Morphologic Hemodynamic and Elastographic Ultrasound criteria in grading liver fibrosis and portal hypertension

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US imaging in chronic hepatitis

Overview
1. 1980-2000: Imaging (US, CT, MRI), needle biopsy, histology
2. 2000-2010: The introduction of Elastography/Fibroscan
3. 2010-...: Establishment of Elastography, Innovations
4. Ongoing Study
5. Perspectives: Medical and technical issues
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1. 1980-2000: Needle biopsy and histology
   ▪ Clinical and biochemical data
   ▪ Introduction of Fibrotest
   ▪ Endoscopy for varices

   - Introduction of US guided liver biopsy
   - Histology
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2. 2000-2010: The introduction of Elastography
   - Clinical and Biochemical Data
   - Establishment of Fibrotest
   - Fibroscan: establishment of the non-traumatic estimation of liver fibrosis
   - Ultrasound, CT and MRI for focal liver lesions
   - CEUS in early diagnosis of HCC
   - Biopsy and Histology still the “gold-standard”
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2. 2000-2010: Introduction of Elastography

- Liver biopsy is considered as the “gold standard” but has limitations
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3. 2010-…: Establishment of Elastography, Innovations

- Different methods for Fibrotest
- Fibroscan becomes a reference
- ShearWave Elastography (SWE): introduction of different technologies (HiRTE, ARFI, TSI)
- Introduction of elastographic criteria for liver lipomatosis/inflammation
- Prevalence of US over CT and MRI for liver morphology/hemodynamics
- CEUS in diagnosis and guided treatment of small HCC
- Rarefaction of liver biopsy
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3. 2010-...: Establishment of Elastography, Innovations

Many similar but different Strain and SWElastography methods
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4. Ongoing Study: Inter/Intra- observer variability

Bland Altman Plot: Difference of ratings vs. mean of ratings

- **ICC**: ICC equal to 1 means that all SWE variability relates to patient variability (patients effect) and that there is no variability related to the examiners (examiner effect)
- As ICC decreases the examiner effect begins to predominate over patient effect
- **Inter-examiner** agreement was calculated as the agreement between the first liver SWE measurement of the two observers.
- **Intra-examiner** agreement was calculated as the agreement between the first and the second SWE measurement of each observer
- **ICC** represents the variability of measurements in relation to the intrinsic variability of measurements of the sample

![Bland-Altman plot of Protocol 1, IntraOVar.](image)
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4. Ongoing Study: Inter/Intra-observer variability

Protocol 1

Protocol 2
One step forward:

Protocol 3

Important Ia-IeOVar, low ICC.
Acceptable Ia-IeOVar.
SWE results according to the fibrosis score (F) of the 60 patients who underwent both SWE and liver biopsy
Bars indicate the minimum, mean and maximum value
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4. Ongoing Study: combining all US Data

Aim: Form a Neural Network intergrading morphology, hemodynamic and elastographic data

4.1 B-Mode/Morphology: US measurements of liver, PV and spleen: LL, CL, RL, PV, SP

4.2 Color/Power Doppler/Vein Flow: Precise imaging and measurements of hemodynamics of portal vein thrombosis and varices

4.3 SW Elastography/ “virtual biopsy”: Many different technologies of SWE: reliable findings of liver stiffness/fibrosis, but non-comparable measurements in kiloPascal
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4. Ongoing Study

4.1 Liver/Spleen Morphology

LL

CL

RL

PV / Resp. variation

Spleen

PV / Pulse Doppler
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4. Ongoing Study

4.2 Hemodynamics: Portal Vein, Hepatic Veins, Splenic Vein, Mesenteric Vein
- Diameter/respiratory variation
- Direction and velocity of flow
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4. Ongoing Study

4.2 **Hemodynamics**: Portal Vein, Hepatic Veins, Splenic Vein, Mesenteric Vein

- Varices
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4. Ongoing Study

4.3 Liver and Spleen Elastography
Measurements in kiloPascal
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4. Ongoing Study

4.3 Liver and Spleen Elastography
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5. Perspectives: Medical and Technical issues

5.1 Combining Morphology, Hemodynamics and Elastography:
- Morphology: liver, PV, spleen
- Hemodynamics: PV speed/direction of flow, Varices
- Elastography: grading Liver/Spleen stiffness
- Neural Network integrating morphologic, hemodynamic, Elastographic data
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5. Perspectives: Medical and Technical issues

5.2 More information from Elastography

- Limit Intra/Inter- Obs. Var.: give the possibility to the examiner to choose a SWE- representative liver ROI and an arbitrary SWE ROI
- Organize clinical and imaging studies in order to determine normal and abnormal kPa measurements of the liver and spleen
- Use unexplored Elastography data: Add SWE features in order to estimate and grade liver inflammatory process (necro-inflammatory score)
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5. Perspectives: Medical and Technical issues

5.2 More information from Elastography:

Novel SWE quantification techniques

- Precise/flexible definition of the SWE region to be analyzed.
- Development & evaluation of new analysis parameters, not available in the system.

STEPS
1. Tracing of an arbitrary ROI
2. Custom quantification program:
   - Uses image color bar to establish quantitative link between RGB colors and Elasticity range
   - Analyzes color pixels inside the ROI and converts them to quantitative Elasticity values (kPa)
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5. Perspectives: Medical and Technical issues
5.2 More information from Elastography

Novel SWE quantification techniques

- $50^{TH}$ percentile (Median) $\rightarrow$ Robust estimator of Average Elasticity within ROI
- $10^{TH}$ percentile $\rightarrow$ Robust estimator of Minimum Elasticity within ROI
- $90^{TH}$ percentile $\rightarrow$ Robust estimator of Maximum Elasticity within ROI
- Kurtosis: $4^{th}$ central moment of the Elasticity Histogram
- Kurtosis $> 3$ indicates an increasingly peaky histogram relative to a Gaussian histogram with the same Mean and Standard Deviation (more pixels in the histogram tails, i.e. outliers)
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5. Perspectives: Medical and Technical issues

5.1 Combining Morphology, Hemodynamics and Elastography

5.2 More information from Elastography

<table>
<thead>
<tr>
<th></th>
<th>Histology</th>
<th>Fibroscan</th>
<th>US/SWE</th>
<th>MRI</th>
<th>CT</th>
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<tbody>
<tr>
<td>Morphology</td>
<td>-</td>
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<tr>
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<td>-</td>
<td>+ (Grade 1-4)</td>
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<td>+</td>
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<td>+ (Stage 1-4)</td>
<td>+ (kPa 1-20)</td>
<td>+ (kPa 1-40)</td>
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<td>+/-</td>
<td>+ (Grade 1-3)</td>
<td>+/-</td>
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<td>+ (Grade 1-4)</td>
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</table>
Ultrasound combined with SWE offer:
- An holistic approach combining morphologic, hemodynamic and elastographic data
- Precise measurements for chronic hepatopathy and cirrhosis including all consequences: fibrosis, lipomatosis, inflammation, HCC development, portal hypertension, portal vein thrombosis, varices, ascites
- Efficient approach for the early diagnosis of the HCC and the follow-up of novel therapies for measuring liver fibrosis
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5. Perspectives: Medical and Technical issues
Designing the Future

- Hemodynamic
- Morphology
- Elastography

- Fibrosis (grading)
- Lipomatosis (grading)
- Inflammation (grading)
- Portal Hypertension (grading)
EUROSON SCHOOL
Elastography & Interventional US

EUROSON SCHOOL 2015
14 - 15 FEBRUARY 2015 • ISTANBUL / TURKEY
Main Topics: Interventional / Elastography