THE ANNALS OF "DUNĂREA DE JOS" UNIVERSITY OF GALAȚI
FASCICLE V, TECHNOLOGIES IN MACHINE BUILDING,
ISSN 1221- 4566, 2012

COUPLING COMPUTER-AIDED ULTRASOUND METHODS WITH V-CAD RECONSTRUCTION TO VIRTUAL CHARACTERIZATION OF HEPATIC STEATOSIS

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ABSTRACT

Steatosis is the most frequent chronic liver disease and one of the most frequent ultrasound finding. At the moment there is no proven treatment applicable for all patients. Correction of the associated risk factors and, improvements of the Body Mass Index and Waist Circumference using diet and exercise alone and combined has the most proven results. No adequate imaging tool to monitor individual steatosis grade in daily practice or interventional studies exists. Our goal is to identify a simple, efficient and affordable method to quantify the evolution of steatosis and to test its reliability vs. human interpretation of ultrasound findings.

KEYWORDS: ultrasonography, numerical analysis, brightness, hepatic steatosis

1. INTRODUCTION

Steatosis is the most common chronic liver disease in the world and one of the most frequent finding in ultrasound investigation [1], [2], [3].

However up to date there is no standard drug treatment based on evidence or guidelines for this disease. In this research field liver biopsy is considered the gold standard but its use is limited by low acceptance of the subjects because unfortunately liver biopsy is an invasive procedure with various side effects (pain, bleeding, even death) [4]. For this reason the number of available patients that can be included in the study is relatively low and there is useless from clinical point of view. Some authors point out that even the biopsy suffers from some sampling errors in a magnitude of 25% [4], [5]. Computer tomography, magnetic resonance imaging, and spectroscopy are other alternative imaging techniques used for the detection of hepatic steatosis, but have failed to show better accuracy and their cost and adverse effects (e.g., radiation) limit their usefulness by comparison with screening tools. Liver enzymes have traditionally been used as surrogate markers of liver disease; however, their accuracy is very limited.

The goal of our study is to identify a simple, efficient and affordable method to quantify modifications in NAFLD grade applicable both in monitoring therapy in everyday practice and in studies of different treatments efficacy.

2. METHODS

To test the efficiency of our method we have chosen 10 subjects, 5 men and 5 women between 28 and 65 years newly diagnosed with NAFLD under different treatments and monitor them at 1,2,3 and 6 months. The inclusion criteria were presence of new diagnosed steatosis by ultrasonography and prescription of a therapy, drugs or lifestyle change: diet or different types of exercise. The exclusion criteria were significant alcohol consumption, history of diabetes mellitus, and evidence of cirrhosis or other forms of chronic liver disease. Alcohol consumption was ascertained by the self-administered "alcohol use disorders identification test" (AUDIT). Use of drugs historically associated with causing NAFLD such as systemic glucocorticoids, tetracyclines, anabolic steroids or other known hepatotoxins was also assessed during screening and their use constituted an excluded case.

The ultrasound image was transformed in a binary form using a digital-analogic converter and transferred to a regular computer running Microsoft Windows. We tested 3 different low cost DAC (digital analogic converters) with similar results. The cost for DACs and connecters was no more than five

times the medium cost of a general ultrasound investigation in our area.

The size of the sample we had chosen was ten because our goal was to determine the ability of the computer-aided method to determine light changes in steatosis modifications compared with a health liver and how soon after the start of the therapy we can detect modifications in the grade of NAFLD.

Patients were scanned in the supine and left lateral decubitus position, utilizing subcostal and intercostal approaches. Sonograms were performed under fasting conditions. The time-gain compensation was set up to a fixed position. A representative sagittal sonographic plane of section demonstrating the hepatic parenchyma and the adjacent right kidney was selected to determine liver echogenicity. Focal masses within the liver or kidney were not considered in the assessment. There are many choices for analyzing with the software starting from very expensive specialized ones to free software. Our choice was ImageJ which is powerful, with very low hardware requirements, written in Java with code source available for custom adaptations and with a batch creator that permits automated analyze with a single click. We used ImageJ software to define region of interest (R.O.I) and created a mask for every pacient to use in all determinations (figure 1).

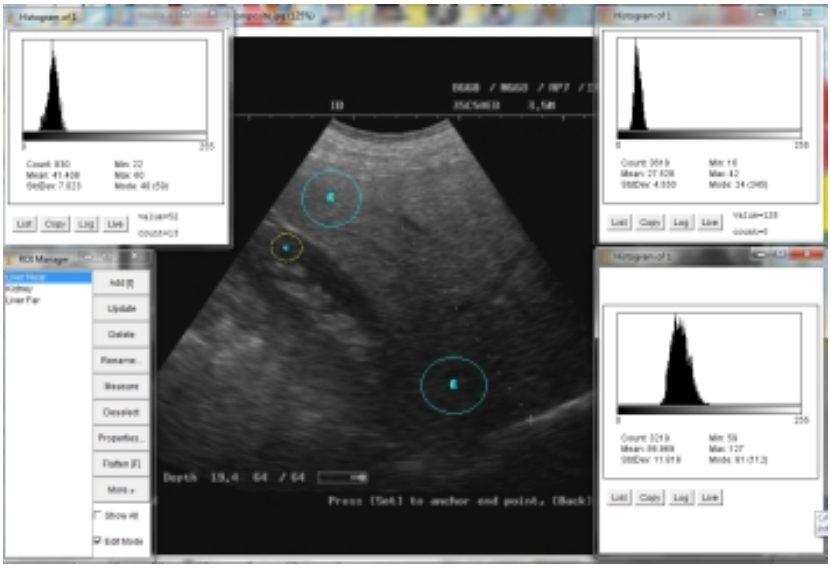

Fig. 1. Selection of ROI and histogram analyze in ImageJ software

Three region of interest were defined for each image: one in the near field of hepatic parenchyma, one in renal cortex and one in the far field near the diaphragm. For interpretation of the image we used mean brightness level in a range of 0-255 values corresponding to the 8 bits image. We determined de variances of the mean brightness level for each ROI in every image. Based on the 3 ROI for each image we tested the best criteria in order to evaluate the modification of steatosis grade between near hepatic field-renal cortex differences, near hepatic field-far hepatic field difference and mean value of near hepatic field alone. We used a second opinion from another ultrasound operator about changes in steatosis grade.

3. RESULTS AND DISCUTIONS

All subjects included in the study had an initial ultrasound evaluation and the results and the therapy are summarized in Table 1. Ultrasound determination of steatosis is primarily based on an increase of the brightness of hepatic parenchyma. "Bright liver" is defined as abnormally intense, high-level echoes arising from the hepatic parenchyma.

Backscattering coefficient measures the quantity of energy that is returned by the tissue back to the receiver as a result of backscattering [6]. Hepatic cell with elevated triglycerides content reflects ultrasounds more and the returning ultrasounds are transposed on the monitor screen as an increased brightness. Median value of the brightness is the key parameters for steatosis. We use a histogram analyze for every ROI and standard deviation to be sure that the image samples were well chosen from a relative homogeneous area of tissue. Standard deviation for all samples ranges from 8.78 to 12.08. Through estimating the dispersion of the mean brightness around area of interest using live mode histogram, it was found variations of maximum ± 2.5 % but for safety reason decided to consider a range of ± 3 % as tolerance level. As brightness range from 0 to 255 that gives as in theory 42 secure grades of brightness. Another decision we have to make is what parameter to choose in evaluation of steatosis evolution.

Comparative liver-kidney brightness as a difference or index between the means is a good

method to diagnose steatosis by minimizing the differences between different ultrasound machines characteristics, settings, and individuals but not necessary in case of the same machine, same settings, same individual and approximate same region.
The near/far hepatic bright difference could not appear in moderate grades of steatosis.

In the present study we decide to test mean brightness value of the near transducer ROI with an generous fault tolerance level of ± 5 % to compare with human interpretation (Table 1). Even if ultrasonography it is known to have a good sensibility in steatosis detection it cannot detect a fat cell percentage under 30% [7]. Also human interpreted ultrasounds lack the ability to differentiate small changes in brightness and has poor results grading the level of steatosis.

Even since 1986 Goldberg [8] proposes a 4 steps scale for steatosis. In 2007 Hamaguchi [9] extends the scale to 6 levels using more parameters: presence of liver-kidney contrast (0-1), parenchymal brightness (0-3), presence of deep beam attenuation (0-1), bright vessel wall thru parenchyma (0-1) and definition of gallbladder walls (0-1).

After two months there is no significant result in steatosis evolution. At three months there are significant differences in 3 cases with mean brightness involution Δ> 10 and one case in human recognition (only one investigator). At 6 months he had 7 cases of significant variation of mean brightness (6 in good and one in worst) and 4 human recognition of improvements (table 2).

Table 1 Initial status of the mean brightness in near hepatic and renal parenchyma R.O.I. and therapy of the subjects

No	Therapy	Liv N	Renal	StdDev	Min	Max	Median
1	LFD,H_1	90.81	43.22	10.64	69.00	119.00	90.00
2	E,LFD,$H_{1,2}$	167.04	105.01	8.78	146.00	190.00	167.00
3	D,A	102.05	68.42	12.08	67.00	133.00	101.00
4	D,H_2	59.98	24.91	9.90	40.00	98.00	59.00
5	D,W,$H_{1,2}$	84.92	31.50	10.94	61.00	110.00	84.00
6	A	69.50	52.68	10.45	44.00	106.00	69.00
7	$H_{3,2}$	80.14	66.46	10.21	56.00	105.00	80.00
8	H_3	97.99	50.78	9.86	72.00	129.00	97.00
9	H_2	88.73	59.54	11.36	59.00	123.00	90.00
10	H_1	119.48	68.53	7.676	94.00	139.00	119.00
No – subject identification number; LivN – mean brightness in the near transducer hepatic R.O.I; Renal – mean brightness in the kidney parenchyma R.O.I; H – hepatoprotectors, E – exercise; LFD – low fat diet, D – diet, A – aerobics, W – walking							

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Table 2. Variations in median brightness vs. human evaluation of steatosis changes at 1, 2, 3 and 6 months

		1 month		2 months		3 months		6 months	
	Therapy	H	Δ B	H	Δ B	H	Δ B	H	Δ B
1	LFD,H_1	N	-5.06	N	-9.77	N	**-11.22**	Y	**-31.43**
2	E,LFD,$H_{1,2}$	N	+4.8	N	-6.87	N	-8.71	N	**+16.8**
3	D,A	N	-4.9	N	-9.63	N	-14.8	Y	**-35.2**
4	D,H_2	N	-2.9	N	+4.43	N	-2.99	N	-9.8
5	D,W,$H_{1,2}$	N	-8.63	N	-7.8	Y/N	**-19.60**	Y	**-28.4**
6	A	N	+2.85	N	-8.94	N	**-15,61**	Y	**- 41,5**
7	$H_{3,2}$	N	+6.93	N	-2.55	N	+9.65	N	**+19.32**
8	H_3	N	-6.25	N	+3.81	N	+9.1	N	+8.4
9	H_2	N	+2.67	N	-3.28	N	+ 4.6	N	-2.6
10	H_1	N	+6.27	N	-2.85	N	-7.8	N	**-12.8**
N-no changes in steatosis detected by both ultrasound operators; Y-changes in steatosis detected by both ultrasound operators									

We conclude that the method we propose is better than human interpretation in terms of discriminative ability and early recognition of modification (Table 3). While the human visual system is very good at such complex tasks as edge detection or form recognition it has many imperfections in brightness perception [10]. It is not possible for people to differentiate between more or less 20 grey tones of all converted grey values [11],

[12]. Below a threshold size the human eyes integrates the perception of two separate areas in view into a single area of uniform intermediate tone. In physics, the luminance of an object is exactingly defined as the luminous flux per unit of projected area per unit solid angle leaving a surface at a given point and in a given direction.

Table 3. Modification of a subject steatosis grade - visual samples of R.O.I. and corresponding mean brightness

R.O.I. Liver near					
Subject 1	Initial	1 month	2 months	3 months	6 months
Mean B	90.8	85.74	81.03	79.58	59.37
	Δ B	-5.06	-9.77	-11.22	-31.43

A more useable definition is the amount of visible light that that reaches the eye from an object. But, when an observer describes how "bright" an object appears, he/she is describing his/her brightness perception of the object. This brightness is the perceptual correlate to luminance and depends on both the light from the object and from the object's background region. More than this sometimes the visual apparatus can alter the appearance of the stimulus in unexpected ways before its message reaches the conscious part of the brain [13]. The grey region surrounded by a dark area looks (is perceived) brighter than the same grey region surrounded by a light region. Hering (1878) [14] attributed this effect to adaptation and local interactions. This phenomenon is just one example of a number of illusions that illustrate problems that can arise when one visual element is viewed in the context of others. Human visual perception of brightness and lightness involves both low-level and higher levels of processing that interact to determine the brightness and lightness of parts of a scene [15] If a scene was scanned by a photodetector, it would measure the amount of luminance energy at each point in the scene; the more light coming from a particular part of the scene the greater the measured value. The human eye's retinal receptors (cones) respond in a similar manner when a scene is imaged unto it. However the appearance (perception) of a region of the scene can be drastically altered without affecting the response of retinal receptors.

4. CONCLUSIONS

Quantitative evaluation of hepatic fat content can be performed using ultrasound investigations augmented by simple computerized analysis and therefore be a valuable analytic tool in monitoring individual patient evolution and clinical investigation.

ACKNOWLEDGEMENTS

The authors would like to express their thanks to KTH DMMS for financial support.

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