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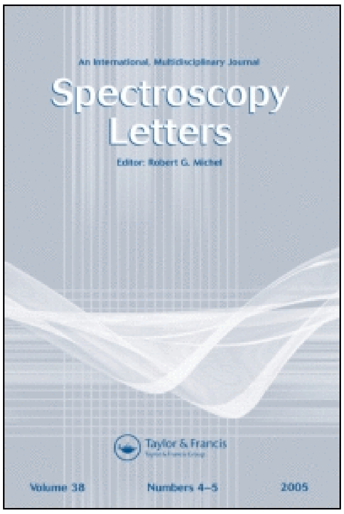

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MAGNETIC RESONANCE IMAGING IN THE PRESENCE OF MECHANICAL WAVES

NMR Frequency Modulation, Mechanical Waves as NMR Factor, Local Temperatur Variations

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ABSTRACT

In the magnetic resonance imaging (MRI) technique the local tissue characterization is accomplished by measurements of the standard NMR parameters.

The present report is concerned with physical factors influencing the MRI tissue characteristics. The effect of mechanical waves on the NMR parameters has been discussed.

1. Introduction

Spectroscopy is finding growing application in examinations of the interiors of complex systems such as biological organisms, geological deposits, underground archeological objects, etc., not only providing information on the structure but also on processes occurring inside the samples under study. The prospects of spectroscopy in the sphere of prompt medical diagnostics are of particular significance.

The principle of spectroecopy lies in obtaining information on the interior of a sample by penetrating it with suitably selected radiation type which, when leaving the sample, carries information on its structure.

An essential condition that should be satisfied in order to obtain possibly adequate information is to use such a radiation type which: (i) in-

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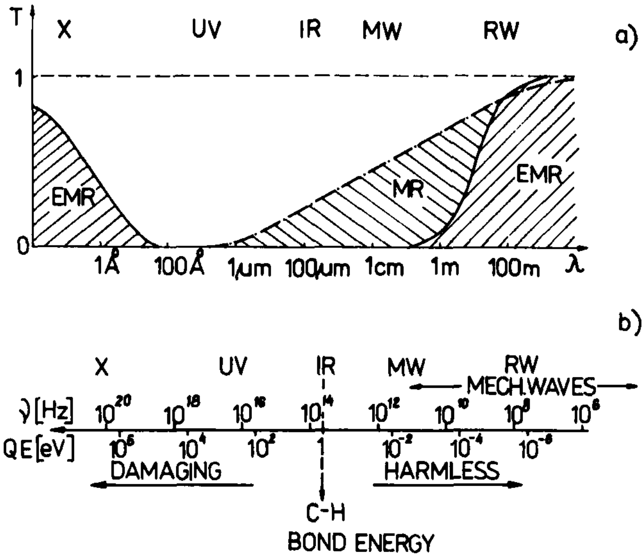

Fig. 1. Transmission of electromagnetic (EMR) and mechanical (MR) waves in soft tissues (a) and the energy scale of both radiation types (b).

teract with the sample matter, (ii) does not induce any substantial structural alternations, and (iii) anables a sufficiently detailed image of the sample interior to be obtained.

The spectroscopy involving electromagnetic radiation ofers two convenient windows to gain an insight deep into human body by using wavelengths from the X-ray and radio wave spectral ranges (Fig. 1), both of which being extensively used.

As regards the resolving power, that in standard procedures of the image creation is limited by the length of waves applied, the X-ray range seems very favourable, contrary to the radio waves. The situation is opposite when considering the problem of invasiveness. The energy of an X-ray quantum exceeds that of the majority of interactions encountered in matter and is therefore capable of producing structural changes in samples, whereas the energy of a radio radiation quantum is incomparably lower than that of the above-mentioned interactions (Fig. 1b), thus being noninvasive. Such spectral windows lie at the extreme ends of the broad

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electromagnetic waves spectrum used in the spectroscopy of abiotic matter. The principle imperfection of the spectroscopy involving electromagnetic radiation when applied to living biological systems consists in the lack of possibilities to use wavelengths from the intermediate spectral range. These are microwaves, infrared (IR), ultraviolet (UV), and visible radiation for which tissues are very weakly penetrable. Since these radiation ranges carry energies comparable to those of the majority of intra- and intermolecular interactions, this disadvantage is particularly revealed in studies concerning the molecular and cellular structure of matter. This shortcoming can in part be eliminated by the application of suitably formed external fields, thus changing the rules for the determination of resolution and offering possibilities to obseve structure in terms of the changes induced by the interaction between certain material elements, e.g., the magnetic or electric multipole moments of nuclei or molecules, with these fields (NMR, EPR, NQR, MRI, etc.).

Other interesting prospects emerge from the application of mechanical waves the spectral range of which is much broader on the wavelength scale than that of the radio waves, covering almost the whole range inaccessible to electromagnetic radiation (Fig. 1a). It can therefore be concluded that in this regard the spectroscopy of mechanical waves supplements the range of diagnostic applications of the spectroscopy involving electromagnetic radiation. It is worth emphasizing that the length of ultrasonic waves is comparable to the dimensions of biological objects as regards the hypermolecular structure. On the frequency and energy scale, this range coincides with the radio wave region (Fig. 1b) owing to markedly lower propagation velocity of the mechanical waves. The mechanical radiation spectral range is finding growing application in diagnostics.

Hence, there emerges an irresistible conclusion that simultaneous use of the electromagnetic radiation and mechanical waves might significantly extend the possibilities to apply spectroscopy for examination of internal structures of human body samples. Joint application of both spectroscopy types should consist in: the direct combination of the spectroscopic techniques used separately until now, or the indirect observation of the effects due to one radiation type emitted as a response to the other type of spectroscopy. In this aspect, spectroscopic observations carried out in that latter radiation field should be pointed out, which are related either to the association of both radiation types or to biophysical and biochemical changes generated by such radiation. The possibilities of employing this type of spec-

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troscopy strongly depend on the frequency range and power of radiation applied as a field in which spectroscopic measurements are carried out, as well as on the choice of a spectroscopic method to be used.

Optosonic |10| and acoustooptical |11| techniques are also extensively used in biological investigations being, however, less useful in tomography in view of strong absorption of electromagnetic radiation by biological tissues in the visible spectral range.

An new research line, proposed in |1-3|, consisting in the employment of the nuclear magnetic resonance (NMR) tomography as a spectroscopic technique used in the mechanical radiation field, seems promising. Such a combination appears favorable for various reasons, among other things in view of: (a) the employment of magnetic field gradients having strictly determined symmetry in the method of magnetic resonance imaging (MRI) which, for the anisotropic displacement of sample elements induced by a mechanical wave, should be manifested in the MRI response by the freaquency fluctuations, (b) the possibilities to generate mechanical waves with lengths comparable to the MRI resolution and cell dimensions, thus enabling spatially controlled displacements of bilogical objects and their effects to be observed at cellular level, (c) low invasiveness of mechanical waves and, hence, the possibility to use higher intensities, I, of the mechanical radiation (of the order of W cm^{-2}) producing changes in acoustic pressure of the order of several atmospheres and, as a result, marked displacements of the eleme ments and considerable veriations in the local density of the sample. High radiation intensities affect also the variations in the local temperature distribution, (d) marked differentiation of the mechanical wave propagation velocities in the environmet (more than 10-fold when passing from gases to solids) related directly to environmental properties, (e) the possibility of inducing controlled movements of whole selected organs or their elements, thus resambling natural motions in biological systems. This refers to such macro elements as the motions of chest, heart, stomach, etc., in the low frequency range, as well as to microelements, for example the cell membranes, intracellular elements, etc., in the high frequency range.

Magnetic resonance imaging was in the past decade significantly developed and adapted for examination and morphological measurements of macroscopic objects. As shown in 1971 by Damadian, the rate of the nuclear relaxation processes in related to the pathological state of tissue |4,5|. This report influenced essentially the interest in the ap-

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plication of the magnetic resonance imaging in medical diagnostics. The investigations in this field received abundant attention and were crowned by the proposition of Lauterbur |6| to employ NMR in tomography of internal structure of great objects.

There exist many nuclei in biological systems that exhibit paramagnetic propeties some of which are of biological significance(see Table I).

The local tissue characterization can be established by measuring the standard NMR parameters, i.e.: the resonance frequency v_L (characteristic of each nucleus type), the magnitude of a signal, proportional to the density, ρ, of selected nuclei, spin-lattice relaxation time T_1, spin-spin relaxation time T_2, diffusion coeficient D, flow velocity v, chemical shift δ , spin-spin coupling J and the spectrum of correlation times τ_0 |7|. The values of these parameters depend on biological, physicochemical, and instrumental factors some of which can be modified by the addition of paramagnetic or ferromagnetic admixtures, the change in the Larmor precession frequency and in the temperature of the element examined. The tomographyc image depends also on the scanning technique used in the MRI method, on the pulse sequence, magnetic field intensity, etc.

The image contrast is affected by numerous factors. The majority of currently used spectrometers afford possibilities to obtain the spatial distribution image only of selected NMR parameters. The images of the spin density and the relaxation times, T_1 and T_2, are most often obtained. Human body contains about 67 % of water distributed inhomogenously over different tissues and organs. The water content and its distribution strongly depend on the state of health, degree of dehydration, and the age of the organism. The differences in the water content in soft tissues do not exceed 30 %, resulting in low dynamics of the proton density images. Greater differentiation has been observed in the case of relaxation times, T_1 and T_2, obtained for these tissues (of the order of 400 %). Hence, the tendency to work out and improve the MRI methods involving those latter parameters. In the MRI methods, the spatial coordinate was transformed to spectral frequency coordinate by application a continuous spatial change in the magnetic field intensity This enable a continuous spectrum to be obtained the intensity of which is proportional to the number of spins in the sample layer with a thickness

$$\Delta x = \Delta\omega / \gamma G \qquad (1)$$

where: $\Delta\omega$ - the width of the receiver transmission band, and G - the magnetic field gradient.

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Equation (1) defines the thickness of the sample layer at which the NMR response is manifested in the spectrum. This thickness depends on the ratio of the receiver transmission band width in the spectrometer to the magnetic field gradient applied. Thus, the resolving power of magnetic resonance imaging is independent of the electromagnetic radiation wavelength and can exceed by several orders of magnitude the resolution achieved in the classical image creating methods.

In the present report, a few additional applications of magnetic resonance imaging will be demonstrated involving the employment of the mechanical wave field as the NMR response modulator. Several siplest effects of the tissue sonification displayed in the NMR response will be shown. It will be futher assumed that only longitudinal waves propagate in soft tissues.

2. Mechanical waves as an NMR factor

The mechanical wave attenuation in soft tissues is relatively weak in the whole wavelength range, being proportional to frequency, i.e., increasing with frequency slower than in pure liquids, thus affording possibilities of sonification of even deep tissue layers. The acoustic resistance and the attenuation coefficients of tissues are varied |8,9|. Theoretical description of interactions between the mechanical waves and biological tissues is complicated. Nevertheless, owing to extensive studies and numerous applications of the ultrasonic techniques in diagnostics, therapeutics, thermography, molecular spectroscopy, etc., the mechanical properties of many tissues have been recognized in sufficient detail. The latest achievements regarding the instrumentation (the formation of acoustic field, detection and data processing) raise hopes of having mastered in the neares future the techniques of controlled sonification of selected elements in various human organs. At present, the data processing procedures in magnetic resonance imaging and in ultrasonic methods are very similarly advanced in many respects requiring similar instrumentation to be used.

Let us now consider several simplest effects produced in tissue by mechanical waves which should be manifested in the NMR response.

A) Frequency modulation

The propagation of a longitudinal wave in viscoelastic medium with a non-zero coefficient of cubic elasticity, K, and shear modulus, Q, is described by the equetion

$$\rho \frac{d^2 \xi}{d t^2} = \left(K + \frac{4}{3} Q \right) \frac{d^2 \xi}{d x^2} \qquad (2)$$

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where ξ - the displacemnt of a point element of the medium,

ρ - density.

Assuming the following solution of equation (2)

$$\xi = \xi_0 \cos(\Omega t - k x) \quad (3)$$

and a non-zero liniear magnetic field gradient in the vicinity of the tissue element considered, the modulation of magnetic field affecting the displaced element consits in fact in the modulation of the resonance frequency, $\omega = \gamma B$, for paramagnetic nuclei contained in this element. The modulation is proportional to the scalar product of the displacement, ξ , and the field gradient, G: (Fig. 2)

$$\Delta \nu_{NMR} = \frac{\gamma}{2\pi} \vec{\xi} \cdot \vec{G} \quad (4)$$

By substituting (3) into (4), the following expression is obtained

$$\Delta \nu_{NMR} = \frac{\gamma}{2\pi} |\vec{\xi}_0| \cdot |\vec{G}| \cos\psi \cos(\Omega t - k x) \quad (5)$$

where $\Delta\nu_0 = (\gamma/2\pi) \, |\vec{\xi}_0| \cdot |\vec{G}| \cos\psi$ denotes the modulation amplitude. Thus, the displacement, ξ , has been transformed into the NMR frequency change, $\Delta\nu$.

Figure 3 shows $\Delta\nu_0/G$ as a function of the mechanical wave frequency for two intensities I = 0.35 and 1 W/cm^2, and several types of paramagnetic nuclei in aqueous medium.

The frequency modulation depth grows with the decrease of the mechanical wave frequency, attaining values markedly exceeding the accuracy of the frequency measurement in the NMR method, up to the frequency $\nu_{mech} = 10^6$ Hz for intensities below the level considered to be invasive. The modulation depth can be adjusted by changing the value of magnetic field gradient G and mechanical wave intensity, depending also on such properties of the medium as the coefficient of cubic elasticity, shear modulus, the presence of the relaxation mechanisms, etc., in other words, on tissue type.

The NMR frequency fluctuations caused by mechanical waves can result from the changes in magnetic susceptibility of tissues due to compressions and rarefactions of the matter. The NMR frequency fluctuations due to magnetoelastic effect may also be anticipated when the biological tissue exhibits a non- zero magnetostriction (for example, an osseous tissue).

B) Temperature changes

For liquids at room temperature the spacific heat at a constant pressure C_p exceeds that at constant volume C_v, and hence $C_p/C_v = \varkappa > 1$. The local pressure changes caused by a mechanical wave result therefore

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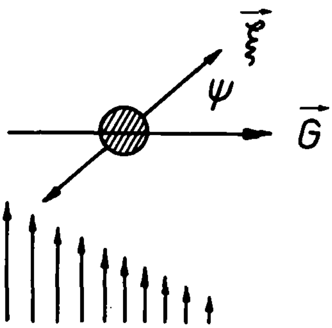

Fig. 2. The displacement, $\vec{\xi}$, and the field gradient, $\vec{G}$, vectors.

in periodic local temperature variations. Assuming adiabatic compression of the medium, the amplitude of the local temperature changes in water was calculated as a function of the mechanical wave intensity (Fig. 4). Periodic temperature fluctuations result in the modulation of some NMR parameters, including the rates of the spin-lattice and spin-spin relaxation processes, as well as the rates of the mass, energy, and momentum transport. Figure 5 shows the range of the relative changes in the proton relaxation time T_1 with the activation energy of this process in soft tissues assumed to range from 10 to 30 kJ/mol.

It seems that the employment of a broad range of mechanical wave frequencies is likely to facilitate the investigation on fast reactions induced by such a periodic disturbance on cellular and molecular level. The temperature and pressure changes result in structural and thermal relaxations.

The mechanical wave energy can in many ways be transferred to the medium. These are the classical ways - viscoelastic mechanisms and heat conduction, and the quantum mechanisms of phonon scattering and absorption. All these processes lead to the increase in the thermal energy of the medium. The precise calculation of the energy absorbed by a system with many relaxation times of different activation energies is difficult. It can, however, be readily found that the value of this energy depends on the wave attenuation coefficient in the medium. It can be also concluded that the temperature changes in a tissue affected by mechanical waves will differ for different attenuation coefficients.

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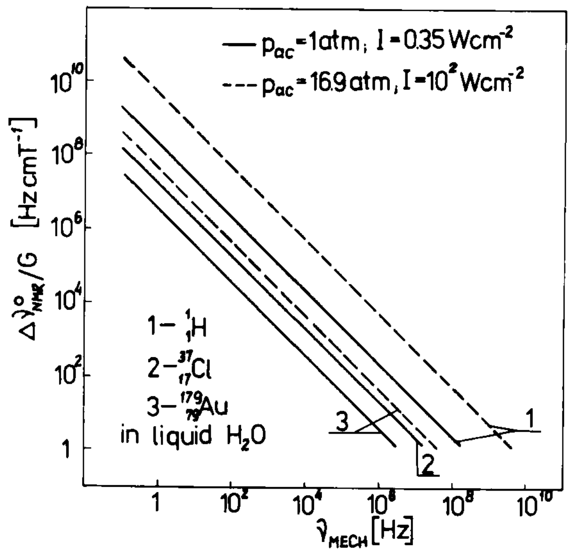

Fig. 3. $\Delta\nu_{NMRo}/G$ as a function of the mechanical wave frequency, ν_{mech} for two intensities I = 0.35 and 1 W cm^{-2}, and several types of paramagnetic nuclei in aqueous medium.

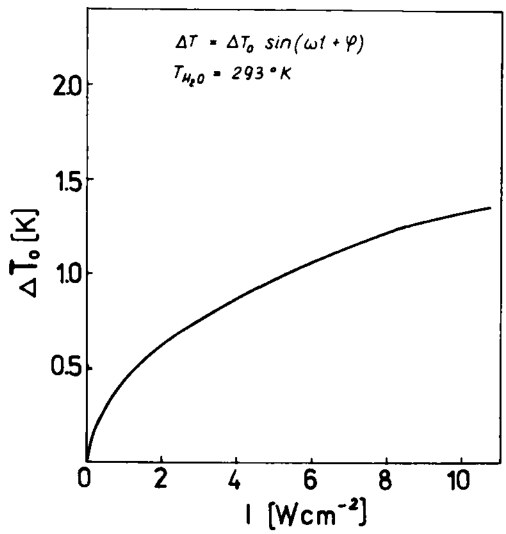

Fig. 4. Amplitude of the local temperature fluctuations induced by the mechanical wave as a function of intensity I.

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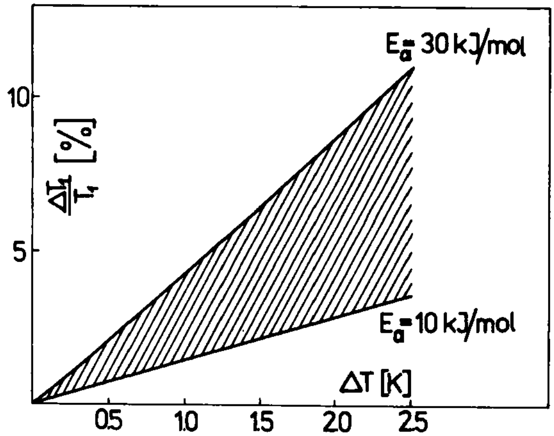

Fig. 5. Amplitude of the changes in T_1 as a function of the tempetature fluctuation amplitude.

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Figure 6 shows the relative energy absorbed by a unit layer in different soft tissues as a function of the mechanical wave frequency. The literature data reported on the propagation velocity and the attenuation coefficient were used in the calculations |8, 9|.

It is worth emphasizing that the efficiency of the transformation of mechanical radiation energy to thermal energy displays discrete character: as a function of frequency - in the regions of the relaxation of the substance examined (of the propagation velocity dispersion), and as a function of position - between the regions of different acoustic impedances.

The thermal effects considered above, following their recognition for biological tissues, can be employed to control and adjust the tomographic image contrast. For example, the contrasts of the T_1 and T_2 images change when the local temperatures of tissues are different.

The ability to induce controlled local temperature changes affords the possibility to obtain information on the energy exchange in living and dead biological systems, for example by the observation of temperature relaxation following the change in the mechanical wave intensity.

It can also be anticipated that the use of the NMR method to observe the sonification effect in tissues will extend the capabilities of thermotherapy and thermography.

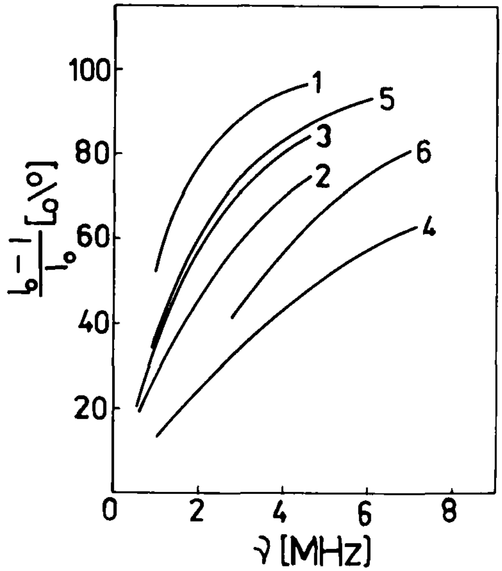

Fig. 6. Relative absorption of the mechanical wave energy in unit tissue layer: 1 - muscular tissue, perpendicularly to the fibers, 2 - muscular tissue, parallel to the fibers, 3 - cardiac muscle, 4 - fat, 5 - eye lens, 6 - neoplasm.

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C) Changes in the NMR signal magnitude

The magnitude of the NMR signal is proportional to the density of spins in samples depending also on the choice of the instrumental parameters, the nuclear relaxation rates, and intensity of all spin system saturating factors.

The sonification of the sample affects the NMR signal by: (i) the change in the nuclear relaxation rate resulting, among other things, from the temperature destributions variations in the sample or structural alterations produced by the mechanical wave, (ii) the saturation of the spin system by a mechanical wave with resonance frequency, (iii) the change in the number of spins in the sample element as a result of its thermal dilatation, displacement, or compression.

The author is aware of the fact that the proposition outlined in the present paper to use mechanical waves as physical factors ac-

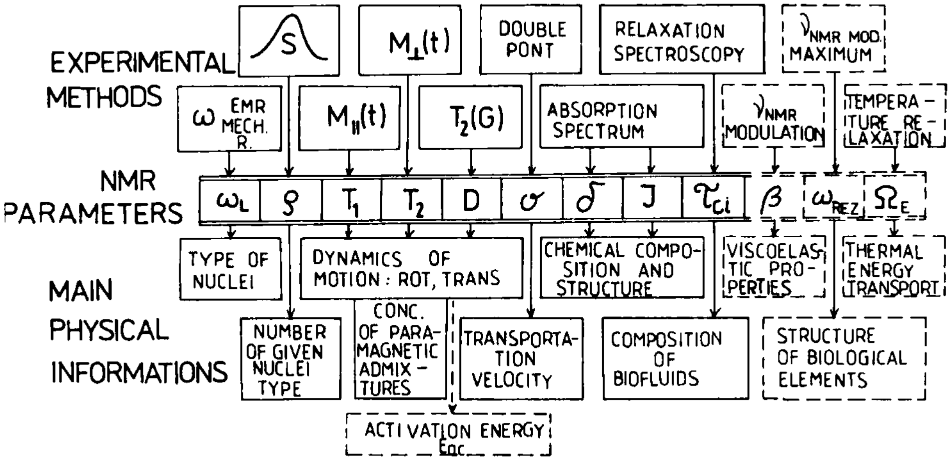

Fig. 7. NMR parameters and the relevant classes of information. The parameters marked with solid line have until now been determined by MRI. Broken lines refer to parameters to be measured by sonification of samples.

tive in the magnetic resonance imaging is difficult from the technical point of view, considering in principle the necessity of inserting the mechanical wave transmitter with controlled parameters into a strong magnetic field. On the other hand, this proposition seems promising as regards the diagnostic, therapeutic, and research prospects, as one might expect that the employment of mechanical waves will extend the scale of information obtained by the magnetic resonance imaging, concerning local characteristics of biological tissues in vivo, to embrace also the following parameters:

- adiabatic compressibility β - by measuring the depth of the NMR frequency modulation resulting from the displacement of the tissue elements,
- the mechanical resonance frequency of selected internal organs or the elements of tissues ω_{res} down to the cellural level,
- thermal conductivity Ω_E - by measuring the local temperature relaxation rate in tissue, following the change in the mechanical wave intensity, and

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- the activation energy of nuclear relaxation processes E_a - by inucing controlled local temperature changes and observing the effects in the tomographic image of these processes.

The NMR parameters determined in the present study (solid line) and discused above (broken lines) and the main information carried by these quantities are listed in figure 7.

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