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Quantitative Examination of Liver Tissue Ultrasound Elastograms

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Methods of computer-aided statistical analysis of ultrasound elastograms are presented. An approach consisting in initial segmentation of elastograms visualizing low-elasticity segments distribution in the tissue of an examined biological organ and in statistical analysis of this distribution is described. Satisfactory correlation between the values of some statistics and medical specialists' description of human liver elastograms was observed. The ways of continuation of the works aimed at improvement of the elastograms-based diagnostic methods are suggested.

K e y w o r d s: image processing, ultrasound elastography, image segmentations, liver fibrosis

1. Introduction

Elastography is a method of biological tissues' stiffness or elasticity examination aimed at a non-invasive detection and classification of lesions. The concept of elastography is based on the observation that soft tissue subjected to a temporal compression in different ways, according to its spatial distribution of elasticity restores its original form. The difference in tissues' responses in the above-mentioned cases in the elastograms are visualized. The result is rendered in a form of color images in which a color scale corresponds to the tissue stiffness gradation. This makes possible to distinguish between normal tissues and those suspected to be affected by lesions.

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Despite the fact that the method was invented in 1991 by J. Ophir et al. [1], till now, its large possibilities have not been sufficiently recognized and should be investigated. Elastography can be combined with various imaging modalities, like ultrasound (*US*, [2]), optical coherence tomography (*OST*, [3]), magnetic resonance (*MR,* [4]) etc. The area of medical application is also large, including, e.g. liver [4], breast [5], or any types of subcutaneous lesions examination. In this paper attention is focused on *US* elastography (sonoelastography). In this case the measuring process is based on registration of differences between pre-compressed and post-compressed ultrasound echo signals stimulated simultaneously with a time-varying external force applied to the examined organ. This, approach also has some shortcomings consisting in the fact that in real clinical conditions the compression applied cannot be accurately controlled. Moreover, the problem of exact relationship between the examined tissue's stiffness and the response signal is still open. Thus the visualized elastograms give rather approximate information about a spatial distribution of the physical elasticity module values in the examined organs. A medical interpretation of the elastograms of the organs needs also high experience and general medical knowledge. On the other hand, the method is highly useful, e.g. in non-invasive detection of hepatic fibrosis in various states of the liver diseases. Investigations of the last problem are conducted, among others, in the Dept. of Gastroenterology of the Cancer Center and Institute of Oncology [3]. A standard ultrasound machine used in this study was equipped with an option enabling qualitative assessment of the stiffness of the tissue. This non-invasive method is called the real-time color-coded sonoelastography. The aim of our work presented below consists in quantitative examination of the elastograms in order to make based on them medical diagnosis more precise and reliable. This work is aimed at investigation of the possibilities of medical diagnostic decisions' improvement by the computer-aided quantitative liver elastogram analysis and making them more accurate and comparable in long-term therapeutic processes. For this purpose, two approaches were tested and compared: a/ based on the morphological spectra of elastograms and b/ based on selected standard statistical parameters. However, it was found that, because of relatively low discrimination power of the elastograms, using only summing-type morphological spectral components for lesions detection is effective. This is why in this paper some preliminary results of using of standard statistical parameters only are presented. The organization of the paper is as follows. In Sec. 2 the experimental materials and the used methods are described. Sec. 3 contains a short presentation of the reached results. The conclusions are given in Sec. 4.

2. Materials and Methods

2.1. Materials

The experiments were based on clinical data provided by the Dept. of Gastroenterology of the Cancer Center and Institute of Oncology in Warsaw, obtained using

a standard ultrasound equipment EUB 9000 (Hitachi Corp. Tokyo, Japan) with 5.0–7.5 MHz linear probe. The data set consisted of elastograms from 29 patients (18 women, 11 men; median age 41 y.) with chronic liver disease (verified by core biopsy and histological examination as a gold standard to detect fibrosis) and 20 healthy voluntaries. Some patients were excluded from the study for the following reasons: overweight assessed as the thickness of the fatty tissue over the liver above 2 centimeters, ascites and the narrow intercostal spaces potentially making the obtainment of elastograms difficult. An experienced pathologist analyzed the histological features according to the fibrosis scoring system. Fibrosis was staged from 0 to 4, with 0 being no fibrosis, 1–2 minimal and mild fibrosis and 3 or 4 considered severe fibrosis or cirrhosis. The painless mechanical pressure with the use of the probe was delivered to an intercostal space and the sequence of elastograms was recorded on a hard drive. The strength of the pressure was controlled by a visual indicator situated on the screen, as visible in the middle of Fig. 1. There are seven levels of the pressure visible on the screen during the examination. In order to achieve the best reproducibility, the results were considered in the analysis when the score was between third and fifth level. Three repeated measurements were performed by the same operator, without moving the patient. In this study all measurments were taken by the investigator after a short training course supervised by an experienced ultrasonographist. In a preliminary study, when these procedures were performed by the same investigator, the satisfying intra-operator reproducibility of the measurement

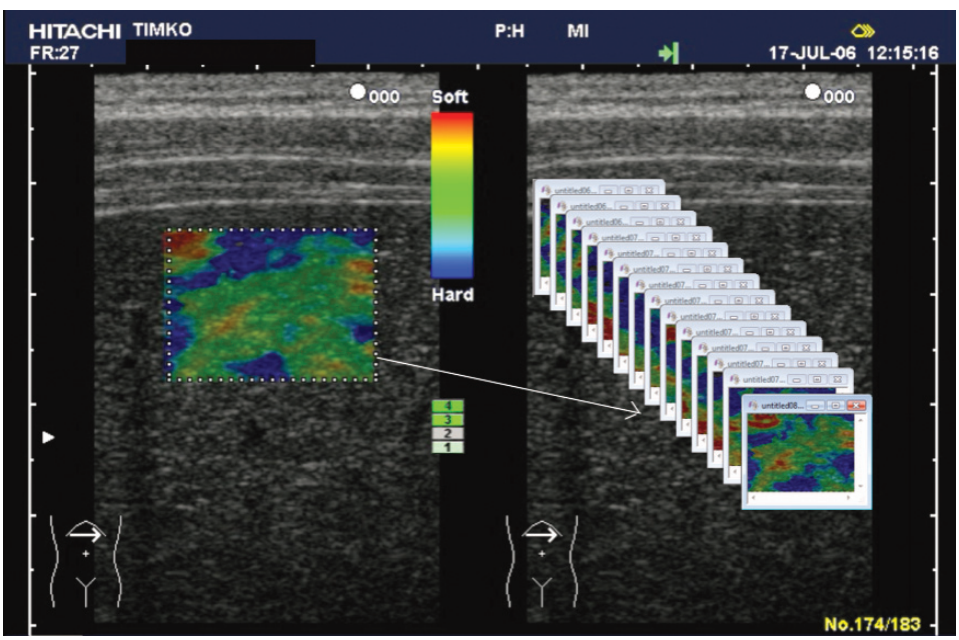

Fig. 1. Example of a single elastogram (left) and of elastogram sequence (right) corresponding to the different projection depths in a patient (other details in the text are explained)

technique was achieved .The technical details of the sonoelastographic procedure can be found in the previous paper [3].

In Figure 1 a typical view of the screen of the ultrasound equipment used in our experiments is shown. The colored frames of the elastograms are visualized on the background of typical USG images in order to show their projection levels (perpendicular to the USG visualization plane). The elastographic projection level is marked by an arrow at the vertical scale on the left side (scaled in mm). On the left part of the screen a single elastogram is shown while on the right side a sequence of elastograms acquired at different visualization depths is visualized. The horizontal scale at the top and the vertical scales on both sides of the screen indicate the distances (in cm) of the USG visualization. All liver sequences of the elastograms of a single patient consisted of about 100 (from 20 to 300) images corresponding to the different visualization depths. However, the depth of projections in fact roughly only could be established and this caused a main difficulty in exact reconstruction of 3D elasticity module distribution.

In the image, a color scale of the detected stiffness levels is visible. Blue color corresponds to the "hard" or "low-elasticity" tissue which medically is classified as "ill", while green up to red colors are assigned to the "soft" tissues or the tissues of middle up to high elasticity which medically are classified as "normal". Generally speaking, the higher is the rate of blue segments with respect to the green, yellow and red ones, the more the examined organ is suspected to be affected by fibrosis.

2.2. Methods

The sequences of elastograms of the individual patients were statistically examined. The examination consisted of two phases:

I. Segmentation of areas corresponding to the different elasticity module,
II. Statistical examination of the segments.

In the phase I original colors assigned by the system to the pixels: blue – *low elasticity*, green – *middle elasticity*, red – *high elasticity*, yellow - *unrecognized* (see Fig. 1) were converted into a numerical scale on which a threshold level discriminating the "normal" (red or green) and pathological (blue) image segments manually, by a medical expert were established. Next, the pathological (low elasticity) segments on the background of normal (middle or high elasticity as well as unrecognized) ones in a binary, black-white form were visualized, as shown in Fig. 2, right.

On the sequences of black-white images the following calculations were performed: total number of the fixed color (in particular – *blue*) segments/image, minimal and maximal numbers of the fixed color segments/image, mean number of the fixed color segments/image, variance, standard deviation, kurtosis and sequences of the fixed color segments/image.

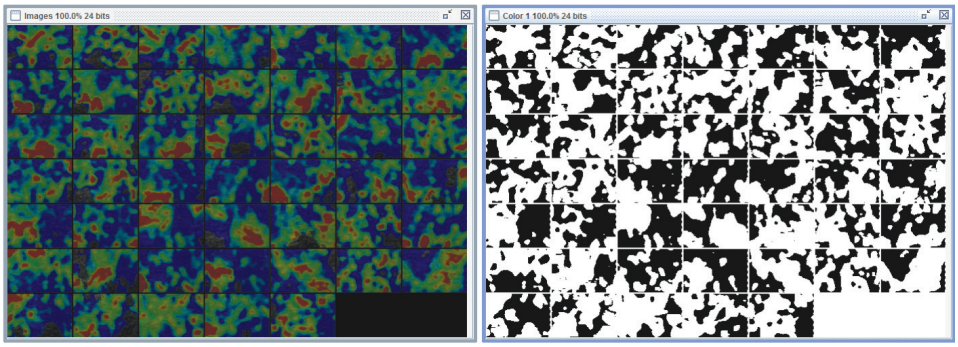

Fig. 2. A series of the liver elastograms in one patient: a) the original images taken at the different projection depths, b) the corresponding binarized (black-white) images prepared for statistical analysis of the low-elasticity (black) segments. The black segments in b) correspond to the blue (low elasticity, ill) segments in a) while the white ones to to the green and red segments (jointly classified as normal) in a) have been assigned

This type of data calculated for four initial colors gave us a rough inspection into the granularity of the elasticity module distribution. The deeper inspection was obtained at the phase II, when the following parameters for the *black* segments were calculated: total segments area, percent of total segment area, minimal, maximal and average segment area, variance standard deviation, kurtosis and sequences of segment area. As an example, in Fig. 3 a histogram of *black* segment areas for a sequence of the elastograms is shown.

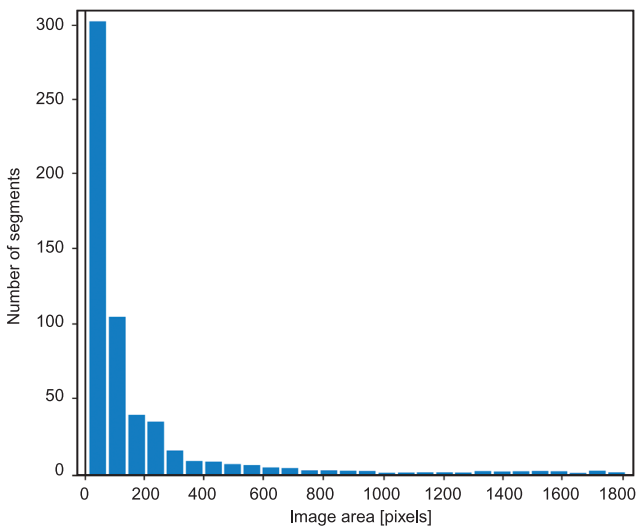

Fig. 3. Histogram of low elasticity segment areas (black after binarization) for a given sequence of the elastograms

It can be observed that in this series of the elastograms disseminated small black segments (corresponding to the high tissue stiffness areas) are dominating while the number of larger black segments is relatively low. However, namely the large black segments are of particular diagnostic interest.

On this basis also the relative volumes of the hard and soft tissues in the individual planar projections and in the total 3D object reconstruction could be calculated, assuming that the distances between the projection surfaces are regular and known (what in clinical practice is not always guaranteed).

For the above-described calculations a standard Image Pro Plus software as well as special elastogram analysis programs (elaborated by M.Sc. D. Wiśniewski) were used.

3. Results

3.1. Planar (2D) Segmentation of Low-elasticity Regions

The elastograms from a total number of 29 patients with chronic liver diseases and 20 healthy voluntaries were evaluated. The distribution of the observed low elasticity values according to fibrosis stages evaluated by the medical experts is shown below in tabular form. The measured mean values were 35.7, 36.1, 42, 42.7, 47.1 , respectively, for F0, F1, F2, F3 and F4 fibrosis scores and 33.2 in the control group (Table 1).

Table 1. Results of the examinations of liver elasticity in the group of patients

Patients with chronic liver diseases			
Fibrosis stage	Number of patients *n*	Mean score of low elasticity (percentage of blue color)	
		Mean value	Range
F0	3	35.71	32.14 – 40.44
F1	9	36.08	30.31 – 47.1
F2	9	41.96	29.56 – 58.42
F3	3	42.67	36.79 – 53.38
F4	5	47.15	40.51 – 51.17
Control group			
	20	33.18	24.03 – 42.1

Liver elasticity was thus positively correlated with the fibrosis stages, what is better visible in Fig. 4.

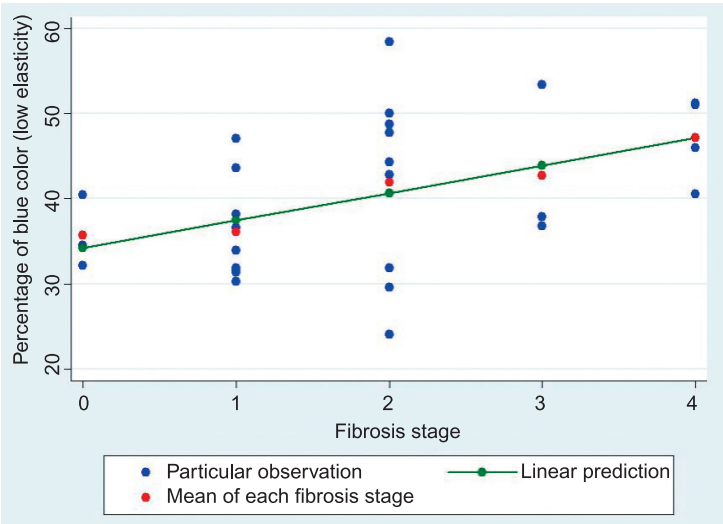

Fig. 4. Plot of liver low elasticity as a function of the liver fibrosis stage

Next observations have shown that the statistics of the total segments' area were well correlated with medical recognition of the low-elastic segments in the elastograms. This is illustrated in Fig. 5 where, as before, blue circular sectors correspond to the low elasticity segments occurring in the elastograms of the healthy volunteers (left image) and the ill patients (right image). Green, red and yellow sectors correspond there to the normal tissues of middle or high elasticity modules.

For examination of general morphological structure of the low-elasticity segments occurring in the elastograms a series of 17 statistical parameters, calculated by a computer program, was taken into consideration. The parameters are listed in

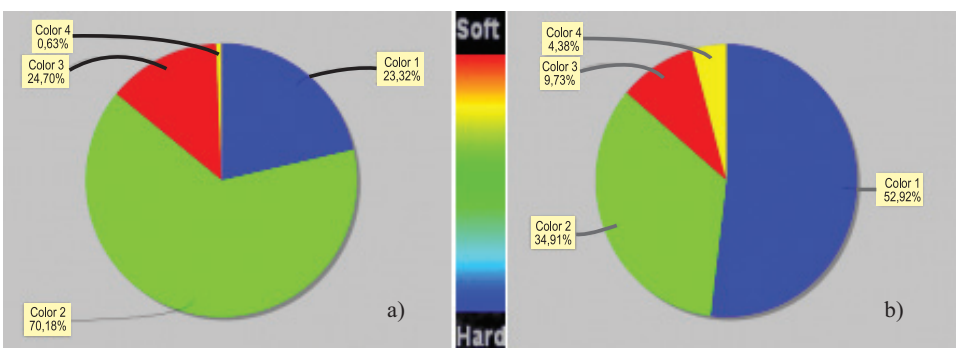

Fig. 5. Global area percentage: of the low elasticity (Hard) segments (represented by blue – color 1 circular sectors) detected in: a) the healthy volunteers and b) the ill patients. Green – color 2, red – color 3 and yellow – color 4 sectors correspond to the normal (Soft) tissues of middle or high elasticity modules

Table 2, where their measured values in 2 cases representing the ill patients (named B and D) and 2 cases representing the healthy persons (A and C) are also given. The cases have been chosen so as to show the range of parameters' values changing.

Table 2. Basic statistics of the elastograms for the selected patients

Patient / Statistic	A	B	C	D
Total number of fixed color segments/image	**553**	**36**	**358**	**195**
Minimal number of segments in image	3	2	2	2
Maximal number of segments in image	13	7	16	16
Average number of segments /image	8.35	4.5	7.31	7.5
Variance of segments number	6.25	2.25	11.36	17.48
Standard deviation of segments number	2.5	1.5	3.37	4.18
Kurtosis of segments number	–0.64	–0.41	–0.29	–0.91
Sequences of segments number	–0.35	0	0.52	0.58
Total segments area	**97313**	**22631**	**90103**	**116342**
Percent of total segments area	**24.03**	**46.53**	**29.78**	**42.06**
Minimal segments area	6	7	6	6
Maximal segments area	3158	3521	3406	7762
Average segments area	**175.98**	**628.64**	**251.68**	**596.63**
Variance of segments area	140254	1017305	253069	1660237
Standard deviation of segments area	374.51	1008.62	503.06	1288.50
Kurtosis of segments area	28.21	1.35	14.06	12.68
Sequences of segments area	4.86	1.69	3.56	3.46

By analysis of the "average segment area" statistic it can be observed that the patients B and D have evidently more of the stiff segments than two other ones. Also percent of the total segments area in the patients B and D is larger than in A and C. This recommends the patients B and D to the deeper medical examination. This also is visible in the low level of the "total number of the fixed color segments/image" statistic. Therefore, it has been observed that only 4 of the initially calculated parameters provide a valuable for medical diagnosis information: total number of the black segments per image, total area of the black segments, percentage of the black segments area and average area of the black segments. The corresponding numerical data have been marked in bold in Table 2. Other statistics seem to be less specific for the high tissue stiffness detection.

3.2. Spatial (3D) Reconstruction of Low-elasticity Regions' Distribution

Series of the binarized elastograms give also an opportunity to look into the 3D structure of the low elasticity segments. For this purpose there can be calculated sums of pairs, triples, etc. of the consecutive binary (black-white) images. As a result, the coextensive thick the high stiffness segments become visible. From a diagnostic point of view such, even small-area segments are non-less important than those of large area occurring in the single images only. However, this method is evidently not equivalent to the exact 3D reconstruction of the liver; it makes only a rough inspection into the existence of the thick high-stiffness structures possible. This is illustrated in Fig. 6 where three consecutive elastograms a), b) and c) (taken from a series of the binarized elastograms visualizing the stiff tissue segments) are shown in the upper row while in the lower row their sums: a)+b), b)+c) and a)+b)+c) are shown. The operations were performed on the binary images according to the rules:

$$0 + 0 = 0,\ 0 + 1 = 1 + 0 = 1 + 1 = 1$$

where 0 corresponds to black (low elasticity) and 1 to white (high elasticity) sectors of the binarized images. According to the above-given rules, in a sum of any images black only such segments remain which are black on all of the components of the sum. Thus the black segments visible in the last case indicate the position of the compact thick lesions inside the examined tissue.

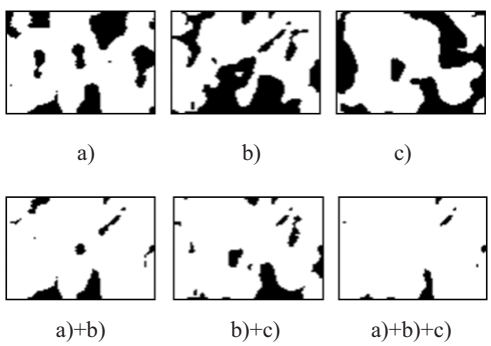

Fig. 6. Visualization of the low elasticity segments' thickness: in the lower row of the images algebraic sums of the upper row images are shown

At last, on the basis of a series of the elestograms acquired on the different projection area depths a rough inspection into the 3D structure of the low-elasticity segments of the examined organ is possible. In Figure 7 an example of a 3D reconstruction of the low-elasticity segments distribution (blue color) under the assumption of the equal inter-slices distances is shown. In fact, as it before has been mentioned, the distances cannot be precisely controlled. As a consequence, in Fig. 7 the *z*-scale is only roughly determined what makes the exact volumes' calculation impossible.

Nevertheless, a rough visualization of the 3D tissue lesions distribution provides a sort of additional useful information about the diagnosed organ. Improvement of the 3D reconstruction method needs a more accurate control of the projection depth of the elastograms, which depends on the future progress of the elastographic imaging modality.

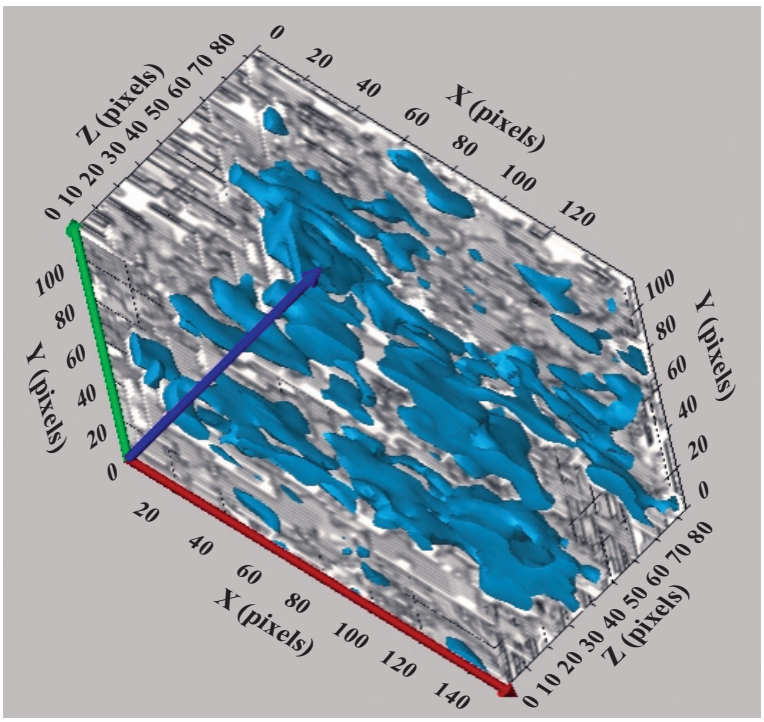

Fig. 7. Example of a 3D reconstruction of the inner elasticity module distribution based on a series of the elastograms corresponding to the "suspicious" objects of minimal elasticity (blue color)

4. Conclusions

Elastography is a relatively new modality of medical imaging whose large possibilities need to be investigated. Diagnostic effectiveness of this modality can be increased if direct examination of the elastogrames is finished by their statistical analysis. In this paper a method of computer-assisted analysis of the elastograms as well as a method of 3D reconstruction of the tissue elasticity have been presented. The first results have shown that the method may be very useful and effective in clinical applications, in particular, if combined with computer-aided image analysis methods. Our observations have also shown that for detection and rough assessment of the liver lesions the low-level morphological spectral components (as described in [7])

can be used. Further works should be focused on elaboration of a computer-aided diagnostic system which will help in classification of the elastograms according to the categories established by medical specialists.

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