

# ULTRASOUND IN CHRONIC LIVER DISEASE

**Prof. Ioan Sporea, MD, PhD**

Head of Department of Gastroenterology and Hepatology  
University of Medicine and Pharmacy,  
Timișoara, Romania

**WFUMB Center of Education (COE),  
EFSUMB Ultrasound Learning Center**



# US EVALUATION OF THE LIVER STRUCTURE

- ▶ Usually, normal liver texture is homogenous, with hepatic and portal veins very well seen;
- ▶ In pathological conditions, we look for *steatosis* (“bright liver” with posterior attenuation) or for *advanced fibrosis* (inhomogenous liver, irregular surface, signs of portal hypertension, size of caudate lobe).

# The value of US evaluation in **NAFLD** and **NASH** (Non Alcoholic Fatty Liver Disease and Non Alcoholic SteatoHepatitis)

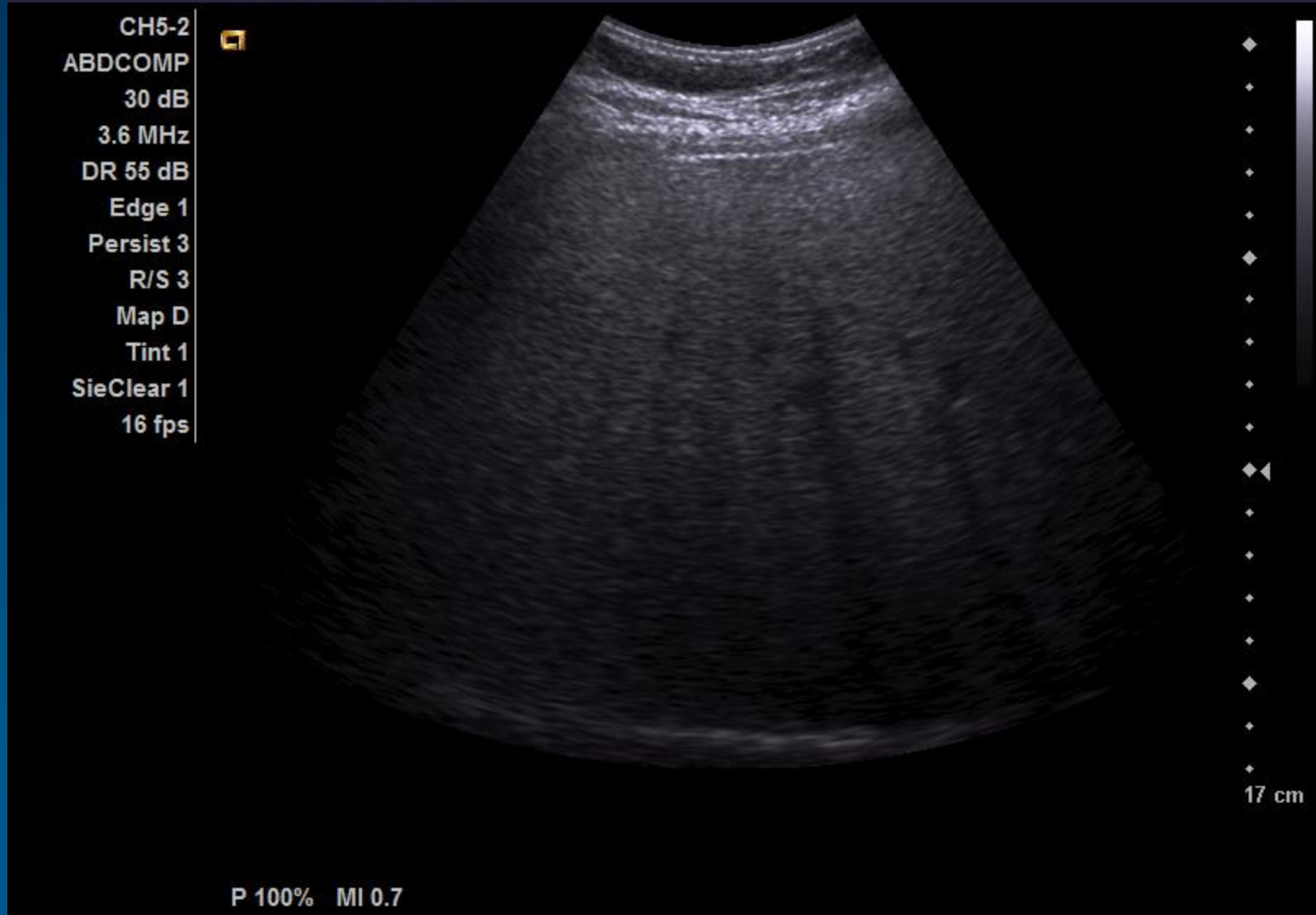


# MODERATE STEATOSIS IN US

SIEMENS

SC SPOREA PRAXIS SRL  
\* 17\_01\_2012\_18\_19\_18

21:54:28 Tu 17/01/2012



# INCREASED HEPATO-RENAL GRADIENT

SIEMENS

SC SPOREA PRAXIS SRL  
\* 31\_01\_2012\_18\_04\_11

21:59:19 Tu 31/01/2012

CH5-2  
ABDCOMP  
30 dB  
3.6 MHz  
DR 55 dB  
Edge 1  
Persist 3  
R/S 3  
Map D  
Tint 1  
SieClear 1  
19 fps



14 cm

P 100% MI 0.7



## ■ “Bright liver echo pattern” with posterior attenuation

■ In a study Palmentieri and al (1) **compared bright liver echo pattern to the liver biopsy**. The study showed in **235 patients** that the **bright liver echo pattern was found in 67% of patients with steatosis of any degree and in 89% of patients with steatosis  $\geq$  30%**.

■ In this study the **sensitivity, specificity, positive predictive value and negative predictive value** of “bright liver” echo pattern and posterior attenuation for steatosis were **64%, 97%, 96% and 65%, respectively**.

■ Among the subgroup of patients who had **steatosis of  $\geq$  30%** the same parameters were: **91%, 93%, 89% and 94%**, respectively.

# US EVALUATION OF STEATOSIS

- In a study performed by our group (1), we tried to evaluate the performance of ultrasound (US) for assessment of the severity of liver steatosis as compared to a pathological examination (LB)
- We performed echo-assisted liver biopsy in **161 patients with chronic hepatitis with the US aspect of “bright liver” with “posterior attenuation”**, using modified Menghini needles.
- In US we divided the aspect in: mild, moderate and severe steatosis.

1. Sporea I et al: "The value of transabdominal ultrasound for assessment of the severity of liver steatosis as compared to liver biopsy". Central. European J. Med. 2009; 4: 490-495

# RESULTS OF THE STUDY

- The results of this study showed that **the sensitivity of US for the prediction of histological steatosis of at least moderate severity was 0.64, with 0.77 specificity, 0.55 positive predictive value, and 0.94 negative predictive value. The overall accuracy was 0.75**
- This study showed that the **transabdominal ultrasound evaluation of the fatty liver is a quite good predictor**, perhaps sufficient for most purposes, **for the estimation of the severity of liver steatosis in the moderate to severe range.**



Mathiesen et al (1) *compared US with hepatic histology for steatosis* in a series of 165 patients.

Steatosis was graded as none, mild, moderate or severe.

In patients with increased echogenicity, 86.7% had liver steatosis *at least moderate*.

For the detection of steatosis, US had a sensitivity of 0.90, specificity 0.82, positive predictive value - 0.87 and negative predictive value - 0.87.

# CAD FOR THE EVALUATION OF STEATOSIS

- ▶ **CAD (Computer Assisted Diagnosis)** was used for the increasing of the accuracy of US for the detection and evaluation of the severity of steatosis (1).
- ▶ In a study performed by our group (2), in 120 subjects, **CAD was able to make a correct classification of the degree of steatosis with an accuracy of 82.2%.**

- ▶ 1. Gaitini D et al: Feasibility study of ultrasonic fatty liver biopsy: texture vs. attenuation and backscatter. *Ultrasound Med Biol.* 2004 ;30(10):1321-7.
- ▶ 2. Mihailescu DM, ...Sporea I. - Computer aided diagnosis method for steatosis rating in ultrasound images using random forests. *Med Ultrason.* 2013 Sep;15(3):184-90.

# META-ANALYSIS-US FOR LIVER STEATOSIS

- ▶ Large meta-analysis (1), with 49 studies and **4720 subjects**, where the **sensitivity of US** for *moderate and severe steatosis* was **84,8% (CI 95%: 79,5-88,9%)**, with a **specificity 93,6% (CI 95%: 87,2-97,0)** in **comparison with liver biopsy**.

- ▶ 1. Hernaez R et al. Diagnostic Accuracy and Reliability of Ultrasonography for the Detection of Fatty Liver: A Meta-Analysis. Hepatology 2011; 54(3): 1082–1090

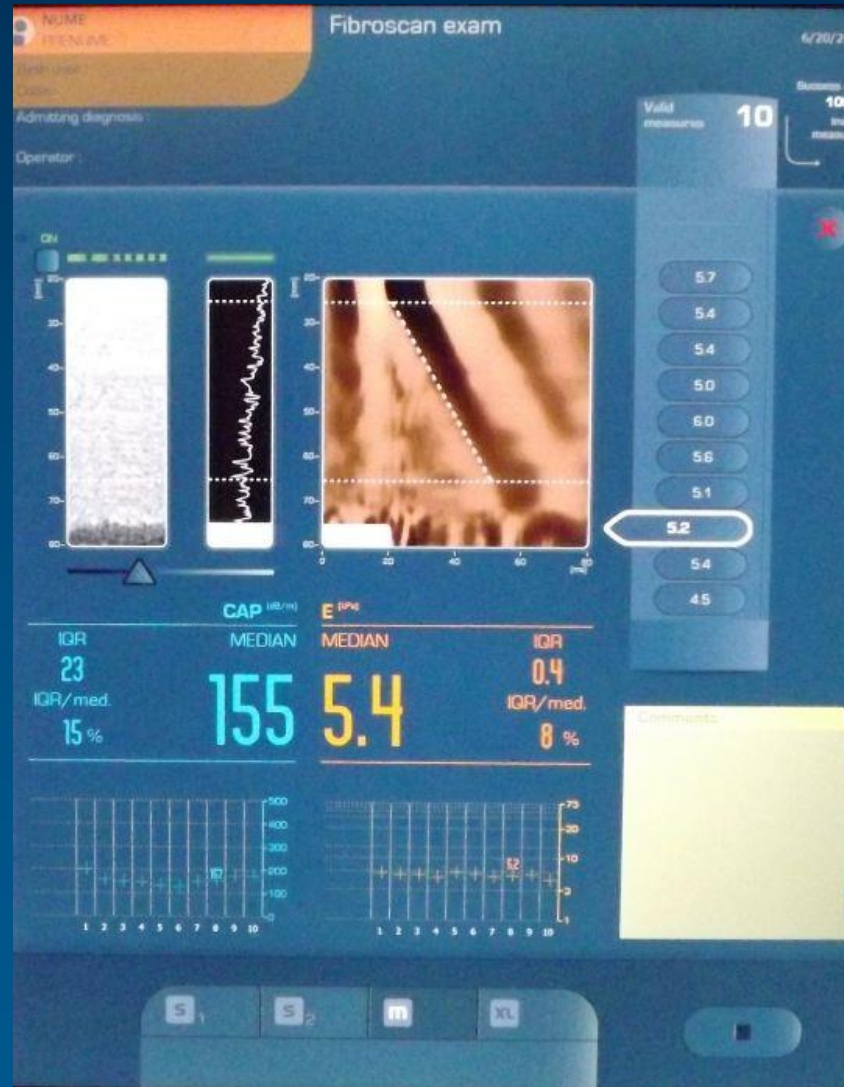
# CONTROLLED ATTENUATION PARAMETER (CAP) - FOR THE EVALUATION OF STEATOSIS

- ▶ The combination in the *same machine (FibroScan) of TE* with **Controlled Attenuation Parameter (CAP)**, which *can objectively evaluate liver steatosis*, is useful for *patients with NAFLD/NASH* (giving an objective quantification of the fatty amount in the liver).
- ▶ In comparison with liver biopsy, **the CAP AUROC's for liver fatty infiltration is between 0.823** (0.809-0.837) and **0.865** (0.850-0.880) % (1,2).

1. Lupşor-Platon M, Feier D, Stefănescu H et al. Diagnostic accuracy of CAP measurement by TE for non-invasive assessment of liver steatosis: a prospective study. J Gastrointest Liver Dis. 2015 Mar; 24(1):35-42

2. Karlas T, Petroff D, Sasso M et al. Individual patient data meta-analysis of controlled attenuation parameter (CAP) technology for assessing steatosis. J. Hepatol. 2017;66:1022-1030

# THE SCREEN OF FIBROSCAN



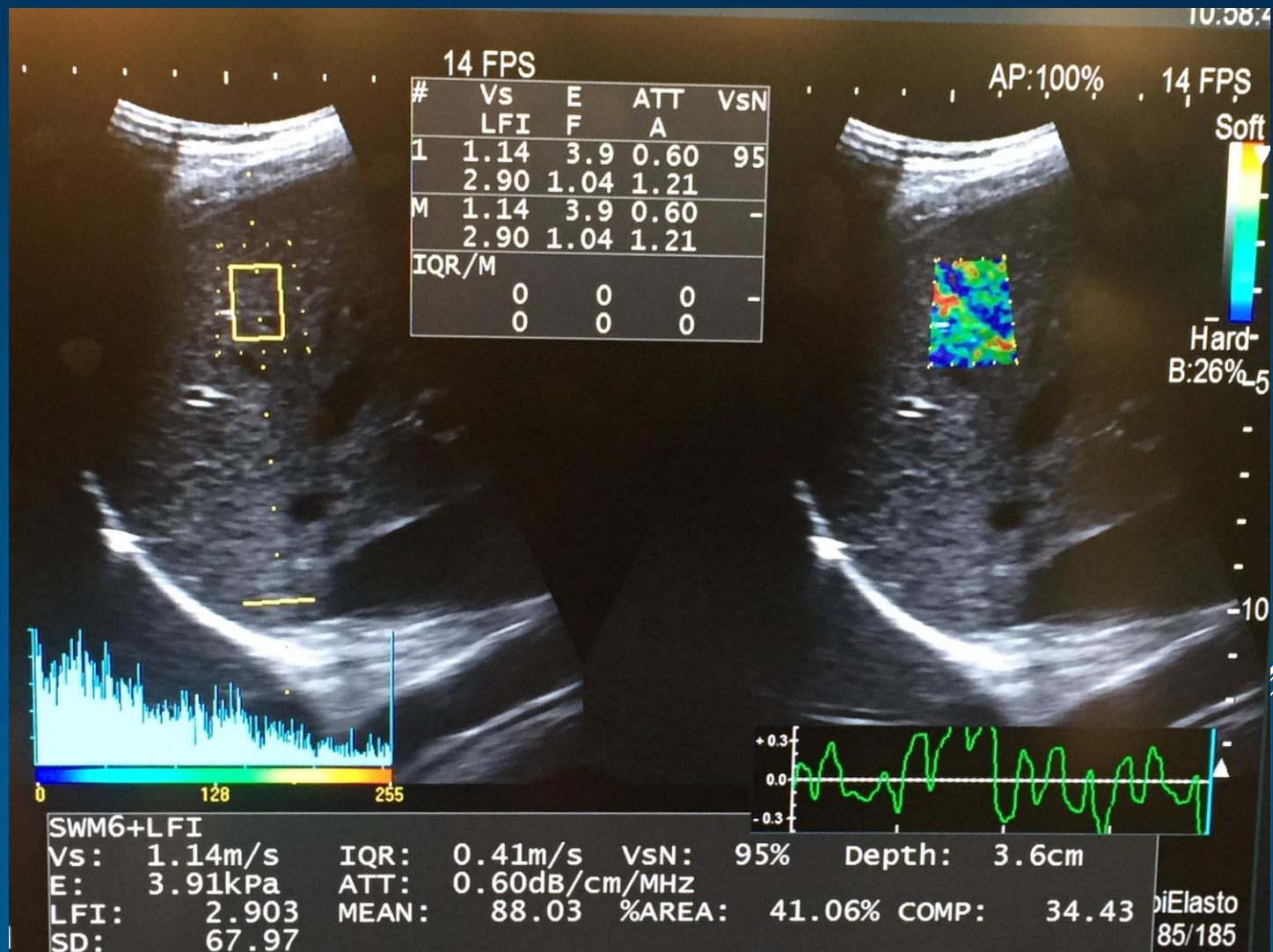
# WHICH ARE THE CUT-OFF VALUES OF CAP ?

- ▶ **Proposed cut-off values for CAP are:**
- ▶ **Mild steatosis > 250 dB/m**
- ▶ **Moderate steatosis > 270 dB/m**
- ▶ **Severe steatosis > 290 dB/m**

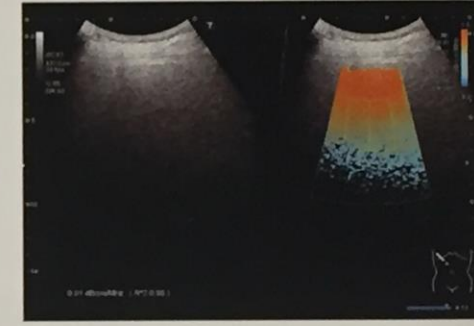
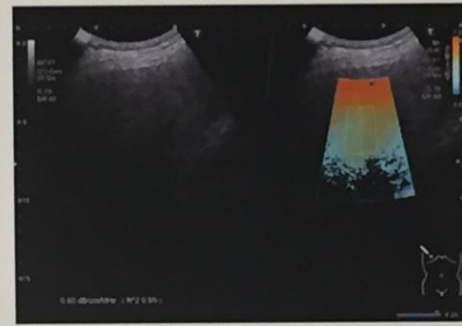
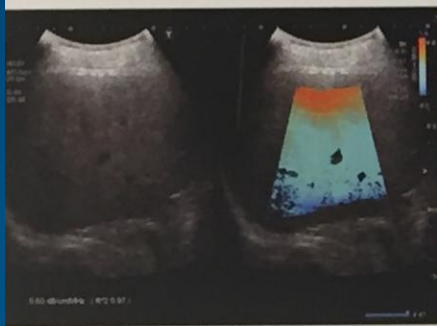


# LAST MINUTE FOR STEATOSIS EVALUATION

## COMBI-ELASTO: POINT SWE + STRAIN + ATTENUATION



# ATTENUATION IMAGING FOR STEATOSIS QUANTIFICATION



Modality	Mild
CAP	0.634* (222 dB/m)
ATI	0.672*
CT (L/S)	1.35
Histology	NA

Modality	Moderate
CAP	0.871* (305 dB/m)
ATI	0.818*
CT (L/S)	1.03
Histology	20%

Modality	Severe
CAP	0.97* (341 dB/m)
ATI	0.938*
CT (L/S)	0.73
Histology	NA

\* In dB/cm/MHz. Average value after 10 measurements.

# CORRELATION CAP/ATI (ATTENUATION IMAGING)

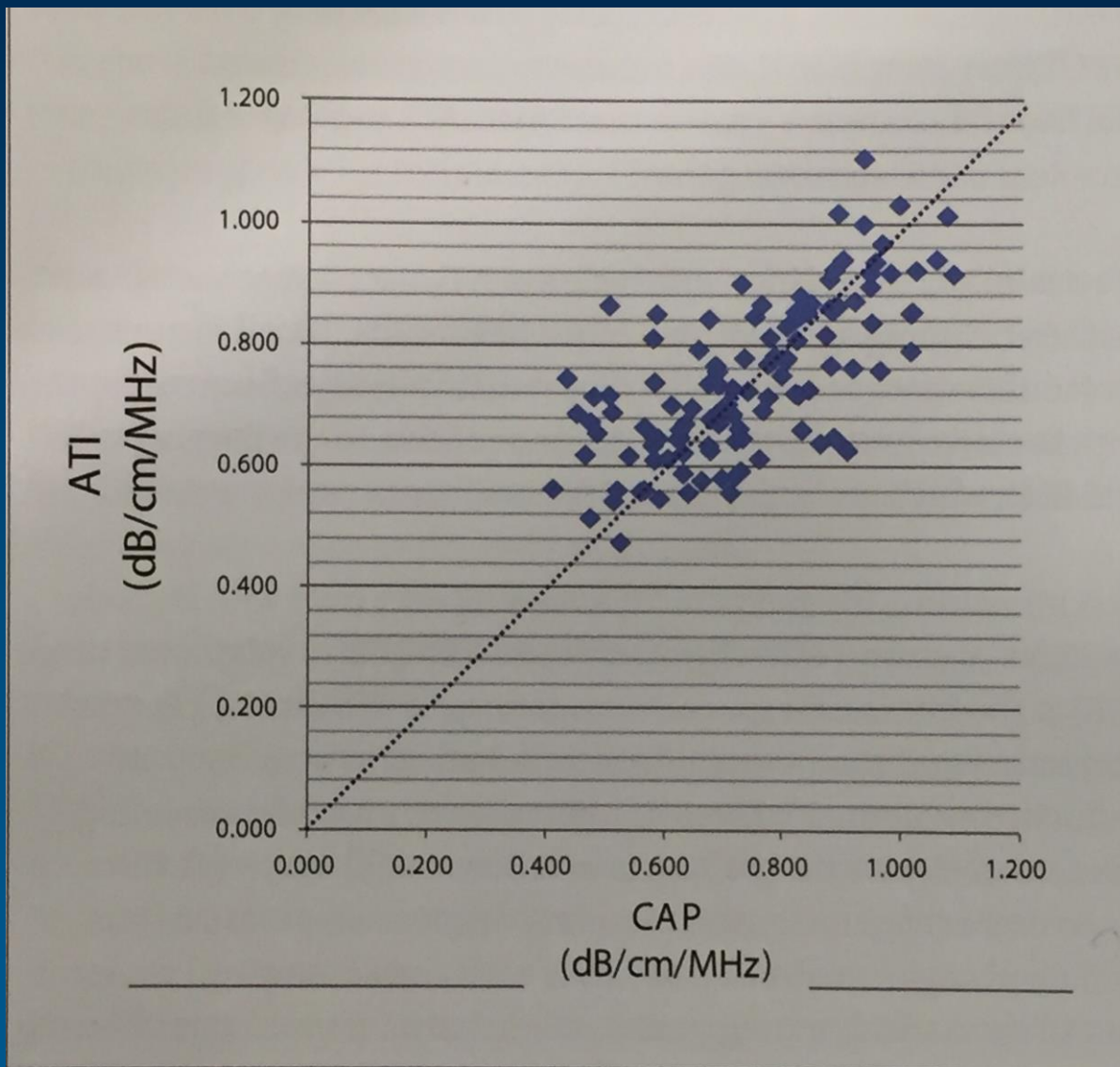


Figure 4. Correlation between ATI and CAP.

# LIMITS OF US IN LIVER STEATOSIS

- **NAFLD and NASH can not be differentiated by US (steatosis vs. steatohepatitis) :**

- Ataseven et al (1): “ultrasonography findings do not reflect the histopathological severity in patients with NASH” (but the results appear the same for CT);
- Saadeh et al (2): “differences between NASH and nonprogressive NAFLD were not apparent with any radiological modality (US, CT, MRI)”
- **Conclusion: for the diagnosis of NASH only the severity of steatosis was reflected by the radiological methods (2)**

1. Ataseven H et al - Acta Gastroenterol Belg. 2005; 68: 221-225

2. Saadeh S et al - Gastroenterology 2002; 123: 745-750



# HOW CAN WE USE ULTRASOUND WAVES FOR THE EVALUATION OF LIVER FIBROSIS?

**1. Using the classic ultrasound evaluation of the liver** (assessment of liver structure, hepatic margins, splenomegaly, caudate lobe dimensions or signs of portal hypertension);

Or

**2. Modern methods of liver stiffness assessment** (Transient Elastography, point SWE, 2D-SWE)

MI: 1.2



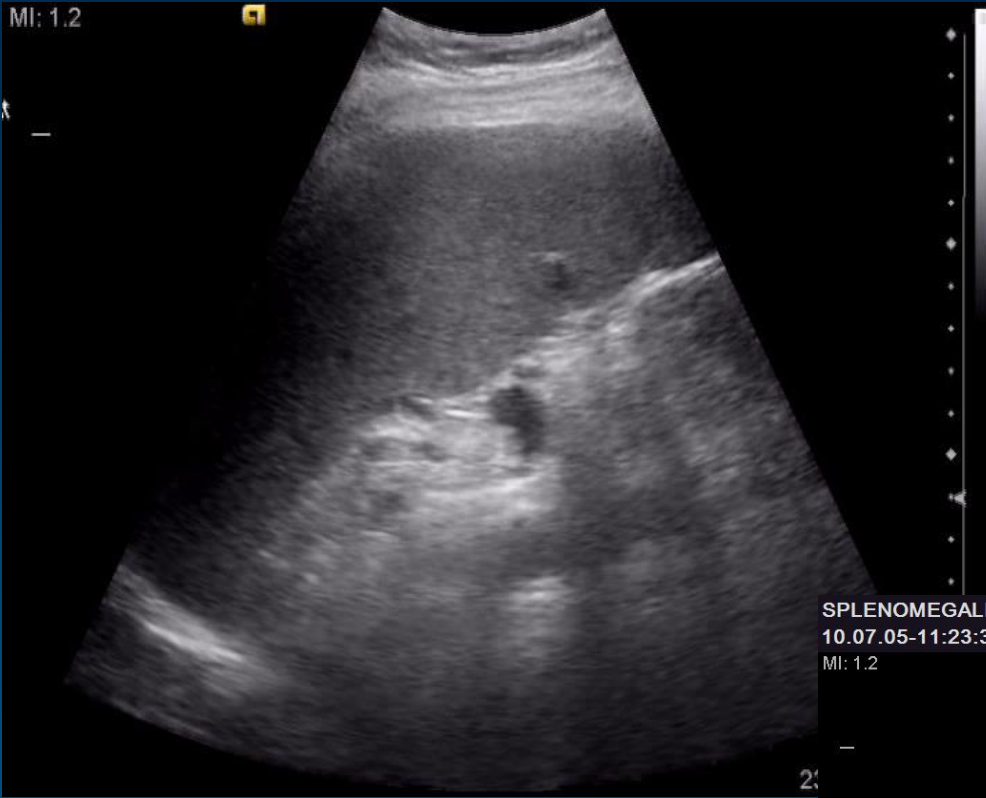
28fps

15cm





MI: 1.2

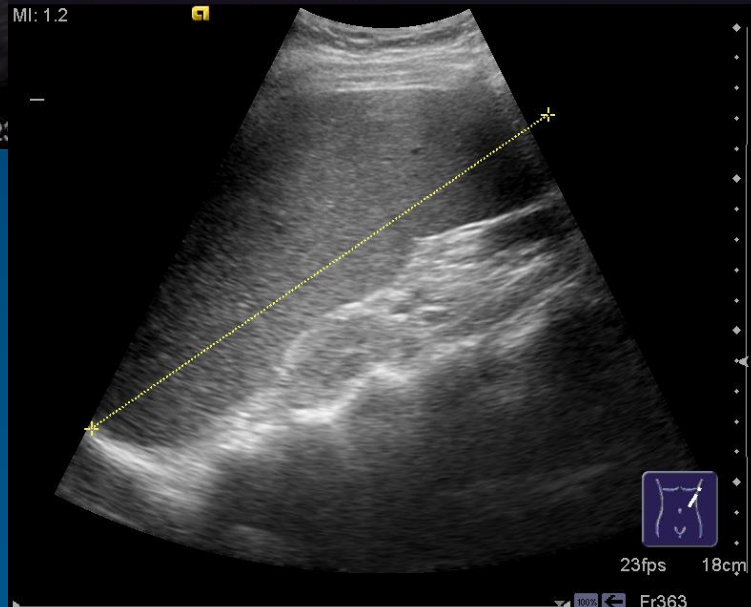


SPLENOMEGALIE

11:24:55 AM 7/5/2010

10.07.05-11:23:33-DST-1.3.12.2.110...

MI: 1.2



SIEMENS

4C1 / Abdomen

General

2D 100%

THI / H4.50 MHz

5 dB / DR 65

ASC 3 / DTCE L

Map J / ST 1

D=182.8 mm



23fps 18cm

Fr363

MI: 1.1



**QUADRAT LOBE ENLARGEMENT**



25fps

17cm



U.M.F. TIMISOARA

SIEMENS

Me 28/10/04

ID1

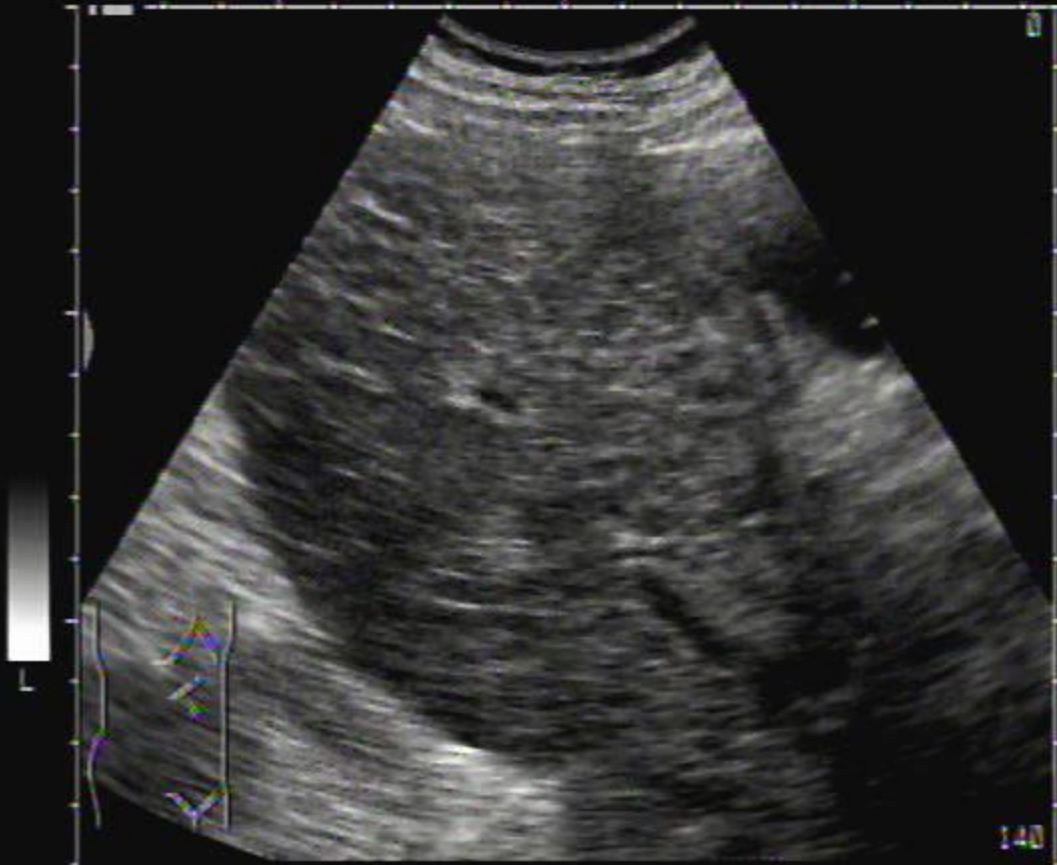
MD1

#11154158

Abd

3C4+ 

FPS 25s

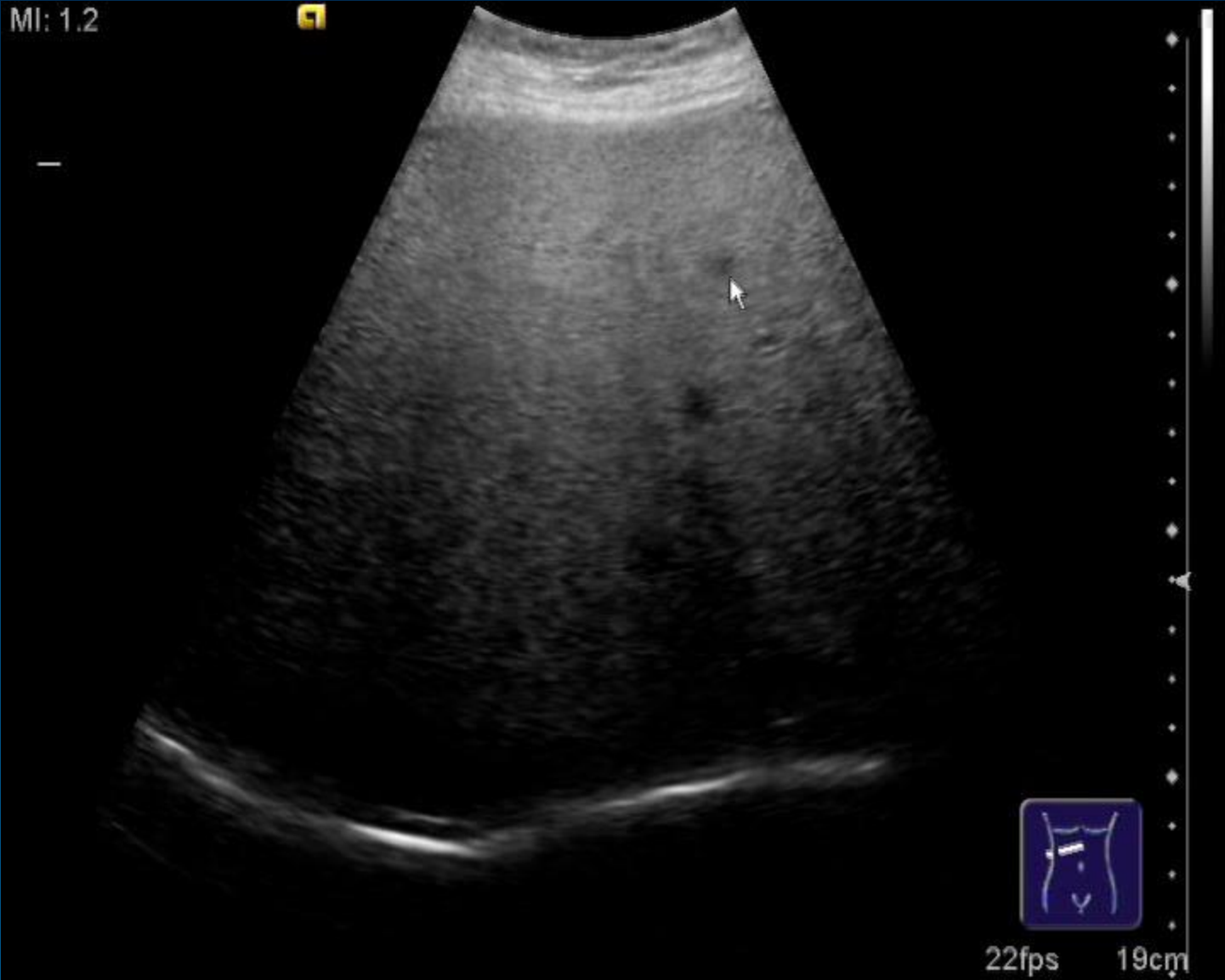


TBIPicto E/1155/1/21

140

M10.6 PWR100%

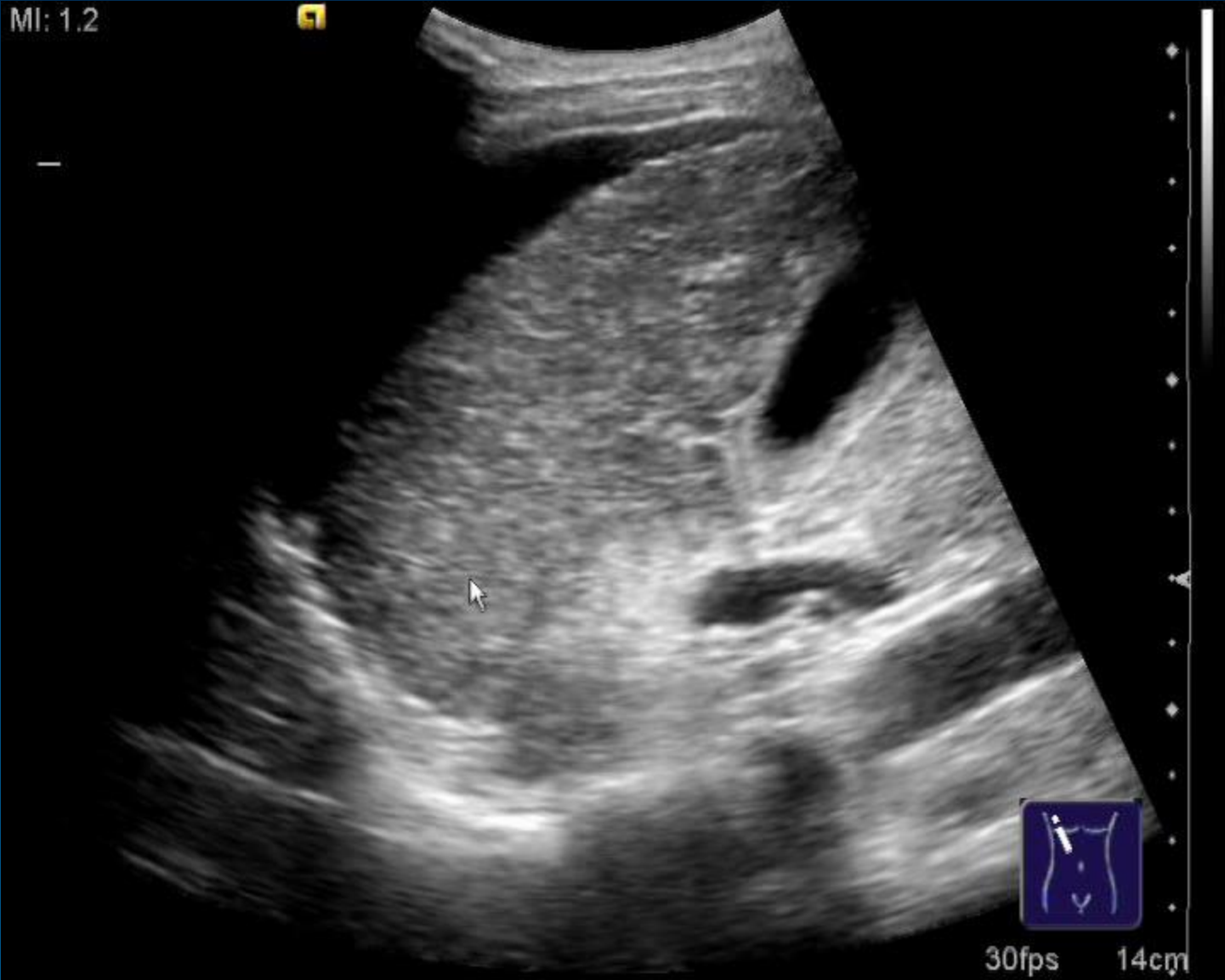
MI: 1.2



22fps

19cm

MI: 1.2

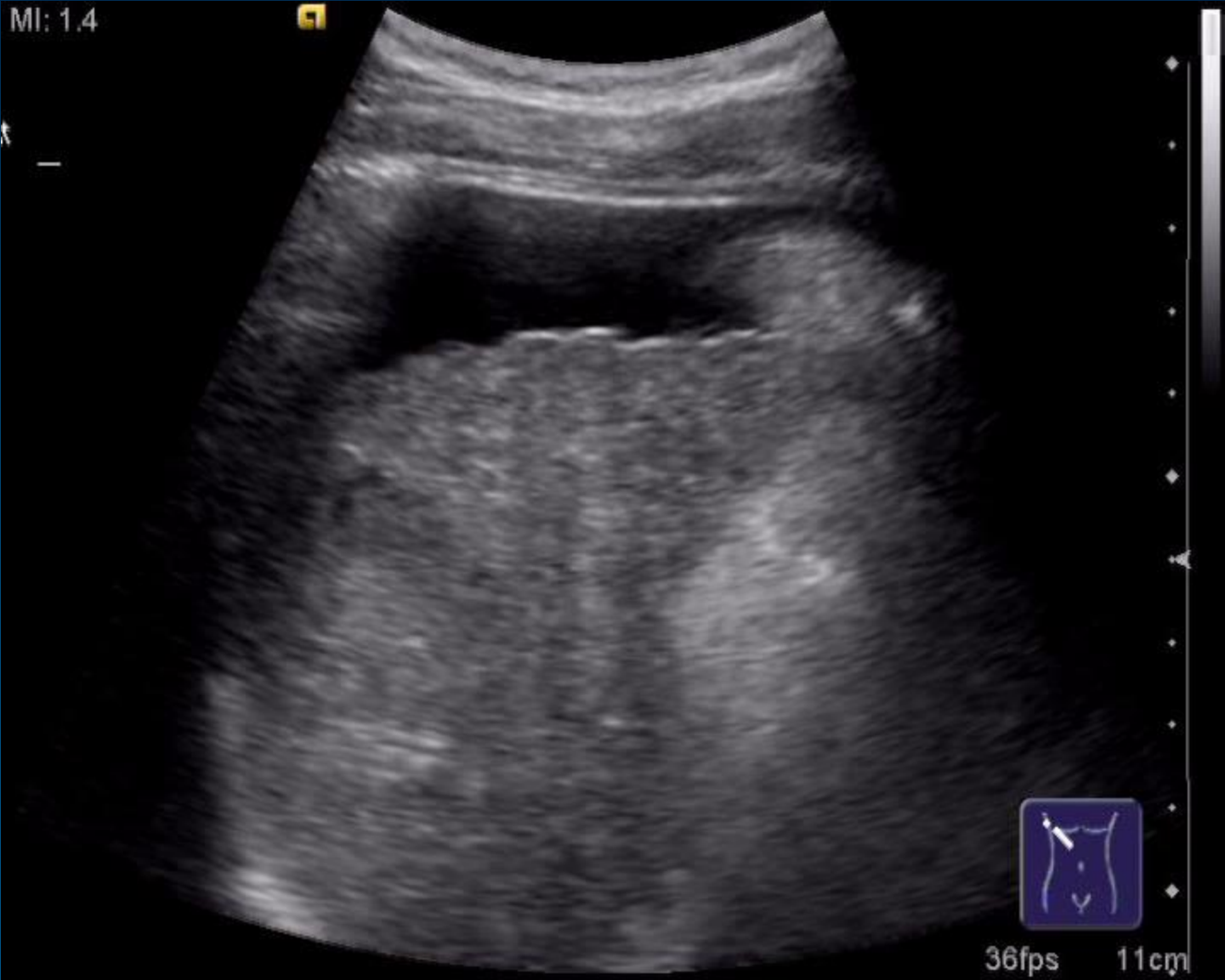


30fps

14cm



MI: 1.4



36fps

11cm



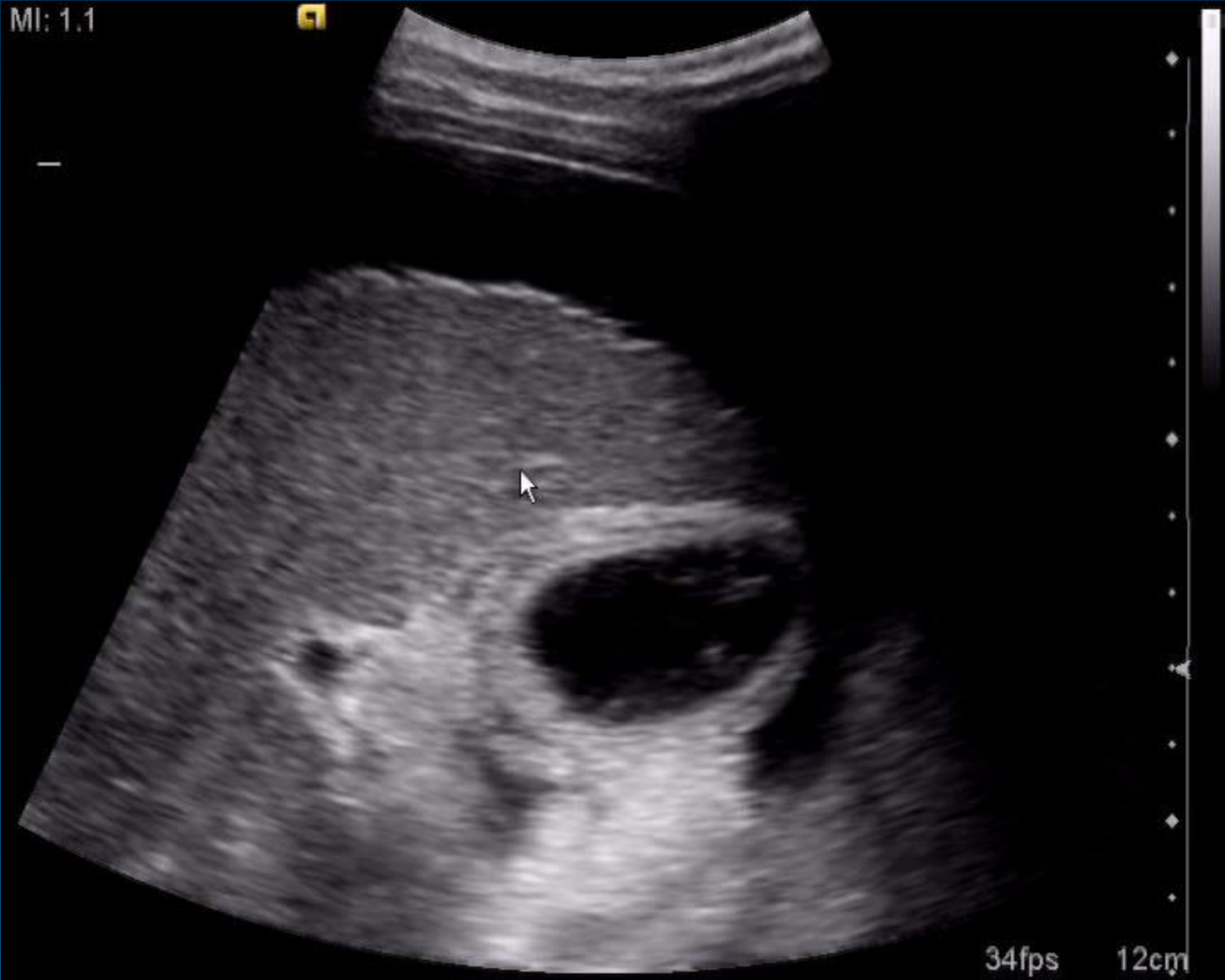
MI: 1.1



34fps

12cm

MI: 1.1



34fps

12cm



# ACCURACY OF ULTRASOUND FOR THE DETECTION OF **LIVER FIBROSIS** IN CHRONIC VIRAL HEPATITIS

- ▶ D'Onofrio and al (1) performed a **prospective study on 105 patients with chronic hepatitis** and compared the results of US to the liver biopsy for the evaluation of hepatic fibrosis. The author evaluated the following US parameters: liver margins, parenchymal echotexture, portal vein caliber and spleen diameter.
- ▶ **US diagnosis of liver fibrosis** in chronic liver disease is possible with **25% sensitivity**, **100% specificity**, 100% positive predictive value and 79% negative predictive value, with a total **diagnostic accuracy of 80%**.

# ADVANCED FIBROSIS (CIRRHOSIS)

- Shen et al (1) evaluated the liver fibrosis in 324 patients with chronic viral hepatitis (the vast majority with HBV infection), both **by needle biopsy and US** (description of the liver surface and parenchyma, diameter of vessels, blood flow velocity and spleen size).
- A single parameter has limited sensitivity and specificity for the diagnosis of early cirrhosis (for ex: the cut-off value of > 12 cm for the spleen's length had 0.60 sensitivity and 0.75 specificity for the diagnosis of liver cirrhosis). But by **using 2 or 3 parameters for the US diagnosis of cirrhosis** (especially the length of spleen, the diameter of splenic vein and the echo pattern of the liver, **the negative predictive value of these parameters was close to 0.95.**

# ADVANCED FIBROSIS (CIRRHOSIS)

- ▶ **Zheng et al** (1) studied the *value of US for the evaluation of liver fibrosis* in comparison with *histology* in **225 patients** with **chronic viral hepatopathies**.
- ▶ They found that the **hepatic parenchymal echo-pattern, the liver surface and the thickness of the gallbladder wall** are independent predictors of liver fibrosis.
- ▶ In this study, the diagnostic **accuracy of US for compensated cirrhosis was 80.7%**.

# WHAT IS THE CRITERION FOR DIFFERENTIATING CHRONIC HEPATITIS FROM COMPENSATED CIRRHOSIS?

- This prospective study **blindly investigates the accuracy of an ultrasonographic score**, derived from **liver, spleen and portal vein features** in predicting the final diagnosis in 212 patients with compensated chronic liver disease **undergoing percutaneous liver biopsy.**

- Gaiani S, Gramantieri L, Venturoli N, Piscaglia F, Siringo S, D'Errico A, Zironi G, Grigioni W, Bolondi L: What is the criterion for differentiating chronic hepatitis from compensated cirrhosis? A prospective study comparing ultrasonography and percutaneous liver biopsy. *J Hepatol* 1997;27(6):979-85.



# RESULTS OF THE STUDY

- Taking biopsy as the standard, the **ultrasonographic score differed significantly between chronic hepatitis** (39+/-33) and **cirrhosis** (100+/-35) ( $p < 0.0001$ ).
- Discriminant analysis with stepwise forward selection of the variables identified **liver surface nodularity and portal flow velocity as independently associated with the diagnosis of cirrhosis** ( $p < 0.005$ ), and a score based on these two variables **correctly identified cirrhosis in 82.2% of cases**.

# ULTRASOUND BASED LIVER ELASTOGRAPHY CAN BE DEVIDED:

## 1. Shear Waves Elastography:

a) **Transient Elastography-TE** (FibroScan)

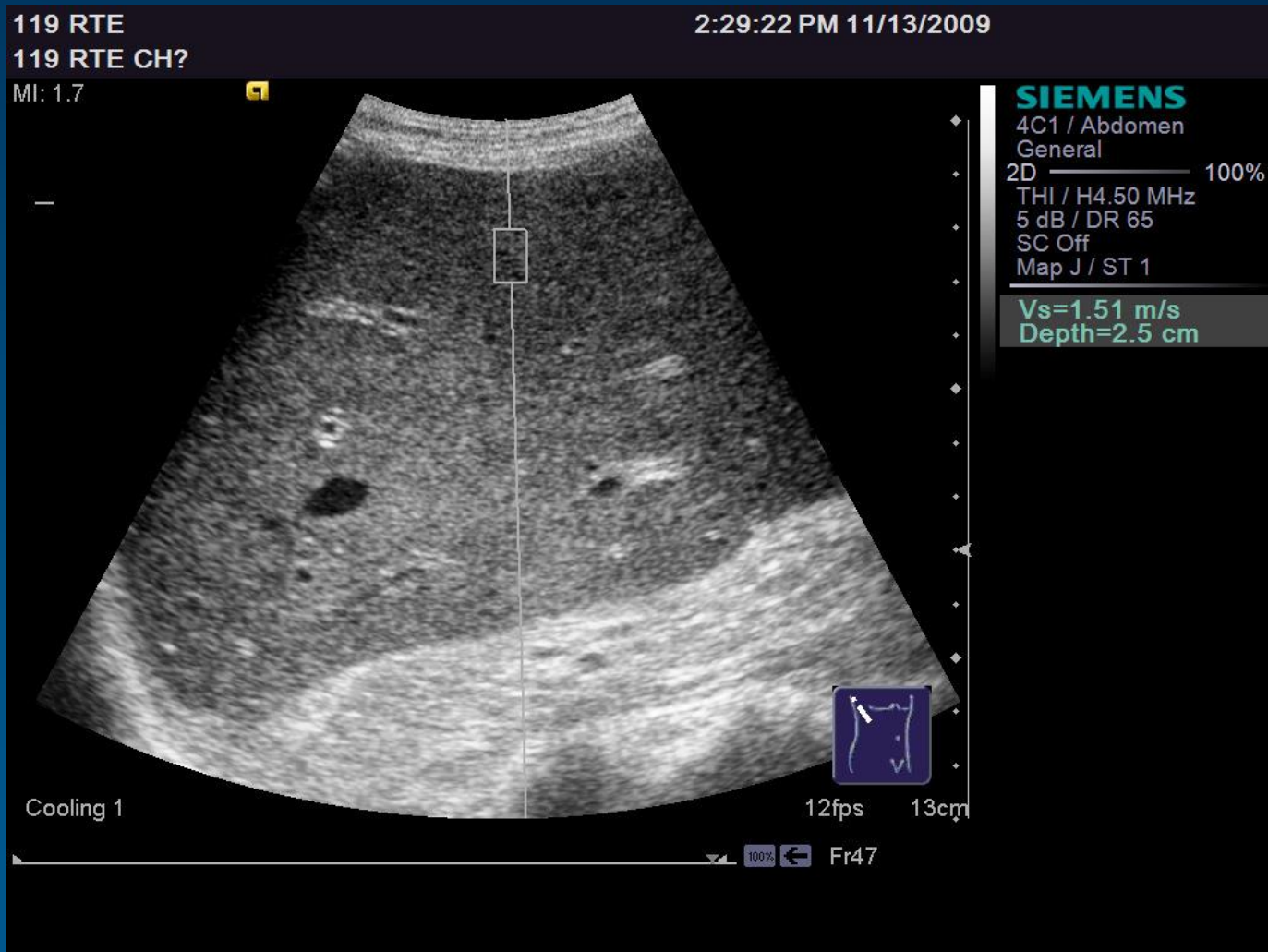
b) **Point Shear Wave Elastography- pSWE** [using **Acoustic Radiation Force Impulse** Quantification: **VTQ** (Siemens), **Elast PQ** (Phillips)]

c) **Real Time Shear Wave Elastography- 2D SWE** [**SuperSonic Imaging Elastography (SSI)** (Aixplorer), **GE**, **Toshiba**]

## 2. Strain Elastography (Hi RTE)

**EFSUMB Guidelines and Recommendations on the Clinical Use of Ultrasound Elastography. Part 1: Basic Principles and Technology:** J. Bamber, D. Cosgrove, C. F. Dietrich, J. Fromageau, J. Bojunga, F. Calliada, V. Cantisani,, J.-M. Correas, M. D'Onofrio, E. Drakonaki, M. Fink, M. Friedrich-Rust ,O. H. Gilja, R. F. Havre, C. Jenssen, A. S. Klauser, R. Ohlinger,,A. Saffoiu, F. Schaefer, I. Sporea, F. Piscaglia. **Ultraschall Med.** 2013 Apr;34(2):169-84.

# POINT SWE USING ARFI TECHNIQUE: VTQ (VIRTUAL TOUCH QUANTIFICATION)



# CAN DOPPLER SONOGRAPHY GRADE THE SEVERITY OF HEPATITIS C-RELATED LIVER DISEASE? (1)

- **CONCLUSION** : “**Doppler-derived indexes, which have previously been recommended** for the assessment of severity in chronic liver disease, **are difficult to reproduce reliably** and therefore **have a limited clinical role in the noninvasive assessment of hepatic fibrosis or inflammation**” (1).

# DIAGNOSIS OF LIVER CIRRHOSIS WITH CONTRAST-ENHANCED ULTRASOUND (CEUS)

- **Hepatic vein arrival time and enhancement level of liver parenchyma in late phase** (in comparison with normal liver) may be valuable clues for the diagnosis of liver cirrhosis with CEUS.
- Some studies shown also that the **hepatic vein arrival time correlated with the severity of liver fibrosis.**

- 1.Liu GJ et al: Diagnosis of liver cirrhosis with contrast-enhanced ultrasound. World J Radiol 2010 ;28; 2(1): 32-36
- 2.Kaneko T et al: Signal intensity of the liver parenchyma in microbubble contrast agent in the late liver phase reflects advanced fibrosis of the liver. Liver Int 2005; 25: 288-293

# CEUS DIAGNOSIS OF FIBROSIS

- Ridolfi et al [1] tried to use low MI CEUS with **SonoVue to evaluate the severity of chronic hepatitis C.**
- They found the **mean hepatic vein arrival time decreased progressively with increasing severity of liver disease** all patients with liver cirrhosis had a hepatic vein arrival time of 17 s or less, whereas values of 18 s or more were recorded for all controls and for almost all patients (20/22) with non-cirrhotic liver disease.
- 1. Ridolfi F et al: Contrast-enhanced ultrasound to evaluate the severity of chronic hepatitis C. *Dig Liver Dis* 2007; 39: 929-935



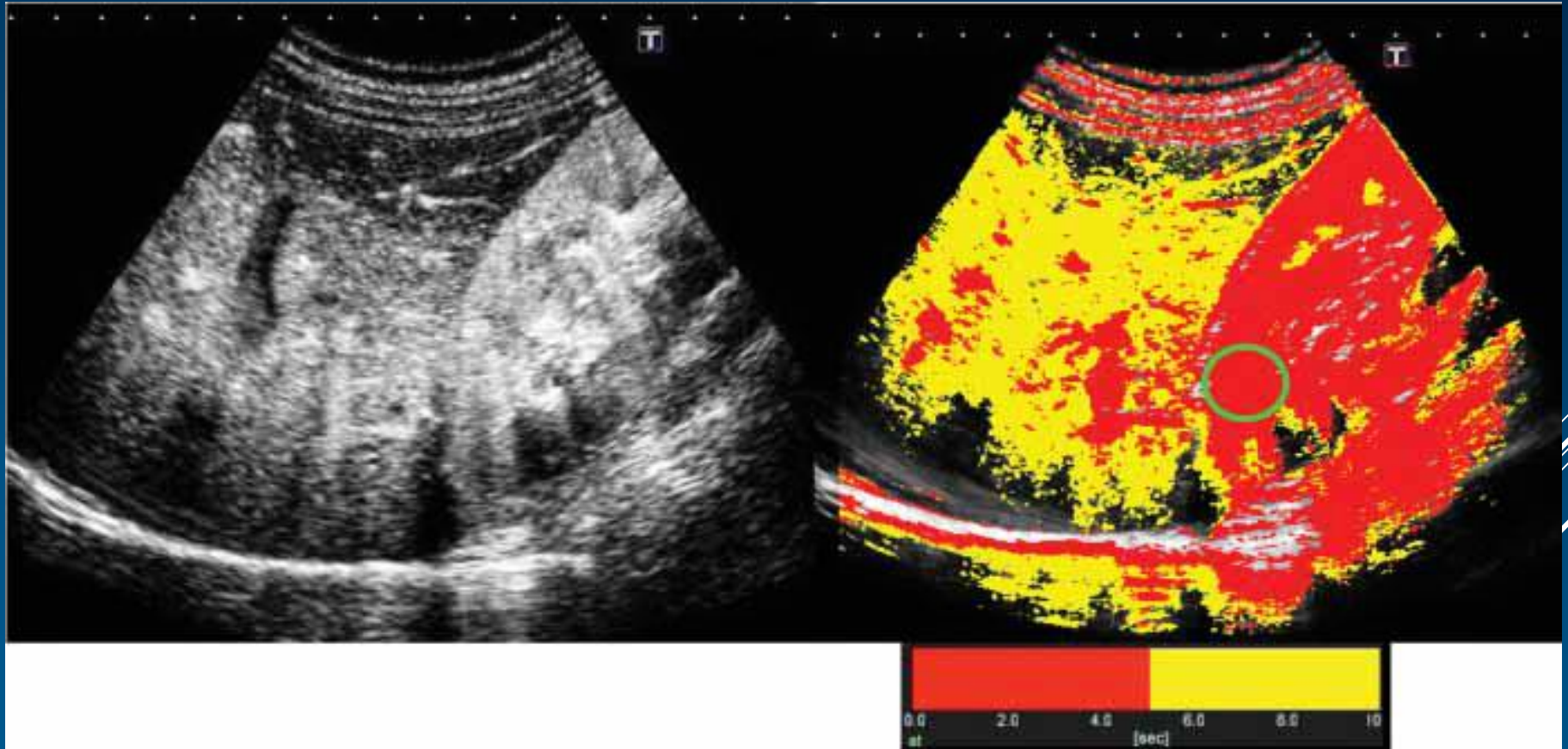
# PREDICTION OF LIVER DISEASES SEVERITY WITH CEUS

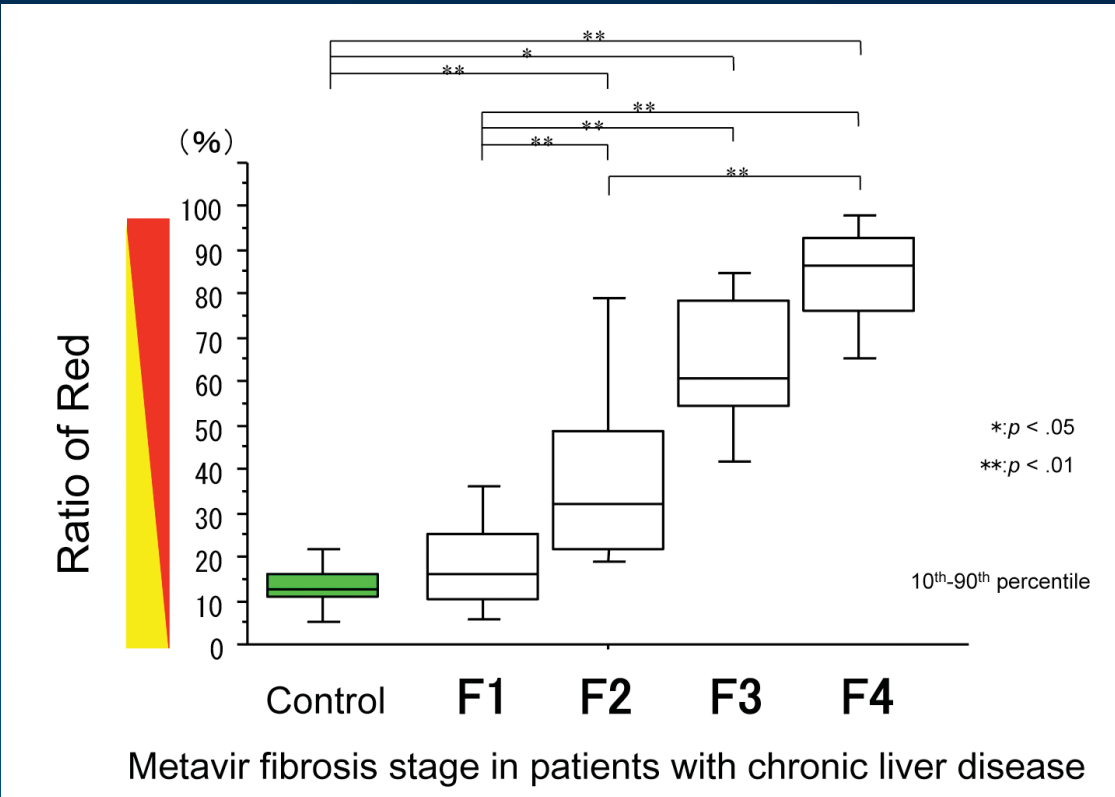
- ▶ **85 untreated patients with biopsy proven HCV** induced liver disease were studied prospectively (1).
- ▶ Was investigated the utility of **hepatic vein transit times (HVTT)** for grading and staging diffuse liver disease (**using Levovist**). HVTT for the mild hepatitis, moderate/severe hepatitis, and cirrhosis groups showed a monotonic decrease of 38.8 , 26.0, and 15.8 seconds, respectively.
- ▶ There was **100% sensitivity and 80% specificity for diagnosing cirrhosis** and **95% sensitivity and 86% specificity for differentiating mild hepatitis from more severe liver disease.**
- ▶ 1. Lim AKP et al: Hepatic vein transit times using a microbubble agent can predict disease severity non-invasively in patients with hepatitis C. Gut 2005;54:128-133

# LIVER CEUS FOR THE EVALUATION OF HEPATIC FIBROSIS

- In this study, **60 patients with liver disease in chronic hepatitis C infection were examined and compared with 10 healthy volunteers** who served as controls.
- Sonographic **contrast agent Sonazoid** was intravenously infused, and the **S5 or S6 region of the liver and right kidney were observed concurrently** while movies of the procedure were saved.
- **Arrival time parametric images of liver parenchymal blood flow** were created, with red pixels to indicate an arrival time of 0 to 5 seconds and yellow pixels to indicate an arrival time of 5 to 10 seconds.
- From the obtained images **the ratio of the red** area to the entire enhanced area of the liver was calculated using image-processing software.
- Wakui N, , Ryuji Takayama R, Takenori Kanekawa T et al. Usefulness of Arrival Time Parametric Imaging in Evaluating the Degree of Liver Disease Progression in Chronic Hepatitis C Infection. J Ultrasound Med 2012; 31:373–382

# ARRIVAL TIME PARAMETRIC IMAGES





RESULTS:

$F \geq 2$ : AUC 0.909

$F = 4$ : AUC 0.962



# OUR CASES: LIVER CIRRHOSIS



Gastroenterology Department  
21/03/16 11:08:13AM ADM

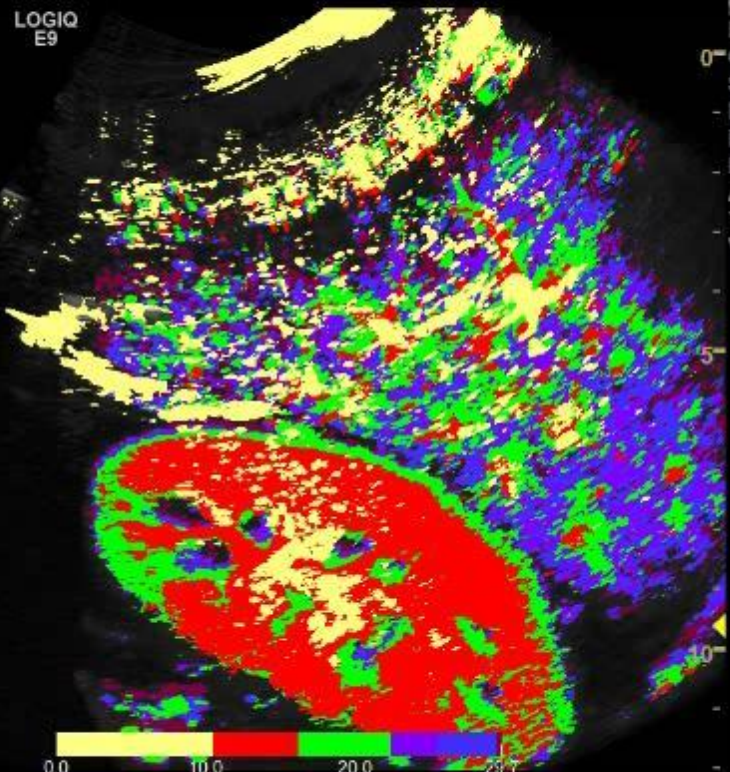
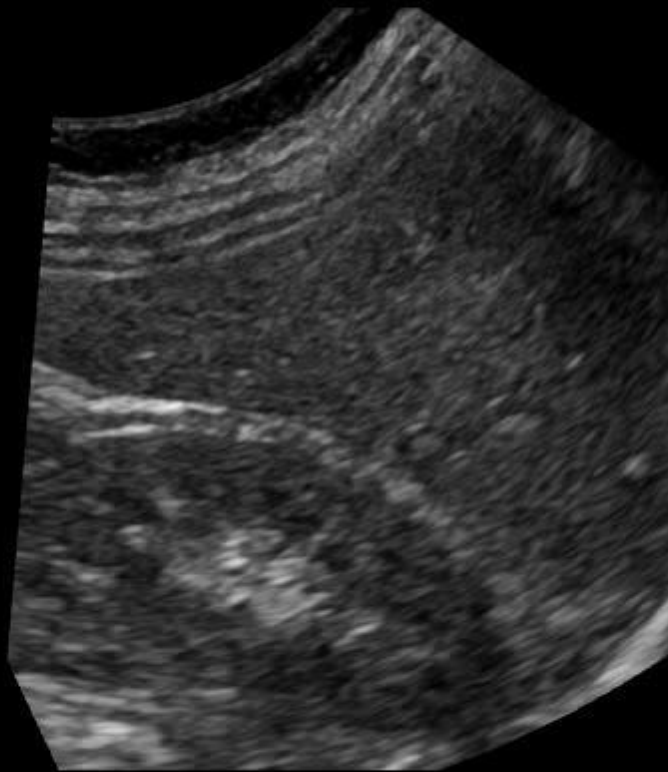
173/2016 EVALFIBROZEI,  
210316-110639AM

MI 0.16 TIs 0.0

C1-6  
Abdomen

21/03/16

FR 10



CON	
Frq	Gen
0-Gn	18
S/A	1/2
-Map	D/0
D	12.0
-DR	69
AO%	9
-Trig	0-1
Vis	C

T1: 0:31

# IN CONCLUSION

- ▶ Regarding the use of (classical) US for the evaluation of fibrosis, this method has low sensitivity, a quite good specificity (for cirrhosis), with a total diagnostic accuracy of 80% (1).
- ▶ Liver steatosis ((at least moderate) can be quite well evaluated with US (sensitivity 75-90%) or maybe can be improved with CAD.
- ▶ At the same time, US is useful for the evaluation of liver cirrhosis (quite good accuracy), because of its low cost, is easy to be perform and due to the high acceptability by the patients.
- ▶ Arrival Time Parametric CEUS can be a promising method for fibrosis evaluation.





## 18<sup>th</sup> World Federation for Ultrasound in Medicine and Biology Congress

MAY 26-29, 2021  
Timisoara, Romania

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