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CE-Ultrasound US Elastography for HCC

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CEUS & US Elastography : Contents

CEUS

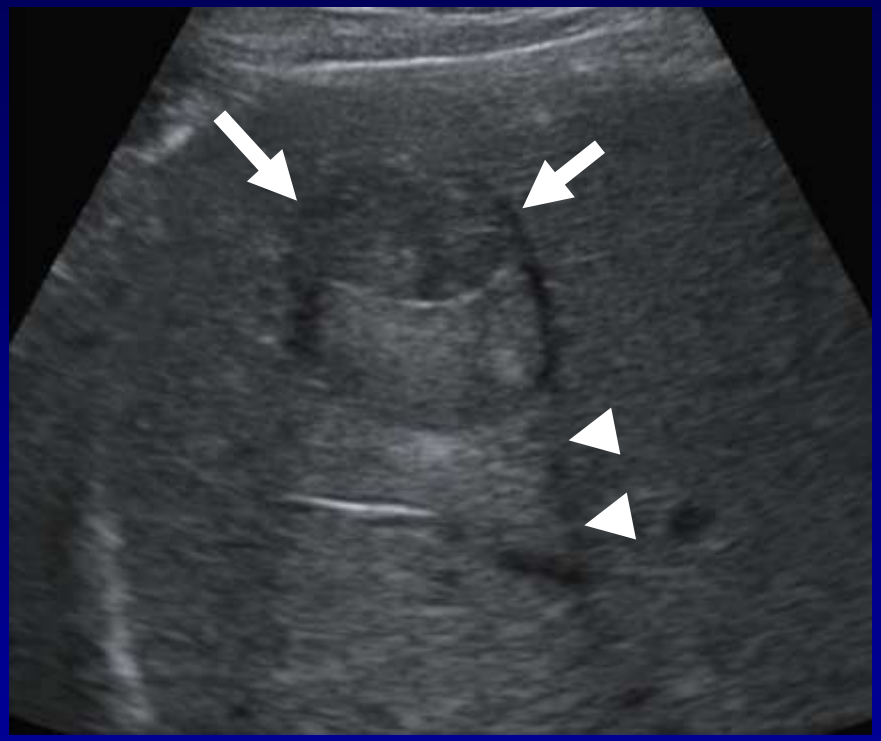
- Introduction
- Contrast agents & imaging
- Clinical application ⇒ US Video WS
- Summary

US Elastography

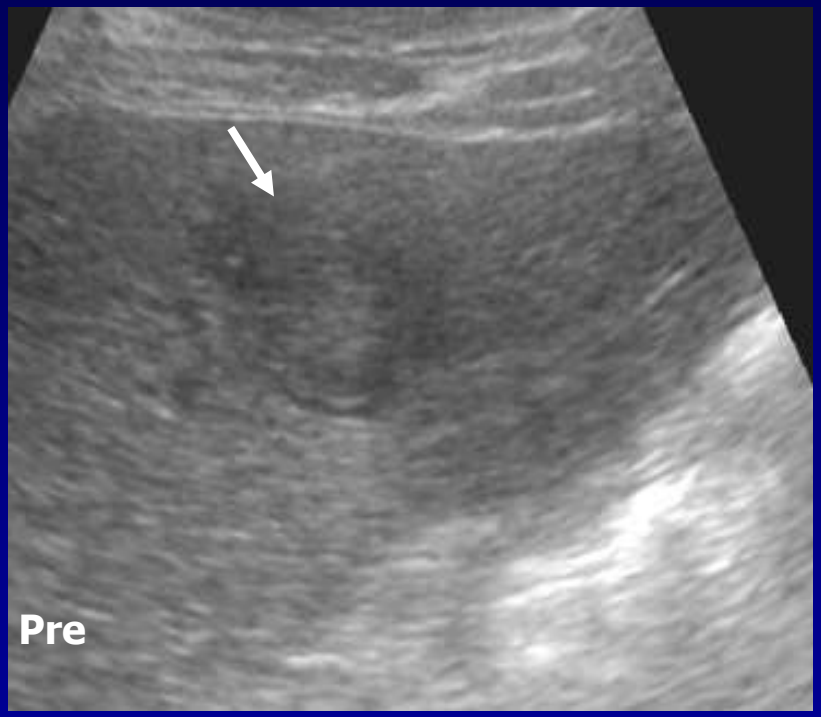
- Introduction
- Clinical application
- Summary

Grayscale US

Diagnosis of liver tumor

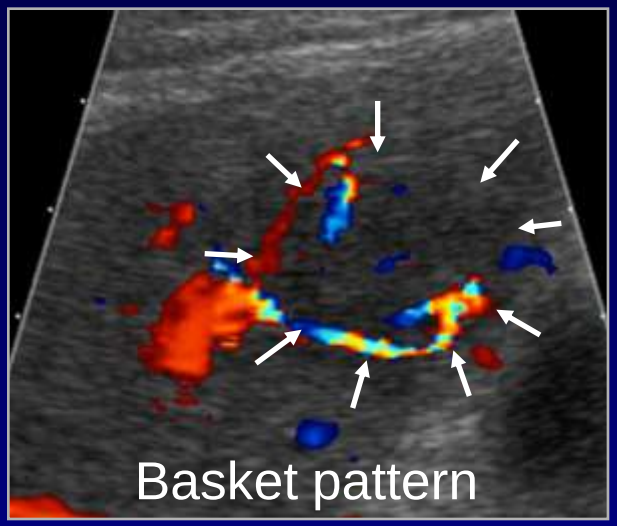


Peripheral halo
Mosaic pattern
Lateral shadowing → HCC



Nonspecific

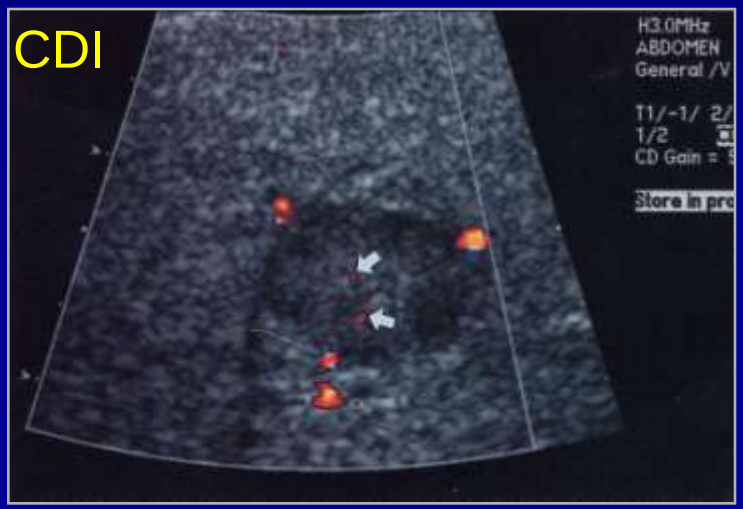
Doppler US : CDI, PDI



Limitations of Doppler

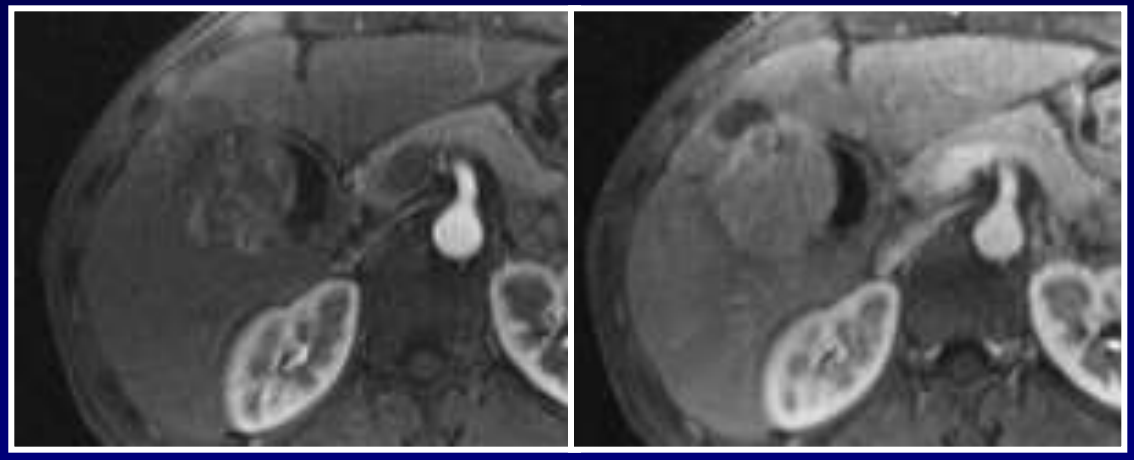
- Not sensitive
- Not specific
- in deeply located small lesion

Detection of Flow in Small Vessels



- Poor Reflectivity of Blood
- Strong Reflectivity of Clutter
- High Attenuation
- Small Doppler Shift

Contrast Agents



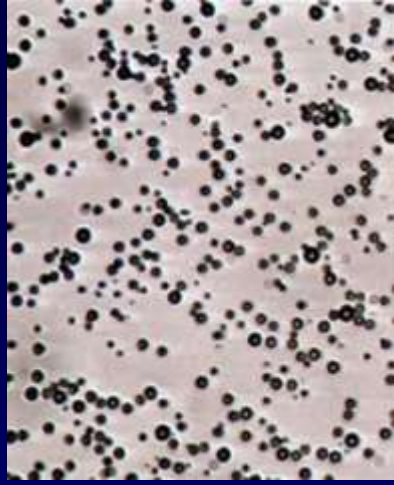
Contrast-enhanced CT or MR has been widely used for

Diagnosis, Characterization of malignant liver tumor

Anatomic mapping

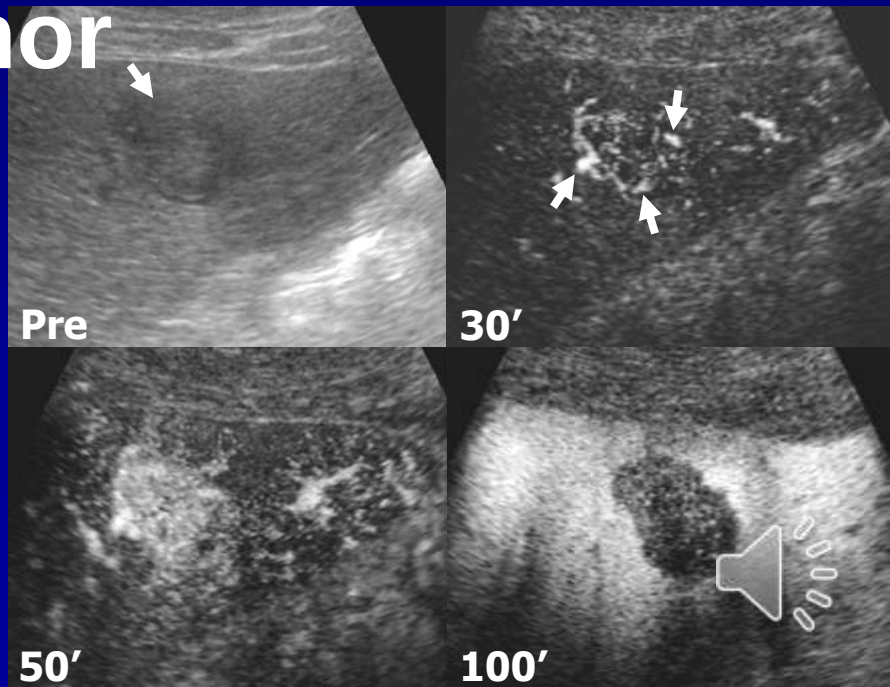
Treatment monitoring

Likewise
US needs contrast agents for



Diagnosis, Characterization
Anatomic mapping
Treatment monitoring
of malignant liver tumor

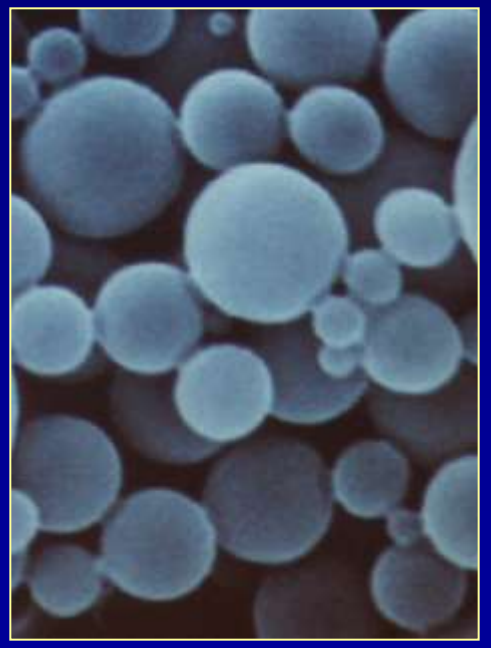
Indication of
CE US



US Contrast Agents

Gas-filled microbubbles with an acoustic impedance different from the blood and relatively permeable shell

- Smaller than 7μm
- Remain within the vascular compartment
- Cross the capillary beds
- Survive passage through the cardiopulmonary circulation



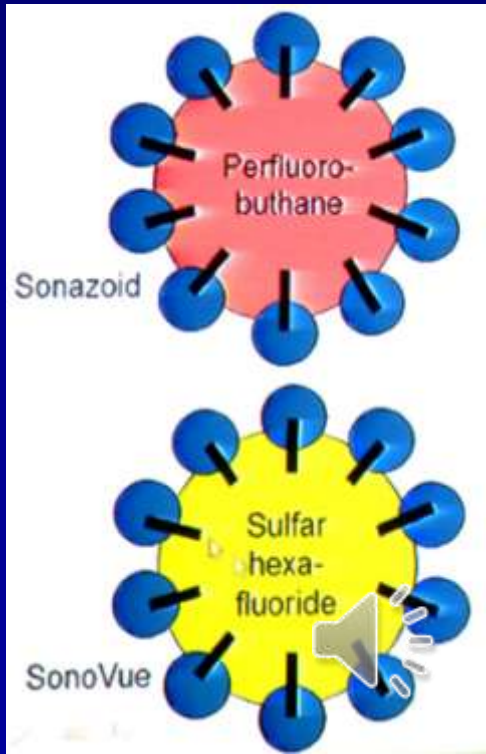
Contrast Agents : Big-5

1st Generation ➔ High MI Imaging

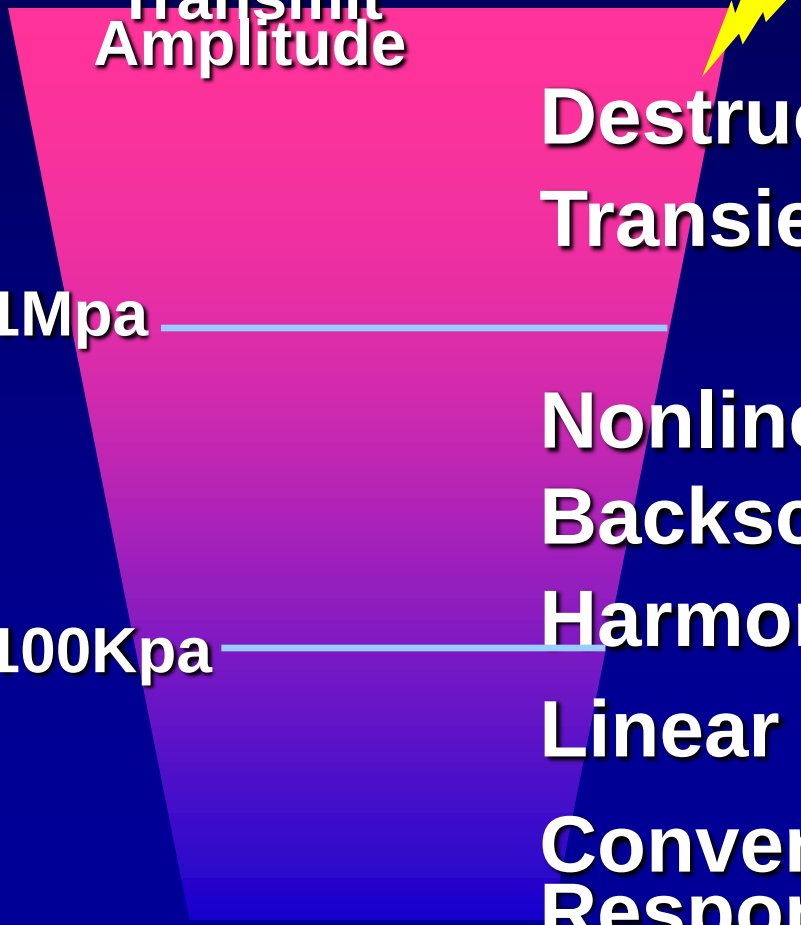
- **Levovist®** ***Schering***

2nd Generation ➔ Low MI Imaging

- **Definity®** **Lantheus Medical**
- **Sonovue®** ***Bracco***
- **Optison®** ***TYCO***
- ***Sonazoid®*** ***GE Healthcare***
  Daiichi-Sankyo



Mechanism for Enhancement



Stimulated Acoustic Emission

Destruction

Transient signal

Nonlinear Backscatter

Harmonic Response

Linear Backscatter

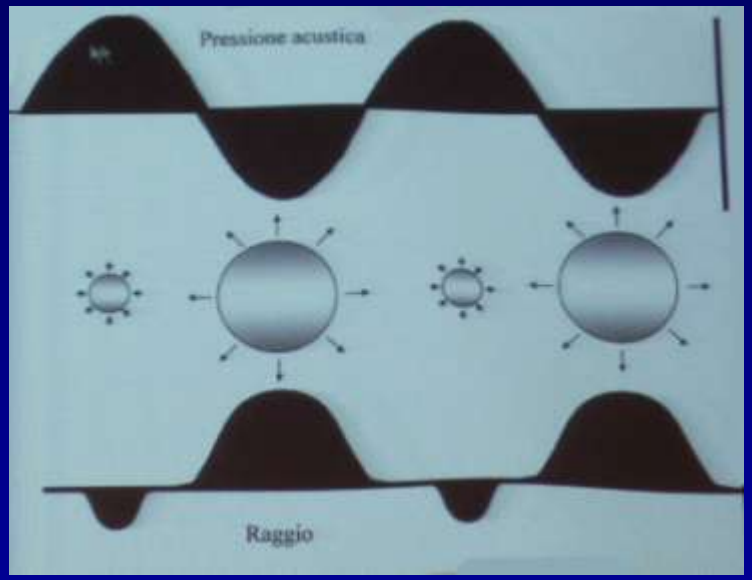
Conventional Response

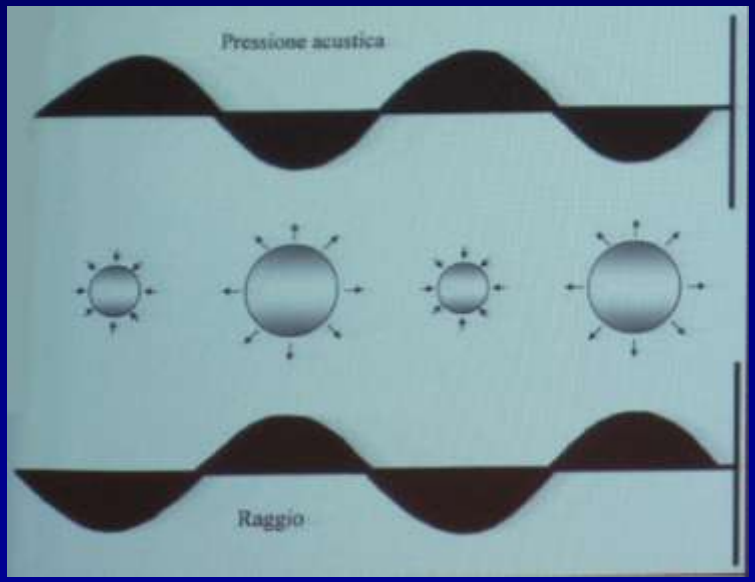
High MI Imaging

Low MI Imaging

Mechanical Index (MI)

- Peak negative pressure of the transmitted pulse
- Indication of the probability of bubble destruction





- **High MI (>0.5)**
  - **Non-linear behaviour**

- **Low MI (< 0.2)**
  - **Symetric behaviour**

Modified from Dr Quaia, ECR 2009

US Imaging Methods for Microbubble

- Fundamental
- Color Doppler (CD)
- Power Doppler (PD)
- Harmonic Power Doppler (HPD)
- Pulse Inversion Harmonic (PIHI)
- Coded Harmonic Angio (CHA)
- Coherent Contrast Imaging (CCI)
- Agent Detection Imaging (ADI)
- Contrast Pulse Sequencing (CPS)

Contrast-enhanced US

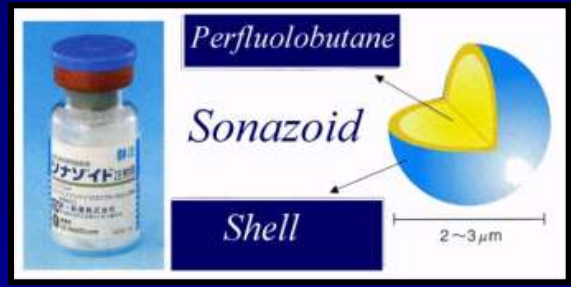
High MI Imaging (> 0.6)

- 1st generation contrast agent
- Disruptive bubble imaging
- Vascular volume assessment

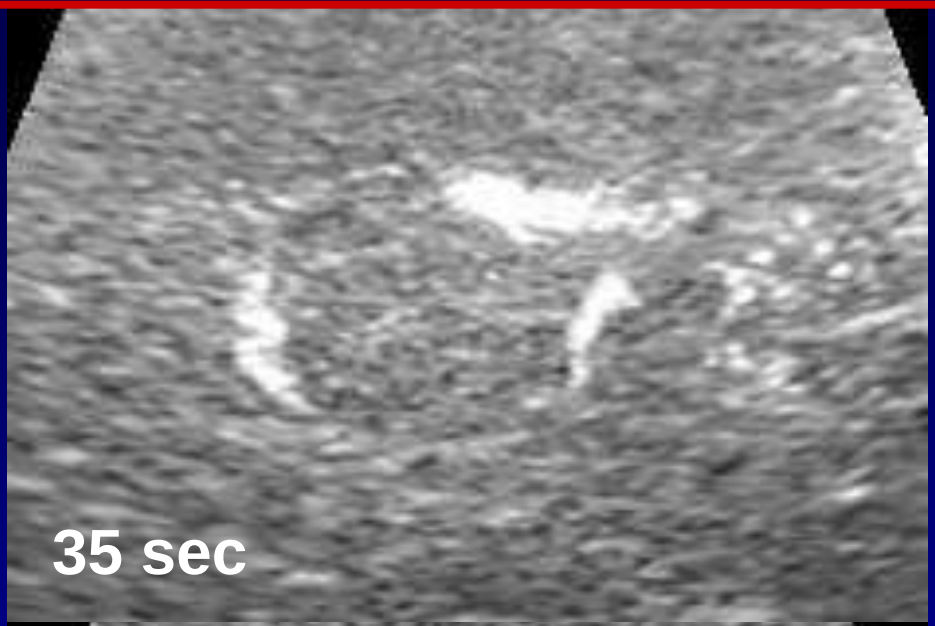
Low MI Imaging (< 0.2)

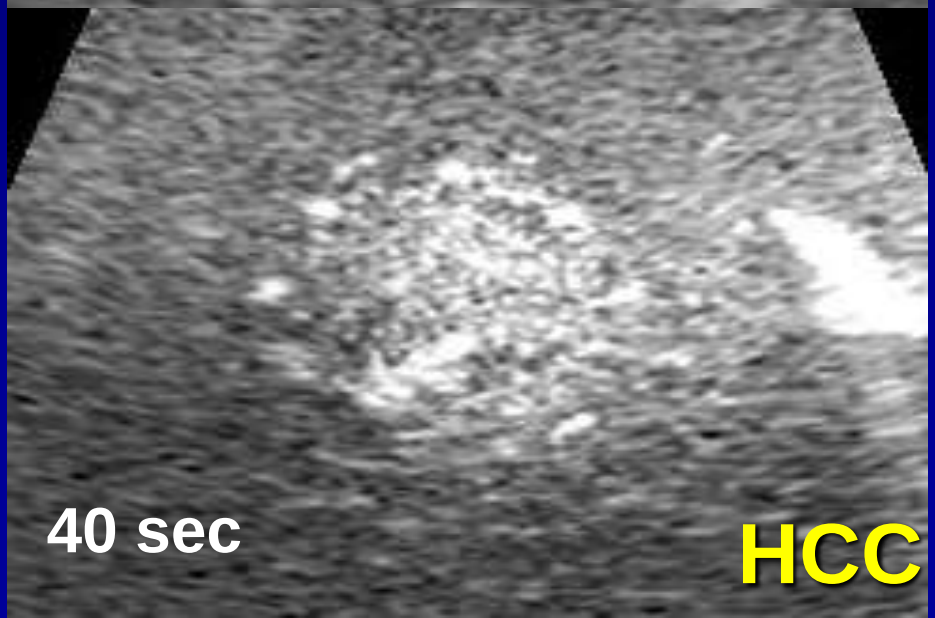
- 2nd generation contrast agent
- Continuous bubble imaging
- Vascularity assessment

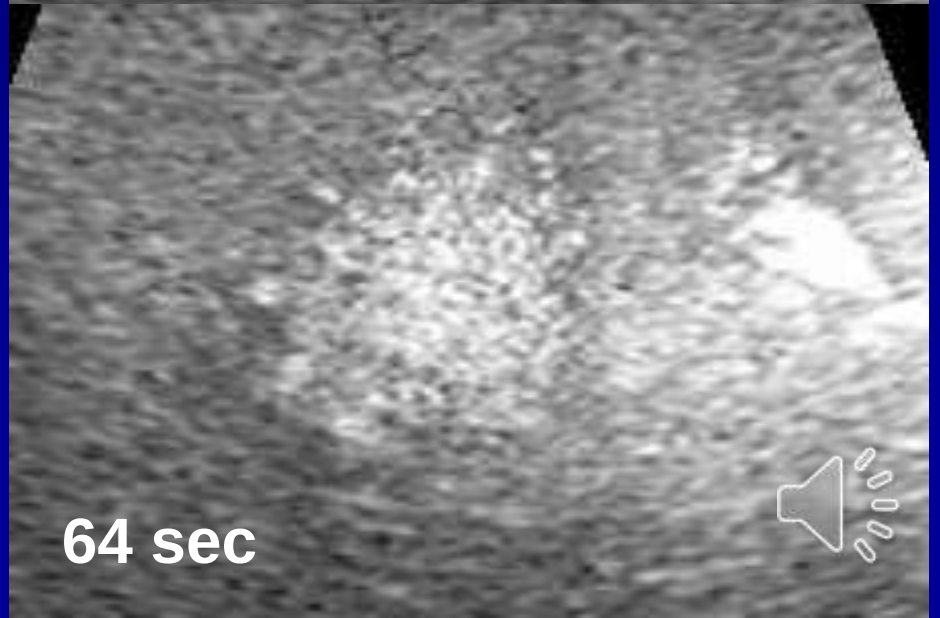
  Kupffer cell function



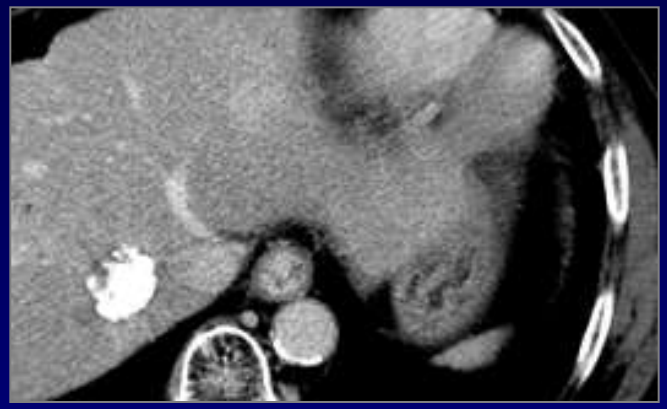
High MI Imaging : CHA







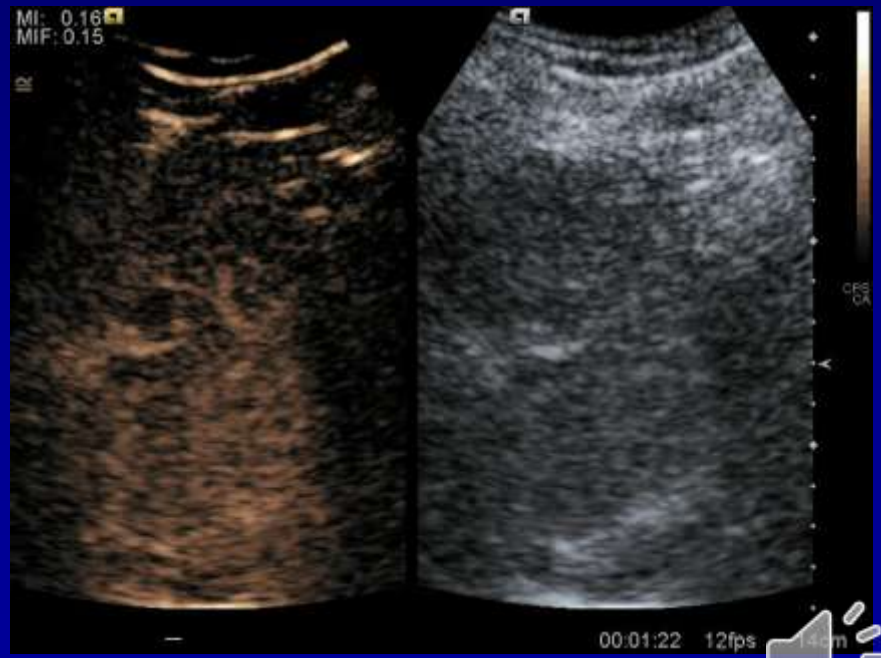
Low MI Imaging



SonoVue

HCC

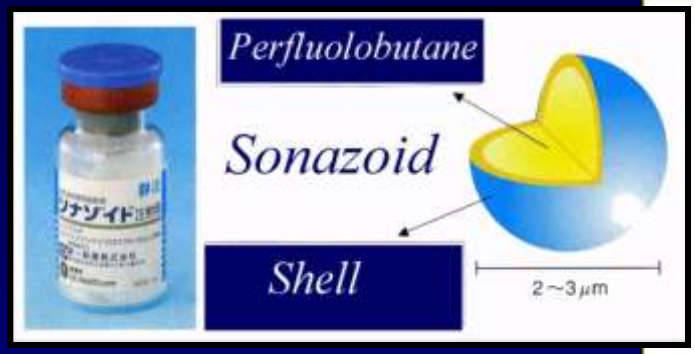
Early phase

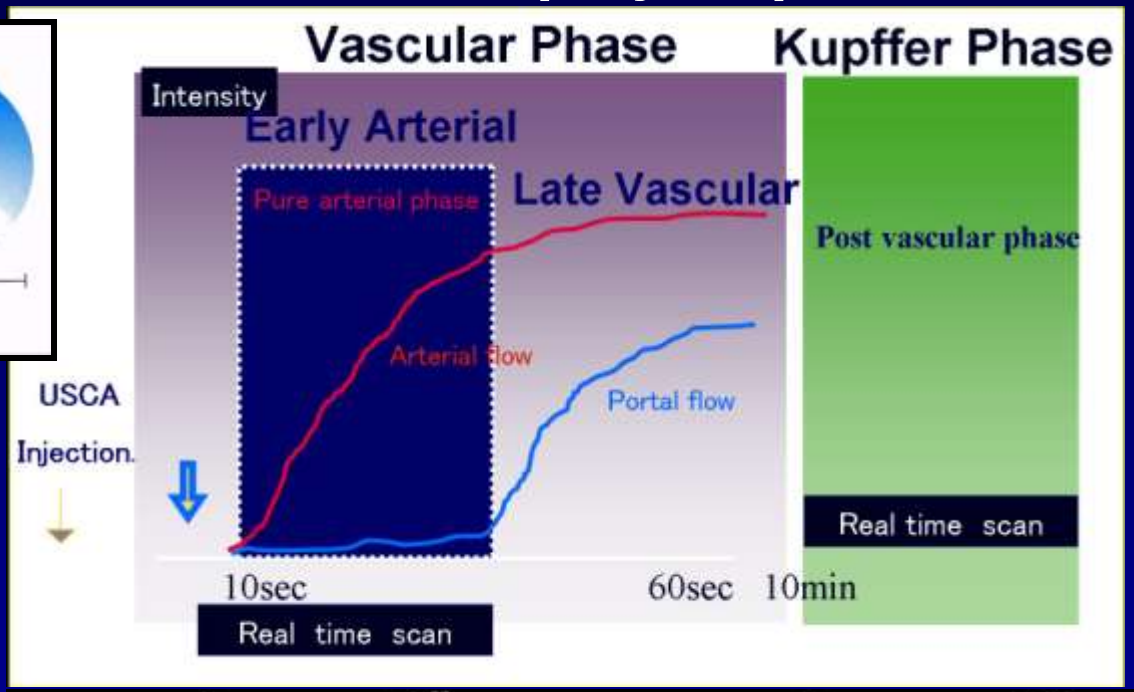


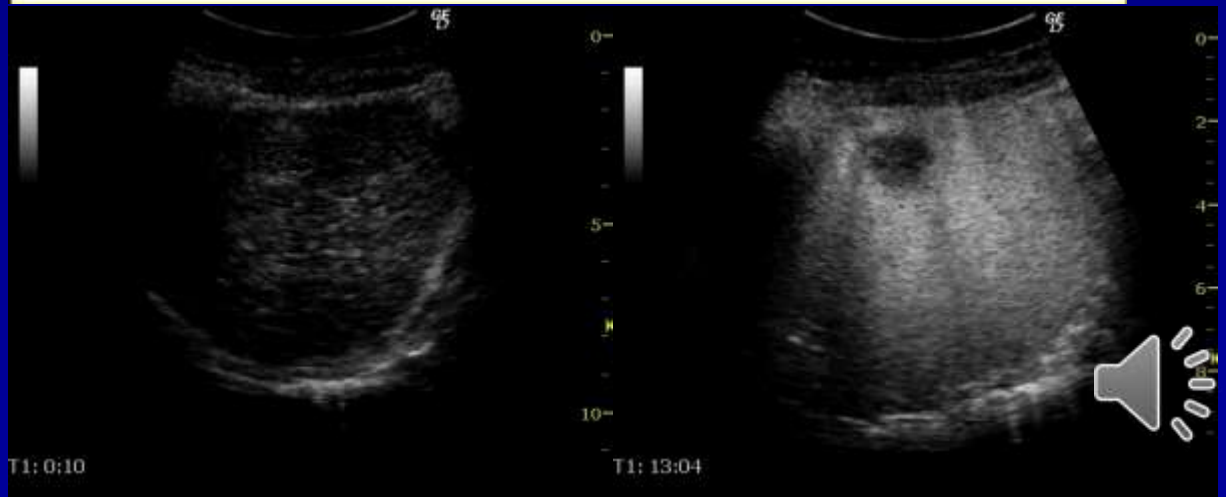
Late phase

Low MI Imaging Sonazoid

Sonazoid Microbubble is taken up by Kupffer cells







Courtesy of Dr Kudo

US Contrast Agent

Agent	Imaging	Approved
Levovist®	Vasclar + (Kupffer)	Worldwide
SonoVue®	Vascular alone	Europe, China, Korea
Definity®	Vascular alone	Canada, Australia, USA
Sonazoid®	Vascular + Kupffer	Japan, Korea

Summary : CE US

- **Focal liver lesion**
  - **Allows lesion characterization**
  - **Reduces the need for CT / MRI**
  - **Improves patient management**
  - **Introduced into guidelines**
- **Percutaneous image-guided tumor ablation**
  - **Allows intra-and post-procedural evaluation**
  - **Might be useful in patient follow-up after therapy as an alternative to CT/MR evaluation**

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Elastography : Hot Issue

From: Joel Gay [mailto:joel.gay@supersonicimagine.com]
Sent: Friday, October 26, 2012 4:26 AM
To: Ziv.Ben-Ari@sheba.health.gov.il; leuyf2@gmail.com; laurent.d.castera@gmail.com; laurent.castera@bjn.aphp.fr; jean-pierre.cercueil@chu-dijon.fr; bichoi@snu.ac.kr; jerome.dumortier@chu-lyon.fr; giovanna.ferraioli@unipv.it; Sven.Francque@uza.be; Mireen.Friedrich-Rust@kgu.de; ivica.grgurevic@zg.htnet.hr; aymeric.guibal@gmail.com; sb328138@skynet.be; keimv@medizin.uni-leipzig.de; didier.lebrec@bjn.aphp.fr; jmsh@snu.ac.kr; olivier.lucidarme@psl.aphp.fr; stanislas.pol@cch.aphp.fr; thierry.poynard@psl.aphp.fr; orensh@tasmc.health.gov.il; james.trotter@baylorhealth.edu; valerie.vilgrain@bjn.aphp.fr; murielw1999@yahoo.fr; p.zoumpoulis@echomed.gr; ushkwang@gmail.com; Dr. Winnie Chu
Cc: Jean-pierre Henry; Aline Criton; Sharon Bruce
Subject: SuperSonic Imagine Aixplorer Liver Users Meeting – Sunday November 11, 7:30 PM, Boston, USA

Dear all,

63rd AASLD Annual Meeting

SuperSonic Imagine is organizing its next worldwide Aixplorer® Liver Users' Meeting in Boston, while attending the 63rd AASLD Annual Meeting (or The Liver Meeting®).
We are very pleased to invite you to join this next meeting in order to discuss how we plan to move forward with the building of proofs of the value of SWE™ in the diagnosis of liver fibrosis.
If you are not planning on attending The Liver Meeting® 2012 and you know some of your hepatologists, gastroenterologists and radiologists colleagues who have worked with Aixplorer® are going, feel free to forward this invitation to them. We will be very happy to welcome them at this Aixplorer® users' meeting.

We thank in advance all sites and representatives who will agree joining this global effort.
Please review the practical details below and inform us on your availability by replying to this email.

The Liver Meeting® is a registered trademark of the American Association for the Study of Liver Diseases.

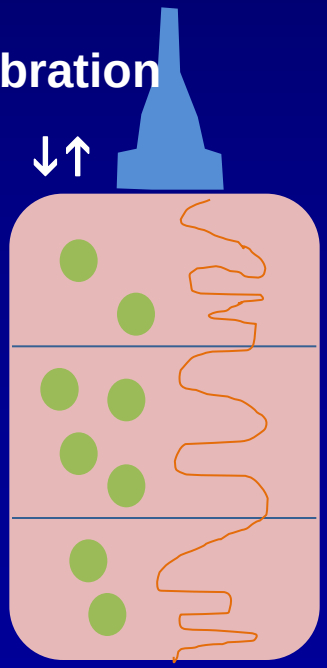
Aixplorer Liver Users' Meeting, Boston, MA, November 2012

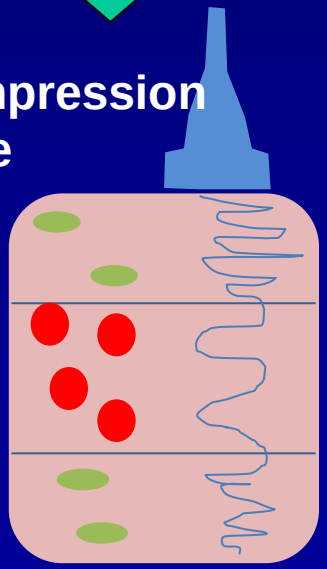
Date and Time
Sunday November 11
7:30-9:00 PM
Location, Venue

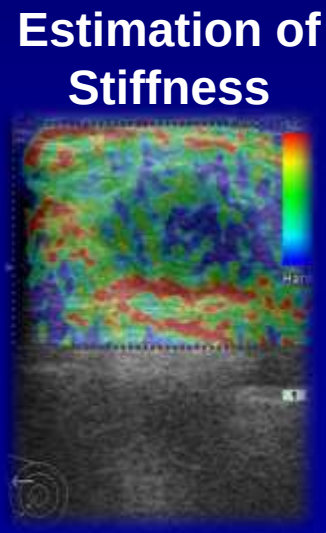
US Elastography

- New technique for studying the elastic property (stiffness) of tissue
- Similar to that obtained with manual palpation, but more sensitive and less subjective

➔ 21C palpation

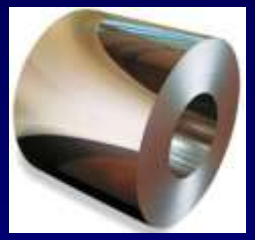






- Limitation (Compression E): Deep organ

What is Elasticity?



Steel is hard

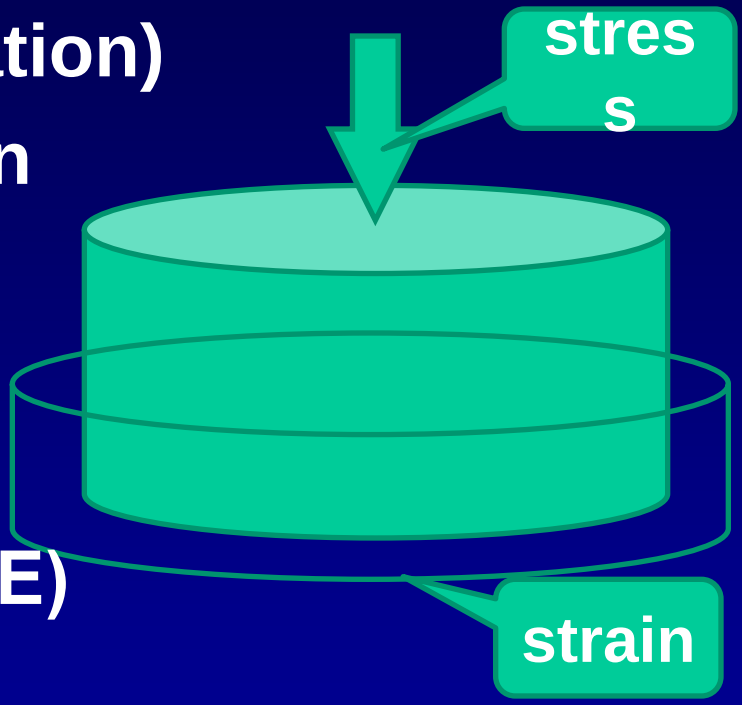
Ice cream is soft

Sponge is elastic

- Elastic material
  - has a resting shape
  - changes its shape when a stress is given
  - restores its shape after the stress is removed
- Elasticity is the degree of shape change (strain) of a given material when a stress is given

Stiffness & Elasticity

- Stress causes strain (deformation)
- Stiff material makes less strain
- The stiffness is in inverse proportion to the elasticity



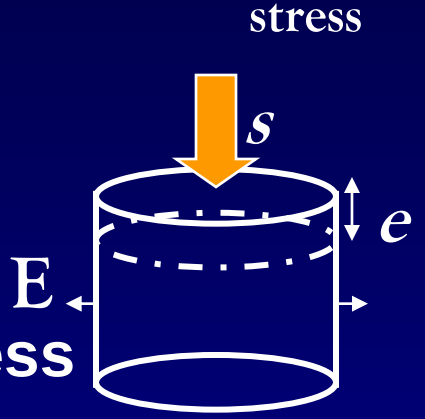
- Stiffness ∝ Young's Modulus (E)
- Tissues show different E

  (normal liver <6 kPa, LC > 15 kPa)
- Measurement of E: $E = S/\varepsilon$ (KPa)

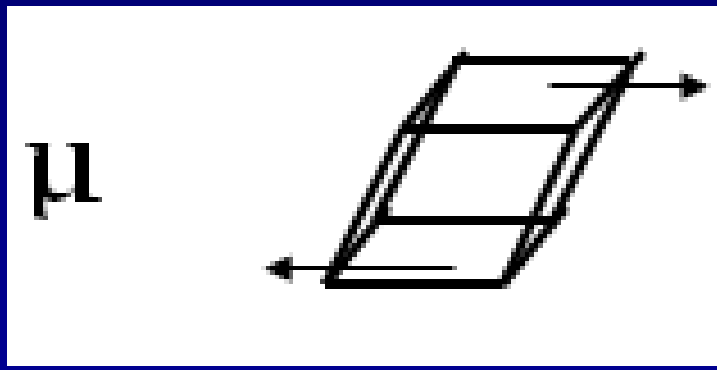
  E: Young's modulus, kPa, S: stress, ε: strain

Elastic Properties of Soft Tissue

- **Young's modulus(E): stress/strain**
  - Elastic property corresponding to palpation
  - Relates longitudinal strain to longitudinal stress



- **Shear modulus:**
  - Relates transverse strain to transverse stress
  - Shear stiffness can be calculated from velocity of shear wave



$$E = 3\rho c_s^2$$

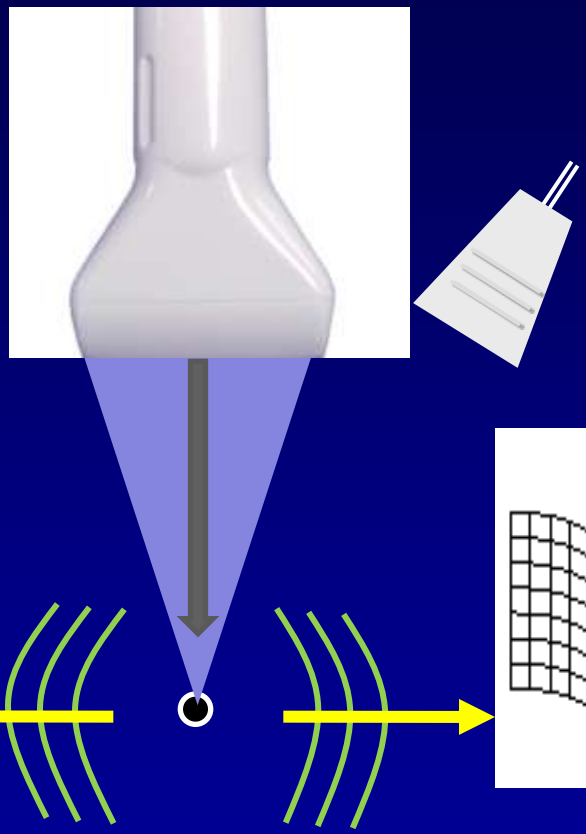
ρ = tissue density, liver: 1000 kg/m3

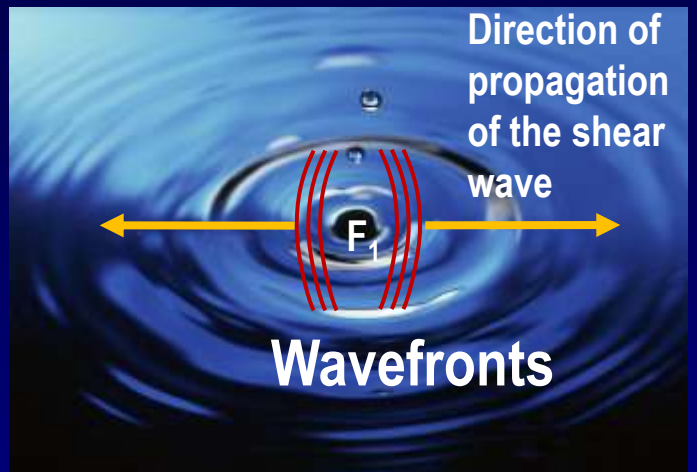
c = shear wave velocity (m/s)

Shear (Transverse) Wave?

Velocity :
~1540
m/s
In tissue

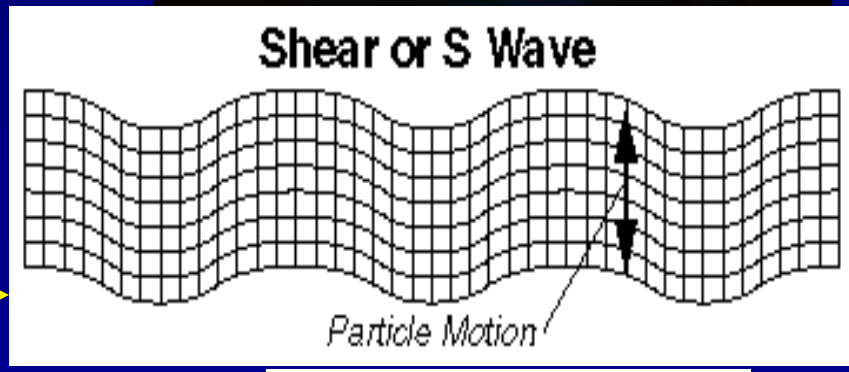
Longitudinal Wave



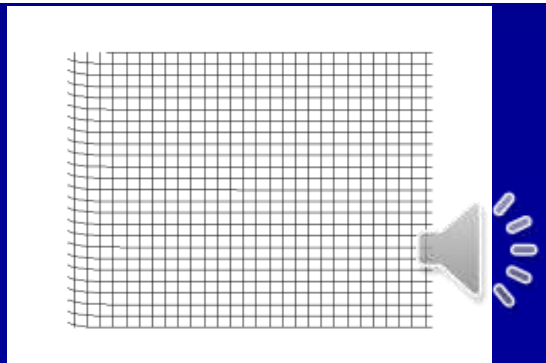


Velocity :
1-10 m/s
In tissue

Shear Wave



$$E = 3\rho c_s^2$$

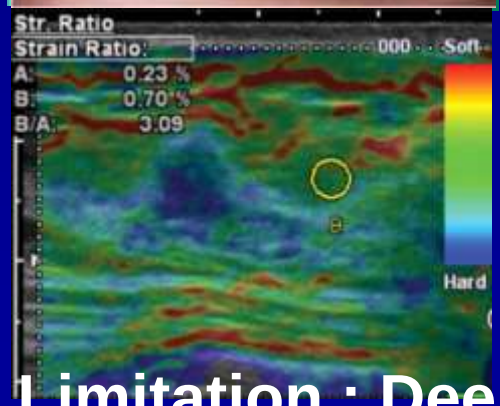


As tissue stiffness increases,
Shear wave velocity increases

US Elastography of liver

Breast vs. Liver by Manual compression

Static elastography



Shear wave-based elastography

Mechanical push

Acoustic Radiation Force Impulse

Transient elastography

ARFI imaging

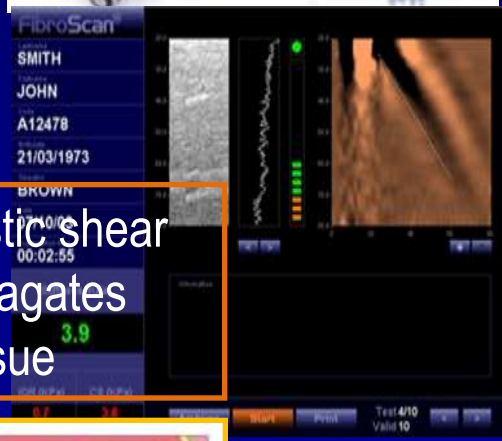
Supersonic SWE

- Limitation : Deep organs

Conventional SWE : TE

Principle of Transient Elastography

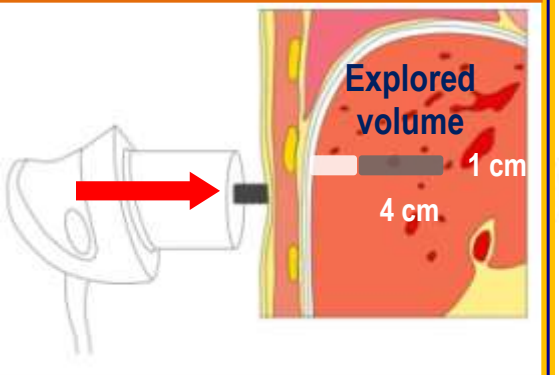
- **Dedicated acquisition platform**
- **External mechanical impulse generating low-frequency shear wave**
- **Recording propagation speed by M-mode acquisition**

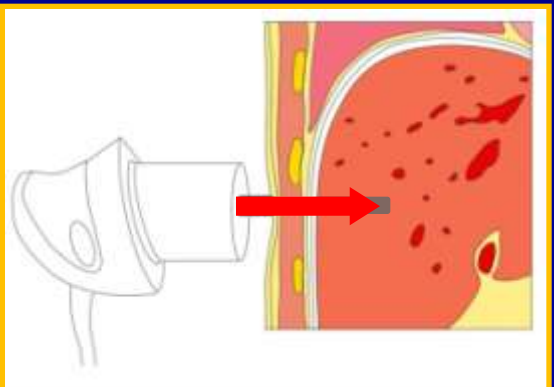


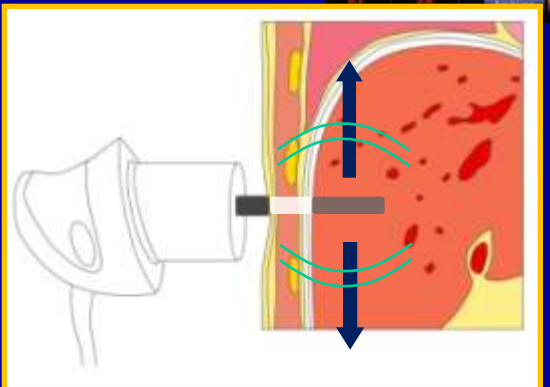
Step 1: Mechanical impulse by a external vibrator

Step 2: Transmitted from the vibrator to the tissues via the transducer

Step 3: An elastic shear wave that propagates through the tissue

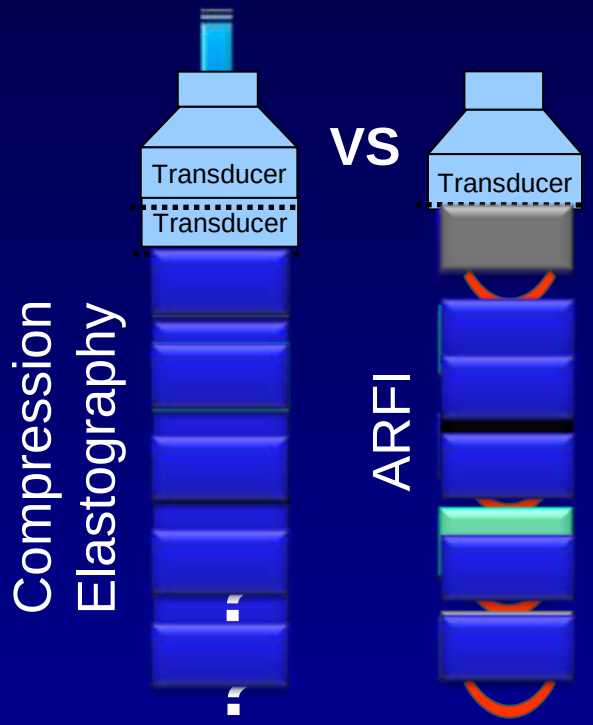


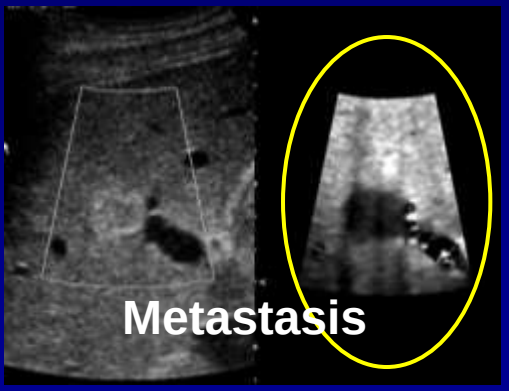


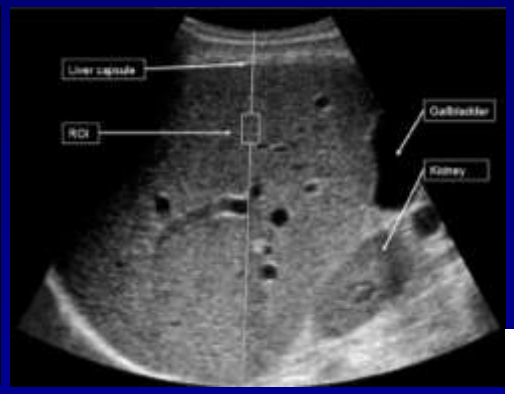


New SWE Imaging

- **Acoustic radiation force impulse Imaging (ARFI): *Siemens***
  - **Virtual Touch Tissue Imaging (I)**
  - **Virtual Touch Tissue Quantification (Q)**

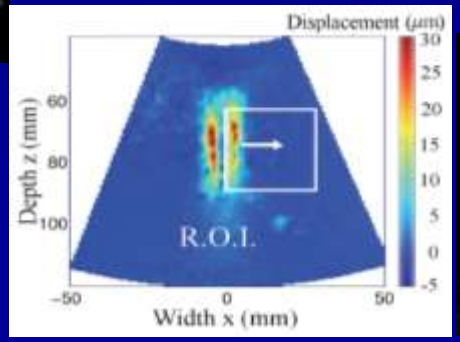




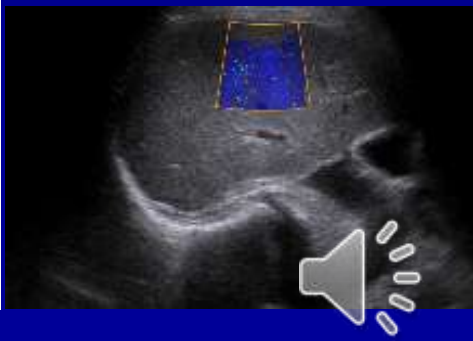


- **Supersonic shear wave E (SSWE):**

  Supersonic Imagine (SSI)



shear wave dispersion



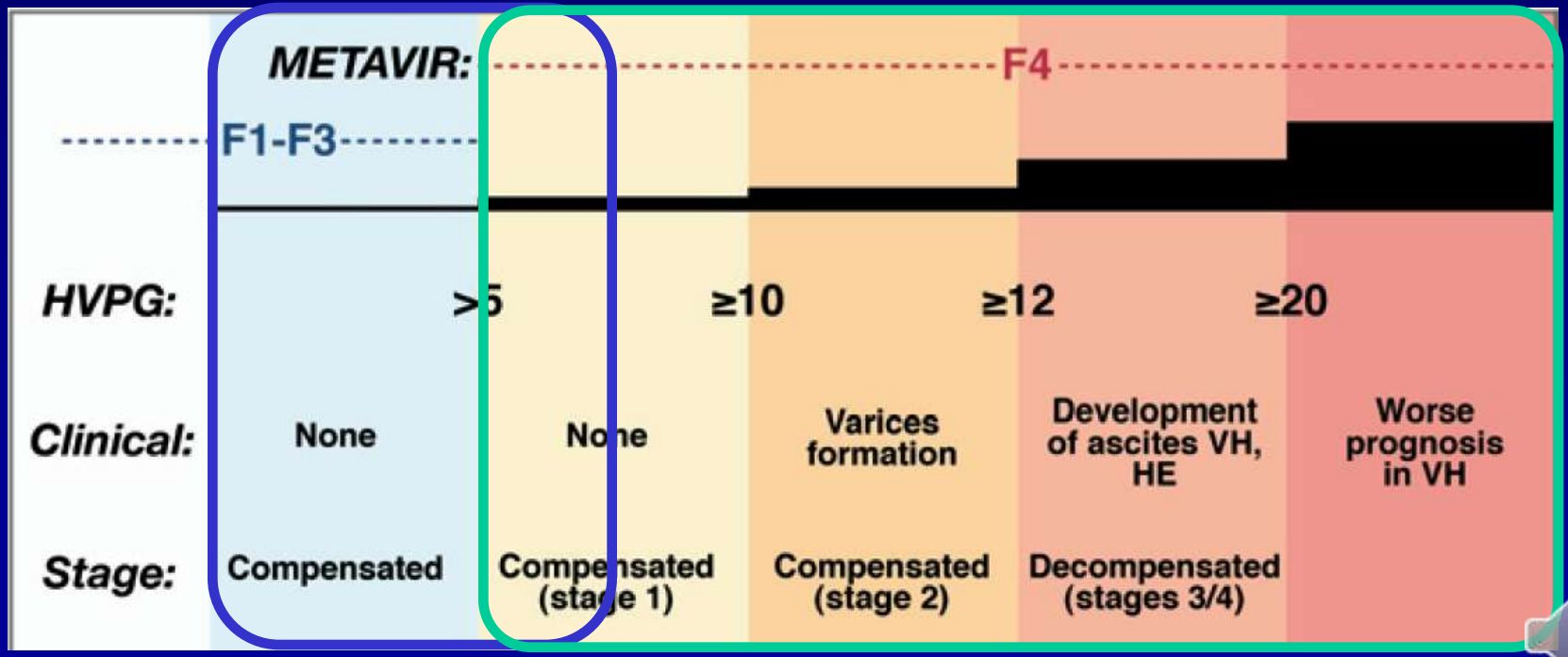
elasticity map

SW-based Elastography

	Product Name	Company	Vibration Source	Frequency
Transient elastography	Fibroscan	Echosens	Mechanical vibrator	50 Hz
ARFI elastography	Acuson S2000	Siemens	Transient radiation force	
Supersonic shear Imaging	Aixplorer	Supersonic Imagine	Transient radiation force	

US Elastography : Hepatic Fibrosis

- **Extensively validated**
  - **Noninvasive**
  - **Easy to repeat**
  - **Quantitative**
  - **Reproducible**

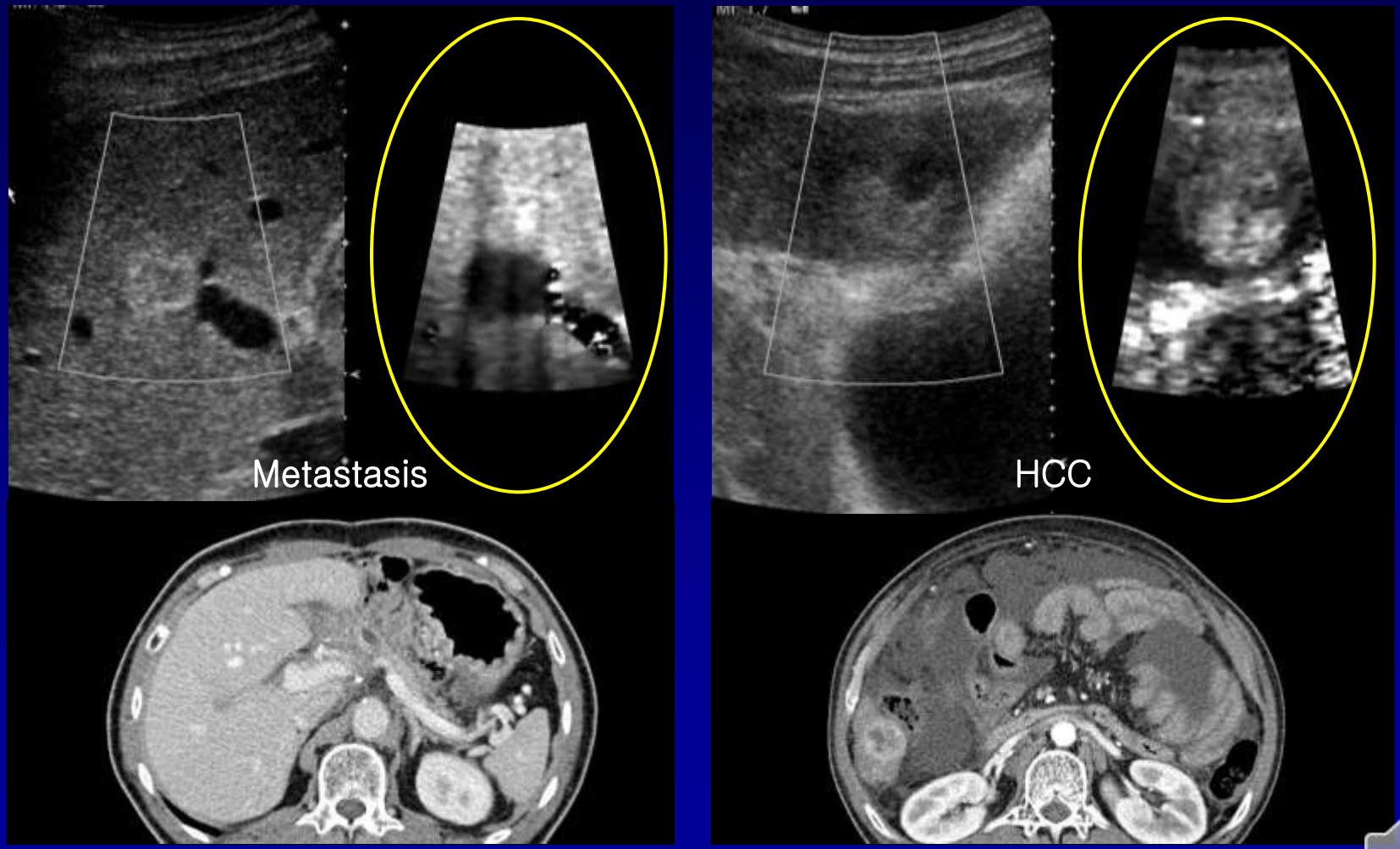


Garcia-Tsao G, et al. Hepatology 2010;51:1-5

Friedman SL. Gastroenterol 2008;134:1655

USE : Focal Liver Lesion

ARFI: Metastasis vs. HCC



Cho SH, et al. Ultrasound Med Biol 2010;36:202-208

Acoustic Radiation Force Impulse Elastography for Focal Hepatic Tumors: Usefulness for Differentiating Hemangiomas from Malignant Tumors

KJR 2013;14:743-753

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Objective: The purpose of this study is to investigate whether acoustic radiat

Table 1. Mean Shear Wave Velocity of Focal Hepatic Tumor Groups

	n	Mean SWV ± SD (m/sec)*
Hemangioma (a)	28	1.80 ± 0.57
HCC (b)	26	2.66 ± 0.94
CCC (c)	3	3.27 ± 0.64
Colon cancer metastasis (d)	20	3.70 ± 0.61
Other metastasis (e)	24	2.82 ± 0.96

SWV for differentiating hemangiomas from malignant tumors was 0.86, with a 65.8% at a cut-off value of 2.73 m/sec ($p < 0.05$). In the ARFI 2D images, the and more conspicuous as compared with the hemangiomas ($p < 0.05$).

Conclusion: ARFI elastography with ARFI quantification and ARFI 2D imaging may be useful for differentiating hepatic hemangiomas from malignant hepatic tumors.

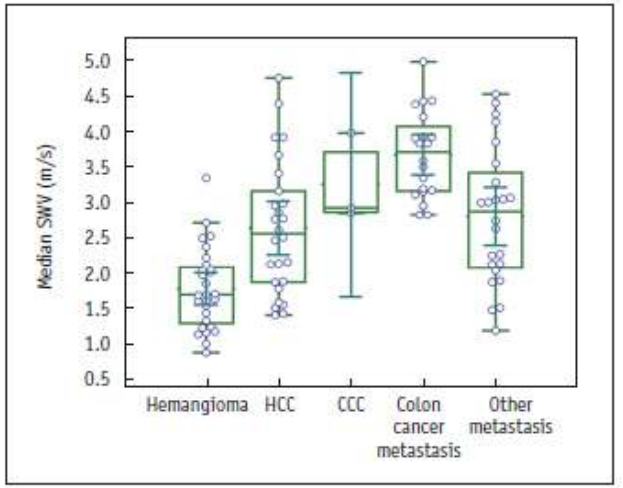
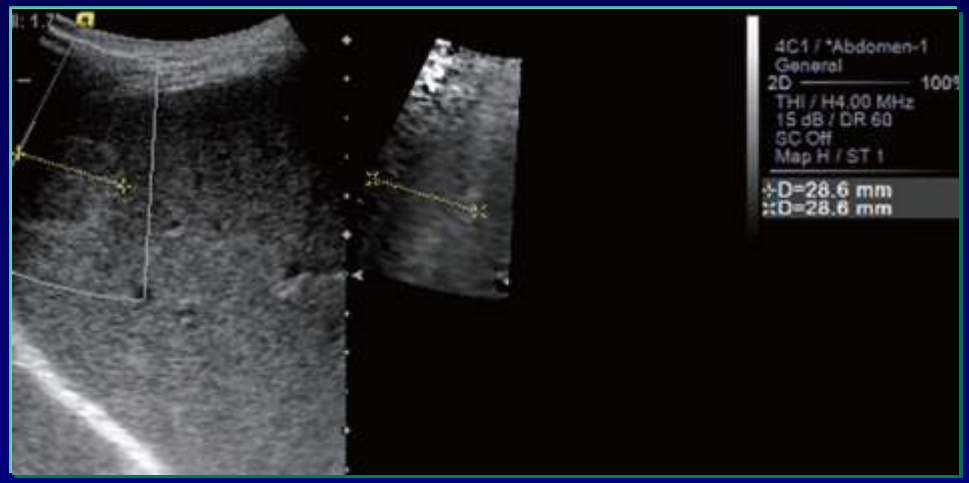
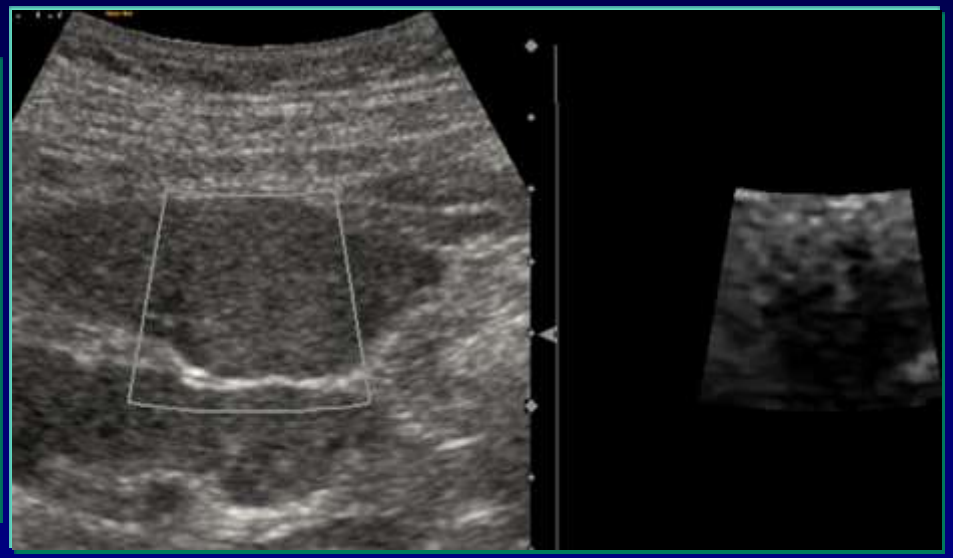
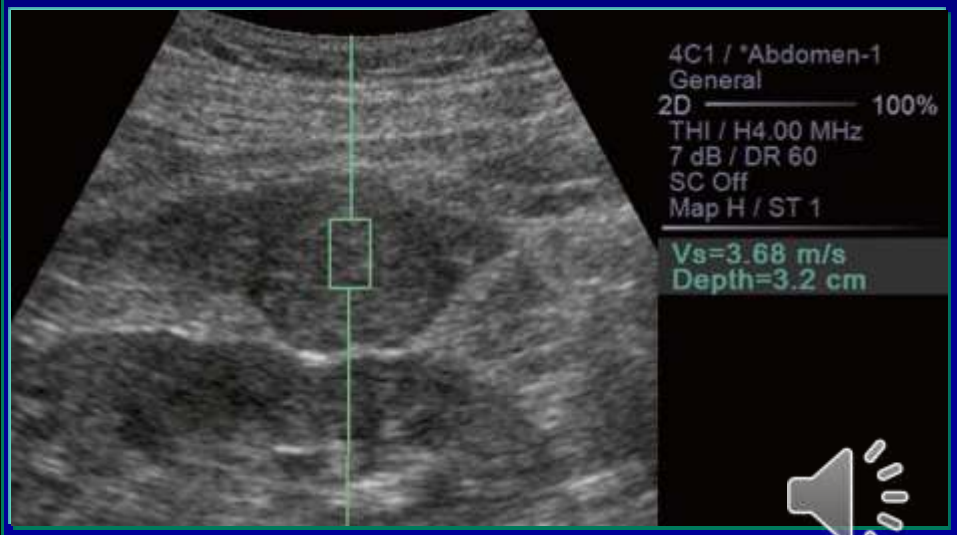


Fig. 1. Combined box-and-whisker and dot plots of median shear wave velocity (SWV) (m/sec, y-axis) among five hepatic tumor groups (x-axis). HCC = hepatocellular carcinoma, CCC = cholangiocarcinoma

ARFI: Hemangioma vs. Mets







KJR 2013;14:743-753

2012 WFUMB USE meeting

EC meeting of WFUMB

2013 WFUMB USE meeting

WORLD FEDERATION FOR ULTRASOUND IN MEDICINE AND BIOLOGY

www.wfumb.org

February 8, 2013

Byung Ihn Choi, MD
Department of Radiology
Seoul National University Hospital
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Dear Dr Choi:

I am writing on behalf of the World Federation for Ultrasound in Medicine and Biology (WFUMB) to invite you to attend a meeting of the WFUMB's Elastography Consensus Committee on March 15-17, 2013 in Washington, D.C.

The schedule of events is as follows:

Friday, March 15
Arrivals
7pm – Group Dinner

Saturday, March 16
8am-6pm – Consensus Meeting
7pm - Group Dinner

Sunday, March 17
8am-1pm – Consensus Meeting
(Meeting may go to 18:00 if it takes longer than we expected together with only available people)
Departures

Your presentation schedule will be on March 16 (Saturday) from 4:00 to 6:00 pm, and your presentation topic is Shear Wave Method of Ultrasound Elastography of the Liver for 20 minutes

WFUMB Elastography Consensus Meeting (Tentative)

Agenda

March 16

1. Welcome and Introduction (8:00-8:20) — Kudo
2. Basics and Terminology (8:20-12:00) — Kudo /Barr (Co-Chair)
3. Liver (13:00-18:00) — Kudo/Cosgrove (Co-Chair)

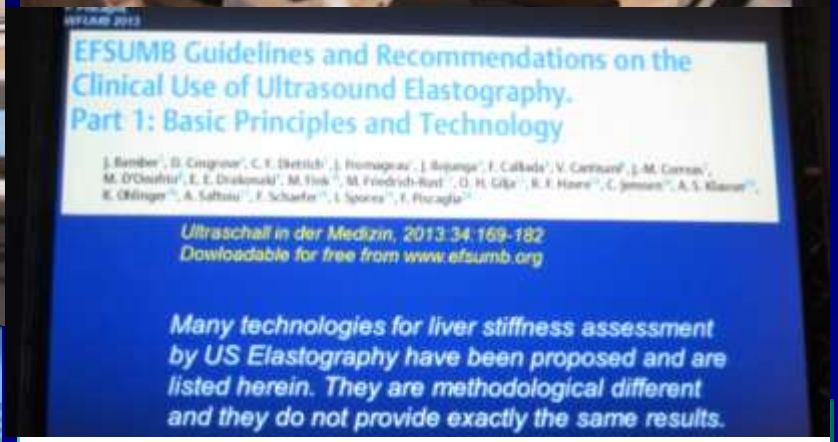
March 17

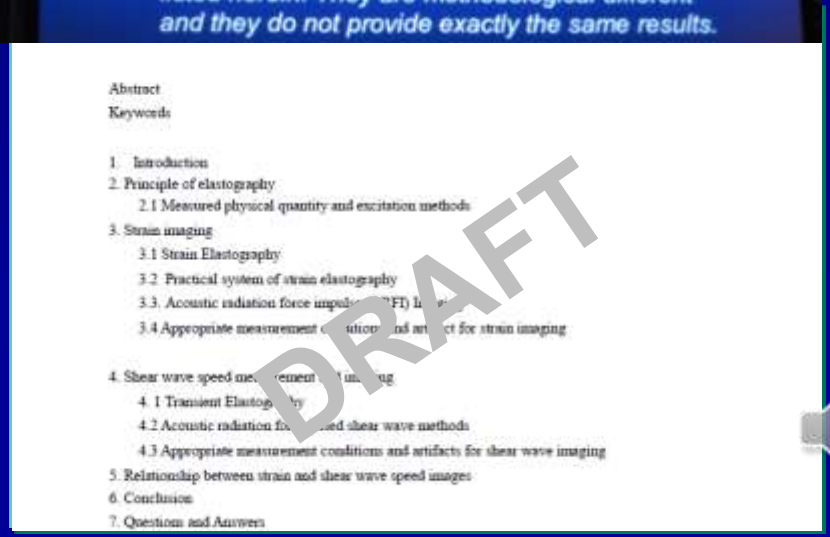
1. Breast (8:00-12:00) — Kudo/Filice (Co-Chair)
2. Thyroid (13:00-16:00) — Kudo/ Wilson (Co-Chair)

- Co-Chair was assigned to the native English speakers (Except Dr. Filice), who are not responsible for draft manuscript writing.
- The allocated time is just tentative. It might be shorter or could be longer depending on the numbers of discussion point.

Washington DC
March 16-17

2013 WFUMB USE meeting





2013 WFUMB USE meeting

The accuracy of elastography methods improves with the severity of fibrosis. The most studied etiology is chronic viral hepatitis. The body of evidence is highly dependent on the method for other etiologies.

-What are the limitations?

Obesity is a common limitation of all ultrasound based elastography methods. Others are narrow intercostal spaces and, for transient elastography, the presence of ascites. Most methods show increased values when amino-transferases are elevated

Some manufacturers do not recommend the use of liver elastography in pregnancy.

-To what extent can elastography reduce liver biopsies?

-Can elastography provide additional information for focal liver lesions?

Currently, the body of evidence concerning the use of elastography in focal liver lesions is not strong enough to recommend its use in clinical practice.

These recommendations are written based on the international literature and on the WFUMB experts group's findings.

WFUMB Guidelines and

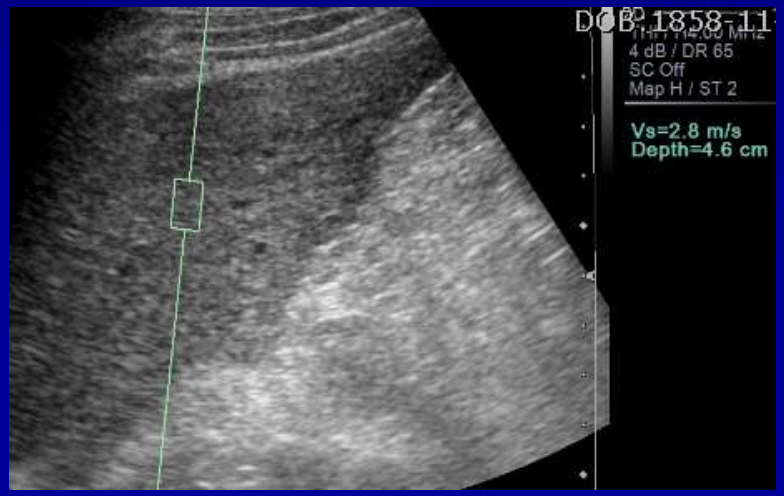
Part 3: Liver

Giovanna Ferraioli, MD [1)]*, Choi, MD(3)[1)], Ioan Sporea, [illegible] F. Dietrich, [5]MD[7)], Dominique Amy, MD (8), Jeffrey C. Bamber, Ph.D(9), Richard Barr, MD, PhD (10), Yi-Hong Chou, MD (11), Hong Ding, MD (12), Andre Farrokh, MD (13), Mireen Friedrich-Rust, MD (14), Timothy J. Hall, Ph.D. (15), Kazutaka Nakashima, (16), Kathryn R. Nightingale, Ph.D. (17), Mark L. Palmeri, MD, Ph.D. (17), Fritz Schafer, MD (18), Tsuyoshi Shiina, Ph.D. (19), Shinichi Suzuki, MD , (20), ~~Carlo Filice[1)]~~, Masatoshi Kudo, MD [21)]

~~*These authors contributed equally to this work.~~

Summary : US Elastography

- Elastography is one of important noninvasive methods to quantify HF more sensitively and objectively
- Currently, the body of evidence concerning the use of US elastography in focal liver lesions is not strong enough to recommend its use in clinical practice
- To avoid confounders of liver stiffness, comprehensive other imaging exams are needed



Thank U