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Ultrasonic Imaging in Liver Disease

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Abstract: Ultrasound is a widely used medical imaging technique. Tissue characterization with ultrasound has become important topic since computer facilities have been available for the analysis of ultrasound signals. Automatic liver tissue characterizations from ultrasonic scans have been long the concern of many researchers. The system advantage is its high accuracy and its computation simplicity. For each available technique, the reproducibility, results and limitations are analyzed, and recommendations are given. This set of guidelines updates the first version, published in 2015. Since the prior guidelines, there have been several advances in technology. The system can be used as a second opinion system to aid the diagnosis of liver diseases.

Keywords: Ultrasound imaging, automatic liver diagnoses, neural networks, quantitative tissue characterization, Liver diseases, Elastography.

INTRODUCTION: Elastography has been used to evaluate liver stiffness for more than 10 y. As chronic liver damage results in hepatic fibrosis, characterized by an increase of extracellular matrix produced by fibroblast-like cells, the liver becomes stiffer than normal. Elastography can be used to assess liver stiffness non-invasively. It measures tissue behavior when an external mechanical actuation or internal push; and (iii) strain elastography (SE) technique, which uses frame-to-frame differences (tissue deformation) with stress, caused by pressing the body surface or by internally occurring physiologic motion. The ARFI techniques can be divided into point shear wave elastography (p-SWE) and 2-D shear wave elastography (2-D SWE) techniques. The shear wave-based techniques (TE and ARFI techniques) measure the speed of shear waves in tissues. The shear waves are generated by an external mechanical push in TE or by the push pulse of a focused ultrasound beam in the ARFI techniques. For both of these techniques, the shear wave speed calculated, which is related to liver stiffness, can be converted into kilopascals, the unit of Young's modulus E (3rv2 , where r is the tissue density and v is the speed of the shear wave), assuming that the tissue is purely elastic, incompressible, its elastic response is linear and that the tissue density is always 1000 kg/m3 . It is important to note that magnetic resonance elastography (MRE) reports the shear modulus in kilopascals and is three times smaller than the Young's modulus used to report the results of the ultrasound techniques (Barr et al. 2016b). Guidelines on the use of US elastography for the assessment of liver diseases were produced by the World Federation for Ultrasound in Medicine and Biology (WFUMB) a few years ago (Ferraioli et al. 2015); however, this is a very rapid growing field and new evidence and improvements are available since that release. Our objectives were to determine, based on the evidence from the literature, what is new since the previous release of the WFUMB guidelines (Ferraioli et al. 2015), regarding the impact of elastography on reduced use and/or replacement of liver biopsy for diffuse liver diseases. The potential role of elastography in the characterization of focal liver lesions is also discussed. Hepatology is an excellent example of how results deriving from basic science influence our everyday clinical practice. This involves diagnostic procedures as well as therapeutic developments. The role of diagnostic imaging in the assessment of liver disease continues to gain in importance. Imaging of the liver has progressed rapidly during the past decade with continued advancement of current ultrasound, computed tomography, and magnetic resonance imaging.

Refinement enabling better anatomic characterization of disease and significant strength from the addition of new techniques and high resolution images were seen. Improvements in ultrasound (US) scanners over the past few decades have been remarkable: advances such as color Doppler and

harmonic imaging have increased image quality and accuracy. Ultrasound is usually the first imaging modality in the evaluation of liver disease because it is easy to perform, widely available, relatively inexpensive and is cost effective. Tissue characterization is a term that usually refers to the quantitative estimation of tissue or image features leading to a more accurate distinction of normal and abnormal tissues, the results of tissue characterization are quantitatively interpreted using numerical values. It aims to provide additional information about tissues not available by viewing ordinary images of the ultrasound B-scan. Thus, gained information are quantitative and is far less operator dependent than the usual B-scan images. Changes in tissue elasticity are generally correlated with pathological phenomena. Many cancers appear as extremely hard nodules which are a result of increased stormal density (collagen content). Other diseases involve fatty and/or collagenous deposits which increase or decrease tissue elasticity. Complicated fluid filled cysts could be invisible in standard ultrasound examination. Diffuse diseases such as cirrhosis are known to significantly reduce the elasticity of the liver, yet they appear normal in conventional ultrasound examinations. The Visual criteria provide low diagnostic accuracy around 70%. Therefore the physicians may have to use further invasive methods such as the pathology investigation of ultrasonically guided needle biopsy [1], [2]. Although this technique is considered to be the best test for diagnosis, it has the disadvantage of being invasive and risky, it may cause a great risk of cancer spread if it cuts through a localized cancer area. The quantitative tissue characterization steps first, are to extract the features (parameters) from the returned signal, (pulse-echo data) and then analyze these features and correlating it to different Pathologies [3], [4]. Quantitative tissue characterization technique (QTCT) is gaining more acceptance and appreciation from the ultrasound diagnosis community. It has the potential to significantly assist sonographers to achieve better diagnostic rates. QTCT is based on extracting parameters from the returned ultrasound echoes for the purpose of identifying the type of tissue present in ultrasound scan plane. These parameters can be divided into two main categories according to their origin: 1) RF Signals parameters: extracted from the returned RF echoes prior to machine processing, attenuation and backscattering parameters. 2) Image texture parameters: extracted from the video image after the echo processing is performed in machine, such parameters include the statistical characteristics of the gray level distribution in certain region of interest (ROI) in the image. RF Signal parameter has the advantage of being free from any machine processing distortions, while the second has the advantage of being easier to implement [5], [6]. The major advantage of using computerized B-mode ultrasound is the possibility of obtaining tissue-specific parameters which are unattainable by visual assessment. These characteristics apply to changes of the tissue texture due to diffuse diseases of organs (e.g., cirrhosis) or caused by focal lesions. In both cases the changes are expressed relative to some standard display of the texture e.g. the normal echogram of the healthy organ. Brightness scale depends on echo strength [7]. The mean gray level physical meaning is the brightness or echogenicity of the texture, which most of the Sonographers write it in their ultrasound report. It is well established that in fatty (Steatosis) and cirrhosis liver classes, the echogenicity is higher, and sometimes they called this group as "bright liver" [8]. Figure 1 shows the ultrasound image for fatty (bright) liver which shows the higher echogenicity, but brightness is not sufficient to diagnose subjectively fatty liver from cirrhosis. Most of the fatty and Cirrhotic livers are Hyper echoic. Figure 2 shows the ultrasound image for the cirrhotic liver. Figure 3 shows the ultrasound image for cancer liver. Figure 4 shows the ultrasound image for the normal liver, it is isoechoic (normal brightness). Figure 5 shows ultrasound images for some samples for the four liver cases. The gray-scale ultrasound images generated in the clinical environment provide significant contributions to the diagnosis of liver diseases. However, at the resolution capabilities practical for abdominal scanning, common diffuse diseases of the liver, such as hepatitis, fatty infiltrations, and early cirrhosis, are difficult to diagnose from normal by visual inspection of the B-mode [9]. Fatty liver containing very little fibrous tissue would produce a similar sonogram to that cirrhotic liver containing similar quantity of fibrous tissue making it difficult for a clinician to differentiate fatty from cirrhotic livers, so the specific texture on B-scan images is believed to be related to tissue properties, i.e., the pathological state of the soft tissue. Therefore, for classification, features can be extracted with the use of image texture analysis techniques. We propose the gray scale statistics for texture characterization. Neural networks [10, 11] provide computational

techniques that are able to deal with our problem. The fundamental objective for neural networks pattern recognition systems is classifying an input to provide a meaningful categorization of its data content. A Pattern recognition system can be considered as a two stages device, the first stage is feature extraction, and the second is classification. Features are the measurements taken on the input pattern that is to be classified; typically we are looking for minimum features that will provide a definite characteristic of that input type.

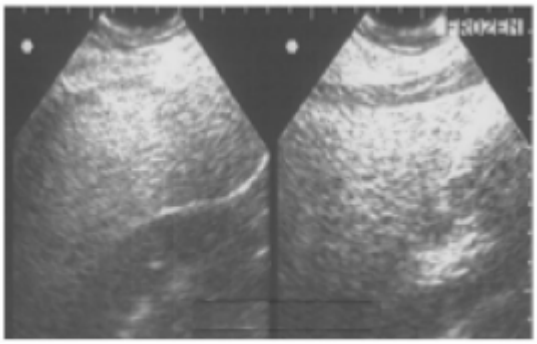

Figure 1. Ultrasound image for bright liver.

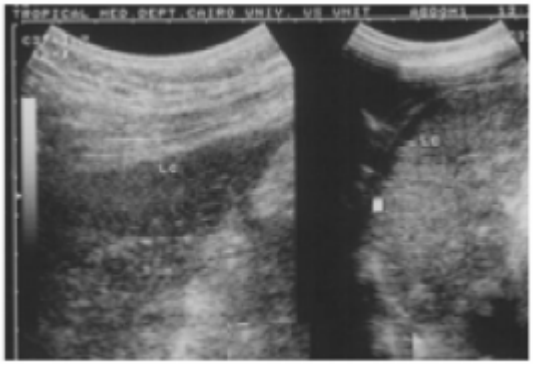

Figure 2. Ultrasound image for cirrhotic liver.

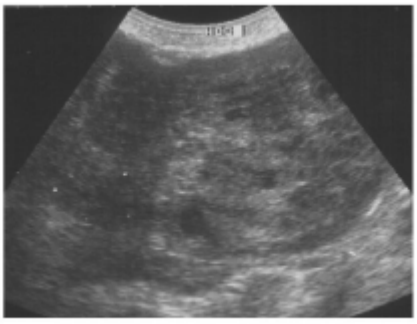

Figure 3. Ultrasound image for cancer liver.

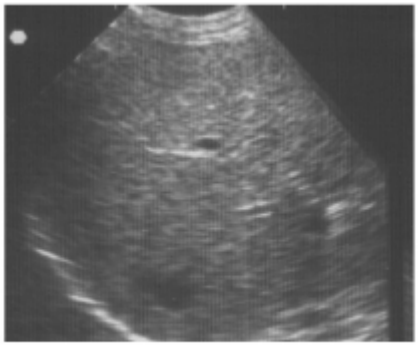

Figure 4. Ultrasound image for normal liver.

Material and methods

The most spread and known diseases in our country such as fatty liver (steatosis), cirrhoses and carcinoma (cancer) are chosen to be our cases in addition to the normal case to be easy to compare the disorder ones with the normal case. Ultrasound images used in our research were obtained on [Toshiba ECCO CEE. and Toshiba SSA-100] with 3.5- MHz.transducer frequency; Images were captured with 512 x 512 pixels and 256 gray-level resolution. Fasting Condition of the patients is substantial, it has been suggested that patients should be fasting for eight hours before any scan to avoid the effect of changing liver glycogen and water storage on ultrasound attenuation. Ultra sound images for different liver cases taken from patients with known histology and accurately diagnosed by specialized sonographer from various hospitals such as, department of tropical medicine and hepatology Cairo University (Kaser El-aini Hospital), Al Moalemeen Hospital Gezira, and Charity Center for Liver Diseases and Researches - Nasser City, Altyseer Medical center and other clinical centers are the assistant to our database. Four sets of images have been taken: Normal, Fatty, Cirrhoses and cancer, for each case we have 160 samples from 80 subjects, 80 samples to find out the learning data for classification and 80 samples for testing each liver case, Except for Normal case we have 200 samples from 100 subjects, after discarding the false negative and false positive samples. From each image, two blocks of 64X64 pixels approximately 2cm x2cm in actual dimension have been selected. Blocks were chosen to include only liver tissue, without blood vessels, acoustic shadowing, or any type of distortion. We select 320 samples from 340 for training set

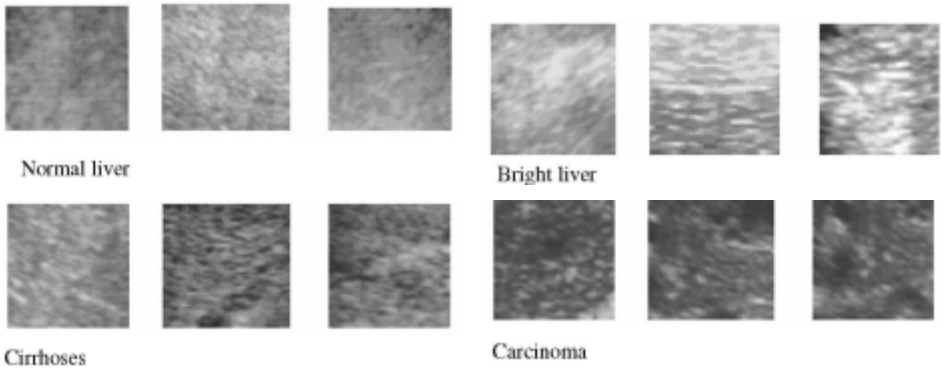

Figure 5. Ultrasound image samples for liver cases.

and 320 samples from 340 for test set were composed out of all blocks from independent images. An important initial step is to divide the data set into two independent subsets, Train and Test sets. This preliminary step effectively avoids introducing false-negative or falsepositive. False-negative rate is the probability that the classification result indicates a normal liver while the true diagnosis is indeed is liver diseases i.e., positive. This case should be completely avoided. False-positive rate is the probability that the classification result indicates liver diseases while the true diagnosis is indeed a normal liver.

VARIABILITY BETWEEN P-SWE AND 2-D SWE SYSTEMS Limitations and system differences The main limitation of these techniques is that different estimates of shear wave speed (SWS) are obtained with different systems. The Quantitative Imaging Biomarker Alliance (QIBA) committee of the Radiologic Society of North America (RSNA) performed an inter-laboratory study of SWS estimation in elastic phantoms. Commercially available SWE systems were used. A statistically significant difference in SWS estimates among systems and a depth-dependent estimate of SWS for each system were obtained. The inter-system variability ranged from 6% to 12%. No statistically significant differences were found among raters using the same system. The study also reported very good agreement between systems (Hall 2013). It was found that in viscoelastic phantoms, the deepest focal depth (7.0 cm) yielded the greatest intersystem variability for each phantom (maximum of 17.7%) as evaluated by the interquartile range (IQR), and the median SWS estimates for the greatest outlier system for each phantom/focal depth combination ranged from 12.7% to 17.6% (Palmeri 2015). A study has evaluated the variability of SWS assessed with a p-SWE technique at various depths using different frequencies. In both the phantom and liver, the mean velocities as measured by two probes at the same depth and at different depths differed. The lowest variability in the phantom was at 4 and 5 cm from surface with the convex probe and at 2 cm with a linear probe. In the liver, the depth with lower variability was 4 cm from the skin with a convex probe and at 3 and 4 cm with a linear probe (Chang et al. 2013). In another study on 89 chronic hepatitis C virus (HCV)-infected patients, the linear probe gave SWS values higher than those obtained with the convex probe (Potthoff et al. 2013). This is expected because the SWS is dependent on the ARFI frequency: The higher the ARFI frequency, the higher the SWS. A recent study has evaluated the inter-system and inter-observer variability of LSMs in patients with varying degrees of liver stiffness (Ferraioli et al. 2018). The assessment of LSMs was performed using six US systems, four with p-SWE and two with 2-D SWE. The Fibroscan was used as the reference standard. There was an agreement >0.80 for all pairs of systems. The mean difference between the values of the systems with 2-D SWE technique was 1.54 kPa, whereas the maximum mean difference between the values of three of four systems with p-SWE technique was 0.79 kPa. The variability between measurements obtained with different systems was higher in stiffer liver. The range of values obtained with the two 2-D SWE systems paralleled that of the Fibroscan in cases of very stiff liver (>15 kPa), whereas the four systems with a p-SWE technology gave lower values in the higher range of liver stiffness. The intra-patient concordance for all systems was 0.89 (95% confidence interval [CI]: 0.830.94). Inter-observer agreement was >0.90. Piscaglia et al. (2017) reported that the correlation between stiffness measurements taken with several systems (including the Fibroscan) in different intercostal spaces was good but not perfect.

Table 2. Recommendations for performing liver elastography

Adherence to a strict protocol is required.
Patient should fast for 4 h before examination.
Exam should be performed with the patient in the supine or slight left lateral position with the arm raised above the head to increase the intercostal space.
Measurements should be taken through an intercostal approach at the location of the best acoustical window.
Measurements should be taken 1.5 to 2.0 cm below the liver capsule to avoid reverberation artifact. The optimal location for maximum shear wave generation is 4.0–4.5 cm from the transducer.
The transducer should be perpendicular to the liver capsule.
Placement of the region of interests should avoid large blood vessels, bile ducts and masses.
For transient elastography, the appropriate transducer should be selected based on patient's body habitus.
Ten measurements should be obtained from 10 independent images, in the same location, with the median value used for transient elastography and point shear wave elastography techniques. Three or five measurements may be appropriate for 2-D shear wave elastography when a quality assessment parameter is used.
The IQR/M (interquartile range/median) should be used as a measure of quality. For kPa measurements the IQR/M should be <0.3 and for m/s it should be <0.15 for an accurate data set.

It is quite important to describe the most significant parameters used to build our quantitative tissue characterization system The Mean Gray Level, physical meaning is the brightness or echogenicity of the texture, It is well established that in fatty and cirrhosis liver classes, the echogenicity is higher, and sometimes they called this group as "Bright Liver" but brightness is not sufficient to diagnose subjectively fatty liver from cirrhosis. Most of the fatty and Cirrhotic livers are Hyperechoic, while the normal texture is isoechoic (normal brightness). It is clear from figures (7, 8, 10, 11 and 12) and table 1 that the mean gray level of cirrhotic and Carcinoma ultrasound pictures are mixed. Fatty livers are the highest mean gray level. The lowest mean gray level is that for Carcinoma liver, and the mean gray level of fatty liver is slightly higher than in cirrhotic Livers.

TRANSIENT ELASTOGRAPHY. The procedure has been fully described in the previous WFUMB guidelines on liver elastography (Ferraioli et al. 2015). The strengths of the TE approach are that it is widely available and a point-of-care technique. Weaknesses are the lack of gray-scale image guidance to determine where the measurement is being obtained, inability to visualize and avoid large vessels and masses at the site of measurement (although these may be generally identified on the time-motion and A-mode), the need for recalibration of the spring in the device at 6- to 12-mo intervals (depending on the type of probe), decreased applicability in cases of obesity and inability to use it in patients with ascites.

ARFI-BASED TECHNIQUES. The procedure has been fully described in the previous guidelines (Barr et al. 2016b). These are listed in Table 2 Although most vendors allow measurements to 8 cm from the transducer, measurement accuracy decreases below 6 cm from the transducer because of attenuation of the ARFI pulse. The literature suggests that 10 measurements should be obtained for p-SWE, and the median value reported. Several studies have indicated that an IQR/ median (M) 30% (measurements in kPa) improves accuracy in staging liver fibrosis. Recent literature suggests that a smaller number of measurements may be accurate (Fang et al. 2018; Ferraioli et al. 2016a); however, at this time there is not enough literature to support this suggestion. The energy deposition of the ARFI push pulse for U.S. Food and Drug Administration (FDA)- approved vendor systems is within current FDA diagnostic limits for livers in adults. Off-label use for other organs and for use during and immediately after the use of US contrast materials should be avoided until further investigated (Cui et al. 2014). In 2-D SWE, a larger field of view (FOV) is placed where the elastogram will be obtained. Within that FOV, regions of interest (ROIs) can be placed to obtain the stiffness value. As opposed to p-SWE, the ROI size can be changed. If possible, the ROI should be placed near the center of the FOV, as there are often errors at the borders of the FOV. Most vendors provide the average and the standard deviation of the stiffness values from the pixels in the ROI, and some of them provide the minimum

and maximum stiffness values as well. The mean value should be used. The standard deviation within the ROI reports the variability of the pixel measurements within the ROI and is not a measure of the quality of the measurement. Not enough studies have been performed to provide recommendations, but several studies using 2-D SWE have used three or five measurements if the system has a quality measure that confirms the area of measurement has high-quality shear waves (Dietrich et al. 2017a). Most vendors with 2-D SWE may allow the placement of many ROIs within the elastogram FOV. This is discouraged, because if there is an error in that image, the error is reproduced in all the measurements from that image.

STRAIN ELASTOGRAPHY. There is no significant change from previous WFUMB liver elastography guidelines (Table 2) (Ferraioli et al. 2015). A limited study using combinational elastography, the combined use of strain and shear wave imaging with a single machine, might increase accuracy in the diagnosis of liver fibrosis and inflammation (Yada et al. 2017a, 2017b). Data mining, which combines SE and serologic tests, is reported to be the novel approach (Yada et al. 2014). In a meta-analysis (Kobayashi et al. 2015) of 15 studies with 1626 patients, SE was found not to have high accuracy for any cutoff stage of fibrosis. REPRODUCIBILITY Shear wave elastography techniques have excellent reproducibility, provided the recommendations of the manufacturer or expert recommendations are followed. For all systems, intra-observer reproducibility assessed with the intra-class correlation coefficient (ICC) was >0.90, and inter-observer reproducibility was >0.80 (Boursier et al. 2008a; Fang et al. 2017; Ferraioli et al. 2012; Fraquelli et al. 2007; Garcovich et al. 2017; Hudson et al. 2013). Factors that influence the reproducibility of the measurement are similar across the different techniques and are related to the operator's experience and to factors dependent on the subject being examined. A learning curve has been consistently observed not only for TE (Boursier et al. 2008b), but also for p-SWE (Fraquelli et al. 2016) and 2-D SWE (Ferraioli et al. 2012; Hudson et al. 2013; Woo et al. 2015), with higher reproducibility achieved by expert operators. Inter-observer variability increases with higher liver fibrosis stages (Boursier et al. 2008a; Fraquelli et al. 2007; Vuppalanchi et al. 2018) and in overweight or obese patients (Boursier et al. 2008a; Fraquelli et al. 2007). Patient position and respiration phase can affect the results, and variability is decreased by using standardization. CONFOUNDING FACTORS AND LIMITATIONS Although liver fibrosis is the main determinant of liver stiffness, a number of factors have been found to influence LSM, often resulting in a false-positive diagnosis of advanced fibrosis or cirrhosis. Clinicians should be aware of these confounding factors and avoid using liver elastography in such situations. Although most of the studies were conducted using TE for historical reasons, studies using p-SWE or 2-D SWE almost always produced similar effects, suggesting that the same confounders should affect all techniques similarly. Confounding factors were already reported in the previous guidelines (Barr et al. 2016b; Dietrich et al. 2017a; Ferraioli et al. 2015). Details on the published studies are available in Supplement 1 (online only). Liver steatosis causes attenuation of the ARFI pulse and can lead to more variability in the measurements, although theoretically it should not affect the SWS, based on current ARFI methods in clinical use, even though some reports have indicated that livers with steatosis have increased viscoelasticity, which can also affect SWS. Published studies have conflicting results.

Comparison with the US signs of liver steatosis. Few studies, all carried out with small samples, are available. Only two studies have performed a head-to head comparison with liver biopsy as reference: one in patients with chronic liver disease (de Ledinghen et al. 2012a) and the other in patients with chronic hepatitis B (Xu et al. 2017a). Both studies indicated that the performance of CAP for detecting and grading liver steatosis was higher than that of US; however, the rate of overestimation was significantly higher for CAP than for US (30.5% vs. 12.4%, $p < 0.05$) (Xu et al. 2017a). A study that has assessed the diagnostic accuracy of CAP in comparison with US for detection and quantification of hepatic steatosis in the general population reported that CAP significantly correlated with steatosis; the AUROCs were 0.94 (95% CI: 0.91———————————0.97) for significant steatosis and 0.95 (95% CI: 0.900.99) for severe steatosis (Carvalhana et al. 2014). It has been reported that in patients with advanced liver fibrosis, CAP performs better than US in assessing liver steatosis (Ferraioli et al. 2016b). The US findings of liver fibrosis and steatosis could be similar, and this may decrease the

diagnostic accuracy of US. No data in NAFLD patients are available. By use of the imperfect gold standard methodology in a series of overweight or obese children, it has been reported that for the evaluation of liver steatosis in children, CAP performs better than US, and a cutoff value for CAP of 249 dB/m rules in liver steatosis with 0.98 (0.970.98) specificity (Ferraioli et al. 2017)

Comparison with magnetic resonance (proton density fat fraction). Studies that have assessed the diagnostic accuracy of CAP compared with proton density fat fraction (PDFF) magnetic resonance (MR) spectroscopy, using liver biopsy as reference, have reported that CAP is outperformed by MRI-PDFF for steatosis grading. In a study on 142 patients with NAFLD, CAP identified hepatic steatosis grade 2 with an AUROC of 0.73 (95% CI: 0.640.81), whereas PDFF yielded an AUROC of 0.90 (95% CI: 0.820.97, $p < 0.001$) (Imajo et al. 2016). In another study on 55 patients suspected of having NAFLD both PDFF and CAP detected histologically proven steatosis (S1), but PDFF had better diagnostic accuracy than CAP in terms of AUROCs (0.99 vs. 0.77, respectively; $p = 0.0334$) (Runge et al. 2017). Likewise, another study in 104 consecutive patients reported that MRI-PDFF is more accurate than CAP in detecting all grades of steatosis in patients with NAFLD (Park et al. 2017). MRI-PDFF identified steatosis of grade 2 or 3 with AUROC values of 0.90 (95% CI: 0.820.97) and 0.92 (95% CI: 0.840.99); CAP identified steatosis of grade 2 or 3 with AUROC values of 0.70 (95% CI: 0.580.82) and 0.73 (95% CI: 0.580.89). A study that assessed the accuracy of CAP using magnetic resonance spectroscopy as the reference standard in HIV-infected patients found that the results obtained with the two techniques correlated well; however, patients with higher body composition parameters were more likely to be misclassified as having hepatic steatosis by CAP (Price et al. 2017).

Follow-up Longitudinal studies are awaited. Recently, a study that followed up 4282 patients who had both a reliable LSM and 10 successful CAP measurements reported that neither the presence nor the severity of hepatic steatosis predicted liver-related events, cancer or cardiovascular events in the short term, while LSM and etiology independently predicted liverrelated events (Liu et al. 2017). Subgroup analyses of viral hepatitis (hepatitis B: 37.0%, hepatitis C: 2.9%) and NAFLD patients (40.7% of the entire cohort) revealed similar results.

Summary. The controlled attenuation parameter is a promising point-of-care technique for rapid and standardized steatosis quantification, but needs to be better validated in patients with NAFLD with the XL probe. CAP quality criteria are not well defined. There are no consensual cutoff values, and the influence of BMI and diabetes should be further explored. More data are needed with the XL probe in NAFLD patients, who are the target population, and for the comparison with US, taking liver biopsy as the reference standard. Longitudinal studies are awaited. CAP is outperformed by MRI-PDFF. Current technological advances of imaging ultrasound systems are directed at grading steatosis. However, no studies are available yet.

RECOMMENDATION: CAP is a point-of-care, standardized and reproducible technique, promising for the detection of liver steatosis. However, for quantifying steatosis there is a large overlap between adjacent grades, there are no consensual cutoffs and quality criteria are not well defined. (LoE 3, GoR C) (10,0,0)

Table 1. Available equipment

SWE technique	System (manufacturer)	Software registered name	Quality criteria and/or additional features (manufacturer derived)	Additional tools
Transient elastography	FibroScan FibroScan 502 Touch (EchoSens, France)	FibroScan	The software determines automatically whether each measurement is successful or not and controls choice between M+ and XL+ probes based on skin-to-liver capsule distance (this second option is available with the newer systems); 10 measurements and IQR/M ≤30%	Controlled Attenuation Parameter (CAP) to detect and quantify liver steatosis.
Point SWE (pSWE)	Acuson S2000 and 3000 (Siemens Healthineers, Germany)	Virtual Touch Quantification (VTQ)	If signal/to noise ratio is low, "XXX" is displayed.	
	iU22, Epiq series, Affiniti (Philips Healthcare, Netherlands)	ElastPQ	No measurement displayed if signal/to noise ratio is low; for each measurement the standard deviation is provided	
	HI-VISION Ascendus, Arietta 70, Arietta 850 (Hitachi Ltd, Japan)	Shear wave measurement (SWM)	No measurement displayed if signal/to noise ratio is low; net amount of effective shear wave velocity (VsN) ≥50%	Combinational elastography (available on the Arietta 850) that combines strain and shear wave elastography. ATT – attenuation software for quantification of liver steatosis.
	MyLab 9 (Esaote, Italy)	QElaXto	No measurement displayed if signal/to noise ratio is low; rate of effective measure for each value shown in the screen (H,M,L)	
	HS70 A, RS80 A (Samsung Medison, South Korea)	S-shearwave	Reliable measurement index (RMI)	
2-D SWE	Aixplorer (SuperSonic Imagine, France)	SSI	No color displayed if signal/to noise ratio is low; stability index (SI)	
	Epiq series (Philips Healthcare, Netherlands)	ElastQ	No color displayed if signal/to noise ratio is low; confidence map	
	Acuson S3000 (Siemens Healthineers, Germany) Logiq E9 (GE Healthcare, USA)	Virtual Touch IQ	Pixels remain blank if result is not "satisfactory"	
	Aplio 500, i-series (Canon Medical Systems, Japan)		Propagation map	Shear wave dispersion imaging, related to tissue viscosity. Attenuation Imaging (ATI) to detect and quantify liver steatosis.
	Resona series, DC-80 system (Mindray, China)	Sound Touch Elastography (STE), Sound Touch Quantification (STQ)	Reliability map (RLB); stability from motion in a period of time frames (M-STB)	

SWE = shear wave elastography

Practical advice for interpretation of liver stiffness values. There is significant overlap of stiffness values for the varying degrees of liver fibrosis. All techniques have high accuracy for normal patients and most patients with cirrhosis. However, degrees of liver stiffness between these two extremes overlap substantially. One approach is to use a cutoff value system as recommended by the SRU, with a low cutoff below which there is a high probability of being normal or having minimal fibrosis and a high cutoff value where there is a high probability of significant fibrosis or cirrhosis (Barr et al. 2016a). Some patients with biopsy-proven cirrhosis have had relatively low stiffness values in many studies. Another clinical approach to interpreting liver stiffness values would be in keeping with that recommended for TE by the Baveno VI Conference (de Franchis and Baveno 2015). The socalled "rule of 5" (Young's modulus 5, 10, 15 and 20 kPa) could be recommended (Fig. 1): LS 15 kPa are highly suggestive of compensated advanced chronic liver disease. Values 2025 kPa can rule in CSPH. Recommendation 16: Interpretation of liver stiffness measurements needs to be taken in context with the other clinical and laboratory data. (LoE 1b, GoR A) (10,0,0)

Table 3. Items to be delineated when performing liver elastography studies

Machine(s) utilized, procedure (transient elastography, point shear wave elastography, 2-D shear wave elastography), probe, quality criteria
Population (body mass index, alcoholism, comorbidities, transaminase levels, platelet count)
Context of use (specialty clinic, general practice, academic institution, *etc.*)
Confounding factors (fasting, *etc.*)
Operators (number, degree of training, experience)
Reference standard for validation study and interventional studies
If liver biopsy is used for gold standard; size of specimens, central reading, interval between liver biopsy and elastographic procedure

Minimal requirements for future studies. When studies evaluating liver elastography are performed, it is recommended that the items in Table 3 be included in the methodology, to allow for better comparison between studies and techniques. The Statement for Reporting Studies of Diagnostic Accuracy (STARD checklist) should be used before starting studies of diagnostic accuracy

REFERENCES

1. Detect Liver Disease Early -Online: [www.vitalimaging.co.uk], 2005.

2. Karl Wernecke, Pierre Vassallo, Ulrich Bick, Stefan Diederich, Peter E. Peters, The Distinction between Benign and Malignant Liver Tumors on Sonography: Value of a Hypoechoic Halo, American Journal of Roentgenology, volume 159(5), Nov.1992, pp. 1005-9
3. A-M. Badawi, A. M. Hashem, Ali El Hendawi, Nabil El Kady, AbouBakr M. Youssef, M. F. Characterization of Different liver pathologies preliminiary Results", Kaser Elaini Midical Congress Conf.1995.
4. Ultrasonic tissue characterization. IEEE.Trans. Ultrasound Ferroelectric. Freq. Control. 2001 Jul; 48 (4):1139-46.PMID: 11477773[PubMed-indexed for MEDLINE].
5. Liver Health Information. The American Liver- Foundation. Online: [www.liver foundation.org/cgi- bin/dbs/articles. cgi? db=articles&uid=default], 2005
6. Liver diseases & CellBiology, Online: [http://www.otterbein.edu/home/fac/wndnjhns/NOTES3.HTML], 2005.
7. Diseases of the Liver. [www.ability.org.uk/Liver_Diseases.html], 2005. Online: [www.cancerindex.org/clinks2m.htm] ,2005. [www.cancerindex.org/geneweb/X070601.htm], 2005.
8. Diffuse Liver Diseases Online. [www.asianradiology.com/sample-page/sampl-chap25.pdf], 2005.
9. C.Wu, Y. Chen, and K. Hsieh, "Texture features for classification of ultrasonic liver images, "IEEE Trans. Med. Imag., vol. 11, pp. 141- 152, june 1992.
10. Training an Artificial Neural Network http://www.dacs.dtic.mil/techs/neural/neural3.html
11. "An automatic diagnostic system for liver image classification in Artificial Neural Network in Biomedicine". Online: [www.medinfo.cs.ucy.ac.cy/documents/medinf 03_NeuralNetworksM edicallmaging.Pdf.], 2005.
12. David J. Dowsett, Patrick A. Kenny and R. Eugene Johnston. The Physics of Diagnostic Imaging. Published by Chapman & Hall, an imprint of Thomson Science, 1998.
13. Rafael C. Gonzalez and Richard E. Woods. Digital Image Processing. Chapman & Hall Medical, New York Don Mills, 1993.
14. Liver diseases characterization, pubMed. http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?cmd=Retriev&db=pub Med&list_uids ...25/02/1427
15. Yasser M. Kadah, Aly A. Farag, Jacek M. Zurada, Ahmed M. Badawi, and Abu-Bakr M. Youssef, Classification Algorithms for Quantitative Tissue Characterization of Diffused Liver Disease from Ultrasound Images, IEEE Transactions on Medical Imaging, volume 15, No. 4, August 1996, pp. 466-478.
16. Y.M. Kadah, A.A. Farag, M. Zurada, A. M. Badawi,and A.M. Youssef, "Classification algorithms for quantitative tissue characterization of diffuse liver diseases from ultrasound images," IEEE Trans. Med. Image., col. 15, no. 4, pp. 466-477, aug. 1996.
17. The Back Propagation Network Learning by Example. http://www2.psy.uq.edu.au/-brainwav/Manual/BackProp.html# Learning Problem.
18. H. Sujana, S. Swarnamani, and S. Suresh, Application of Artificial Neural Networks for the Classification of Liver Lesions by Image Texture parameters, Ultrasound in Medicine and Biology, volume 22, No. 9, 1996, pp. 1177-1181.
19. Jacek M. Zurada. Artifical Neural Systeems. PWS Publishing Company, United States of America, 1999.

20. An Introduction to Neural Networks. Online: [www.cs.stir.ac.uk/!lss/NNIntro/InvSlides.html],2005.
21. M. Unser, "Texture classification and segmentation using wavelet fraMES, 'IEEE Tran. Image Processing. Vol. 4, pp. 1549-1569, Nov. 1995.
22. Wavelet-Based Texture Classification of Tissues in Computed Tomography [http://doi.ieeecomputersociety.org/10.1109/CBMS]. 2005.105
23. Characterization, based on nonseparable wavelet decomposition and its application for the discrimination of visually similar. Diffuse diseases of liver. www.research.ibm.com/people/a/aleksand/pdf/00730399.pdf