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Acoustical characterization of polysaccharide polymers tissue-mimicking materials

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ABSTRACT

Tissue-mimicking phantoms play a crucial role in medical ultrasound research because they can simulate biological soft tissues. In last years, many types of polymeric tissues have been proposed and characterized from an acoustical and a thermal point of view, but, rarely, a deep discussion about the quality of the measurements, in terms of the uncertainty evaluation, has been reported. In this work, considering the necessity to develop laboratory standards for the measurement of ultrasonic exposure and dose quantities, a detailed description of the experimental apparatuses for the sound speed and the attenuation coefficient measurements is given, focusing the attention on the uncertainty evaluation both of the results and analysis algorithms. In particular, this algorithm reveals a novel empirical relation, fixing a limit to the energy content (therefore limits the number of cycles) of the three parts in which the authors have proposed to divide the acoustical signal.

Furthermore, the realisation of multi-components phantoms, Agar and Phytagel based tissue-mimicking gels along with others long chain molecules (dextrane or polyvinyl alcohol) and scattering materials (silicon carbide and kieselguhr) are investigated.

This paper reports accurate speed of sound and attenuation coefficient measurements. Speed of sound is measured by a *pulse-echo* technique in *far-field* condition, using an optical glass buffer rod; while attenuation coefficient is determined by an insertion technique, using demineralized water as reference material.

The experimental sound speed results are subjected to an overall estimated relative uncertainty of about 1.5% and the attenuation coefficient uncertainty is less than 2.5%.

For the development of laboratory standards, a detailed analysis of the measurement uncertainty is fundamental to make sample properties comparable. The authors believe this study could represent the right direction to make phantoms characterizations referable and traceable.

1. Introduction

Ultrasounds are widely applied in biomedical field, both for diagnostic aims [1–3] and for therapeutic intents [4–6]. In last years, the necessity of guidelines for safe applications of ultrasounds on patients and personal treatment plans and the need of laboratory standards for the measurement of ultrasonic exposure and dose quantities have induced the proliferation of studies about tissue-mimicking materials (TMMs). Many types of polymeric tissues have been proposed and characterized from an acoustical and thermal point of view with the aim to verify if their thermophysical and mechanical characteristics could be considered similar to those of human tissues.

Among quantities useful for the characterisation of TMMs, the density, ρ, the speed of sound, w, the attenuation coefficient, α, and the heat capacity, c_p, have an essential role, especially in medical applications. For example, density and speed of sound are often used to distinguish an health tissue from an affected one (such as in osteoporosis diagnosis [7–10]), while the attenuation coefficient can be used to predict the ultrasonic beam behavior inside a tissue in terms of absorbed and scattered energy. Moreover, the evaluation of attenuation dependence with frequency supplies information about the proper working frequency range to be used in different applications [11]. Finally, the heat capacity lets to foresee how much of the absorbed energy will be transformed in heat and, as a consequence, in tissue temperature increase.

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Many relevant and informative papers about TMMs can be found in literature [12–15], even if a detailed and accurate uncertainty evaluation of the measured parameters for materials under investigation is not always presented. Despite that, a number of useful comparisons have been completed, providing guidance on achievable uncertainties [16,17] (obtained considering the dispersion of values measured by different laboratories). The data comparison procedure would be improved if an accurate uncertainty evaluation was associated to each considered measure [18]. For this reason, in this work the experimental apparatuses for the speed of sound and the attenuation coefficient measurements have been described in detail and particular attention is focused on the uncertainty evaluation both of the results and of the analysis algorithms.

Considering, as starting point, the TMMs recipes reported in last years in literature [19,20] and thinking about the realisation of multi-components phantoms, Agar and Phytagel based tissue-mimicking gels have been investigated. The effects on w and α values of long chain molecules, such as dextrane or polyvinyl alcohol, and scattering materials, like silicon carbide and kieselguhr, have been examined.

2. Preparation of tissue mimicking materials

Over last 25 years, different TMMs have been proposed and studied [21] in terms of their mechanical, thermal and acoustic properties. In this work, two of the most used polysaccharide polymers for TMMs, Agar and Phytagel have been investigated. Indeed, the study of these molecules is interesting since ultrasonic absorption from gelling molecules is given by various phenomena, such as chemical relaxation processes associated to molecular volumes modification due to conformational changes, exchange processes involving free water molecules or bound to the polymer, interactions with junction zones (i.e. the double helix structure with which the polymerization of polysaccharides occurs) or aggregates of junction zones [22]. On the other hand, because of the high attenuation value required for phantoms simulating human tissues and organs in therapeutic applications of ultrasounds, attenuation increase given by other long chain of polysaccharides, like dextrane and PVA (polyvinyl alcohol) added to the solution, and the effect of scattering particles like kieselguhr and silicon carbide, have also been investigated. All materials used in this work have been provided by Sigma Aldrich. In particular, it has been used a medium molecular weight (M_w 100,000) Dextran, a high molecular weight PVA (M_w 98,000), a silicon carbide with a mean dimension of 37 μm, a diatomaceous earth also known as kieselguhr, that is a siliceous sedimentary rock crumbled in a white fine powder, with a particles size dimension in the range from 10 to 200 μm have been used.

Original recipes of phantoms tested in this work are described in the following.

The first gel, hereafter referred to as TMM 1, is prepared heating an aqueous solution of Agar (3% in wt) at 100 °C for 5 min under stirring and adding Benzalkonium chloride (0.9% in wt) as an antifungal agent. Successively, while the sample is cooling, it is cast carefully into a cylindrical mould to avoid bubbles formation and to obtain smooth and flat surfaces, needed to optimize the ultrasonic coupling for the measurements. The second gel, referred to as TMM 1a, is prepared starting from the same solution used for the TMM 1, but Dextran (1.5% in wt) and PVA (1.5% in wt) are added during the heating step.

Moreover, subsequent gel samples are based on Phytagel. The polymerisation of this molecule is catalysed by the presence of cationic ions (Na^+, Ca^{++} Mg^{++}), thus, in our case, for the preparation of the third gel, referred to as TMM 2, an aqueous solution of Ca_2SO_4 (0.5% in wt) is kept under stirring while it is gradually heated at 90 °C for 10 min. During the heating step, Phytagel (2% in wt) powder is added carefully under stirring to prevent lumps formation. After that, while the sample is cooling, it is cast carefully into the cylindrical mould. The fourth gel, TMM 2a, is prepared with the same procedure described for TMM 2 but, during the heating step, scattering agents, kieselguhr (1.5% in wt) and SiC (1% in wt), are added to the solution and kept under stirring until any visible lumps are no more longer present. Finally, a fifth gel, referred to as TMM 2b, is prepared as TMM 2a but with the variation in percentage of weight of kieselguhr (3% in wt) and SiC (2% in wt).

3. Measurement method and experimental apparatus for the speed of sound

The speed of sound has been measured using the traditional *pulse-echo* technique and an optical glass buffer rod has been interposed between the ultrasound transmitter and the sample to ensure that *far-field* conditions are reached before the signal passes through the sample as shown in Fig. 1. In the *pulse-echo* technique, the source transducer transmits a signal that travels through the sample and is reflected at the opposite surface of the material, generating a series of echoes. The time τ between two successive echoes, detected by the same transducer (in this case the receiver), corresponds to the time spent by the signal to travel a double path, therefore outward and return [23]. So the speed of sound w is determined as:

$$w = \frac{2d}{\tau}, \tag{1}$$

where d is the length or thickness of the sample. In this work the quantity d has been determined as average of ten length measurements carried out by means of a digital callipers having a resolution of 0.01 mm.

Since the reliability of the speed of sound determination strongly depends on the accuracy of the time-of-flight measurement, this one has been subjected of special attention and analysis. The measurement of the time delay between the acquisition of two successive echoes has been carried out using a numerical technique based on the possibility to digitize the received signals with an high sampling rate (a digital oscilloscope with 8 bit resolution and time sampling of 0.20 ns has been used). In this frame, echoes can be represented as continuous functions of time, $V_1(t)$ and $V_2(t)$ for the first and the second echo respectively, and their temporal delay can be estimated determining the value of τ which maximizes the correlation function:

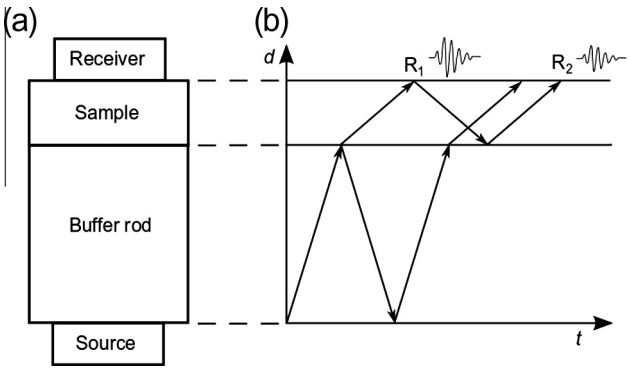

Fig. 1. Assembly of transducers and sample with buffer rod (a) and the corresponding (b) diagram of the acoustic signal path. R_1 and R_2 refer to the first and second echoes used for the speed of sound determination. R_1 crosses the sample once, while R_2 three times.