebral stroke treatment

What can ultrasound do in cardiovascular therapy?

- Diagnostic level ultrasound has thrombolytic properties
- Mechanisms not yet understood...
- Combined with microbubbles, therapy levels enhanced
- HIFU operates through thermal, mechanical effects, but also has thrombolytic properties (different mechanisms?)

1. Coronary and Microvascular Thrombolysis Xie, F., Porter, T., et al, U. Nebraska

- Goal: examine effects of impulses from 3D ultrasound on microvascular and epicardial reflow in porcine model of coronary thrombosis.
- Uses diagnostic level Usnd, high MI, nontargeted microbubbles
- Coronaries: porcine atherosclerotic and normal controls





Video: Coronary and Microvascular Thrombolysis Xie, F., Porter, T., et al, U. Nebraska

Before Usnd

After Usnd





1. Coronary and microvascular thrombolysis Xie, F., Porter, T., et al, U. Nebraska

Porcine Acute ST-segment elevation myocardial infarction and resolution by use of 3D ultrasound (US), Micro Bubbles (MB) and Tenecteplase (TP)



2. Deep Vein Thrombolysis by Histotripsy in a Porcine Model

Xu, Z., Maxwell, A, et al, University of Michigan, Ann Arbor

B-Mode



Color Doppler

<u>Histotripsy</u> = short, HIFU pulses to cause soft tissue or clot breakdown by <u>cavitation</u>

Cavitation cloud guided left to right inside the occluded vein,-----disintegrates clot sections ----allows blood to flow again,



2. Deep-Vein Thrombolysis by Histotripsy in a Porcine Model

Xu, Z., Maxwell, A., et al, University of Michigan, Ann Arbor



Video shows cavitation cloud dissolving clot in vein (left to right)



Conclusion: histotripsy has potential to be an effective non-invasive thrombolysis technique

3. HIFU Ablation for Treatment of Atrial Fibrillation

C. Deng, and M.Gudur et al, U. Mich

• Clinical significance

- Abnormal electrical activity in the atria
- Most common arrhythmia
- Affect 2.2 million adults in U.S.
- Initiation mechanisms
 - Automatic focal source
 - Pulmonary Vein (Major)
 - Coronary sinus, SVC, etc.
- Treatment Options
 - Cox-Maze-surgical--gold std.
 - Complex, long procedure
 - Ablation (RF, Cryo, MW, Laser, HIFU)
 - Minimally invasive, some problems
 - Pharmacotherapy
 - Global side effect and low efficacy

[1] Dewire, J & Calkins, H. *Nat. Rev. Cardiol.* 7:129-138. (2010) [2] *Atkas, M., Daubert, J, Hall, B., Cardiol. J.,* 15:1:87-94; (2008)

3. HIFU Ablation for Treatment of Atrial Fibrillation

Cheri X. Deng, et al, U. Michigan

- High Intensity Focused Ultrasound (HIFU)
 - Goal: develop efficient & safe HIFU ablation for treating AF
 - But—current ablation techniques not optimal:
 - Safety (AE fistula, phrenic nerve injury)
 - Efficacy (1/3 recurrence of AF, especially RF)
 - Technique Problems (HIFU)
 - Overheating
 - Cavitation
 - Incomplete lesions

Critical need for Real-time Monitoring for HIFU based on feedback control

[2] Atkas, M., Daubert, J, Hall, B., Cardiol. J., 15:1:87-94; (2008)

Yokoyama et al., Circ Arrhythm Electrophysiol, 2:41-49. (2009)
Kumon et al., Ultrasound in Med. & Biol. 2012
Laughner et al., Circ Arrhythm Electrophysiol. 2012



3. HIFU Ablation for Treatment of Atrial Fibrillation

M. Gudur, C. Deng, et al, U. of Michigan

Ultrasound imaging techniques

Integrated Backscatter (IBS): Echo

Acoustic Radiation Force Imaging (ARFI): stiffness property

Spectral analysis: spectral response \rightarrow scatterer size, acoustic concentration

Shear Wave Elasticity Imaging

Harmonic motion imaging

Differential attenuation maps

Echo de-correlation



H. Zhong, et al., Ultr. Med. Biol. vol. 33, pp. 82-94, 2007





Eyerly SA, *et al.*, *J. Card. Elect.* 2010;21(5):557-563



Conclusion: Feedback from Imaging, functional, quant. methods will increase safety and efficacy of HIFU ablation

R. E. Kumon *et al.*, *IEEE Int. Ultr. Symp. Proc.* 2009, pp. 244-247

4. HIFU Treatment of Acute Stroke

K. Hynynen, et al, U. Toronto

- Goal: develop new phased-array technology for treatment of stroke
- Transcranial sonication using patient-specific skull information from CT scans
- Precise localization of Usnd energy

4. HIFU Treatment of Cerebral Stroke

K. Hynynen, et al, U. Toronto

"Helmet "Applicator

High-power phased array with very large number of elements

Use patient-specific skull information from CT scans

Precision of beam eliminates need for thrombolytic agent



Kullervo Hynynen PhD, et al-- R01 EB3268, Sunnybrook Health Center, U. Toronto

4. HIFU Treatment of Acute Stroke

Burgess, Hynynen et al, AIUM 2012

1.5MHz transducer, 1ms pulses, 0.1% duty cycle, 20sec duration







HIFU Treatment of Acute Stroke

Burgess, Hynynen, et al, AIUM 2012

- Rabbit study :
 - Effective thrombolysis in embolic model of stroke
 - Effectiveness of high frequency phased array capable of focusing and transmitting high power through skull
 - Encouraging results for transfer to the clinical setting

HIFU Treatment of essential tremor



Private Co. and U. Va. study currently conducting FDA clinical trials (not funded by NIH)

PI that developed system concepts: K.Hynynen, U. Toronto, et al R01EB 3268, F. Jolesz, et al, **BW** pinducting clinical study: W. Jeffrey Elias, MD., U.Va.

Evolution of Surgical Tools in Medicine

Conventional Surgical Instruments and invasive procedures (1000's years) Minimally invasive surgical instruments and procedures Noninvasive ultrasound?

