Concentric Tube Robotics: Non-Linear Trajectories for Epilepsy Surgery

The Harvard community has made this article openly available. Please share how this access benefits you. Your story matters

<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Citable link</td>
<td><a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:27007762">http://nrs.harvard.edu/urn-3:HUL.InstRepos:27007762</a></td>
</tr>
<tr>
<td>Terms of Use</td>
<td>This article was downloaded from Harvard University’s DASH repository, and is made available under the terms and conditions applicable to Other Posted Material, as set forth at <a href="http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA">http://nrs.harvard.edu/urn-3:HUL.InstRepos:dash.current.terms-of-use#LAA</a></td>
</tr>
</tbody>
</table>


Concentric Tube Robotics: Non-linear Trajectories for Epilepsy Surgery

Isdin M. Oke
Harvard Medical School, Irving London Society, Class of 2016

Tomer Anor PhD, Patrick Codd MD, Joseph R. Madsen MD
Department of Neurosurgery
Boston Children’s Hospital

Recurrent and unprovoked epilepsy seizures affect more than 50 million people worldwide. Despite advances in antiepileptic drugs, more than 30% of patients continue to demonstrate abnormal neuronal activity; at present, this is primarily treated with surgical intervention\(^1,2\). In 80% of patients with medically intractable seizures, the epileptic focus is located in the medial temporal lobe and neurosurgical treatment of these foci requires large skin incisions, extensive bone removal, and potentially harmful excision of brain tissue, several times the size of the epileptic focus\(^3\).

Minimally invasive approaches rely on straight endoscopic cannula to either deliver depth electrodes to further refine the target area or lasers to ablate the epileptogenic tissue. However, straight cannulas struggle to properly access non-linear targets such as the amygdalo-hippocampal region often implicated in medial temporal lobe epilepsy. Furthermore, the cannulas must be positioned to avoid critical structures such as blood vessels and cerebrospinal fluid filled ventricles. We propose to overcome the limitations of straight cannulas by introducing curved concentric tubes to perform non-linear 3D minimally invasive trajectories.

Concentric tube robots are composed of multiple superelastic Nitinol tubes arranged telescopically\(^4\). Each segment can be independently translated and rotated giving rise to two degrees of freedom that can be modeled computationally. Parameterization of the robot characteristics in conjunction with a global pattern search optimization method can determine the optimal trajectory to achieve the greatest coverage of a target volume\(^5\). Semi-automatic segmentation of MRI images can generate surface models of target structures as well as obtain coordinates for entry points and boundary constraints. In addition, we can incorporate weighted constraints for surgically critical structures such as ventricular spaces and blood vessels.

We demonstrate that a multi-segmented concentric tube trajectory can consistently achieve a greater percent coverage of a target hippocampus than a manually defined linear trajectory. We also demonstrate that the total skull surface area from which the target can be approached increases as a function of trajectory complexity. Most interestingly, the magnitude of benefit for each additional segment was found to decay such that the greatest increase in target coverage occurs between \(N = 1\) and \(N = 2\) with very gradual improvement for \(N > 3\). Results suggest that the addition of a single curved segment to a linear laser probe will dramatically increase both the target coverage and potential entry positions. Ultimately, the optimized parameters generated will serve as guidelines to fabricate a prototype concentric tube navigation system. As a novel non-linear surgical platform, concentric tube robotics promises an exciting advance in laser ablation neurosurgery.
Table of Contents

I. Introduction ........................................................................................................................... 3
   a. Epilepsy definition, epidemiology and medical/surgical treatments................................. 3
   b. Limitations of current minimally invasive surgical approaches ........................................... 4
   c. Novel proposed non-linear approach ................................................................................... 5
      i. Hardware: Concentric tube trajectory .............................................................................. 5
      ii. Software: Optimization algorithm .................................................................................. 6
   d. Specific Aims ....................................................................................................................... 7

II. Materials and Methods ......................................................................................................... 9
   a. Sample patient population .................................................................................................. 9
   b. Model generation ............................................................................................................... 9
      i. Freesurfer segmentation .................................................................................................. 9
      ii. 3D Slicer model generation ......................................................................................... 10
      iii. Meshlab, Netfab, Matlab triangular mesh generation .................................................. 10
   c. Parameterization ............................................................................................................... 12
      i. Modeling concentric tube trajectory .............................................................................. 12
      ii. Modeling depth electrode trajectories ......................................................................... 13
      iii. Modeling laser tip behavior ......................................................................................... 13
   d. Global patternsearch optimization algorithm ...................................................................... 14
   e. Graphic user interface ........................................................................................................ 15

III. Results ............................................................................................................................... 17
   a. Curved depth electrode modeling ..................................................................................... 17
   b. Distribution of solutions from the optimization algorithm .................................................. 17
   c. Single entry point analysis ................................................................................................ 18
   d. Optimized trajectories vs. manual trajectory ..................................................................... 18
   e. Global entry analysis ........................................................................................................ 19
   f. Challenging entry meta analysis ....................................................................................... 19

IV. Discussion ........................................................................................................................... 20
   a. Assumptions underlying model, parameterization and optimization ................................... 20
      i. Defining target and navigable brain region ..................................................................... 20
      ii. Defining probe tip and trajectory .................................................................................. 21
      iii. Defining skull surface entry ......................................................................................... 22
   b. Curved depth electrode modeling ..................................................................................... 22
   c. Distribution of solutions from the optimization algorithm .................................................. 23
      i. Initial position problem .................................................................................................. 23
      ii. Distribution of solutions ............................................................................................... 25
   c. Single entry point analysis ................................................................................................ 25
   d. Optimal trajectories vs. manual trajectories ..................................................................... 26
   e. Global entry analysis ........................................................................................................ 27
   f. Challenging entry analysis ............................................................................................... 27

V. Future Directions ................................................................................................................ 28
   a. Improving the algorithm .................................................................................................. 28
   b. Surgical interface .............................................................................................................. 28
   b. Meta analysis of skull entry ............................................................................................. 29

VI. Figures ............................................................................................................................... 30

VII. Tables ................................................................................................................................. 40

VIII. References ........................................................................................................................ 41
1. Introduction

a. Epilepsy definition, epidemiology and medical/surgical treatments

Recurrent and unprovoked epilepsy seizures affect more than 50 million people worldwide.6 A seizure is the clinical expression of abnormal synchronous discharge of neurons in the cerebral cortex. Focal seizures have a restricted regional onset followed by spread to neighboring local or remote brain regions potentially causing significant clinical consequences. Electrodes placed on the surface of the brain or embedded within the brain can be used to localize the epileptogenic region. Long-term monitoring allows neurologists to further define the neuroanatomical origin and develop treatment strategies7,8. The medial temporal lobe is an important region that is often implicated as the source of debilitating seizures that generalize and spread throughout the brain9,10. Within the medial temporal lobe, foci are often localized to the parahippocampal structures, a region responsible for the consolidation of memories11. Antiepileptic therapy traditionally involves polytherapy from a selection of antiepileptic drugs that is titrated to a maximally tolerated dosage providing optimal seizure control12. Despite advances in antiepileptic drugs, more than 30% of patients continue to demonstrate abnormal neuronal activity; at present, this is primarily treated with surgical intervention1,2. Current neurosurgical treatment of these foci requires large skin incisions, extensive bone removal, and potentially harmful excision of brain tissue, several times the size of the defined epileptogenic focus13. In attempt to minimize the amount of tissue damaged during surgical procedures, several minimally invasive techniques have been developed. The majority of
minimally invasive approaches rely on straight cannula to either deliver depth electrodes to further refine the epileptogenic area or laser probes to ablate the epileptogenic tissue\textsuperscript{14}.

b. Limitations of current minimally invasive surgical approaches

As mentioned, current minimally invasive approaches to epilepsy surgery rely on defining a surgical target, finding an appropriate skull entry point and using a linear laser probe to access and ablate the epileptogenic brain region (\textit{Figure 1}). The Visualase laser-induced interstitial thermal ablation apparatus is a commercially available device that introduces a laser fiber to raise the temperature of target tissue and irreversibly destroy the region surrounding the probe tip\textsuperscript{15}. Despite the dramatic improvement of such technology over removing large amounts of cortical tissue, there are two major limitations that pose challenges to effectiveness and widespread use. The first limitation is that the surgeon must manually define the best entry and target locations for the linear probe aided by only the pre-operative MRI images. Working in two dimensions from the coronal MRI slices, the surgeon must define points for the entry and target locations. Naturally, the brain is a three dimensional structure filled with obstacles such as blood vessels, ventricles and nuclei that must be avoided in trajectory planning. The challenge of finding an optimal trajectory solution given the complexity of the anatomical constraints is non-trivial. Therefore, manual definition is both difficult and time consuming for the surgeon, often requiring over an hour of iteratively cycling through MRI slices to ensure an appropriate selected trajectory. The second major disadvantage stems from the geometric constraints of a linear trajectory. The surgeon is very limited in the locations on the skull surface from which he/she can select to approach the deep epileptogenic region. The surgeon must aim
to align the axial direction of the probe tip with the axial dimension of the desired target. Because of the linear trajectory, the surgeon has no way to avoid obstacles between the skull entry and targets without selecting a different initial entry position. Therefore, the two major limitations for current minimally invasive epileptic surgery involve the non-trivial challenge for the surgeon to manually find the trajectory that covers the greatest amount of target as well as the total diversity in the possible entry locations.

c. Novel proposed non-linear approach

We hope to address the limitations of current minimally invasive epilepsy surgery by tackling challenges in both the hardware and software (Figure 1). An overview of both challenges and plans to overcome them are described, however the majority of the thesis will focus on the software optimization problem.

i. Hardware: Concentric tube trajectory

To overcome the restrictions imposed by linear trajectories, we hope to introduce the use of non-linear concentric tube trajectories to navigate around neuroanatomical obstacles. Concentric tube cannula are composed of multiple superelastic Nitinol segments arranged telescopically. Each segment can be independently translated and rotated giving rise to the ability to make complex motions in three-dimensional space. Since the shape and displacement of each telescoping section is kinematically decoupled from that of the proximal sections the cannula can reliably navigate in constrained environments. A robotic platform can control the trajectory of the concentric tube cannula, which is ideally suited for performing complex tasks required in minimally invasive neurosurgery. The cannula
possess cross sections comparable to needles and catheters, but are capable of substantial actively-controlled lateral motion and force application along their entire length. In the last few years, substantial progress has been made in developing concentric tube robotic technology. Mechanics models have been developed for computing the kinematics and deformation due to external loading. Solution of the anatomically constrained inverse kinematic problem has been considered. Real-time implementations of position control and stiffness control have been demonstrated in the laboratory and in intracardiac animal trials\textsuperscript{16–21}. In addition to developing the hardware robotics to control the motion of the concentric cannula, we will be optimizing the mechanical properties of the tip to achieve smaller diameters and tighter radii of curvature (Figure 2). Overall the hardware improvements will dramatically increase the flexibility and adaptability of the laser trajectory to avoid critical obstacles.

ii. Software: Optimization algorithm

In order to streamline the process for the surgeon to select and define the surgical target and the skull entry position, we hope to apply a number of algorithms to transform the patient specific MRI into a series of three dimensional models and develop an algorithm to model the concentric curved trajectory given the neuroanatomical constraints. Segmentation is the process of parceling an MRI scan into the relevant structures. Although this can be achieved manually, high throughput automated segmentation algorithms have been developed that can effectively assign values to each voxel in an MRI a probability of belonging to a specific structure\textsuperscript{22,23}. The segmented label maps can then be transformed into three-dimensional models that will represent the surgical targets and neuroanatomical
obstacles (Figure 3). Parameterization of the robot characteristics in conjunction with a global pattern search optimization method can determine the optimal trajectory to achieve the greatest coverage of a target volume. Details of the algorithm approach and goals will be discussed in Section II. The goal is to develop an interface that can provide the optimal skull surface entry location to ablate the maximum amount of hippocampal target given the defined neuroanatomical obstacles.

d. Specific Aims

This thesis hopes to contribute to the development of the novel approach to optimal design of concentric tube robots targeted at applications in neurosurgery. The work will be presented as follows: We will conclude the introduction with a summary of the concrete project aims. In Section II we present the methodology behind transforming patient MRIs into compatible volume representations, provide a new concentric trajectory parameterization particularly suited for a given optimization strategy, and define the optimization, objective and cost functions employed in the algorithm. In Section III we present the results of applying the algorithm to four clinically challenging cases. In Section IV we will discuss the significance of the results and in Section V we will summarize our results and present the next steps for future investigation.
Aim 1: Develop algorithm for concentric tube behavior given neurosurgical constraints.

We seek to develop an interface to solve multiple non-linear optimization problems. Building on existing algorithms developed by our group, we will model the trajectory of an N segment concentric tube cannula in the brain. We will focus on integrating and prioritizing neurosurgical constraints. We will apply semi-automatic segmentation of MRI images to define surgical targets, optimal entry points and critical structures. We will incorporate into the algorithm user controllable weighting factors for each critical structure. The resulting algorithm will allow the surgical planning team flexibility to find the optimal trajectory given a patient specific problem.

Aim 2: Demonstrate principles of non-linear trajectories in depth electrode placement

We will use theoretic models of epileptogenic regions of interest to demonstrate the ability of curved electrode trajectories to replace multiple linear trajectories. We will categorize the general approaches for designing non-linear trajectories. As proof of concept, we will illustrate a patient case where multiple straight depth electrodes used to define an epileptogenic region can be replaced with curved depth electrodes.

Aim 3: Quantify effectiveness of concentric tube approach in laser ablation epilepsy surgery

We will model the ablation radius of a Visualase MRI guided laser. Given the geometry of a defined hippocampal target, we hope to compare the effectiveness of a straight cannula to the multi-segmented curved cannula and determine how much each additional segment contributes to the ablated fraction of the surgical target.
II. Materials and Methods

a. Sample patient population

In this IRB approved investigation we will be using the pre- and post-operative T1 sagittal MPRAGE MRIs of one patient who underwent depth electrode placement and four patients who underwent a Visualase laser ablation procedure to remove epileptogenic tissue. The operations were performed between August 2012 and December 2015 and the pediatric patient population was between the ages of 14 and 18. In each Visualase case, the patient was experiencing medically intractable seizures originating from epileptogenic foci within the hippocampal region and each patient was treated with MRI guided straight laser ablation. The surgeon manually defined the entry and target positions pre-operatively and the Visualase software (http://www.visualaseinc.com/) determined the linear trajectory between the two points. Post-operative MRIs were analyzed using 3D Slicer (http://www.slicer.org) to obtain the coordinates of entry and target points and interpret the performed trajectory. Furthermore the radius of ablation was calculated based on the region of damaged tissue surrounding the probe tip from the post-operative scan.

b. Model generation

i. Freesurfer segmentation

Freesurfer is an open source software suite for processing and analyzing human brain MRI images developed at the Martinos Centre for Biomedical Imaging by the Laboratory for Computational Neuroimaging. A series of algorithms can be applied to fully characterize cortical anatomy, thickness, regions of interest and subcortical structural boundaries. In essence, Freesurfer generates a probability for each voxel in the MRI of
belonging to a specific neuroanatomical region. The software generates a label map for the MRI corresponding to the predicted anatomical distribution of structures. We applied the automatic segmentation process using default T1 settings to each patient MRI and manually reviewed the outputs to ensure appropriate segmentation. The segmentation solution typically converged within 16 hours (*Figure 3*). Minimal manual curating of the outputs was necessary, in only one case was the post-operative MRI abnormal ablated tissue not recognized by the algorithm and was manually segmented in addition to the automatic output.

ii. 3D Slicer model generation

Patient MRIs were imported into 3D Slicer, an open source software platform for working with and manipulating imaging output files. The segmentation derived from the Freesurfer algorithm was superimposed onto the MRIs as a label map and used as a template to generate models of various subcortical structures. A number of structures could be generated including the ventricular system, the basal ganglia nuclei, hippocampal targets and navigable volume of brain. Each model was generated from a surface representing the volume boundary that underwent Laplacian smoothing with 10 iterations using a Sinc type filter and 25% decimation. The resulting models were saved and exported as .ply files (*Figure 4*).

iii. Meshlab, Netfab, Matlab triangular mesh generation

Each .ply model was imported into MeshLab (http://meshlab.sourceforge.net/), an open source software designed to perform a number of filtering, smoothing and
reconstructive operations on triangular and quadrangular meshes. We used the quadratic edge collapse decimation to reduce the number of faces on each model by a factor of 4. After the decimation, each model underwent a Laplacian smooth (3 iterations, cotangent smoothing) and Taubin smooth (lambda = 0.5, mu = -0.53, iterations = 10) with care taken to ensure that the total size of the mesh remained constant. Simplification of each model proceeded with iterative cycles of decimation and smoothing to gradually reduce total number of faces within the desired range while preserving overall surface structure and model integrity (in most cases an acceptable range was between 100 and 5000 faces in order to maximize the speed of computations in MatLab, particularly with the inpolyhedron() function). Between each step, the cleaning and repairing filters remove duplicate vertices; faces and unreferenced vertices were applied to each model. After simplification and smoothing, each model was imported into NETFAB basic (http://www.netfabb.com/), an open source software for preparing models for 3D printing in order to remove any holes and irregularities from the triangular mesh. The automatic repair function was applied to each model, which filled in holes in the matrix appropriately in order to fulfill the underlying assumption that the produced surfaces are closed and non-intersecting. Each repaired .ply file imported into MatLab using the plyread() function and saved as a variable for later use with the parameters face organization, point 3D location, and direction of face normal. The models could be displayed using the MatLab function trisurf() and an appropriate color scheme function. This representation is referred to the surface model (Figure 4a). The models can also be represented in an additional method for later use in the optimization function. A 3D meshgrid with a 0.1 mm³ density is defined and all of the points lying within a surface model are selected. The result is a point distribution
that matches the geometry of the original surface model. This representation is referred to the point distribution model (*Figure 4b*). Both the surface model and point distribution models are used throughout in the optimization algorithm, each to represent two navigable volumes. $T_S$ and $T_P$ represents the surface and point distribution models of the hippocampal target respectively. $B_S$ and $B_P$ represents the surface and point distribution models of the brain volume from which is subtracted all the obstacle volumes representing the volume within which the probe is free to travel (*Figure 5*).

c. Parameterization

i. Modeling concentric tube trajectory

In this investigation, we will be working with an N segment trajectory. To define the N segment trajectory we will use the following convention, which will be used through this manuscript. $N = 1$ represents a linear trajectory as is currently preformed by the Visualase straight laser ablation. $N = 2$ represents an additional degree of complexity where there is a straight trajectory attached to a circular trajectory at the tip that has a constant radius of curvature. $N > 3$ represents a straight trajectory along with $N - 1$ constant radius circular trajectories at the tip of each preceding segment that are arranged in a series. Therefore, a $N = 5$ trajectory represents a straight entry trajectory followed by 4 circular paths connected end to end each with independent rotations, radii of curvature and trajectory lengths (*Figure 6*).

The overall trajectory can be described by $3N$ degrees of freedom ($x_1, x_2, ..., x_{3N}$). The initial straight trajectory that is common to all the paths is defined based on the rotation around the $x$ axis ($x_1$) and the rotation around the $y$ axis ($x_2$) and the length of the
trajectory ($x_3$). Each additional segment is defined by an axial rotation perpendicular to the plane of motion of the preceding segment representing the twisting between segments on the robot ($x_{3(N-1)+1}$), a radius of curvature defining the circular trajectory ($x_{3(N-1)+2}$) and a length defining the distance along the specified circular path ($x_{3(N-1)+3}$). Finally the entry point is important for defining the trajectory as it is the point from which the straight segment common to all trajectories originates ($x,y,z$). It will not be optimized for using the optimization algorithm, but will be defined for each optimization as is discussed in the following section (Figure 7).

ii. Modeling depth electrode trajectories

We modeled the region of interest (ROI) in which lies an epileptogenic focus as a box with dimensions $l \times w \times h$ (Figure 8). We defined three scenarios for the ROI with respect to the electrode trajectory. Case 1 is where $h >> l \sim w$ such that the ROI follows the linear electrode trajectory. Case 2 is where $h \sim l >> w$ such the ROI lies in the plane parallel to the electrode trajectories. Case 3 is where $l \sim w >> h$ such that the ROI lies in the plane perpendicular to the electrode trajectories.

iii. Modeling laser tip behavior

We define a surface that surrounds the trajectory with a radius of $C_R$ and length of $C_L$ from the tip of the robot. This surface represents the ablative radius and trajectory of the laser probe. This is the cylinder tip model and the volume encompassed by this surface is expressed by $C_S$ (Figure 9). Alternatively the ablative region can be defined as a series of spheres with variable spacing between the spheres to represent point ablation and retraction of a tip. In this case, the radius of sphere $n$ is $S_{Rn}$ and the spacing between
adjacent spheres is $S_{\text{Ln}}$. This could also be used to model the position of a depth electrode within the hippocampal region of the brain and is explored in more detail in Section IV.

d. Global patternsearch optimization algorithm

We apply the global patternsearch algorithm from the optimization toolbox of MatLab to minimize the desired objective function. The objective function we defined consists of three distinct components:

\[ f_1 = \frac{1}{\sqrt{(t_x - p_x)^2 + (t_y - p_y)^2 + (t_z - p_z)^2}} \]  
\[ f_2 = \frac{P_{\text{inside}}}{\sum_{i=1}^{N} P_i} \]  
\[ f_3 = \frac{T_{\text{inside}}}{\sum_{i=1}^{N} T_i} \]

where:
- $t_{xyz}$ = x,y,z coordinates of target centre of mass.
- $p_{xyz}$ = x,y,z coordinates of probe tip.
- $P_{\text{inside}}$ = # of probe points within the navigable brain model.
- $\Sigma P$ = total # of probe points.
- $T_{\text{inside}}$ = # of target points in ablation surface model.
- $\Sigma T$ = total # of target points.

The first stage ($f_1$) is defined as minimizing the distance between the probe tip and the target in order to ensure that the trajectory falls within the desired target region. Once within the target region, the second stage ($f_2$) ensures that the trajectory does not pass through any of the predefined obstacle models. This includes models of the basal ganglia nuclei, CSF, blood vessels which are integrated to create a navigable brain model ($B_s$ and $B_p$) indicating the region within the brain that is safe for the trajectory to traverse. At this stage the user may modify the relative weight of traversing each section. Once the
algorithm gives a solution that obeys the obstacle condition above the defined threshold, the third and final level of the objective function \( f_3 \) is to maximize the amount of the trajectory within the target. This is defined as the inverse of the greatest number of points from the point distribution model of the target that fall within the surface model of the laser tip at the end of the trajectory \( (T_p \text{ inside } C_3) \). The patternsearch algorithm minimizes the objective function and gives rise to the optimal solution given a specific starting location:

Define objective function:

\[
 f = \begin{cases} 
 2 + f_1 & \text{if } f_3 = 0 \\
 1 + f_2 & \text{if } f_2 > 0 \\
 f_3 & \text{if } f_2 = 0 
\end{cases} 
\]  

(4)

Define optimization algorithm

a. set surface entry point \((x,y,z)\)

b. compute \(\arg \min f(x_1,x_2,\ldots,x_N)\)

c. repeat for \(N = 1:1:5\)

Several additional constraints to the trajectory are implemented including limiting the total length and ratio of segment length to radius of curvature in order to avoid forbidden looping trajectories.

e. Graphic user interface

The final task is to incorporate the model generation, display, parameter selection and optimization algorithm runs into an interface that can be used to explore a wide variety of starting locations and different anatomical geometries (Figure 10). Some of the specifics of the interface and plotting capabilities will be discussed in further sections but
the ultimate goal of this interface as will be discussed in Section V is to develop a simple way for the surgeon to define the optimal entry and target locations for a specific operation given his/her expertise and specific requirements.
III. Results

a. Curved depth electrode modeling

Hypothesis: A single curved depth electrode may replace several straight depth electrodes.  
(Figure 7) and (Figure 11)

Results: Three linear depth electrodes can be effectively replaced by single non-linear trajectories that can be generally subdivided into two approaches: branched vs. circular. Branched approaches employ a single entry trajectory from which multiple curved electrodes may fan out from. Circular approaches employ multiple concentric curved electrodes such that the outer diameter is formed by the larger radius of curvature and the inner by the smaller radius of curvature.

b. Distribution of solutions from the optimization algorithm

Hypothesis: We are optimizing a function with potentially a large landscape of possible solutions. Each optimization from a single entry point will need to be performed multiple times. The probability of obtaining the minimum desired target coverage should increase as a function of the number of optimization iterations.  
(Figure 12) and (Table 1)

Result: Regardless of the number of segments (N), a single iteration will have at least 50% chance of obtaining a solution within the 10th percent of the optimal solution. Therefore, the algorithm workflow should be designed to take into account that each iteration may not necessarily yield an appropriate solution.
c. Single entry point analysis

Hypothesis: Adding each additional circular segment should provide a solution at least as complete as the one before. Percent coverage of hippocampal target from a single entry point should increase as a function of trajectory complexity (N) regardless of entry location.

(Figure 13)

Results: Percent coverage of target from a single entry point increases, as a function of trajectory complexity regardless of the occipital, parietal, temporal or frontal entry location. The most significant shift in percent coverage is consistently between N = 1 and N = 2. The temporal approach appears to benefit most from additional degrees of trajectory complexity (N > 3). The occipital approach appears to benefit the least from additional degrees of trajectory complexity.

d. Optimized trajectories vs. manual trajectory

Hypothesis: Given any starting entry point, we are interested in how an N-segment trajectory compare to a manually selected linear approach. We hypothesize that optimized trajectories will produce greater target coverage than manually selected trajectories. Hippocampal target coverage will increase as a function of trajectory complexity (N).

(Figure 14) and (Table 2)

Results: 1) Optimized trajectories consistently produce greater target coverage as a function of trajectory complexity than manually selected trajectories. 2) The rate of change
of target coverage decreases as a function of trajectory complexity and does not change substantially when $N > 3$.

e. Global entry analysis

Hypothesis: Finally, we are interested in how the profile of surface coverage changes as a function of trajectory complexity. We hypothesize that the total potential skull surface area from which the target can be accessed will increase as a function of trajectory complexity ($N$).

(Figure 15) and (Figure 16)

Results: 1) Significant increase in potential surface entry locations between $N = 1$ and $N = 2$ segment trajectories. 2) Number of entry locations continues to increase as a function of trajectory complexity but the rate of increase diminishes substantially when $N > 3$

f. Challenging entry meta analysis

Hypothesis: In some cases it takes the surgeon upwards of one hour to define the trajectory. We hypothesize that optimization algorithm should find unique solutions to challenging cases where the ventricles are enlarged, and it is difficult for the surgeon to define a direct trajectory.

(Figure 17)

Results: Surface analysis of challenging cases reveal a number of potential entry points that may have been overlooked in the linear trajectory planning. Additional degrees of freedom dramatically simplify the challenge of finding a suitable entry point.
IV. Discussion

a. Assumptions underlying model, parameterization and optimization

i. Defining target and navigable brain region

In this investigation, we generate a three-dimensional model of the hippocampus as the surgical target. We assume that the goal of the procedure is to remove as much of the hippocampus as possible in order to minimize the probability of an epileptogenic region escaping ablation. In practice the goal of minimally invasive approach is to minimize tissue damage and in theory to remove only the tissue responsible for generating the seizures. Another assumption for our model is that the hippocampus is the target and not the hippocampal-amygdal region, which is may often be surgically removed especially in cases where the epileptogenic region is poorly defined.

We rely on the Freesurfer algorithm to segment and identify the critical subcortical structures that we wish to avoid. Each output was analyzed to ensure it matched expectation of regional anatomy. There were limits in the ability of the algorithm to identify the venous system of the brain as well as the smaller vasculature. The addition of gadolinium contrast enhancement or specific SWI or T2 sequences may help identify blood vessels. Future efforts should focus on one of three options, exploring Freesurfer parameters, manually identifying additional obstacles to avoid or preparing short automated mechanism to identify desired obstacles.
ii. Defining probe tip and trajectory

A second assumption we made revolves around the shape of the laser ablative region. As discussed in Section II, the laser ablation method can be either modeled as a cylinder surrounding the tip of the robot or a series of spheres along the distal tip at variable areas. We chose to use the cylindrical method for two major reasons. Retrospective analysis suggests that the majority of the Visualase cases post-ablation could be modeled as a cylinder (Figure 8). Additionally the cylindrical approximation simplifies the algorithm by avoiding introducing changing radii for each sphere for an unlimited number of spheres potentially adding incomputable degrees of complexity to the algorithm.

An additional factor concerning the laser tip that was assumed to be minimal was the ablation of surrounding non-target tissues. We chose to ignore this parameter because the fluid filled temporal horn of the lateral ventricle that surrounds the majority of the hippocampus acts as barrier to heat transmission, a property employed by Visualase to limit undesired external off-target damage. The ablation radius inside tissue that isn’t part of the target could be accounted for with a variable parameter that takes into account the structure of the surrounding tissue, but to simplify our model, we assume that the extra target damage would be minimal given a high degree of optimization.

Finally, in modeling the trajectory, we assume that the diameter of the probe tip in brain tissue is non-existent. This is an appropriate simplification for modeling purposes but in reality the diameter of the robot tip can range anywhere from 3.0 mm to 0.2 mm from the outermost to the innermost segment diameter. One of the major challenges on the hardware side is to decrease this total diameter and minimize tissue disruption. From a software point of view an additional condition could be introduced to minimize the total
volume based on the segment trajectory of the specified segment occupies. Again, from a hardware point of view, the goal is to minimize the diameter of the concentric tube laser probe, so the current model reflects the trajectory of a laser probe in an ideal case.

iii. Defining skull surface entry

In attempt to explore the spectrum of novel entry approaches to the optimization problem, we explore a wide variety of potential entry positions on the surface of the skull. We impose limitations to the potential locations such as avoiding the face, ears, and contralateral skull surface (to prevent traversing the falx cerebri). However, factors that were not necessarily accounted for include any areas that may have some superficial fat surfaces, muscles or large amounts of subcutaneous tissue or regions that overly any of the sutures. Ultimately given a subset of surgical trajectories the surgeon can select the most appropriate and least challenging entry trajectory, but in this modeling approach we are interested in perhaps discovering new patterns and trends in the trajectories and potential entry locations.

b. Curved depth electrode modeling

Our theoretical models of achieving electrode coverage within a region of interest demonstrates that there is variable benefit to using non-linear trajectories that Case 3 > Case 2 > Case 1 (Figure 7). Case 1 shows that a ROI in line with the depth electrode path can best be covered with a straight electrode whereas Case 3 shows that a ROI in a plane perpendicular to the depth electrode path requires many straight electrodes to achieve adequate coverage. As illustrated by the case example, both branched and circular electrode trajectory configurations are able to replace the coverage of three depth
electrodes within a ROI (Figure 11). Both trajectories from a single entry point, eliminating the need for multiple skull entry sites which further increases the probability for complications. The major benefit of the branched configuration is that it relines on curved electrodes with larger radii of curvature which may be more easily manufacturable. The major advantage of the circular configuration is that a single electrode trajectory is required to achieve coverage. Ultimately a combination of branched and curved trajectories originated from a single entry point may prove to be most effective. One final case that was not explored in this investigation would be where \( h = l = w \). We chose not to investigate this model on the basis of having a perfectly cuboidal ROI would be quite rare and more likely than not, at least one dimension of the ROI would be different such as to better fit within one of aforementioned case models.

c. Distribution of solutions from the optimization algorithm

i. Initial position problem.

Perhaps the most challenging problem to a successful result from the optimization algorithm is finding an optimal initial position from which to seed the algorithm. Initial attempts involved developing a framework from which to be able to manually select and position the probe. The user interface includes 3N slider panels with which the operator can precisely define the initial configuration of the probe for a given entry position (Figure 10). There are three major limitations to this technique. The first is the unavoidable tedious and slow nature of probe positioning. Care must be taken to configure the proximal segments prior to the distal segments, otherwise shifts can impact the distal tube conformation. Moving each parameter individually is a slow process and doing so for each segment configuration is tedious thus a mimic function as developed to expedite the
process. The second challenge is understanding exactly where in the navigable brain region the trajectory traverses outside the target. The overlapping brain mesh can be overwhelming for a user and therefore a module was developed to highlight parts of the trajectory that were outside a given boundary condition. Further improvements to benefit the end user include incorporating a slice-by-slice view of the patient’s MRI in axial, coronal, sagittal and custom plane perpendicular to the direction of the probe. The final challenge is that the human seeded solution is not necessarily the ideal solution that can be determined. This is best highlighted where an optimally selected initial and final probe positions are compared to an iteratively randomly initialized positions. However, despite the challenges, the manual selection has proven to allow high degree of user control and ability to dictate the general desired trajectories and will have value in end user surgical planning where an individual trajectory is carefully optimized. Before such optimization can occur finding the best optimized solution will require a large number of well selected initial seed positions and this is a challenging problem that was approached in the following way:

Seeding $N = 1$ and $N = 2$ segment trajectories: Given the entry point and center of mass of target, determine the center of mass of the target. Transform the linear trajectory between the entry and center of mass into $\theta$ and $\phi$ angles for the $x_1$ and $x_2$ parameters respectively. For each subsequent iteration, $x_1$ and $x_2$ was modified to be initial value +/- a scaling factor.

Seeding $N \geq 3$ segment trajectories: Four iterations with the method for seeding 1 and 2 segment trajectories were performed. Each resulting trajectory was then compared to that of the path for $N-1$ segment. If the objective function value was less, the
conformation of the N-1 segment was used to seed a new iteration of the optimization which constantly produced a resulting value of $f_1(N)$ equal to or lower than the $f_1(N-1)$ trajectory.

ii. Distribution of solutions.

The pattern search algorithm seeks to minimize the objective function. However there are many possible solutions that give similar values for the function. In fact, there is a spectrum of peaks and values that can be obtained. It is important to establish the minimum number of iterations necessary to give an optimal solution in order to optimize the efficiency of the algorithm especially for the surface analysis. Figure 12 highlights that each individual optimization has approximately a 50% chance of providing an optimal solution. We define an optimal solution as one that is within the 10% target coverage bracket of the maximum attainable value. Therefore, the spectrum profiles obtained suggest that at least 4 iterations should be performed for up to 5 segment trajectories in order to have a high probability of finding a successful trajectory. It takes approximately 10s, 20s, 40s, 80s and 120s for an $N = 1, 2, 3, 4$ and 5 segment trajectory respectively. The main constraint and disadvantage of this strategy is the time involved in performing multiple iterations in order to be sure an appropriate solution is obtained. Further techniques to speed up the process may involve devising a novel solution to the initial position problem or introducing more geometric constraints in the navigable brain volume such that there is a narrower landscape of possible solutions.

c. Single entry point analysis.
Figure 13 presents representative trajectory for an N = 1 to 5 trajectory from entry points in the occipital, temporal, parietal and frontal lobes of the brain. In all cases the percent hippocampal coverage increases as a function of trajectory complexity. The optimal trajectories appear to come from the occipital area of the brain but a complete surface analysis as discussed in Figure 16 provides a more in depth analysis. We can conclude however that the rate of change in improvement changes dramatically as a function of trajectory complexity. This suggests that trajectories with 3 or more degrees of complexity may not contribute significantly to the overall coverage of the hippocampal target region.

d. Optimal trajectories vs. manual trajectories

Using the surface analysis method previously described we sought to determine the optimum trajectories from any point on the surface. As demonstrated in Figure 14, the coverage increases as a function of trajectory complexity and in all cases is above the manually selected trajectory. Interestingly, the manual trajectory is not that far from that of the optimized linear trajectory, which was observed consistently. This suggests that the trajectory the surgeon selects despite the challenge and time-consuming activity is generally quite effective. Regardless the optimizations are not only superior but present a wide variety of potential trajectories. This ability to provide additional entry locations particularly following non-linear trajectories fulfills the second hypothesis we sought to explore in this investigation.
e. Global entry analysis

Here we hypothesized that the total skull surface area from which the target can be accessed will increase as a function of trajectory complexity. We ran the algorithm on multiple cases giving rise to Figure 16. The area from which the probe can enter the surface increases dramatically as a function of trajectory complexity. However as shown by Figure 16, the biggest leap in overall target coverage is from N = 1 and N = 2. Very complex trajectories (N > 3) do not show such a dramatic change as a function of trajectory complexity. Figure 15 provides a histogram that highlights the distribution of solutions for an N segment trajectory. These findings suggests that even introducing a single degree of curvature, potentially something that could be managed manually, not necessarily robotically increasing its potential for clinical use could dramatically increase the ability to reach non linear targets in the brain.

f. Challenging entry analysis

Finally, we present in Figure 17 three additional Visualase cases, which were determined to be challenging for the surgeon to determine a linear trajectory. As demonstrated by the surface maps of entry positions, a number of non-linear solutions were obtained given a wide variety of initial entry positions. Again, the most significant increase in surface coverage is between N=1 and N=2 and the rate of increases levels of after N > 3. These results suggest that concentric tube trajectories with a single degree of curvature can drastically improve the versatility of laser ablative epilepsy surgery.
V. Future Directions

a. Improving the algorithm

One important and perhaps significant improvement to the optimization algorithm would be to incorporate the results of DTI imaging into the objective function. An additional condition that optimizes for the degree of parallel direction between the trajectory and fiber tracts could be valuable to minimizing the disruption of white matter tracts that the trajectory introduces in the brain.

Other ways to improve the optimization algorithm include making changes to the initialization function as discussed in Section IV. Determining a way to initialize appropriate radii of curvature and arc lengths in addition to the general probe orientation would be a valuable tool that would help shrink the spectrum of possible solutions and increase the speed of the optimization.

b. Surgical interface

A fluid segmentation workflow is essential to the translation of this research toolbox into clinical practice. We currently perform an intensive segmentation protocol, which requires 24 hours to complete. However, the level of detail and substructure segmentation is greater than would be necessary to assist surgical approaches to treatment. For this reason developing a simplified version of the segmentation protocol that can be used real time to generate label maps would be very beneficial.

Additionally the next challenge would be integrating the various components of the workflow in order to develop a unified surgical toolkit. As it stands, different software is
required to go from patient MRI to optimized solution. Integrating the necessary components of each tool into a single interface that the surgeon can employ in real time would greatly benefit and provide increased clinical use potential of the technique.

Finally from a hardware point of view, results suggest that a two segment optimized trajectory can dramatically increase both the target coverage and the total assessable surface area. Optimization algorithm will guide the design of two-segment concentric tube cannula for further investigation ex vivo using 3D printed brain models and cadaveric heads.

b. Meta analysis of skull entry

Generating surface maps from multiple different cases may yield interesting trends and patterns that can be extrapolated upon to create rules and guidelines for performing non-linear surgical techniques. Running the optimization algorithm on multiple cases may reveal some interesting insights on ways to navigate the neuroanatomical obstacles and challenges facing current linear laser ablative surgery.

VI. Summary

This investigation introduces non-linear trajectories for electrode placement and laser ablation in epilepsy surgery. Single curved depth electrodes are shown to replace multiple linear depth electrodes. Curved laser trajectories are shown to be more effective at ablating a hippocampal target than linear trajectories and furthermore dramatically increase the number of potential skull surface entry points.
VI. Figures

**Figure 1:** Current minimally invasive surgical approaches to epilepsy surgery rely on MRI guided straight laser probes to ablate epileptogenic tissue. We propose to improve the hardware by introducing concentric tube trajectories and improve the software by optimizing laser probe trajectory based on patient-specific geometry.

**Figure 2:** Prototype of concentric tube tip (a) and robotic driver (b). Tip dimensions are comparable to needle catheters. Each nitinol segment is controlled by two motors and may be translated or rotated giving rise complex motions in three dimensional space.
**Figure 3:** Sample volumetric segmentation of neuroanatomical structures by FreeSurfer. Algorithm output provides both subcortical (a) and cortical (b) segmentation.

**Figure 4:** 3D models generated using Slicer and triangular meshes generated for MatLab computations.

**Figure 4:** Surface model (a), point distribution model (b) and composite (c) of a left hippocampus target. Similar models are generated for each anatomical obstacle.
Figure 5: Surface model of navigable brain region. Model was generated by total brain region and subtracting from it the volumes of critical structures that must be avoided such as blood vessels, ventricular system, cranial nerves and basal ganglia nuclei.

Figure 6: Sample N segment trajectories. N = 1 represents a straight trajectory and each additional segment can be represented by an arc with a constant radius of curvature and a defined segment length. The potential complexity of the trajectory increases with N.

Figure 7: Parameterization example for a N = 2 segment trajectory. Each additional circular segment requires 3 additional parameters: twist angle $\phi$, radius of curvature and arc length.
Figure 8: Theoretical models of depth electrode placement within a given region of interest (ROI). The benefit of curved trajectories increases from Case 1 to Case 3 as the ROI lies more perpendicular with respect to the electrode paths. Both branched and circular trajectories can be employed to achieve non-linear coverage of a given ROI.

Figure 9: Modeling laser ablation radius as a cylindrical volume with a constant radius $C_R$ that extends a length $C_L$. 
**Figure 10:** Example of interface used to perform calculations. A similar simplified version of the interface could be useful for the surgeon to determine optimal trajectories in real-time.
**Figure 11:** Proof of concept highlights a patient case where the cingulate cortex was mapped with 3 depth electrodes (B). A similar result could have been achieved by a single non-linear electrode with either a branched (C) or circular approach (D).

**Figure 12:** Optimization function was run 100 times to determine optimization solution profile of $N = 1, 2, 3, 4$ and 5. At least 50% of the solutions are within 10% of the optimal solution. Results are summarized in Table 1.
Figure 13: Sample optimized N segment trajectories from an occipital, parietal, temporal and frontal approach. Three views of the same entry position are shown to highlight trajectory diversity. Bar plots represent the percent hippocampal coverage for each degree of trajectory complexity (N).
Figure 14: Optimized compared to manually selected trajectories. Optimized trajectories consistently produce greater target coverage as a function of trajectory complexity than manually selected trajectories. The rate of change of target coverage decreases as a function of trajectory complexity and does not change substantially when $N > 3$. Results are summarized in Table 2.
Figure 15: Histogram representing distribution of target coverage fraction as a function of trajectory complexity. Bin size is 0.1 of the target coverage.

Figure 16: Optimization algorithm was performed iteratively on points across the skull surface. Surface plots highlighting the ability of various surface entry points to yield coverage of the hippocampal target. Coverage >70% is considered surgically acceptable. Box plot below represents the distribution of optimized trajectories. Greatest increase in surface coverage occurs between N = 1 and N = 2. Distribution of acceptable entry positions does not change significantly when N > 3.
Figure 17: Surface distributions and corresponding histograms for three additional surgically challenging cases. In each situation the manually selected trajectory took significant time (>1h) to be selected. Surface plots and histograms demonstrate a dramatic increase in potential surface entry locations as a function of trajectory complexity with the most significant change occurring between N = 1 and N = 2.
Table 1: Algorithm was performed with identical starting point and variable initial trajectory parameters to determine the probability of obtaining an optimal trajectory. Results in this table correspond to Figure 16. The minimum fraction of successful trajectories for the highest solution bracket was 0.48 which suggests each optimization iteration should be performed at least 2 times in order to ensure a solution in the highest coverage bin. In our cases we ran the simulation 4 times in order to be extra certain an optimal trajectory was achieved. Similar distributions were obtained using different initial positions.

Table 2: % coverage of hippocampal trajectory for manual vs optimized trajectory in four Visualase cases. Results in table correspond to Figure 17.
VIII. References


