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Review report of the doctoral thesis of Olga DOUBROVINA, entitled "WAVELET ANALYSIS OF ULTRASONIC SIGNALS IN SOFT TISSUE STRUCTURE CHARACTERIZATION"

The PhD thesis submitted by Olga Doubrovina concerns a problem that receives a lot of attention because nowadays cancer is one of the major causes of mortality worldwide. Researchers still make, considerable effort in the field of non-invasive diagnosis aimed at improving the sensitivity of in vivo imaging techniques. Of all medical diagnostic techniques, ultrasound imaging is one of the most popular, however, the sensitivity, and specificity, of ultrasound for the examination of different tissues is often susceptible to low contrast between cancer and healthy tissues. The main objective of the thesis presented by Olga Doubrovina was to show that thanks to the use of the wavelet decomposition of the raw ultrasonic backscattered signals, several new markers characterizing the soft tissue scattering microstructure can be found.

Overall assessment

The document is decomposed in seven parts. References are listening after the conclusions. Three appendixes close the document. The first chapter contains a general theoretical background of ultrasound signals generated by ultrasound transducers to study tissue structure properties. The mathematical definition of the chaoticity measure, a "scale index" based on a signal wavelet decomposition was introduced. Chapter 1 also shows the author's point of view as a mathematician of physical modeling. In particular, chapter 1.3 about non-classical absorption contains the contribution in the form of proposing a new general equation containing fractional Laplace operators. The second chapter describes a method of differentiating the density of scatterers by using the statistical properties of

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different wavelet approximation levels and the details coefficients of the Daubechies 6 family. The backscattered signals collected from three types of tissue-mimicking agar-gel phantoms with glass beads with low density and high density are compared. In chapter three the statistical properties of the wavelet approximation of the signal envelope were used to measure temperature changes. PhD student showed that wavelet approximations application to the temperature tracking improves the method of temperature tracking by statistical parameter changes.

Chapter four was devoted to the problem of the differentiation of scatterers' randomness type through a numerical model of random structures. According to the results obtained by PhD student, the scale index shows the strictly periodic structure for media with a regular distribution of scatterers. The larger value of scale index corresponds to the media with a random distribution of scatterers. In Chapter five it was shown how the collected RF (radio frequency) signals backscattered from self-made "threads" phantom with periodic structure can be used for validation the improvement of accuracy of MSS (mean scatterer spacing) parameter determined from a special wavelet approximation level of RF signals. The threads are in three different environments, water, oil, and starch gel. The RF echo signals from these phantoms will be also used to the validation of the scale index, the quantitative parameter introduced by PhD student for the first time to ultrasound signal chaoticity analysis. Chapter six presented the analysis of data sets containing signals from the human liver samples, collected by a radiologist in vivo. One dataset consists of the regions of tumor, the second dataset consists of the other regions with the healthy tissue. It was applied to the "scale index" to classify the tissue areas as healthy or cancerous.

The dissertation is well planned, carefully conducted and analyzed in detail. Also, balanced conclusions were drowned from the observed results. However, readability of the same parts of the manuscripts is poor because of numerous (mainly grammatical, vocabulary, typographical) errors. At some place, the manuscript certainly needs some polishing. The descriptions of many figures are illegible.

Specific assessment of section

In chapter 1 dedicated to the theoretical background, an important point is a discussion concerning absorption. However, there was a lack of detailed explanation of the acoustic energy conversin into the biochemical type, no description of relaxation processes.

In the following chapters, I appreciate the combination of experimental work and numerical modeling. The author used phantoms and real tissues in experimental studies. In the chapter dedicated to the scatterers' density differentiation, a focus is made on estimate the quantitative parameters connected with effective scatterers numbers by studying envelopes of the raw RF backscattered signals from agar-gel samples with a different number of scatterers. How was the uniformity of scatterers' distribution in the phantom checked? Figure 2.1 was published in [43] but there is no mention of it at the dissertation.

In my opinion, the most interesting part is chapter 3 – the examine of temperature changes in tissue during the heating process by registering the changes in the ultrasound echo signals. New methods of thermal treatment are constantly being sought and the currently existing are constantly being optimized, especially magnetic hyperthermia using

magnetite nanoparticles. The real-time measurement of temperature in tissue during therapy is a very important problem. It can be done using invasive temperature sensors, however, a much better solution is the so-called passive acoustic mapping. The candidate has shown the functional dependence on the temperature of statistical parameters allows to track of the direction of rising and following down of points in agreement with the heating process. However, the relationship between the acoustic properties and the temperature varies between patients depending on their individual characteristics e.g. state of health. So it is a problem with the scaling of the acoustic results to the values expressed in Celsius degrees. How to scale parameter α_0 to Celsius degrees? It is also interesting whether the area with magnetic nanoparticles can be detected by RF signals? Why were experiments performed using different phantoms: agar and PVA in chapters 2 and 3?

Chapter 4 is dedicated to studying the wavelet transformation of backscattered signal numerically generated from different types of scattering media. It was shown the scale index is a quantitative parameter of structure periodicity and randomness degree and is a very fine tool that can be used to discover qualitative differences in the random structure. Was it impossible to make such phantoms with the structure as in Figure 4.1 and compare the numerical results with the experimental ones?

In the further part of the dissertation, the possibility of using the "scale index" to measure the chaoticity degree of a structure was experimentally tested. In Chapter 5, phantoms were used, while in Chapter 6, the liver structure. It was shown that in the phantom the value of the scale index was sensitive to the environment scatterers size, and the value of the index ordered the size of environmental scatterers size. The scale index also quantifies the structure of the liver as more periodic in healthy areas than in tumor areas. A weaker point here is that some aspects might be approached more critically. The question is how practically can the use of the scale index look like? Will the ultrasonography calculate this parameter and display a specific value? Will there be any values "in the norm"?

It's worth appreciating that the results connected with her dissertation candidate published in 5 articles, 2 chapters of books, and 24 papers at scientific conferences. She is also a co-author of other scientific papers, mainly in Russian-language journals.

Conclusion

The results of the research, included in the doctoral thesis, contribute to the broadening of knowledge regarding the use of wavelet analysis of ultrasonic signals in soft tissue structure characterization. The PhD thesis also demonstrated the candidate's general theoretical knowledge of the discipline, as well as her ability to perform scientific work independently. **Thus, my final appraisal is to recommend the admission of Olga Doubrovina to publicly defend the doctoral thesis.** Candidate meets the conditions for awarding the degree of doctor specified in the Act of 14 March 2003 on Academic Degrees and Title and Degrees and Title in the Arts.

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