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Feasibility study of trans-cranial Direct Current Stimulation in presence of Brain tumor

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Feasibility study of trans-cranial Direct Current Stimulation in presence of Brain tumor

Thesis
Submitted in partial fulfillment of the requirement for the Degree
Master of Engineering (Biomedical)
at
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Approved:

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Abstract

Feasibility study of trans-cranial Direct Current Stimulation in presence of Brain Tumor.

Trans-cranial Direct Current Stimulation has been shown to modulate cortical neuronal activity. Weak constant current is applied to the scalp using electrodes, leading to sub-threshold changes in neuronal membrane potential. Before actual clinical stimulation is performed, such systems are validated by simulating the stimulation and the resulting current flow patterns using finite element solvers. However, the reliability of such models depends upon the accuracy with which the underlying anatomy has been modeled [1]. In earlier studies it has been shown that the current flow patterns within the brain are altered due to the presence of lesioned brain tissues[2]. Here we present the first investigations of the use of tDCS in patients with brain tumors. We created a brain model from MRI scans of a patient who had a left hemisphere Glioblastoma Multiforme tumor, we modeled the resulting brain current flow and also compared the results across different tDCS modalities like conventional, HD-tDCS. Our results demonstrate the effect of tumor on the resulting current flow and the ability to modulate current pattern through the brain. However it is important to understand that tDCS is not being suggested as a treatment modality for brain tumors, but as a tool for management of the co-morbidities associated with brain tumors.
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1.0 Introduction

Trans-cranial Direct Current Stimulation (tDCS) is a non-invasive and safe technique that has the capability to modulate cortical neuronal activity, by electrodes placed on the scalp that deliver weak polarizing current. Clinical and scientific studies have shown that this technique of stimulating the brain quite often produces the desired outcomes, Finite Element Models have guided tDCS into discovering new stimulation modalities like the 4x1 ring configuration (also known as HD-tDCS) which has been shown to restrict current within the ring perimeter while still stimulating the target [3]. Newer and better configuration are being suggested, a recent study on a new montage shows that the current can be optimally delivered to a specific target with the option of maximum focality at the target or maximum intensity at the target [4].

The purpose of this thesis is to focus on investigating how a brain tumor will modulate the current flow in brain, upon stimulation using conventional one anode-one cathode tDCS. It is important to consider that a brain tumor is a mass of unnecessary cells growing in the brain. Also, every year more than 66,000 Americans alone are diagnosed with a form of brain tumor (American Brain Tumor Association.). The central nervous system (CNS) is the core of our existence and is responsible for the control of our personality, thoughts, memory, intelligence, speech, understanding; our senses- vision, hearing, taste, smell and touch; our basic body functions- breathing, heart beat and blood pressure; and how we function in our environment – movement and balance and co-ordination. Thus a brain tumor is a punishing situation for any individual. It is worth taking a note that, the current treatments associated with the brain tumor treatment, though now much improvised than earlier treatment options, it is still very harsh on the patient.
In this study, we are focusing on GBM (Glio-Blastoma Multiforme) a grade IV tumor, as classified by WHO tumor classification system. GBM tumors are generally found in the cerebral hemisphere’s of the brain, but can be found anywhere in the brain, and have a general tendency to grow rapidly. The normal steps in treating a Glioblastoma Tumor is to have a surgery and relieve pressure and remove as much of the tumor as possible. Radiation therapy and chemotherapy are always an intermittent part of the treatment. A peculiar feature of the Glioblastoma type tumors is that they arise from the supportive tissue of the brain; the glial tissue helps to keep the neurons in place and functioning well. In this study, we will investigate how using tDCS therapy in the presence of a tumor will modulate the normal current flow patterns in the brain and how tDCS could turn out to be a viable option for management of side-effects arising due to the regular cancer treatment modalities. The safety and tolerability of tDCS when used within accepted safety guidelines is well established in adults.[5][6][7].
2.0 **Background:**

Trans-cranial electrical stimulation is a promising tool in rehabilitation based on the growing body of evidence that delivery of current to specific brain regions can promote desirable neural plasticity changes. In order to better understand trans-cranial stimulation, we will briefly indulge into understanding the anatomy of the brain. The brain is comprised of two major parts the brain and the CNS (Central Nervous System). It is important to understand before performing neuronal stimulation, as electrical brain stimulation is quite often referred to as, that what region of the brain corresponds to what bodily function. The major structures of the CNS are:

a) **Cerebrum/ Cerebral Hemispheres**

- It is the largest area of the brain and consists of two hemispheres, left and right. The right cerebral hemisphere controls the left side of the body and the left hemisphere controls the right.
- The right cerebral hemisphere is responsible for creativity, intuition and innovation.
- Left side for analytic thought, logic and language.

b) **Corpus Callosum**

It is the region of the brain that connects the two hemispheres and is typically all nerve fibers.

c) **Cerebellum**

- It is the second largest brain region and again has two halves, this region of the brain is connected to the brain stem as well.
- Each hemisphere has four sections know as lobes, named as temporal, frontal, parietal and occipital.
• Frontal Lobe: It is responsible for movement, intelligence, reasoning, personality, planning, decision making, judgment initiation, inhibition and mood.

• Parietal Lobe: Has the control of intelligence, reasoning, differentiating left from right, language, reading and sensation comes from this lobe.

• Temporal Lobe: Speech, behavior, hearing, vision, smell and emotions are controlled by this lobe.

• Occipital Lobe majorly deals with vision.

d) Brain Stem

• It connects the spinal cord to the cerebrum and is the lowermost portion of the brain.

• Mid-brain, Medulla oblongata, Pons, reticular formation form the brain stem.

• The pons contains the origin of the cranial nerves

e) Mid-brain

f) Medulla Oblongata

g) Ventricles

These are the connected cavities that contain CSF (Cerebrospinal Fluid), which is produced in the choroid plexus.

h) Glial tissues (Neuroglia)

Glia is the supportive tissue of the brain. It is named from Glial cells, that form these type of tissue. The most common types of Glial cells are Astrocytes and Oligodendrocytes.

i) Cranial Nerves

j) Spinal Cord

k) Meninges
It is important to note that brain as any other organ of the body is vulnerable to diseases, which could be chronic or acute. Here for the purpose of this thesis we are investigating the effects of performing tDCS in the presence of brain tumors, specifically GBM type tumors.

2.1 Properties of Cancer Cells

One feature of both proliferating cells and cancer cells is that these cells have resting cell membrane potentials that are lower than the cell membrane potentials of healthy adults cells. Also, cancer cells are more easily detached and do not exhibit contact inhibition of their growth. In a sense cancer cells have become desynchronized from the rest of the body [8]. The major hypothesis is that cancer cells have different electrical and metabolic properties due to abnormalities in structure outside of the nucleus. Characteristic feature of cancerous cells that affect their electrical activity:

- Cancer cells are less efficient in their production of cellular energy (ATP)
- Cancer cells have cell membranes that exhibit different electrochemical properties and a different distribution of electrical charges than normal tissues
- Cancer cells have different lipid and sterol content than normal cells
- Cancer cells have altered cell membrane compositions and membrane permeability, which results in the movement of potassium, magnesium and calcium out of the cell and the accumulation of sodium and water into the cell.
- Cancer cells have lower potassium concentrations and higher sodium and water content than normal cells[8]

Also electrical properties of cancer cells are different than that of the electrical properties of the normal tissues, that surround them. Cancer cells have a negative charge on their cell surfaces. These abnormalities result in cancer cells having lower trans-membrane potentials than normal
cells and altered membrane permeability [8]. As mentioned before the conventional treatment for any form of cancer involves a surgical removal of the tumor, and depending upon the type and stage of tumor, it is followed by chemotherapy by drugs or radiation. It has been observed that post-treatment patients show side-effects like depression, pain. They also complain about reduced cognitive function. These side-effects are not limited to any particular kind of cancer, but are linked with the treatment modality.

2.2 transcranial Direct Current Stimulation (tDCS)

Weak electric currents modulate neuronal activity.[9] Trans-cranial Electrical Stimulation is a promising tool in rehabilitation based on the growing body of evidence that delivery of current to specific brain regions can promote desirable plastic changes[10]. Electroconvulsive Therapy( ECT) and trans-cranial Direct Current Stimulation (tDCS) are the two important forms of trans-cranial electrical stimulation. However of particular interest are neurostimulation modalities that are low cost, portable and simple to implement. Further-more stimulation should be applied using low intensity current in a manner that is safe, well tolerated and can be delivered concurrently with physical rehabilitation and other therapies. Currently trans-cranial Direct Current Stimulation has been gaining considerable interest because it possess all these desired qualities [11]

A constant direct current (DC) is a flow of electrical charge whose magnitude and direction remains unchanged. tDCS is a non-invasive form of brain stimulation which employs a relatively low magnitude, non-convulsive constant DC current targeted to the cerebral cortex through patch electrodes against the head[12]. Historically, the inception of the idea of weak electrical current stimulation began in the late 18th Century, when Giovanni Aldini reported successful treatment of a melancholic patient with the application of DC to the head[13]. Since
the 1960’s systemic studies have been undertaken to investigate the effects of tDCS on depression, using experimental protocols fundamentally different than those used today[14].

The turning point in tDCS history was in late 1990’s when it was discovered that weak direct currents were able to penetrate the skull and stimulate the vestibular system[15]. In a later study , it was shown that tDCS had similar but faster beneficial effects compared to pharmacological treatment[16]. In contrast to pharmacotherapy, non-invasive electrotherapy offers the potential for both anatomically specific brain activation and complete temporal control—since electricity is delivered at the desired dose instantly and there is no electrical “residue” as the generated brain current disappears when stimulation is turned off. Thus, transcranial Direct Current Stimulation can be customized and individualized to specific brain targets in ways not possible with other interventions in order to optimize a particular rehabilitative outcome[1].

Conventionally tDCS is performed with a DC generator delivering a constant current and two electrodes . The DC source can be adjusted for the desired current, whose amplitude is generally varied between 0.5 to 2mA [17]. The current is usually delivered through large electrodes generally having an area of 25-35cm²[3].Generally tDCS lasts for 10-20 minutes per session, with the current amplitude kept at a constant value, however the current is commonly ramped up and down, at the beginning and the end of the session in order to reduce cutaneous sensation and avoid retinal phosphenes[17]. tDCS flows in a single direction, from anode (positively charged electrode), to the cathode (negatively charged electrode). Thus, based on the targeted cortical area, tDS is classified into ‘anodal’ or ‘cathodal’ type stimulation. Studies have suggested that anodal tDCS enhances the activity of the neurons, whereas cathodal tDCS suppresses it.
It is important to understand that the precise pattern of current flow through the brain is determined not only by the stimulation dose, but also by the underlying anatomy and tissue properties. In predicting brain current flow using computational models, it is thus important to precisely model both the stimulation itself and the relevant anatomy upon which it is delivered, on an individual to individual basis. Especially important is the recognition that individual anatomical idiosyncrasies can result in significant distortions in current flow. This is particularly evident when skull defects, brain lesions occur.
3.0 Methods

3.1 MRI Derived Computational Modeling

Computational models of tDCS range in complexity from concentric spheres to high resolution models based on individual’s magnetic resonance image (MRI). The appropriate level of modeling detail depends on the clinical question asked (as well as the computational resources available). Whereas simple geometries may be solved analytically[18], realistic geometries employ specialized softwares including numerical solver’s (namely finite element methods [FEM]) [19]. Regardless of the complexity, all forward models share the primary outcome of correctly predicting brain current flow during transcranial stimulation to guide clinical therapeutic delivery[19]. It has to be understood that as tDCS continues to prove more and more efficient in dealing with neurological disorders and its clinical relevance is shown across various neurological disorders, it becomes more and more important to understand the role of such computational forwards models.

Figure 1(a)  Figure 1(b)  Figure1(c)
**Figure 1:** Model renderings. Figure 1(a) Showing the complete model with the scalp, Figure 1(b) showing the brain matter, Figure 1(c) Cut segment of the entire brain showing various tissue masks, tumor is shown in yellow.

As shown in the Figure 1, the computational model has been generated from the MRI scans of a patient having a GBM type brain tumor in the left hemisphere. The tumor is shown in yellow in the images. Figure 1(c) shows the tumor in a cut segment view of the head. The different colors represent different tissue masks that have been segmented and modeled in this particular study. The tumor masks that have been modeled are skin, skull, csf (cerebrospinal fluid), gray matter, white matter and tumor. The MRI was derived using a 1.5 T GE scanner, the scan was anonymized hence no information regarding the patient is available.

The individualized head model was created using 1mm\(^3\) resolution using T1 weighted magnetic resonance imaging (MRI) scans of the patient. Automated segmentation algorithm was initially used to accomplish the segmentation, the algorithm used was Statistical Parametric Mapping (SPM8). Additional post-processing was applied via MATLAB(2010b, The MathWorks, MA) algorithms developed at the Neural Engineering Lab, City College of New York. Also, tumor was not segmented in automated segmentation thus additional manual segmentation was done to segment the tumor and certain anatomical elements have overlapping intensities and boundaries which needed manual correction. Hence Manual Correction was performed using ScanIP+FE (Simpleware LTD, UK). Filters were used to clear rough patches of tumor (figure 1a.) The figure 2(a) shows the segmentation results for a healthy head. As it can be observed from the figure 2(b) and figure 2(c). The normal anatomy of the brain has been altered.
On creating the 3D models, a peculiar finding was that in the subject of study, the anatomy of the brain had been altered due to the presence of the tumor. As seen in Figure 2, the gray matter had been pushed forward.

**Figure 2**: The tumor head model compared to the normal head anatomy, depicting the shift in change/modulation in the normal anatomy of the brain.

As it can be observed that the normal anatomy of the brain has been modified and the gray matter has been pushed towards the front of the head. The following Figure 3 shows us the exact location and the positioning of the tumor within the skull relative to other tissues.
**Figure 3:** A detailed depiction of the tumor within the head, with all other masks shown with transparency, to give an estimate of the size and the location of the tumor within the head.

Sponge pads and electrodes measuring 5x7cm, were created in Computer Aided Design(CAD) program (SOLIDWORKS, DS Solid Works, MA.) The large electrodes were rectangular in shape with a minutely curved trajectory to accommodate for the scalp anatomy. Similarly a curve was sketched in an orthogonal plane along which the cross-sectional profile of the pad was swept. The process was repeated for all the pad positioning using the larger pads, taking into consideration the curvature at the site of placement.

The pad and the electrode were then imported into ScanCAD (Simpleware LTD, UK.) alongside the segmentation model as a Standard Tessellation Language( STL) file. The pads were then placed according to the specific montage, with the return electrode over the supra-
orbital. Once these models CAD models were placed onto the head, they were imported back into the ScanIP+FE for meshing.

In order to accommodate for the shift in the anatomical structures the pads need to be placed in accordance to the underlying anatomy. Such a method of placing pads is more optimized for the underlying anatomy and hence relatively more accurate in accommodating and predicting the change in current flow patterns. In predicting brain current flow using computational models, it is extremely important to precisely model both the stimulation itself and the relevant anatomy upon which it is delivered on an individual basis [1]. Also, relevant is the recognition that individual anatomical idiosyncrasies can result in significant distortions in current flow. Such that could be evident due to presence of a non-bodily matter. This is particularly apparent when skull defects and brain lesions occur [2]. Hence, we hypothesize that the presence of brain tumor will have a significant impact on the current flow through the adjacent brain regions.
Figure 4: Figure 4(a) Anatomical placement of the pads in order to accommodate for the shift in the anatomy. Figure 4(b) Standard placement of the pads referencing to the 10/20 electrode placement paradigm. Figure 4(c) Showing how the shift in the anatomy has caused a separation of 46.8mm (from center to center).

Here in this research, there are two parts, one being to show that using conventional tDCS, we hypothesize that, the presence of the tumor will modulate the current flow, having taken that hypothesis it is important to note that, the shift as it is evident from Figure 2, and thus the clinicians should take into consideration the placement of pads onto patient scalp in conditions such as these will need to be optimized corresponding to the amount of change in the anatomy.

Figure 4 indicates that the distance between the two pad placements (i) Standard: Placed by standard placement procedure i.e. 10/20 Electrode placement paradigm, without accommodation of the change in the underlying anatomy. (ii) Anatomical: Optimized by accommodating for the underlying anatomy, by shifting the pads 46.8mm towards the front.

As a second part of this research will show that conventional tDCS though proven to have advantages lacks the focality, in order to show this a 4x1 ring configuration has been used. The HD-tDCS configuration has been shown to restrict the physiological effects of the current to an area within the ring perimeter [3].

3.2 Finite Element Modeling (FEM)
A FE (Finite Element) model based on electrostatic volume conduction physics was created in COMSOL Multiphysics 3.5a (COMSOL, Inc., MA). Each mesh was imported into this FE solver and isotropic conductivities were assigned as given in the following table:

<table>
<thead>
<tr>
<th>No.</th>
<th>Tissue mask</th>
<th>Assigned Conductivity (Siemens/Meter)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Gray Matter</td>
<td>0.276</td>
</tr>
<tr>
<td>2</td>
<td>White Matter</td>
<td>0.126</td>
</tr>
<tr>
<td>3</td>
<td>CSF (Cerebro Spinal Fluid)</td>
<td>1.65</td>
</tr>
<tr>
<td>4</td>
<td>Skull</td>
<td>0.01</td>
</tr>
<tr>
<td>5</td>
<td>Scalp/Skin</td>
<td>0.465</td>
</tr>
<tr>
<td>6</td>
<td>Tumor</td>
<td>0.200</td>
</tr>
<tr>
<td>7</td>
<td>Air</td>
<td>1e^-15</td>
</tr>
<tr>
<td>8</td>
<td>Sponge Pad</td>
<td>1.4</td>
</tr>
<tr>
<td>9</td>
<td>Gel</td>
<td>0.3</td>
</tr>
<tr>
<td>10</td>
<td>Electrode</td>
<td>5.99e^7</td>
</tr>
</tbody>
</table>

Due to the data suggesting that the tumor mass can be electrically conductive[8]. We inorder to have a robust result set, assigned the tumor with a range of conductivity values. The values and the naming convention used are:

- Resistive (Comparative) : 0.126 s/m ~ White matter
- Conductive (Comparative) : 1.1 s/m
- Very Conductive/Merged : 1.65 s/m ~ CSF (to replicate post-surgery condition)
Boundaries conditions were applied as electrically insulated to all exterior boundaries and continuous to all interior boundaries. The exterior boundaries of the electrodes were modified to be 1A/m² corresponding to an inward current injection of about 1mA in the heterogeneous skin model. The Laplace equation was solved and linear system iterative solver of conjugate gradients was used (with a relative tolerance of 1x10⁻⁶).

After solving, boundary plots of the cortical surface (gray matter) were plotted with a false color map and scaled to a visible range. This scale was then normalized to per 1mA of current injection. Additional lighting was used in some images to better visualize brain morphology and the spatial distribution of electric field.

In order to accommodate for the further studies smaller electrodes and gel measuring 11.00mm were created using the same CAD program. Like before the CAD models were imported into ScanCAD( Simpleware LTD, UK) alongside the segmentation model as a STL file. The pads were placed according to the 4x1 configuration[3]. Once the CAD models had been appropriately placed they were converted to segmentation masks and exported back into ScanIP+FE for meshing. For the optimized model was generated by using the international 10/10 system (electrode distance is 10% of the circumference from nasion to inion and from left to right preauricular points); each electrode is modeled as a cylinder of 11mm diameter and 2mm depth. Additionally, a 1mm thick gel layer with a surface area equal to that of the cylinder rests directly under the electrode. The labeled volume is then translated to a finite element mesh using Scan FE(Simpleware LTD, UK).

Here, based upon the literature suggesting tumor to be a mass of conductive tissues, we have performed stimulations using 4 values of tumor conductivity. The four values used a re
0.126, 0.200, 1.1 and 1.65 s/m these replicate the white matter, mixture of glial/Schwann cells, and 1.65 ~ CSF respectively.
4.0 Results

Conventional tDCS (one anode – one cathode), used here has been shown to target the desired cortical region, directly underneath the pads which has been previously demonstrated by our research group. As mentioned before the tumor has been modeled to have varying conductivity values. Hence the results are grouped according to the conductivity value of the tumor.

4.1 Results I: Tumor Conductivity = 0.200 s/m

The following Figure 5 shows the stimulation results for the Standard Electrode placement montage. According to the previous studies, the peak cortical stimulation is seen directly underneath the pads and between the two electrodes. Fortunately enough, even though the motor strip has been shifted, peak cortical stimulation can be seen at the motor cortex. The peak electric field and the current density (in cortex) for this montage was reported as 0.330 V/m/mA and 0.091mA respectively.

Figure 5: Stimulation results for Standard Montage for tumor conductivity 0.200 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
Figure 6 shows the stimulation results for the Anatomical Electrode placement montage. However contrary to the expectation of having peak cortical stimulation under the pads, it has moved towards the front. The peak electric field and the current density for this montage was reported as 0.330 V/m/mA and 0.091 mA respectively.

**Figure 6:** Stimulation results for the Anatomical Montage, the tumor conductivity is 0.200 s/m. On the right, additional lighting has been used in order to represent that anatomy with higher clarity. The peak cortical intensity is 0.330 V/m/mA.
From the slice plots of the electric field taken through the center of the tumor, it can be observed that there is a higher electric field in the region around the tumor in the standard electrode placement montage, which can be seen from the Figure 7.

**Figure 7:** Slice plot for Electric field for the tumor conductivity of 0.200 s/m. The peak cortical stimulation intensity in both montages is 0.330 V/m/A. The slice is taken through the center of the tumor.
Comparing the current density plots in both the montages, however does not indicate a notable difference. The current density plot is shown in Figure 8. The peak cortical current density was 0.091 mA. However the peak current density across the tumor was 0.066 mA.

**Figure 8:** Slice plots for current density, for tumor conductivity of 0.200 s/m. The peak current density seen through the cortical region is 0.091 mA. The slice is taken through the center of the tumor.
4.2 Results II: Tumor Conductivity = 0.126 s/m (~ White Matter)

The stimulation results seen here in this section are for the tumor conductivity value 0.126 s/m which is equal to the conductivity of the white matter. However this condition can be said to be a resistive condition where in the tumor is resistive as compared to the previous condition.

![Standard Montage (0.126)](image)

Figure 9: Stimulation results for Standard Montage for tumor conductivity 0.126 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
As seen from the Figure 9 and Figure 10, the stimulation results are not much different from that seen in the previous condition, for both the Standard and the Anatomical Montages.

**Figure 10:** Stimulation results for Anatomical Montage for tumor conductivity 0.126 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
The peak electric field and current density for this condition was reported as 0.330 V/m/mA and 0.091 mA respectively for Standard montage and 0.330 V/m/mA and 0.091 mA respectively for the anatomical montage.

Figure 11: Slice plot of the electric field for the tumor conductivity of 0.126 s/m. The peak stimulation value for both the montages is 0.330 V/m/mA. The slice is through the center of the tumor.

The Slice plot for the electric field has been shown in Figure 11 and as it can be observe there is no significant change in the electric field from what was seen in the condition of tumor conductivity being 0.200 s/m.
However the slice plot for current density shows that there is less current flow through the tumor as compared to the previous condition of tumor conductivity 0.200 s/m. This is shown in Figure 12.

The peak cortical current density was 0.091 mA. However the peak current density across the tumor was 0.041 mA.

Figure 12: Slice plot of the current density for the tumor conductivity of 0.126 s/m. The peak current density for both the montages is 0.091 mA. The slice is taken through the center of the tumor.
4.3 Results III : Tumor Conductivity = 1.1 s/m

The stimulation results in this section are for the tumor conductivity value of 1.1 s/m which can be inferred to as conductive to both the previous conditions, where the tumor conductivity were 0.200 and 0.126 s/m.

The Figure 13 shows the stimulation results for the Standard montage, and the reported peak electric field and current density values were 0.330 V/m/ mA and 0.091mA respectively, which are comparable to the values from the previous conditions.

Figure 13: Stimulation results for Standard Montage for tumor conductivity 1.1 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
The Figure 14 shows the stimulation results for the anatomical montage and peak electric field and current density values reported for this montage are 0.330 V/m/mA and 0.091mA.

Anatomical Montage (1.1)

**Figure 14:** Stimulation results for Standard Montage for tumor conductivity 1.1 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
The slice plots for electric field for both the anatomical and the standard montage are shown in the Figure 15 and it can be observed that there is an increase in the electric field as compared to the previous conditions, also hot spots can be seen around the periphery of the tumor.

**Figure 15:** Slice plot of the electric field for the tumor conductivity of 1.1 s/m, The peak stimulation intensity for both the montages is 0.330 V/m/mA. The slice was taken from the center of the tumor.
Figure 16 shows the current density plots for the anatomical and standard montage, which clearly indicate an increased current flow through the tumor in both the conditions as compared to the previous conditions. The peak cortical current density was 0.091 mA. However the peak current density across the tumor was 0.363 mA.

**Figure 16:** Slice plot of current density for the tumor conductivity of 1.1 s/m. The peak current density for both the montages is 0.091 mA. The slice has been taken through the center of the tumor.
4.4 Results IV: tumor conductivity = 1.65 s/m (~CSF)

This condition was modeled in order to replicate the post-surgery condition of the tumor, where the tumor is replaced by CSF, which relates to the previous study by our research group on stroke heads. The stimulation results are as shown in Figure 17.

**Figure 17:** Stimulation results for Standard Montage for tumor conductivity 1.65 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
The Figure 17 shows the stimulation results for the standard montage, where the reported peak stimulation intensity was 0.330 V/m/mA and the current density (in cortex) was 0.091mA. The peak cortical stimulation intensity for the anatomical montage was 0.330 V/m/mA and the current density was 0.091mA, which can be seen in the Figure 18.

Figure 18: Stimulation results for Anatomical Montage for tumor conductivity 1.65 s/m, on right is the stimulation result with additional lighting in order to better represent the anatomy. The peak cortical intensity is 0.33 V/m/mA.
However the slice plots show that an increased electric field in the cortical region around the tumor, as seen previously in the condition, where the tumor conductivity was 1.1 s/m. The slice plot is shown in Figure 19

**Figure 19:** Slice plot of the electric field for the tumor conductivity 1.65 s/m. The peak cortical stimulation was 0.330V/m/mA. The slice has been taken through the center of the tumor.
The current density slice plots again show an increased current flow through the tumor, as seen in Figure 20 for both anatomical and standard montages. Which is again similar to what was seen for the condition where the tumor conductivity was 1.65.

The peak cortical current density was 0.091 mA. However the peak current density across the tumor was 0.5 mA.

**Figure 20:** *Slice plot of current density for the tumor conductivity 1.65 (CSF). The peak current density (Cortex) is 0.091mA. The slice has been taken through the center of the tumor.*
5.0 Discussion and Future Work:

From the stimulation results in for condition I with tumor conductivity value 0.200 s/m, it can be seen that the peak electric field intensity 0.330 V/m/mA for both the anatomical and standard montages lies within the normal peak stimulation intensity range for healthy heads. However for the Anatomical and Standard montage, the peak stimulation is seen at different locations. Which can be reasoned to be because of the pads are moved closer to each other the current tries to take the least resistive and the shortest path to the ground electrode.

The peculiar feature of the stimulation pattern with the tumor conductivity to be 1.1 and 1.65 s/m is that comparing to the condition where the tumor conductivity was 0.126 and 0.200 s/m is that a higher electric field is seen towards the back of the head, this is in convergence with the results obtained from the slice plots for current density. The characteristic property, that current is inversely proportional to the resistivity holds and hence as the conductivity of the tumor increases, a higher current flow is seen through the tumor.

As discussed before, post completion of conventional cancer treatment, a variety of complications arise in general with the cancer treatment, which include neurological disorders like depression, pain, reduced cognitive ability. Also, depending upon the surgical removal, there might be loss of function, hence requiring rehabilitation.

Previous studies from our research group has shown the effectiveness of tDCS in the mentioned neurological conditions. Though optimizing for the change in the underlying anatomy (Anatomical Montage), as seen from the stimulation results, the motor cortex, which is the target of such stimulation is not being activated with peak stimulation intensities. It holds that the peak
cortical stimulation using large pads is less targeted and between the two pads. Hence newer approaches like HD-tDCS (High Definition- transcranial Direct Current Stimulation) are being developed and being validated to replace the conventional one anode one cathode transcranial Direct Current Stimulation with large electrodes.

The figure shows the stimulation results for the same tumor head but with the HD-tDCS 4x1 ring configuration, where 4x1 stands for 4 return and 1 active electrode. As it can be seen, the current flow is restricted to within the ring perimeter and the peak stimulation intensity and current density noted are ---- and ----- respectively. Which are within the normal healthy subject peak cortical intensities as shown by previous studies by our research group. It has also been shown that in the 4x1 montage, varying electrode center position ring diameter, stimulation polarity, duration and amplitude represents a large parameter space.[3]

As seen from the results above, though conventional tDCS, fortunately in this case, using the standard placement does activate/ stimulate the targeted cortical region, though it is not directly underneath the sponge pads. Hence, as previously shown [3], tDCS using large sponge electrodes is not a good at targeted neuronal stimulation and depends heavily on the underlying anatomy. However, newer tDCS approaches like HD-tDCS are being developed which has been shown to have a higher focality as compared to conventional tDCS (One anode –One cathode).

The following set of images show the stimulation results for the 4x1 (HD-tDCS). 4x1 is the naming convention used to suggest that, there is 1 anode in the center and 4 cathodes around it, for anodal stimulation, it can also be reversed to achieve cathodal stimulation. It has also been shown that in the 4x1 montage, varying electrode center position ring diameter, stimulation polarity, duration and amplitude represents a large parameter space.[3]
The following are the results of stimulation for the HD-tDCS, the peak cortical stimulation intensity is 0.313 V/m/mA and the peak cortical current is 0.86mA.

Figure 21: Stimulation results for HD-tDCS montage, for the tumor conductivity of 0.200 s/m. The peak cortical stimulation is 0.313 V/m/mA. Additional lighting has been used in the figure on the right to represent the anatomy with higher clarity.
Figure 22: The figure shows the stimulation results for the HD-tDCS montages, for the tumor conductivities 0.126 and 1.1 s/m. The peak cortical stimulation is 0.313 V/m/mA. Additional lighting has been used in order to represent the anatomy with higher clarity.
6.0 References


