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# Bioacoustics Response of Small Benign or Malignant Nodules

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*Abstract*— **One of the most important features of separation between benign or malignant tissues is their smooth or rough shape. This article presents a new method for early diagnosis of thyroid cancer by knowing the resonance frequencies of a certain tissue. Two types of nodules were investigated: spherical and elliptical. Their external surfaces were smooth or rough with different values of spicules. Propagation of sound through the human body was modeled by a classical partial differential equation associated with Neumann or Dirichlet boundary conditions. The assessments of about ten acoustic eigenfrequencies are enough to decide the type of external surfaces: smooth or rough, or whether nodule is benign or malignant. Data obtained by this method refers to the result of investigating 3D bodies smaller than 5 mm, when other medical devices such as ultrasound or CT cannot evaluate their surface shape because of their limited spatial resolution.**

## I. Introduction

THE cancer diseases are characterized by uncontrolled growth of abnormal cells and their uncontrolled spread could result death. It is the second most common cause of death in many countries. Improvement in survival rate reflects progress in diagnosing certain cancers at an earlier stage. According to WHO projections over the next 20 years, the number of deaths from cancer will increase by over 45% [1]. Noninvasive medical imaging techniques such as magnetic resonance tomography, computerized tomography or ultrasound, supervised by expert radiologists, contribute to the early detection, assessment, and follow up of the nodules [2], [3]. However, the subjectivity involved in the interpretation of the medical images made by these techniques can be regarded as their major drawback. A system that would be able to interpret these images based on explicit features could contribute to the objectification of medical diagnosis, as it could provide the experts with a second opinion, and could lead to a consequent reduction in misdiagnosis rates [4].

When a nodule volume is too small, one of the most important features that allow detection between benign or malignant character of the tissue is its outer surface shape. As a result of cellular multiplication and apoptosis phenomena there are significant differences ($p < 0.05$) between the benign and malignant soft-tissue tumors in terms of parameters including tumor margin, shape and size. Benign lesions did not have infiltrated margins or a scalloped shape and malignant tumors tended to be large [5].

This clue can be used but the spatial resolution of the modern medical investigation devices such as ultrasound or computer tomograph is limited at about 1 mm, so they can appreciate the body shape only its diameter is bigger than about 5 to 10 mm. It is possible to have an idea about the object dimension taking in consideration that at resonance, the diameter has to be an integer number of half-wavelength of the signal propagating through it. In the case of smooth shapes, there is a certain frequency that meets this condition. In the case of rough shapes, there will be more frequencies, around central frequency, meeting this condition.

So, our objective was to detect for small 3D body whether its surface is smooth or not, and to appreciate how big the body is. From mathematical point of view, the minimum diameter is not important, but in this study we limited it at 1 mm, for matching it to practical investigation.

In this paper, we modeled nodules by homogenous elliptical and spherical bodies. The malignant tissue is modeled to have many spicules around a base shape and the benign tissue to have a smooth shape [6], [7]. By adding random values with normal distribution, the rough surfaces were obtained. Spiculated masses are highly malignant and failing to detect these findings early can prove fatal. Unfortunately, detecting these findings is not easy as these masses are invariably submerged in the dense tissue background. Studies have shown spiculated masses account for a fairly large percentage of missed cancers by both radiologists and computer-aided detection algorithms.

This paper develops a method for calculating tumor features for nodules located in thyroid gland. The thyroid was modeled using a generic pattern presented in [8]. The investigated nodule is located in the left lobe of thyroid. Most of adults have nodules or cysts inside thyroid, generally of benign nature. Some of them may grow and become cancerous. A medical endocrinologist is interested in distinguishing between a node of a malignant nature and one of the benign nature when their volumes are very low. Moreover, he is interested in speed of evolution of the tumor. The shape and dimensions of tumors are in direct relation with its evolution stage. The two scenarios, benign and malignant, are tested by evaluating the acoustic pressure generated by high frequency sounds, a noninvasive method.

The absolute values of the first ten eigenfrequencies give information on the size of nodules.

Distribution of these eigenfrequencies offers a reliable

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indicator of the degree of surface roughness and hence about malignancy character of nodules.

## II. Materials and methods

In this paper the thyroid is investigated from acoustic point of view. The internal structure is considered to be uniformly filled with blood. As investigating signal, the sound was chosen because it propagates though human body with a relative small attenuation and it is not dangerously. Under normal conditions we may assume that the wavelength of the sounds wave is much longer than the mean free path of the thyroid molecules. Then, we may treat the thyroid as a continuous medium instead of as single molecule. With the assumptions of small perturbations, undamped system, zero mean flow, and negligible temperature gradient, the acoustic pressure equation *p* is essentially the time-domain wave equation.

Sound waves in a lossless medium are governed by the following equation [2] for the acoustic pressure, *p* (Pa):

$$\frac{1}{K}\frac{\partial^2 p}{\partial t^2} - \nabla.\left(-\frac{1}{\rho_0}(\nabla p - q)\right) = Q \qquad (1)$$

where $K$ (Pa)=$\rho_0\, c_s^2$ is called the adiabatic bulk modulus, $\rho_0$ (kg/m$^3$) is the density, $c_s$ (m/s) denotes the speed of sound, q (N/m$^3$) is the dipole source, and Q (1/s$^2$) is the monopole source. We treated this equation as an eigenvalue of a partial differential equation to solve for eigenmodes and eigenfrequencies [9]:

$$\nabla.\left(-\frac{1}{\rho_0}(\nabla p - q)\right) + \frac{\lambda^2 p}{K} = Q \qquad (2)$$

The eigenvalue $\lambda$ introduced in this equation is related to the eigenfrequency, $f$, and the angular frequency, $\omega$, through $\lambda = i\ 2\pi\ f = i\ \omega$. A general boundary condition was impedance boundary condition ($Z$):

$$n.\left(\frac{1}{\rho_0}(\nabla p - q)\right) + \frac{\lambda p}{Z} = 0 \qquad (3)$$

where $Z$ (Pa·s/m ) is the acoustic input impedance of the external domain and $n$ is for the wave-direction vector. From a physical point of view, the acoustic input impedance is the ratio between the sound pressure and the normal particle velocity. The two opposite limits: $Z\to\infty$ and $Z\to 0$ are for the sound-hard and sound-soft boundary conditions (Dirichlet and Neumann boundary conditions).

By using finite difference method, in space and time, (3) has the following general form [7]:

$$\det([D] - \lambda[I]) = [0] \qquad (4)$$

The eigenfrequencies correspond to resonance frequencies, and eigenvectors are connected with the acoustic pressure of a particular excitation for which the answer is proportional to excitation, the proportionality factor being the eigenvalue [8], [9]. Computation of characteristic equation roots (4), in finite precision, may be highly unstable since small perturbations in the coefficients may lead to large perturbations of the roots [10].

Two kinds of 3D objects were investigated: ellipsoid and sphere. The smooth surfaces of these objects are shown in fig. 1a. To simulate the size of spicules, the rough surfaces were generated by adding random values to smooth object radius. These values have normal distribution, with different mean and standard deviation values. The rough surfaces for the same types objects are shown in fig. 1b.

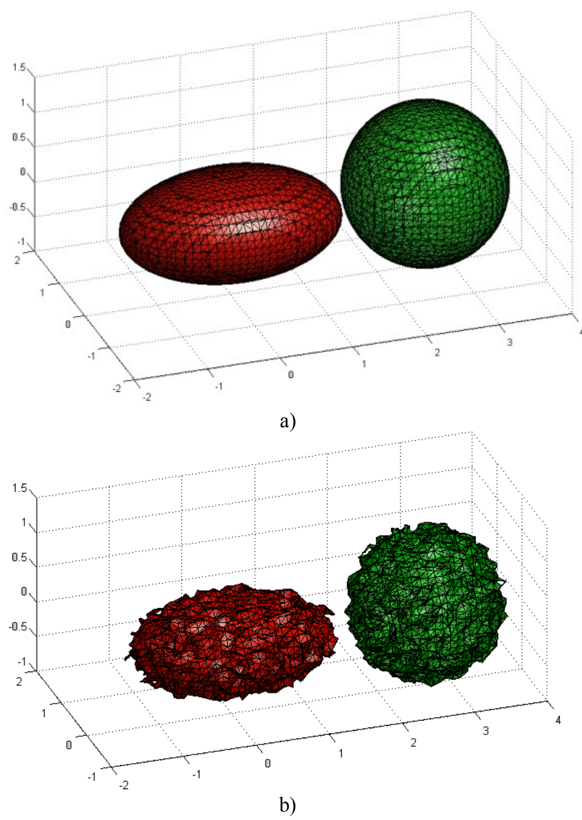

Fig. 1 The objects with smooth surfaces, a) and rough surfaces, b).

## III. Results

The left lobe of thyroid was modeled by an ellipsoid with axes 6x4x3 mm. It is considered to be homogeneously and filled in with blood, sound speed in blood $\rho_0$ = 1540 km/s, and blood density $c_s$ = 1025 km/m$^3$. Material parameters for nodules are considered to be 2o% higher [8].

Equation (4) was numerically solved by using finite element method. The first ten eigenfrequencies values for acoustic pressure of the sound, corresponding to the spheres with smooth surfaces, were evaluated. Table I shows these ten eigenfrequencies for a sphere with 5 mm radius.

Frequencies ratio between the first and second spatial harmonic is greater than 1.5, and the frequency ratio between the first and the tenth spatial harmonic is approximately 4.5.

To study the possibility of early malignancy, three kinds of spicules were modeled by normal distributed variables, $N_1(.1, .1)$, $N_2(.2, .2)$ and $N_3(.5, .5)$. In the same Table I, the corresponding eigenfrequencies for the other three spheres with rough surfaces having a variable radius, $5 \pm N_i$ mm (i=1, 2, 3), are shown as well.

When sphere irregularities are small, about 2%, significant differences between sound waves received cannot be detected. In analysis of the worst case, when random variable $N_3$ acts on sphere, frequencies ratio between the first and second spatial harmonic is about 1.05, and the frequency ratio between the first and the tenth spatial harmonic is approximately 2.7.

Fig. 2 offers a better view of influence of mean value of random variable on the spectral distribution of the eigenfrequencies. Higher spatial harmonics decrease their values and tend to be grouped around the fundamental frequency.

TABLE I

Ten eigenfrequencies for spheres with 5 mm medium radius

| Eigenfrequncy [kHz] | Smooth sphere | Sphere with $N_1$ | Sphere with $N_2$ | Sphere with $N_3$ |
|---|---|---|---|---|
| F1 | 102 | 100 | 96 | 93 |
| F2 | 163 | 158 | 126 | 97 |
| F3 | 220 | 213 | 163 | 121 |
| F4 | 273 | 258 | 181 | 140 |
| F5 | 291 | 263 | 194 | 161 |
| F6 | 324 | 305 | 263 | 211 |
| F7 | 351 | 314 | 270 | 216 |
| F8 | 382 | 347 | 289 | 225 |
| F9 | 419 | 392 | 316 | 241 |
| F10 | 447 | 418 | 328 | 249 |

Table II shows the first ten eigenfrequencies for an ellipsoid with axes: 7x4x3 mm. Spatial harmonic frequency of ellipsoid is smaller than the sphere, about 1.32 times because the sphere radius is smaller than the ellipsoid axis, 1.4 times. This error could be done by finite element method.

In this case, the frequencies ratio between the first and second spatial harmonic is about 1.7, and the frequency ratio between the first and the tenth spatial harmonic is approximately 4.45.

The early detection possibility was simulated in the same manner as in sphere case, by using of three normal distributed variables. So, in the same Table II, the corresponding eigenfrequencies for an ellipsoid with axes: $(7 \pm .N_i)x(4 \pm . N_i)x(3 \pm . N_i)$ mm are shown as well.

The influence of small irregularities of the surface will have more effect on the frequencies of spatial harmonics, because the small axis of the ellipsoid is smaller than the sphere radius previously analyzed. So, ratio between the first and second spatial harmonic is about 1.4, and the frequency ratio between the first and the tenth spatial harmonic is approximately 3.76.

The frequencies ratio between the first and second spatial harmonic is about 1.06, when random variable $N_3$ acts on the axes ellipsoid, and the frequency ratio between the first and the tenth spatial harmonic is about 2.27.

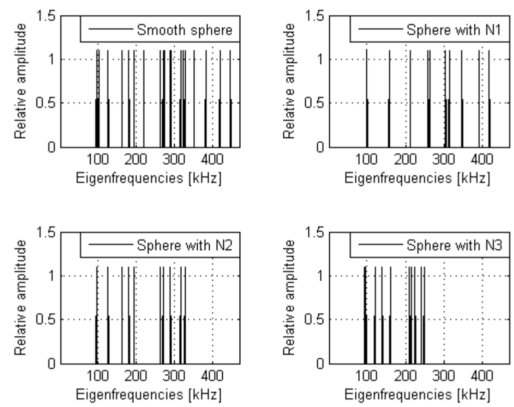


Fig. 2 Spectral distribution of ten eigenfrequencies for smooth and rough spheres

As at the sphere, increasing roughness causes shrinking spatial frequencies values that clump together around the fundamental frequency. This thing can be seen on Fig. 3, by noticing how spatial harmonic frequencies shrink and are grouped around the fundamental frequency as a function of random variable amplitude.

TABLE II

Ten eigenfrequencies for smooth and rough ellipsoids

| Eigenfrequncy [kHz] | Smooth ellipsoid | Ellipsoid with $N_1$ | Ellipsoid with $N_2$ | Ellipsoid with $N_3$ |
|---|---|---|---|---|
| F1 | 74 | 72 | 65 | 59 |
| F2 | 125 | 101 | 84 | 63 |
| F3 | 162 | 147 | 105 | 71 |
| F4 | 181 | 159 | 115 | 78 |
| F5 | 201 | 174 | 127 | 82 |
| F6 | 232 | 196 | 152 | 113 |
| F7 | 256 | 204 | 163 | 119 |
| F8 | 283 | 217 | 158 | 125 |
| F9 | 302 | 259 | 183 | 129 |
| F10 | 329 | 271 | 179 | 134 |

## IV. Conclusions

The absolute value of the first resonant frequency is very strongly connected by the maximum diameter value of the nodule, and consequently, by the stage of the tumor evolution. The dimensions chosen in these simulations correspond to early stages at evolution of nodules.

The second eigenfrequency of smooth objects such as spheres and ellipsoids is far enough from the first one, more than 1.5 times. This may be an important clue in the identification between malignant and benign tissue.

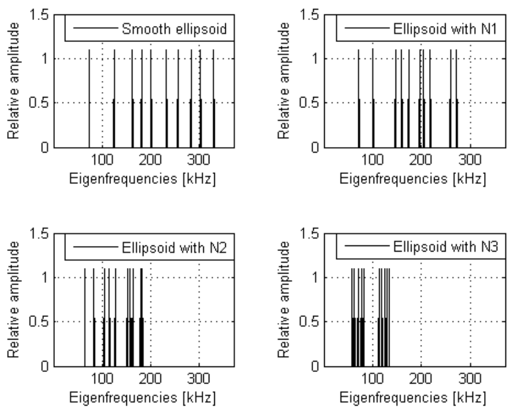


Fig. 3 Spectral distribution of ten eigenfrequencies for smooth and rough ellipsoids

The bodies with rough surfaces have many resonant frequencies around the first resonant frequency, depending how big the roughness is. Analysis of scattering eigenfrequencies around the fundamental frequency may allow physicians to follow up the time evolution of the cancer disease.

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