

Reproducibility of transient elastography among chronic HCV patients in Egypt

Aisha Elsharkawy

Assistant lecturer of tropical medicine-Cairo university



Background:

Management of hepatitis C virus infection

- Treatment indication depends on the extent of liver fibrosis
 - Fibrosis stage \geq F2
- Liver biopsy considered as a gold standard for liver fibrosis assessment but
 - Invasive procedure, poor acceptance
 - Poor reliability when length <15 mm
 - Sample variability.
 - Cost, limited availability

Non invasive methods

- Non invasive methods have been validated:
 - Serum markers: Fibrotest®, Fibrometre®,
 - Transient elastography (Fibroscan®)

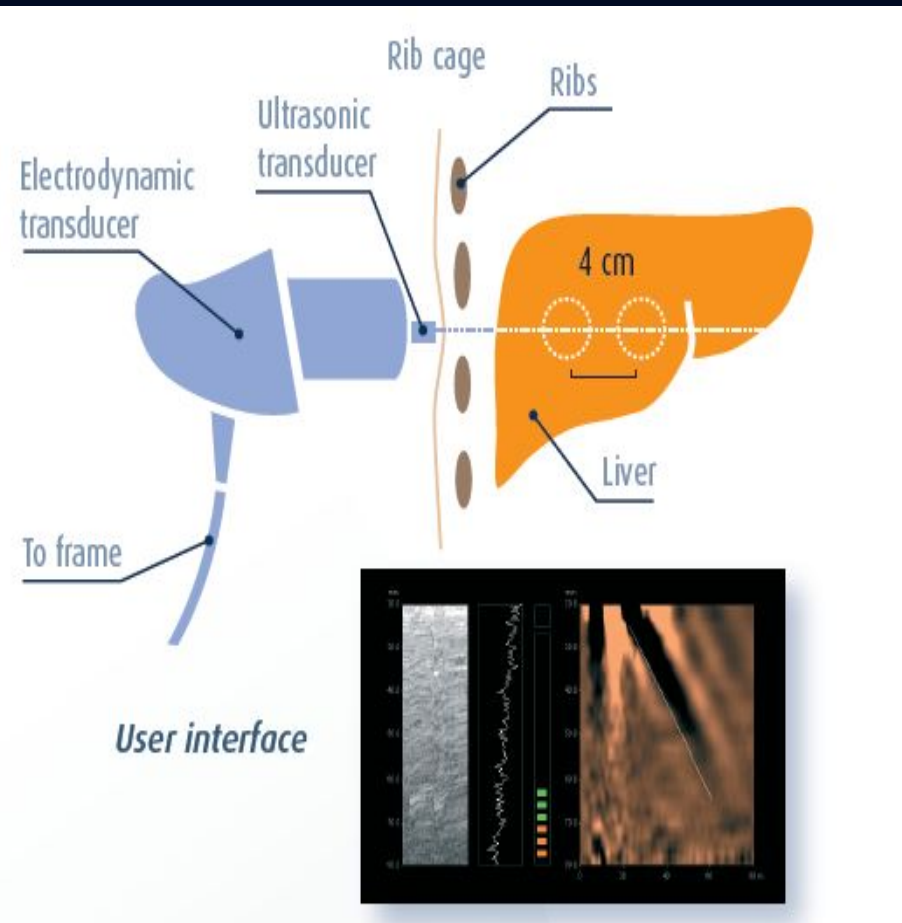
Fibroscan®

FibroScan®



- Examination duration < 5 mn
- 10 successful acquisitions
- Median value = correct value
- Results expressed in kPa





FibroScan®

Lastname: **SMITH**
 Firstname: **JOHN**
 Code: **A12478**
 Birthdate: **21/03/1973**
 Operator: **BROWN**
 Date: **07/10/03**
 Examination time: **00:02:55**

Stiffness (KPa): **3.9**

IQR (KPa): **0.7** CS (KPa): **3.6**

Archives Start Print Test 4/10 Valid 10

- 10 valid measurements, Success rate $\geq 60\%$, IQR $< 30\%$ of the median

Background

Previous studies on reproducibility

- Transient elastography (TE) is a **highly reproducible** and user-friendly technique for assessing liver fibrosis in patients with CLD
- with **excellent** interobserver and intraobserver agreement
- reproducibility is significantly **reduced** in patients with
 - steatosis ,
 - increased BMI
 - and lower degrees of hepatic fibrosis

(Fraquelli M et al , Gut 2007)

What is reproducibility?

- Refers to the ability of a test or experiment to be accurately reproduced, or replicated.

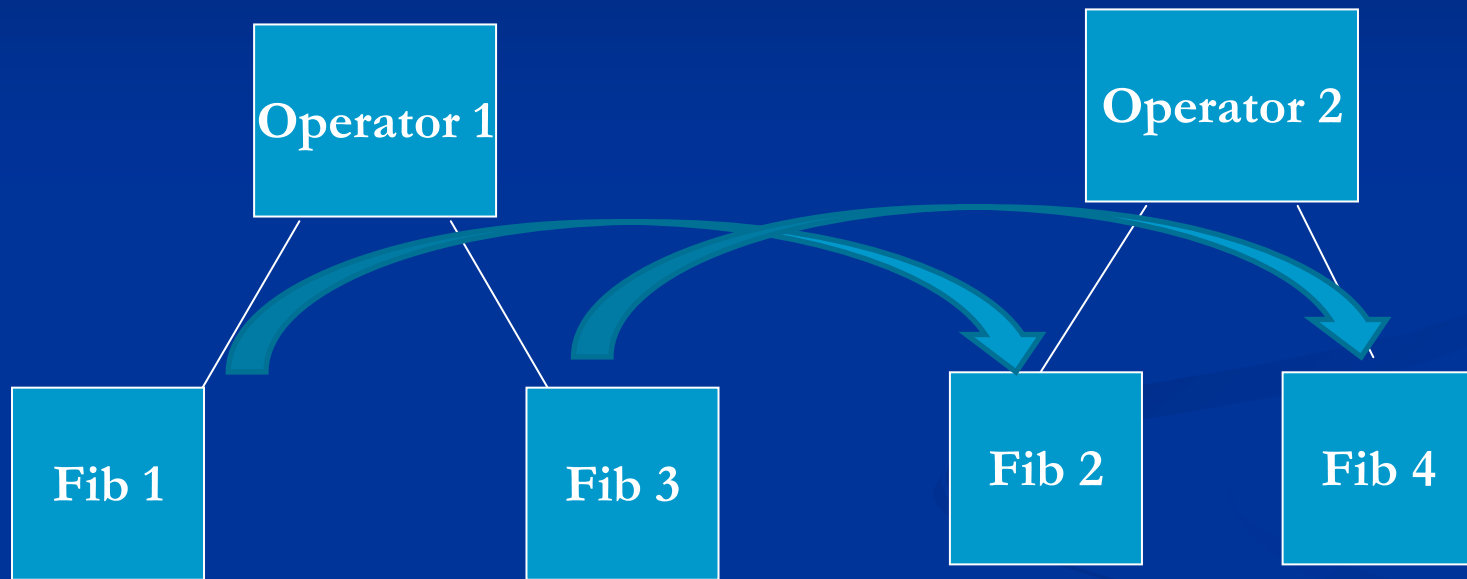
Objectives

- To assess the intra and inter-operator reproducibility of Liver Stiffness Measurement among chronically HCV infected patients in Egypt.

Methods: population

- Chronic HCV patients included in "fibrosis markers study "(ANRS 12184 PIs: Gamal Esmat, Philippe Bonnard)
- Inclusion criteria:
 - ≥ 18 years
 - No interferon treatment or liver biopsy contra-indication
 - BMI < 35
 - Willing to be treated if indicated
 - Consent to participate

Methods: Design



Blinded To other Operators results
Random order of operator 1, 2
Free choice of anatomical site

Methods: Analysis

- **Reproducibility analysis**
 - *Graphic method of **Bland and Altman***
 - Quantitative analysis
 - ***Intraclass Correlation Coefficient (ANOVA)***
 - Qualitative variable:
 - ***Kappa Coefficient***

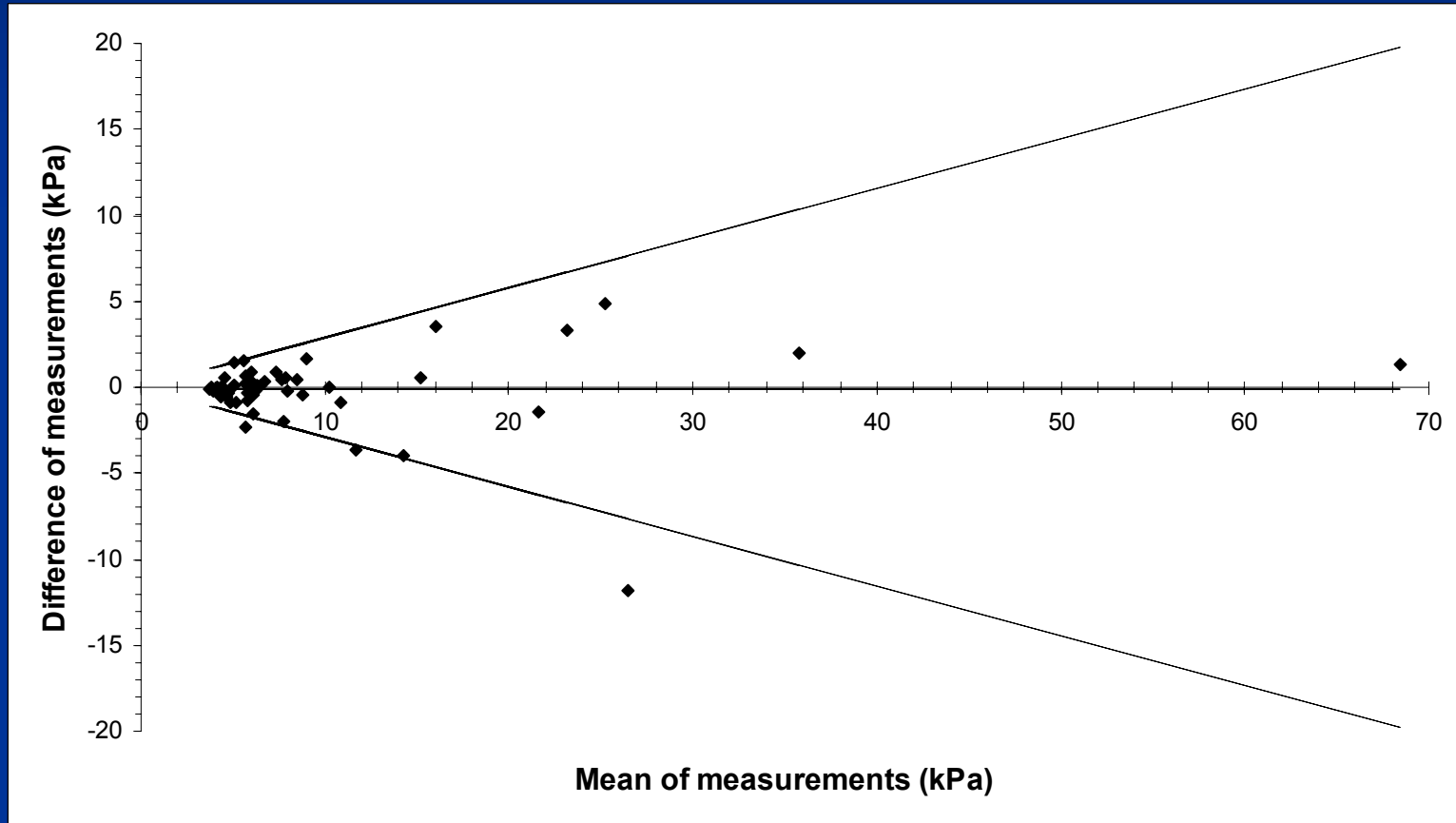
Patients characteristics (N=58)

	% or median[IQ1, IQ3]
Gender (male)	74%
Age (years)	39 [37 - 42]
Overweight (BMI>25)	74%
Obesity (BMI>30)	28%
ALT≥N	66%
Schistosomia serology +	35%

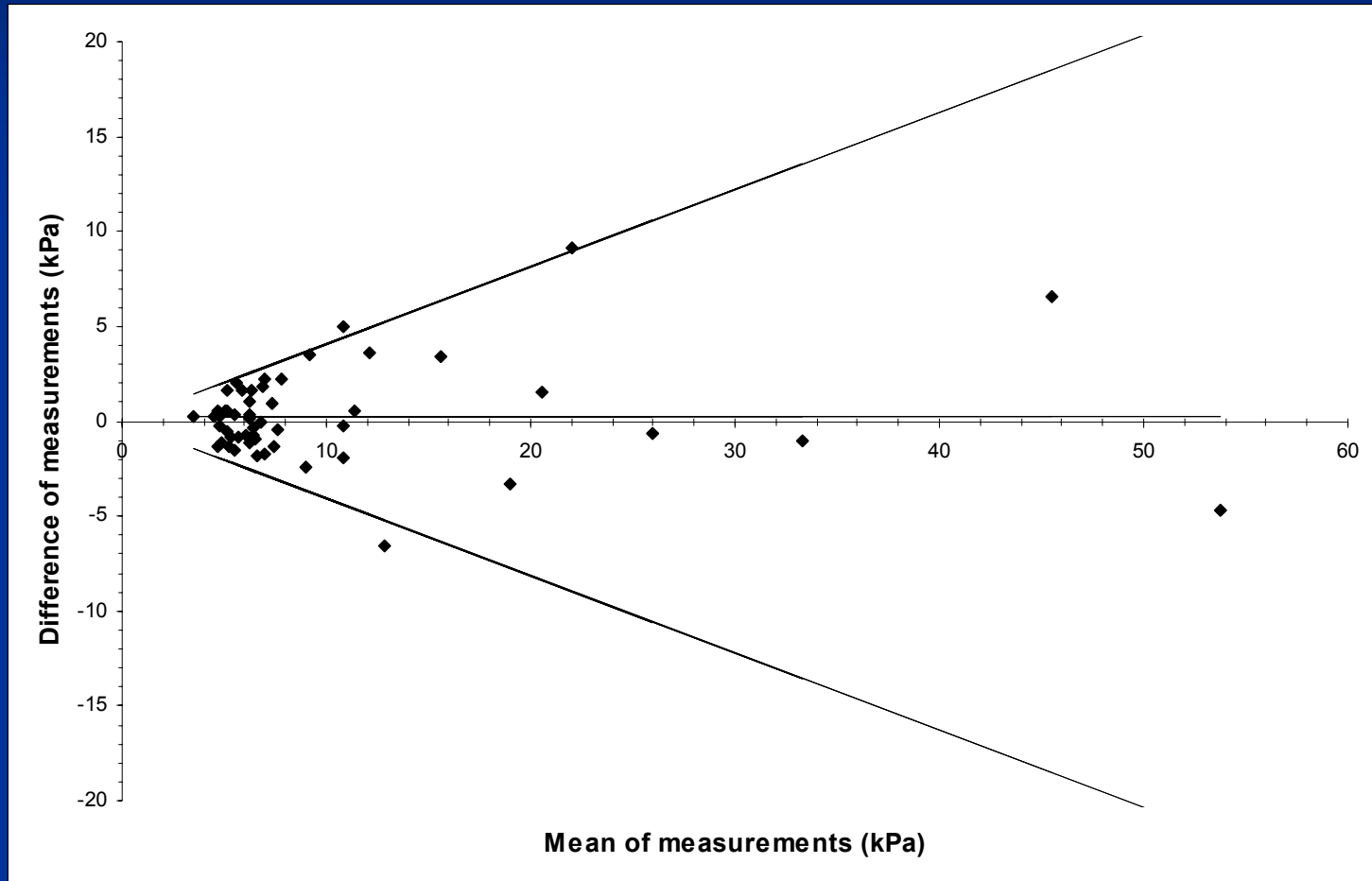
Liver Stiffness Measurements

- Failure rate 7% (N=4)
 - overweight
- Liver Stiffness Measurement
 - N=54 patients, N=216 LSM
 - Median=6,3 kPa, from 2,8 to 69,1 kPa

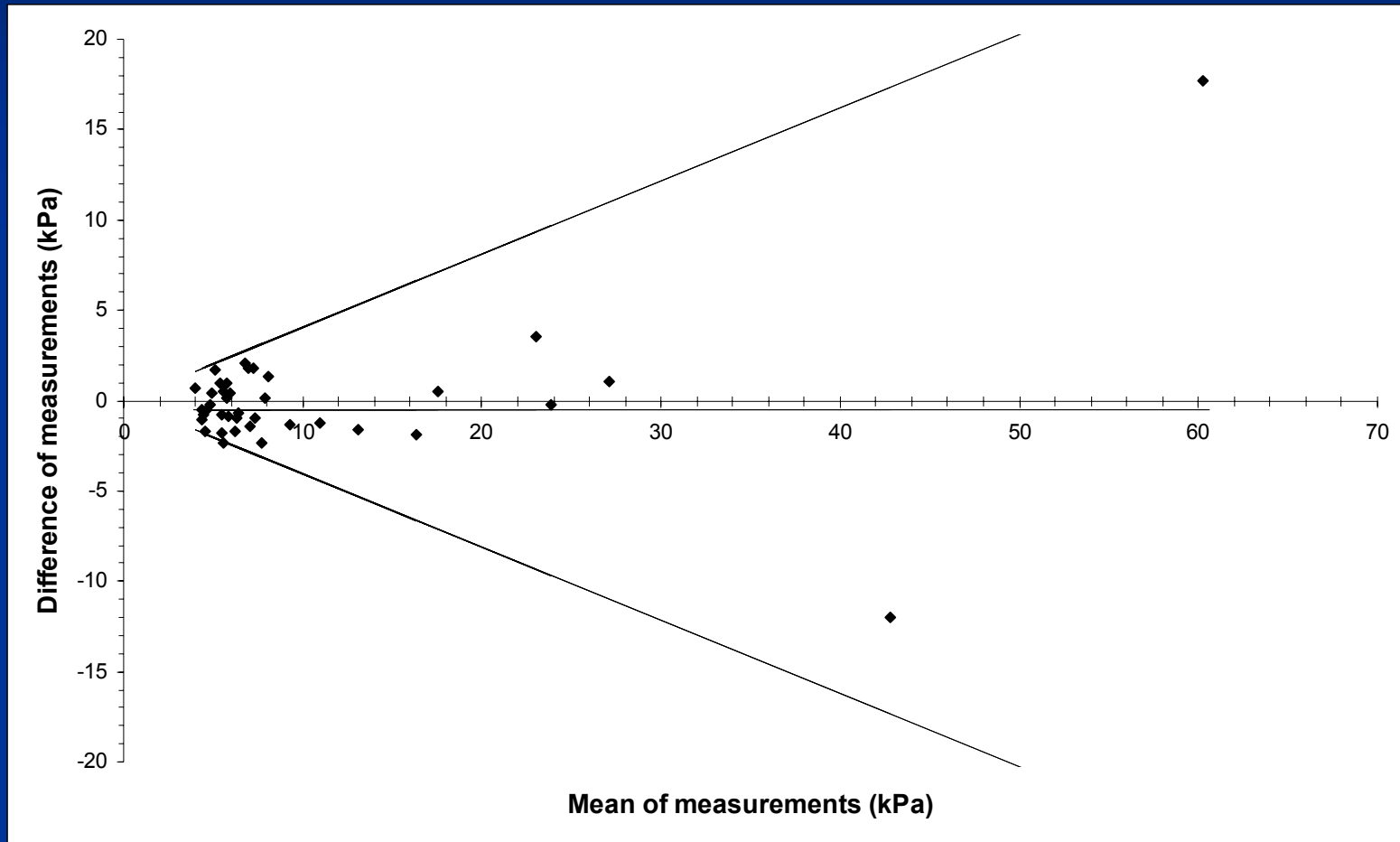
Results: Bland and Altman graphic Operator 1



Results: Bland and Altman graphic Operator 2



Results: Bland and Altman graphic Inter-operator



Results: Intraclass Correlation Coefficient

$$\hat{\rho}_{inter} = CCI_{inter} = \frac{\sigma_b^2}{\sigma_b^2 + \sigma_o^2 + \sigma_h^2 + \sigma_e^2}$$

■ Intra-operator

- Oper1: ICC=0,97 PI 95% [0,95-0,99]
- Oper2: ICC=0,94 PI 95% [0,91-0,97]

■ Inter-operator

- 1st: ICC=0,94 PI 95%[0,86-0,97]
- 2nd: ICC=0,95 PI 95%[0,89-0,97]

ICC	Meaning
<0,5	bad
0,5-0,71	fair
0,71-0,87	good
>0,87	excellent

Results: Intraclass Correlation Coefficient

- LSM \leq 14.5 kPa
- Intra-operator
 - Oper1: ICC=0,83 PI95% [0,74-0,92]
 - Oper2: ICC=0,82 PI95% [0,72-0,92]
- Inter-operator
 - 1st: ICC=0,75 PI95% [0,55-0,87]
 - 2nd: ICC=0,80 PI95% [0,66-0,87]

ICC	Meaning
<0,5	bad
0,5-0,71	fair
0,71-0,87	good
>0,87	excellent

Rousselet et al. Hepatology 2005

Results: Kappa Coefficient ($<F2/\geq F2$): threshold 7,1 kPa

■ Intra-operator

- Oper1: $\kappa=0,92$ [0,81-1,00]
- Oper2: $\kappa=0,69$ [0,49-0,88]

■ Inter-operator

- 1st: $\kappa=0,65$ [0,44-0,88]
- 2nd: $\kappa=0,80$ [0,63-0,97]

K	Meaning
$<0,2$	bad
0,4-0,6	fair
0,6-0,8	good
$>0,8$	excellent

Castera et al., Gastroenterology 2005
Landis-Koch et al. Biometrics 1997

Conclusions

- ICC (intraclass correlation coefficient)
 - Excellent, as in previous publications.
 - However, ICC is not a good indicator as it gives too much weight to the differences between subjects compared to the differences between operators.
 - When restricted to patients with LSM ≤ 14.5 kPa, ICC is much less satisfactory.

Conclusions

- Alternative approach based on qualitative indicators i.e, patients are classified in 2 categories ($<F2$ / $\geq F2$) corresponding to “do not treat / treat”:
 - Overall agreement (Kappa coefficient) was good
 - However, it may suffer from the fact that at the threshold value (e.g., 7.1 kPa for $<F2/\geq F2$), there is a high variability (± 2.8 kPa).

Conclusions

- We need to
 - To confirm the results with a larger number of patients
 - To identify the factors associated with lack of reproducibility
 - To discuss these results in comparison with the performance of other methods in identifying $\geq F2$ patients

Acknowledgement

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THANK YOU