

US Modality Committee Report

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History of our Committee

- Initial discussions at 2011 RSNA meeting
- Debate to select initial biomarker effort at 2012 AIUM conference (March.2012)
 - Initial biomarker chosen
 - Committee Co-Chairs selected
- A Committee formed to investigate QIBA potential
 - Subcommittees formed
 - Draft charge to each subcommittee established
 - Membership and leadership being determined

History of our Committee

- Lively discussions at both meetings
- MANY options for quantitative biomarkers from ultrasound systems
 - For more than 30yrs we've had a conference dedicated to this specific area (quantitative ultrasound)

Proposed Initial Biomarker

- Shear wave speed for quantifying liver fibrosis
 - Fibrosis is known to increase liver stiffness
 - Shear modulus is proportional to the square of shear wave speed
 - At least two ultrasound imaging system manufacturers produce systems capable of estimating shear wave speed in soft tissues
 - At least one non-imaging system also commercially available
 - Initial reports of clinical tests in the literature

Relating material parameters

- Young's modulus: E
- Shear modulus: μ
- Shear wave speed: c_T

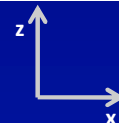
$$E = 3\mu = 3\rho(c_T)^2$$

- Linear, isotropic, elastic solid (anisotropy?)
- Incompressible ($\nu = 0.5$), $[-1:0.5]$
- May be a function of viscosity (dispersive)
- May be a function of strain (nonlinear)
- Poroelastic?

Wave Propagation in Soft Tissues

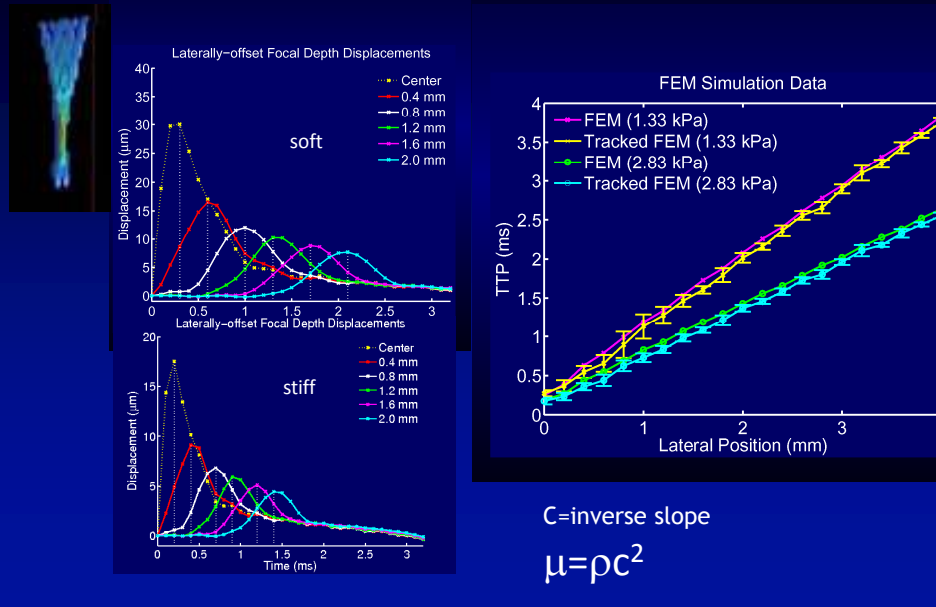
Transverse (Shear) Wave (1-5 m/s)

Ultrasound (compression) Wave
(1540 m/s)



<http://www.kettering.edu/%7Edrussell/Demos/waves/wavemotion.html>

Estimate shear wave speed with linear regression



Liver Biopsy

- Diagnostic gold-standard
 - Invasive
 - Infection
 - Hemorrhage
 - Pain
 - Limited sampling
 - Costly (time and money)
 - Not suitable for longitudinal monitoring of disease progression / resolution
- Can a non-invasive liver stiffness estimate be used as a surrogate measure of liver health?



<http://www.medandlife.ro/assets/images/Vol%2011%20N0%204/generalarticles/fierbinteanu/image005.jpg>

Fibrosis in Chronic Liver Disease

Appearance	Ischaic stage Categorical description	Ischaic stage Categorical assignment	Fibrosis measurement*
	No fibrosis (normal)	0	1.9%
	Fibrous expansion of some portal tracts + short fibrous septa	1	3.0%
	Fibrous expansion of most portal tracts + short fibrous septa	2	3.6%
	Fibrous expansion of most portal tracts with occasional portal to portal (P-P) bridging	3	6.5%
	Fibrous expansion of portal tracts with mixed bridging (portal to portal (P-P) as well as portal to central (P-C))	4	13.7%
	Mixed bridging (P-P and/or P-C) with occasional nodules (incomplete cirrhosis)	5	24.3%
	Cirrhosis, probable or definite	6	27.5%

*Proportion (%) of area of illustrated section showing Sirius red staining for collagen (collagen proportionate area, CPA)

Available



SuperSonic Aixplorer



EchoSens Fibroscan



Siemens S2000

ARFI / Shear Wave Clinical Use

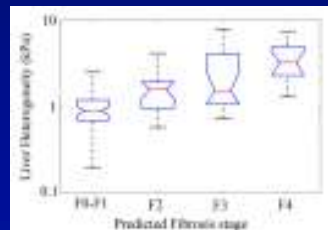
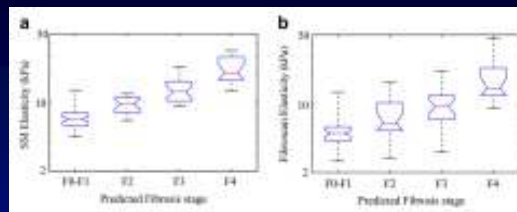
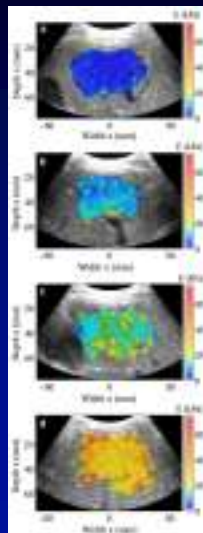


Conclusion: ARFI imaging and serum fibrosis marker test results correlated significantly with histologic fibrosis stage.

ARFI imaging is a promising US-based method for assessing liver fibrosis in chronic viral hepatitis

* This product is not commercially available in the United States

Supersonic Shear Imaging: Liver Fibrosis



Bavu et al. "Noninvasive In Vivo Liver Fibrosis Evaluation Using Supersonic Shear Imaging: A Clinical Study on 113 Hepatitis C Virus Patients," UMB, 37(9), 2011.

Siemens S2000 – Liver Fibrosis – HCV

Study:	Disease	Total N	AUROC			
			F0 vs F1,2,3,4	F0, 1 vs F2,3,4	F0,1,2 vs F3,4	F0,1,2,3 vs F4
Iijima et al (Japan)	CLD	160				0.925
Sporea, et al (Romania)	HCV, HBV (N=54,17)	183		0.839		0.907
Friedrich-Rust et al (Germany)	HCV, HBV	81		0.84	0.93	0.95
Lupsor, et al (Romania)	HCV	112	0.709	0.851	0.869	0.911
Fier.-Brat. (Romania)	HCV	74		0.902	0.993	0.993
Takahasji et al (Japan)	CLD	80		0.94	0.94	0.96
Goertz et al (Germany)	HCV, HBV (N=36,21)	77		0.85	0.92	0.87
Cabasa et al (Italy)	CLD	60				0.9
Yoneda et al (Japan)	NAFLD	64			0.973	0.976
Barcelona Study	CLD, transplants (N=49, 62)	111		0.855 (CLD), 0.921 (trplants)		
Palmeri et al (Duke)	NAFLD	135			0.9	
Mean Values			0.709	0.875	0.932	0.932

Shear Wave Speed as a Biomarker

- Each ultrasound system produces a shear wave with different frequency characteristics
 - Soft tissues are dispersive (different shear wave speed at different frequencies)
- The (viscous) loss mechanism might make simple (Voigt) model approximation invalid
 - Proportionality between squared shear wave speed and shear modulus might be inaccurate
- Under what clinical conditions can these measurements be made with confidence

Ultrasound QIBA Committee

- Three Co-Chairs
 - Medical Physicist
 - Radiologist
 - Industry Leader

Ultrasound QIBA Committee

- Three subcommittees
 - Evaluate system dependencies
 - Develop/test/select ultrasound phantoms
 - Determine confounding clinical parameters
- Subcommittee formation nearly complete
 - Draft charge to each subcommittee has been circulated
 - Currently determining leadership
 - Determining meeting schedules

Conclusions

- Potential biomarkers identified
 - Shear wave speed for staging liver fibrosis
- Underlying physics reasonably well understood
- Degree of fit with QIBA biomarker selection criteria:
 - Transformative: Likely to change clinical workflow
 - Translational: Laboratory studies and preliminary clinical trials completed
 - Feasible: In clinical use outside of USA
 - Practical: Easy to perform
 - Collaborative: world-wide interest
- Implementations by the various manufacturers
 - At least two ultrasound system manufacturers