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Review Article

On ultrasound classification of stroke risk factors from randomly chosen respondents using non-invasive multispectral ultrasonic brain measurements and adaptive profiles

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ABSTRACT

In this paper, we present a new brain diagnostic method based on a computer aided multispectral ultrasound diagnostics method (CAMUD). We explored the standard values of the relative time of flight (RIT), as well as the attenuation, ATN, of multispectral longitudinal ultrasound waves propagated non-invasively through the brains of a standard Caucasian volunteer population across different ages and genders. For the interpretation of the volunteers health questionnaire and ultrasound data we explored various clustering and classification algorithms, such as PCA and ANOVA. We showed that the RIT and ATN values provide very good estimators of possible physiological changes in the brain tissue and can differentiate the possible high-risk groups obtained by other groups and methods (Russo et al. [1]; Lloyd-Jones et al. [2]; Medscape [3]).

Special attention should be given to the subgroup which included almost 39% of the volunteers. Respondents in this group have a significantly increased minimum ATN value (see Classification Trees). These values are strongly correlated with the identified risk of stroke factors being: age, increased alcohol consumption, cases of heart disease and stroke in the family as already shown by Rusco and as incorporated into Lloyd-Jones et al., ''Heart Disease and Stroke Statistics – 2009 Update'', by the American Heart Association (AHA) and American Stroke Association (ASA), as updated recently in the 2015 ''Stroke Prevention Guidelines''.

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1. Introduction

1.1. *Aim and methodology*

1.1.1. *Aim*

Currently, scientific advances in medical diagnostic imaging such as magnetic resonance imaging (MRI), computed tomography (CT) or even ultrasound, have reached very high standards. These technologies provide comprehensive geometrical information about a patient's internal tissue structure but contain little information about its bio-chemical composition. On the other hand, laboratory analysis of biological and chemical components of a patient's blood, cerebrospinal fluid (CSF) or brain tissue provides very good information about the composition of all single substances, for instance by using chromatography, but not about the tissue structure. Furthermore, many brain tissue pathologies are often difficult to detect with standard medical imaging as those minor changes in the brain tissue do not show any discrepancies in picture that was taken. A good diagnosis, in the early phases of such brain disorders, can only be made by a very experienced specialist, such as a neurologist or psychiatrist, who can interpret a patient's initial symptoms. Unfortunately, similar to mental health problems, other brain illnesses such as traumatic brain injuries are hard to detect or to track with standard imaging or bio-chemical analysis. On the one hand, these are often too minor to occur on the single image, and on the other hand, they are too fast for chemical analysis, thus making it difficult to treat them effectively.

To overcome the shortcomings of brain diagnostic technologies that exist today, this paper will present a novel concept called "computer aided multispectral ultrasound diagnostics" (CAMUD) for brain health monitoring. Our solution use longitudinal mechanical ultrasound waves with frequencies in the range of lower MHz and incorporates the following components:

1. Proprietary multispectral ultrasound brain scanner SoNovum UltraEASY™ [6];
2. Innovative form of brain health data analytics; and
3. Machine-learning prediction tool to diagnose, prevent possible brain impairment with early detection and to track brain disorder conditions and treatment in real time.

The first two steps will be described and discussed in detail in this paper. The third step will form the basis of a corresponding research study and the results will be presented in a subsequent paper.

The first application to employ ultrasonic methods to examine the brain relied on a simple echo reflection method. Echoencephaloscopes, devices that employ reflected ultrasonic waves to examine the position of brain structures, allowing mainly for the diagnosis of the asymmetry of anatomical structures, based on echo presented in "A Mode" (amplitude presentation), were created in the mid-1960s. The first Polish echoencephaloscope was developed in 1966 at the Institute of Fundamental Technological Research, Polish Academy of Sciences, under the direction of Professor Filipczynski. Successive ultrasound brain diagnostic methods like transcranial Doppler (TCD) and scanning (ultrasonography) have been widely adopted in practice. The first experiments involving a transcranial ultrasound densitometry system were made by Prof. Roman Mazur back in 2000 and published in «Udar Mózgu» [4]. The ultrasound system used in this clinical experiment examined 62 patient's brain tissue with only one frequency. The authors interpreted the recorded changes in the ultrasound signal as simple density changes of the brain tissue due to absence of blood, its hydrolyze or edema. We will demonstrate that using multiple frequencies will show the dispersive character of the brain tissue and provide some other interpretation to the signal changes. In non-linear material, as, for example biological tissue and especially human brain tissue, an effect of longitudinal wave dispersion can be clearly observed and measured. It is such effect, in which the non-linear frequency-dependent mediums bulk modulus results in different propagation speeds for different ultrasound frequencies [6]. In addition to the observed changes in propagation speed, different attenuation profiles can also be observed. Interdependence between wave speed and attenuation is in accordance with Kramers–Kronig equations ([5], (29)) where it is shown among others that

$$\frac{1}{c_2}-\frac{1}{c_1}=-\frac{2}{\pi}\cdot\int_{\omega_1}^{\omega_2}\frac{\alpha(\omega)}{\omega^2}\mathrm{d}\omega \qquad (1)$$

where c_1, c_2 are propagation velocities for waves with circular frequencies ω_1 and ω_2, respectively, and $\alpha(\omega)$ is the attenuation for wave with circular frequency ω. The above, after introducing $\omega = 2\pi\cdot f$, $\omega_1 = 2\pi\cdot f_1$ and $\omega_2 = 2\pi\cdot f_2$, takes the form of:

$$\frac{1}{c_2}-\frac{1}{c_1}=-\frac{1}{\pi^2}\cdot\int_{f_1}^{f_2}\frac{\alpha(f)}{f^2}\mathrm{d}f \qquad (2)$$

As will be presented further in this paper, such pattern of frequency-dependent attenuations and the corresponding propagation speeds can be used to identify the state of a medium or to track possible changes to the brain tissue in real time.

To fulfill the paper's goals, a "SoNovum UltraEASY™)" [6] ultrasound system for data acquisition was built by E3-Technology, SonoMED and SoNovum and used for multispectral signal collection. Data was collected by MTZ Clinical Research Warsaw (MTZ), during the medical experiment approved by Bioethics Committee Vote Reg. No. KB/916/14 (Bioethics Board Resolution no. 07/14 of the District Physicians Chamber in Warsaw from March 13, 2014) from almost 250 volunteers with representative ages and gender (see Fig. 1).

1.1.2. *Experimental procedure*

The collection of the ultrasound data, conducting the medical examination, and administering the volunteers' questionnaire, was performed by MTZ according to the approved protocol. The duration of the entire procedure for each healthy volunteer did not exceed 20 min. It consisted of three steps:

(A) Preparation for the main ultrasound examination

- Volunteer identification and signing informed consent.
- Answering the questionnaires (described below).