

STUDY OF NIRS BASED MOTOR CORTEX ACTIVATION PATTERNS  
IN CEREBRAL PALSY AFFECTED KIDS  
USING IMAGE BASED METRICS

by

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## ABSTRACT

### STUDY OF NIRS BASED MOTOR CORTEX ACTIVATION PATTERNS IN CEREBRAL PALSY AFFECTED KIDS USING IMAGE BASED METRICS

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In recent years the National Institutes of Health has placed great emphasis on addressing the emergent need to accelerate translation of laboratory discoveries into clinical practice. The proposed study is very much aligned with this NIH emphasis, targeting on the translation of near infrared (NIR) brain imaging to clinical assessment for children with cerebral palsy.

Over ten million Americans are affected by central nervous system disorders that result in motor deficits. Cerebral palsy (CP) is the most common motor disorder of central origin in childhood and affects at least 2 children per 1000 live births every year [1]. One of the most prevalent types of cerebral palsy is hemiparetic CP, an incomplete paralysis of one half of the body. These motor deficits profoundly affect a child's ability to develop age-typical motor skills and to engage fully in play, exploration and self-help activities.

Cortical reorganization or neuroplasticity results from adapting to abnormal development, disease, injury, or learning. Changes in neuronal network micro-circuitry in turn affect gross

synaptic currents, the spread of neural activation, and the morphology of local field potentials that are concomitant with a particular function [2]. It has been suggested that evaluation of brain activity in patients with CP can be used as a diagnostic tool to test: (a) the functional activation of motor areas, (b) the recovery or change in brain activity over time, and (c) the response of brain activity to a particular treatment.

Available neuroimaging techniques in general are useful to study neuroplastic rearrangements in the human brain *in vivo*. These techniques include measurements of the regional cerebral blood flow (rCBF), regional cerebral metabolism of glucose or oxygen, and of neuroreceptor and neurotransmitter systems by positron emission tomography (PET). Importantly, functional magnetic resonance imaging (fMRI) has mapped cerebral structures that participate in movement, sensation, or cognitive problem solving. Unfortunately, accurate imaging from these techniques requires the patients' complete body confinement, steadiness and minimal noise for a period of 30-40 minutes. The practical challenges of fulfilling such requirements in children results in a success rate of less than 50% in normal children [3] and are extremely difficult to perform in those with motor disorders, particularly for children with CP. Therefore, advanced, image acquisition and analysis technologies are necessary to non-invasively image or map *in vivo* changes in brain activities that relate to complex movement.

In recent years, functional near infrared spectroscopy (fNIRS) has been increasingly utilized to investigate neural activities in the human brain during a variety of functional stimulations [4, 5, 6, 7, 8]. This technology measures detectable changes in oxygenated (HbO), de-oxygenated (HbR), and total (HbT) hemoglobin concentrations in the cerebral cortex, thereby providing an indirect measurement of the changes in cerebral neuronal activity as they closely correlate with changes in cortical oxygen exchange. Various studies have demonstrated that fNIRS is a sensitive method to detect and map functional activities from the human motor cortex [5, 6, 7, 8, 9, 10, 11, 12].

I hypothesize that analysis of fNIRS images can identify quantitative image based metrics that can help differentiate between CP affected and normal children. Accordingly, my specific goal is to propose such metrics and identify the ones that have the greatest sensitivity in identifying the CP affected children.

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## CHAPTER 1

### INTRODUCTION

#### 1.1. Near Infrared Spectroscopy (NIRS) and Functional NIRS Imaging (fNIRS)

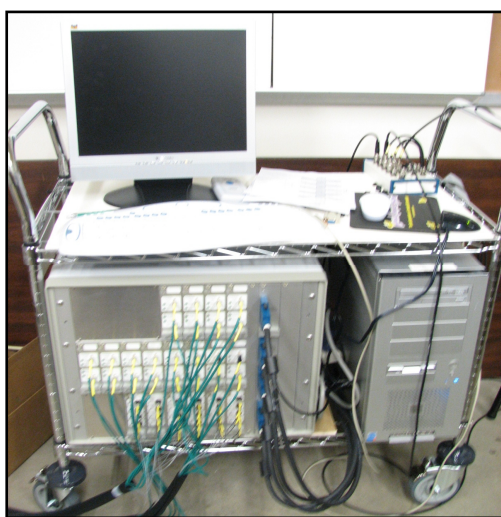
It is well established that near infrared (NIR) light (650-900 nm) can penetrate the human scalp/skull and reach the brain. The principle of functional NIR imaging (fNIRI) relies on the fact that NIR light is differentially and minimally absorbed by the oxygenated hemoglobin (HbO) and de-oxygenated hemoglobin (HbR) in the tissue. In the last 15 years, NIRS and functional NIRS-based brain imaging have evolved as sensitive methods for safe and non-invasive evaluation of hemodynamics and oxygenation in the normal [13,14] or injured [5] human brain, as well as for the determination of cerebro-vascular functional brain imaging in response to a variety of neurological stimuli [16,17,18,19]. In particular, fNIRI has increasingly emerged as a unique imaging modality for studying neuro-hemodynamic responses to brain activation [5, 6, 7, and 8].

In pediatric applications, fNIRI technology exhibits many advantages over fMRI including: (a) avoiding the need to expose children to high magnetic fields or RF pulses, (b) providing real-time cerebral activation measurements despite head-movements, a considerable constraint of MRI, and (c) providing separate measures of HbO and HbR (fMRI/BOLD only measures deoxy-Hb). The two independent measures of HbR and HbO are potentially advantageous in separating signals due to increased oxygen consumption, an issue of considerable concern in studies of fMRI/BOLD. Importantly, fNIRI has been safely used to gather hemodynamic data that correlates with neural activity in neonates and children [20, 21]. Data from multiple human subjects have consistently demonstrated that brain imaging using fNIRI can reliably locate and image activated brain regions during motor stimulation with a good signal-to-noise ratio [22].

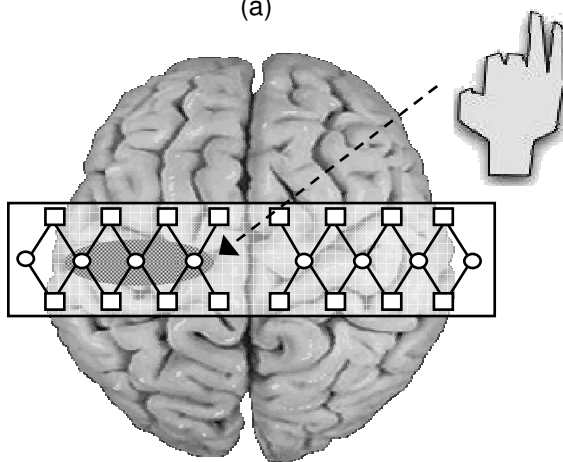


## 1.2 Instrumentation for Functional NIR Brain Imaging

Instrumentation for fNIRS is based on frequency, time and continuous wave analysis. Although frequency-domain [23, 24, 25, 26, 27] and time-domain NIRS imaging systems [28, 29] can provide quantitative hemodynamic measurements, those based on continuous wave (CW) analysis are better suited for functional NIR brain imaging [30, 31, 32, 33, 34, 35, 36] due to faster data acquisition, portability, and lower cost.



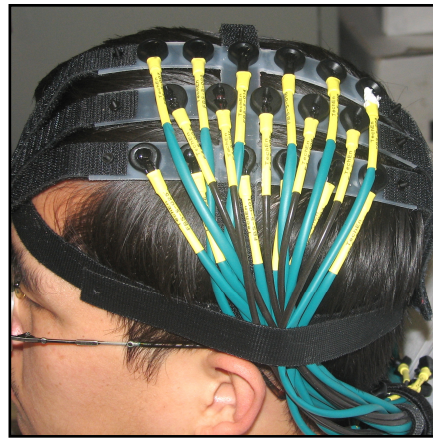
(a)



(b)

Figure 1.1 (a) Main Body of CW-5 (b) the geometry of CW-5 probe on the motor cortex (circle: light source; square: detector).

Currently, there are three commercial fNIRS brain imagers available in the US, two of which are CW-based. We have recently acquired a state-of-the-art CW-5 system (TechEn, Inc; Milford, MA), as shown in Figure 1.1 (a). The CW-5 NIRS imager is CW-based and fMRI compatible, consisting of 24 laser diode sources and 24 avalanche photodiode detectors. The 24 sources (12 at 690 nm and 12 at 830 nm) and 24 detectors system can analyze a relative large area of the sensorimotor brain simultaneously (Figure 1.1 (b)), as all the laser sources are continually ON and frequency-modulated, so that the detectors can see different sources simultaneously. This allows an increased number of measurements to be obtained, providing a more accurate image reconstruction with improved spatial resolution.



(a)



(b)

Figure 1.2 (a) Close look at the source detector attachment to the head (b) The experimental setup while a pediatric subject was doing the motion task.

Light sources and optical detectors are coupled to optical fibers that are arranged on a plastic probe assembly and can be placed symmetrically on the head of each participant according to the arrangement shown in Figure 1.1 (b) and Figure 1.2 (b). The distance between two adjacent sources can be designed according to our needs. Figure 1.2 (b) shows an overall experimental setup of CW-5 with a normal pediatric control, who was reading the protocol instruction from a lap-top computer while performing a finger tapping experiment.

The optical source-detector probes of the CW-5 system are relatively comfortable (Figure 1.2(b)) for pediatric subjects since the probes are light-weight and flexible, having non-sharp-edge contact with the subject's head.

### 1.3 Need for Translation of fNIR Brain Imaging to Clinical Assessment for Children with Cerebral Palsy

Although the fNIRS and fNIRI methodologies have been developed in research laboratories and have been proven valid and reliable for functional brain imaging over the last decade, as reviewed in Sections B1 and B2, there has been little clinical utilization for such a non-invasive brain imaging technology. The reasons for slow translational progress from bench to bedside may result from several possible factors listed below:

- (1) The limitation of the penetration depth of light to reach deeper areas in the human brain,
- (2) The lack of accuracy in spatial location of the activated areas in the human brain due to the diffusive nature of NIR light propagation through tissues,
- (3) The lack of appropriate match between the fNIRI technology and specific clinical problems
- (4) Inadequate effort on translational research to create patient-friendly, clinician-friendly fNIRI systems for specific clinical applications.

Given extensive development and abundant scientific papers published in this research field in the last 15 years, we believe that fNIRI technology can be translated from bench to bedside in a short period of time if we can:

- (1) Target a specific clinical problem that is associated mainly with cortical function,

- (2) Demonstrate the feasibility in translating fNIRI to clinical assessment for the specific group of patients.

Few studies have been reported on using fNIR brain imaging to evaluate cortical regions activated through voluntary movement of the affected upper extremity in hemiparetic CP children. Little is known on the reliability and accuracy of the fNIR brain imaging when it is used in hemiparetic CP children. There are challenges in both engineering and neurological aspects; the following questions provide a few examples:

- (1) How robust are fNIRI measurements to motion artifacts given that most of pediatric CP subjects have uncontrolled movement?
- (2) Can we detect the differences between healthy pediatric controls and children with CP, or between abnormal from normal regions in pediatric CP patients?

These questions are necessary to answer, and will be answered through the proposed study, in order to prove that fNIR brain imaging is useful for monitoring neuroplasticity in children with CP.

#### 1.4 Need for Improvement in Spatial Resolution of fNIR Brain Imaging

While the probe holder assembly from CW-5 together with a reconstruction algorithm (HOMer) [35] results in a reasonable spatial resolution for a fNIR brain image [36], recent reports [37, 38] and our own tissue phantom experiments show that the limited number of source-detectors pairs used for image reconstruction lead to distorted, shifted, or blurred reconstructed images as compared with the true location of the hidden object.

Regarding the image reconstruction algorithm, although it has been incorporated within the CW-5 system, it has two deficiencies: (a) it assumes that NIR light propagates through optically homogeneous tissues, i.e., it does not consider the significant changes in absorption and scattering that light experiences while it travels through the scalp and the skull; (b) it has no depth localization for the detected fNIR signals, i.e., it creates two-dimensional images at an assumed cortical surface depth. The main consequence of (a) is that the spatial resolution of

reconstructed images is degraded, causing blurring effects. The main consequence of (b) is that detected cortical hemodynamic signals may contain 'contaminated' contributions from concurrent hemodynamic changes occurring superficially in the scalp and skull, which would reduce signal specificity.

To improve these deficiencies, in future work, we plan to advance the fNIRI reconstruction algorithm so that it will enable us to immediately reap the benefits of improved specificity and spatial resolution. Deficiency (a) will be addressed by adapting the image reconstruction algorithm to model light propagation in the head based on a two-layer tissue geometry [39], or a patient-specific MRI image volume [40]. Deficiency (b) will be addressed by reconstructing hemodynamic change maps simultaneously at two different tissue depths corresponding to those of the scalp and the cortex.

Before the improvements can be incorporated in the reconstruction algorithm, we need the data modeling technique to simulate the required data with appropriate pixel density, source detector density, number of photons etc. We used Monte Carlo Photon Transport algorithm to simulate the data.

#### 1.5 The tMCimg Monte Carlo Transport Program

tMCimg uses a Monte Carlo algorithm to model the transport of photons through 3D highly volumes with spatially varying optical properties and arbitrary boundary conditions. Both highly-scattering tissues (e.g. white matter) and weakly scattering tissues (e.g. cerebral spinal fluid) are supported. Using the clinical structural information provided by MRI, X-Ray CT, or ultrasound, accurate solutions to the photon migration forward problem are found in times ranging from minutes to hours, depending on the optical properties and the computing resources available. In brief, each photon is propagated as follows; for every photon in the simulation:

- (1) Set the initial position and direction according to the configuration file
- (2) Until the photon ``escapes"

- (a) Select the distance to the next scattering event (an exponentially distributed random variable).
  - (b) Move, possibly reflecting or refracting off of interfaces, to the next scattering event. As the photon is moved from voxel to voxel, it is attenuated according to the local absorption and the distance traveled in each type of tissue is recorded.
  - (c) As the photon moves, its position is sampled at regular time intervals and this is used to update the accumulated photon density.
  - (d) Scatter into a new direction according to some (possibly isotropic) phase function.
  - (e) Iterate until the photon leaves the system, or the time limit is exceeded.
  - (f) If the photon exists near a detector, add a line to the history file.
- (3) Finally, save the final photon density to disk.

Geometry used was of size 110 x 110 x 110 cms.cms.cms. Following optical properties were used:  $\mu_s'=10\text{cm}^{-1}$ ,  $\mu_a= 0.1 \text{ cm}^{-1}$ ,  $n=1.4$ ,  $g=0$ . Source and detector were located at 1cm depth. Now Monte Carlo program when run for 10,000000 photons takes around 3 hours to generate required data files for this geometry. We reduced the computational time by generating this data only once wherein a 6 x 6 block of pixels is tagged as a tissue and thus we have much number of tissues on the layer to be reconstructed. Now suppose we want to have a blob at a particular location, then the tissue block corresponding to that location is selected as blob. If another region needs to be selected as blob, then tissue block corresponding to that location is selected as blob, In this way we do not need to run the complete Monte Carlo program again and again for generating blobs at different regions. We call this data as master data. This simulated data needs to be reconstructed for different source detector densities, different pixel densities, different heterogeneity locations and thus come up with an optimal solution for better spatial resolution.

## 1.6 Long Term Goals

Here we propose to use advanced functional fNIRS for the real-time evaluation of brain activity associated with motor movements. We intend to identify the spatial characteristics of cortical activation during upper extremity movements in normal children, and compare it to those activated in children with CP while performing the same movements. The project will study hemodynamic/neurological changes in sensorimotor network activity during upper extremity motor tasks that might occur as a result of CP, by measuring the dynamic oxygenation levels of hemoglobin during repetitive intentional movements in this patient population. The long-term goal of this study is to translate fNIRS brain imaging as a sensitive diagnostic, prognostic, and monitoring tool for this motor disorder. The knowledge obtained from this project bears the potential to uncover specific brain functional changes in CP, may help develop new therapeutic strategies for these patients, contribute towards our understanding of the pathophysiology of CP, and perhaps be used as a predictor of a child's prognosis.

## 1.7 Previous Studies

Some previous studies done by our group are described here:

### *1.7.1. The Repeatability of fNIR Brain Mapping/Imaging Induced by Hand Waving Activation*

The motivation to examine the fNIR responses of hand waving was that some pediatric CP subjects may not be able to perform finger tapping well due to limited fine motor skills; instead, they may be able to adequately perform hand waving following the instructed protocols. In an initial study, a pediatric control was measured twice on two separate days, performing the same right-hand-waving protocol. His/Her motor activation patterns show good consistency. As an example, Figure 1.3 illustrates the motor activations induced by right hand waving from the subject. A broad area on the left hemisphere is consistently activated; a smaller area on the right-anterior hemisphere is also involved.

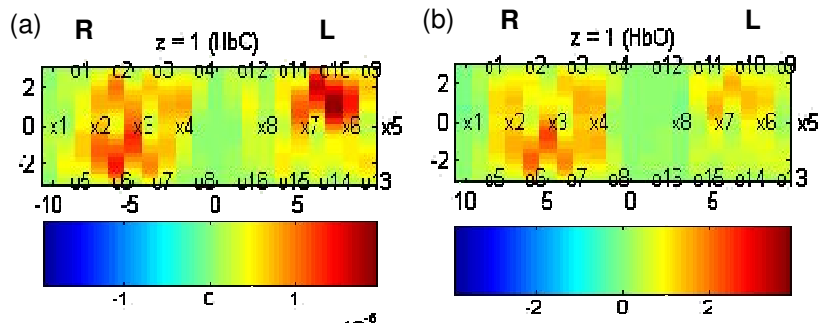


Figure 1.3 The repeatability of fNIRS images due to motor activation by right hand waving on two different days. The consistent patterns between the two days are seen, while the intensities of the responses differ slightly (a) data collected on first occasion (b) data collected on second occasion.

### 1.7.2 Comparison of Motor Cortex Activation Patterns Induced by Finger Tapping versus Hand Waving

In general, the motor activation by finger tapping shows a concentrated area of involvement. In normal pediatric subjects, it follows the mirror projection that the activated cortex is on the opposite side to the moving hand. On the same side of the moving hand, little activation is observed (Figure 1.4(a)). In comparison, the motor activation by hand waving shows a broader area of involvement than that for finger tapping (Figure 1.3 and 1.4(b)). If we look at the anatomy of the human cortex (Figure 1.4(c)), the cortical motor area responsible for hand waving appears closer to the vertex, possibly causing an extended area of response. Moreover, although it still follows the mirror projection in pediatric controls, slight activation on the same side of the waving hand is also observed (Figure 1.3 and 1.4(b)). We speculate that this phenomenon might result from the hand waving action itself and needs to be further investigated in our future studies.



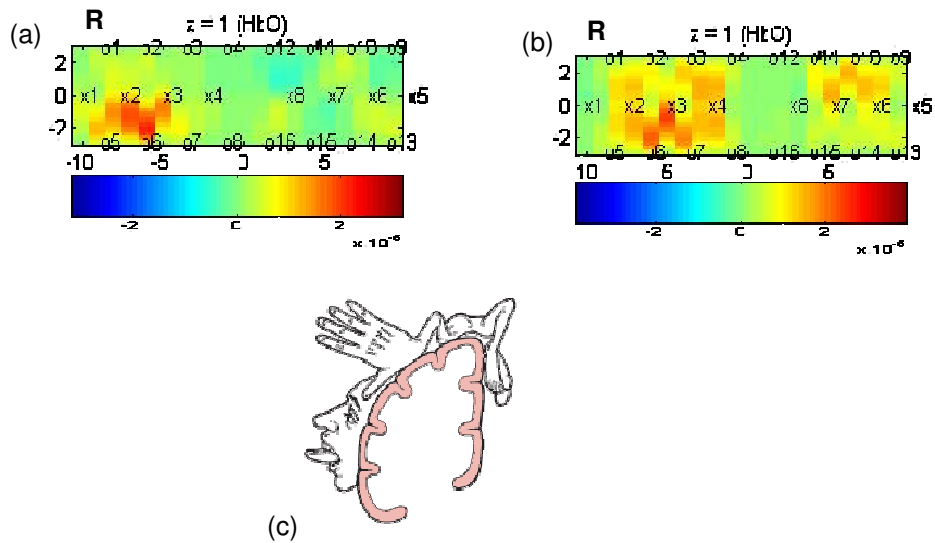


Figure 1.4 Comparison of motor activations (control #4) in response to (a) right hand finger tapping and (b) right hand waving. (c) shows the projection of body parts to the motor cortex.

### 1.7.3 Comparison of the Motor Activation Patterns in Pediatric Controls versus Children with CP

Although in pediatric controls the motor activation is seen on the contralateral side, the side of motor activation varies in children with CP. As an example, Figure 1.5 (a) shows the motor activation induced by left hand finger tapping from a pediatric control, illustrating clear activation on the opposite side (right hand side). In comparison, Figure 1.5 (b) shows the same motor activation from a child with CP with **left hand impairment**. As we observed during the measurement, when that subject tapped her left fingers, her right hand also moved involuntarily (mirror movements). The fNIRS images (Figure 1.4) show that both her left and right sides of her motor cortex were accordingly activated.

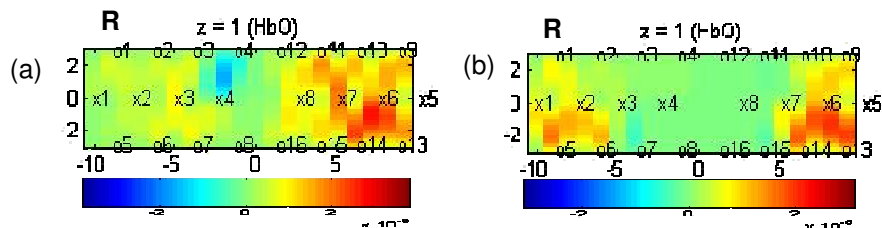


Figure 1.5 Comparison of the left hand finger-tapping activations between (a) a pediatric control and (b) a child with CP who has an impaired left

### 1.8 Motivation

At the present time simple visual inspection of fNIRS motor cortex activation images yield not clearly distinguishable patterns between normal and CP affected Kids. For the described problem, our possible solution will be to explore the possibility of utilizing other data analysis tools, such as pattern recognition methods and image based metrics Analysis to enhance hemodynamic distinction between normal and abnormal brain anatomy obtained from the pediatric controls and children with CP.

### 1.9 Aims

Following are the specific aims of my study:

- (1) Study Reproducibility Using Image Based Metrics.
- (2) Compare Finger Tapping and Hand Waving in Normal Subjects Using Image Based Metrics.
- (3) Compare Normal Subjects with Cerebral Palsy (CP) Affected Kids Using Image Based Metrics.
  - (a) Differentiate between healthy pediatric controls and children with CP.
  - (b) Differentiate abnormal from normal regions.

### 1.10 Proposed Image Metrics

Following Image based metrics are selected for this study:

- (1) **Activation:** Sum of all the pixel values above threshold level.
- (2) **Activated Area:** Number of pixels whose values are above the threshold level. Here number of such pixels would be same as activated area, because each pixel size is 1 x 1 cm.cm.
- (3) **Percentage Coefficient of Variation:**  
Percentage Cv =  $(\sigma / \mu) * 100$ , where  $\sigma$  is standard deviation and  $\mu$  is mean.
- (4) **Location of Blob with respect to Center line of brain**

### 1.11 Segmentation

Histogram in ideal case has two peaks, representing background and objects respectively. Between two peaks is a sharp valley. Ideally we can select threshold level as bottom of this valley. But in reality, valley is sometimes flat, broad, not traceable, noisy. So we need to use sophisticated discrimination analysis algorithm. In discrimination analysis only histogram of the image is required, no other a prior knowledge required. It solves unsupervised decision problem in pattern recognition. It automatically selects optimal threshold.  $\eta$  is used as criterion measure to evaluate the “goodness” (or separability) of the threshold at level  $k$ .  $\eta$  is the discriminant measure (or the measure of separability of the resultant classes in gray levels). The optimal threshold level  $k$  that maximizes  $\eta$  is selected [45].

## CHAPTER 2

### METHODS

#### 2.1 fNIR Brain Imaging on Pediatric Controls and Children with CP

##### *2.1.1. Human Subjects and Experimental Protocols*

Six healthy controls and 6 children with hemiparetic CP between the ages of 6 and 18 years old were be enrolled. Informed consent was obtained for all 20 subjects. The subjects were evaluated at Texas Scottish Rite Hospital for Children on two different occasions less than one month apart to prove test reliability. The physician performed a neurological examination at the first study visit. The nurse obtained vital signs and documented any concurrent illnesses, changes in medications or adverse events on a data collection tool at each study visit. All classifications and evaluations were performed by the same occupational therapist. At each visit, both upper extremities for all subjects were be classified according to the Manual Ability Classification System (MACS) [41, 42] and upper extremity function was evaluated by the Shriners Hospital for Children Upper Extremity Evaluation (SHUEE). Surface EMG recordings from both affected and unaffected upper limb muscles were used to monitor for mirror movements, artifact and movement reassurance of the correct motor activity requested from the subject during fNIRS. In addition, a soft strap was applied to stabilize the extremity during the motor task (Figure 1.1 (d)). At each study visit, all subjects were tested using fNIRS imaging while performing a repetitive upper extremity motor task (both finger tapping and hand waving).

The 24-channel, high-density, fNIRS brain imager (CW-5) was used to identify and map the brain functions during motor stimulation. The probes were attached to the subject's head as shown in Figure 1.1 (c) and 1.1 (d). The stimulation protocol of repetitive upper extremity locomotion was performed for a period of time, e.g., 15 sec, followed by a period of rest of 15

sec. This rest-stimulation-rest episode was repeated 8 times during the measurement, and the entire measurement lasted about 15 minutes, including baseline readings. All sessions for all subjects were videotaped.

### *2.1.2. Stimulation Design of Motor Activity for fNIRS Brain Imaging Measurements*

After testing and calibrating CW-5, fNIRS hemodynamic readings for changes of HbO, HbR, and HbT induced by motor stimulation were taken. A finger tapping and hand waving stimulation protocol was utilized during the fNIRS measurements. Both the left and right hand performed finger tapping followed by hand waving (repeated flexion and extension movements of the wrist) for a period of time, e.g., 15 seconds, followed by a period of rest of 15 seconds. This rest-stimulation-rest activation train was repeated 8-10 times during the measurement for both the control group and the children with CP. Specifically, after mounting the light sources and detectors on the subject's head the individual was instructed to tap his/her fingers and then to wave his/her hands, without moving the upper arm, during the stimulus period and remain relaxed and relative motionless at other times. Stimulus timing was provided through e-prime software on a computer screen. An entire measurement lasted about 15 minutes. To examine the reproducibility of the fNIRS imaging system, the same experiment was performed twice within one month for both the control and CP groups.

### *2.1.3. Protocols for Motion Task Used for Pediatric Subjects with and without CP*

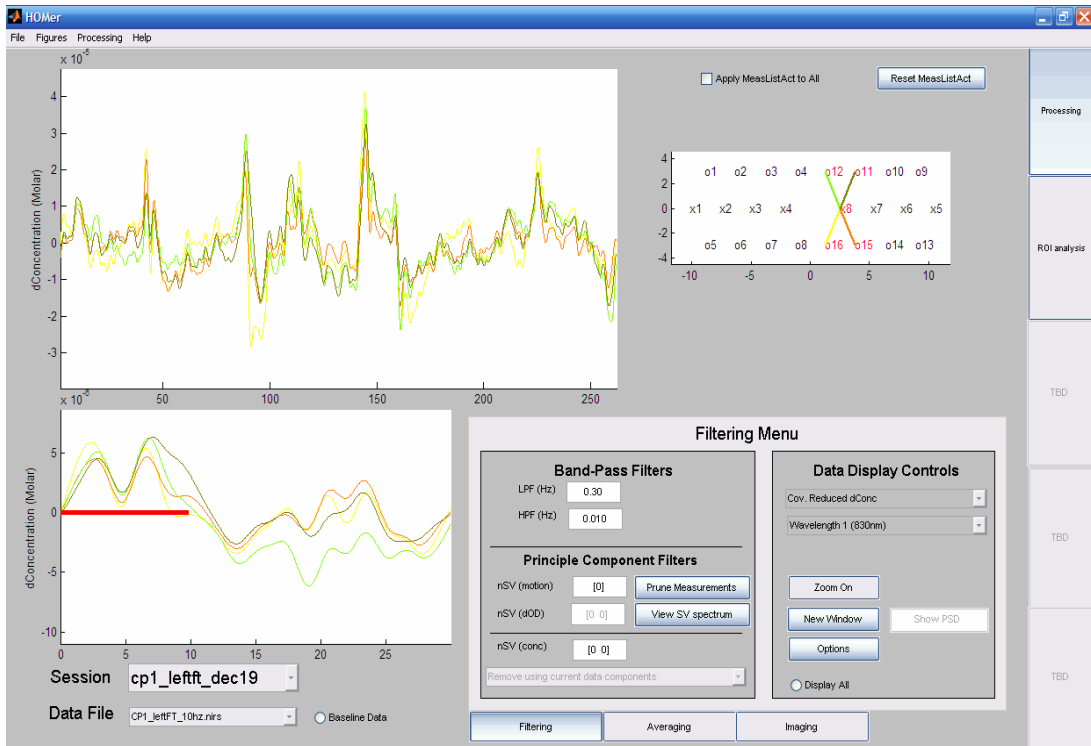
The finger tapping task required the subject to bring the index and middle fingers toward to the thumb at a pre-determined paced rhythm (about 1.5 Hz). The pediatric subject continued this action for 15 seconds according to a flash cue on screen and then relaxed for 15 seconds. The subject repeated this tapping-relaxation cycle 8 times for each measurement; his/her motor activation was averaged over the 8 cycles in the data processing. For comparison, a hand-waving task was also tested, requiring the subject to wave his/her wrist joint, while his/her fingers were not moved individually. The rhythm of waving was also at a pre-determined pace (about 1.5 Hz). The timing of hand-waving task was the same as that in finger-tapping protocol:

the subject continued the action for 15 seconds and then relaxed for 15 seconds; the entire cycle was repeated 8 times in each measurement.

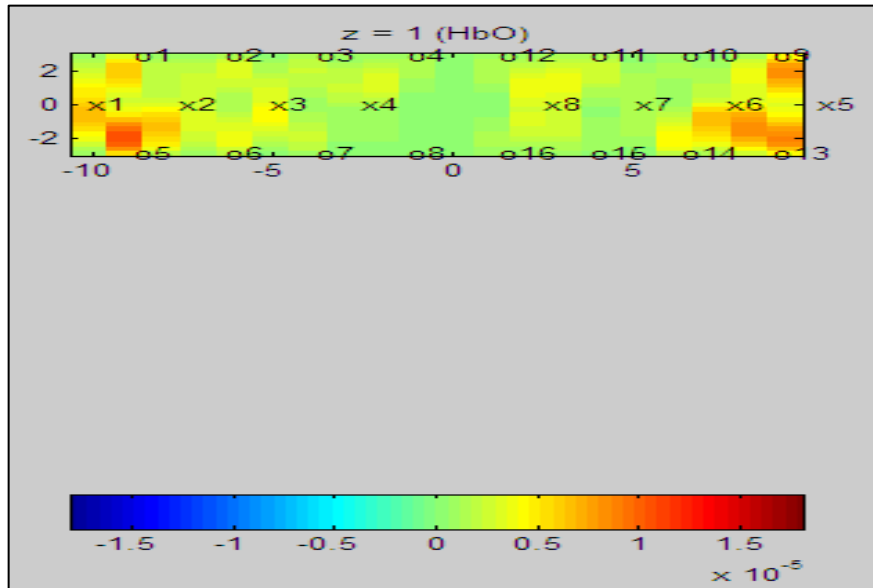
For each subject, the experiment started from right hand finger tapping, followed by right hand waving. Then, the subject performed left hand finger tapping, followed by left hand waving. The subjects sat on a comfortable chair during the entire experiment (Figure 1.2(b)). A short break was allowed between every two measurements so that the pediatric subject could rest. Moreover, to investigate the repeatability of the experiment, the subjects were measured twice, several weeks apart, using the same protocol. Six pediatric controls and 6 children with hemiplegic CP were measured. The ages of the pediatric subjects were between 6-18 yrs.

### 2.2 Data Analysis in HOMer

Once data acquisition is done, acquired data files are exported to software called HOMer for initial processing and reconstruction of images. The preprocessing includes filtering, averaging, and reconstruction. The frequency threshold value used for high pass filter was 0.01 Hz to keep out low frequency drifts in signal. The hemodynamic response is also low frequency, but we do not want respiration and cardiac pulsation interfering with the signal, so we select 0.3 Hz as threshold value for our lowpass filter. Signal with 0.4 Hz low pass filter was seen to be noisier. After that in imaging section, reconstruction is done by regularized inversion or backprojection method. Figure 2.1(a) shows a typical session in HOMer software. Figure 2.1(b) shows a typical HbO reconstructed image of a Cerebral Palsy subject.



(a)



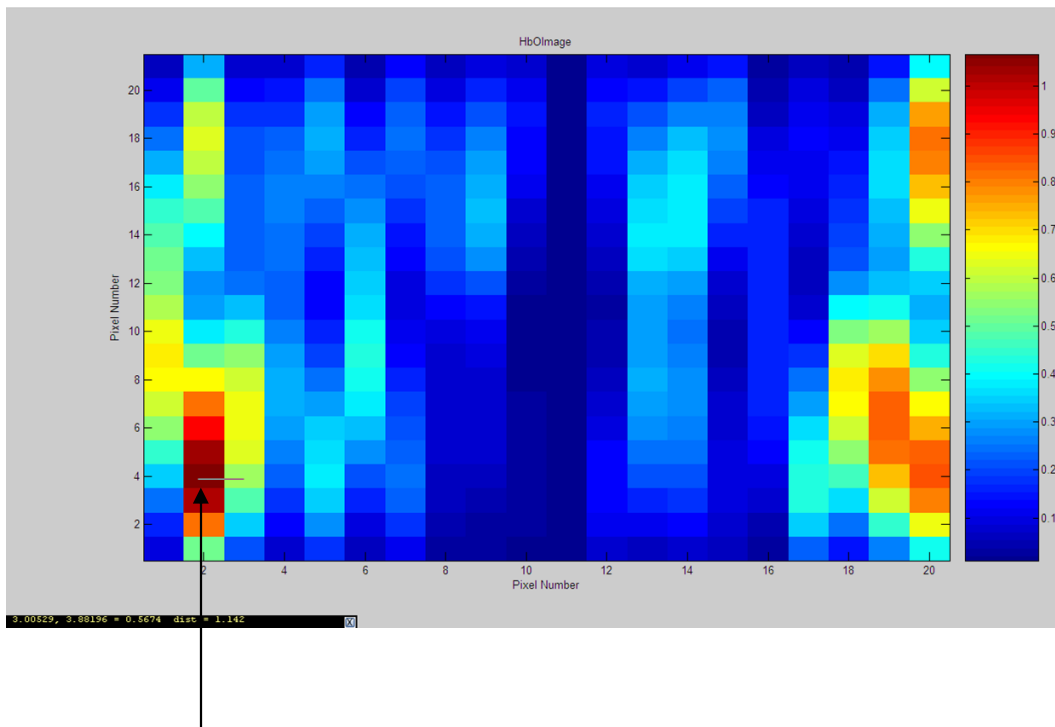
(b)

Figure 2.1 (a) shows a typical session in HOMer software. (b) shows a typical HbO reconstructed image of a Cerebral Palsy subject.

## 2.3 Image Analysis Software

### 2.3.1. Measuring Distance Interactively

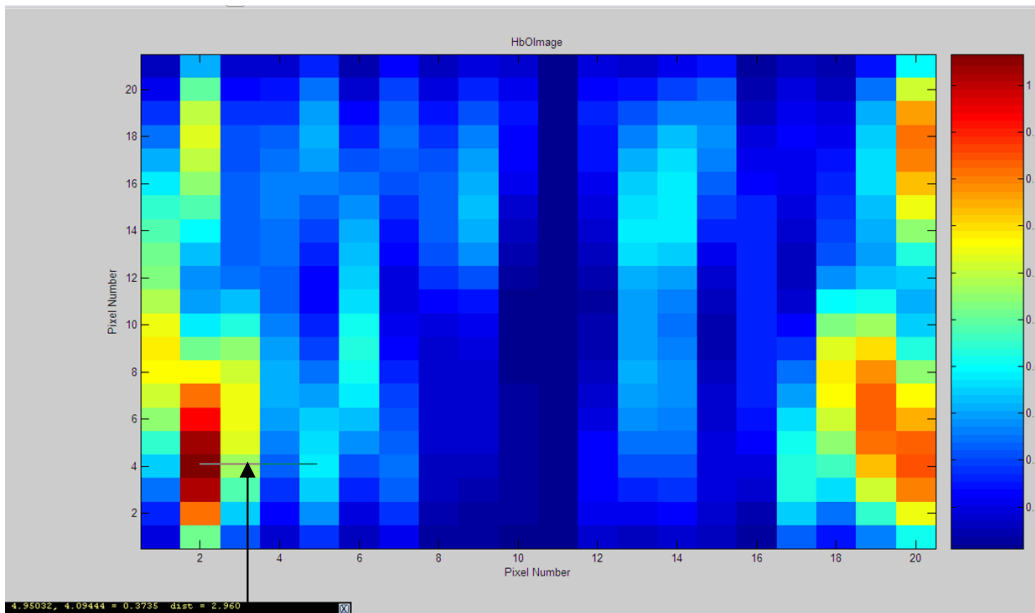
Figure 2.2 to 2.5. shows how the location of the blob from the centerline of the brain can be measured. Here we select the most intense pixel. For this colormap it's the reddest pixel. One places the mouse at the center of that pixel and drags it until the centerline of the brain as shown in figure 2.2 to 2.5. The measured horizontal distance between the initial point (that is the most intense pixel) and the final point (that is the centerline of brain) can be seen in a small black window at the bottom of the image.



Line showing the horizontal distance measured

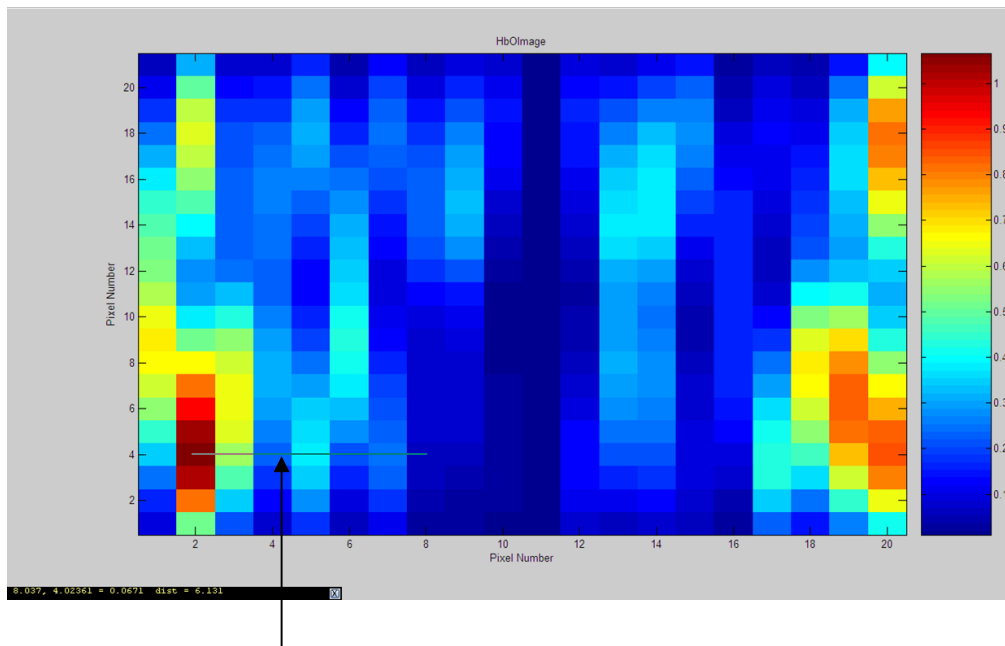
Figure 2.2 shows the distance measured between two points as 1 cm.





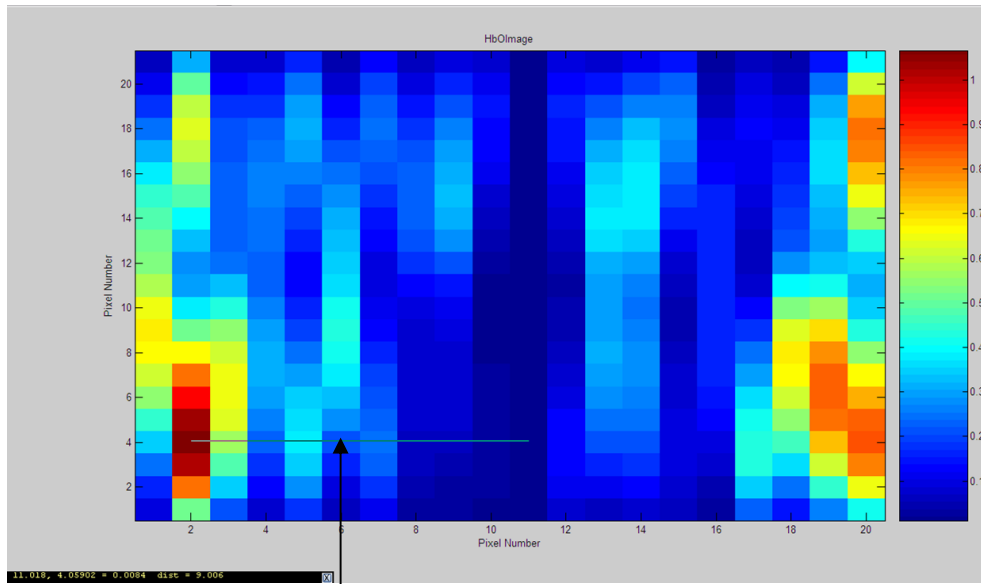
Line showing horizontal distance measured

Figure 2.3 shows the distance measured between two points as 3 cms.



Line showing horizontal distance measured

Figure 2.4 shows the distance measured between two points as 6 cms.



Line showing horizontal distance measured

Figure 2.5 shows the distance measured between the activated pixel and brains centerline as 9 cms.

### 2.3.2 Image Segmentation Using Interactive GUI

The Image Analysis software has a GUI where in user can interactively threshold the image. On the GUI one can load the image. On the left hand side top one can see the input image. At the bottom of the GUI is the histogram of the input gray scale image. On the top right hand side is the segmented image. On the histogram, there is a slider which is used for selecting the threshold. Figures 2.6 to 2.13 show how the slider is dragged by the user at different threshold levels of the pixel value histogram resulting in a corresponding increase or decrease of the segmented, where the pixel values represent change in HbO concentration measured in Molars. However the software selects the optimal threshold level by use of a discrimination analysis algorithm [45]. All analysis was done based on the automatic threshold selection and the slider dragging is an additional feature in case manual threshold adjustment is required.

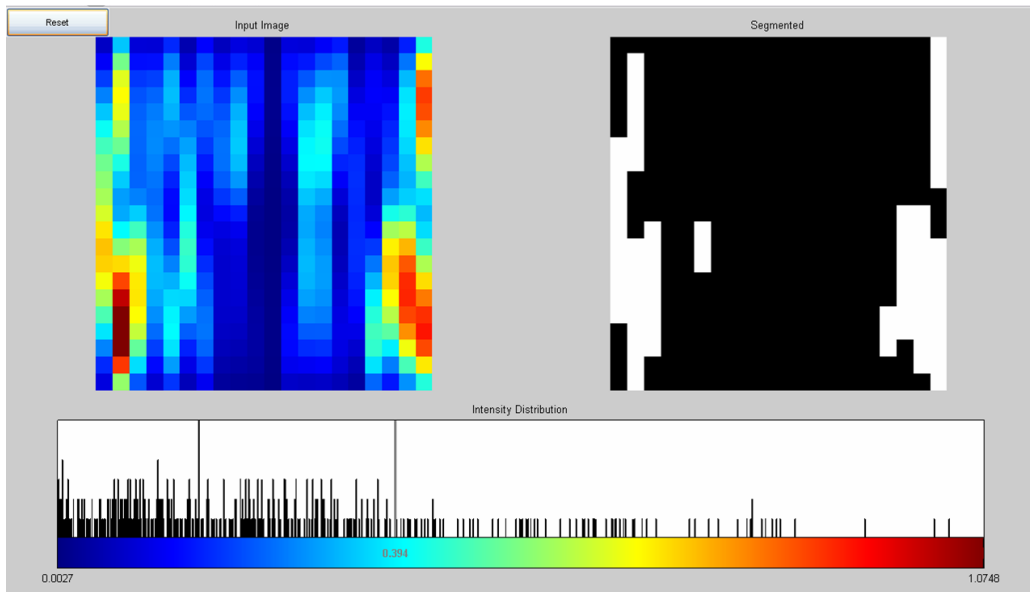


Figure 2.6 shows original image and its segmented image at a threshold of 0.394

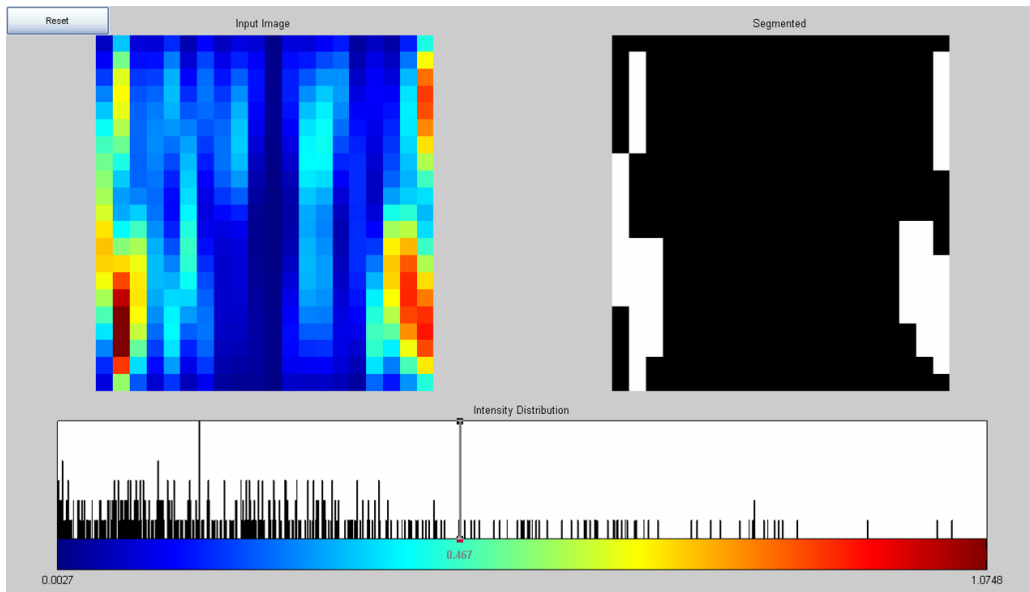


Figure 2.7 shows the original image and its segmented image at a threshold of 0.467

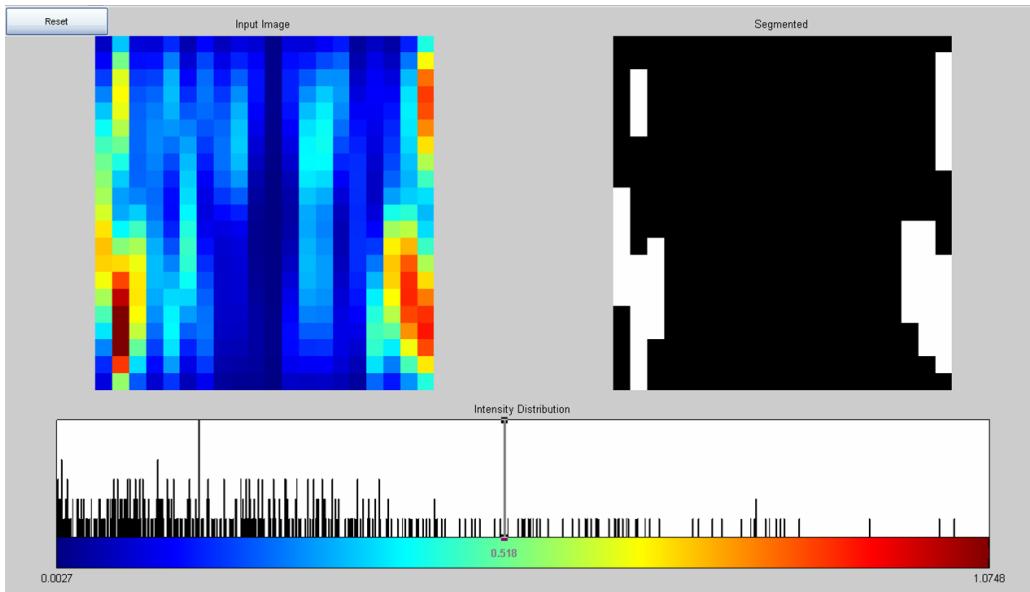


Figure 2.8 shows original image and its segmented image at a threshold of 0.518

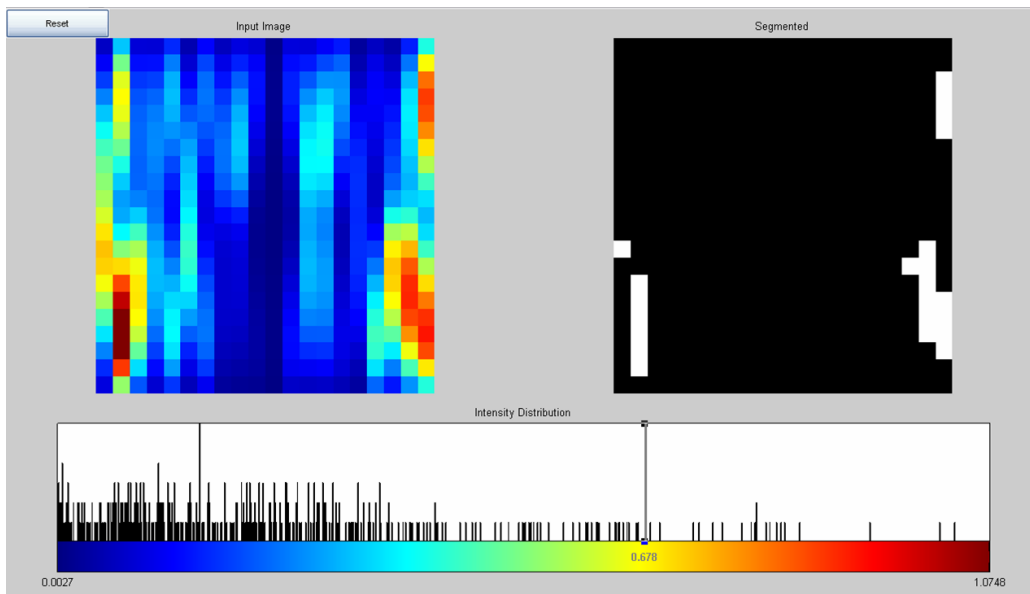


Figure 2.9 shows original image and its segmented image at a threshold of 0.678

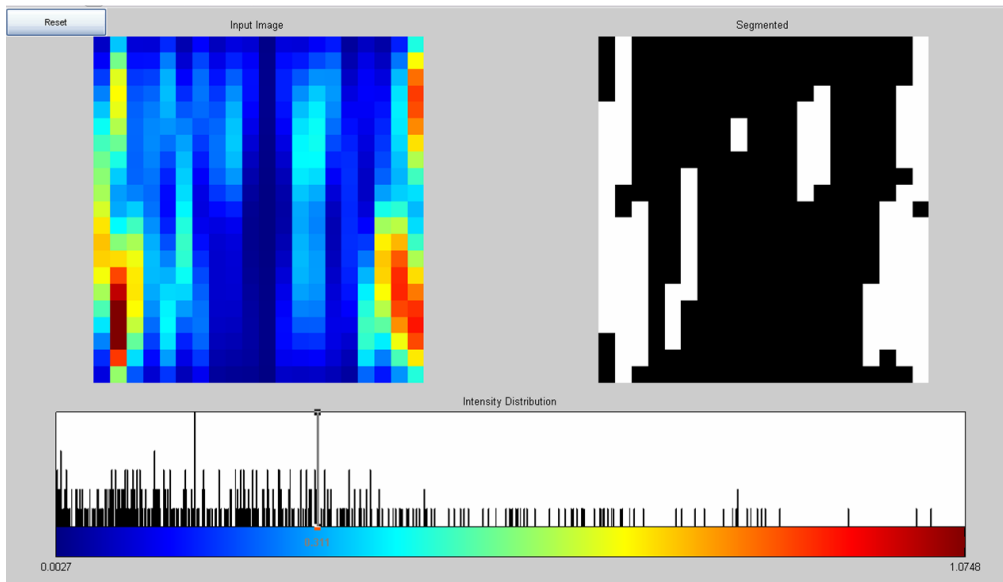


Figure 2.10 shows original image and its segmented image at a threshold of 0.311

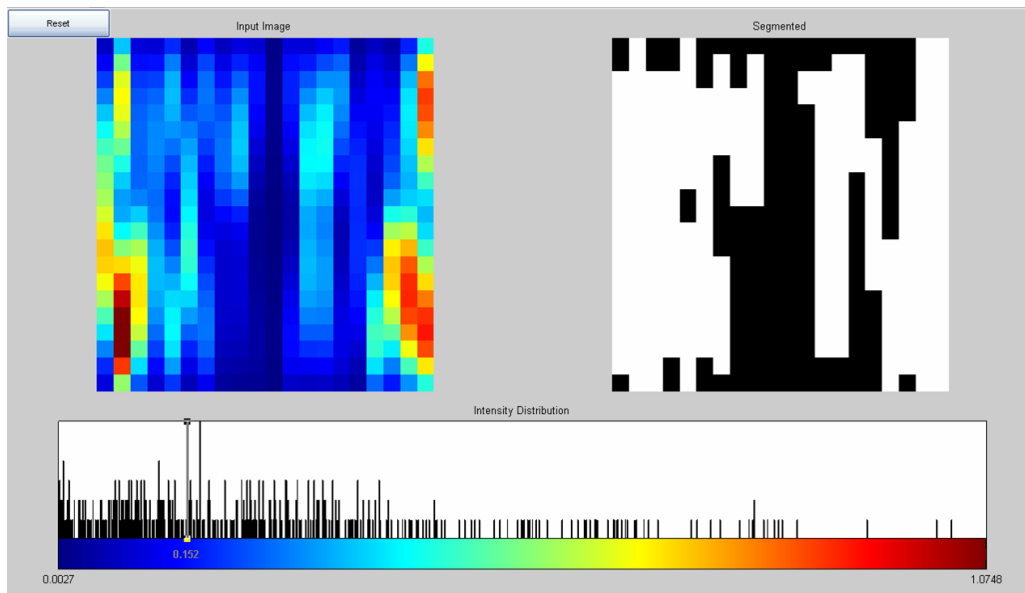


Figure 2.11 shows original image and its segmented image at a threshold of 0.152

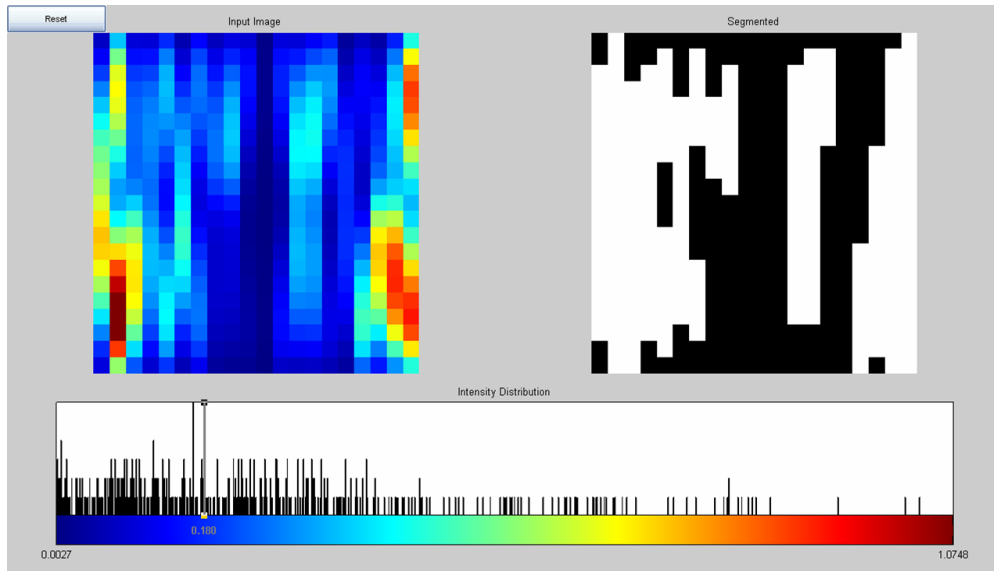


Figure 2.12 shows original image and its segmented image at a threshold of 0.180

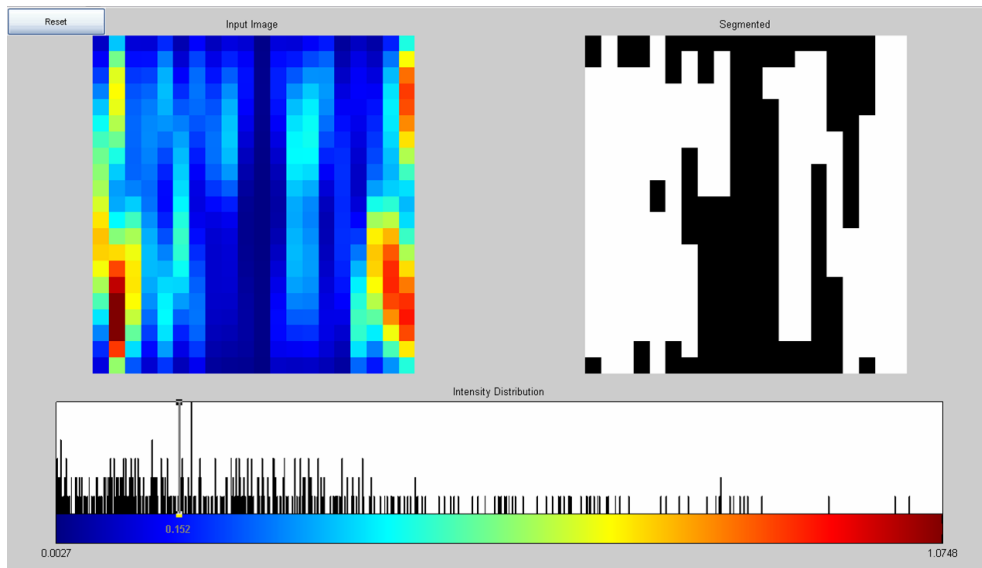


Figure 2.13 shows original image and its segmented image at a threshold of 0.152

## 2.4 Computing Image Metrics

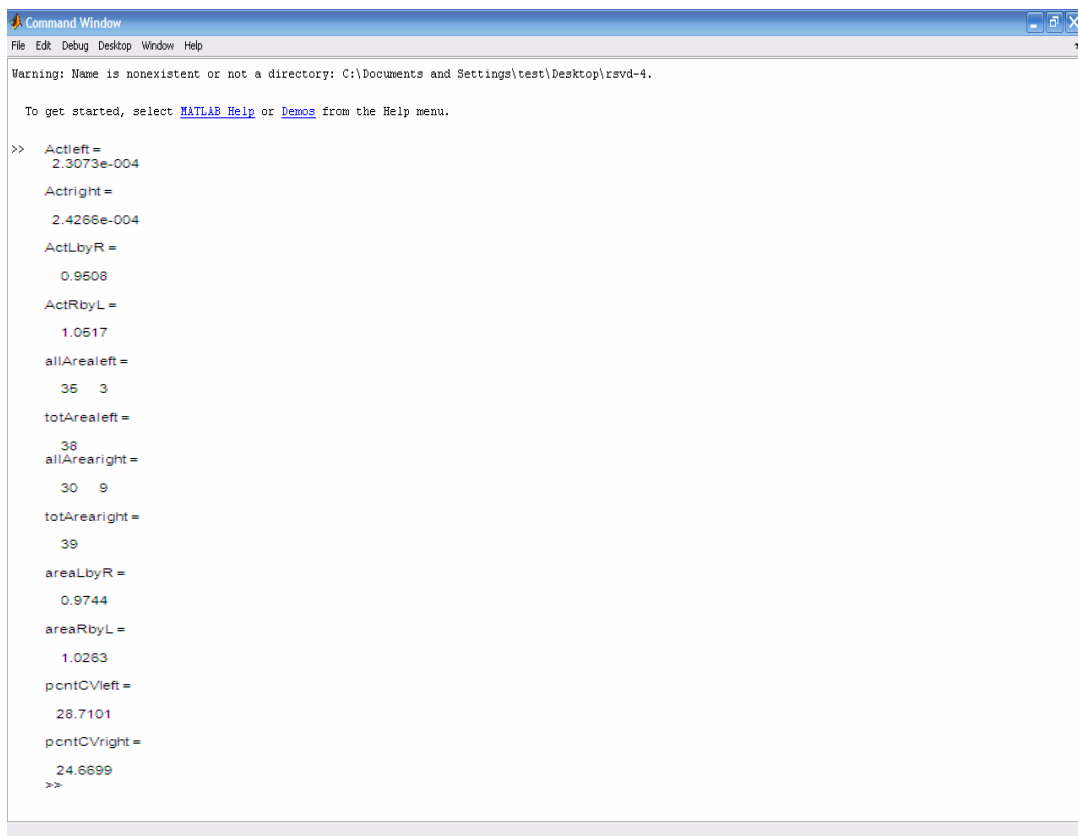
The following Image metrics are calculated by software and are printed on the matlab command window as shown in Figure 2.14:

- (1) **ActLeft:** Is activation on the left hand side of the image.
- (2) **ActRight:** Is activation on the right hand side of the image.
- (3) **ActLbyR:** Is ratio of activation on left hand side of the image to right hand side of the image.
- (4) **ActRbyL:** Is ratio of activation on right hand side of the image to left hand side of the image.
- (5) **allAreaLeft:** Gives area of each segmented region on left hand side of the image
- (6) **totAreaLeft:** Gives sum of area of all the segmented regions on left hand side of the image. That is it gives the total activated area on the left hand side of the image.
- (7) **allAreaRight:** Gives area of each segmented region on right hand side of the image
- (8) **totAreaRight:** Gives sum of area of all the segmented regions on right hand side of the image. That is it gives the total activated area on the right hand side of the image.
- (9) **areaLbyR:** Gives the ratio of total activated area on left side of the image to total activated area on right side of the image.
- (10) **areaRbyL:** Gives the ratio of total activated area on right side of the image to total activated area on left side of the image.
- (11) **pcntCVleft:** Gives the percentage coefficient of variation of all the values corresponding to activated region in segmented image on left hand side of the image.
- (12) **pcntCVright:** Gives the percentage coefficient of variation of all the values corresponding to activated region in segmented image on right hand side of the image.

Fig 2.15(a) is the histogram of the left half of the segmented image. If we put data cursor on the number of pixels having intensity 1, than number of pixels it shows is same as the

activated area on the left hand side of the image. This is just another way of finding the activated area.

Fig 2.15(b) is the histogram of the right half of the segmented image. If we put data cursor on the number of pixels having intensity 1, than number of pixels it shows is same as the activated area on the right hand side of the image. This is just another way of finding the activated area.



```
Command Window
File Edit Debug Desktop Window Help
Warning: Name is nonexistent or not a directory: C:\Documents and Settings\test\Desktop\rsvd-4.

To get started, select MATLAB Help or Demos from the Help menu.

>> Actleft =
2.3073e-004
Actright =
2.4266e-004
ActLbyR =
0.9508
ActRbyL =
1.0517
allArealeft =
35 3
totArealeft =
38
allArearight =
30 9
totArearight =
39
areaLbyR =
0.9744
areaRbyL =
1.0263
pntCVleft =
28.7101
pntCVright =
24.6699
>>
```

Figure 2.14 Computed Image Metrics on Matlab command Window





(a)



(b)

Figure 2.15(a) Histogram of the left half of the segmented image (b) Histogram of the right half of the segmented image.

## 2.5 Exporting Image Metrics and Other Information to MS Excel Automatically:

The software creates an excel file named results on the first time it is run. It creates one sheet for each metric listed in section 2.4. It automatically exports the values of all the metrics to their respective sheet in the excel file. Also along with the metrics it states in each sheet against each value, the subject number, protocol used and the date on which the data was collected.

Fig 2.16 shows the results file.

The above computed image metrics and the segmented images will be used to:

- (1) Study Reproducibility.
- (2) Compare Finger Tapping and Hand Waving in Normal Subjects.
- (3) Compare Normal Subjects with Cerebral Palsy (CP) Affected Kids.
  - (a) Differentiate between healthy pediatric controls and children with CP.
  - (b) Differentiate abnormal from normal regions.

| A  | B           | C | D | E | F | G | H | I | J | K | L | M | N | O | P | Q | R | S |   |   |   |
|----|-------------|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1  | ActLeft     |   |   |   | S | u | b |   | 2 |   | l | e | f | t | F | T |   | i | m |   |   |
| 2  | 3.58374E-05 |   |   |   | S | u | b |   | 2 |   | l | e | f | t | H | W |   | i | m |   |   |
| 3  | 0.000114045 |   |   |   | S | u | b |   | 2 |   | l | e | f | t | F | T |   |   | 1 |   |   |
| 4  | 8.4358E-05  |   |   |   | s | u | b |   | 2 |   | l | e | f | t | h | w |   |   | e |   |   |
| 5  | 0.00021216  |   |   |   | S | u | b |   | 6 |   | l | e | f | t | H | W |   |   | m |   |   |
| 6  | 0.000511291 |   |   |   | S | u | b |   | 6 |   | l | e | f | t | H | W |   |   | m |   |   |
| 7  | 0.000211192 |   |   |   | S | u | b |   | 6 |   | l | e | f | t | H | W |   |   | m |   |   |
| 8  | 0.000349297 |   |   |   | s | u | b |   | 2 | r | i | g | h | t | f | t |   |   | n | o |   |
| 9  | 0.000502385 |   |   |   | s | u | b |   | 2 | r | i | g | h | t | f | t |   |   | f | e |   |
| 10 | 0.000739338 |   |   |   | s | u | b |   | 2 | r | i | g | h | t | h | w |   |   | f | e |   |
| 11 | 0.000165321 |   |   |   | s | u | b |   | 2 | r | i | g | h | t | h | w |   |   | n | o |   |
| 12 | 0.00045919  |   |   |   | s | u | b |   | 6 | r | i | g | h | t | h | w |   |   | o | c |   |
| 13 | 0.001672886 |   |   |   | s | u | b |   | 6 | r | i | g | h | t | h | w |   |   | n | o |   |
| 14 | 0.000195576 |   |   |   | s | u | b |   | 4 | r | i | g | h | t | f | t |   |   | o | c |   |
| 15 | 0.000591834 |   |   |   | s | u | b |   | 4 | r | i | g | h | t | h | w |   |   | o | c |   |
| 16 | 0.000400473 |   |   |   | s | u | b |   | 1 | 2 | r | i | g | h | t | f | t |   |   |   |   |
| 17 | 0.000814137 |   |   |   | s | u | b |   | 1 | 2 | r | i | g | h | t | h | w |   |   |   |   |
| 18 | 2.42823E-05 |   |   |   | s | u | b |   | 4 | r | i | g | h | t | f | t |   |   | o | c |   |
| 19 | 1.89018E-05 |   |   |   | s | u | b |   | 4 | r | i | g | h | t | h | w |   |   | o | c |   |
| 20 | 9.1094E-05  |   |   |   | s | u | b |   | 5 | r | i | g | h | t | f | t |   |   | o | c |   |
| 21 | 0           |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 22 | 0.000161613 |   |   |   | s | u | b |   | 1 | 2 | r | i | g | h | t | f | t |   |   | d |   |
| 23 | 0.000284722 |   |   |   | s | u | b |   | 1 | 2 | r | i | g | h | t | h | w |   |   | d |   |
| 24 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 25 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 26 | 0.000365188 |   |   |   | c | p |   |   | 1 |   | l | e | f | t | f | t |   |   | n | o | v |
| 27 | 0.000230725 |   |   |   | c | p |   |   | 1 |   | l | e | f | t | f | t |   |   | d | e | c |
| 28 | 0.000142575 |   |   |   | c | p |   |   | 1 |   | l | e | f | t | h | w |   |   | n | o | v |
| 29 | 0.000104222 |   |   |   | c | p |   |   | 1 |   | l | e | f | t | h | w |   |   | d | e | c |
| 30 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 31 |             |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |
| 32 | 0.000211877 |   |   |   | c | p |   |   | 1 |   | r | i | g | h | t | f | t |   |   | n | o |
| 33 | 0.00053082  |   |   |   | c | p |   |   | 1 |   | r | i | g | h | t | f | t |   |   | d | e |
| 34 | 0.000722768 |   |   |   | c | p |   |   | 1 |   | r | i | g | h | t | h | w |   |   | n | o |
| 35 | 0.000503692 |   |   |   | c | p |   |   | 1 |   | r | i | g | h | t | h | w |   |   | d | e |
| 36 | 0.000720845 |   |   |   | c | p |   |   | 2 |   | r | i | g | h | t | f | t |   |   | n | o |

Figure 2.16 MS Excel result file wherein the computed Image Metrics are exported automatically

## CHAPTER 3

### RESULTS

#### 3.1. Evaluating Reproducibility Using Image Metrics

For assessing reproducibility in finger tapping protocol we follow criterion (1) described below for percentage coefficient of variation on left and right side and criterion (2) for activation and activated area:

(1) If the value of the metrics on the second occasion is in  $\pm 20\%$  tolerance of the value obtained on the first occasion, then we can consider it as reproducible. If 30% is selected as reproducibility criterion, results lose their significance. 10% is too strict a criterion for initial studies. So to come up with an optimal criterion, 20% was selected as reproducibility criterion.

(2) In finger tapping protocol, it has been seen that activation on contralateral side is higher than activation on ipsilateral side, So according if we take ratio of activation on contralateral side to ipsilateral side, the value would be higher than 1. So if this ratio is higher than 1 on both occasions, then it can be considered reproducible. Same applies to activated area in case of finger tapping protocols.

For assessing reproducibility in hand waving protocol we follow criterion (1) described below for percentage coefficient of variation on left and right side and criterion (2) for activation and activated area:

(1) If the value of the metrics on the second occasion is in  $\pm 20\%$  tolerance of the value obtained on the first occasion, then we can consider it as reproducible.

(2) In hand waving protocol, it has been seen that activation on contralateral side is almost equal to activation on ipsilateral side, though sometimes activation becomes a little higher or

little lower on contralateral side than ipsilateral side. So according if we take ratio of activation on contralateral side to ipsilateral side, the value would be either 1, little higher than 1, or little lower than 1. So if the values on first and second occasion are either little less than 1, little higher than 1 or equal to 1 than they can be considered reproducible. Same applies to activated area in case of hand waving protocols.

Figure 3.1 shows the image metrics for subject 2, left finger tapping protocol. The data was collected twice and so we can assess if the image metrics for both times were reproducible or not. In finger tapping protocol, from previous studies it was found from viewing the images that activation on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activation on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be ActRbyL. So if Act RbyL is higher than 1, it can be called reproducible for our purpose. Here it can be seen that it is higher than 1, both the times. So it is reproducible.

Also from previous studies it was found from viewing the images that activated area on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activated area on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be AreaRbyL. So if Area RbyL is higher than 1, it can be called reproducible for our purpose. Here it can be seen that it is higher than 1, both the times. So it is reproducible.

For this subject pcntCVleft is not reproducible because its value on second occasion does not fall within +/- 20% of the value obtained on the first occasion, whereas pcntCvright is reproducible because its value on second occasion falls within +/- 20% of the value obtained on first occasion.

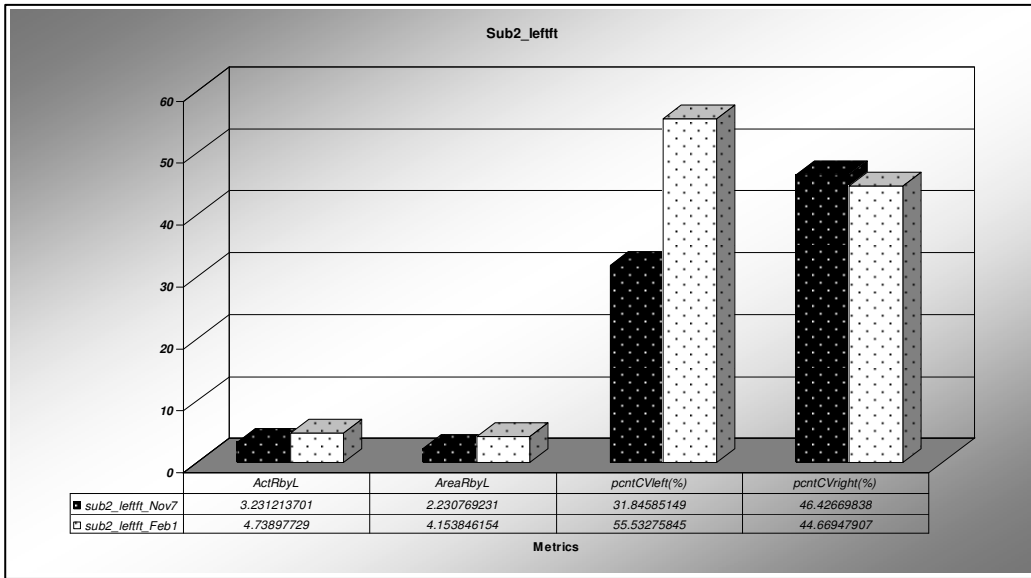


Figure 3.1 shows the image metrics reproduced over a period of time for subject 2, left finger tapping protocol.

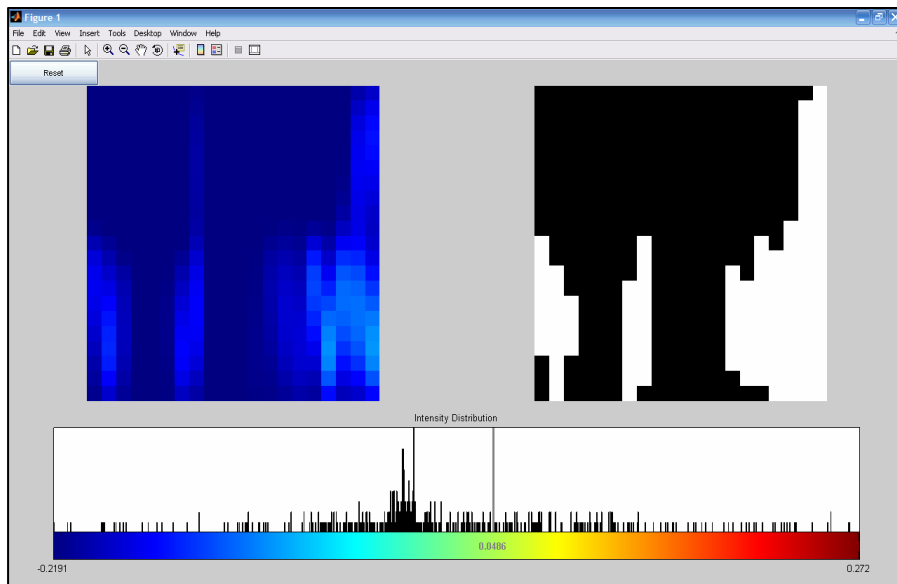


Figure 3.2 shows HbO image, its histogram and its segmented image for subject 2, left finger tapping protocol, collected on first occasion

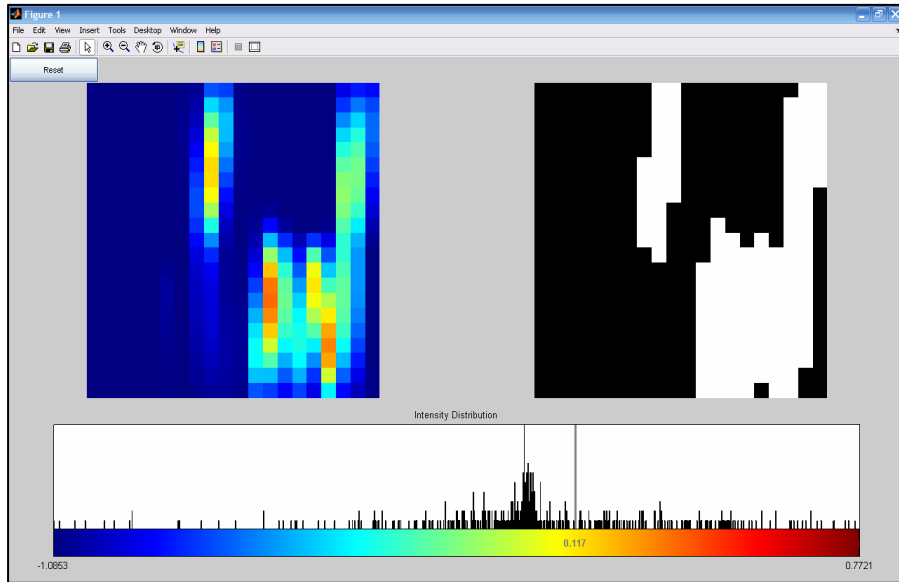


Figure 3.3. shows HbO image, its histogram and its segmented image for subject 2, left finger tapping protocol, collected on second occasion

The automated threshold selection algorithm eliminated any possible inconsistencies arising from manual threshold selection and produced results that were visually consistent with the corresponding color maps as seen in Figs. 3.2 and 3.3. Also the activated areas on the two occasions look similar.

Figure 3.4 shows the image metrics for subject 2, left hand waving protocol. The data was collected twice and so we could assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is higher than 1 for both the occasions. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little less than 1 on first occasion and little higher than 1 on second occasion. So activated area in this case is reproducible. Percentage Coefficient of Variation on left side (pcntCVleft) is not reproducible, whereas percentage Coefficient of Variation on right side (pcntCVright) on second occasion falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on right side is reproducible.

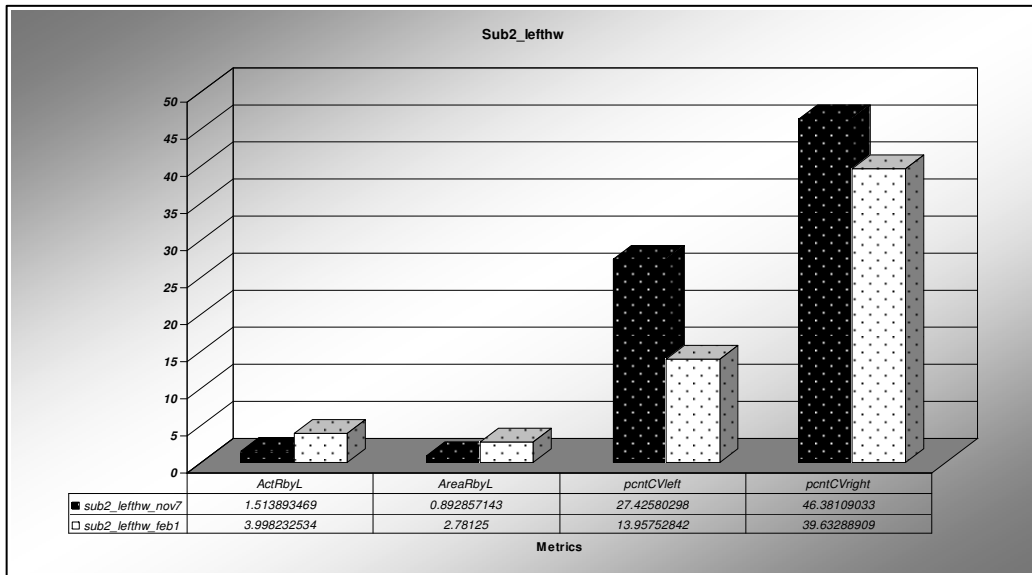


Figure 3.4 shows the image metrics reproduced over a period of time for subject 2, left hand waving protocol.

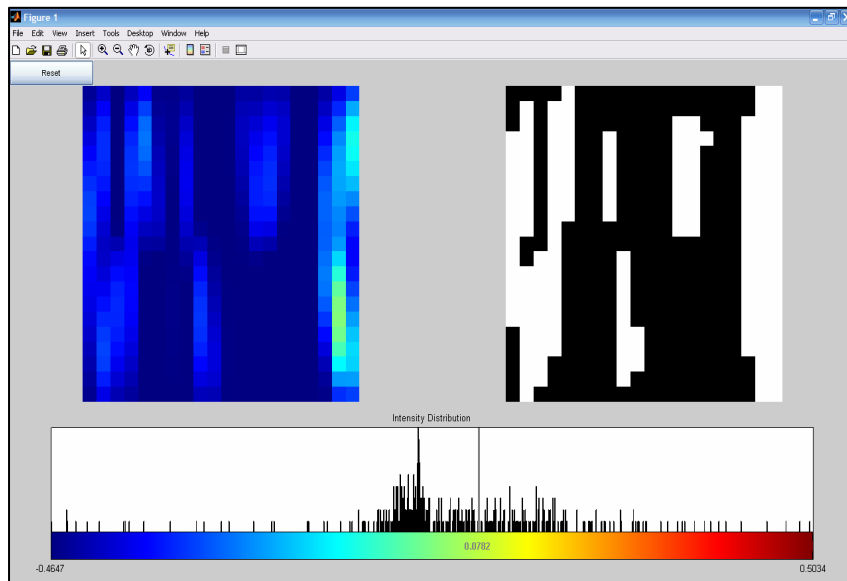


Figure 3.5 shows HbO image, its histogram and its segmented image for subject 2, left hand waving protocol, collected on first occasion

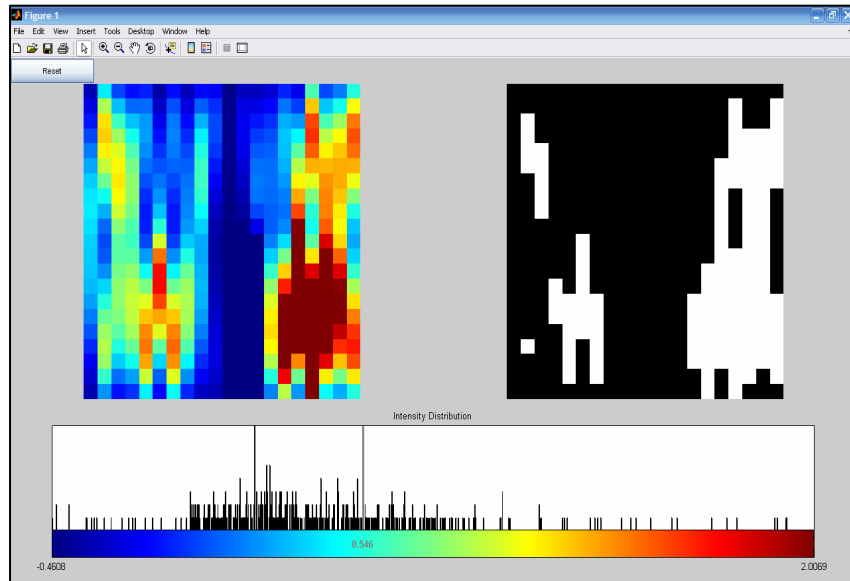


Figure 3.6 shows HbO image, its histogram and its segmented image for subject 2, left hand waving protocol, collected on second occasion

If we have a look at the segmented images for subject 2, left hand waving protocol in Figure 3.5 and 3.6 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.7 shows the image metrics for subject 6, left hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is higher than 1 for first occasion and little lower than 1 on second occasion. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little less than 1 on both occasions. So activated area in this case is reproducible. Percentage Coefficient of Variation on left side(pcntCVleft) is not reproducible, whereas percentage Coefficient of Variation on right side(pcntCVright) on second occasion falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on right side is reproducible.



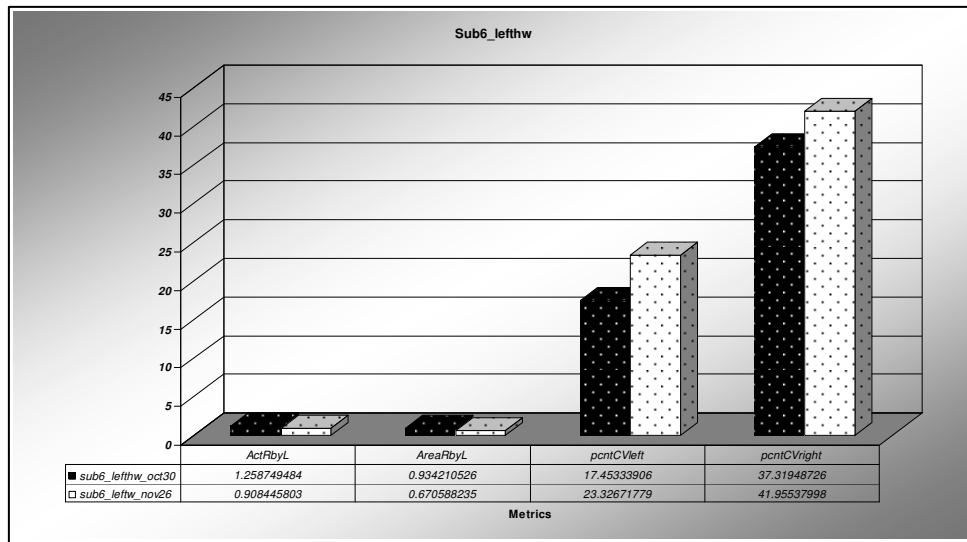


Figure 3.7 shows the image metrics reproduced over a period of time for subject 6, left hand waving protocol.

Figure 3.8 shows the image metrics for subject 2, right finger tapping protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. In finger tapping protocol, from previous studies it was found from viewing the images that activation on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activation on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be ActLbyR. So if ActLbyR is higher than 1, it can be called reproducible for our purpose. Here it can be seen that it is higher than 1, both the times. So it is reproducible.

Also from previous studies it was found from viewing the images that activated area on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activated area on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be AreaLbyR. So if AreaLbyR is higher than 1, it can be called reproducible for our purpose. Here it can be seen that it is higher than 1, both the times. So it is reproducible. For this subject pcntCVright is not reproducible whereas pcntCVleft is reproducible.

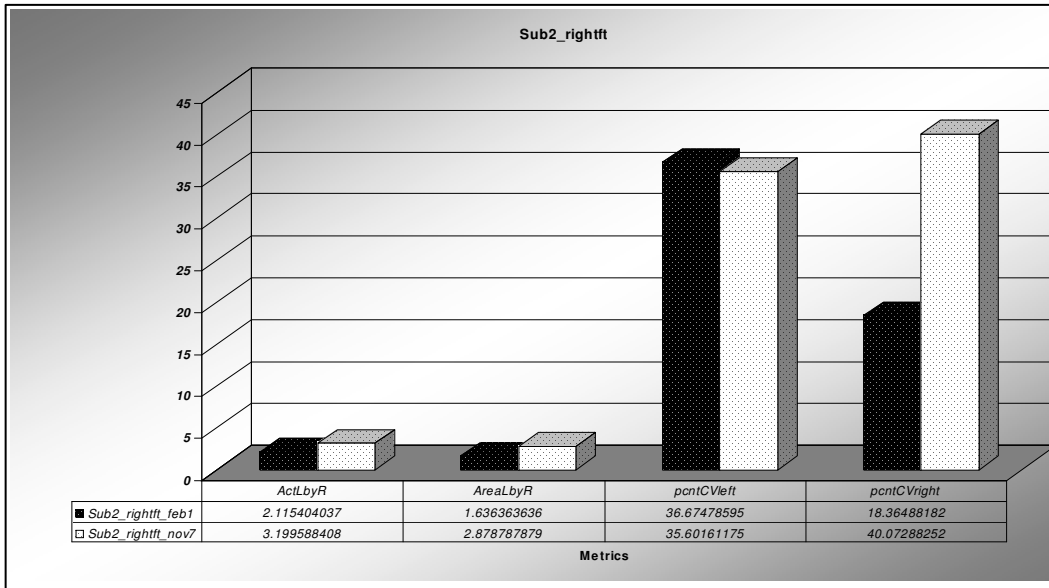


Figure 3.8 shows the image metrics reproduced over a period of time for subject 2, right finger tapping protocol.

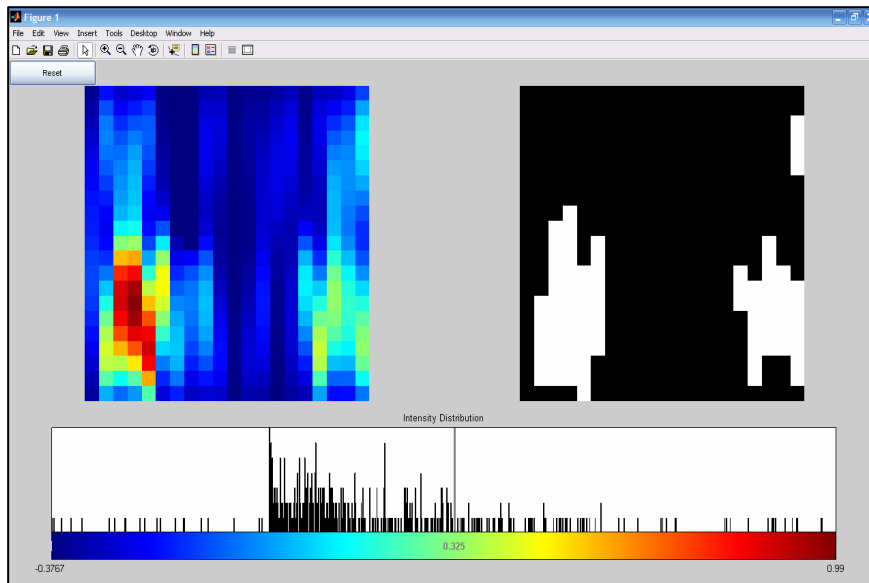


Figure 3.9 shows HbO image, its histogram and its segmented image for subject 2, right finger tapping protocol, collected on first

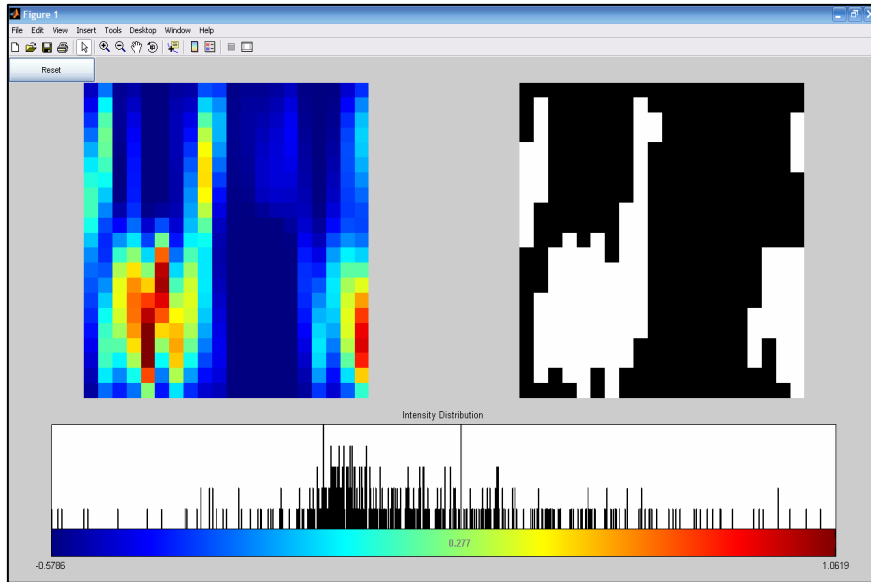


Figure 3.10 shows HbO image, its histogram and its segmented image for subject 2, right finger tapping protocol, collected on second occasion

If we have a look at the segmented images for subject 2, right finger tapping protocol in Figure 3.9 and 3.10 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.11 shows the image metrics for subject 2, right hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is higher than 1 for both the occasions. But on the second occasion the value is much much higher than that on first occasion, this can be attributed to some unusual physiology that occurred on second occasion because of subject carrying out some mental or physical activity out of the defined protocol. Same pattern is seen for the activated area as activation in this particular subject. Percentage Coefficient of Variation on right side(pcntCVright) is not reproducible, whereas percentage Coefficient of Variation on left side(pcntCVleft) on second occasion falls within +/-20% of the value on the first occasion. So percentage Coefficient of Variation on left side is reproducible.

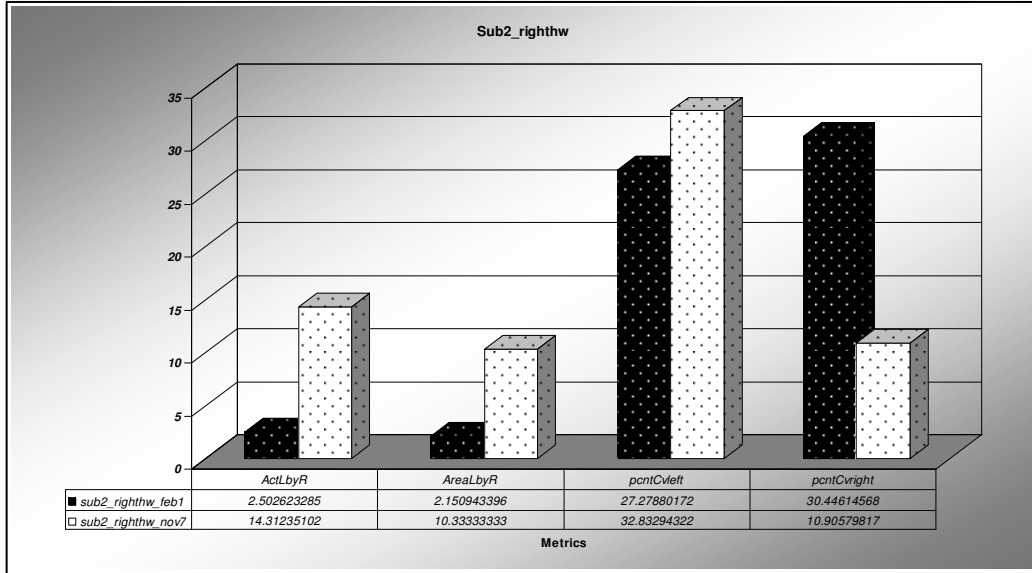


Figure 3.11 shows the image metrics reproduced over a period of time for subject 2, right hand waving protocol.

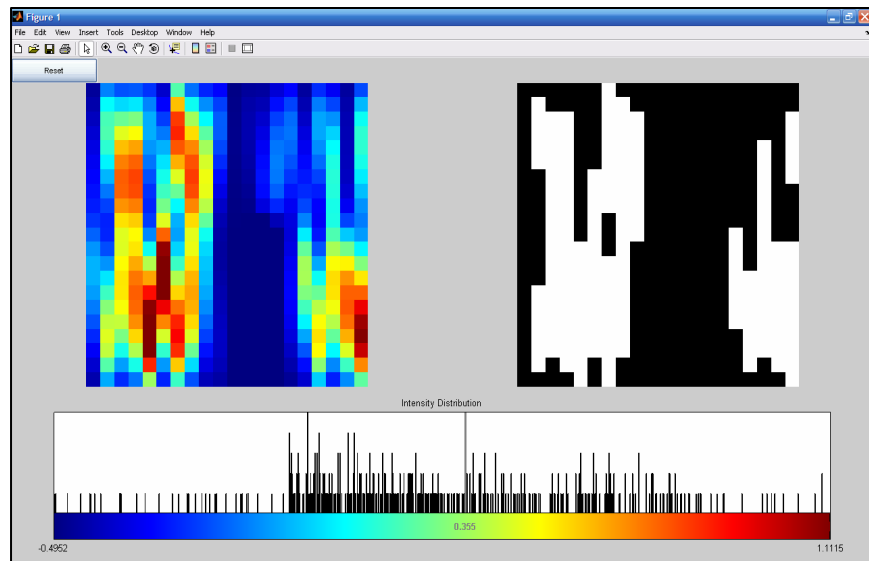


Figure 3.12 shows HbO image, its histogram and its segmented image for subject 2, right hand waving protocol, collected on first occasion

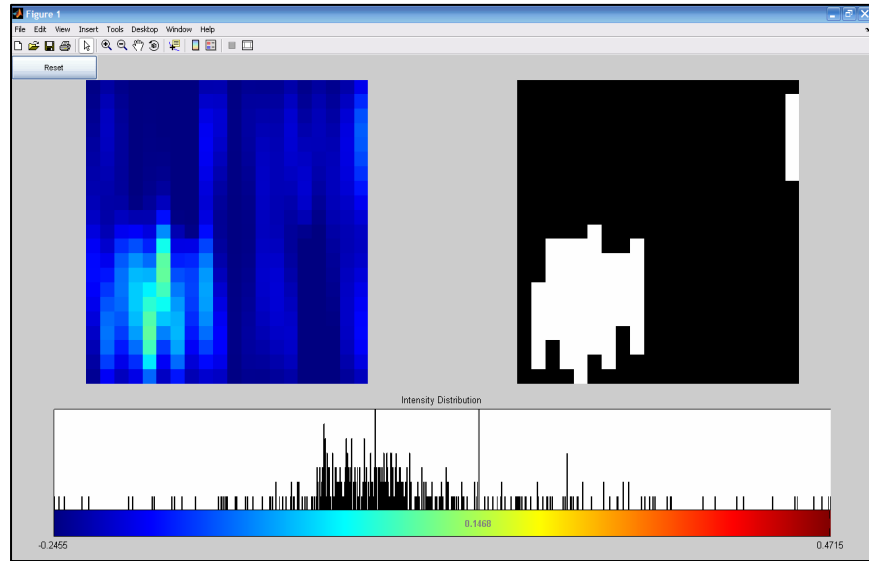


Figure 3.13 shows HbO image, its histogram and its segmented image for subject 2, right hand waving protocol, collected on second occasion

If we have a look at the segmented images for subject 2, right hand waving protocol in Figure 3.12 and 3.13 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.14 shows the image metrics for subject 6, right hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is little higher than 1 for both the occasions. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little higher than 1 on both occasions. So activated area in this case is reproducible. Both percentage coefficient of variation on left side (pcntCVleft) and percentage Coefficient of Variation on right side (pcntCVright) on second occasion do not falls within  $\pm 20\%$  of their respective values on the first occasion. So percentage Coefficient of Variation on right as well as left side is not reproducible.

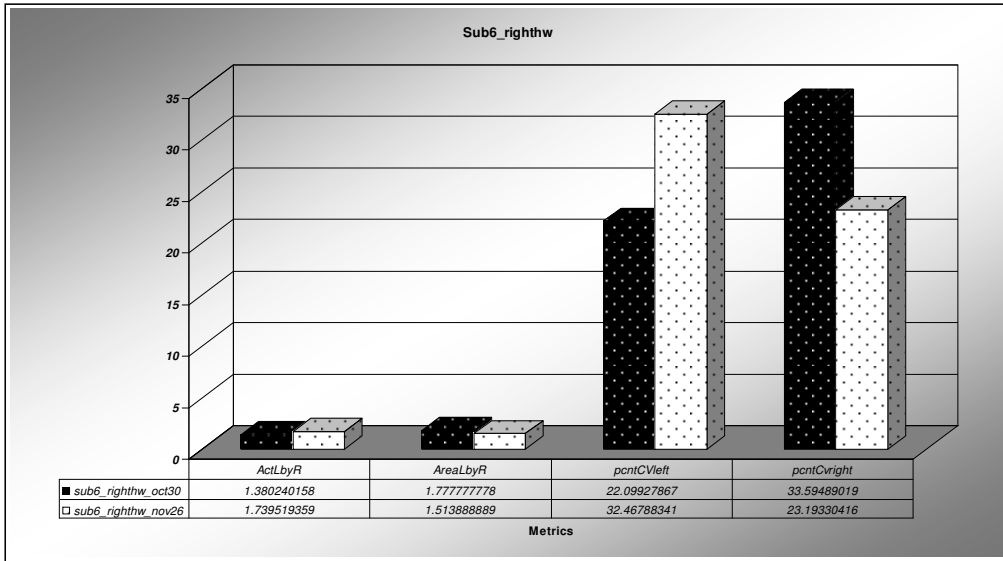


Figure 3.14 shows the image metrics reproduced over a period of time for subject 6, right hand waving protocol.

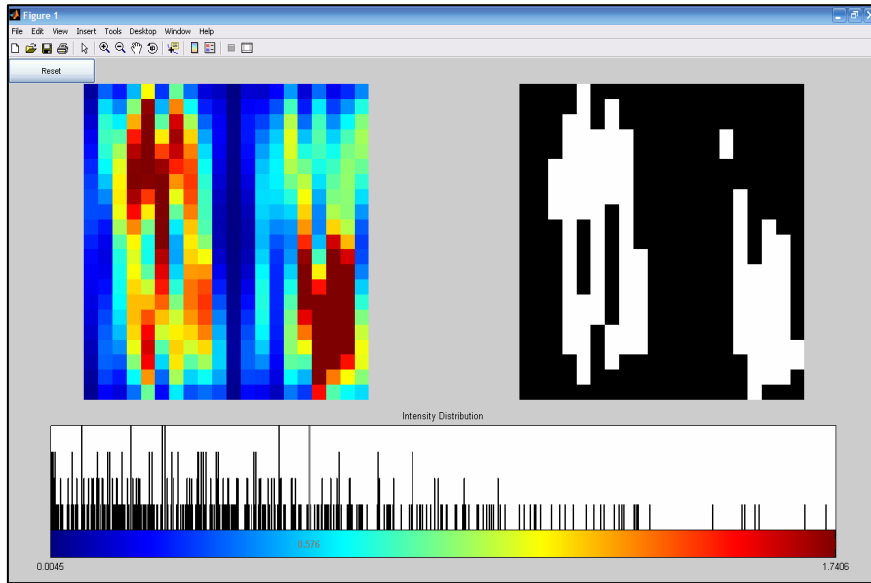


Figure 3.15 shows HbO image, its histogram and its segmented image for subject 6, right hand waving protocol, collected on first occasion

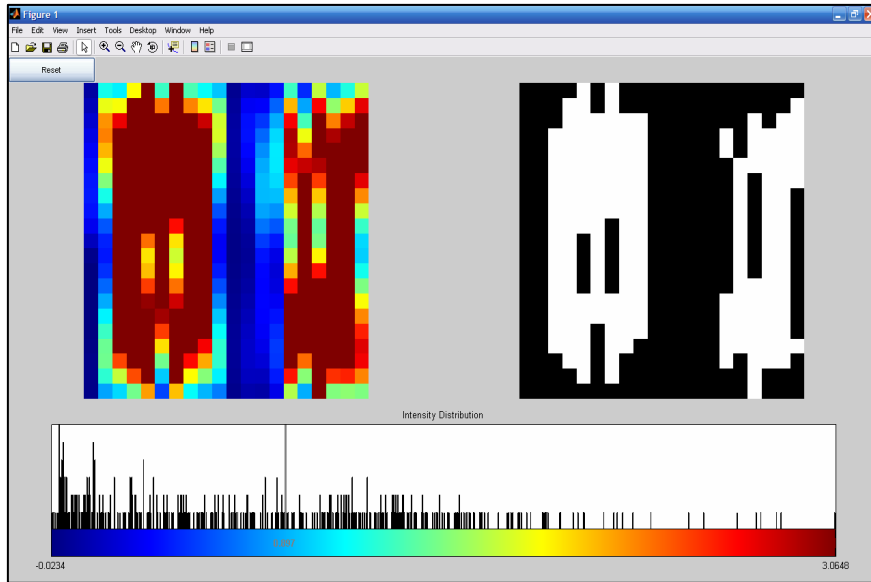


Figure 3.16 shows HbO image, its histogram and its segmented image for subject 6, right hand waving protocol, collected on second occasion

If we have a look at the segmented images for subject 6, right hand waving protocol in Figure 3.15 and 3.16 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.17 shows the image metrics for CP subject 1, left hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is little less than 1 for both the occasions. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little less than 1 on both occasions. So activated area in this case is reproducible. Percentage Coefficient of Variation on left side (pcntCVleft) on second occasion does not falls within +/-20% of the value on the first occasion. So percentage Coefficient of Variation on left side is not reproducible. Also Percentage Coefficient of Variation on right side (pcntCVright) on second occasion does not falls within +/-20% of the value on the first occasion. So percentage Coefficient of Variation on right side is not reproducible.

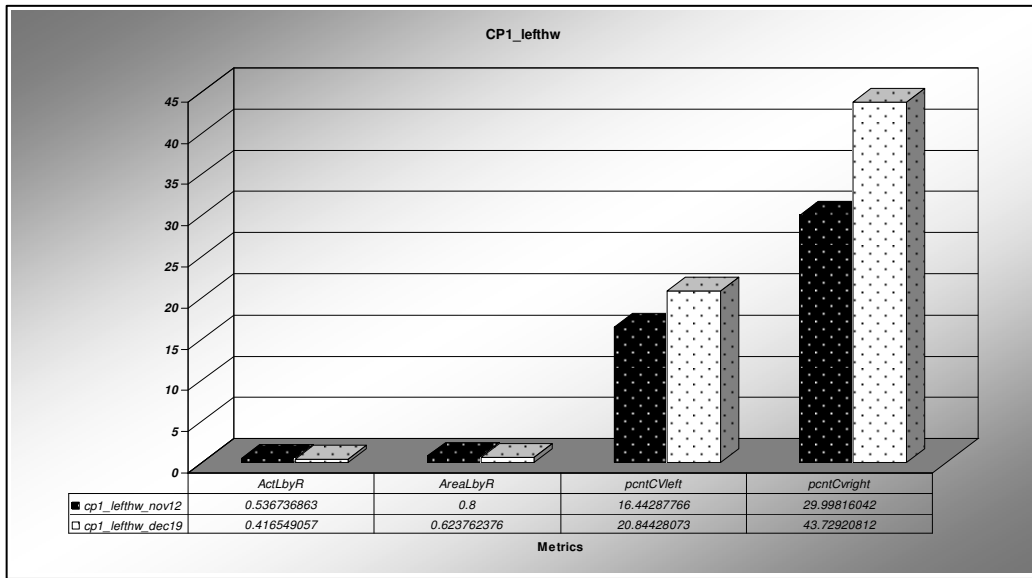


Figure 3.17 shows the image metrics reproduced over a period of time for CP subject 1, left hand waving protocol.

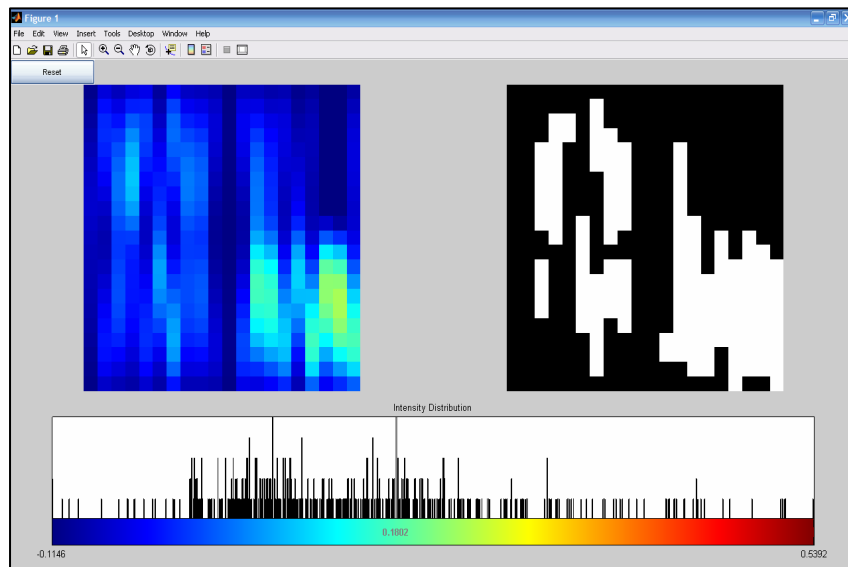


Figure 3.18 shows HbO image, its histogram and its segmented image for CP subject 1, left hand waving protocol, collected on first occasion



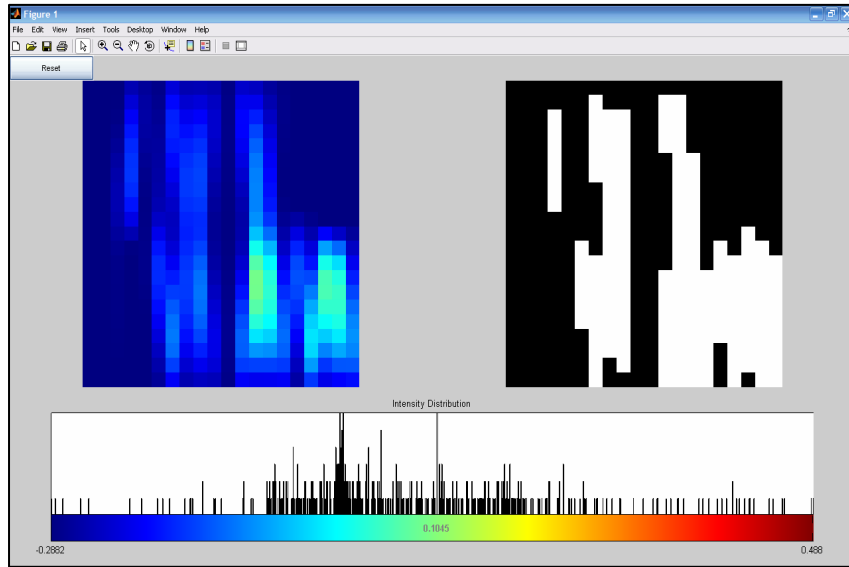


Figure 3.19 shows HbO image, its histogram and its segmented image for CP subject 1, left hand waving protocol, collected on second occasion

If we have a look at the segmented images for CP subject 1, left hand waving protocol in Figure 3.18 and 3.19 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.20 shows the image metrics for CP subject 1, right hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is little less than 1 for both the occasions. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little less than 1 on both occasions. So activated area in this case is reproducible. Percentage Coefficient of Variation on left side (pcntCVleft) on second occasion does not falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on left side is not reproducible. Also Percentage Coefficient of Variation on right side (pcntCVright) on second occasion does not falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on right side also is not reproducible.

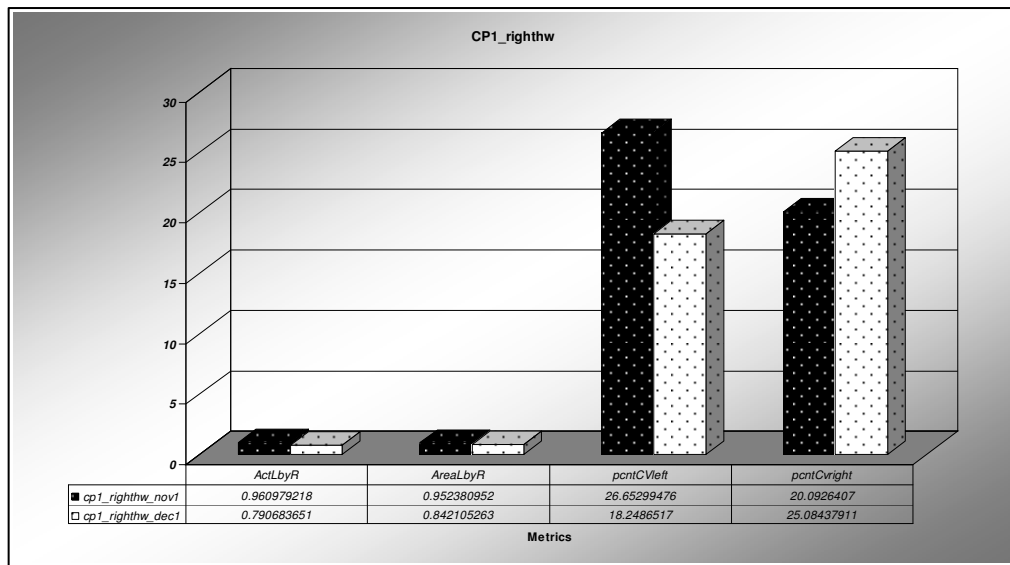


Figure 3.20 shows the image metrics reproduced over a period of time for CP subject 1, right hand waving protocol.

Figure 3.21 shows the image metrics for CP subject 5, right hand waving protocol. The data was collected twice and so we can assess if the image metrics were reproducible or not. The ratio of the activation on contralateral side to ipsilateral side (here ActRbyL) is little less than 1 for both the occasions. So activation is reproducible for this case. The ratio of the activated area on contralateral side to ipsilateral side (here AreaRbyL) is little less than 1 on both occasions. So activated area in this case is reproducible. Percentage Coefficient of Variation on left side (pcntCVleft) on second occasion does not falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on left side is not reproducible. Also Percentage Coefficient of Variation on right side (pcntCVright) on second occasion does not falls within  $\pm 20\%$  of the value on the first occasion. So percentage Coefficient of Variation on right side also is not reproducible.

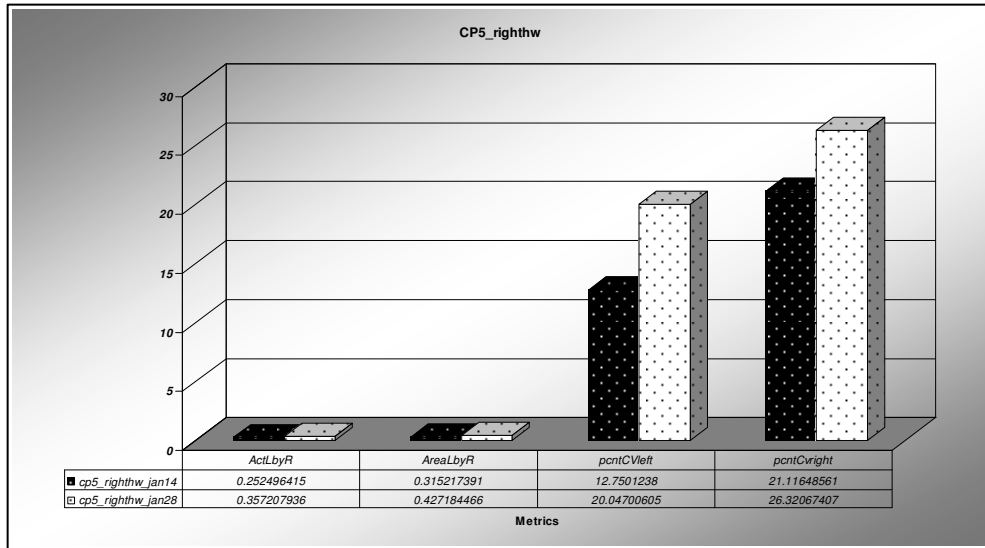


Figure 21 shows the image metrics reproduced over a period of time for CP subject 5, right hand waving protocol.

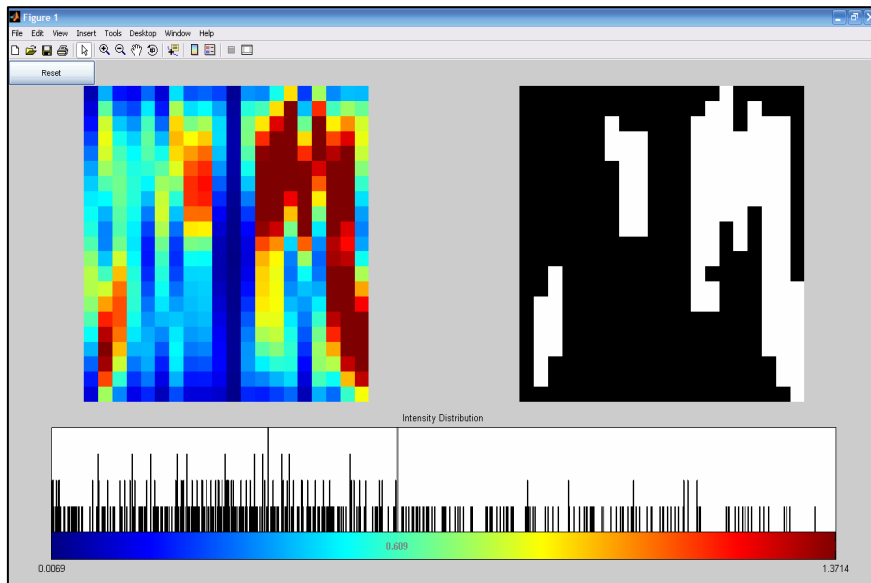


Figure 3.22 shows HbO image, its histogram and its segmented image for CP subject 5, right hand waving protocol, collected on first occasion

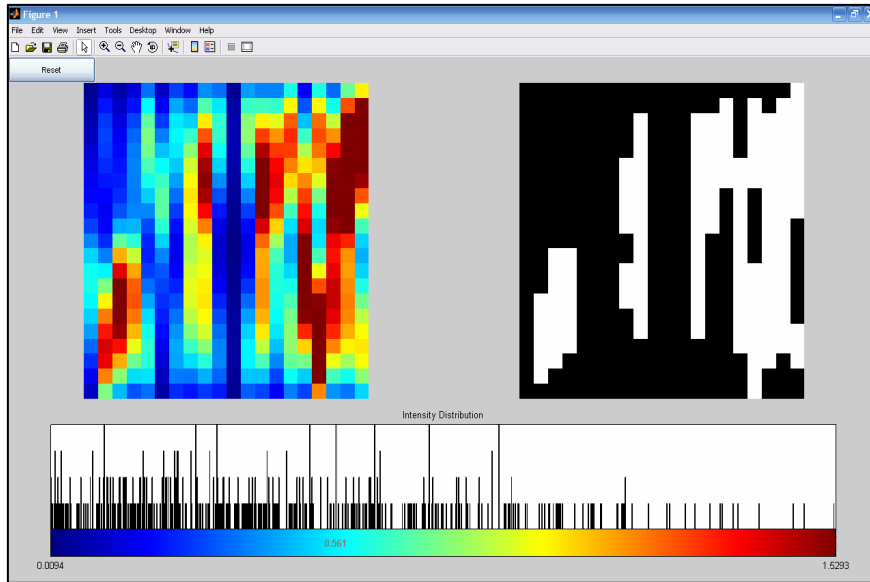


Figure 3.23 shows HbO image, its histogram and its segmented image for CP subject 5, right hand waving protocol, collected on second occasion

If we have a look at the segmented images for CP subject 5, right hand waving protocol in Figure 3.22 and 3.23 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Figure 3.24 shows the image metrics for CP subject 4, left finger tapping protocol. The data was collected twice and so we can assess if the image metrics were reproduced or not. In finger tapping protocol, from previous studies it was found from viewing the images that activation on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activation on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be ActRbyL. So if Act RbyL is higher than 1, it can be called reproducible for our purpose. Here it can be seen that it is higher than 1, both the times. So it is reproducible.

Also from previous studies it was found from viewing the images that activated area on contralateral side was higher than on ipsilateral side. So if we take the ratio of the activated area on contralateral side to ipsilateral side, it should be higher than 1. Here that ratio would be AreaRbyL. So if Area RbyL is higher than 1, it can be called reproducible for our purpose. Here

it can be seen that it is higher than 1, both the times. So it is reproducible. For this subject pcntCVright is reproducible whereas pcntCVleft is not reproducible.

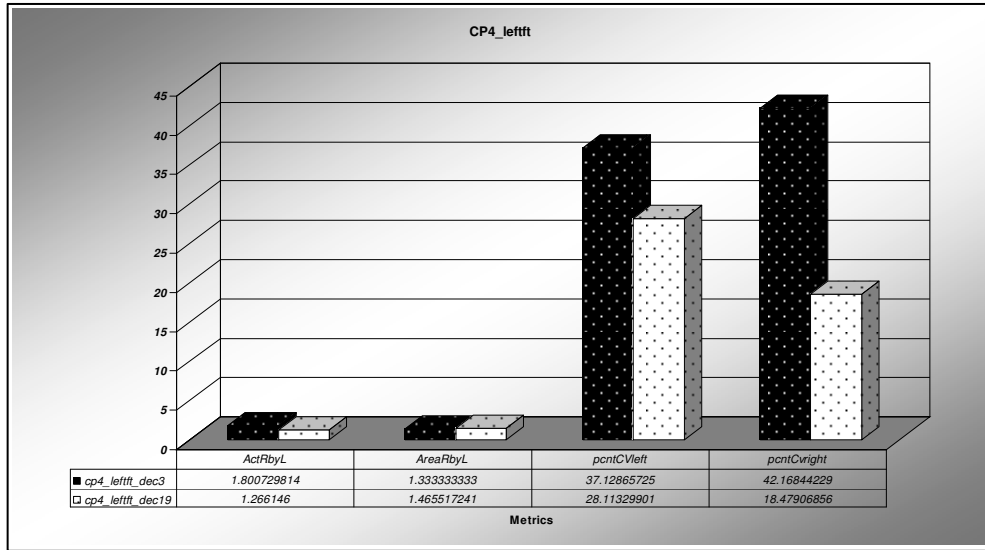


Figure 3.24 shows the image metrics reproduced over a period of time for CP subject 4, left finger tapping protocol.

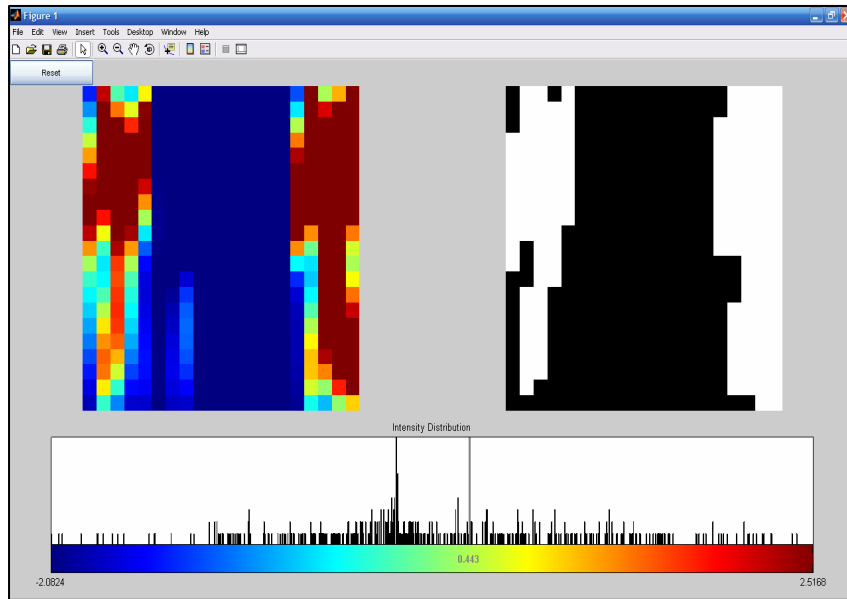


Figure 3.25 shows HbO image, its histogram and its segmented image for CP subject 4, left finger tapping protocol, collected on first occasion

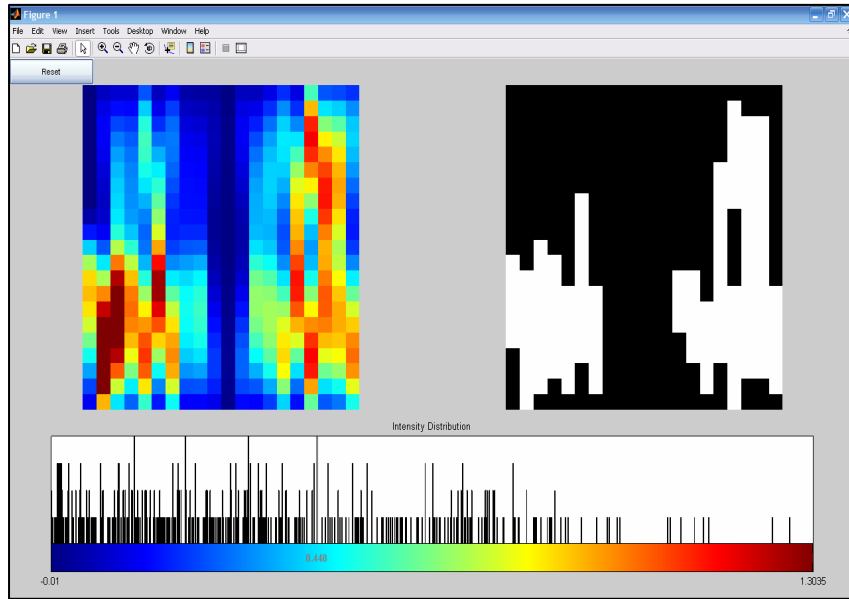


Figure 3.26 shows HbO image, its histogram and its segmented image for CP subject 4, left finger tapping protocol, collected on second occasion

If we have a look at the segmented images for CP subject 4, left finger tapping protocol in Figure 3.25 and 3.26 we can exactly know which region is activated without any decision issues. The activated areas on the two occasions look similar.

Table 3.1 summarizes the results described in section 3.1, columns indicate subNumber and the protocol, rows indicate the metric, Yes indicates that the corresponding metric for the corresponding subject and protocol is reproducible, whereas No indicates that the corresponding metric for corresponding subject and protocol is not reproducible. Criterion 1 mentioned at beginning of section 3.1 is used for assessing reproducibility of activation and activated area metrics, whereas criterion 2 mentioned at beginning of section 3.1, is used for assessing reproducibility of percentage coefficient of variation on left and right side of image.

| subNo_protocol | Metrics |          |            |             |
|----------------|---------|----------|------------|-------------|
|                | ActRbyL | AreaRbyL | pcntCVleft | pcntCVright |
| sub2_leftft    | Yes     | Yes      | No         | Yes         |
| sub2_lefthw    | Yes     | Yes      | No         | Yes         |
| sub6_lefthw    | Yes     | Yes      | No         | Yes         |
| sub2_rightft   | Yes     | Yes      | Yes        | No          |
| sub2_righthw   | No      | No       | Yes        | No          |
| sub6_righthw   | Yes     | Yes      | No         | No          |
| cp1_lefthw     | Yes     | Yes      | No         | No          |
| cp1_righthw    | Yes     | Yes      | No         | No          |
| cp5_righthw    | Yes     | Yes      | No         | No          |
| cp4_leftft     | Yes     | Yes      | No         | Yes         |

Table 3.1 summarizes the results of reproducibility study

### 3.2. Assessing Variability in Normal Subjects

To assess variability in normal subjects, average of each metric along with its standard error is shown in the bargraphs below (Figure 3.27 to Figure 3.32). The metrics for which variability is assessed are ActLeft, ActRight, totAreaLeft, totAreaRight, pcntCVLeft, pcntCVRight. Averages and standard error for these image metrics are calculated for four different protocols namely left finger tapping, left hand waving, right finger tapping, right hand waving.

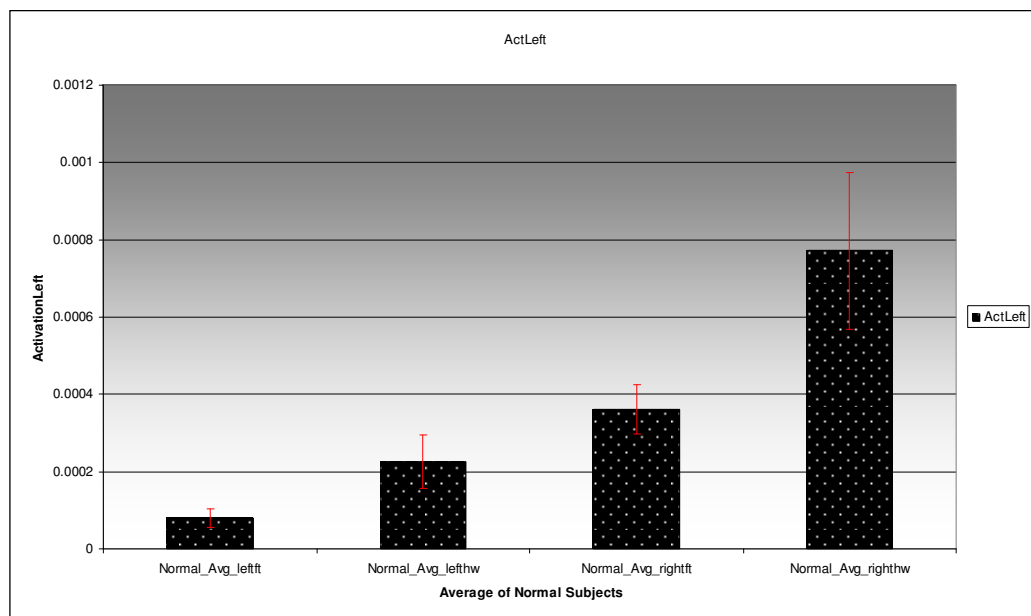


Figure 3.27 shows Average and Standard error for the metric ActLeft for all Normal Subjects

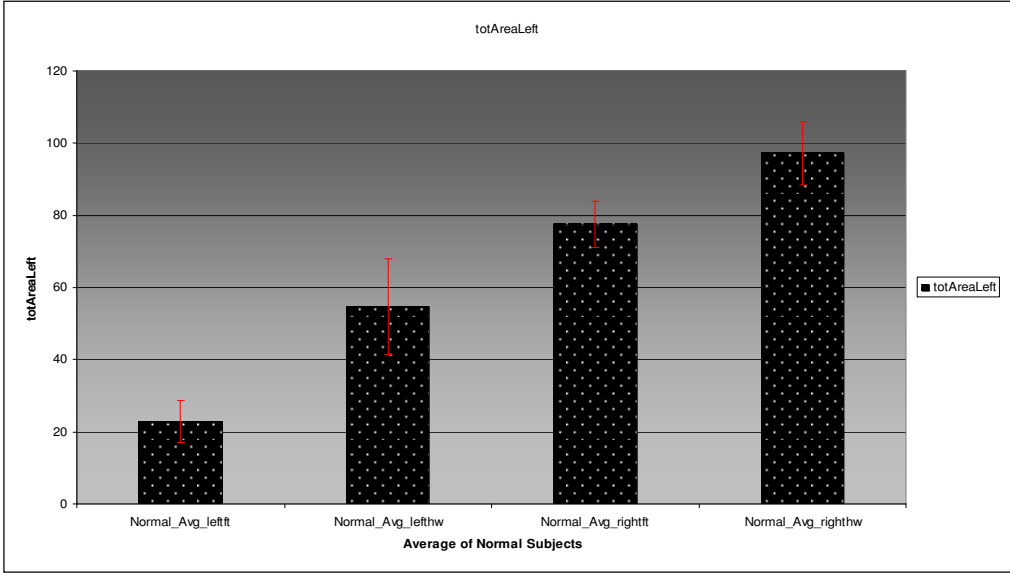


Figure 3.28 shows Average and Standard error for the metric totAreaLeft for all Normal Subjects

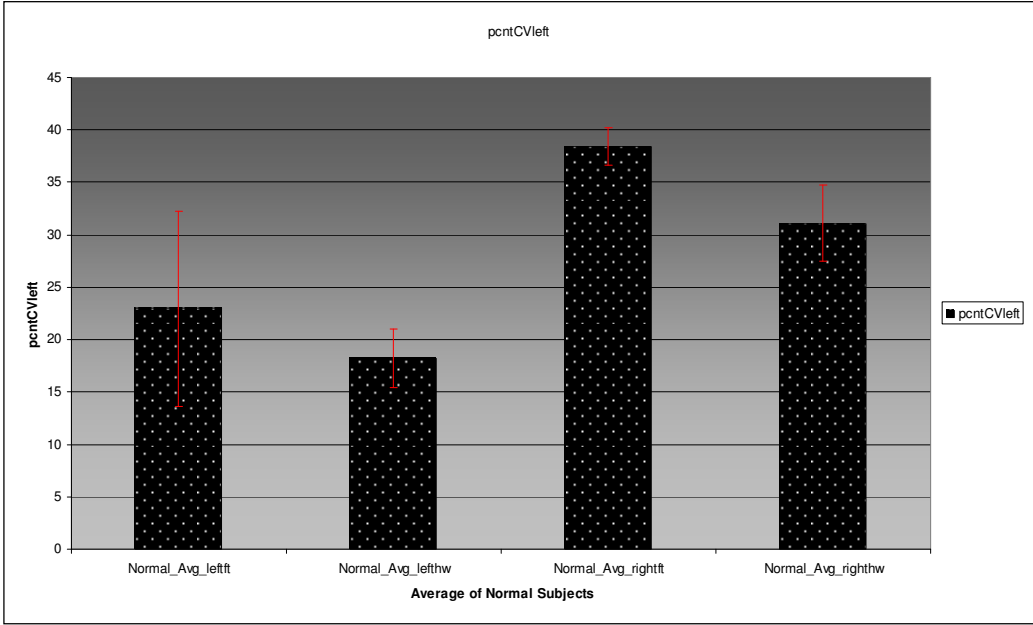


Figure 3.29 shows Average and Standard error for the metric pcntVLeft for all Normal Subjects



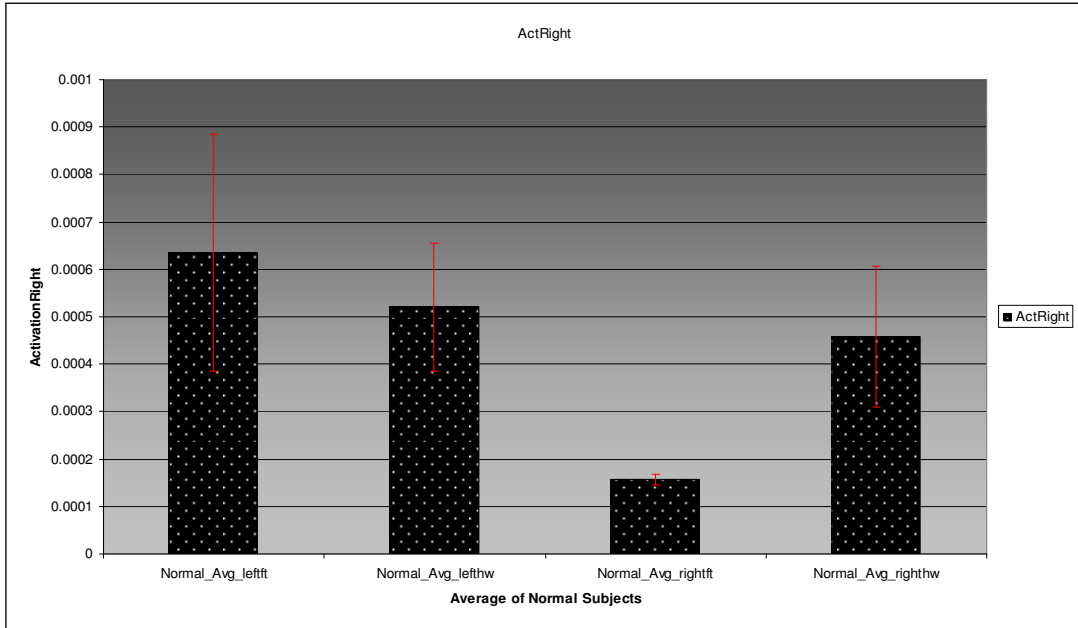


Figure 3.30 shows Average and Standard error for the metric ActRight for all Normal Subjects

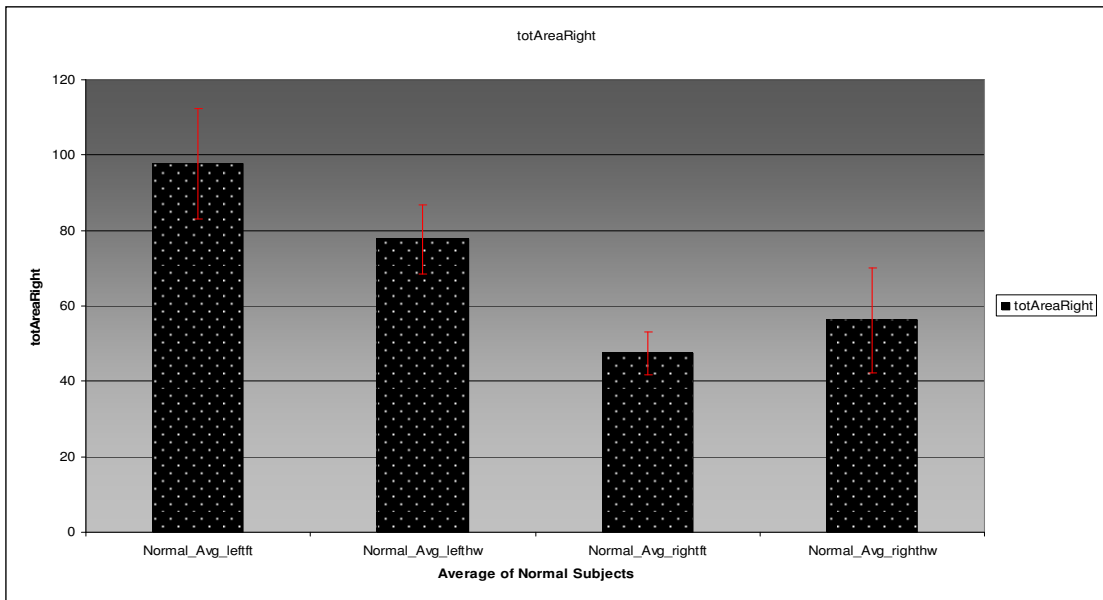


Figure 3.31 shows Average and Standard error for the metric totAreaRight for all Normal Subjects

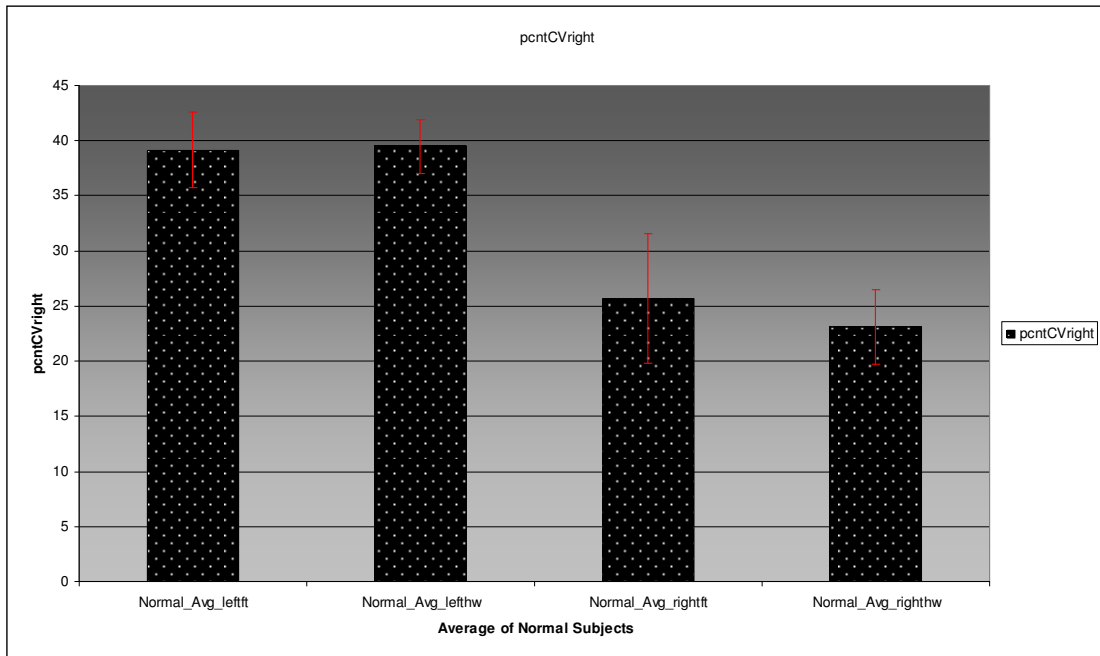


Figure 3.32 shows Average and Standard error for the metric pcntCVright for all Normal Subjects

### 3.3 Comparing Finger Tapping and Hand Waving in Normal Subjects using Image Metrics

Act\_hw\_by\_ft\_ipsi stands for ratio of activation on ipsilateral side in hand waving protocol to activation on ipsilateral side in finger tapping protocol for same subject. When Act\_hw\_by\_ft\_ipsi is greater than 1, it means that activation is higher on ipsilateral side in handwaving protocol than finger tapping protocol for the same subject. In Figure 3.33 we can see that for different protocols Act\_hw\_by\_ft\_ipsi is always greater than 1, which suggests that activation is always higher on ipsilateral side in handwaving protocol than finger tapping protocol for the same subject.

Area\_hw\_by\_ft\_ipsi stands for ratio of activated area on ipsilateral side in hand waving protocol to activated area on ipsilateral side in finger tapping protocol for same subject. When Area\_hw\_by\_ft\_ipsi is greater than 1, it means that activated area is higher on ipsilateral side in handwaving protocol than finger tapping protocol for the same subject. In Figure 3.34 we can see that for different protocols Area\_hw\_by\_ft\_ipsi is always greater than 1, which suggests that

activated area is always higher on ipsilateral side in handwaving protocol than finger tapping protocol for the same subject.

Act\_hw\_by\_ft\_contra stands for ratio of activation on contralateral side in hand waving protocol to activation on contralateral side in finger tapping protocol for same subject. In Figure 3.35 we can see that for different protocols, Act\_hw\_by\_ft\_contra is a little less, equal or little greater than 1, which means activation in hand waving on contralateral side is a little less, equal or little greater than, activation in finger tapping on contralateral side.

Area\_hw\_by\_ft\_contra stands for ratio of activated area on contralateral side in hand waving protocol to activated area on contralateral side in finger tapping protocol for same subject. In Figure 3.36 we can see that for different protocols, Area\_hw\_by\_ft\_contra is a little less, equal or little greater than 1, which means activated area in hand waving protocol on contralateral side is a little less, equal or little greater than, activation in finger tapping on contralateral side.

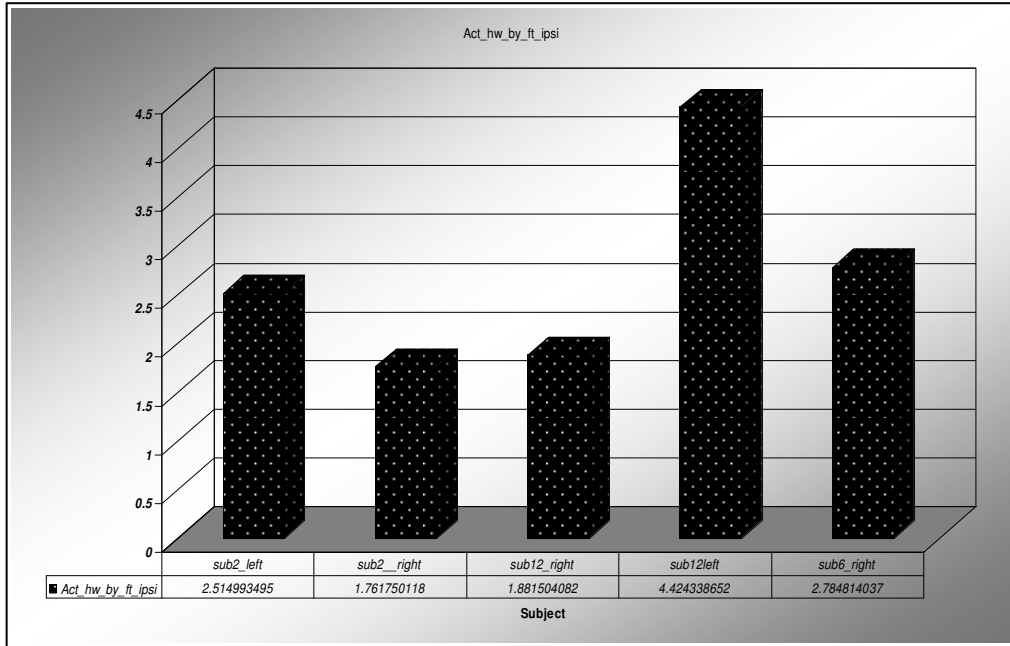


Figure 3.33 shows ratio of activation on ipsilateral side in handwaving protocol to activation on ipsilateral side in finger tapping protocol

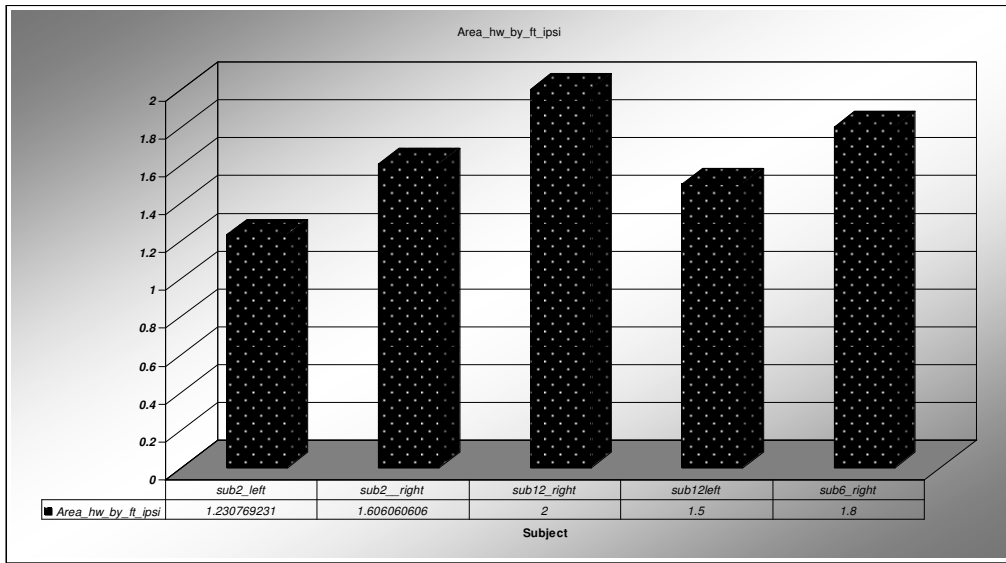


Figure 3.34 shows ratio of activated area on ipsilateral side in handwaving protocol to activated area on ipsilateral side in finger tapping protocol

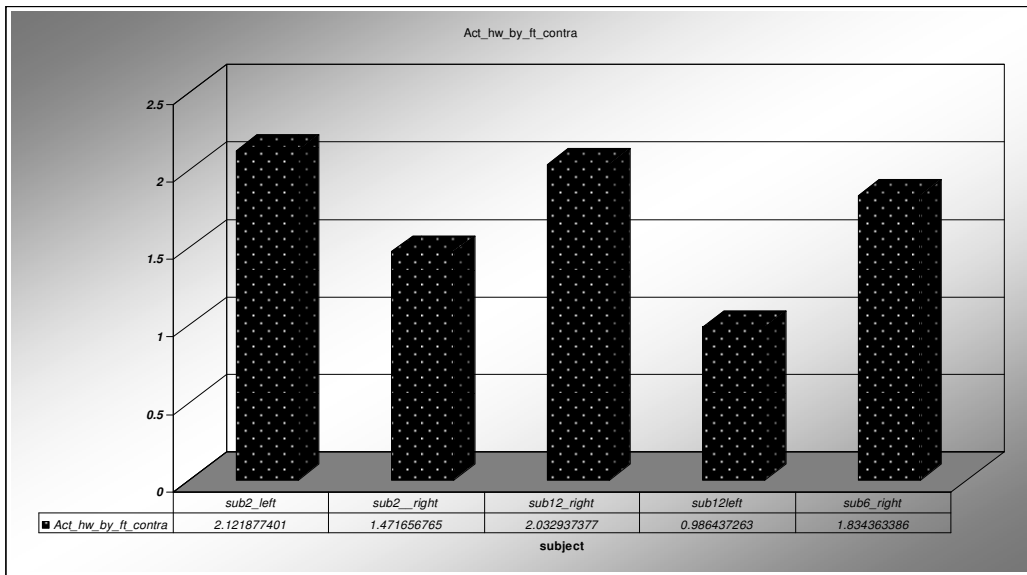


Figure 3.35 shows ratio of activation on contralateral side in handwaving protocol to activation on contralateral side in finger tapping protocol

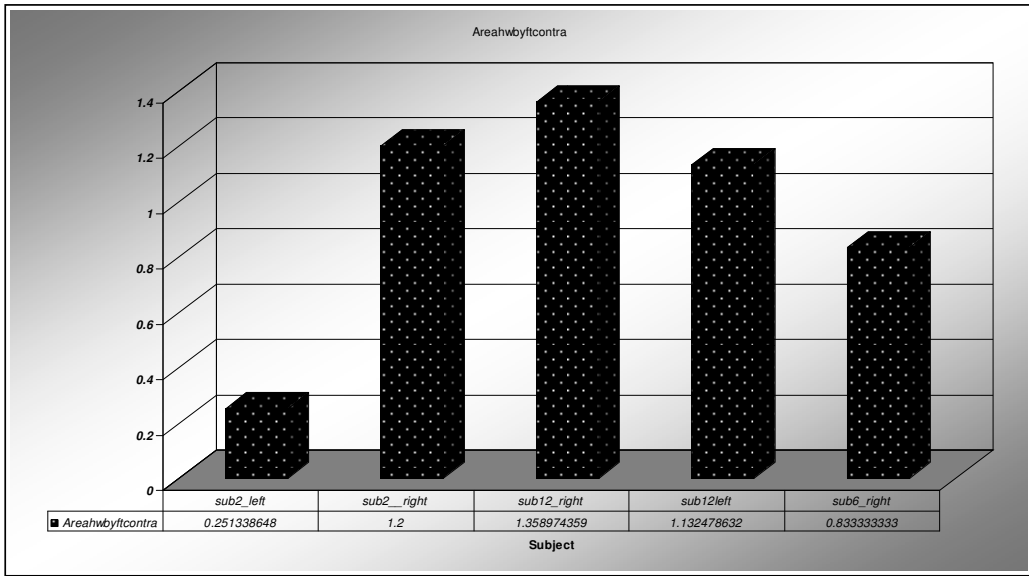


Figure 3.36 shows ratio of activated area on contralateral side in hand waving protocol to activated area on contralateral side in finger tapping protocol

### 3.4 Comparing Cerebral Palsy Kids with control group

Figure 3.37 shows comparison of Cerebral Palsy Kids having hemiparesis on right side with control group. Here the metric compared is activation on ipsilateral side.

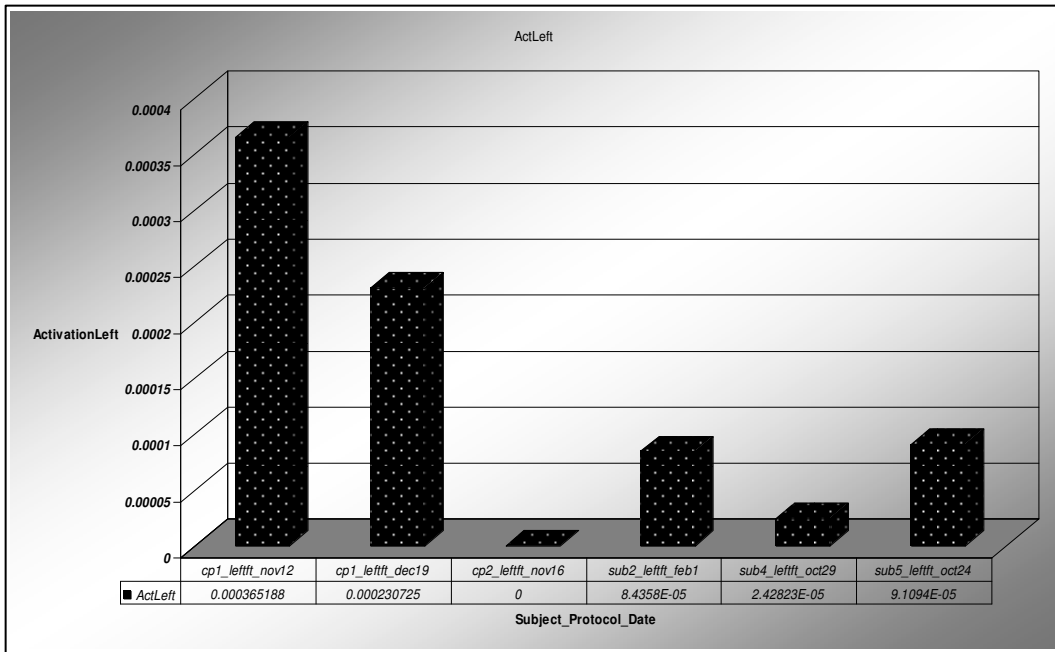


Figure 3.37 shows activation on ipsilateral (left) side for CP Subjects and Normal subjects

It is seen that activation on ipsilateral side is significantly higher in CP Kids than normal subjects.

Figure 3.38 shows comparison of Cerebral Palsy Kids having hemiparesis on right side with control group. Here the metric compared is activated area on ipsilateral side.

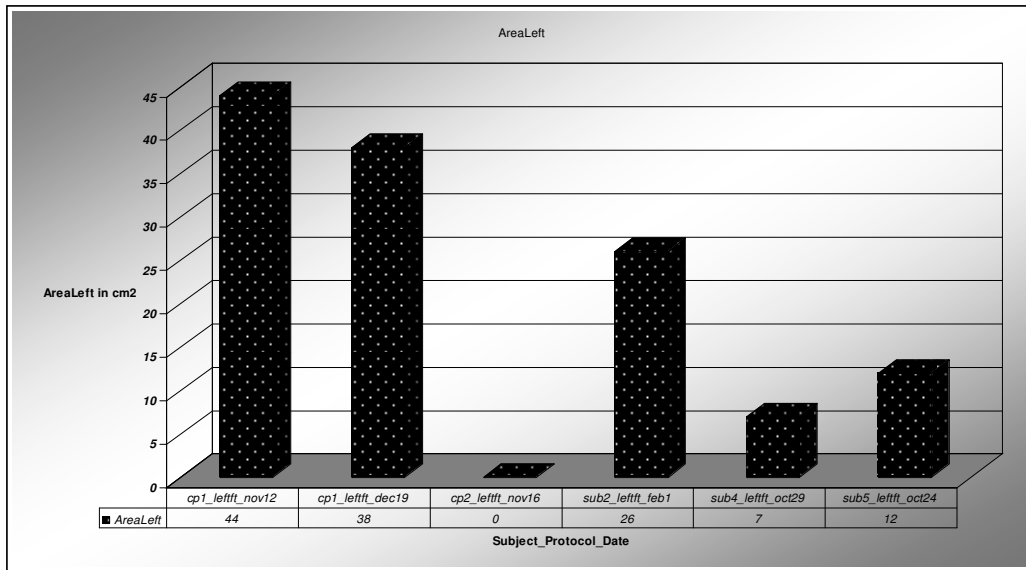


Figure 3.38 shows activated area on ipsilateral (left) side for CP subjects and Normal subjects

It is seen that activated area on ipsilateral side is significantly higher in CP Kids than normal subjects.

Figure 3.39 shows comparison of CP Kids having hemiparesis on left side with control group. Here the compared metric is activation on ipsilateral side.

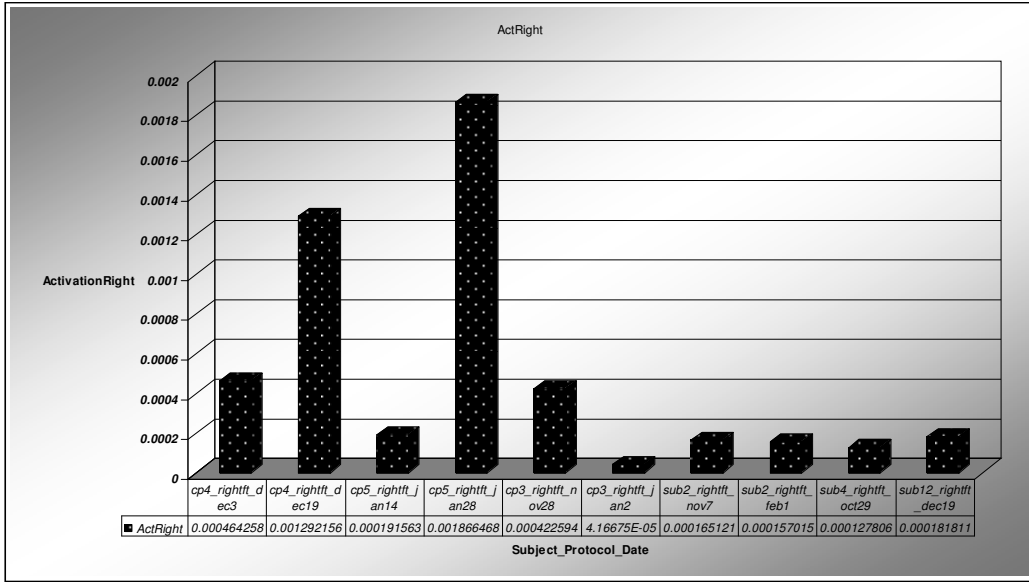


Figure 3.39 shows activation on ipsilateral (right) side for CP Subjects and Normal subjects. It is seen that activation on ipsilateral side is significantly higher in CP kids than in normal subjects.

Figure 3.40 shows comparison of CP Kids having hemiparesis on left side with control group. Here the metric compared is activated area on ipsilateral side.

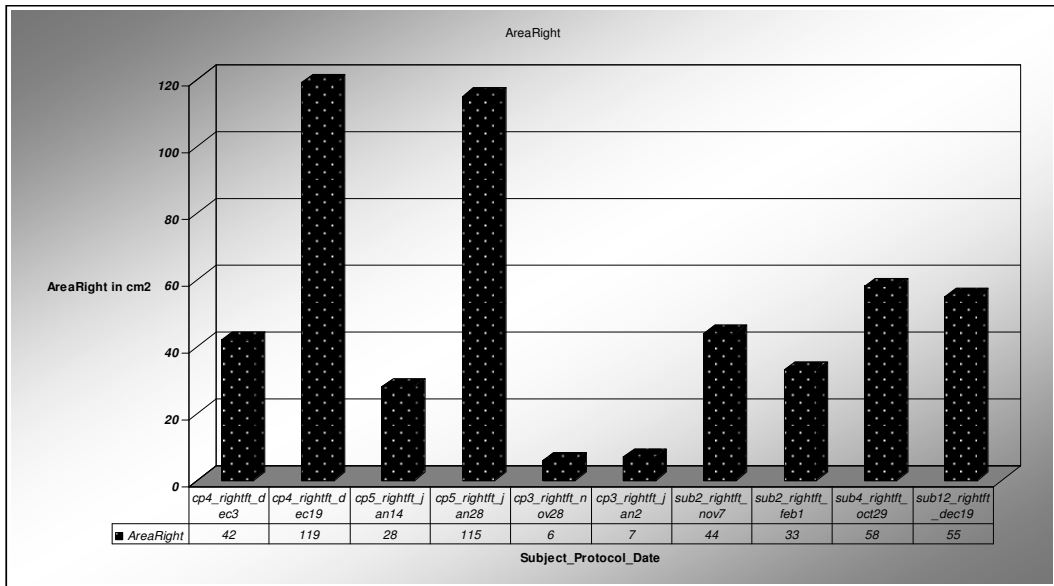


Figure 3.40 shows activated area on ipsilateral (right) side for CP subjects and Normal subjects.

It is seen that activated area on ipsilateral side is significantly higher in CP kids than in normal subjects.

The brain is constantly reorganizing structurally and functionally as it responds to stimuli and to injury. This ability to reorganize is referred to as "neuroplasticity". Homologous Region Adoption is a mechanism of neuroplasticity that provides for one area of the brain to take over the function of a distant area that has been injured. The new functional area can be in the same half or in the other half of the brain. The human brain has two halves connected by a bridge. Each half controls somewhat different functions, but can share in control of a single function. The mechanism involved is thought to be possible because of the existence of a minor, but existing neural pathway in the distant area which has been non-functional as long as the major pathway was in operation. Here the CP Kids had damage on the contralateral side, and higher activation was seen on the ipsilateral side, which indicates the neuroplastic behaviour of the brain. Thus our method is capable to assess neuroplasticity in CP Kids.

#### *3.4.1 Comparing the location of activation on ipsilateral side in Cerebral Palsy Kids and Normal Subjects*

Distances for top 15% of peak pixels were measured from the centerline of the brain. Out of which the distance of the closest pixel from the centerline was noted down. When the CP subject has hemiparesis on left side and we analyze the images for right finger tapping, and right hand waving protocol, the closest activated pixel on ipsilateral side was found to be significantly closer to brains centerline than in images for right finger tapping and handwaving for normal subjects. In other words activation on ipsilateral side was found to be significantly closer to brains centerline in Cerebral Palsy Kids than normal subjects. Figure 3.41 shows the distances of the closest activated pixel on ipsilateral side in Cerebral Palsy affected Kids and normal subjects. The activated region in Cerebral Palsy Kids is around 2 to 3 cms away from centerline of the brain, whereas the activated region in normal subjects is around 7-9 cms away from centerline of the brain. A two tailed unpaired t-test was performed for the distances of the



closest peak pixels from the brains centerline for the affected and normal group. Variance for the two groups is considered unequal for this t-test. The associated probability found was 0.000249 which is a lot less than 0.05. So the difference in location of the activation in CP Kids and normals is statistically significant.

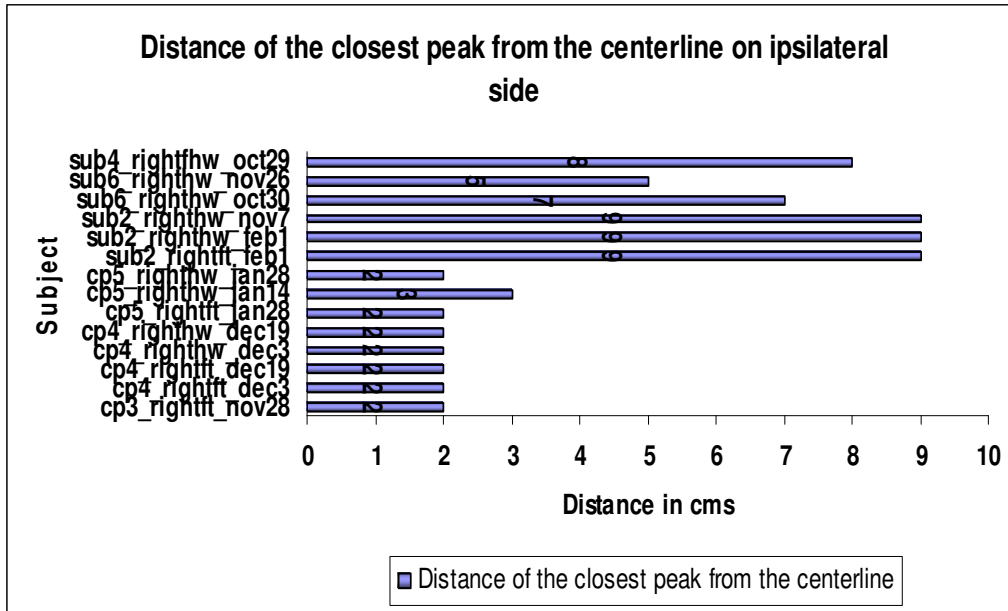


Figure 3.41 shows the distance of the closest peak from the centerline on ipsilateral side in CP and normal subjects

Pixel having highest value was denoted as peak pixel and pixels having values greater than 0.85 times of the peak pixel were taken as top 15% peak pixels. When the CP subject has hemiparesis on left side and we analyze the images for right finger tapping, and right hand waving protocol, the number of such peak pixels on ipsilateral side were found to be more than in images for right finger tapping and handwaving for normal subjects. The above fact can be seen in Figure 3.42.

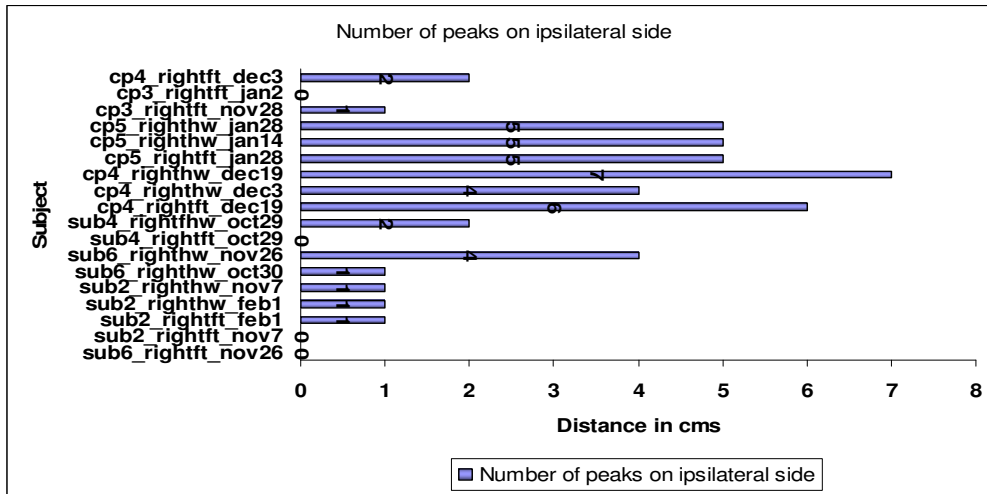


Figure 3.42 shows Number of peak pixels on ipsilateral side for Cerebral Palsy Kids as well as Normal subjects

3.4.2 Comparing the location of activation on contralateral side in Cerebral Palsy Kids and Normal Subjects

Figure 3.43 shows comparison of activation on contralateral (right) side for CP Subjects and Normal subjects.

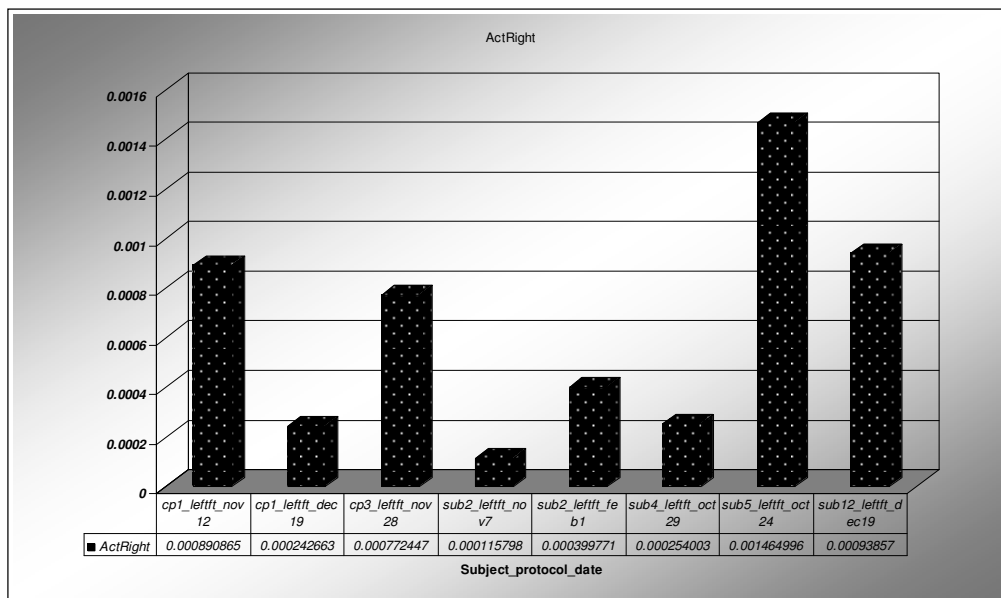


Figure 3.43 shows activation on contralateral (right) side for CP Subjects and Normal subjects

As can be seen in the figure, no particular pattern could be figured from it, as to differentiate between CP Kids and normal subjects.

Figure 3.44 shows comparison of activated area on contralateral (right) side for CP subjects and Normal subjects.

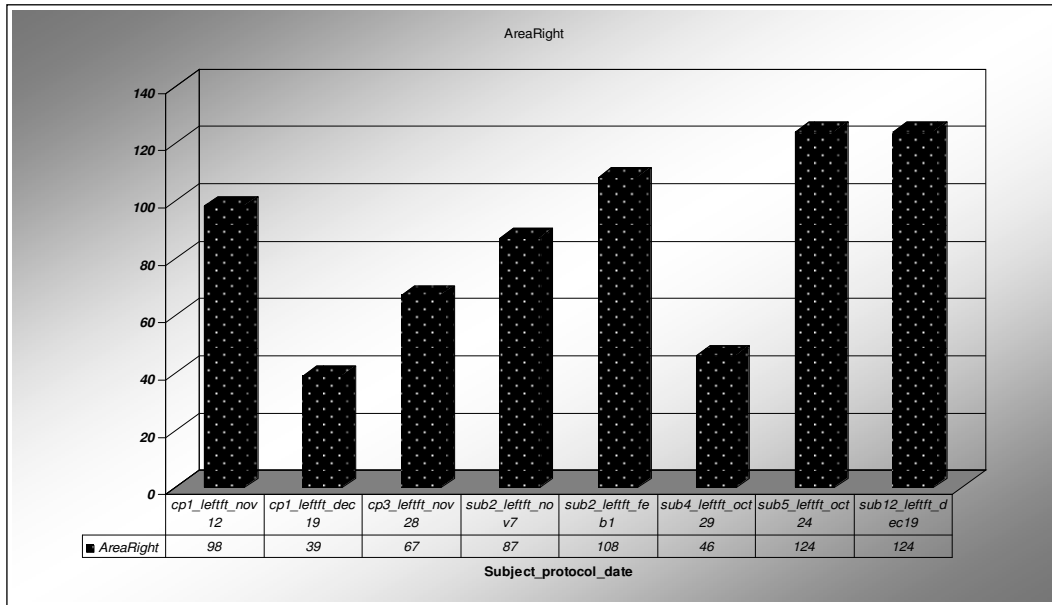


Figure 3.44 shows the comparison of activated area on contralateral (right) side for CP subjects and Normal subjects

As can be seen in the figure, no particular pattern could be figured from it, as to differentiate between CP Kids and normal subjects.

Figure 3.45 shows comparison of the distance of the closest peak from the centerline on contralateral side in CP and normal subjects.

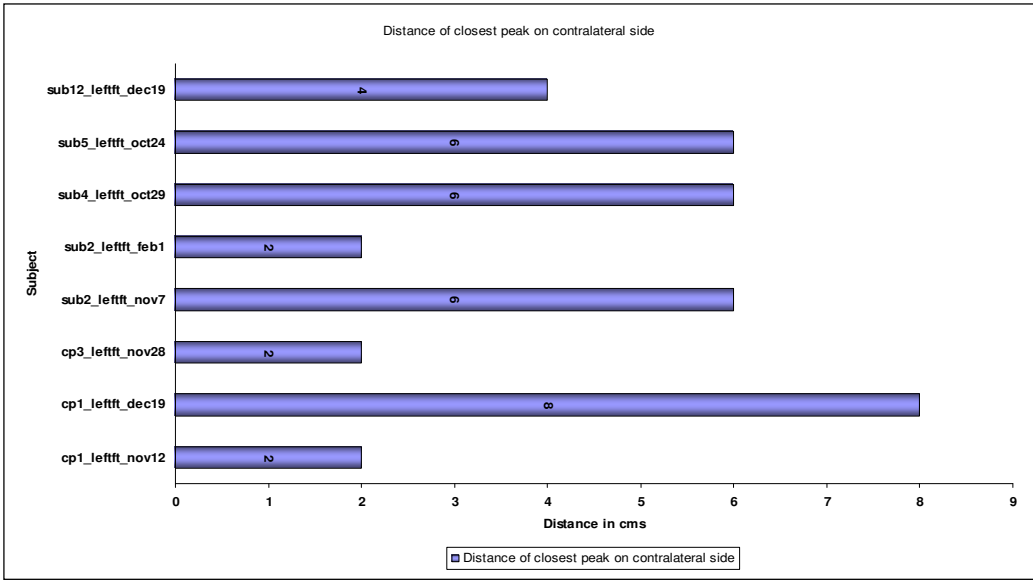


Figure 3.45 shows the distance of the closest peak from the centerline on contralateral side in CP and normal subjects

Figure 3.46 shows comparison of the number of peak pixels on Contralateral side for Cerebral Palsy Kids as well as Normal subjects.

As can be seen in the figure, no particular pattern could be figured from even this metric, as to differentiate between CP Kids and normal subjects.

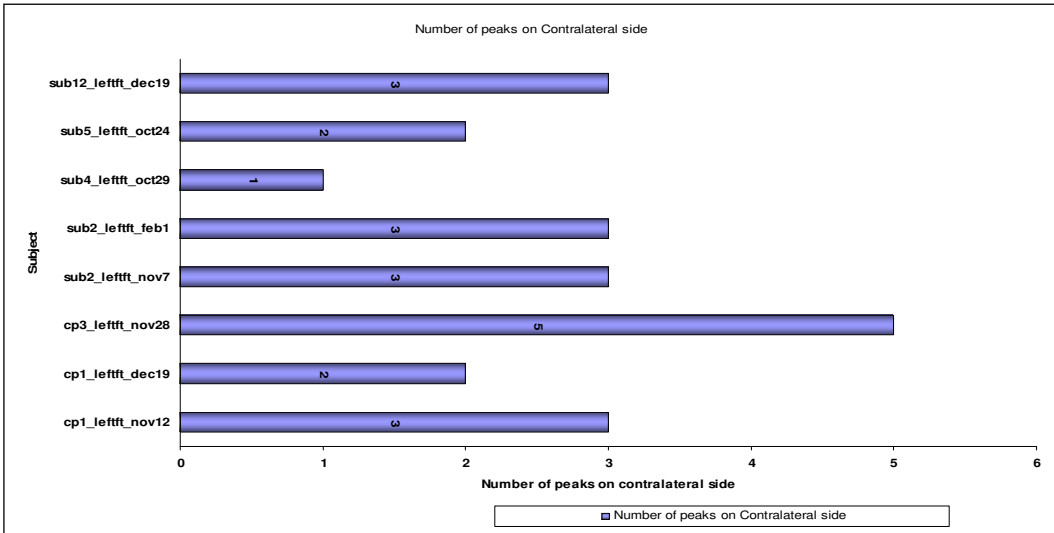


Figure 3.46 shows Number of peak pixels on Contralateral side for Cerebral Palsy Kids as well as Normal subjects

No particular pattern was figured from even this metric, as to differentiate between CP Kids and normal subjects.

In all assessing contralateral side for differentiating CP Kids from the normal subjects did not proved to be of much usefulness.

### 3.4.3 Assessing evolution of the activated area on ipsilateral side with respect to time

In Figure 3.47, activated area for CP subject 4, for right finger tapping protocol collected on dec19 seems to be higher than normals, but the activated area for the same subject same protocol collected on dec3, is not greater than normals. Same pattern in seen for CP subject 5, that is on one occasion the activated area is greater than normals, and on another occasion it is not.

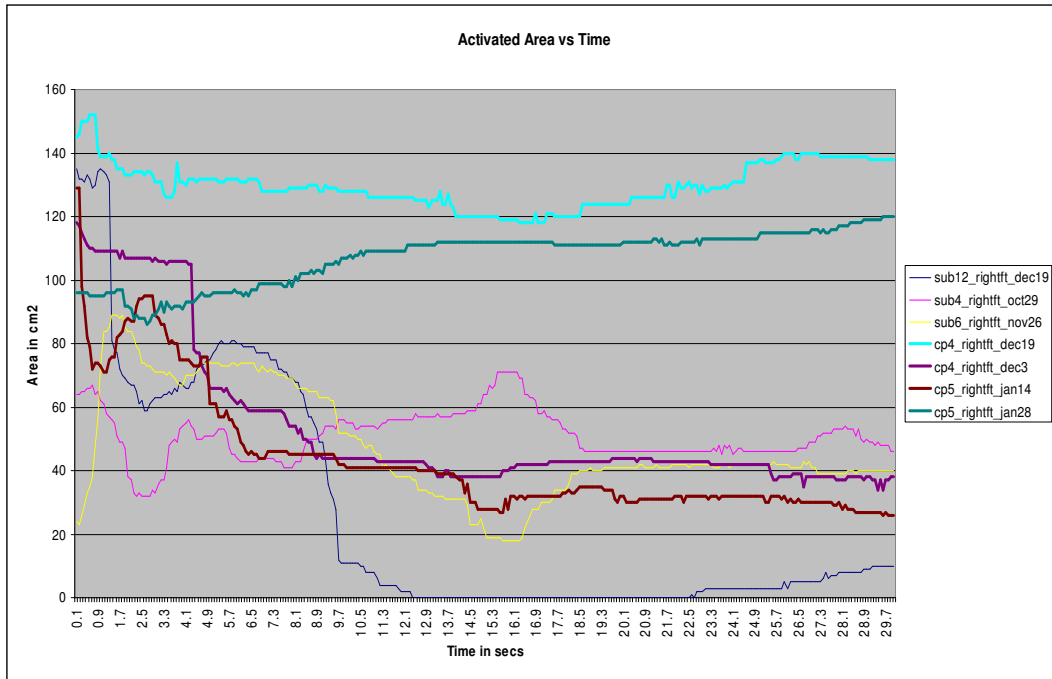


Figure 3.47 shows Average Activated area on ipsilateral side over 30 seconds for CP Kids and normal subjects

## CHAPTER 4

### CONCLUSIONS

#### 4.1 Reproducibility

Image metrics and the segmented images are very well reproduced over a period of time for both CP and Normal subjects. Activation and Activated Area are the image metrics that are reproduced quite well, whereas percentage coefficient of variation is sometimes reproduced and sometimes not. Small variations in activation and activated area can be attributed to physiology occurring corresponding to events defined in protocol. Large variations (very rarely), as seen for subject 2 right hand waving protocol, can be attributed to physiology occurring due to the events occurring that are not defined in protocol.

#### 4.2 Comparison of Finger Tapping and Hand Waving in Normal Subjects using Image Metrics

Activation and activated area is found higher in handwaving than finger tapping on ipsilateral side for normal subjects. Activation in hand waving on contralateral side is a little less, equal to or little greater than activation in finger tapping on Contralateral side. Activated area in hand waving on contralateral side is a little less, equal to or little greater than activated area in finger tapping on contralateral side. Thus we can use activation and activated area for differentiating between finger tapping and handwaving protocols in normal subjects.

#### 4.3 Comparison of Cerebral Palsy Kids with control group

Activation on ipsilateral side is significantly higher in CP kids than in normal subjects. Activated area on ipsilateral side is significantly higher in CP kids than in normal subjects. When the CP subject has hemiparesis on left side and we analyze the images for right finger tapping , and right hand waving protocol, the activation on ipsilateral side was found to be significantly closer to brains centerline than in images for right finger tapping and handwaving for normal subjects. When the CP subject has hemiparesis on left side and we analyze the images for right finger tapping, and right hand waving protocol, the number of peaks on ipsilateral side were found to be more than in images for right finger tapping and handwaving for normal subjects. Thus activation on ipsilateral side, activated area on ipsilateral side, number of peak pixels on ipsilateral side, and distance of closest peak pixel from brains centerline are the image metrics that prove to be promising for differentiating the Cerebral Palsy affected Kids from normal subjects, whereas percentage coefficient of variations on both ipsilateral and contralateral side did not prove to be useful for differentiating between Cerebral Palsy affected Kids and normal subjects. It would be good to conduct t-test to assess if the promising image metrics are statistically different in CP affected kids than normals, but an insufficient CP Kids data was available and the data also had to be divided in a large number of sub-categories, making it impossible to perform t-tests. It is shown with the help of t-test, that difference in the location of activation in CP Kids and normals is statistically significant. Activation, activated area, distance of the closest peak from brains centerline and number of peaks were the image metrics assessed on the contralateral side in both CP Kids and normal subjects, to see if they are useful for differentiating CP Kids from normal subjects. None out of these four metrics on contralateral side proved to be useful. Whereas same four image metrics on ipsilateral side proved to be useful for differentiating CP Kids from normal subjects.

APPENDIX A

IMAGE ANALYSIS ALGORITHM  
AND SOURCE CODE



```

close all;
clear all;

%Load the file
load -mat cp1_leftft_dec19.hmr

% Get average HbO
HbOimage = DOT.IMG.img(:,:,1,1,1);
nmax = max(HbOimage(:));
nmin = min(HbOimage(:));
n = 2;
while n < 100
    HbOimage = HbOimage + DOT.IMG.img(:,:,1,n,1);
    S = DOT.IMG.img(:,:,1,n,1);
    if nmax < max(S(:))
        nmax = max(S(:));
    end
    if nmin > min(S(:))
        nmin = min(S(:));
    end
    n = n + 1;
end
HbOimageavg = HbOimage./99;
figure, imagesc(HbOimageavg*1e5);
title('HbOimage');
xlabel('Pixel Number');
ylabel('Pixel Number');
set(gca,'YDir','default');
colormap jet
colorbar('location','eastoutside')

%Measure distance interactively
pixval;

%Get the level and binary image
[LEVEL, BW] = thresh_tool(HbOimageavg);

%Crop the bw and color image into left and right
bwleft = BW(1:21,1:10);
bwright = BW (1:21, 11:20);
HbOleft=HbOimageavg(1:21,1:10);
HbOright=HbOimageavg(1:21,11:20);

%Calculate activation of left side of the image
t=LEVEL;
s=0;

for x= 1:1:21
    for y=1:1:10
        n1= HbOleft(x,y);

```

```

        if (n1>=t)
            s=s+n1;
        else
            s=s;
        end
    end
end
end
Actleft=s;
Actleft

```

*%Calculate activation of right side of the image*

```

t=LEVEL;
s1=0;

```

```

for x= 1:1:21
    for y=1:1:10
        n2=HbOright(x,y);

        if (n2>=t)
            s1=s1+n2;
        else
            s1=s1;
        end
    end
end
end
Actright=s1;
Actright

```

*%Calculate ratios of activation on left and right side of image*

```

ActLbyR=s./s1;
ActLbyR

```

```

ActRbyL=s1./s;
ActRbyL

```

*%Calculate area of left side of image by three methods, also showing  
%histogram of binary image*

```

figure
imhist(bwleft);
title('Histogram of Left Half of Image');
ylabel('Number of Pixels');
xlabel('Intensity');
L = bwlabel(bwleft);
stats= regionprops(L,'Area','Centroid');
allArealeft = [stats.Area]
c=sum(sum(bwleft));
totArealeft=c;
totArealeft

```

*%Calculate area of right side of image by three methods, also showing  
%histogram of binary image*

```

figure

```

```

imhist(bwright);
title('Histogram of Right Half of Image');
ylabel('Number of Pixels');
xlabel('Intensity');
set(gca, 'XTickMode', 'manual');
L = bwlabel(bwright);
stats= regionprops(L,'Area','Centroid');
allArearight = [stats.Area]
c1=sum(sum(bwright));
totArearight=c1;
totArearight

```

**%Calculate ratio of areas on left and right side of image**

```

areaLbyR=c./c1;
areaLbyR

```

```

areaRbyL=c1./c;
areaRbyL

```

**%calculate standard deviatio of left activated part**

```

f=HbOleft.*bwleft;
i=1;
clear sta

```

```

for x= 1:1:21
    for y=1:1:10

```

```

        g= f(x,y);
        if g~=0
            sta(i,1)=g;
            i=i+1;

```

```

        end

```

```

    end

```

```

end

```

```

z=std(sta);
z1=mean(sta);
z2=(z./z1)*100;

```

```

pcntCVleft=z2;
pcntCVleft

```

**%Calculate standard deviation of right activated part**

```

p=HbOright.*bwright;
q=1;
clear stb

```

```

for x= 1:1:21
    for y=1:1:10

        r= p(x,y);
        if r~=0
            stb(q,1)=r;
            q=q+1;

        end

    end

end
end

```

```

u=std(stb);
u1=mean(stb);
u2=(u./u1)*100;
pcntCVright=u2;
pcntCVright

```

```

%Show all peaks on left side of image, for calculating number of blobs
peak=max(max(HbOleft));

```

```

d=0;

```

```

leftblobs=0;

```

```

re=HbOleft;
for x=1:1:21
    for y=1:1:10

```

```

        p2=0.85*peak;

```

```

        rd=re(x,y);

```

```

        if (rd>=p2)

```

```

            d=d+1;

```

```

            leftblobs(d,1)=d;
            leftblobs(d,2)=x;

```

```

                leftblobs(d,3)=y;

```

```

                    leftblobs(d,4)=rd;

```

```

        end
    end
end

```

```

    end

end

%Show all peaks on right side of image, for calculating number of blobs
peakn=max(max(HbOright));

dn=0;

rightblobs=0;

ren=HbOright;
for x=1:1:21
    for y=1:1:10

        p2n=0.85*peakn;

        rdn=ren(x,y);

        if (rdn>=p2)

            dn=dn+1;

            rightblobs(dn,1)=dn;
            rightblobs(dn,2)=x;

                rightblobs(dn,3)=y+10;

                    rightblobs(dn,4)=rdn;

            end

        end

    end

end

end

%Display original image, thresholded image, and slider for thresholding
thresh_tool(HbOimageavg*1e5);

%Automatically export the following parameters to excel results file:
%image metrics, subject number, protocol, and date of data collection

xlswrite('results', Actleft, 'Actleft', 'A56');
xlswrite('results', Actright, 'Actright', 'A56');
xlswrite('results', ActLbyR, 'ActLbyR', 'A56');
xlswrite('results', ActRbyL, 'ActRbyL', 'A56');
xlswrite('results', allArealeft, 'allArealeft', 'A56');
xlswrite('results', totArealeft, 'totArealeft', 'A56');
xlswrite('results', allArearight, 'allArearight', 'A56');
xlswrite('results', totArearight, 'totArearight', 'A56');
xlswrite('results', areaLbyR, 'AreaLbyR', 'A56');

```

```
xlswrite('results', areaRbyL, 'AreaRbyL', 'A56');  
xlswrite('results', pcntCVleft, 'pcntCVleft', 'A56');  
xlswrite('results', pcntCVright, 'pcntCVright', 'A56');
```

```
name=('sub6_rightft_nov26');  
xlswrite('results', name, 'Distance', 'F170');  
xlswrite('results', name, 'Actleft', 'F56');  
xlswrite('results', name, 'Actright', 'F56');  
xlswrite('results', name, 'ActLbyR', 'F56');  
xlswrite('results', name, 'ActRbyL', 'F56');  
xlswrite('results', name, 'allArealeft', 'F56');  
xlswrite('results', name, 'totArealeft', 'F56');  
xlswrite('results', name, 'allArearight', 'F56');  
xlswrite('results', name, 'totArearight', 'F56');  
xlswrite('results', name, 'AreaLbyR', 'F56');  
xlswrite('results', name, 'AreaRbyL', 'F56');  
xlswrite('results', name, 'pcntCVleft', 'F56');  
xlswrite('results', name, 'pcntCVright', 'F56');
```

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## BIOGRAPHICAL INFORMATION

Nayan Asanani got his B.S.E.E degree from India. His father and mother both being physicians, medicine was always at back of his mind. So he decided to pursue further studies as Masters Student at Biomedical Engineering Department, University of Texas at Arlington and University of Texas Southwestern Medical Center at Dallas. His research area during this period was Optical Image Processing and Analysis. His future goal is to develop and or market healthcare products for the betterment of humankind.