Studies on Rat Brain Phantoms for the Development of Near-Infrared Spectroscopy (NIRS) System

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**Equal contribution*

Keywords: Agarose, Intralipid, Near-Infrared Spectroscopy, Phantom, Rat Brain.

Abstract: The present work aims at developing static phantom for rat brain to model the inhomogeneities in the brain tissues. The inhomogeneities have been modelled by varying the concentration of the fluids that mimic those inhomogeneities. The local variations in various parts of brain can be considered as different concentration of substances and accordingly having different optical attributes. Near-infrared spectroscopy (NIRS) has been used to detect and estimate these local changes that indicate different brain activities. The paper presents the development of static rat brain tissue phantoms and its analysis using a single channel near-infrared spectroscopy (NIRS) system. Homogeneous phantoms have been prepared with different concentrations of agarose and intralipid. For different concentrations, the NIRS signal has been acquired at dual wavelengths (770 nm and 850 nm). With increase in the concentration of intralipid, an increase in the amplitude of NIRS signal was noted. The response obtained due to 770 nm and 850 nm sources corresponded to lower and upper amplitude respectively.

1 INTRODUCTION

Near-infrared spectroscopy (NIRS) is increasingly becoming popular for monitoring cerebral oxygenation level by measuring the time variations in the concentrations of oxygenated haemoglobin (HbO_2) and deoxygenated haemoglobin. Cross-sectional studies on cerebrovascular artery reveal that impaired cerebral hemodynamics precede transient ischemic attack and ipsilateral stroke (Markus and Cullinane, 2001). The NIRS is a non-invasive analytical tool that uses the electromagnetic spectrum of wavelength range 700 nm to 2500 nm. This spectroscopy technique involves both vibration and electronic transitions. The basic instrumentation consists of light sources, photo detectors and dispersive component. This technology is widely used in functional mapping of cerebral cortex. The basic idea behind this technique is the fact that absorption spectra of oxy- and deoxy- hemoglobin are different in the optical window of 700 nm to 900 nm (Jobsis, 1977). Hence, these absorption spectra are used as biomarkers in the analyses that relates to the changes in hemoglobin concentration.

NIR light range is capable of penetrating a few centimetres deep into the human brain tissue because the absorption by the tissues is rather low in the NIR window (Lin et al. 2002). The most favourable choice of the dual wavelengths in the NIR range is crucial for signal sensitivity and minimal crosstalk (Villringer and Chance 1997). Typically, it is required to choose one wavelength from greater than NIR light window and other from lower than NIR light window (Biswal et al. 2011). The selection of pair of wavelength is used to measure oxy-hemoglobin (HbO_2) and deoxy-hemoglobin (Hb) (Reynolds, 1988). Electrical stimulus response can also be analyzed using NIRS. This is emerging as a powerful non invasive diagnostic technique for monitoring cerebral micro vessels (Sharma et al. 2016). The analyses with NIRS provide an aid in studying various neural disorders (Dutta et al. 2015; Arora et al. 2016).

In order to develop and evaluate the performance of a spectroscopic system, a test on a suitable phantom is required. The phantom should be a replica of biological tissue and mimic the optical properties as desirable for a NIRS system (Jindal et al. 2015). The most popular phantom used in research is a mixture of intralipid and agarose solution (Cubeddu et al 1997; Lindquist et al 1996).

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Some research groups also use gelatine for the phantom preparations (Madsen et al 1992; Vitkin et al 1995; Hielscher et al 1996).

In this paper we present an approach of designing and implementing static phantom of rat brain with varying concentration of intralipid in agarose solution. A static phantom is the one whose properties are almost constant throughout the experiment whereas in case of dynamic phantom, the experiment is done by varying the properties of the phantom. Agarose solution allows more hardening of the sample in comparison to ink or gelatine solution and is therefore easy to handle. The phantoms are placed on NIRS setup that constitutes of two light emitting diodes and a photodiode. Our work demonstrates the use of NIRS system on rat brain phantoms which helps in quantifying the performance of the NIRS system that can be used for testing brain structures.

The paper is divided into four sections. Section I presents the introduction to the study. Section II describes the various materials used and procedures followed up in the study. The description of NIRS signal acquired by a single channel setup is given in section III. Various issues related to phantom design and NIRS functionality are discussed in section IV.

2 METHODS & PREPARATIONS

2.1 Phantom Preparation

The flowchart for preparing a static rat brain tissue phantom model is shown in Figure1. The development of static phantom of a rat brain follows a four step process.

In the first step, a 3-dimensional rat brain structure was simulated in Siemens PLM Software SOLID EDGE ST9. Generally, model designs are based on length, width, height and volume of specific rat brain. The final simulation rat brain model is stored in the ".par" format. This format is compatible with 3D printer.

The second step involves positioning the rat brain. In order to minimise the amount of supporting material, best settings and position of rat brain model was selected. The various processing methods, take different amounts of time mainly depending upon selected material. Polylactic Acid (PLA) material is used in our experiment. It took around thirty minutes to print the structure. Acetone solution was used for surface finish and removal of the supporting material.

In the third step, PDMS (Polydimethylsiloxane) was used to make the mould around the printed rat brain structure. The mould was prepared in two halves using clay as a separating agent. For curing, the mould structure was heated in microwave oven for an hour at 90° C. After curing both the sides, a cavity is formed in two moulds by removing the PLA structure.

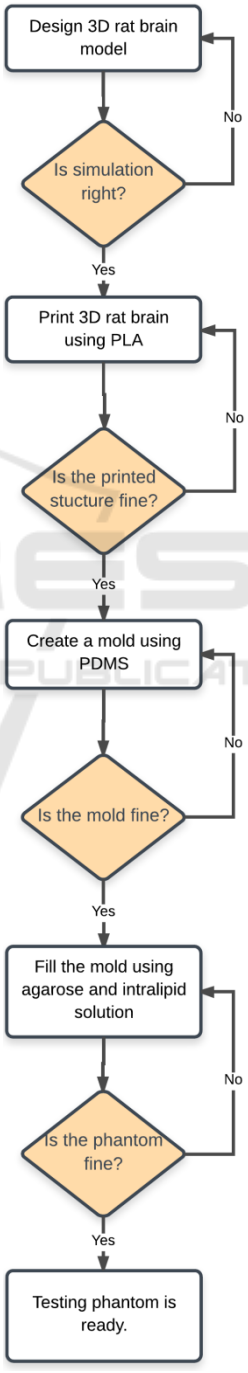

Figure 1: Flowchart to prepare a static phantom.

In the final step, a solution of 1% of agarose in distilled water was prepared by heating in the microwave oven at 90°C. This solution has very low absorption and therefore intralipid is used as a scattering agent to get the preferred optical properties. The important concern in designing a phantom that closely resembles rat brain is the amount of scattering and absorption agents. Agarose powder (A9539, Sigma, and Life Science) was used to make a solution in distilled water. Samples of the solution were prepared by adding different concentrations of intralipid in 1% of agarose solution. The amount of intralipid in different samples was: 0.625%, 1.25% and 2.5%. The solution was stirred continuously to get the uniformity in the sample. The mixing of intralipid in agarose solution was done at 53°C and the mould was filled using this solution at about 40°C. It was then kept for some time to get proper hardening and shape. It can be immersed in cold water for some time for hardening. Later, the mould was removed. The phantoms were stored in a moist petri dish sealed with parafilm in refrigerator. Figure 2 depicts the steps followed in preparing the phantoms.

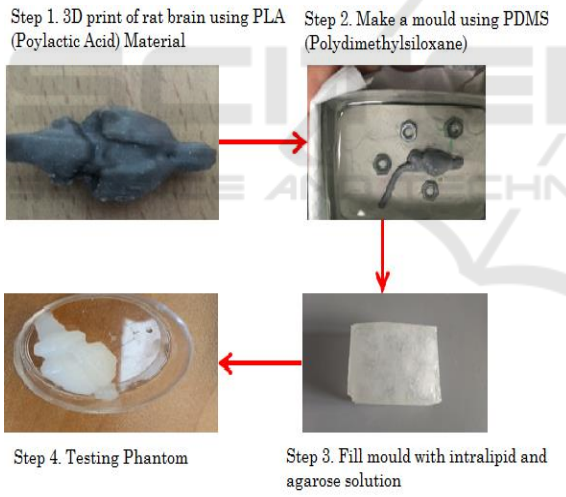

Figure 2: Steps involved in preparing phantom.

2.2 Near Infrared Spectroscopy System Set-up

Our NIRS system is shown in Figure 3. The NIRS system consists of two light emitting diodes of 770 nm and 850 nm, one photodiode on neoprene fabric base and NI myRIO board. NI myRIO board is used as a controller for LEDs and signal acquiring unit for the photodetector. The two wavelengths of 770 nm and 850 nm are chosen because they are on the opposite sides of the point: ~810 nm where oxy-hemoglobin and deoxy- hemoglobin have identical absorption coefficients (Villringer et al. 1993). The two LEDS are placed together and photo diode is at a distance of 1cm from the LEDs.

NI LabVIEW system design software has been used for signal analysis. The simulate LabVIEW VI was used to provide alternate analog input to both LEDs and also for acquiring signal in the waveform chart. This VI is compatible with NI myRIO board as shown in Figure 4.

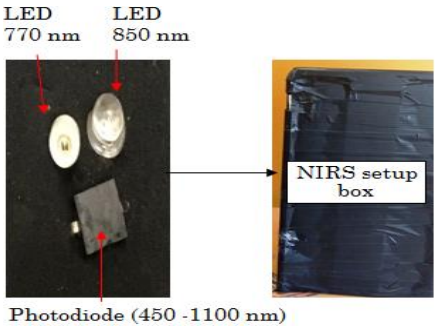

Figure 3: One channel NIRS setup.

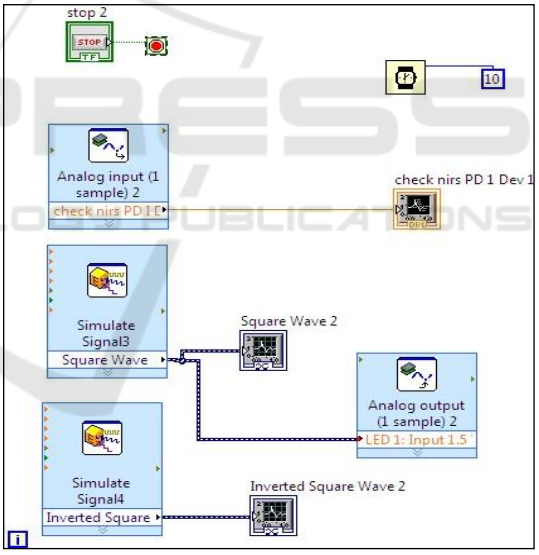

Figure 4: LabVIEW VI for one channel NIRS system setup.

2.3 Experimental Set-up

The phantom has been placed on NIRS set-up and it has been covered with a black box to avoid ambient light interference in the experiment as depicted in Figure 5. The two LEDs were alternately made on and off. The test is done for three phantoms: 0.625% of intralipid in 1% agarose solution, 1.25% of intralipid in 1% agarose solution and 2.5% of

intralipid in 1% agarose solution.

The duration of experiment for each phantom is 10 minutes. The signal sample points are recorded from each phantom using NI myRIO board. In this experimental approach dual wavelength LEDs were alternately made on and off. The signal samples have been recorded at the rate of eleven samples per second. The first five sample points corresponded to first LED (850 nm) and last five sample points corresponded to second LED (770 nm).

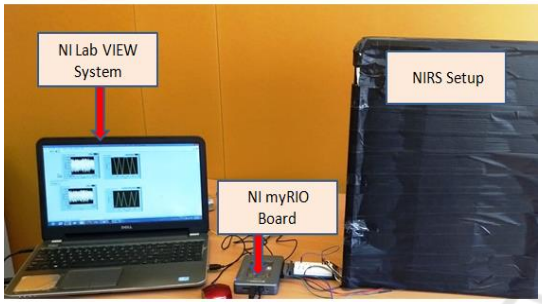

Figure 5: Experimental set-up for testing phantoms.

3 RESULTS & DISCUSSION

The experimental measurements are taken on three phantom samples: 0.625% of intralipid in 1% agarose solution, 1.25% of intralipid in 1% agarose solution and 2.5% of intralipid in 1% agarose solution. The photo diode voltage output for the samples is shown in Figure 6. Figure 7 illustrates the photodiode output variation in the first testing phantom sample 0.625% of intralipid in 1% agarose solution.

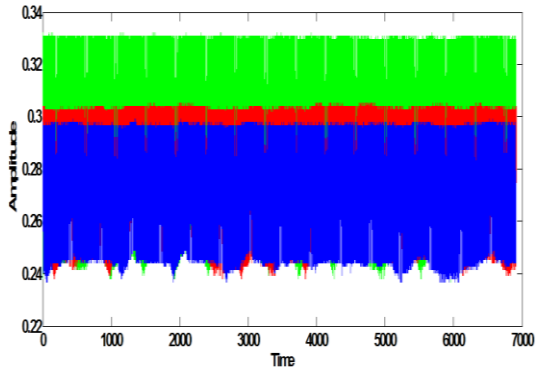

Figure 6: Photodetector output voltage for three test phantoms.

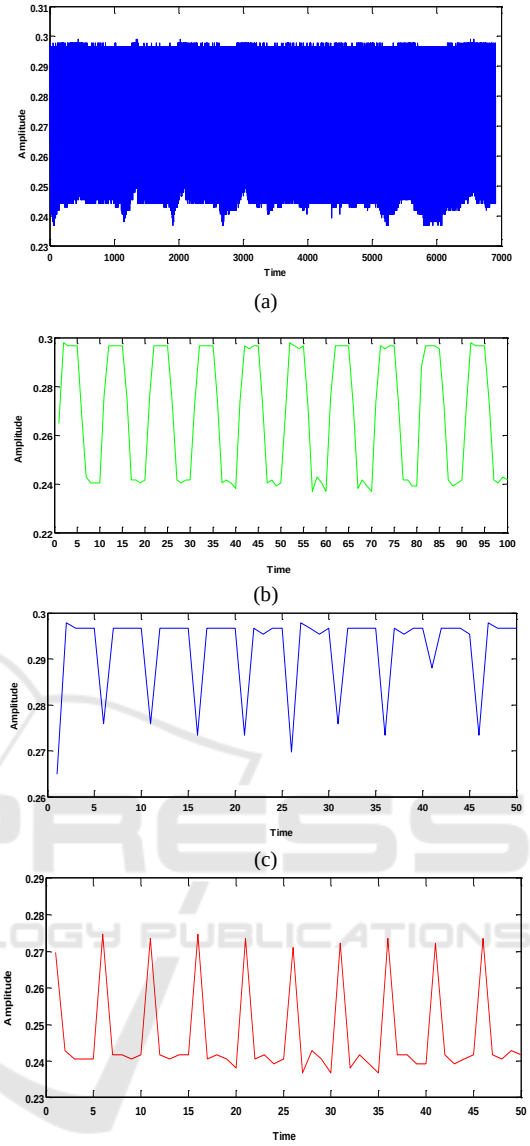

Figure 7: (a) Photodiode output signal in the first testing phantom: 0.625% of intralipid in 1% agarose solution, (b) First 100 sample points of recorded signal, (c) Upper amplitude variation in the signal which corresponded to on time period of LED source 850 nm, (d) Lower amplitude variation in the signal which corresponded to on time period of LED source 770 nm.

The output signal behaviour observed in the second testing phantom sample: 1.25% of intralipid in 1% agarose solution is shown in Figure 8. In the second phantom, sample percentage concentration of intralipid was increased twice as compared to the first testing phantom sample. The photodiode output signal performance detected in the third testing

phantom sample: 2.50% of intralipid in 1% agarose solution is shown in Figure 9.

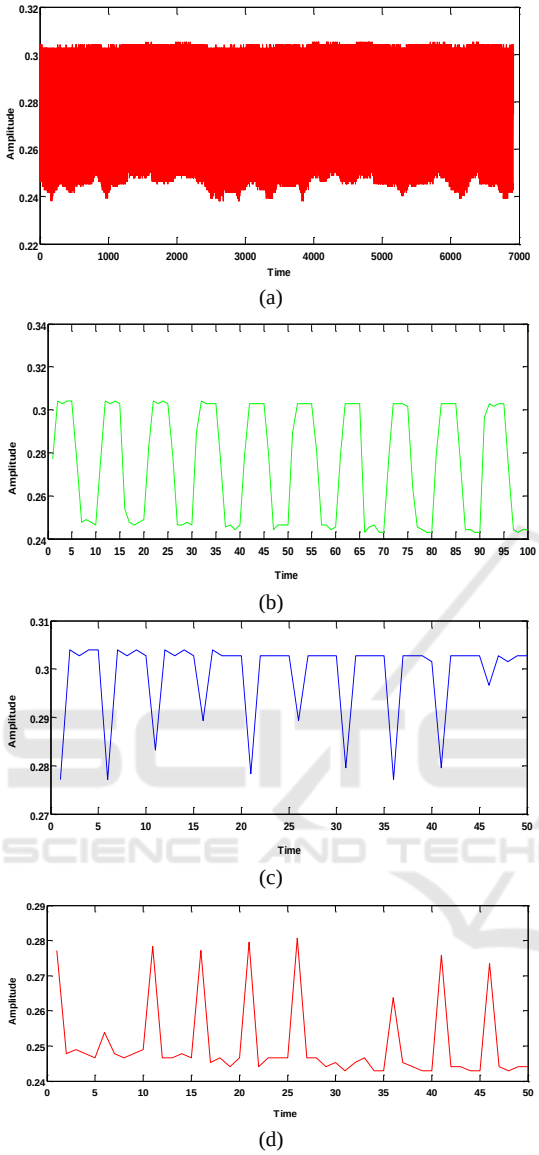

Figure 8: (a) Photodiode output signal in thesecond testing phantom: 1.25% of intralipid in 1% agarose solution, (b) First 100 sample points of recorded signal, (c) Upper amplitude variation in the signal which corresponded to on time period of LED source 850 nm, (d) Lower amplitude variation in the signal which corresponded to on time period of LED source 770 nm.

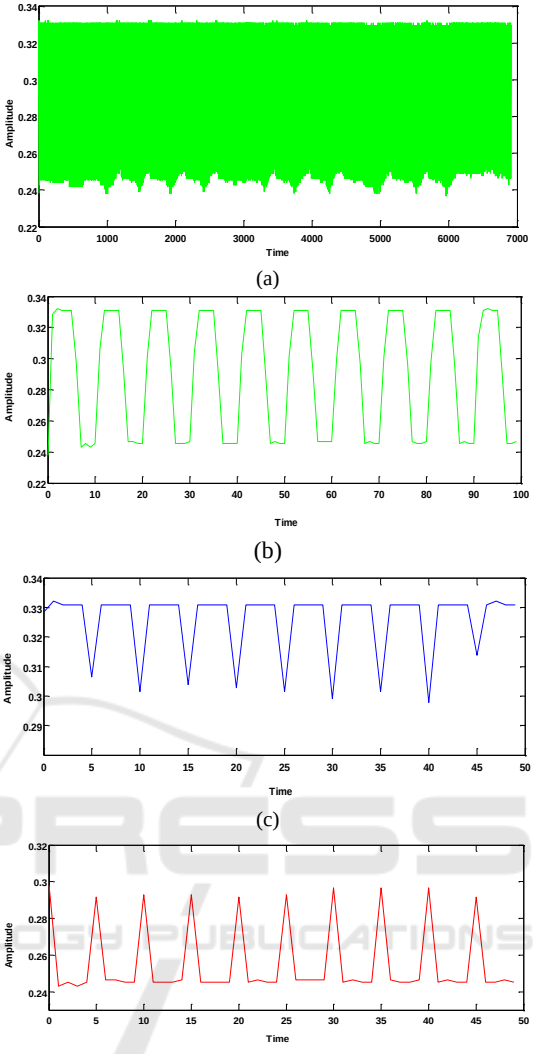

Figure 9: (a) Photodiode output signal in the third testing phantom: 2.5% of intralipid in 1% agarose solution, (b) First 100 sample points of recorded signal, (c) Upper amplitude variation in the signal which corresponded to on time period of LED source 850 nm, (d) Lower amplitude variation in the signal which corresponded to on time period of LED source 770 nm.

The increase in photo diode voltage with increase in concentration of intralipid is clearly visible. Intralipid is a scattering agent. Therefore more is the concentration of intralipid in the sample, more is the back scattering, and hence more will be the output voltage of photo diode. The effect is clearly visible on higher amplitude of NIRS acquired signal that corresponds to higher wavelength of 850 nm as depicted in Figure 10. This effect is less prominent in case of lower wavelength of 770 nm. The intensities profile due to the phenomenon of

backscattering is linked to the structural and functional parameters of tissues. These analyses are required for characterization of optical phantoms in medical applications.

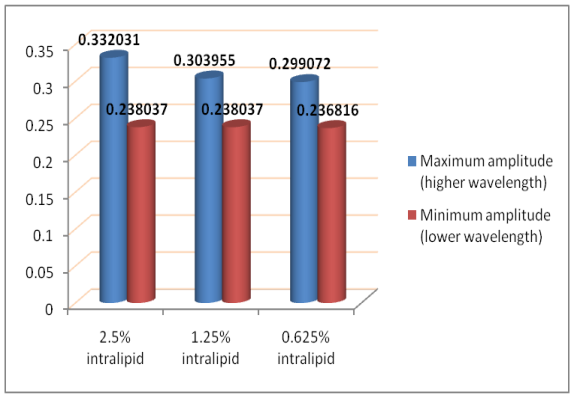

Figure 10: Amplitude profile for the three phantoms.

4 CONCLUSIONS

The work presented here describes the preparation of solid static phantoms of agarose and intralipid. They are tested using single-channel time domain NIRS system. The phantom design presented is easy to prepare and can be used to get inhomogeneous samples with preferred optical properties. Using similar procedures, it is possible to get multi-layered structure with varying optical properties so as to mimic real brain tissues. The NIRS system design is based on a dual-core ARM Cortex-A9 processor (myRIO Student Embedded Device) and have high speed NIRS data acquisition rate. For this study, we attempted to see the affect of scattering agent in the medium on photo detector output. Similar attempts can be made on sophisticated designed phantoms that replicate the real brain. Such experiments provide an insight in analysis of in vitro complex structures.

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