

The assessment of the applicability of shear wave elastography in modelling of the mechanical parameters of the liver

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Purpose: The development of haptic technology in laparoscopic simulations indicates a demand of constant upgrade of tactile feedback, which is currently considered to be unsatisfactory. Presumably, one of its causes may be insufficiently examined and described mechanical parameters of soft tissues *in vivo*, including liver tissue. The aim of the following work was the attempt at assessing the applicability of data from shear wave elastography in organ modelling by correlating the mechanical parameters of the liver obtained by this noninvasive method, with the mechanical parameters obtained by indentation. *Methods:* Each one out of 12 porcine livers, was subjected to elastography and subsequently to the indentation test. The mean Young's modulus for each liver lobe was obtained using elastography, while in indentation Young's moduli in three different strain ranges and maximum load were calculated. *Results:* Differences between mechanical parameters of lobes were not found but the parameters were calculated for different methods and strain ranges. *Conclusions:* The limitations of both methods prevent the unambiguous assessment of the applicability of elastography in liver modelling for laparoscopic simulations, at the presented stage of research. Nevertheless, the presented study provides a valuable introduction to the development of a methodology for testing the mechanical parameters of liver tissue.

Key words: shear wave elastography, indentation, Young's modulus, porcine liver

1. Introduction

Technological advances in medicine bring about constant changes in diagnostic methods and treatment of patients as well as in ways of simulating procedures as well as training of medical students. They are well illustrated by visible progress on the market of laparoscopic simulators. Over the last dozen or so years, simulators using virtual reality and haptic feedback technology have become standard in highly developed countries. In addition to hardware implementations, an important aspect are simulations of the intraoperative environment, whose level of advancement sets the pace for the above-mentioned technological developments.

Simulations used in training simulators cover several areas of surgery, including orthopaedic, gynaecological, and general surgery [14]. A potential problem area in the design of training procedures, especially in the context of reproduction of the mechanical properties, are all parenchymatous organs [17], such as the liver. This is corroborated by research by Wilson et al. [18], according to which current simulators with haptic feedback do not improve the skills of doctors. One of the suggested reasons is the force response of the modelled tissues, which is inadequate for the operating conditions.

This phenomenon may have several causes. The process of developing organ and tissue simulations involves many simplifications, such as applying linear elastic models to represent the mechanical properties

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of soft tissues [5] and acquiring their mechanical parameters under *ex vivo* conditions [15].

In addition, the mechanical properties of soft tissues, of parenchymatous tissues in particular, are still not sufficiently understood or described. Experimental studies are usually carried out without considering key factors, such as blood supply and pressure in the living body.

A relatively well-described organ, present in many laparoscopic simulations and made of parenchymatous tissue, is the liver. The methods for testing the mechanical parameters of the liver are highly inconsistent. Studies on this subject include tensile and compression tests [16], indentation test [3], [10] as well as dynamic tests. Different models are used (porcine, canine, bovine, and human) and tested with the adoption of various boundary conditions. The geometry of the specimens differs in each case. A comparison of the results is also hampered by different parameters (among others, stiffness, Young's modulus, and maximum tensile strength) determined by individual authors. The results obtained in individual studies differ significantly from each other [15]. These variables make it difficult to choose the values of the determined objective parameters – existing in the living body – that can be used to create laparoscopic simulations.

Presumably, most of the above-mentioned simplifications and inconsistencies can be eliminated by means of elastography. This relatively new and still developing technique enables a non-invasive estimation of selected mechanical parameters of organs *in vivo*. There are many types of elastography, including compression elastography, acoustic radiation force impulse (ARFI) imaging, and magnetic resonance elastography (MRE). However, the greatest interest is aroused by shear wave elastography (SWE) [9], widely used for diagnosis of liver diseases [20]. SWE uses ultrasound imaging, with an additional shear wave introduced to the region of interest (ROI). The character and velocity of wave propagation is used to assess the shear modulus of tissue, which is then converted to Young's modulus [9]. SWE is the type of elastography causing least interference with the body of the patient. This method has limitations related to simplifications adopted in signal processing, including the linear elastic tissue response; however, it is highly repeatable [2], [20], suggesting that appropriately adjusted results can be useful for laparoscopic simulations with force feedback.

There are very few studies comparing the results of experimental tests of the mechanical properties of tissues, particularly of the liver, to elastography. Research using MRE was done by Reiter [19] and Hagh-

panahi [8], while ultrasound elastography was used by Ferraioli [6] and Chatelin [4]. However, only Ferraioli used the SWE method in his research.

The present study is a preliminary attempt at assessing the applicability of data from shear wave elastography in organ modelling by correlating the mechanical parameters of the liver obtained by SWE with the mechanical parameters of the liver obtained by indentation.

2. Material and methods

The test material consisted of 12 fresh livers of healthy domestic pigs with an average weight of 1.9 ± 0.1 kg. The testing was carried out within 84 hours of the slaughter of the animals. The material was stored at a temperature of $4\text{ }^{\circ}\text{C}$ and the tests were carried out at room temperature, protecting specimens from loss of moisture.

The first stage was an SWE examination using an ultrasound system (Aixplorer, SuperSonic Imagine). A linear transducer (SuperLinear SL10-2) was used with a frequency range of 2–10 MHz. The specimens were placed on a flat surface that did not restrict the geometry of the organ. Four measurements were made on each lobe. The lobes were marked in accordance with the anatomy of the porcine liver [13]: I – left lateral lobe, II – left medial lobe, III – right medial lobe, and IV – right lateral lobe. The measurements were carried out on the diaphragmatic side of the organ in such way that each time there was a layer of ultrasound gel, visible in imaging, between the transducer and the surface of the examined material.

The second stage of the research was an indentation test performed on an MTS Synergie 100 testing machine using a spherical indenter with a diameter of 10 mm. Four measurements were made on each lobe, preloading the specimen to approximately 0.05 N, with the indentation speed of 1 mm/min. The test was each time carried out until a discontinuity in the recorded force-displacement curve was observed.

The strain in each test was calculated as the ratio of indenter displacement to the initial specimen height [23]. Stresses were determined using a linear elastic model of the material [3], [9], which made it possible to relate the obtained indentation results to the SWE data.

Young's modulus of individual specimens was determined as tangent modulus to the curve, in each case at three strain ranges: $\varepsilon = 0.025 \div 0.075$ [5], $\varepsilon = 0.05 \div 0.1$ [25], and $\varepsilon = 0.1 \div 0.2$ [24], used in the literature to analyse parenchymatous tissues.

Statistical analysis (GraphPad Prism) of the obtained results included D’Agostino–Pearson’s K2 test ($p = 0.05$) to determine the distribution of the obtained data. Then, the calculated values of Young’s modulus of all groups were compared to each other using the Mann–Whitney U -test ($p = 0.0001$, $p = 0.05$). In addition, differences in results between individual lobes were tested for statistical significance using ANOVA test ($p = 0.05$).

3. Results

The results obtained by SWE were each time presented in the form of an image (elastogram) and a numerical value of Young’s modulus, as shown in Fig. 1. In the upper part of the image, above the tissue border, there is a visible dark area, which is a layer of ultrasound gel. The description of the elastogram shows the mean (Mean), minimum (Min), and maximum (Max) values as well as standard deviation (SD) of Young’s modulus in the examined ROI, including its diameter (Diam).

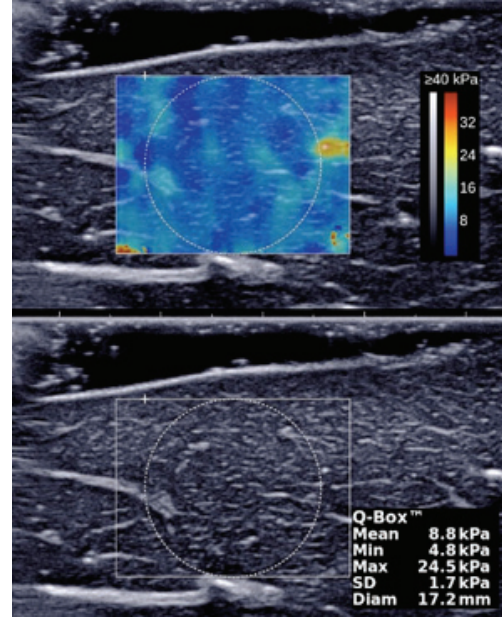


Fig. 1. A sample liver elastogram with the obtained mean Young’s modulus value – *Mean* in the ROI

The force-displacement curves (Fig. 2) were used to determine values of force after which discontinuity

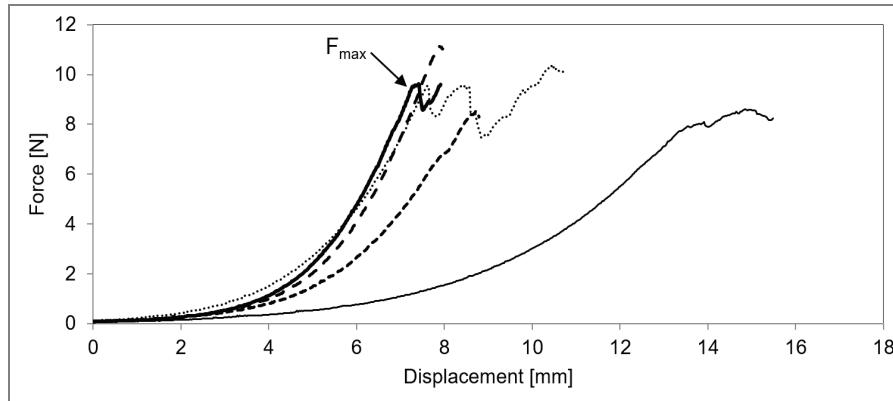


Fig. 2. A sample force-displacement curve; continuous line marks sample F_{max} value

Table 1. Obtained results: F_{max} – mean force at which discontinuity occurred in the curve of a given specimen; E_{SWE} – Young’s modulus obtained in elastography; $E_{2.5-7.5}$, E_{5-10} , and E_{10-20} – individual mean values of Young’s modulus in successive specimens, calculated for each strain range ϵ

No. of specimen	F_{max} , N	E_{SWE} , kPa	$E_{2.5-7.5}$, kPa	E_{5-10} , kPa	E_{10-20} , kPa
1	10.98 ± 3.65	14.06 ± 3.98	7.97 ± 3.45	10.62 ± 4.67	26.58 ± 14.31
2	24.94 ± 4.09	15.94 ± 2.74	12.53 ± 6.10	23.19 ± 25.09	58.92 ± 66.39
3	17.96 ± 4.39	17.88 ± 3.60	14.44 ± 6.81	18.97 ± 9.54	46.14 ± 27.94
4	28.10 ± 9.09	16.43 ± 2.90	25.97 ± 16.71	39.24 ± 20.00	93.25 ± 58.20
5	18.91 ± 4.56	12.09 ± 1.42	28.19 ± 10.86	31.87 ± 18.81	77.23 ± 37.67
6	30.02 ± 6.47	16.54 ± 2.84	34.97 ± 19.54	48.77 ± 30.06	136.18 ± 89.76
7	15.98 ± 5.27	11.08 ± 2.56	15.96 ± 6.30	22.37 ± 7.96	57.71 ± 18.88
8	17.88 ± 3.97	12.33 ± 1.96	16.87 ± 6.67	24.98 ± 11.92	68.61 ± 39.87
9	10.29 ± 2.03	12.80 ± 1.21	5.51 ± 2.61	7.57 ± 3.93	19.52 ± 10.75
10	22.12 ± 6.88	11.28 ± 2.12	4.65 ± 1.85	5.93 ± 2.60	12.93 ± 6.85
11	16.82 ± 4.11	13.14 ± 1.40	6.69 ± 3.35	9.33 ± 5.34	27.74 ± 24.47
12	14.97 ± 3.43	15.91 ± 1.39	4.49 ± 1.59	5.94 ± 2.50	18.58 ± 11.24

was observed. The values obtained this way for individual specimens, together with Young's modulus values, are shown in Table 1.

The performed D'Agostino–Pearson's omnibus test ($\alpha = 0.05$) confirmed normal distribution of data only in the E_{SWE} group. The Mann–Whitney U -test confirmed statistically significant differences ($p < 0.0001$ and $p < 0.05$) between Young's modulus values determined at different strain ranges and a statistically significant difference ($p < 0.0001$) between the groups E_{SWE} and E_{10-20} . There were no statistically significant differences ($p < 0.05$) observed between the E_{SWE} group and the groups E_{5-10} and $E_{2.5-7.5}$. These results are shown in Fig. 3.

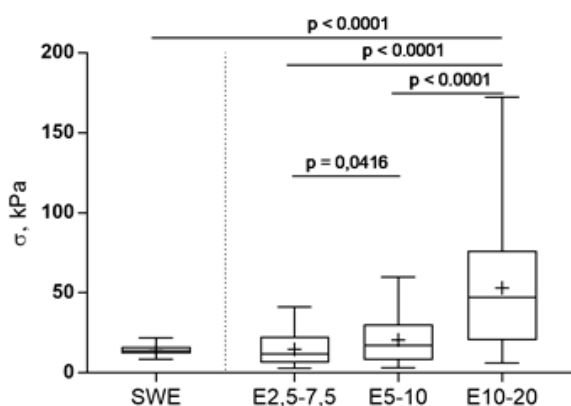


Fig. 3. Young's modulus values obtained with various methods

Table 2. Mean F_{max} values of individual lobes and of Young's modulus of individual lobes

Lobe	F_{max}, N	E_{SWE}	$E_{2.5-7.5}$	E_{5-10}
I	20.85 ± 6.90	13.76 ± 3.38	10.73 ± 7.04	13.63 ± 8.50
II	21.71 ± 7.68	14.94 ± 2.72	16.96 ± 12.14	23.64 ± 18.37
III	20.75 ± 8.69	14.37 ± 2.01	15.72 ± 12.28	23.53 ± 16.26
IV	14.49 ± 5.68	13.47 ± 3.40	15.48 ± 10.45	21.34 ± 14.60

The obtained measurement results were also analysed for differences in the measured mechanical parameters between individual lobes; however, the ANOVA analysis ($p < 0.05$) showed no statistically significant differences between the groups either in the case of mean F_{max} values or in the case of mean Young's moduli (Table 2). The analysis was performed omitting the E_{10-20} group.

4. Discussion

The values determined in the conducted tests enable preliminary assessment of the applicability of

data from shear wave elastography in organ modelling. Their comparison to the values obtained through indentation tests in individual strain ranges also allows to evaluate and correlate the results of SWE with the mechanical parameters determined in a specific range of liver tissue strains.

The obtained F_{max} values of the liver are lower than those obtained by Kaneta et al. [10], but comparable to those determined by Tamura et al. [23]. The differences may result, among others, from the geometry of the used indenter and the specimen loading rate. For example, Kaneta [10] used in his study four different types of indenters, in each case receiving different values of the determined parameters. Tamura [23] found no differences in the obtained results with respect to the specimen loading rate; however, differences in modulus values amounting to several orders of magnitude were found in a study by Saraf et al. (2006).

According to Hoskins [9], the values of Young's modulus in SWE examination of healthy soft tissues (the author does not differentiate liver tissue or parenchymatous tissues) fall in the range of 0.5–70 kPa; therefore, the values of Young's modulus of the liver determined through indentation do not exceed its upper limit except for the E_{10-20} parameter. The values of Young's modulus obtained through elastography in each case fell within the range described by Hoskins [9]. The elastographic examination was carried out

with care to preserve the gel layer between the transducer of the apparatus and the surface of the specimen so that the pressure of the transducer on the organ was as low as possible. During the procedure performed under these conditions, no change was observed in the geometry of the specimen. Considering that for parenchymatous tissue the strain range $\varepsilon = 0.1-0.2$ is a range of large strains [25] and that the values E_{10-20} are higher than E_{SWE} , we can conclude that during the elastographic examination lower-value strains were induced in the organ, not reaching the range of large strains. Thus, tissue strains induced by elastographic examination reach similar values as strain ranges analysed by indentation: $\varepsilon = 0.025 \div 0.075$ and $\varepsilon = 0.05 \div 0.1$.

The value of Young's modulus of the liver in SWE was described in detail in an article by Barr et al. [1]. The study analysed the results of tests performed with the use of various elastography systems. The values of Young's modulus of a healthy human liver obtained with an Aixplorer ultrasound system did not exceed 7 kPa. As indicated by Mattei and Ahluwalia [15], the human liver is characterized by a lower Young's modulus compared to the porcine liver. In research conducted by Carter [3], this value was almost fifteen times lower. By comparison, in his *in vivo* study of porcine livers using SWE, Sugimoto [22] obtained a mean Young's modulus of 6.37 ± 2.42 kPa. The results thus confirm the findings of a study by Kerdok [11], i.e., that the liver deprived of blood flow is characterized by higher values of the mechanical parameters compared to the perfused liver.

The lack of statistically significant differences between the groups E_{SWE} and $E_{2.5-7.5}$ and the groups E_{SWE} and E_{5-10} may provide a basis for further analyses in the given strain ranges, where a significant but missing information is the range of tissue strain present during the SWE procedure. The force with which the operator applies the transducer to the specimen has a noticeable effect on the results obtained with this method. Determination of its absolute value would enable the calculation of the range of strains occurring during the test and correlate the imaging results with the results of the indentation test. Similar research with an attempt to correlate results was carried out by Carter [3]. However, the methods used by the researcher required direct contact of the tool with the liver of the patient (research was conducted on the human model) during surgery. In addition, the values obtained significantly exceeded the values given in other sources and averaged 270 ± 81 kPa.

The lack of statistically significant differences in the mechanical parameters determined for individual lobes is supported by the literature [7],[10]. Both Chui and Kaneta used the porcine model with specimens having different geometries. Chui examined cylinders excised from liver parenchyma by squeezing them, while Kaneta compared the influence of indenter geometry on the entire organ. On this basis, it can be concluded that the liver is a homogeneous organ. At the same time, as emphasised by Reiter [19], the applied experimental method is extremely sensitive to local inhomogeneity of tissue; therefore, an important issue in this context is the area of the organ in which the test is carried out. Rich vascularity, especially in the central part of the liver, can be a source of incorrect assessment of the parenchymatous tissue structure.

The mathematical model used to analyse the results is based on the same assumptions as shear wave elastography [9]. This allowed to obtain comparable or even similar results, but at the same time prevented their relating to real intraoperative conditions, which are also desirable in laparoscopic simulation. Correct interpretation of the results seems to require application of a mathematical model assuming viscoelastic nature of the liver, as many other soft tissues [12], [21].

It is also worth mentioning other limitations of the method: use of a spherical indenter results in complex phenomena at its border with the specimen and uneven loading of the specimen. The method also limits the possible indentation depth. In addition, the tests were performed outside of the animal body, and thus in the absence of intra-abdominal pressure and the accompanying tension of other tissues as well as perfusion. It has been shown [11] that the mechanical properties of the liver obtained *ex vivo* differ from those obtained *in vivo*. In addition, the animal model was studied and its differences from the human model should be taken into consideration. Studies of the mechanical properties of the liver mention many parameters that affect the obtained values. Also, the analysis is hindered by the diversity of the models used, and the parameters determined, in the literature, which Mattei [15] goes so far as to call "a Pandora's box." Nonetheless, the performed tests made it possible to identify some of the errors and areas of improvement of the methodology.

Because of the limitations of both indentation tests and SWE imaging, the search for connection between their results is a difficult task, virtually impossible without further research. The conducted experiments are an introduction to the development of liver test methodology. An attempt was made to compare the results obtained with two different measurement methods; however, the current stage of research is not advanced enough to either accept or reject elastography as a method of acquiring actual values of the mechanical parameters of soft tissues. Further research should consider the mathematical model used in the calculations.

Concluding:

- statistically significant differences between SWE elastography Young's modulus (E_{SWE}) and indentation Young's modulus ($E_{0.1-0.2}$) were observed.
- No statistical significant differences between SWE elastography Young's modulus (E_{SWE}) and indentation Young's moduli ($E_{2.5-7.5}$ and E_{5-10}) were shown.
- No statistical significant differences between liver lobes were found, regardless of the measurement method.

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