

PROPOSTA DI UN NUOVO ALGORIMO PER LA DIAGNOSI ECOGRAFICA DELLE MALATTIE CRONICHE DEL FEGATO



Corso Residenziale di
ECOGRAFIA
ed **ECO-INTERVENTISTICA**

Informazioni per i partecipanti

La quota d'iscrizione al corso è di € 385,00 per partecipante, inclusiva della

Direttore **Prof. Antonio Giorgio**

A. Giorgio

Direttore del servizio di Ecografia
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Consultant Ecografia Interventistica Istituto
Clinico Tortorella -Salerno



5 - 8 Giugno 2013
Maiori (Salerno)

Palazzo Mezzacapo,
Sala Consiliare – Corso Regina

con il patrocinio della **SIEMC**

Conflict of interest

None to declare

DIAGNOSTIC AND THERAPEUTIC ADVANCES IN HEPATOLOGY

Noninvasive Assessment of Liver Fibrosis

Doris Nguyen¹ and Jayant A. Talwalkar^{2,3}

Hepatology-2012

Real-time elastography- a new application in the field
of liver disease

Gheorghe L et al, J Gastrointestin Liver Dis 2008

Elasticity imaging promises to make an important
contribution to ultrasound practice

Real-time elastography for noninvasive assessment of liver fibrosis in chronic viral hepatitis

Friedric - Rust M et al, AJR 2007



Non invasive assessment of liver fibrosis using US based real-time elastography which can be performed with conventional US probes during a routine US examination

- ✓ real-time elastography is a new method for measurement of tissue elasticity integrated in a sonography machine and is technically different from transient elastography
- ✓ recently, researchers have evaluated real-time elastography for the characterization and detection of focal lesions in the breast, thyroid and prostate

Real-Time Tissue Elastography and Transient Elastography for Evaluation of Hepatic Fibrosis

Hiroyasu Morikawa

2013

	Principle	Mode of generation	Imaging modality
Real-time Tissue Elastography (RTE)	Tissue distortion	Pulsing of the aorta	Ultrasound
Vibration-Controlled Transient Elastography (VCTE, Fibroscan)	Propagating shear wave	Mechanical vibration	Ultrasound
Acoustic Radiation Force Impulse (ARFI)	Propagating shear wave	Radiation force	Ultrasound
Magnetic Resonance Elastography (MRE)	Propagating shear wave	Mechanical vibration	Magnetic resonance imaging
Supersonic Shear Imaging (SSI)	Propagating shear wave	Radiation force	Ultrasound

Table 1. Elastography techniques for measurement of liver stiffness.

ALOKA

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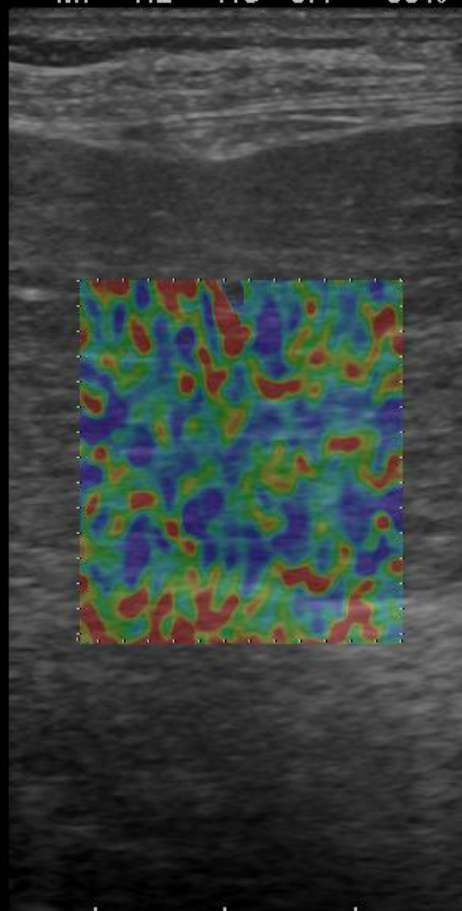
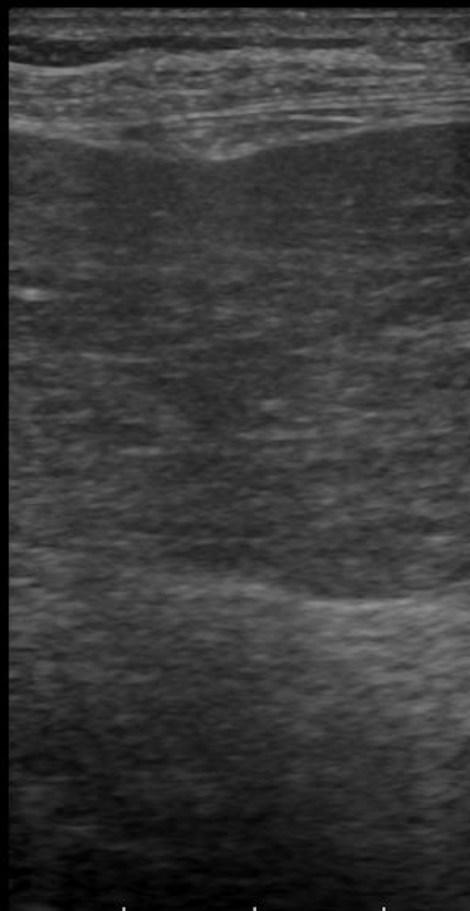
21-04-'11
13:46:39

18Hz 1

278/376	278/376
5.00M	5.00M
R7.0	R7.0
G44	G44
D86	D86
A2	A2

MI = 1.2 TIS < 0.4 80%

18Hz 1



40:Elasto Add. @@ Probe:5415

AIP

SCI

ALOKA

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21-04-'11

13:47:48

18Hz 1

273/278 273/278

5.00M 5.00M

R7.0 R7.0

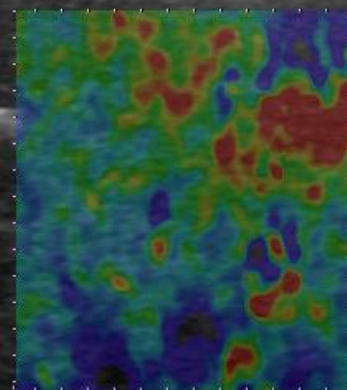
G44 G44

D86 D86

A2 A2

MI = 1.2 TIS < 0.4 80%



18Hz 1



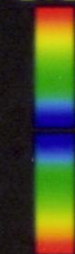
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AIP

SCI

Reconstruct 
Pre-process 

0.07




0.07

● Image Select ●

Gray Scale

Velocity

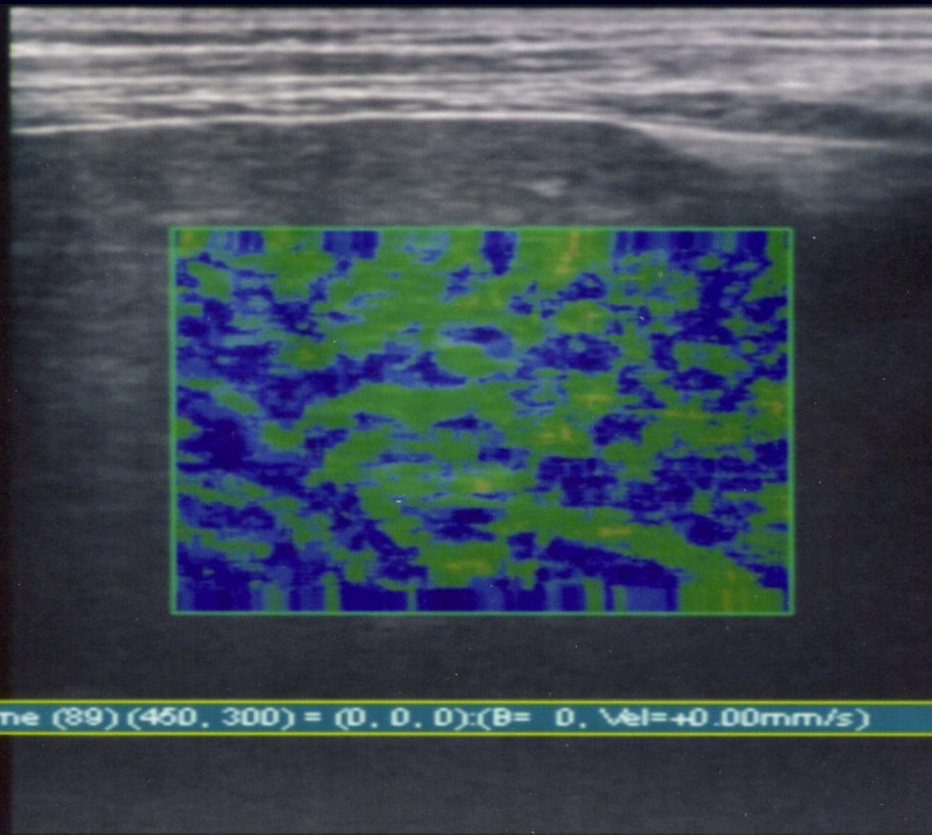
Vel. Grad. 

Strain 

Auto

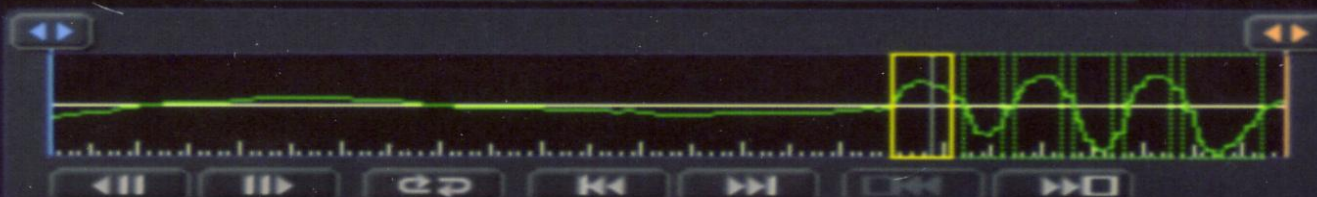
Color

BW



25fps
CF 4.7
10.0

Frame (89) (450, 300) = (0, 0, 0):(B= 0, Vel=+0.00mm/s)



Current:089

TCA

M-Graph

CH1

Set
Draw

CH2

Set
Draw

CH3

Set
Draw

CH4

Set
Draw



ROI Tracking



off



on



auto

Del All

File

Quit

TOSHIBA

201305

20/05/2013

11:40:40

Reconstruct

0.45

Pre-process

● Image Select ●

Gray Scale

Velocity

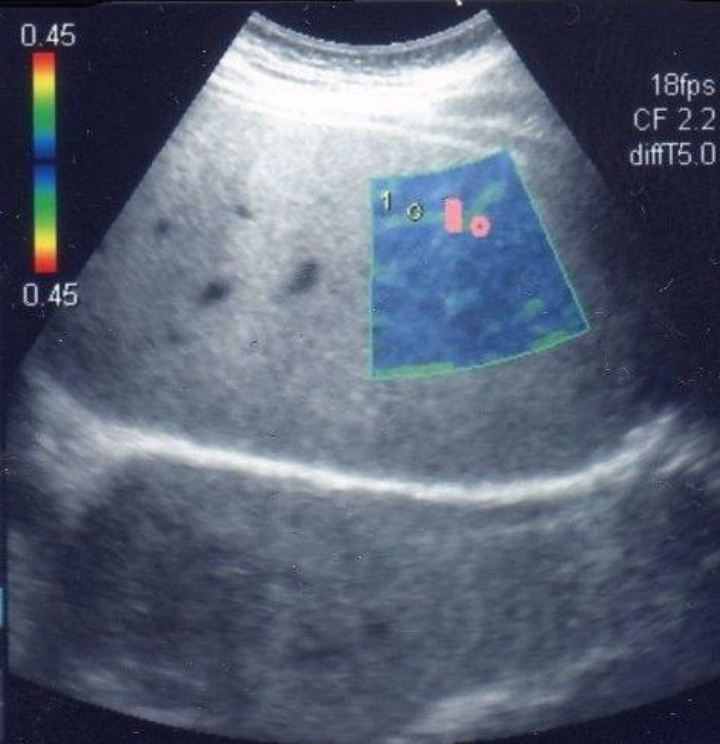
Vel. Grad.

Strain

Auto

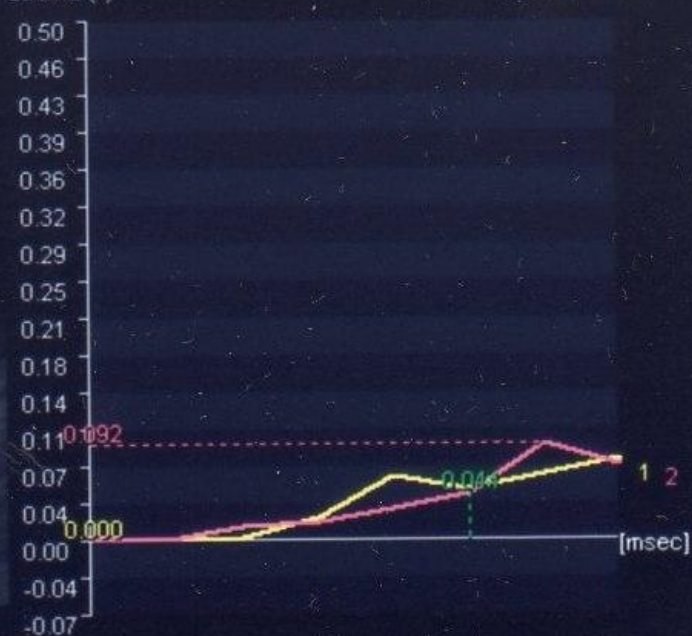
Color

BW



Strain2 (-)

Time: 283 msec



Current:038

TCA

M-Graph

CH1

Set

Draw

CH2

Set

Draw

CH3

Set

Draw

CH4

Set

Draw

ROI Tracking

off

on

auto

Del All

ROI info.

max

min

current

CH1: 0.078 (397)

CH2: 0.092 (340)

CH3:

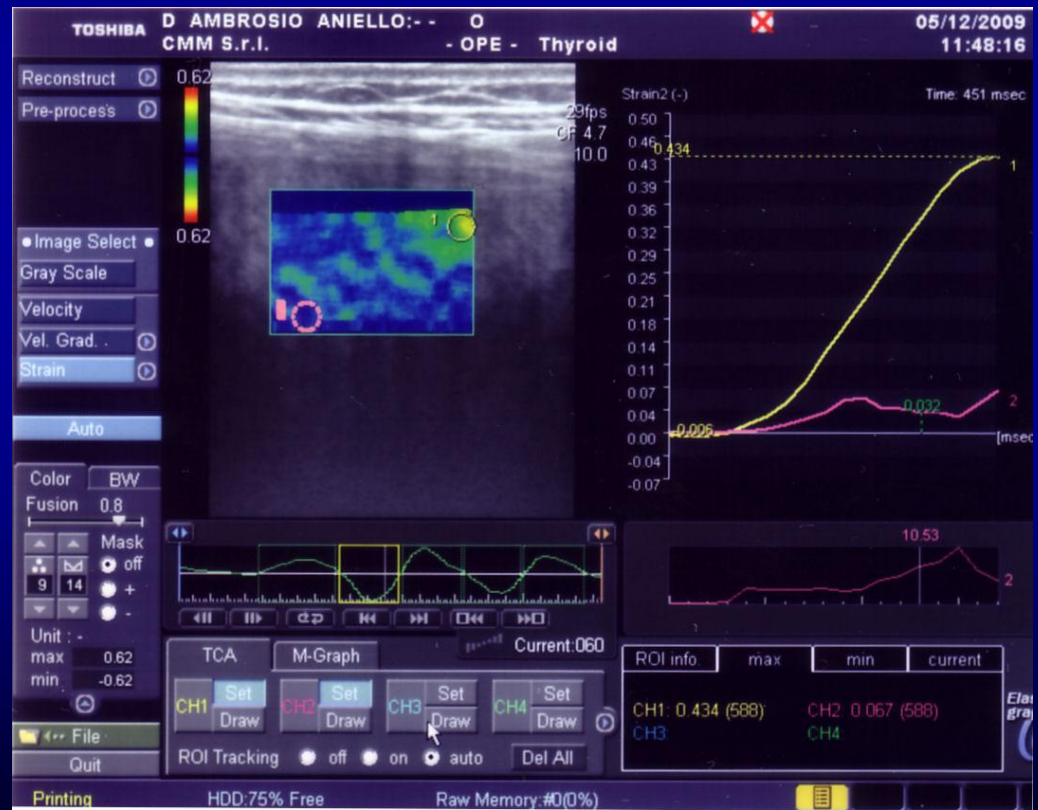
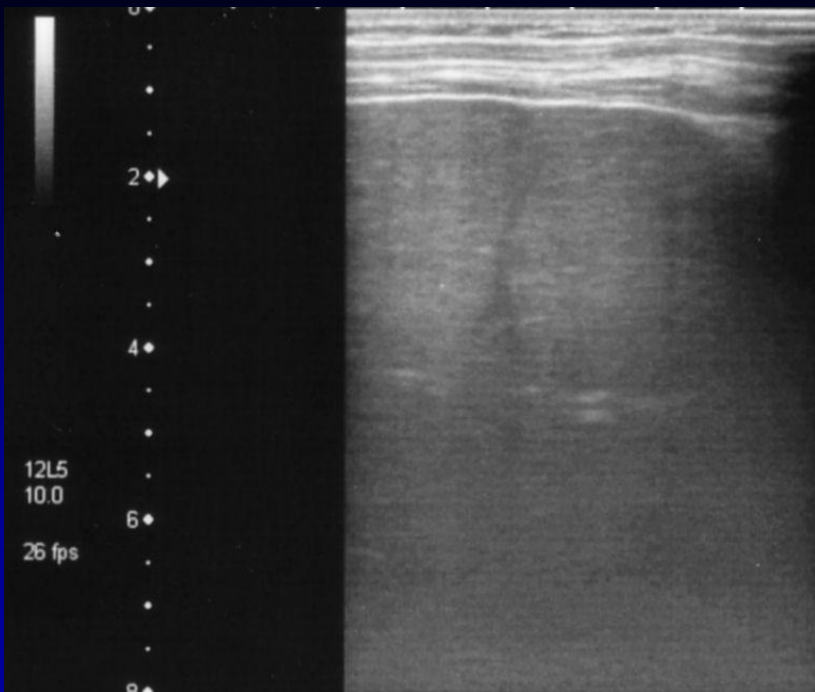
CH4:

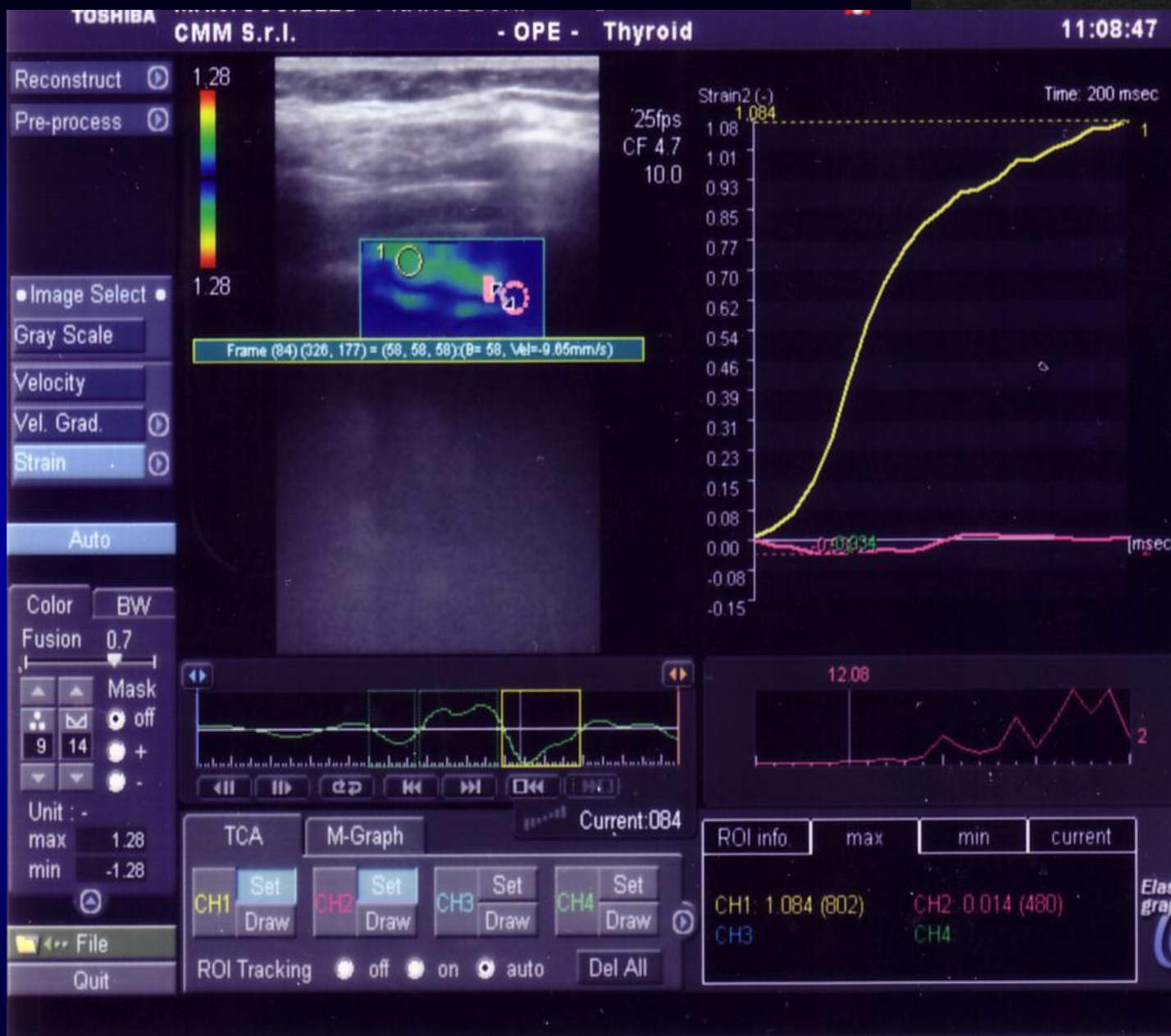
Elasto-
graphy

Printing

HDD:48% Free

Raw Memory:#0(0%)





Real-time elastography for noninvasive assessment of liver fibrosis in chronic viral hepatitis

Friedric - Rust M et al, AJR 2007

materials & methods

✓ 79 pts chronic viral hepatitis and known fibrosis stage

✓ 20 healthy volunteers

- specially developed program was used for quantification of tissue elasticity
- aspartate transaminase-to -platelet ratio index (APRI) and routine laboratory values were included in the analysis

Real-time elastography for noninvasive assessment of liver fibrosis in chronic viral hepatitis

Friedric - Rust M et al, AJR 2007

results

- ✓ Spearman's correlation coefficient between the elasticity scores obtained using real-time elastography and the histologic fibrosis stage was 0.48 which is highly significant ($p < 0.01$)
- ✓ **diagnostic accuracy** expressed as areas under the ROC curves were **0.75** for the diagnosis of **significant fibrosis**



fibrosis stage according to METAVIR scoring system
 $F \geq F2$

Real-time elastography for noninvasive assessment of liver fibrosis in chronic viral hepatitis

Friedric - Rust M et al, AJR 2007

results

- ✓ diagnostic accuracy (ROC curves) were 0.73 for the diagnosis of severe fibrosis ($F \geq F3$) and 0.69 cirrhosis
- ✓ for a combined elasticity-laboratory score, the areas under the ROC curves were 0.93 (significant fibrosis), 0.95 (severe fibrosis) and 0.91 (cirrhosis)

conclusion

real-time elastography is a new and promising US-based noninvasive method for the assessment of liver fibrosis in pts with chronic viral hepatitis

Real-time elastography for noninvasive diagnosis of liver fibrosis

Kanamoto M et al, J Hepatobiliary Pancreat Surg 2009

objective

to evaluate the usefulness of
real-time tissue elastography for the
preoperative assessment of liver
fibrosis stage

methods

- ✓ the liver fibrosis stages were finally determined in the operative specimens from 41 pts
it was examined the correlation between the elastic ratio and the histological fibrosis stage

Real-time elastography for noninvasive diagnosis of liver fibrosis

Kanamoto M et al, J Hepatobiliary Pancreat Surg 2009

results

- ✓ significant correlation between the elastic ratio and the histological fibrosis stage was found

conclusion

- ✓ real time elastography is a promising US-based noninvasive method for the preoperative assessment of liver fibrosis



Noninvasive evaluation of hepatic fibrosis using serum fibrotic markers ,transient elastography (fibroscan) and real-time tissue elastography **Tatsumi C et al, Intervirology 2008**

objectives

- ✓ To investigate the accuracy of noninvasive tests: serum fibrotic markers, transient elastography (TE) and real-time tissue elastography (real-TE) in the diagnosis of hepatic fibrosis
- ✓ To determine whether they can replace liver biopsy

119 pts with chronic liver disease

Noninvasive evaluation of hepatic fibrosis using serum fibrotic markers transient elastography (fibroscan) and real-time tissue elastography Tatsumi C et al, Intervirology 2008

results

✓ fibrotic stage by histopathology no correlate as well with serum fibrotic markers although it was useful to diagnose cirrhosis

✓ the stage of hepatic fibrosis correlated well with liver stiffness measured with **fibroscan**



the levels of liver strain measured by real-Time elastography correlated well with liver stiffness ($p < 0.05$)

fibroscan was also a much better predictor of liver cirrhosis than APRI

Noninvasive evaluation of hepatic fibrosis using serum fibrotic markers transient elastography (fibroscan) and real-time tissue elastography **Tatsumi C et al, Intervirology 2008**

conclusion

- ✓ serum fibrotic markers and fibroscan are useful for distinguishing liver cirrhosis (F4) from chronic liver hepatitis (F1-F3)

Real-Time elastography is a novel and promising method to determine the stage of hepatic fibrosis

Real-time elastography- a non-invasive diagnostic method of small HCC in cirrhosis

Gheorghe L et al, J Gastrointestin Liver Dis 2009

aim

- ✓ to evaluate real-time sonoelastography as a noninvasive tool for the diagnosis of small HCC in cirrhotic pts (nodules under 3 cm represent the most challenging category for noninvasive diagnosis HCC)

methods

- ✓ 42 cirrhotic pts/58 nodules (1-3 cm)
the mean intensity of colors red, blue, green were measured using a semi-quantitative method

Real-time elastography- a non-invasive diagnostic method of small HCC in cirrhosis Gheorghe L et al, J Gastrointestin Liver Dis 2009

conclusion

- ✓ US elastography is a promising method for the non-invasive diagnosis of early HCC

blue color at elastography and hypervascular aspects are independent predictors of HCC

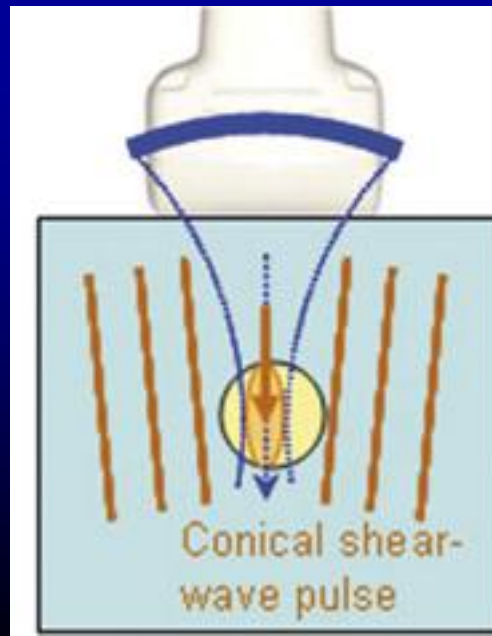
NEW SONOGRAPHIC
QUANTITATIVE TOOLS IN
EVALUATION OF LIVER
FIBROSIS :

ARFI, SWE, ASQ

Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography Friedrich-Rust M et al Radiology; 2009

aim

to compare in a pilot study **acoustic radiation force impulse (ARFI)** imaging technology integrated into a conventional US system **with both transient elastography (TE) and serologic fibrosis marker testing for the noninvasive assessment of liver fibrosis**



Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography Friedrich-Rust M et al Radiology; 2009

Materials & methods

- ✓ **ARFI** imaging involved the mechanical excitation of tissue with Use of short-duration acoustic pulses to generate localized displacements in tissue
- ✓ the displacements resulted in shear-wave propagation, which was tracked by using US correlation-based methods and recorded in meters per second
- ✓ 86 pts with chronic viral hepatitis underwent TE, ARFI imaging and serum fibrosis marker testing

Unknown

10:41:26 AM 8/17/2010

10.08.17-10:39:54-DST-1.3.12.2.110...

ML: 1.7



SIEMENS

4C1 / Abdomen

General

2D 100%

THI / H4.50 MHz

-1 dB / DR 65

SC Off

Map J / ST 1

Vs=2.61 m/s

Depth=4.4 cm



16fps

9cm

Fr374

Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography Friedrich-Rust M et al Radiology; 2009

results

- ✓ were compared with liver biopsy findings which served as the reference standard
- ✓ ARFI imaging ($\rho=0.71$), TE ($\rho=0.73$), and serum fibrosis marker test ($\rho=0.66$) results correlated significantly with histologic fibrosis stage ($p<0.01$)
- ✓ median ARFI velocities ranged from 0.84 to 3.83 m/sec

Liver fibrosis in viral hepatitis: noninvasive assessment with acoustic radiation force impulse imaging versus transient elastography

Friedrich-Rust M et al Radiology; 2009

results

areas under the receiving operating characteristic curve for the accuracy of ARFI imaging, TE and serum fibrosis marker testing were 0.82, 0.84 and 0.82 respectively, for the diagnosis of moderate fibrosis histologic fibrosis stage \geq 2 and 0.91, 0.91 and 0.82 respectively for the diagnosis of cirrhosis

conclusion

ARFI imaging is a promising US-based method for assessing liver fibrosis in chronic viral hepatitis with diagnostic accuracy comparable to that of TE

Noninvasive Evaluation of Hepatic Fibrosis using Acoustic Radiation Force-Based Shear Stiffness in Patients with Nonalcoholic Fatty Liver Disease

Mark L. Palmeri¹, Michael H. Wang¹, Ned C. Rouze¹, Manal F. Abdelmalek², Cynthia D. Guy³, Barry Moser⁴, Anna Mae Diehl², and Kathryn R. Nightingale¹

J Hepatol. 2011 September

Reconstructed shear stiffnesses were not associated with ballooned hepatocytes ($p = 0.11$), inflammation ($p = 0.69$), nor imaging location ($p = 0.11$). Using a predictive shear stiffness threshold of 4.24 kPa, shear stiffness distinguished low (fibrosis stage 0–2) from high (fibrosis stage 3–4) fibrosis stages with a sensitivity of 90% and a specificity of 90% (AUC of 0.90). Shear stiffness had a mild correlation with APRI ($R^2 = 0.22$). BMI > 40 kg/m² was not a limiting factor for ARFI imaging, and no correlation was noted between BMI and shear stiffness ($R^2 = 0.05$).

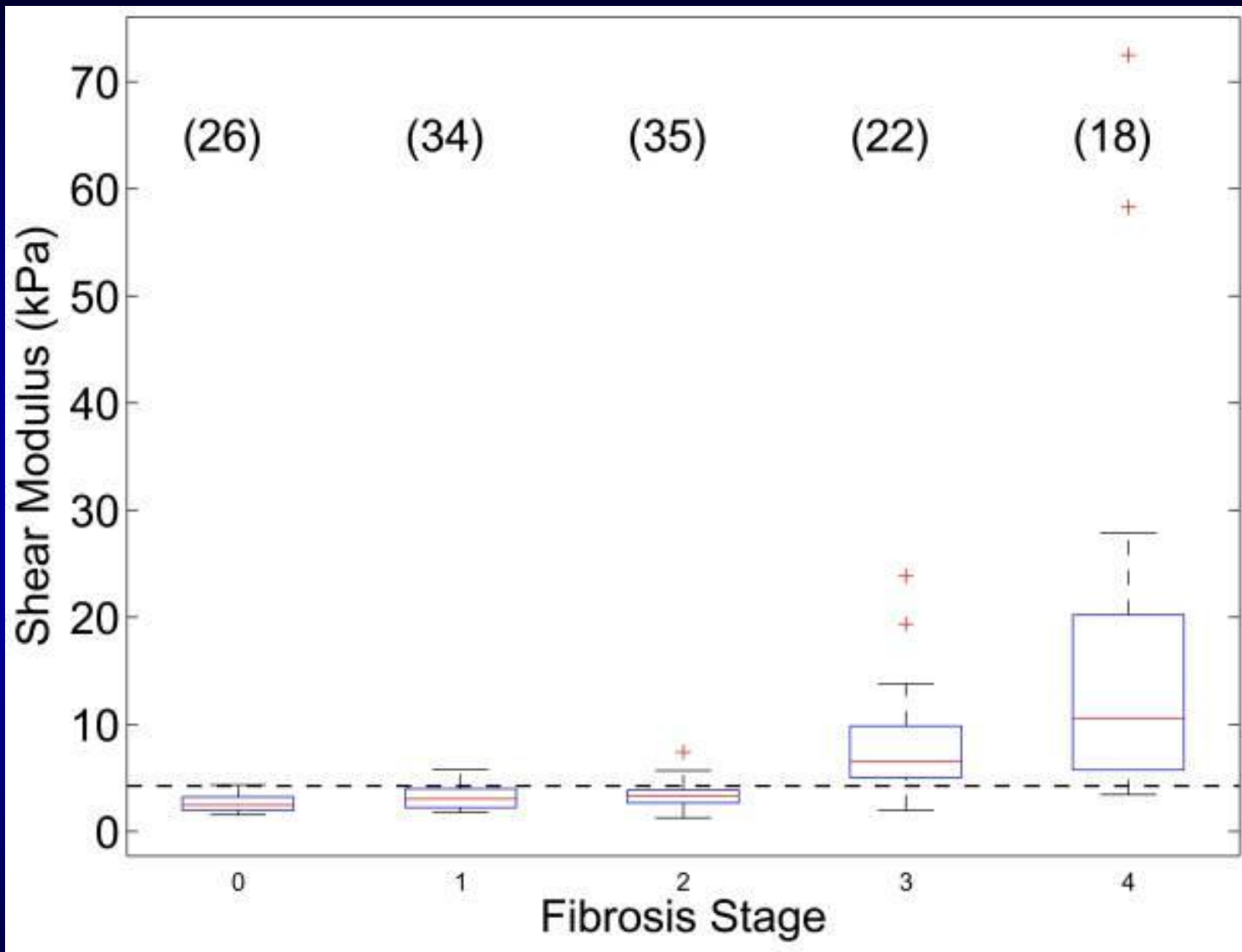
Noninvasive Evaluation of Hepatic Fibrosis using Acoustic Radiation Force-Based Shear Stiffness in Patients with Nonalcoholic Fatty Liver Disease

Mark L. Palmeri¹, Michael H. Wang¹, Ned C. Rouze¹, Manal F. Abdelmalek², Cynthia D. Guy³, Barry Moser⁴, Anna Mae Diehl², and Kathryn R. Nightingale¹

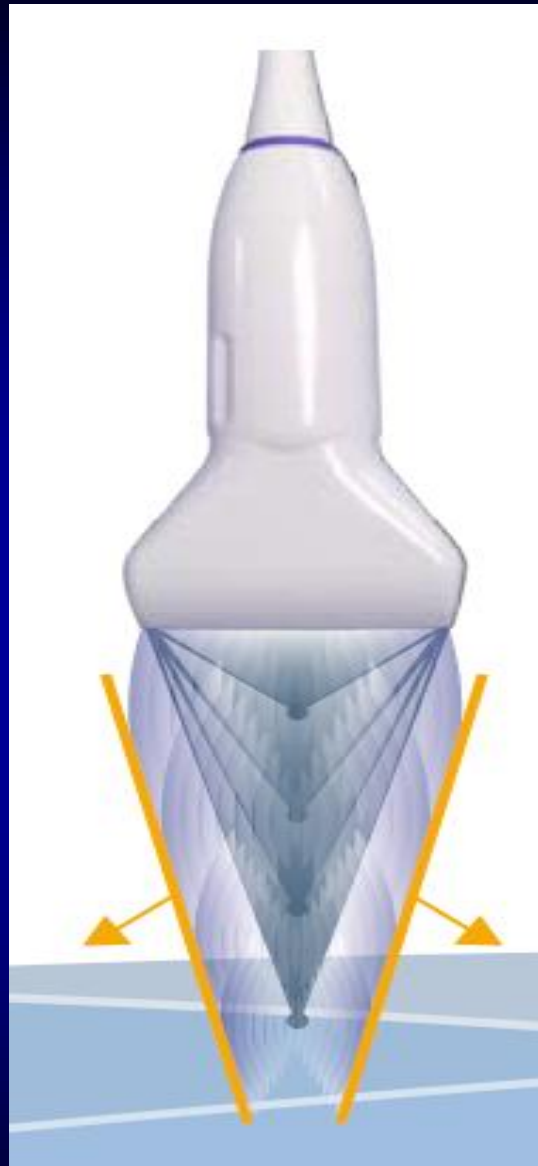
J Hepatol. 2011 September

Conclusions

—ARFI imaging is a promising imaging modality for assessing the presence or absence of advanced fibrosis in patients with obesity-related liver disease.

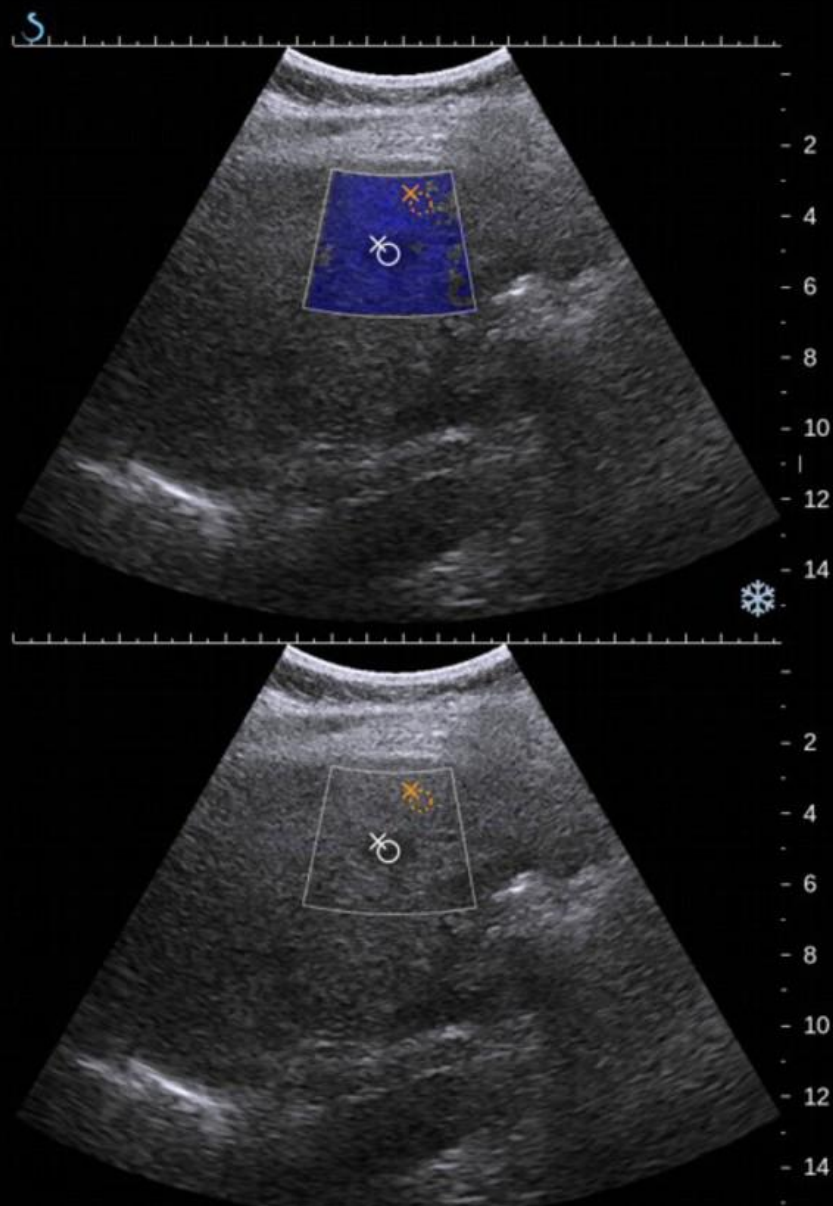


Shear-waves
Radiation
Force Impulse



Tissue 1540 m/s
 Super Compound On
 SuperRes 2
 Pen / FR
 Map 3 / 64 dB / Medium
 Gain 40 %
 Fr. 7 Hz
 Zoom 100 %

WE™
 Gen
 Map 1
 Opa, 50 %
 Persist. Medium
 Smooth, 5
 Gain 70 %
 SWE Standard



+70 kPa



× **Q-Box™ ratio**
 Mean 2.69 kPa
 Min 1.22 kPa
 Max 4.46 kPa
 Std Dev 0.9
 Mean 3.84 kPa
 Min 1.05 kPa
 Max 9.73 kPa
 Std Dev 2.1
 Ratio 0.7

Shear wave elastography for assessing liver fibrosis in chronic hepatitis C: a pilot study.

Ferraioli G et al

Hepatology. 2012 Dec;56(6):2125-33.

Real-time shear wave elastography (SWE) is a novel, noninvasive method to assess liver fibrosis by measuring liver stiffness. This single-center study was conducted to assess the accuracy of SWE in patients with chronic hepatitis C (CHC), in comparison with transient elastography (TE), by using liver biopsy (LB) as the reference standard. Consecutive patients with CHC scheduled for LB by referring physicians were studied. One hundred and twenty-one patients met inclusion criteria. On the same day, real-time SWE using the ultrasound (US) system, Aixplorer (SuperSonic Imagine S.A., Aix-en-Provence, France), TE using FibroScan (Echosens, Paris, France), and US-assisted LB were consecutively performed. Fibrosis was staged according to the METAVIR scoring system. Analyses of receiver operating characteristic (ROC) curve were performed to calculate optimal area under the ROC curve (AUROC) for F0-F1 versus F2-F4, F0- F2 versus F3-F4, and F0-F3 versus F4 for both real-time SWE and TE.

Liver stiffness values increased in parallel with degree of liver fibrosis, both with SWE and TE. AUROCs were 0.92 (95% confidence interval [CI]: 0.85-0.96) for SWE and 0.84 (95% CI: 0.76-0.90) for TE (P = 0.002), 0.98 (95% CI: 0.94-1.00) for SWE and 0.96 (95% CI: 0.90-0.99) for TE (P = 0.14), and 0.98 (95% CI: 0.93-1.00) for SWE and 0.96 (95% CI: 0.91-0.99) for TE (P = 0.48), when comparing F0-F1 versus F2- F4, F0- F2 versus F3-F4, and F0 -F3 versus F4, respectively.

CONCLUSION: The results of this study show that real-time SWE is more accurate than TE in assessing significant fibrosis (\geq F2). With respect to TE, SWE has the advantage of imaging liver stiffness in real time while guided by a B-mode image. Thus, the region of measurement can be guided with both anatomical and tissue stiffness information.

Spleen Stiffness and splenoportal venous flow

Ran Hai-Tao et al
J Ultrasound Med , Feb 2013

Liver elastography is able to predict increase of liver stiffness in portal hypertension and to predict variceal bleeding with high sensitivity and specificity.

Moreover it can be used to evaluate decrease of portal pressure after TIPS placement

Liver elastography for the diagnosis of portal hypertension in patients with liver cirrhosis

Roxana S et al
Med Ultrasonics, 2012

Performance of ARFI for the staging of liver fibrosis: a pooled meta-analysis


**J Viral Hepatitis 2012
Friederich-Rust et al**

518 patients - 8 studies

The mean diagnostic accuracy for cirrhosis: 0.93%

**In the sub-group of patients undergoing both ARFI
and TE: comparable results**


Acoustic Structure Quantification (ASQ) a new diagnostic tool in ultrasonography of the liver



over the last decade methods to quantify the changes of ultrasonic texture have focused on non-invasive tissue classification of parenchymal organs, primarily the liver, by using different mathematical procedures

- ✓ ASQ describes the elastic scattering of light that passes gas atoms which have a much smaller diameter than the wave-length of the light
- ✓ normal liver parenchyma is mainly composed of a 3D arrangement of many structures that are smaller than the wavelength of the typical ultrasound pulse used in clinical examinations

Acoustic Structure Quantification (ASQ) a new diagnostic tool in ultrasonography of the liver



- ✓ in livers containing fibrosis or cirrhosis, nodules and fibrous structures are larger than the ultrasound wavelength

- ✓ **ASQ measures the difference between this theoretical echo amplitudes distribution and the real measurement in a ROI of a patient, using the chi-square as statistical tool**

- ✓ the results of this comparison, the $Cm2$ values, are shown in histogram form

Precision QPure+



TOSHIBA

0:- - O
Prof. Giorgio - Napoli

- OPE - ASQ

09/04/2010
10:00:43

ASQ



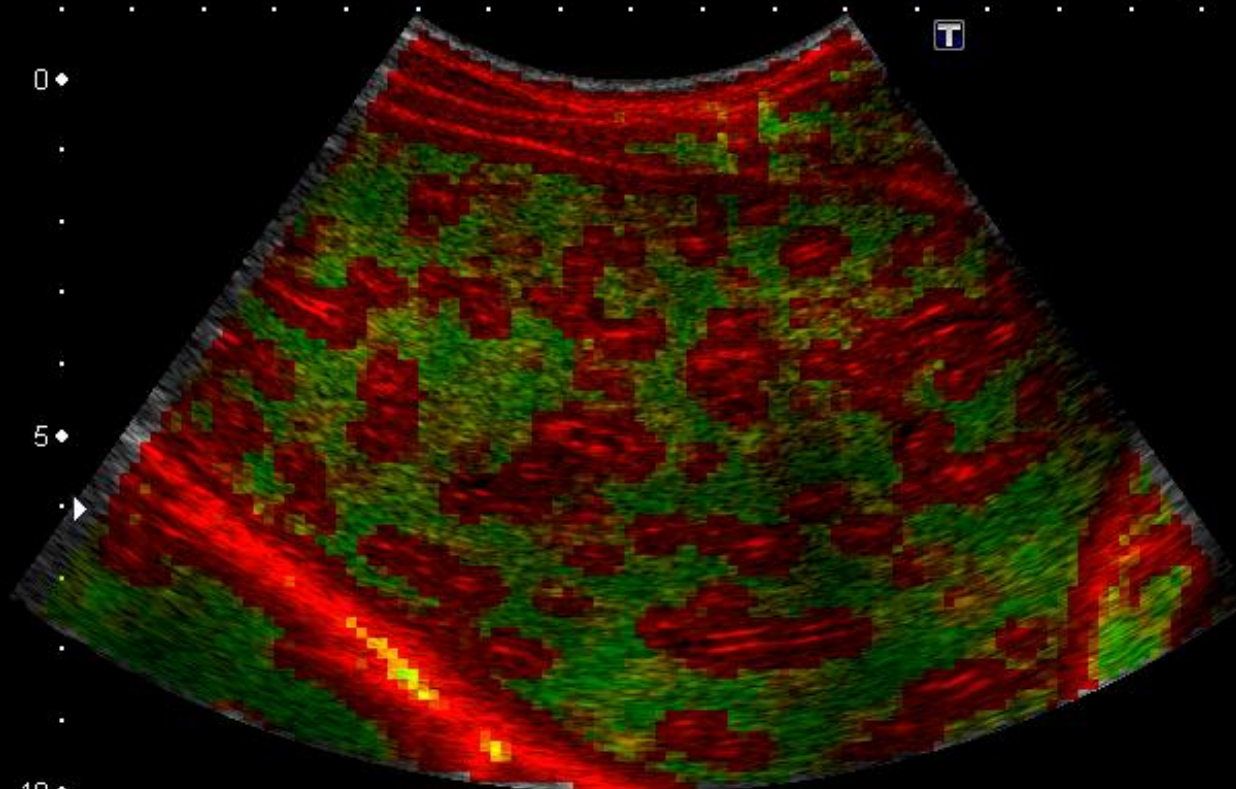
0 ♦

5 ♦

6C1
T5.0

7 fps

10 ♦



MI: (1.5)
2DG
80
DR
65



1/3



100 150 200 Cm²



Quit

Storing

HDD:94% Free



TOSHIBA

01:- - O
Prof. Giorgio - Napoli

- OPE - ASQ

09/04/2010

10:09:19

ASQ



0

5

10

6C1
T5.0

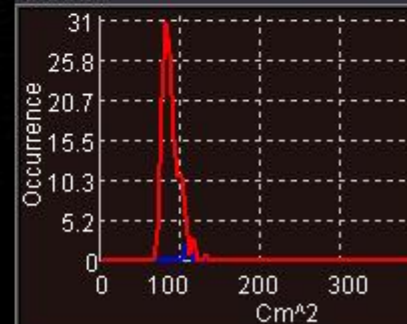
7 fps



MI: (1.5)

2DG
80DR
65

Result



2/2

ROI Type

1

2

All

Mode	82
Average	88
SD	10

Distrib

Graph

Quit

Accum

Large

Storing

HDD:94% Free

B-Mode Ultrasound with algorithm based on statistical analysis of signals: evaluation of liver fibrosis in patients with chronic hepatitis C

Toyoda H et al, AJR; 2009

- ✓ 148 pts with histologically proven chronic hepatitis C without cirrhosis
- ✓ the peak value of the Cm2 histogram was calculated from B-mode US images and the resulting value was compared with the histologic fibrosis grade

✓ the values were 124.5 (range 109.5 – 148.0) for pts with fibrosis grade F0 or F1, 131.5 (range, 116.0 – 146.0) for pts with fibrosis grade F2, and 144.0 (range, 117.5 – 154.0) for pts with fibrosis grade F3

✓ the peak C2m histogram value for F3 was higher than that for F0 or F1 ($p < 0.001$) and F2 ($p = 0.0003$), and the value for F2 was higher than that for F0 or F1 ($p = 0.0027$)

results

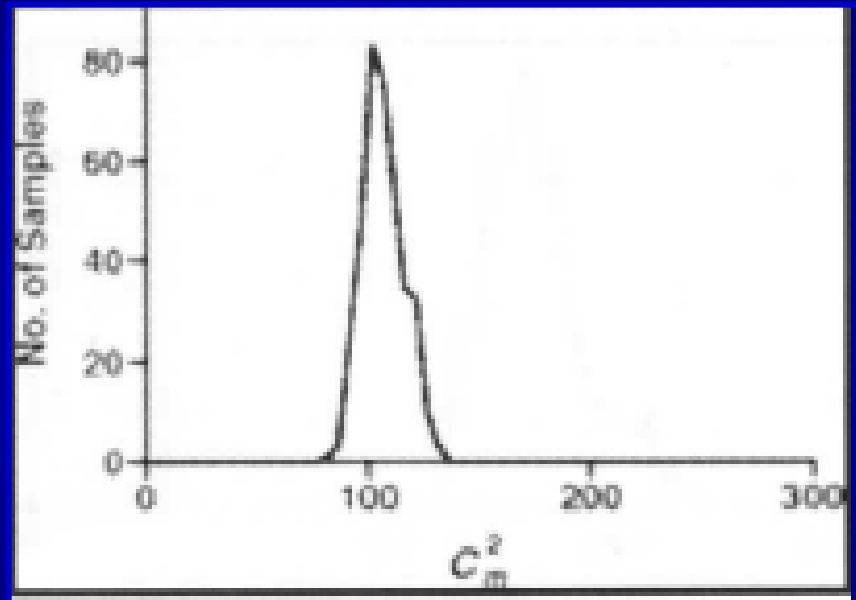
- ✓ a significant increase in the median peak C2m histogram value was observed with progression of fibrosis grade, however, no statistically significant increase in the median peak C2m histogram value was observed between pts with grade F0 fibrosis and those with F1 fibrosis

B-Mode Ultrasound with algorithm based on statistical analysis of signals: evaluation of liver fibrosis in patients with chronic hepatitis C Toyoda H et al, AJR; 2009

conclusion

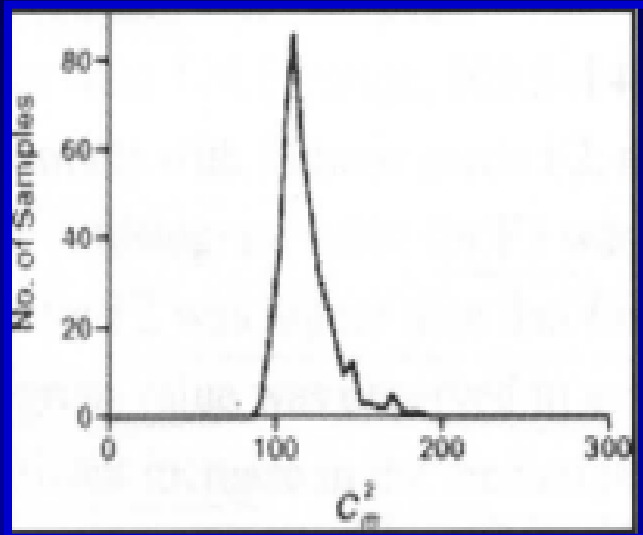
- ✓ these results shown that peak value of a C2m histogram may be associated with an increase in the grade of liver fibrosis, making it possible to evaluate the degree of liver fibrosis by analysis of B-mode images

B-Mode Ultrasound with algorithm based on statistical analysis of signals: evaluation of liver fibrosis in patients with chronic hepatitis C Toyoda H et al, AJR; 2009

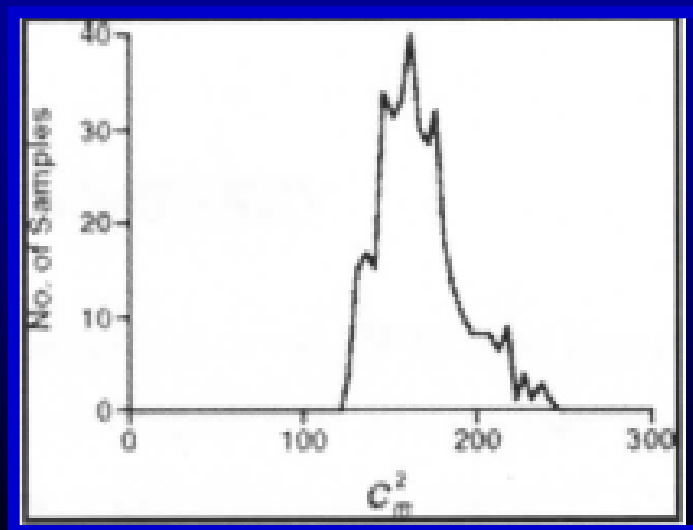
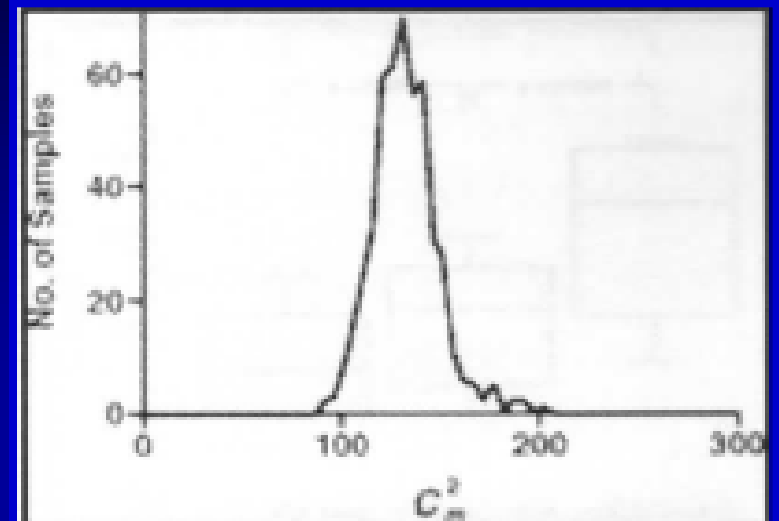


examples of C_{2m}
histograms Agar
Phantom

liver with grade F-1 fibrosis



liver with grade F-2 fibrosis



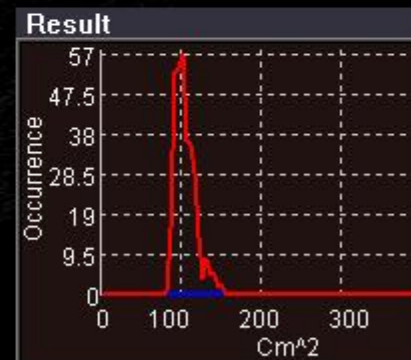
liver with grade F-3 fibrosis

ASQ



6C1
T5.0
7 fps

MI: (1.5)
2DG
87
DR
65



5/5

ROI Type

Buttons: [Triangle], [Circle], [Trash], [2], [Trash], [3], [Trash], [All]

Storing

HDD: 94% Free

Buttons: [List], [Empty Box], [Empty Box], [Empty Box], [Empty Box]

TOSHIBA

9:- - O

Prof. Giorgio - Napoli

- OPE - ASQ

08/04/2010

12:45:37



0 ♦

5 ♦

10 ♦

6C1
T5.0

7 fps



MI: (1.5)

2DG
80

DR
65

TOSHIBA

9:- - O
Prof. Giorgio - Napoli

- OPE - ASQ

08/04/2010

12:46:16

ASQ



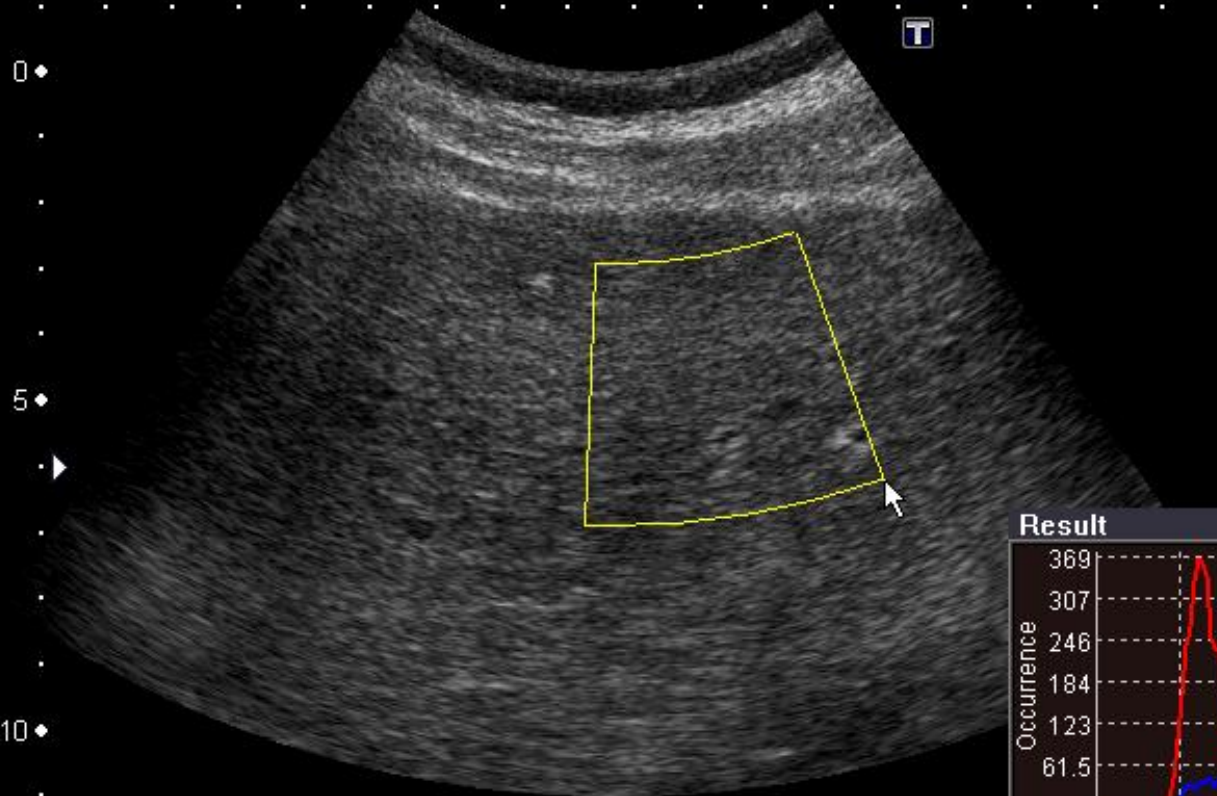
0 ♦

5 ♦

10 ♦

6C1
T5.0

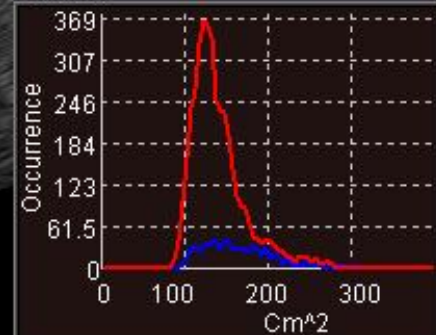
7 fps



MI: (1.5)

2DG
80DR
65

Result



1/2

ROI Type

1



All

Mode 125

Average 142

SD 39

Distrib

Graph

Accum

Large

Quit

Storing

HDD:95% Free



TOSHIBA

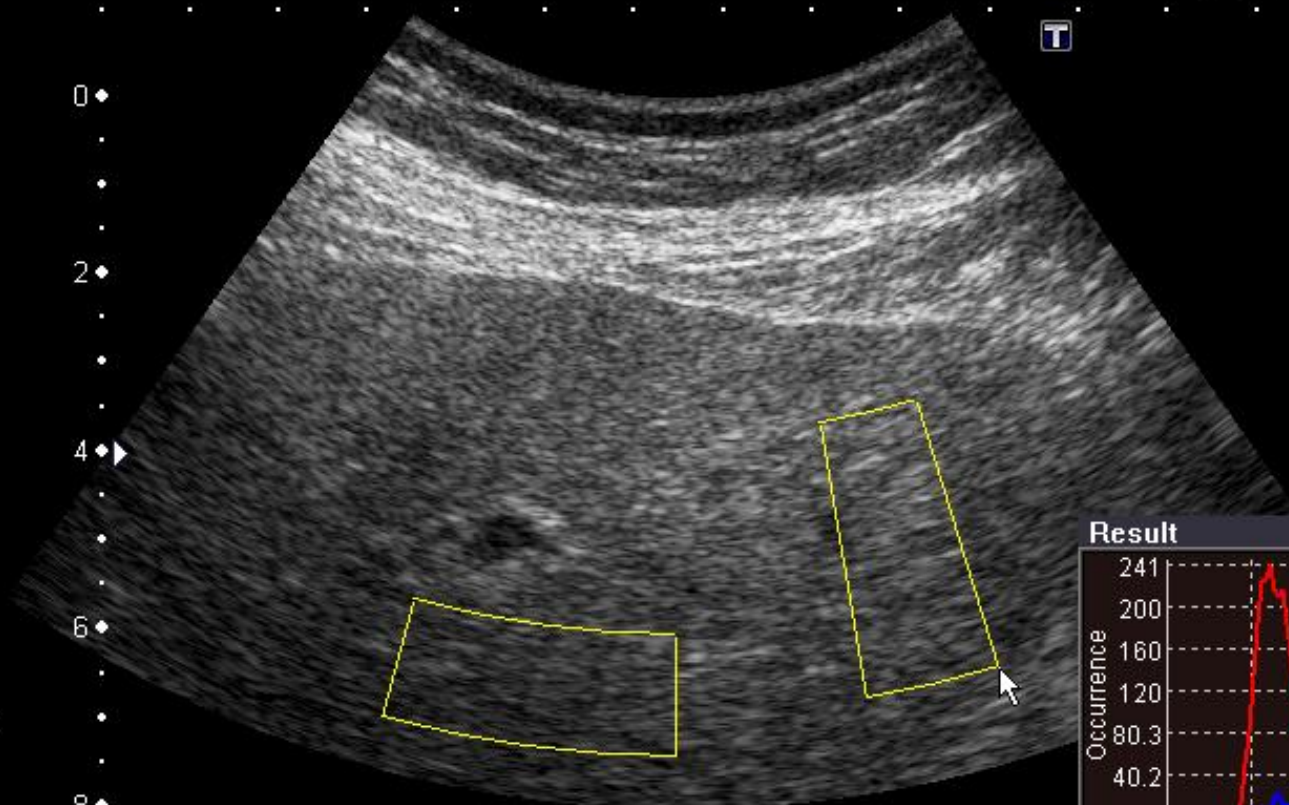
8:- - O
Prof. Giorgio - Napoli

- OPE - ASQ

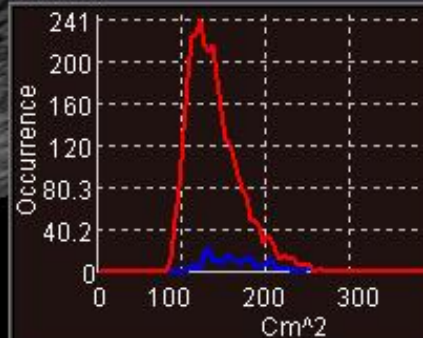
08/04/2010

12:37:30

ASQ

6C1
T5.0
7 fps0 ♦
.
2 ♦
.
4 ♦ ▶
.
6 ♦
.
8 ♦MI: (1.5)
2DG
80
DR
65

Result



1/2

ROI Type

1 2

All

Mode 124
Average 140
SD 33

Distrib Graph
Accum Large

Quit

Storing HDD:95% Free

TOSHIBA

20100408.105250.TSB_Hosp.ID:20100408.10... O
Prof. Giorgio - Napoli - OPE - Abdomen

08/04/2010
10:56:06

Precision APure+

T

0 ♦

5 ♦

10 ♦

15 ♦

6C1
diffT5.0
21 fps

MI: (1.5)

2DG
85

DR
65



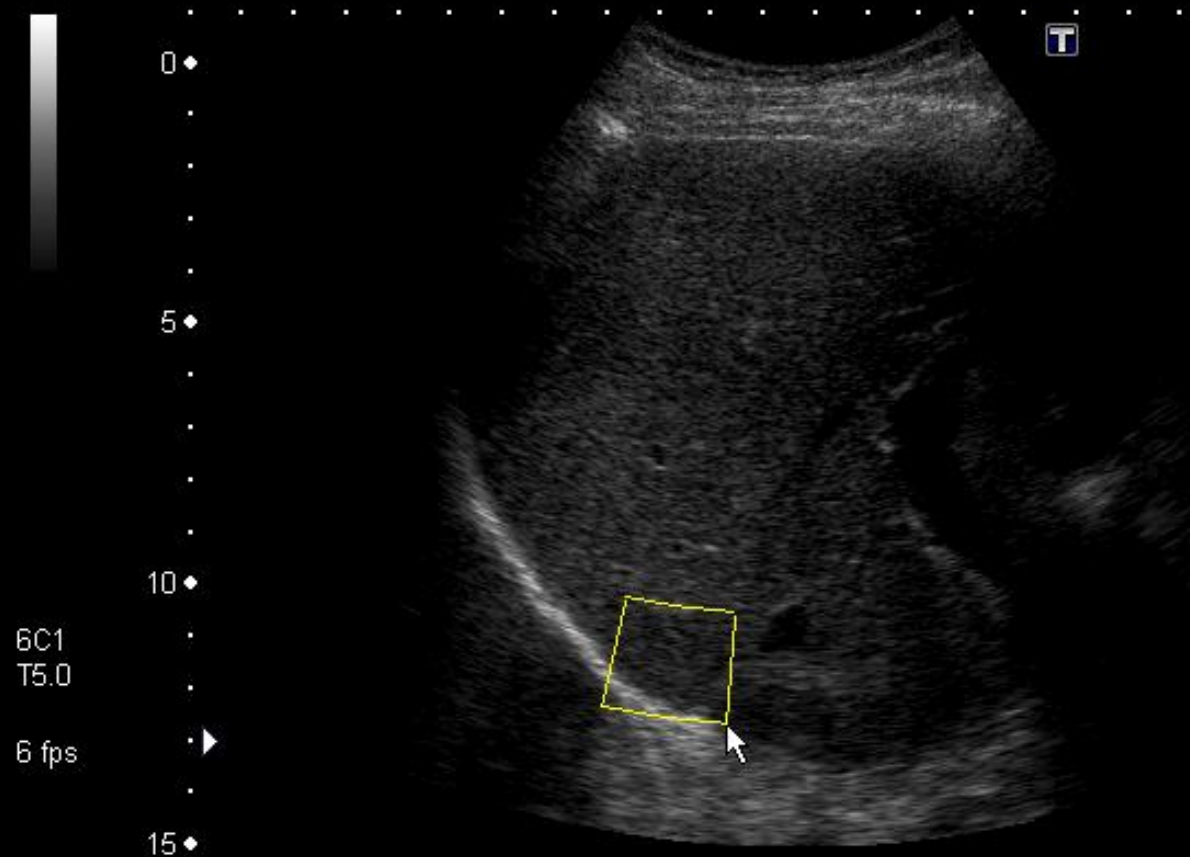
TOSHIBA

20100408.105250.TSB_Hosp.ID:20100408.10... O
Prof. Giorgio - Napoli - OPE - ASQ

08/04/2010

10:57:10

ASQ



MI:(1.4)

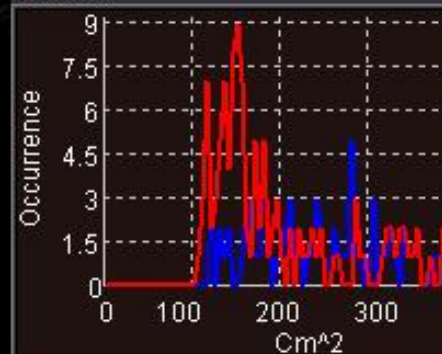
2DG

80

DR

65

Result



3/3

ROI Type

1

All

Mode 154

Average 193

SD 74

Distrib

Graph

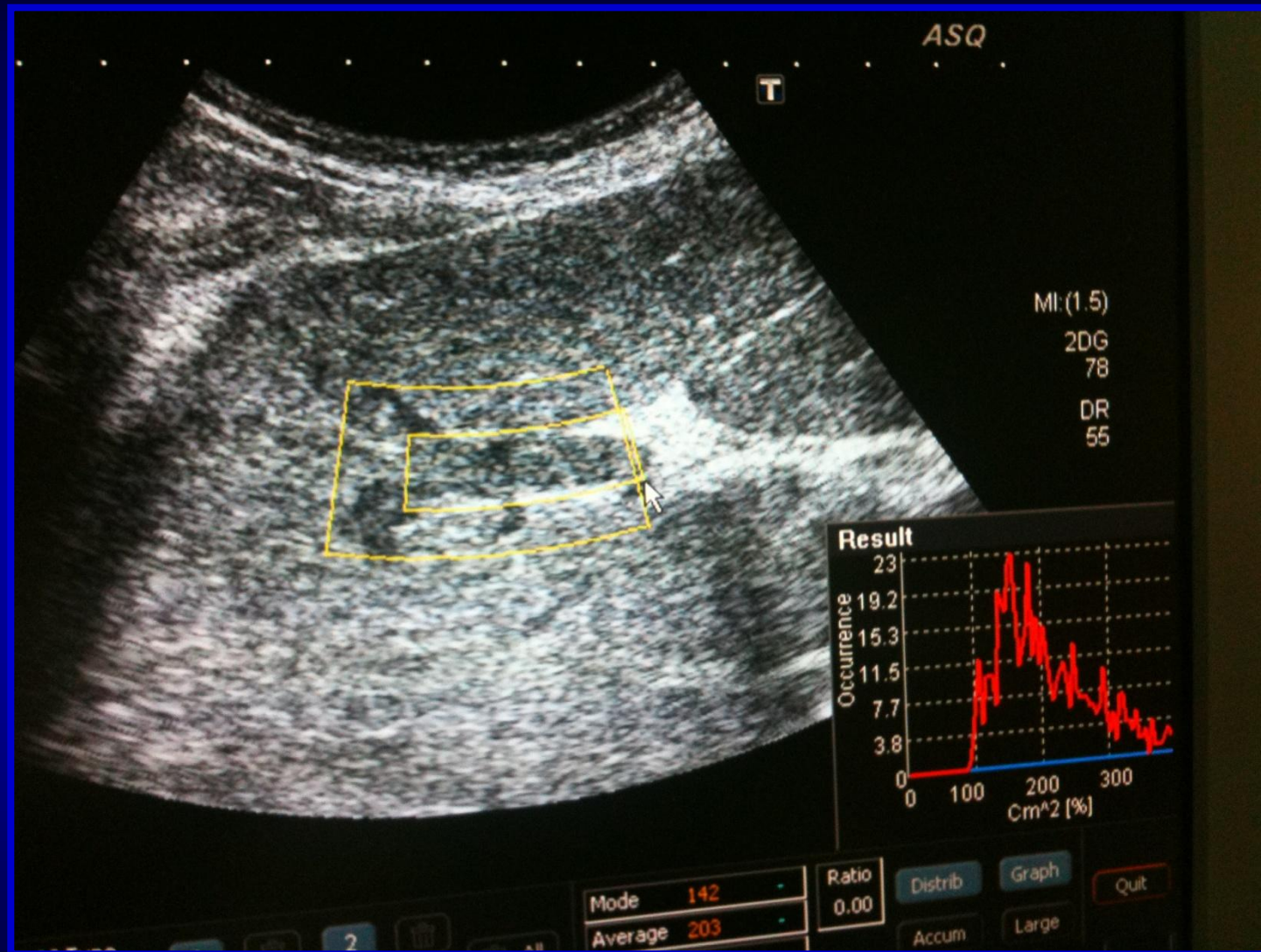
Quit

Accum

Large

Storing

HDD:98% Free

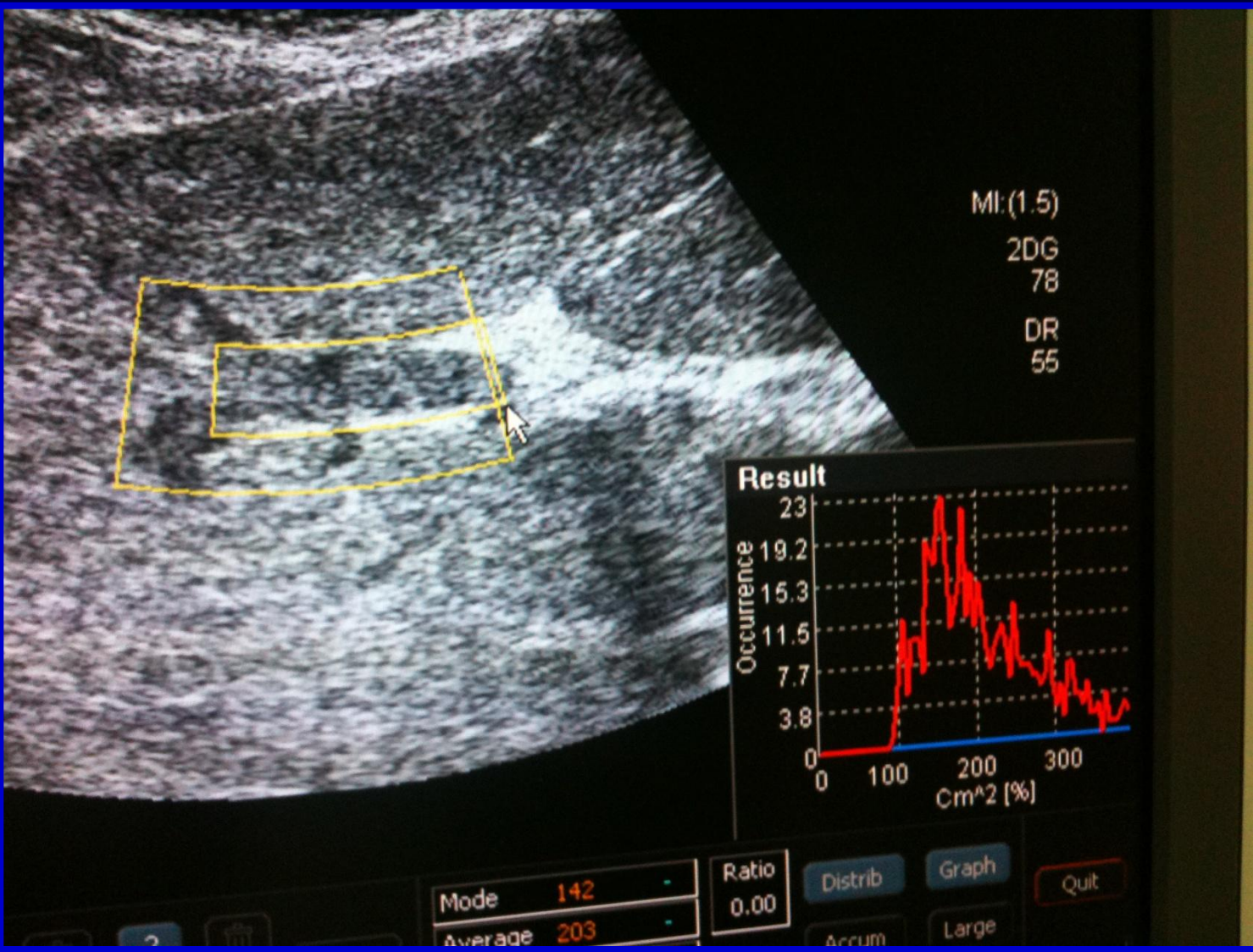


TOSHIBA

20110413.114322.TSB_Hosp.ID:20110413.11... O
PROF. A. GIORGIO Napoli - OPE - Abdomen

13.04.2011
11:46:05





	Pazienti SANI (28)	Pazienti con CHC (76)	Pazienti con Cirrosi (49)	Pazienti con HCC (18)	p
CM²	73 (69-77)			204 (199-248)	F1 vs F0: ∞
F1		82 (79-88)			F2 vs F1: ∞
F2		100 (89-118)			F3 vs F2: ∞
F3		120 (117-131)			F4 vs F3: ∞
F4			140 (138-147)		HCC vs F4: ∞

Giorgio et al, SIMIT 2011

	Pazienti SANI (28)	Pazienti con CHC (9)	Pazienti con Cirrosi (1)	p
CM²	73 (69-77)			F1 vs F0: ∞
F1		82 (79-88)		F2 vs F1: ∞
F2		100 (89-118)		F3 vs F2: ∞
F3		120 (117-131)		F4 vs F3: ∞
F4			140 (138-147)	

Giorgio et al, SIMIT 2011

DIAGNOSTIC AND THERAPEUTIC ADVANCES IN HEPATOLOGY

Noninvasive Assessment of Liver Fibrosis

Doris Nguyen¹ and Jayant A. Talwalkar^{2,3}

Hepatology-2012

Evidence for chronic liver disease

CONVENTIONAL
ULTRASOUND



Fibrotest or elastography
(TE, MRE)

ARFI, SWE, ASQ



Results consistent with
F0-F1 fibrosis

Results consistent with
F2-F4 fibrosis

Results consistent with
cirrhosis (F4)

Biopsy not mandatory but
may be needed for clinical
decision making

Biopsy if needed for clinical
decision making

Biopsy not mandatory

