Is Acoustocerebrography a new noninvasive method for early detection of the brain changes in patients with hypertension?

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Background: Hypertension (HT) is the leading cause of global disease burden and overall health loss. The brain is one of the main target organs affected by HT. Age and systolic blood pressure are independent predictors for asymptomatic cerebro-vascular damage, even in the absence of neurologic abnormalities. HT is a potentially modifiable risk factor that leads to the formation of large vessel macroangiopathy, small vessel disease, microangiopathy, and microhemorrhages. Early detection of the brain changes (BC) gives a chance to receive appropriate treatment and protection from irreversible damage. Acoustocerebrography (ACG) is a set of techniques to capture the states of human brain tissue, and its changes on its molecular and cellular level. It is based on noninvasive measurements of various parameters obtained by analyzing an ultrasound pulse emitted across the human's skull (Wrobel et al. 2015). The main idea of this method relies in the relation between the tissue density, bulk modulus, and speed of propagation, for ultrasound waves in this medium. In our previous study we showed that ACG is an effective method for brain examination and detecting WML in the brains of patients with asymptomatic atrial fibrillation compared to Magnetic Resonance Imaging (Dobkowska et al. 2016). Additionally we showed that ACG allows to obtain a differentiated signal originates from atrial fibrillation (AF) patients and high-risk patients wit AF and HT (Olszewski et al. 2017).

Aim: The aim of the study was early detection of the brain changes in patients with hypertension using Acoustocerebrography.

Methods: The study included 136 female and 98 male volunteers (age 43.6 ± 15.7 years) who were surveyed in the clinical research. The patients were divided into two groups: group I (patients with HT) n=33, and control group II (patients without HT) n=201. Phase and amplitude of all frequency components of the received signals from the brain path were extracted and compared to the phase and amplitude of the transmitted pulse. By doing so, the time of flight and the attenuation of each frequency component were calculated. Additionally, a fast Fourier transformation (FFT) was performed and its features were extracted.

Fig. 1 An outline of the process of forming multidimensional phase bundle: The compound multi-spectral signal is being emitted at one side of a patient's head and after transversing skull bones and the brain tissue it is being received on the other side

Acoustocerebrography

Acoustocerebrography is based on noninvasive measurements of various parameters obtained by analyzing an ultrasound pulses propagating along the human's brain (Fig. 1). The main idea of this method relies on the relation between the tissue density ρ, bulk modulus K, and speed of sound c, in the tissue under examination. The most important parameters estimated in the ACG method are: attenuation, absorption coefficient, frequency dependent attenuation, speed of sound and tissue elasticity. Speed of sound or, equivalently, times of arriving (ToA) of pulses propagating along the brain path, can be inferred from phase relations between spectral components of the received spectra (Wrobel et al. 2015). Basically, the ToA for the transmitted pulse through a skull is calculated from transmission/reception phases for two sine bursts with carrier frequencies f1 and f2, respectively. This rather elementary idea was modified by introducing a new multifrequency (10 components within the 1.3 MHz bandwidth, from 0.7 to 2 MHz) transmitting/receiving system that considerably improved the precision of the estimations of velocities and attenuations in intra-cranial tissue. The phase and amplitude of all 10 frequency components of the received signals from the brain path were extracted and compared to the phase and amplitude of the transmitted pulse with the precision of 0.1° to 1° for phase and 5.6 ns for estimation of time of flight. It results in very high precision of measurements of speed of sound in brain tissue $\Delta c = 1.25$ m/s and change in local tissue density $Dr/r = 1.6 \cdot 10^{-3}$. The bulk elasticity modulus K is calculated with a precision exceeding $\Delta K/K = 2{,}52 * 10^{-5}$
The ACG examination times takes 30 sec. We performed the examination three times for each patient and used the average signals for further processing using the multi-spectral ultrasound brain scanner Sonovum UltraEASY™. (Fig. 2)

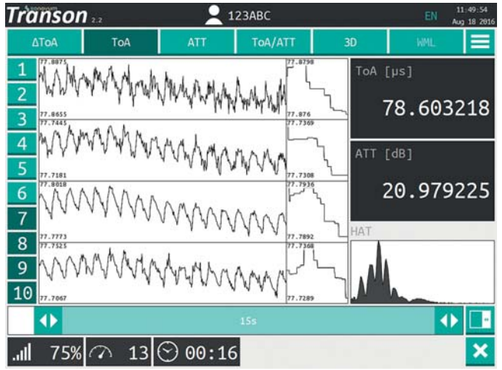

Fig. 2
Sample screen shot of the ACG signal recording

Results: After introducing a machine learning technique, the ROC plot with an AUC of 0.929 with sensitivity 0.879 and specificity 0.831 was obtained. Fig. 3

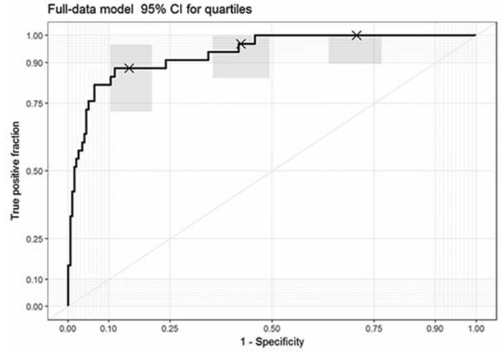

Fig. 3
ROC plot for the discrimination HT patients with 95% confidence intervals for quartiles of 1-specificity and sensitivity

Conclusion: ACG is new promising method, which allows for early detection of change in the brain in the patients with HT.

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