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Over-Hydration Detection in Brain by Magnetic Induction Spectroscopy

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Abstract. Detection and continuous monitoring of edema in the brain in early stages is useful for assessment of medical condition and treatment. We have proposed a solution in which the bulk measurements of the tissue electrical properties to detect edema or in general accumulation of fluids are made through measurement of the magnetic induction phase shift between applied and measured currents at different frequencies (Magnetic Induction Spectroscopy; MIS). Magnetic Resonant Imaging (MRI) has been characterized because its capability to detect different levels of brain tissue hydration by differences in diffusion-weighted (DW) sequences and it´s involve apparent diffusion coefficient (ADC). The objective of this study was to explore the viability to use measurements of the bulk tissue electrical properties to detect edema or in general accumulation of fluids by MIS. We have induced a transitory and generalized tissue over-hydration condition in ten volunteers ingesting 1.5 to 2 liters of water in ten minutes. Basal and over-hydration conditions were monitored by MIS and MRI. Changes in the inductive phase shift at certain frequencies were consistent with changes in the brain tissue hydration level observed by DW-ADC. The results suggest that MIS has the potential to detect pathologies associated to changes in the content of fluids in brain tissue such as edema and hematomas.

1. Introduction

Edema is a medical condition in which the relative amount of liquid in tissue increases. It is of substantial concern when it occurs in the brain. The characteristic of brain edema is that it develops in a delayed fashion, over a period of hours or days, after a brain trauma or event has occurred and is a cause of substantial mortality [1]. Detection and continuous monitoring of edema in the brain is essential for assessment of the medical condition and treatment.

We have suggested the use of MIS as a potential tool for non-invasive detection of tissue edema using multy-frequency induced magnetic fields. In earlier studies we have shown that measuring induction phase shift throughout the bulk of the tissue in time and in a broad range of frequencies could be used as an alternative technique for detection of the tissue edema formation [2] and [3]. Detecting the change in phase shift in time after the occurrence of a suspect episode could serve as a first order clinical warning to detect the presence and progression of edema.

MRI-DW has been used for the evaluation of acute cerebral stroke, intracranial tumours, demyelinating diseases and edema [4]. A water loading in healthy young adults have shown a measurable increase in brain tissue T2 relaxation times moderately correlated to the peripheral osmolality [5]. The diffusion of water molecules in the human brain is restricted by the tissue microstructure and water content. An increase in water ADC in the lentiform nucleus region of the brain has been reported as an early warning of brain edema detectable by conventional MRI [6].

The goal of this study was to test experimentally the feasibility to use MIS to detect the water content in the brain of young volunteers influenced by an over-hydration condition. The experimental system employs a two-coil induction system configuration to detect volumetric fluid changes by inductive phase shift measurements. MIS and DW-ADC data were estimated and compared.

2. Material and Methods

2.1. Biophysical Considerations for Inductive Phase Shift Measurements.

We consider the human head/coil configuration shown in figure 1. An alternating current Ie^{jwt} flowing through the inductor coil generates a magnetic field **B** surrounding the head volume. The induced eddy currents inside the brain promote a perturbation of the primary magnetic field **ΔB** as a function of the tissue electrical properties (σ, ε). The composite magnetic field given by **B**+**ΔB** is detected in the sensor coil as an inductive phase shift. We define a basal induced current argument in the sensor coil as ($\omega t + \Theta$) and the argument influenced by an over-hydration tissue condition as ($\omega t + \Theta_1$). To estimate the inductive phase shift ($\Delta\theta$) we can use the argument differences at specific frequency and time according to the following expression:

$$\Delta\theta=(\omega t+\theta_1)-(\omega t+\theta)=\theta_1-\theta \tag{1}$$

2.2. Experimental Inductive Spectrometer

An experimental Inductive Spectrometer was designed and constructed. Figure 1 shows a block diagram of the experimental prototype. The system consists of five modules: function generator, transceiver, phase detector, data acquisition and a PC as data processing unit. The function generator was implemented by a commercial radiofrequency signal generator (Rohde & Schwarz SMP02), which supplies an alternating current Ie^{jwt} of approximately 10mA rms in the range of 10 to 200 MHz. The transceiver consists of two different diameter coils coaxially centered at a distance d=10cm with radii of R1=2 cm and R2=8.5 cm. Both coils were built from ten turns of magnet wire AWG22 rolled on a plastic harness specifically designed for an adult human head. The coil inductances, as calculated on the basis of Faraday's law, are approximately 44.4μH and 7.73mH for the inductor and sensor coils respectively. The inductor coil induces a current in the sensor coil by magnetic induction, it involves an inductive phase shift ($\Delta\theta$) in the sensor coil as a function of the brain electrical properties. The phase detector was designed on the basis of the AD8302 (Analog Devices Inc. Norwood, MA USA). The AD8302 is a fully integrated RF IC for measuring differences in phase between two signals with a resolution of 10mV/degree. The signals of the inductor and sensor coils were connected directly to the phase detector module as shown in figure 1. The data acquisition module uses the A/D converter USB-1408FS (Computing Measurements Inc. Norton, MA USA) with a sample rate of 48kS/s. For each frequency, the data is an average of 1024 measurements. The data processing system is controlled by a personal computer Dell Precision 490 (Dell Inc. Round Rock, Texas USA). The fundament hypothesis in this study is that the changes in phase measured with the detection coil will be representative of the changes in electrical conductivity and permittivity inside the brain.

2.3. Diffusion-weighted MRI and ADC estimations
DW images with slice thickness of 7 mm and interslice gap of 1 mm were obtained in the axial plane by using a single-shot spin-echo echo planar imaging (SE EPI) sequence (repetition time (TR) 6000 ms, echo time (TE) 80 ms), 20 slices of 256x256 matrix, with b values of 0 and 1000 s/mm^2. DW images were spatially registered and the ADC maps were produced at the base-line and in hydration state to each subject. The ADC value was calculated with an algorithm implemented according to the following equation:

$$ADC\left[\mathrm{mm}^2/_s\right] = \frac{1}{b1}\ln\left(\frac{IS(bo)}{IS(b1)}\right) \qquad (2)$$

where IS(*b0*) and IS(*b1*) are the signal intensities voxel by voxel in the DW images obtained with two different gradient factors (*b0* and *b1*). All regions-of-interest (ROIs) were 1 cm^3 volume approximately localized in the lentiform nucleus region for the measurement of ADC values. For each ROI the mean ADC value was calculated.

2.4. Experimental Design
The experimental concept is shown in Figure 2. It consists of the induction of a generalized and transitory over-hydration condition in ten healthy adult volunteers by ingesting 1.5 to 2 litters of water (25 ml/kg) in ten minutes. Spectra of $\Delta\theta$ in the range of 10 to 200 MHz at 20 pre-programmed frequencies (lineally spaced) were measured by the spectrometer prototype described in subsection 2.2. DW images and water ADC values were estimated in the ROIs brain of the volunteers as described in previous section by the use of a 1.5-T General Electric system (Fairfield CT, USA). Spectra of $\Delta\theta$ and DW-ADC measurements were taken in normal brain tissue and thirty minutes after over-hydration as basal and over-hydration conditions respectively. Changes in $\Delta\theta$ and ADC at specific frequencies and ROIs respectively were compared in basal *vs* over-hydration conditions by a t-student paired (P<0.5). All statics analysis was done by a STATISTICA V7.0 (Stat Soft. Inc). The experimental protocol was developed in the Sectional Image Department of the Military Hospital of the Mexican Army and was previously approved by the Committees of Research and Bio-ethical of the Institution.

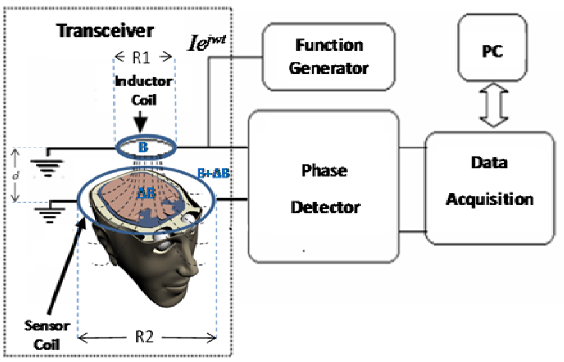

Figure 1. Head/coil configuration and block diagram of the experimental inductive spectrometer prototype.

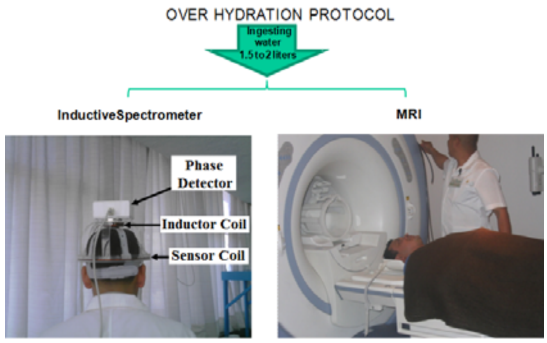

Figure 2. Experimental concept. Over-hydration induction in healthy volunteers by water ingests. MRI *vs* MIS data are compared.

3. Results
Figure 3 shows axial slice diffusion MRI images in basal and over-hydration conditions in the brain of one volunteer as representative behavior of the physiological event. A widespread change in the intensity of the brightness is evident. Figure 4 shows the average spectra of inductive phase shift values estimated in all volunteers in basal and over-hydration conditions. Significant inductive phase shift changes after 100MHz are evident and an important increment of the sensitivity around 150 MHz highlights. Figure 5 shows a box plot of the average assessment water ADC in basal and over-

hydration conditions estimated in all volunteers. A moderated increment of the average water ADC value estimated in the ROIs after the over-hydration induction with respect to basal conditions is observed, nevertheless; a t-student paired test not shows significant changes of water ADC values in the evaluated ROIs.

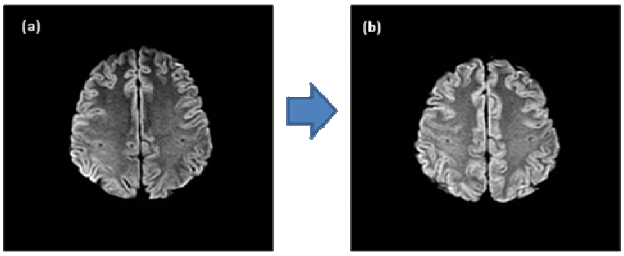

Figure 3. Box plot of the average assessment water ADC in basal and over-hydration conditions estimated in all volunteers.

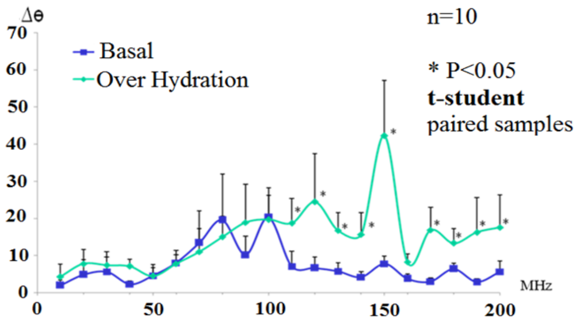

Figure 4. Average spectra of inductive phase shift values estimated in all volunteers in basal and over-hydration conditions. Bars represent one standard deviation.

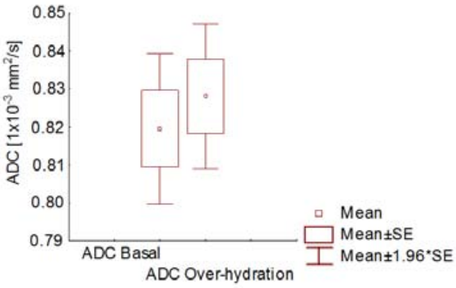

Figure 5. Box plot of the average assessment water ADC in basal and over-hydration conditions estimated in all volunteers.

4. Discussion and Conclusions

The comparisons of basal *vs* overhydration volumetric inductive phase shift values were significant at high frequencies consistently with previous studies [2] and [3]; such condition is explained by the MIS sensitivity to the water dipole effect. The comparison of ADC values not show significant changes in the evaluated ROIs, it´s explained in part by a moderate change in the water content of the brain as the experimental model is intended to induce and in agreement with Rossmiller et al [5]. The results suggest that MIS has the potential to detect in early stages pathologies associated to changes in the content of fluids in brain tissue such as edema and hematomas.

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