A new instrument for deep brain stimulation surgery

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A new instrument for Deep Brain Stimulation surgery
A new instrument for Deep Brain Stimulation surgery

PROEFONTWERP

ter verkrijging van de graad van doctor aan de
Technische Universiteit Eindhoven, op gezag van de
rector magnificus prof.dr.ir. F.P.T. Baaijens, voor een
commissie aangewezen door het College voor Promoties,
in het openbaar te verdedigen op maandag 25 juni 2018 om 11.00 uur

door

Marc Janssens

geboren te Roosendaal en Nispen
Dit proefschrift is goedgekeurd door de promotoren en de samenstelling van de promotiecommissie is als volgt:

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Het onderzoek dat in dit proefontwerp wordt beschreven, is uitgevoerd in overeenstemming met de TU/e Gedragscode Wetenschapsbeoefening.
ἄνθρωπος μέτρον
Summary

A new instrument for Deep Brain Stimulation surgery

Deep brain stimulation (DBS) is the stimulation of regions in the brain using electrical pulses. This is realized by transmitting pulses over an insulated lead wire with a distal exposed electrode. The lead wire runs from a burr hole in the patient’s skull to a specific target in the brain. The stimulation pulses are generated by an implantable pulse generator connected to the lead wire. This pulse generator is usually implanted under the patient’s clavicle. DBS can provide symptom relief for various neurophysiological ailments, like Parkinson’s disease, epilepsy, and dystonia. The stimulation target’s location depends on the ailment addressed and magnetic resonance imaging (MRI) is used to determine the exact location of the target in the patient’s skull. The main clinical application of DBS is for Parkinson’s disease, with the subthalamic nucleus (STN) as typical stimulation target. The STN measures approximately 8 by 4 by 4 millimeters and accurate positioning of the stimulation electrode in the target is essential to minimize stimulation side-effects.

The current day surgical procedure uses a stereotactic frame to implant the electrode along a trajectory chosen by the surgeon, based on the MRI scan made of the patient’s brain. This scan typically does not include a frame reference. An additional computed tomography (CT) scan is made of the patient’s skull with part of the frame attached, and the CT and MRI scans are fused to translate the MRI derived coordinates of the stimulation target and skull entry point to frame settings.

The fusion process introduces an error to the initial imaging accuracy. Combined with shortcomings with respect to stiffness in the stereotactic frame’s design, dating back to the 1980’s, this leads to only highly experienced surgeons being able to implant the stimulation electrode accurately in the intended target. An altered procedure with a less ambiguous translation of the MRI-derived trajectory to settings for the then used instrument, could lower surgery time, risk, and cost, and improve overall treatment efficacy.

Two new surgical instruments, for the implantation of DBS electrodes in the brain, have been designed and realized. The main goal was to achieve unambiguous translation of target and entry point coordinates to instrument settings. This is realized by introducing an adapter disc which gets fixated with screws to the back of the patient’s skull, before the MRI scan for targeting is made. It serves as both a visual reference for imaging and a structural reference for the instrument.

The first instrument prototype is completely made from PEEK. This material ensures full MRI compatibility, allowing for implantation under real time MRI, would this be desired. For the second prototype, the requirement for MRI compatibility is left behind. The freedom in material choice is exploited in the design, together with experience gained from the PEEK instrument. The resulting prototype is more compact and dedicated to DBS surgery, although still in the same style as the PEEK instrument.
Next to the two instrument prototypes, an MRI compatible actuator has been designed and realized. It is required for the possible application of the PEEK instrument in the confined environment of an MRI scanner. Only the straight lined insertion of the electrode needs to be motorized, as the other instrument settings are adjusted before attaching the instrument to the patient’s head. The goal of the design process was to keep the drive as compact as possible, in line with the limited forces at play during electrode insertion in the brain.

Moving the scope of this thesis broader than only DBS, surgery to the brain is intrinsically characterized by elevated risk and the requirement for precision. As all burr hole surgery to the brain can be complicated by brain shift, a small device is proposed to prevent this shift from occurring. It could be used in conjunction with the new instruments to further improve electrode positioning accuracy, or the positioning accuracy of specific tools for other treatments which could benefit from the new instruments. Some of such treatments are discussed in the final part of this thesis.
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Nomenclature

Throughout this thesis a right-handed coordinate system is used, which is defined as follows:

The symbols $x$, $y$, $z$, $\varphi$, $\psi$, and $\theta$, are used throughout this thesis to indicate the respective degrees of freedom. Subscripts are added (e.g. $y_j$, $z_2$, $\psi_i$) to indicate the various adjustments the instruments have for these degrees of freedom.

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
</tr>
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<tbody>
<tr>
<td>AC</td>
<td>Anterior Commissure</td>
</tr>
<tr>
<td>CNS</td>
<td>Central Nervous System</td>
</tr>
<tr>
<td>CSF</td>
<td>Cerebrospinal Fluid</td>
</tr>
<tr>
<td>CT</td>
<td>Computed Tomography</td>
</tr>
<tr>
<td>DBS</td>
<td>Deep Brain Stimulation</td>
</tr>
<tr>
<td>DOF</td>
<td>Degree Of Freedom</td>
</tr>
<tr>
<td>FDA</td>
<td>Food and Drug Administration</td>
</tr>
<tr>
<td>FEM</td>
<td>Finite Element Method</td>
</tr>
<tr>
<td>GPi</td>
<td>Globus Pallidus internus</td>
</tr>
<tr>
<td>ICP</td>
<td>Intracranial Pressure</td>
</tr>
<tr>
<td>MER</td>
<td>Micro Electrode Recording</td>
</tr>
<tr>
<td>MRI</td>
<td>Magnetic Resonance Imaging</td>
</tr>
<tr>
<td>PC</td>
<td>Posterior Commissure</td>
</tr>
<tr>
<td>PD</td>
<td>Parkinson’s Disease</td>
</tr>
<tr>
<td>PEEK</td>
<td>Polyetheretherketone</td>
</tr>
<tr>
<td>STN</td>
<td>Subthalamic Nucleus</td>
</tr>
<tr>
<td>Vim</td>
<td>Ventral intermediate nucleus of the thalamus</td>
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Chapter 1: Deep Brain Stimulation

1.1 Introduction
Deep Brain Stimulation (DBS) is the stimulation of regions in the brain using electrical pulses, transmitted over an insulated lead wire with a distal exposed electrode (figure 1.1). The stimulation pulses are generated by a pacemaker, which is usually implanted under the patient’s clavicle. Implantation in the abdominal area is occasionally performed as well. A lead wire runs subcutaneously from the pacemaker to a burr hole in the skull. Through this hole, the intracranial part of the lead wire with the electrode tip is implanted in the brain. The electrode tip is positioned at a location of which is known its electrical stimulation yields the desired effect for the ailment addressed.

DBS is used for the treatment of multiple motoric, stroke and tremor disorders like dystonia, essential tremor and Parkinson’s disease. Further application includes the treatment of epilepsy and neuropsychiatric disorders like Tourette syndrome, obsessive-compulsive disorder and major depression. The aim of the treatment is to achieve symptom relief for the patient, since a cure is in most cases not available for neurophysiological/-psychological disorders. DBS provides an adjustable and reversible surgical treatment for the various disorders, potentially without side effects. The major challenge lies with controlling the success rate and risks.

Figure 1.1: Typical layout of DBS system components after implantation in a patient [1].
Deep brain stimulation shows great potential in the treatment of various disorders, despite concerns with respect to the current procedure. When it could be offered to more patients who qualify for the procedure, it could have a great impact on their quality of life. The focus of the project accompanied by this thesis, is to address the concerns with the current procedure from a mechanical engineering point of view. This translates to the design and realization of a new instrument for DBS electrode implantation.

A basic knowledge of the anatomy of the brain is needed to understand the different aspects of deep brain stimulation surgery. This anatomy will be elaborated first (section 1.2), followed by an introduction to Parkinson’s disease (section 1.3), and an overview of the current day surgical procedure for DBS (section 1.4). After elaborating several alternatives to the currently used surgical equipment for the implantation of DBS electrodes (section 1.5), the project goal (section 1.6) and outline of this thesis (section 1.7) are presented.

### 1.2 Anatomy of the brain

The brain is the central node in the nervous system. It is a vital organ in the human body and controls most of the conscious body functions. Contained within the skull, it sits on top of the spinal column and is connected to the majority of the body via the spinal cord.

![Functional Areas of the Cerebral Cortex](image)

Three main parts of the brain can be distinguished: the brain stem, the cerebellum or ‘little brain’, and the cerebrum. The brain stem and cerebellum are indicated separately in figure 1.2; the cerebrum consists of all the rest of the brain.

![Anatomy and functional areas of the brain](image)
The brain stem connects the brain to the spinal cord. It plays an important role in regulating breathing, heart rate, and sleep. The cerebellum lies behind the brain stem and underneath the cerebrum in the lower back of the head. Its most important function is maintaining coordination, precision, and timing of motor functions. The cerebrum forms the largest part of the human brain and contains the cerebral cortex, together with several subcortical structures like the hippocampus, basal ganglia, and the olfactory bulb (sense of smell). Together with the cerebellum, the cerebrum controls all voluntary actions of the body. The cerebral cortex makes up most of the cerebrum, and figure 1.2 shows some of the functional areas it contains.

The cerebral cortex consists of two halves, called the cerebral hemispheres, which are interconnected via five commissures. To indicate specific areas on the cortex, both hemispheres are divided in four lobes, being the frontal, parietal, occipital, and temporal lobe. Most body functions are represented symmetrically within the two hemispheres, with exceptions being language and communication (left hemisphere), and visual-spatial ability (right hemisphere). The occipital lobes, containing the visual cortex, are completely dedicated to the sense of sight.

1.2.1 Neurons
The brain contains approximately 86 billion neurons [3]. These are electrically excitable cells which can receive, process, and transmit signal pulses. Neurons consist of a central cell body with attached multiple dendrites and one axon (see figure 1.3). The dendrites normally act as the signal receivers for a neuron, with the axon terminals acting as transmitters. In rare cases, dendrite-to-dendrite or dendrite-to-cell body communication between two neurons is also possible.
In the brain these neurons form an intricate network in which intercellular communication takes place over synapses. To transfer a signal, the transmitting neuron will release neurotransmitter molecules from its axon terminals. These neurotransmitters diffuse over the synapses and get picked up by the receiving neurons’ dendrites. When enough neurotransmitter molecules have been received, an action potential is generated in the receiving neurons and the signal transfer is successful. Such action potential is transmitted electrochemically over a receiving neuron’s axon, resulting in neurotransmitter release from its axon terminals, and thereby continuing the signal transfer chain. Although neuron cell bodies are small (order of micrometers), the length of axons can be orders of magnitude larger (up to 1 meter). To maximize the speed of the electrochemical signal transfer over the axon, it is covered in a sheath of myelin (figure 1.4). This reduces the capacitance of the axon itself, whilst forming an electrically insulating layer towards its surroundings. The action potential can reach speeds up to 100 m/s when traveling along a fully myelinated axon.
Myelin has a typical whitish color compared to the gray-pink color of (living) neuron cell bodies. As such, the myelinated tissue (axons) can be easily recognized in a cross section of the brain (figure 1.5).

Several nuclei of the brain are indicated in figure 1.5. These form a group called the basal ganglia. As can be seen by the strongly myelinated ‘tracts’ surrounding them, they are strongly connected to the cortex, thalamus, and brainstem. Functions to which they are associated are, amongst others: control of voluntary motor functions, learning, routine behavior, and emotion.

1.2.2 Cerebrospinal fluid and the meninges

The brain and spinal cord form the central nervous system (CNS) and are protected from trauma and pathogens in several ways. The blood-brain barrier is present along all blood vessels and capillaries in the brain. It consists of endothelial cells preventing microscopic objects like bacteria and large or hydrophilic molecules in circulating blood from reaching the brain cells or entering the cerebrospinal fluid (CSF). The blood-brain barrier cells allow diffusion of small hydrophobic molecules like O₂, CO₂ and hormones and facilitate the transport of metabolic products across the barrier [7].
The cerebrospinal fluid completely surrounds the brain and spinal cord and flows through the inner ventricular system. The circulating volume of CSF lies between 135 and 150 ml, whilst it is produced at a rate of 500 ml/day [8]. The resulting turnover of about 3.5 times a day provides a chemically stabilizing function for the CNS, rinsing metabolic waste when CSF is absorbed back into the bloodstream. Furthermore, CSF provides buoyancy to the brain, reducing its weight to the equivalence of a mass of 50 grams whereas the brain itself has, on average, a mass of 1500 grams [8]. This prevents the brain from being impaired by its own weight, which could lead to a restriction in blood supply in lower sections. CSF also protects brain tissue when the head is shaken or hit, by preventing, to a certain extent, the brain from contacting the skull. This protective function is limited and cannot prevent brain injury: when impact forces acting on the head become too large over a too long time span, the energy transfer to the brain can cause concussion or more severe traumatic brain injury.

The meninges form a layer of membranes that envelope the central nervous system and contain the cerebrospinal fluid. They consist of three layers: the dura mater, the arachnoid mater and the pia mater; arranged in that order moving from outside to in. The dura mater is thickest and provides the major shielding function; the arachnoid mater has a spider web-like structure and provides a cushioning effect for the CNS. Figure 1.6 shows the how the meninges are arranged around the brain, within the skull.

![Figure 1.6: The meninges, consisting of the dura mater, arachnoid mater, and pia mater, arranged within the skull [9].](image-url)

In neurosurgical procedures to the CNS the meninges need to be opened to provide access. Closure of the meninges after surgery is crucial to prevent leakage or contamination of CSF and infection of the CNS. It is realized by suturing the dura matter as is done with skin.

### 1.3 Interventions in the brain

Despite general knowledge of functional areas in the brain, it is an ongoing challenge to discover exactly where in the brain what specific physical functionality is managed. When surgical intervention is discussed, this knowledge is critical for maximizing the treatment’s efficacy. This forms a contrast with pharmacological treatment, as drugs could be considered to find their own way based on their composition and the chemical processes they address. With the aging population, the prevalence of neurophysiological diseases related to age increases. One of which is Parkinson’s disease, next to for example dementia and Alzheimer’s disease. Although conventional treatment for these ailments is pharmacological,
surgical intervention is also possible. A growing interest in this context lies with Deep Brain Stimulation [10, 11].

**Parkinson’s disease**
The main clinical application of DBS at the moment, is for the treatment of symptoms related to Parkinson’s disease (PD). It is the distortion of the balance between dopamine and acetylcholine caused by the degeneration of dopamine producing neurons in the brain. Dopamine is a neurotransmitter for signal transfer between, amongst others, the substantia nigra and the corpus striatum to realize continuous, purposeful motions. A loss of dopamine results in uncontrolled firing of the neuronal cells in the corpus striatum. Acetylcholine is a neurotransmitter related to signal transfer between nervous cells and skeletal muscular cells and plays an important role as neurotransmitter in the autonomic nervous system. The motor symptoms of Parkinson’s are the most obvious, especially early in the course of the disease, and they include shaking, rigidity, slowness of movement and difficulty with walking and gait. Cognitive and behavioral problems may arise in later stages of the disease, with a possibility of the patient developing dementia [12].

Common treatment of PD consists of administering medicine like Levodopa and dopamine agonists. These act as dopamine precursors being able to transfer the blood-brain barrier whereas dopamine itself cannot. As the disease progresses and dopaminergic neurons continue to be lost, drugs eventually become ineffective at treating symptoms and at the same time can cause a complication called *dyskinesia*. Dyskinesia is characterized by diminished voluntary movements and the occurrence of involuntary movements [13].

In this advanced stage of the disease, surgical intervention can be used as a last resort to improve patients' quality of life. Traditionally this involves creating lesions in specific regions in the brain, usually the subthalamic nucleus and the substantia nigra, to reduce the amount of uncontrolled firing of nervous cells in these areas and thereby diminish the intensity of motor symptoms related to PD. The major drawback of such intervention lies in its irreversibility. Thalamotomy is another intervention used for tremors, being the surgical destruction of specific parts of the thalamus. DBS provides an alternative to lesional surgery by realizing the same effect but at the same time being adjustable and reversible. DBS is however not suitable for all patients: patients who suffer from immunodeficiencies are an example of a situation in which DBS is not a suitable procedure. Furthermore, DBS is (still) a costly procedure [11].

For Parkinson’s disease, the stimulation target (subthalamic nucleus, STN) measures approximately 8 by 4 by 4 mm and should be stimulated ideally in its motoric core (figure 1.7). The success rate of DBS surgery currently lies between 72-85%, with the 28% failure resulting mainly from the inability to hit the right target [14].
Stimulation pulses reaching not only the target area but also surrounding brain tissue have been shown to cause side effects typically in emotional behavior. As conventional electrodes stimulate 360 degrees around their centerline, any positioning of the electrode off center from the target area will result in such parasitic stimulation. The stimulation pulse intensity could be reduced to minimize this, lowering the reach of the stimulation signals in the non-targeted tissue. This however will compromise the efficacy of the targeted tissue’s stimulation.

1.4 Current day procedure

1.4.1 Overview

The procedure starts with making a magnetic resonance imaging (MRI) scan of the patient’s brain. This is done without any reference markers on the head and typically days before surgery. On the day of surgery, this MRI image needs to be mapped onto the patient’s head to allow for image-based targeting.

The base ring of the stereotactic frame used during surgery is fixated to the skull with four skull pins (figure 1.8). These pins are set up in a roughly circular pattern around the skull, pointing roughly inwards. The pins are screwed in, until their points puncture the skin and outer osseous layer of the skull, forming a clamp around the skull.

![Figure 1.8: Base ring of stereotactic frame attached to patient’s head [16].](image)

The base ring remains fixated to the skull until the implantation is completed. A computed tomography (CT) scan is made of the patient’s head with the base ring attached. The ring acts as a reference and after image fusion of the MRI and CT scan, the MRI scan can be related to the ring and thereby mapped onto the head. The stimulation target and skull entry point can now be pointed out on the MRI scan, and the corresponding coordinates are converted to settings for the stereotactic frame (center-of-arc principle).
The frame is now attached to the base ring (figure 1.9) and can be used to indicate the location on the skull where the burr hole should be made. The frame is swiveled away, and back after drilling. The meninges are opened locally after drilling the hole, and a cluster of up to five recording electrodes (one central and four surrounding radially at 2 mm at each quartile) is inserted in the brain along the planned trajectory. These electrodes are used to measure the local neuron firing patterns and thereby either verify the initially planned path and depth were right, or look for the most ideal trajectory (of the five available) and depth if the initial path proves sub optimal. This micro electrode recording (MER) ads up to two hours to the overall surgery time and requires the patient to be awake during the procedure. After selecting the best trajectory of the five available, the recording electrodes are removed and the stimulation electrode is implanted. For bilateral surgery, the procedure is repeated for the other brain half.

The current DBS surgical procedure dates back to the mid 1990’s. Since then, the imaging techniques used for targeting have improved, as has the understanding of how the electrical stimulation of brain regions can beneficially affect them. However, the equipment used for electrode implantation has not undergone any noteworthy evolution and still relies on the center-of-arc principle of the Leksell stereotactic frame. Figure 1.10 shows the frames as used in 1980 and 2016 side by side.
Shortcomings with respect to the unambiguous definition of the stimulation target coordinates can be pointed out with respect to:

- the surgical instrument;
- imaging and planning;
- brain shift.

1.4.2 Surgical instrument
The limited mechanical stiffness of the surgical instrument translates to a limited positioning accuracy of the electrode during implantation. Several structural members are subject to a bending and torsional load, whilst the main arc seems to lack any torsional stiffness needed to properly define the rotation around the axis perpendicular to the sagittal plane.

The fixation of the frame to the skull with four circumferential pins means the clamping force loop is closed around the circumference of the skull. This implies the skull itself is subject to a clamping force. The pins should ideally land perpendicular to the skull surface. This is often not achievable for all four pins due to limited adjustability of the pin orientation, resulting in non-optimal frame fixation. Furthermore, with the patient in supine position during surgery, the frontal pins of the frame will be unloaded due to deformation of the skull.

Although the skin and peristomeum covering the skull are locally anesthetized, the patient is still able to sense this clamping force. Patient feedback points out this is regarded as a highly uncomfortable aspect of the procedure, as the patient remains conscious for the rest of the treatment.

1.4.3 Imaging
The imaging and planning step form a second source of inaccuracy in the implantation procedure. It is not common practice to attach the currently used frame to the patient’s head during the MRI scan. This is primarily because the frame, although not ferromagnetic, causes imaging artifacts which can compromise image quality and accuracy in the target area. Therefore the implantation trajectory planning requires MRI and CT image fusion. This software-based image fusion causes an error as two different image types with limited accuracy each (1 – 3 mm), are fused, again with limited accuracy. In addition, MRI has some shortcomings as imaging technique as well in this application.

MRI is used as a medical imaging technique for visualizing body anatomy and physiology. It is based on the interaction of matter with electromagnetic fields. The spin magnetic moment is a property many atomic nuclei have. It is a measure for the total orbital moment of the constituents of the nucleus around the rotation axis. The spin magnetic moment can be excited by applying electromagnetic field changes at a specific frequency, on top of a static magnetic field. After excitation, it falls back to equilibrium under emission of electromagnetic energy waves with a frequency dependent on the strength of the static magnetic field. By creating a precise gradient in the static field, nuclei at different positions will emit at different frequencies. Analysis of these frequencies shows where the nuclei are located in 3D space. Contrast in images is determined by the rate at which excited nuclei return to equilibrium. As the human body consists for approximately 70% of water molecules, the spin magnetic moment of the associated hydrogen nuclei is targeted with the excitation frequency in most MRI scans for medical use. As a result, MRI is primarily used for imaging soft tissue in the body. However, if a volume of tissue is physically homogeneous but contains different functional regions, this volume is shown as homogeneous on the scan
image. Therefore the imaging of the brain is twofold: on the one hand, it is ideal for showing anomalies like tumors and hemorrhages; on the other hand, it can be difficult to identify different functional regions.

The primary DBS target for Parkinson’s disease, the subthalamic nucleus, lies in a physically homogeneous region in the brain. This implies it is difficult to precisely define its boundaries based on the MRI scan. Therefore its location is often approximated using a general stereotactic atlas. Such atlas uses for example the more clearly distinguishable anterior and posterior commissures as landmarks: the average locations of the left and right subthalamic nuclei are expressed in relation to the midpoint of the so called AC-PC line (figure 1.11).

![Figure 1.11: AC-PC-line indicated on MRI-scan along sagittal plane [20].](image)

This is the straight line connecting the anterior and posterior commissures on the scan images. Other landmarks often used for STN targeting are the substantiae nigra: these nuclei, one on the left and one on the right side, are clearly visible as two dark spots on the scan images as a result of their composition.

Given a perfect instrument, it is because of this shortcoming in MRI-based targeting the micro electrode recording is needed. The use of a general stereotactic atlas or limited contrast image results in target coordinates with a relatively large uncertainty. An iterative electrode positioning procedure is performed, which involves the micro electrode recording and takes two hours in an overall procedure time of five to six hours. However, there is also the phenomenon of ongoing brain shift.

### 1.4.4 Brain shift

The intracranial pressure (ICP) is the pressure inside the skull and thus in the brain tissue and CSF. For a supine adult at rest its value lies between 7 and 15 mmHg\(^1\). An ICP value between 20 and 25 mmHg is considered as the upper limit of normal, above which ICP reducing measures should be considered. Opening of the meninges usually leads to leakage of CSF. Subdural air ingress takes place simultaneously and as a result the ICP will drop. This leads to reduced buoyancy of the brain resulting in deformation of the brain called brain shift.

---

\(^{1}\) mmHg is a traditional measure of pressure in medical context; it is defined as 1 mmHg = 133.322 Pa.
A clinical study by Hartkens et al. [21], based on interventional MRI during neurosurgery, shows brain deformation does not only occur at the surface, but also in deeper brain structures. Furthermore, the principal direction of displacement does not always correspond with the direction of gravity. Brain shift also occurs in the contralateral hemisphere in unilateral brain surgery, although not as explicit as in the ipsilateral hemisphere. For deep brain stimulation surgery, the occurrence of brain shift together with inaccuracy on the exact stimulation target location requires a micro-electrode recording to be part of the surgical procedure. Brain shift is usually not accounted for in the planning stage of the surgery, in which is determined where the stimulation target is located. Bilger et al. [22] state this can lead to the effective location of the electrode being 5 mm or more away from the planned location. During the first electrode insertion an initial brain shift takes place. This shift is locally hindered by the rigid guiding cannula surrounding the flexible electrode. When this cannula is removed a second local shift can be observed which imposes the first deformation of the flexible electrode. Several days or weeks after surgery, the brain returns to its initial state when the air introduced during surgery is resorbed and the CSF replenished. This inverse brain shift leads to a displacement of the electrode in its axial direction (figure 1.12). Bilger et al. [22] state even deep brain structures such as the subthalamic nucleus may shift up to 5 mm during surgery. As this nucleus measures approximately 8 by 4 millimeters, and for effective stimulation in movement disorders one would like to stimulate the motoric sub-region of the STN, such brain shift may result in completely ineffective stimulation. Current work on the influence of brain shift on neurosurgical procedures focusses on the development of models to predict brain shift (Bilger et al. [22]) and methods to detect brain shift using interventional MRI and to correct for it (Hartkens et al. [21], Pallavaram et al. [23]).

Figure 1.12: Postoperative (left) and follow-up (right) CT scans showing brain shift at the end of the procedure and electrode displacement due to inverse brain shift [22].

Without adding any dedicated device, reduction of the time the meninges remain opened is key to minimize the error resulting from brain shift. This means omitting the MER should be considered as its efficacy is questionable.

1.5 Alternatives
Several alternatives to the currently used stereotactic Leksell frame are available (figure 1.13). These can be divided into passive instruments and active robotic systems. Most noticeable passive instruments are the STarFix Platform System by FHC and the Nexframe Stereotactic System by Medtronic. Examples of active robots are the Neuromate Stereotactic Robot by Renishaw and the ROSA robot by Medtech. The focus of the passive instruments seems to lie in providing a more dedicated solution for DBS, resulting in systems that are
more compact and easier to use than the stereotactic Leksell frame. The robotic alternatives aim at the opposite: a versatile surgical robotic system, capable of performing DBS surgery.

From a mechanical engineering perspective, the active robotic alternatives seem overly complicated and even unfit to perform DBS electrode implantation. Their multi-DOF actuated arms have no added value since a set-and-hold operation is requested. The force loops from patient skull to instrument tip are long, compromising absolute positioning accuracy. Thoughts of the ‘palm tree effect’ come to mind.

The passive instrument alternatives are both criticized in the way they translate targeting coordinates to instrument settings. The FHC system uses a patient-specific platform, which needs to be attached to the patient’s skull at a very specific location. A location with questionable reproducibility given the multi-day lead time of the platform after the MRI targeting scan. The Medtronic device uses vision-based navigation (Metronic StealthStation)
in the setup procedure of the instrument. The instrument basically functions as a navigation stylus attached to the patient’s skull, with the corresponding limited accuracy.

For both categories their limited extent of use appears to result from the inability to outperform the accuracy of the Leksell frame and therewith the unwillingness of neurosurgeons to adapt to the associated procedural alterations. The primary competition is therefore identified to be the traditional stereotactic Leksell frame, dating back to the 1980’s, with its associated procedure.

A recent development in the field of stimulation electrodes is the steering brain stimulation electrode by Sapiens / Medtronic (figure 1.14).

![Figure 1.14: Schematic representation of conventional stimulation electrode (left) and the recently introduced steering brain electrode (right) [28].](image)

This new type of electrode facilitates non-axisymmetric stimulation to compensate for off-center placement in the stimulation target. The approach of compensating for inaccurate electrode placement with a new electrode design, is considered to be complementary to the development of a new surgical instrument for electrode implantation. As the resolution of MRI is limited, even pin-point accuracy in implantation could still yield suboptimal results. A steerable stimulation field could provide the final step needed to achieve successful and side-effect free stimulation.

### 1.6 Project goal

DBS shows great potential in the treatment of various disorders, despite the concerns with respect to the current procedure. When it could be offered to more patients who qualify for the procedure, earlier in the treatment of their respective disease, it could improve the quality of life of both them and the people around them. But the benefits reach further than the direct social environment of the patient: instead of being disabled to the extent of needing daily personal care, patients could actively participate in society, reducing cost of social security and medical insurance.

This leads to the goal of the PhD project described in this thesis:
Increase the efficacy of DBS treatment by increasing implantation accuracy and optimizing the surgical procedure.

As the project is done in the field of precision mechanics design, the means to achieve this goal are defined:

Design and develop a new surgical instrument for implantation of DBS electrodes, together with a redefinition of the accompanying procedure.

A success rate over 90% is believed to be achievable when sub-millimeter accuracy in targeting and implantation of the stimulation electrode can be realized.

1.7 Outline
The steps taken in the PhD project to achieve the goal described, are elaborated upon in the following five chapters of this thesis.

- **Chapter 2: Dealing with brain shift and complications during DBS surgery**
  Surgery to the brain is intrinsically characterized by elevated risk and the requirement for precision. As all burr hole surgery to the brain can be complicated by brain shift, a small device is proposed to prevent this shift from occurring. For DBS surgery specifically, various error sources are elaborated and categorized by whether they can be improved upon with a new surgical instrument and optimized procedure.

- **Chapter 3: PEEK instrument**
  The first design for a new instrument for DBS electrode implantation, has resulted in a prototype completely made from PEEK. The main goal was to achieve unambiguous translation of target and entry point coordinates to instrument settings. This is realized by introducing an adapter disc which gets fixated with screws to the back of the patient’s skull, before the initial MRI scan for targeting is made. It serves as both a visual reference for imaging and a structural reference for the instrument. The instrument material ensures full MRI compatibility, allowing for implantation under real time MRI, would this be desired.

- **Chapter 4: The aluminum instrument**
  With the second generation instrument, the requirement for MRI compatibility is left behind. The freedom in material choice is exploited in the design, together with experience gained from the PEEK instrument. The resulting prototype is more compact and dedicated for DBS surgery, although still in the same style as the PEEK instrument.

- **Chapter 5: MRI-compatible actuator**
  The requirement for an MRI compatible drive results from the possible application of the PEEK instrument in the confined environment of an MRI scanner. Only the straight lined insertion of the electrode needs to be motorized, as the other instrument settings are adjusted before attaching the instrument to the patient’s head. The goal of the design process was to keep the drive as compact as possible, in line with the limited forces at play during electrode insertion in the brain.
• **Chapter 6: Prospect on future applications**
The intended use of the new instruments is the implantation of electrodes in the brain for DBS. More applications are seen however, as for example the removal of brain hemorrhages and brachytherapy for the brain. Accurate positioning in the skull, based on MR imaging is a common aspect, together with access via a skull burr hole.

• **Concluding remarks**
This thesis is the accompanying writing of a four year research project on the design and realization of a surgical instrument. The interaction between the fields of mechanical engineering and (neuro)surgery has led to some insights which could be useful for future work on this topic. In the last chapter of this thesis, these insights are shared for their recomendative value.
Chapter 2:

Dealing with brain shift and complications during DBS surgery

Errors and complications related to DBS surgery can be subdivided according to whether they occur before, during or after surgery. Human error in identifying the stimulation target (for example the subthalamic nucleus) in MR images is the first step towards incorrect electrode placement. Fusion of CT and MR images to append stereotactic coordinates to the target is also susceptible to error. Using scanners with a higher field strength (MRI) or higher radiation intensity (CT) provides higher image resolution and can result in smaller fusion errors.

Hemorrhage is the most common complication during surgery. Bakay & Smith [29] report an incidence in DBS procedures of 0.7-3.3% per lead, with an increased risk in hypertensive patients. Careful preoperative planning is crucial to avoid vessel crossings in the electrode insertion trajectory. The occurrence of brain shift during surgery could however compromise this planning. Together with the image fusion errors, this makes it common practice to maintain safety margins, typically 2 to 5 mm, on the minimum distance between vessels and the insertion trajectory. When a micro electrode recording is performed with a maximum of five measuring electrodes, the risk of hemorrhage is increased. One of the measuring electrodes will be inserted along the planned trajectory, whilst the other four are centered around this trajectory with an offset of around 2 mm. The safety margin on the minimum distance towards the vessels should be adjusted correspondingly.

Post-operative complications are primarily device related. DBS hardware forms a foreign body and is therefore susceptible to infection. Abrasive skin wear, especially where the lead wires run over bone under thin skin, can result in surfacing of components with the resulting added risk of infection. Lead fracture and migration form another common complication of DBS, with an incidence reported by Bakay & Smith [29] of ~1.8% and ~4.4% per lead respectively. Lead fracture requires re-operation to remove the damaged lead and to replace it; lead migration is most commonly detected between six months and three years after surgery.

In this chapter a sealing device is proposed as a means to prevent brain shift during DBS surgery (section 2.1). After this, the possibilities for a new type of stimulation implant and electrode are explored (section 2.2).
2.1 Preventing brain shift
Minimizing brain shift during surgery seems, in all cases, beneficial for the targeting accuracy of electrode placement. Although different techniques are practiced to minimize the leakage of cerebrospinal fluid during current day surgery, they pose additional constraints to the implantation trajectory with respect to choosing the brain entry point location.

A sealing device is proposed to prevent CSF from leaking out of the brain after the dura mater is opened for electrode implantation. This will minimize the amount of brain shift occurring during DBS surgery. General dimensions of the seal are 7.5 millimeters in diameter and 2 millimeters in height. It is attached to the dura mater with glue (e.g. DuraSeal, Integra), and proposed to leave attached after completion of the surgical procedure, making it a consumable item. Therefore the same material is chosen for the seal as the insulation material of the electrode lead wire. It is designed as a single component suitable for injection molding, which implies low product cost when produced in large quantities.

The sealing quality depends on the fit of the central hole around the electrode lead wire. As the seal material is elastomeric, the hole is chosen smaller than the lead wire diameter. In this an optimum is found between sealing quality and required axial force for relative displacement of the tube and seal.

The following figures give a description of the seal design.

Figure 2.1: The seal is made from the same fluoropolymer as the insulation of the DBS electrode lead wire.

Figure 2.2: A cross-sectional view shows the seal to be a single-piece product highly suitable for injection molding.
Figure 2.3: The seal is placed on the dura mater through an 8 mm burr hole in the skull.

Figure 2.4: The seal is glued to the dura mater along its edge with surgical glue.

Figure 2.5: A cross-shaped incision in the dura mater is made through the seal opening, allowing access to the brain.
2.1.1 Concerns

The sealing device needs to seal against both the electrode lead wire and the dura mater to function properly. Glue is proposed as a means to achieve the latter function, as this is less invasive than other methods (suturing, clamping). As it is nearly not possible to create a leak free passage of the lead wire through the dura mater, the seal should remain in place after implantation. This will prevent any leakage of CSF and ongoing brain shift after surgery. This proposal to leave a foreign object behind in the body after surgery is expected to raise concerns. The risk of infection is a valid argument against such practice. In this case, the concerns should be weighed against the benefit for the procedure success rate. The brain shift value of 5 mm mentioned might be an extreme case, but given the stimulation target dimensions, any shift is detrimental to the procedure outcome.

A second concern lies within the positioning of the skull burr hole. It is desired to keep the hole as small as possible, as this reduces the risk of infection and promotes healing. With an outer seal diameter of 7.5 millimeter, an 8 millimeter burr hole should be sufficient to allow for proper seal placement. However, this rules out any possible play in the seal’s position, would an unforeseen factor require so. It is therefore advisable to use a 10 millimeter burr hole, unless it is absolutely certain an 8 millimeter hole will suffice. A 10 millimeter burr hole would still be an improvement upon the nowadays common 14 millimeters.

2.1.2 Patentability

A sealing device as proposed above is not currently used during DBS surgery. It is also not known to be commercially available. This raises the question of patentability of such device, as its potential in terms of improvement of surgical accuracy seems substantial.

At the time the sealing device was designed, it was unknown whether such device was invented already or not. A patent search was carried out, resulting in the find of a patent owned by Boston Scientific, titled ‘Burr hole sealing device for preventing brain shift’ [30]. This patent describes a device with a similar intended function as the sealing device discussed above. Although different in appearance, the fundamentals are similar in such a way, that valorization of the proposed device could result in infringement of the patent mentioned.

Knowing a renowned company as Boston Scientific owns a patent, which is not actively valorized by means of a commercially available product, raises questions regarding the value
of the idea behind the patent. Besides the foreseen concerns mentioned in section 2.1.1, there might be further reasons for the lack of a demand for such product.

2.2 Implant alternative

Complications related to DBS lead wires could be resolved by situating the complete system on and in the skull. This eliminates the risk of component surfacing due to skin abrasion. The intracranial volume used should not exceed that of the current electrode and lead, to minimize the compression of surrounding brain tissue. This implies all electronics and the battery should be located in a milled pocket in the skull bone. This is already done for cochlear implants, albeit in a different location on the skull (mastoid bone). Current day DBS pulse generators typically have an internal battery with a capacity of 1 to 2 years’ worth of use. The battery makes most of the pulse generator’s volume, resulting in the medium sized matchbox-like size they usually have. To keep the pocket for the proposed DBS system as compact as possible, the battery capacity of the system will most likely need to be reduced, given current day approved battery technology. A rechargeable battery is proposed to allow minimal battery volume without the need for (frequent) surgical replacement.

For the three most common stimulation targets in the brain, the nominal stimulation characteristics are shown in table 2.1.

Table 2.1: Nominal stimulation characteristics for subthalamic nucleus (STN), globus pallidus internus (GPi), and ventral intermediate nucleus of the thalamus (Vim), [31].

<table>
<thead>
<tr>
<th></th>
<th>STN</th>
<th>GPi</th>
<th>Vim</th>
</tr>
</thead>
<tbody>
<tr>
<td>amplitude [V]</td>
<td>2.1 – 3.0</td>
<td>2.8 – 3.5</td>
<td>2.1 – 3.2</td>
</tr>
<tr>
<td>pulse width [µs]</td>
<td>60 – 90</td>
<td>90 – 150</td>
<td>60 – 120</td>
</tr>
<tr>
<td>pulse rate [s⁻¹]</td>
<td>138 – 158</td>
<td>145 – 160</td>
<td>144 – 163</td>
</tr>
<tr>
<td>impedance [Ω]</td>
<td>1285</td>
<td>1079</td>
<td>1348</td>
</tr>
</tbody>
</table>

The maximum total energy use of the system per day can be calculated from these characteristics. It is shown in table 2.2.

Table 2.2: Maximum total energy use of typical DBS system for stimulation of STN, GPi, and Vim.

<table>
<thead>
<tr>
<th></th>
<th>STN</th>
<th>GPi</th>
<th>Vim</th>
</tr>
</thead>
<tbody>
<tr>
<td>voltage [V]</td>
<td>3.0</td>
<td>3.5</td>
<td>3.2</td>
</tr>
<tr>
<td>current [mA]</td>
<td>2.33</td>
<td>3.24</td>
<td>2.37</td>
</tr>
<tr>
<td>activity [s/day]</td>
<td>1229</td>
<td>2074</td>
<td>1690</td>
</tr>
<tr>
<td>energy use [J/day]</td>
<td>8.6</td>
<td>23.5</td>
<td>12.8</td>
</tr>
</tbody>
</table>

The battery capacity required for one day of system operation can now be determined:

- for STN stimulation: 0.8 mAh @ 3 V
- for GPi stimulation: 1.9 mAh @ 3.5 V
- for Vim stimulation: 1.1 mAh @ 3.2 V

As a patient should be able to recharge the system every 24 hours, a battery capacity for 48 hours is considered to provide the necessary redundancy. Current day lithium-ion battery technology allows for a volumetric energy density of 250 to 620 Wh/l [32], corresponding to
between 900 and 2232 J/cm³. This means a theoretical battery volume of 0.05 cm³ should be enough for 48 hours of GPi stimulation. Although it is unlikely such a small battery would be manufactured, the numbers show a substantial reduction in size compared to the current day pulse generator should be possible. Combined with all electronics needed for pulse generation and recharging, a new unit the size of a 2 Euro coin is estimated feasible. Recharging of the battery is proposed to be done inductively. Depending on the charge rate, it could be done during sleep or a short period of seated activity. The charging loop, attached to a bedside or tabletop device, could be placed in a hat the patient should wear for the duration of the recharging process.

The new system discussed conceptually above, could resolve some of the complications related to current day DBS systems. However, stimulation pulses are still transmitted from a fixed location on the skull to a nucleus in the soft tissue of the brain via a physical medium, being some kind of lead wire and electrode. Such system will always either exercise tractive forces on the brain tissue or result in relative motion between the stimulation target and electrode. Thoughts have risen of a system where the stimulation signal is transferred wirelessly from a transmitter located on the skull to some sort of passive (i.e. without its own power source) transponder implanted in the stimulation target. Migration of the transponder with respect to the stimulation target in such solution should be guaranteed to be impossible. During this research, no physical form of such transponder has been found.
Chapter 3:

PEEK instrument

The first prototype realized as an alternative to the currently used stereotactic frame, was designed with the recent trend of MRI-guided surgery in mind. Real-time imaging during surgery could possibly aid electrode positioning accuracy as compensation for brain movement and deformation during surgery. PEEK was chosen as material, based on its full MRI-compatibility, excellent machinability, and availability as FDA-approved for medical appliance. Furthermore, from all technical polymers commonly available, it has superior mechanical properties (e.g. specific stiffness and functional temperature window). The instrument has been designed to provide an unambiguous translation of MRI-derived stimulation target and entry point coordinates, to instrument settings. The instrument serves as a tool for the implantation of the DBS electrode along a straight-lined path from these entry point coordinates, to the coordinates of the stimulation target.

3.1 Instrument fixation
As the complete force loop from the patient’s skull to the electrode tip is ultimately decisive for the positioning accuracy during implantation, a rigid fixation of the instrument to the skull is crucial.
Two methods of fixation are considered, being the use of skull pins and bone screws. The skull pins are used for the current stereotactic frames (figure 3.1).

Figure 3.1: Conventional (base of) stereotactic frame attached to the skull with skull pins [33].
The skull pin consists of a cylindrical metal rod, partially threaded, with a pointed tip (figure 3.2). The pin is threaded into a support beam, which in turn mounts to the frame base ring. Upon tightening the pin, the pointed tip punctures the skin and outer osseous layer of the skull. The brittle osseous layer will fracture locally at each pin tip, requiring delicacy and experience during fixation. This local skull fracture will introduce play in the fixation upon dynamic loading. The tip should in no way puncture or fracture the inner osseous layer of the skull; this could damage the meninges and potentially the brain. A total of four such pins fixates the frame base ring to the skull. They require a frame design which encloses the skull such that the latter can be clamped. The relatively compliant skull is loaded over its greatest length by the clamping force, compromising fixation stiffness. Ideally, for each pin the clamping force vector should coincide with its respective center line. Given the variety of skull geometries, this is hardly achievable.

Despite local anesthetization of the skin and periosteum at the locations of the skull pins, the patient still experiences a sensation of the skull being clamped. Patient feedback points out this is considered as highly uncomfortable, especially when the patient needs to remain conscious for the remainder of the procedure.

Alternatively, bone screws could be used for fixation of the instrument to the patient’s skull. Such screws are already commonly used in orthopedics and for closing craniotomies\(^2\) in brain surgery. Figure 3.3 gives a few examples of typical bone screws used.

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\(^2\) A method of gaining access to the brain by drilling a hole and subsequently sawing out the contour of the fragment of skull bone to be removed.
Using such screws allows for a design in which the force loop, needed to maintain contact between two touching objects, remains small. When the corresponding preload in the loop is high enough, backlash in the contact can be avoided.

The connection established with a bone screw should be strong enough to handle the desired preload force in the contact. As bone is weaker than (screw) metal, the shear stresses imposed on the bone by the screw should be minimized. For this the screw requires a large pitch-to-diameter ratio. To prevent damage to the meninges and brain, and to minimize the risk of infection, the screws should not penetrate the skull bone. Their length should therefore be chosen carefully.

Based on the benefits in terms of stiffness and size of trauma, fixation by means of bone screws is preferred for the new instrument.

### 3.2 The adapter disc

A fundamental part of the new instrument’s design, is to have a shared reference for both the targeting MRI scan and the fixation of the instrument to the patient’s head. For this, an adapter disc is introduced which is attached to the back of the patient’s head (figure 3.4). The disc is fixated to the prepared skull bone with three bone screws via three titanium sleeves. These sleeves are the only components having invasive contact with the patient. Therefore titanium alloy is chosen as material, as this is MRI compatible and inert in this specific environment. The disc serves as a reference for the target and entry point coordinates and is made from the MRI-compatible polymer PEEK, as is the instrument itself. This material is chosen based on its full MRI-compatibility, excellent machinability and availability as FDA-approved for medical appliance. Furthermore, from all technical polymers commonly available, it has superior mechanical properties (e.g. specific stiffness and functional temperature window).

The location of fixation for the disc on the back of the skull is chosen to have minimal interference with the surgery, and provide enough bone thickness. Furthermore the patient is in supine position on the table, keeping the shear load on the screws and sleeves as a result of the head’s weight to a minimum with the disc placed on the back of the head. The local bone thickness is sufficient to support a rigid fixation with the screws mentioned and resulting scars upon recovery lie within the patient’s hair line.

![Figure 3.4: PEEK adapter disc with three titanium sleeves (left) attached to the patient’s head (right).](image)

The adapter disc provides a kinematic coupling for the instrument (figure 3.5). This means every degree of freedom (DOF) in the coupling is fixed only once. The coupling is designed
such that it can be closed in two ways separated by a relative rotation of 180 degrees. This value of 180 degrees follows naturally from the desire to setup the instrument either along the right or left side of the patient’s head. Furthermore, it simplifies the manufacturing process since the three slots needed for the kinematic coupling now lie on a single line.

Figure 3.5: Statically determined fixation of adapter disc to instrument.

All three locating pins protruding from the surface to which the disc mounts (instrument), fit in a rounded rectangular slot in the mating surface of the disc (figure 3.6). The width of these slots corresponds to the diameter of the pins; the length of the slots is slightly larger than the pin diameter. There are only two contact lines between each pin and the slot walls on the pin’s circumference. For the outer two pins, these contacts are in tangential direction of the disc; for the central pin in the perpendicular radial direction. Together the three locating pins, fitted in their respective slots, fixate the two in-plane translations between the disc and the instrument and also the relative rotation around the out-of-plane axis.
When the disc lands on the mating surface of the instrument, it does so on a ring with the same outer diameter as the disc’s contact surface and an inner diameter several millimeters smaller (figures 3.5 & 3.6). This results in a ring-shaped contact surface fixating the out-of-plane translation and the rotations around the two in-plane axes.

After the disc has landed, it is secured with two bolts approaching from underneath. When the bolts are tightened, the disc is fixated by friction to the mating surface, with the ring-shaped surface mentioned above as contact plane. The result is an extremely rigid and reliable connection which can be made and disassembled over and over without significant wear or loss of position.

The reproducibility of the coupling between the adapter disc and the instrument, is determined by their manufacturing tolerances. For accurate manual machining work, a tolerance of ±0.01mm can be used as rule of thumb for workpieces the size of the adapter disc [36].

The manufacturing tolerances on the position of the locating pins on the instrument, and the corresponding slots in the disc, result in play in the coupling between the disc and the instrument. This play is primarily in the direction of the two in-plane translations between the disc and the instrument, and the relative rotation around the out-of-plane axis.

For the two translations mentioned, the manufacturing tolerances of ±0.01mm on the locations of both the pins and slots, can lead to a worst-case play of 0.04 millimeters in each respective direction. The relative rotation can have a worst-case play of 0.6 milliradians. As these play values can be present in the coupling between the instrument and the adapter disc (and therewith the stimulation target), they can be directly superimposed onto the instrument accuracy.

### 3.3 Integration of reference marker in MRI-transparent PEEK

MRI requires protons with a certain mobility to render a sharp image. The more mobile a proton, the longer the relaxation time of its spin magnetic moment after excitation by the electromagnetic field changes in the MRI scanner. A longer relaxation time corresponds to a longer period of electromagnetic wave emission by the proton, which can then be picked up by the scanner more easily. This results in a sharper image.
The hydrogen atoms in PEEK are bonded too tight, meaning the relaxation time after excitation of the spin magnetic moment is too short. The electromagnetic wave emission by the protons is not picked up by the scanner, so the material appears ‘transparent’ on the scan image.

To provide a usable reference for the targeting MRI scan, the PEEK adapter disc features an internal cavity filled with a solution of sodium chloride and copper sulfate in water (figure 3.7). Although simple water would do, the relaxation times of the protons would in that case be longer than needed for the MRI scanner to produce a sharp image. This would result in a long scanning time. By adding the two salts mentioned, the relaxation time and thereby the scanning time are reduced. The ideal concentration of the salts in water is determined empirically to be 700 mg CuSO₄·5H₂O and 2000 mg NaCl in 1000 ml of demineralized water [37].

The cavity containing the solution is shaped as a triangle. It is oriented such that one of its sides coincides with the reference y-axis and the other two sides point in the direction of the negative x-axis. The positive z-axis is oriented perpendicular to the plane of the triangle, in the direction of the patient’s head. The center of the triangle is identified as $(x,y,z) = (0,0,0)$. As the center of the triangle can be hard to define in the MRI-images, its coordinates can be deduced from the coordinates of the corners. A choice should be made whether the inside or outside corners of the triangle are used, both of the upper and lower level of the triangle (6 points in total). The center point is then defined as the vector average of the sum of all corner coordinate vectors.

Figure 3.7: Representation of how the MRI reference fluid-containing cavity is realized in the PEEK adapter disc. In the bottom picture, the insert is displayed translucent.

The visibility of the MRI reference has been verified using a Philips Medical Systems Intera 1.5T MRI scanner, located at the TU/e Darcy Lab. Figures 3.8 and 3.9 show resulting scan images in a left- to-right, top-to-bottom succession of slices with 0.5 millimeters thickness.
The two scans were made, each with a different setting for the display field of view: 150mm for the scan represented in figure 3.8, and 250mm for the scan represented in figure 3.9. The triangular reference can be made out clearly for both scans, with the smaller display field of view of the first scan providing a larger resolution when determining the coordinates of the corners.
Figure 3.10 shows a close-up of the triangular reference for each of the two scans. The lengths of the inner sides of the triangle have been measured with the imaging software for both scans. For this, the corners have been selected as accurately as possible. The real length, as would be measured with a caliper on the machined part, is 34.6 millimeters. From the figures it becomes clear that the limited MRI resolution causes the inner sides to appear somewhat shorter (and the outer sides longer). As the largest deviation is less than three percent, the averaging used of the six corner coordinates to find the center point coordinates, is still expected to give an accurate value.

Figure 3.10: Measurement of reference triangle side lengths for both the 150mm DFOV (left) and 250mm DFOV (right) scans.

3.4 The new instrument

The new surgical instrument is designed specifically for implantation of the electrode and intracranial part of the lead wire in the brain. It therefore has an operating range wide enough to cover all usual skull and brain anatomies, but not wider than strictly necessary. A larger operating range will typically lead to an increased size of structural components, compromising the stiffness-to-weight ratio and thereby accuracy. The result is a compact and lightweight system, providing accurate electrode placement after a shortened and optimized implantation trajectory planning procedure. It requires the adapter disc described in section 3.2 to be attached to the patient’s skull.

Overall MRI compatibility of the instrument allows for electrode implantation under real-time MRI. This is of interest to research groups studying the behavior of brain tissue when penetrated by a foreign object. Knowledge gained can also be used in harvesting brain tumor biopsies, brachytherapy and ventricle catheterization for hydrocephalus.

Combined with an optimized planning procedure, the new instrument is intended to have a positioning accuracy an order of magnitude higher than what is achievable with the currently used frames. This should result in an increase in surgery success rate.
3.4.1 Instrument design and proposed procedure

Figure 3.11: New instrument for DBS surgery.

The instrument consists of a manually adjustable frame which is attached to the back of the patient’s head via the intermediate adapter disc. All steps in the procedure are taken on one single day which starts with attaching the concave adapter disc to the back of the patient’s skull. An MRI scan is made of the patient’s head, after which the stimulation target and entry point can be pointed out by the surgeon. Their coordinates are defined with respect to a clearly distinguishable landmark on the disc. The target and entry point coordinates are now directly translated to instrument settings via a mathematical algorithm which follows directly from the instrument’s kinematics. Figure 3.12 shows the instrument with its seven degrees of freedom (DOF) indicated (\(y_1, y_2, z_1, z_2, \phi, \psi_1, \psi_2\)). The instrument has been designed with stiff connections between all system points, in both torsion and bending. The resulting setup process is unambiguous and user friendly.
In figure 3.12, the $y_1, \psi_1$-tube is used to define translation $y_1$ and rotation $\psi_1$; the $y_2, \psi_2$-tube for $y_2$ and $\psi_2$. The ways in which the translation and rotation are defined, are the same for both. Figure 3.13 shows a close-up of the translation and rotation adjustment for $y_2$ and $\psi_2$. 
The translation $y_2$ is achieved with a spindle which engages in a thread segment in the tube. The spindle is completely concealed in a housing, avoiding contamination of the threads (figure 3.14). The spindle is fixed in the housing in all its DOF, except the rotation around its axis. The housing contains a key in a keyway on the tube.
The rotation $\psi_2$ is set via an incremental coarse adjustment (15° increments) and an additional fine adjustment (0.5° resolution). For the coarse adjustment, the rotation adjustment arm is released from a notch on the outer surface of the translation spindle housing by sliding the arm in axial direction (figure 3.15b). The housing can now be rotated separately from the arm, realizing the coarse rotation (figure 3.15c). The desired coarse adjustment increment in the arm is mated to the rotation adjustment arm again (figure 3.15d). From this point, the rotation fine-adjustment screw is used to manipulate the arm to reach the final angular value desired (figure 3.15e). A locking mechanism is provided to prevent the adjustment of the translation to influence the rotation (this influence is possible due to friction in the threads). When both rotation and translation are set, an elastic clamp is closed over the tube, effectively fixating the tube with respect to the body it runs through (figure 3.16).

Figure 3.15: Coarse and fine adjustment of rotation $\psi_1$ and $\psi_2$. 
The $z_1$-tube in figure 3.12 defines translation $z_1$. This translation is realized in the same way as $y_1$ and $y_2$. Also here an elastic clamp is present to fixate the tube in the body it runs through after the translation is set. The rotation of this tube is locked with a removable key (figure 3.13). The key can be removed to be able to swivel the instrument head out of the way when access to the skull burr hole is required.

Rotation $\varphi_1$ is adjusted with a spindle (figure 3.17). The electrode drive is hinged over a line indicated as point $C$ in (2 dimensional) figure 3.17. The hinge line, centerline of the $y_2, \psi_2$-tube and the centerline of the electrode/$z_2$-translation intersect in one point.
A remark is given on this use of spindles for the adjustment of various instrument DOFs. The spindles used are all designed to be non-backdrivable; they will hold their setting when no specific adjustment is performed. Their pitch is chosen such that for the various DOFs the desired adjustment resolution is achievable. The threads of the components, the different spindles engage with, are cut for their specific spindle each, minimizing backlash. After the instrument is set up accordingly, it is placed on the same support structure used currently to support the stereotactic frame and patient’s head weight in the OR. This instrument support is attached at the head’s end of the surgical table. Depending on the specific support used, various adapters are available to connect the instrument to the support (figure 3.18 & 3.19).

Figure 3.18: Interchangeable adapter to fixate instrument to support structure.

Figure 3.19: Representation of how the new instrument can be mounted to the currently used support.
The patient is placed on the table in supine position, with the head resting on the instrument base. The adapter disc will hereby land on its mating surface on the instrument base. The adapter disc is then fixated to the instrument base with two screws (figure 3.18).

The burr hole is made in the skull manually, at the location indicated by the instrument. Fixation of the instrument to the back of the patient’s head ensures good visibility and access to the burr hole. To further improve access, the instrument head can be rotated out of the way around the z1-axis after removing the dedicated key (see figure 3.12).

With the burr hole made, the meninges can be opened by incision. If the instrument head has been rotated away for improved access, it should be put back in the correct position by reinstalling the key removed earlier. The stimulation electrode can then be implanted with the electrode drive.

The electrode drive consists of a straight guided sled, driven by a spindle. The sled can carry the stimulation electrode or any other equivalent needle-like object. It is straight guided by the spindle and the housing combined. The electrode drive is operated manually with a finger knob connected to the spindle with a timing belt (figure 3.20).

3.4.2 Instrument kinematics

The instrument kinematics describe how the adjustment of the different DOF of the instrument translates to the coordinates and trajectory of the electrode (tip). As the angular adjustments (ψ1,ψ2,φ) operate in series, the use of coordinate transformation matrices is needed. Figure 3.21 shows the instrument, its DOF, and the first order perpendicularity errors within its construction. The instrument kinematics are described based on this figure. For the various DOF, the operating range limits are given in table 3.1.
Table 3.1: Instrument DOF operating ranges lower and upper limits.

<table>
<thead>
<tr>
<th></th>
<th>Lower limit:</th>
<th>Upper limit:</th>
</tr>
</thead>
<tbody>
<tr>
<td>$y_1$</td>
<td>86 mm</td>
<td>160 mm</td>
</tr>
<tr>
<td>$y_2$</td>
<td>88 mm</td>
<td>175 mm</td>
</tr>
<tr>
<td>$z_1$</td>
<td>192 mm</td>
<td>286 mm</td>
</tr>
<tr>
<td>$z_2$</td>
<td>0 mm (+ offset)</td>
<td>78 mm (+ offset)</td>
</tr>
<tr>
<td>$\varphi$</td>
<td>-20°</td>
<td>28°</td>
</tr>
<tr>
<td>$\psi_1$</td>
<td>-60°</td>
<td>75°</td>
</tr>
<tr>
<td>$\psi_2$</td>
<td>-75°</td>
<td>60°</td>
</tr>
</tbody>
</table>

For the translational adjustments, the absolute values for their limits are given. Whether their contribution to the instrument settings is positive or negative, is taken into account in the vector/matrix-equations describing the kinematics.
Figure 3.21: Instrument with its DOF and first order perpendicularly errors indicated.
Define:

\[
M_1 = \begin{pmatrix}
\cos \psi_1 & 0 & -\sin \psi_1 \\
0 & 1 & 0 \\
\sin \psi_1 & 0 & \cos \psi_1
\end{pmatrix},
M_2 = \begin{pmatrix}
\cos \psi_2 & 0 & -\sin \psi_2 \\
0 & 1 & 0 \\
\sin \psi_2 & 0 & \cos \psi_2
\end{pmatrix},
\]

\[
M_3 = \begin{pmatrix}
1 & 0 & 0 \\
0 & \cos \varphi & \sin \varphi \\
0 & -\sin \varphi & \cos \varphi
\end{pmatrix}
\]

\[
A_1 = \begin{pmatrix}
\cos \theta_{p,1} & \sin \theta_{p,1} & 0 \\
-\sin \theta_{p,1} & \cos \theta_{p,1} & 0 \\
0 & 0 & 1
\end{pmatrix},
A_2 = \begin{pmatrix}
1 & 0 & 0 \\
0 & \cos \varphi_{p,1} & \sin \varphi_{p,1} \\
0 & -\sin \varphi_{p,1} & \cos \varphi_{p,1}
\end{pmatrix},
A = A_1 A_2
\]

\[
B_1 = \begin{pmatrix}
\cos \psi_{p,1} & 0 & -\sin \psi_{p,1} \\
0 & 1 & 0 \\
\sin \psi_{p,1} & 0 & \cos \psi_{p,1}
\end{pmatrix},
B_2 = \begin{pmatrix}
1 & 0 & 0 \\
0 & \cos \varphi_{p,2} & \sin \varphi_{p,2} \\
0 & -\sin \varphi_{p,2} & \cos \varphi_{p,2}
\end{pmatrix},
B = B_1 B_2
\]

\[
C_1 = \begin{pmatrix}
\cos \theta_{p,2} & \sin \theta_{p,2} & 0 \\
-\sin \theta_{p,2} & \cos \theta_{p,2} & 0 \\
0 & 0 & 1
\end{pmatrix},
C_2 = \begin{pmatrix}
1 & 0 & 0 \\
0 & \cos \varphi_{p,3} & \sin \varphi_{p,3} \\
0 & -\sin \varphi_{p,3} & \cos \varphi_{p,3}
\end{pmatrix},
C = C_1 C_2
\]

then

\[
\vec{r}_d = \begin{pmatrix}
0 \\
y_1 - r_{e,3} \\
0
\end{pmatrix}^T + \begin{pmatrix}
0 \\
r_{e,1} \\
0
\end{pmatrix}^T AM_1
\]

(1)

which is the coordinate vector of point \(A\) (figure 3.21).

Furthermore

\[
\vec{r}_b = \vec{r}_d + \begin{pmatrix}
0 \\
0 \\
z_1 - r_{e,2}
\end{pmatrix}^T AM_1 + \begin{pmatrix}
0 \\
0 \\
r_{e,2}
\end{pmatrix}^T B AM_1
\]

(2)

which is the coordinate vector of point \(B\) (figure 3.21), and

\[
\vec{r}_c = \vec{r}_b + \begin{pmatrix}
0 \\
- (y_2 - r_{e,3}) \\
0
\end{pmatrix}^T B AM_1 + \begin{pmatrix}
0 \\
-r_{e,3} \\
0
\end{pmatrix}^T C M_1 B AM_1
\]

(3)

which is the coordinate vector of point \(C\) (figure 3.21).
The coordinate vector of point \( T \) (target point, figure 3.21) is then defined as:

\[
\vec{r}_T = \vec{r}_C + \begin{pmatrix} 0 \\ 0 \\ -z_2 \end{pmatrix} M, CM, BAM. \tag{4}
\]

When the perpendicularly error angles all are zero, i.e. \( \phi_{p,1} = 0, \psi_{p,1} = 0, \theta_{p,1} = 0, \phi_{p,2} = 0, \theta_{p,2} = 0 \) and \( \phi_{p,3} = 0 \), then matrices \( A, B \) and \( C \) are unit matrices. It then follows:

\[
\vec{r}'_A = \begin{pmatrix} 0 \\ y_1 \\ 0 \end{pmatrix} \tag{5}
\]

\[
\vec{r}'_B = \begin{pmatrix} z_1 \sin \psi_1 \\ y_1 \\ z_1 \cos \psi_1 \end{pmatrix} \tag{6}
\]

\[
\vec{r}'_C = \begin{pmatrix} z_1 \sin \psi_1 \\ y_1 - y_2 \\ z_1 \cos \psi_1 \end{pmatrix} \tag{7}
\]

\[
\vec{r}'_T = \begin{pmatrix} z_1 \sin \psi_1 - z_2 \cos \phi \sin (\psi_1 + \psi_2) \\ y_1 - y_2 + z_2 \sin \phi \\ z_1 \cos \psi_1 - z_2 \cos \phi \cos (\psi_1 + \psi_2) \end{pmatrix} \tag{8}
\]

When the desired target and cardan joint coordinates, \( \vec{r}_T = \begin{pmatrix} x_T \\ y_T \\ z_T \end{pmatrix} \) and \( \vec{r}_C = \begin{pmatrix} x_C \\ y_C \\ z_C \end{pmatrix} \), are determined from the MRI scan, the corresponding instrument settings are calculated as follows:

\( y_1 \to \) choose value based on patient head size

\( y_2 = y_1 - y_C \)

\( z_1 = \sqrt{x_C^2 + z_C^2} \)

\( \psi_1 = \arcsin \frac{x_C}{z_1} = \arccos \frac{z_C}{z_1} \)

\( z_2 = \sqrt{(x_T - x_C)^2 + (y_T - y_C)^2 + (z_T - z_C)^2} \)
\( \varphi = \arcsin \left( \frac{y_T - y_C}{z_2} \right) \) \hspace{1cm} (13)

\( \Psi_2 = \arcsin \left( \frac{x_C - x_T}{z_2 \cos \psi_1} \right) - \psi_1 = \arccos \left( \frac{z_C - z_T}{z_2 \cos \varphi} \right) - \psi_1 \) \hspace{1cm} (14)

**3.4.3 Sensitivity analysis**

For any variable \( f \) which is a function of multiple variables, say \( k, l, \) and \( m \), the value of \( f \) in the point \( (k, l, m) = (a + \varepsilon, b, c) \) can be written as

\[
\frac{\partial}{\partial k} f(a + \varepsilon, b, c) = f(a, b, c) + \varepsilon \frac{\partial}{\partial k} f(a, b, c)
\]

for small \( \varepsilon \). The expression \( \varepsilon \frac{\partial}{\partial k} f(a, b, c) \) can be considered the first order sensitivity of the variable \( f \) to small variations in variable \( k \) in the point \( (k, l, m) = (a, b, c) \). This is applied to the expressions for the target point and cardan joint coordinates as defined by the instrument, to determine their first order sensitivity to small errors in the instrument settings. The expressions for the target point coordinates as defined by the instrument are, as derived in equation (8):

\[
x_T(z_1, z_2, \varphi, \psi_1, \psi_2) = z_1 \sin \psi_1 - z_2 \cos \varphi \sin (\psi_1 + \psi_2) \hspace{1cm} (15)
\]

\[
y_T(y_1, y_2, z_2, \varphi) = y_1 - y_2 + z_2 \sin \varphi \hspace{1cm} (16)
\]

\[
z_T(z_1, z_2, \varphi, \psi_1, \psi_2) = z_1 \cos \psi_1 - z_2 \cos \varphi \cos (\psi_1 + \psi_2) \hspace{1cm} (17)
\]

The partial derivatives of these expressions in their constituent variables are listed in table 3.2.
Table 3.2: Partial derivatives of the instrument target point coordinate expressions in their constituent variables.

<table>
<thead>
<tr>
<th></th>
<th>$x_r$</th>
<th>$y_r$</th>
<th>$z_r$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\frac{\partial}{\partial y_1}$</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial y_2}$</td>
<td>0</td>
<td>-1</td>
<td>0</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial z_1}$</td>
<td>$\sin \psi_1$</td>
<td>0</td>
<td>$\cos \psi_1$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial z_2}$</td>
<td>$-\cos \phi \sin (\psi_1 + \psi_2)$</td>
<td>$\sin \phi$</td>
<td>$-\cos \phi \cos (\psi_1 + \psi_2)$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial \phi}$</td>
<td>$z_1 \sin (\psi_1 + \psi_2) \sin \phi$</td>
<td>$z_2 \cos \phi$</td>
<td>$z_2 \cos (\psi_1 + \psi_2) \sin \phi$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial \psi_1}$</td>
<td>$z_1 \cos \psi_1 - z_2 \cos \phi \cos (\psi_1 + \psi_2)$</td>
<td>0</td>
<td>$-z_1 \sin \psi_1 + z_2 \cos \phi \sin (\psi_1 + \psi_2)$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial \psi_2}$</td>
<td>$-z_2 \cos \phi \cos (\psi_1 + \psi_2)$</td>
<td>0</td>
<td>$z_2 \cos \phi \sin (\psi_1 + \psi_2)$</td>
</tr>
</tbody>
</table>

The magnitude of the individual setting errors is chosen as half of the respective scale interval length. These values are listed in table 3.3.

Table 3.3: Magnitude of the instrument setting errors.

<p>| | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>$\varepsilon_{x_1}$</td>
<td>0.05 mm</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{x_2}$</td>
<td>0.05 mm</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{y_1}$</td>
<td>0.05 mm</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{y_2}$</td>
<td>0.5 mm</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{\phi}$</td>
<td>0.0087 rad</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{\psi_1}$</td>
<td>0.0087 rad</td>
<td></td>
</tr>
<tr>
<td>$\varepsilon_{\psi_2}$</td>
<td>0.0087 rad</td>
<td></td>
</tr>
</tbody>
</table>

The expressions for the cardan joint coordinates as defined by the instrument are, as derived in equation (7):

\[x_c(z_1, \psi_1) = z_1 \sin \psi_1\]  \hspace{1cm} (18)
\[y_c(y_1, y_2) = y_1 - y_2\]  \hspace{1cm} (19)
\[ z_c(z_1, \psi_1) = z_1 \cos \psi_1 \] (20)

The partial derivatives of these expressions in their constituent variables are listed in table 3.4.

Table 3.4: Partial derivatives of the instrument cardan joint coordinate expressions in their constituent variables.

<table>
<thead>
<tr>
<th></th>
<th>( x_c )</th>
<th>( y_c )</th>
<th>( z_c )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \frac{\partial}{\partial y_1} )</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial y_2} )</td>
<td>0</td>
<td>-1</td>
<td>0</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial z_1} )</td>
<td>( \sin \psi_1 )</td>
<td>0</td>
<td>( \cos \psi_1 )</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial z_2} )</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial \phi} )</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial \psi_1} )</td>
<td>( z_1 \cos \psi_1 )</td>
<td>0</td>
<td>( -z_1 \sin \psi_1 )</td>
</tr>
<tr>
<td>( \frac{\partial}{\partial \psi_2} )</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Given the ranges for the instrument settings, the maximum absolute values for the partial derivatives from table 3.2 and 3.4 can be determined. Multiplying these with the respective setting errors from table 3.3, gives the theoretical first order sensitivity of the instrument in the target point and cardan joint coordinates for that specific parameter setting. The results are shown in table 3.5.
The adjustment resolution of $\psi_1$ has a major influence on the theoretical absolute first order sensitivity of the instrument. Inherent to placing various degrees of freedom in series, any angular adjustment error at the beginning of the chain will be magnified at the end. This holds for both manufacturing tolerances and adjustments upon use. The former can be dealt with by a specification on the tolerances allowed, and measurements of the actual errors after manufacturing. Providing the end user with a report on these measurements allows him or her to compensate for them when a protocol for this is defined.

Given the kinematics of the instrument, the values in table 3.5 can only be altered (i.e. reduced) by altering the magnitudes of the instrument setting errors from table 3.3. This translates to increasing the resolution with which the user can adjust the settings of the different DOFs, which can be done in a compact way by adding vernier scales to the read-outs of the DOF adjustment settings. An increase in resolution by a factor of 10 can be easily done and is common on basic measuring calipers. Here, the vernier scale increases the resolution of a ruler with millimeter scale, from 0.5 millimeters to 0.05 millimeters.

For the PEEK instrument prototype, the adjustment of the settings for $y_1$, $y_2$ and $z_1$ is already measured with a measuring caliper with vernier scale. This explains the order of magnitude difference between their related sensitivity values, and those for the other four DOFs. Adding vernier scales to these latter DOF setting read-outs, could reduce their related sensitivity values by a factor of 10, depending on the choice of scale. The maximum value in table 3.5 would then reduce to 0.25 millimeters.

Bear in mind that the positioning errors due to play in the coupling between the adapter disc and the instrument, still need to be added to these sensitivity values. As the value of 0.04 millimeters for the translational play in the coupling is an order of magnitude smaller than
calculated maximum sensitivity value, the overall instrument accuracy will not be significantly altered.

3.5 PEEK instrument stiffness
The structural stiffness of the instrument has been mentioned several times as a key contributor to instrument accuracy. It is a measure for how much the instrument deflects under a specific load. When this load is applied in a situation where the instrument is intended to maintain a certain spatial configuration, it will lead to a change in said configuration. More specific, any load applied to the instrument during electrode implantation in the brain, will deform the instrument and change the implantation trajectory defined by the instrument. The result is a deviation of the electrode from its intended path, meaning a loss in accuracy.

The force necessary to implant the stimulation electrode wire in the brain, is small. A numerical value for this force has not been found in literature. Numerical values for insertion forces of slender probes in rat and monkey brains are documented [38], but these probes are typically an order of magnitude smaller in diameter than DBS stimulation electrodes. Furthermore, the experiments conducted in [38] include puncturing the meninges. Force levels up to 200mN are mentioned, supporting the statement of DBS electrode implantation forces being small, i.e. in the order of newtons. Franceschini [39] conducted mechanical tensile tests on swine brain tissue, reporting an average tensile stress at which fracture occurs of 3.43kPa. Given a DBS electrode diameter of 1.27 millimeters (area: ~5mm²), this translates to a penetration (i.e. implantation) force of 17mN, based solely on the required separation of tissue. Friction between the electrode and brain tissue will add to the required penetration force. This additional force is expected to be small, because of the presence of cerebrospinal fluid. It seems reasonable to assume the total force required for implanting a stimulation electrode in the brain will not exceed 1 newton.

3.5.1 FEM analysis
Considering the relatively small force involved with the actual electrode implantation, the largest forces acting on the instrument during surgery come from gravity and user input. To assess the extent to which the instrument deforms under influence of these and other forces, the instrument stiffness is calculated using a finite element method. For the analysis, only the relevant structural parts of the instrument have been modeled. Figure 3.22 shows a subdivision of the instrument; the base and different stages are partly disassembled to show their boundaries more clearly.
The total mass of the instrument is 2682 grams; the masses of the instrument base and stages indicated in figure 3.22, are as follows:

- base: 776 grams
- y1-stage: 768 grams
- y2-stage: 367 grams
- z1-stage: 771 grams

After removing all irrelevant instrument parts (knobs, levers, housings), the instrument is meshed and boundary conditions are applied. The instrument is configured with the y1, y2, and z1 degrees of freedom fully extended. This provides a worst case scenario for stiffness as all bending and torsion lengths are maximized. The coordinate system used in the FEM analyses is rotated by 90 degrees around the z-axis with respect to the coordinate system used throughout this chapter. This means the FEM x-axis corresponds to the instrument y-axis, and the FEM y-axis corresponds to the instrument negative x-axis.

A force of 1 newton is applied in the cardan point, consecutively in the x, y, and z directions, to calculate the stiffness in each respective direction. The results of the three analyses are shown in figure 3.23.
3.23a: Instrument x-stiffness in cardan point 1N/0.081mm = 1.2e4 N/m.

3.23b: Instrument y-stiffness in cardan point 1N/0.046mm = 2.2e4 N/m.

3.23c: Instrument z-stiffness in cardan point 1N/0.03mm = 3.3e4 N/m.

Figure 3.23: Nodal displacement in instrument negative x-direction (3.23a), y-direction (3.23b), and negative z-direction (3.23c), when load force of 1N is applied in said direction in cardan point.

Based on the stiffness values calculated, one can conclude the electrode implantation force will not cause any noteworthy instrument deformation. Even in the worst case scenario of a fully extended instrument and a load in the instrument’s most compliant direction, the displacement of the cardan point is less than 0.1 millimeters.
Figure 3.24 shows the results of FEM analyses on the instrument deformation under a gravity load, consecutively in x, y, and z directions.

3.24a: Cardan point displacement = 0.31mm.

3.24b: Cardan point displacement = 0.31mm.

3.24c: Cardan point displacement = 0.06mm.

Figure 3.24: Absolute nodal displacement under gravity load in instrument negative x-direction (3.24a), y-direction (3.24b), and negative z-direction (3.24c).
One should bear in mind, the results shown in figure 3.24 are not fully veracious as some instrument components have been excluded from the FEM analyses. This was justified for the calculation of the stiffness values, as the removed components would not have any noteworthy contribution to stiffness. They do however contribute to the instrument mass; approximately 700 grams or 27 percent. As these components (electrode drive, spindles, spindle housings, levers, and screws) are quite evenly distributed over the instrument, their removal did not significantly alter the location of the instrument’s center of mass. This allows multiplying the nodal displacements presented in figure 3.24 by 1.37 (≈ 1/0.73), giving a maximum cardan point displacement (worst case) of 0.41 millimeters.

3.5.2 Electrode stiffness
On top of the stiffness of the instrument, the stiffness of the electrode lead wire itself plays a major role in the accuracy with which it can be implanted. The lead wire consists of a platinum-iridium conductor core, surrounded by a fluoropolymer insulator sleeve. The wire is stiffened by a tungsten stylet which runs through the complete length of the lead wire. The stylet can be removed from the proximal end of the lead wire, where the connector to the wiring from the pacemaker is located. The lead wire has a diameter of 1.27 millimeters, and total length of 50 centimeters, including the electrode tip and connector for the pacemaker wire. Figure 3.25 shows a schematic view of a common electrode used.

![Figure 3.25: Schematic view of DBS electrode lead wire (Medtronic Model 3387) [40].](image)

The stylet provides the lead wire with some axial stiffness needed for penetrating brain tissue upon implantation. Because of its slender shape, the lead wire with installed stylus is susceptible to buckling. Furthermore, the lateral stiffness is low, despite the stylus. After implanting the electrode lead wire, the stylus is removed to make the wire as compliant as possible with the brain tissue.

The length of lead wire extended into the skull can be seen as a cantilevered beam. As the wire cannot be held or supported by the instrument over the length it extends into the skull, only its own lateral stiffness, and the support by the brain tissue, can keep it from deviating from its intended straight-lined trajectory. It should ideally be as short as possible to maximize its stiffness in bending. For the instrument this implies the location of the cardan joint should be chosen as close to the skull burr hole as possible. The instrument kinematics give the user complete freedom in where to position this point.
3.6 Conclusion
In Chapter 1, the current day surgical procedure for DBS electrode implantation has been discussed. Concerns with the procedure and instrument used have been expressed, and taken as input for the design and realization of a new surgical instrument.

The fixation of the instrument to the patient’s head was the first concern addressed. An adapter disc is proposed to be attached to the back of the patient’s skull prior to the MRI scan used for target and trajectory planning. Bone screws are used to attach the disc to the skull. The disc contains a reference visible on the scan images, and the disc itself provides a mechanical interface to the instrument. Because of the way the disc is attached to the skull, and the way it is loaded during surgery, it provides a less invasive and stiffer connection between the instrument and skull than the currently used skull pins. Furthermore, patient comfort is improved as there is no sensation of the skull being clamped, as is the case with the currently used stereotactic frames.

A completely new instrument for electrode implantation has been designed and realized. Full MRI-compatibility was set as a requirement, leading to a design completely in PEEK. The instrument is designed to be compact and slender, with an unambiguous definition of stimulation and entry point coordinates. It contains an interface to the currently used head support, keeping the required changes in the current workflow to a minimum.

Analysis of the instrument kinematics shows a direct translation of target and entry point coordinates to instrument settings. The procedure is put into a protocol prescribing the user how to set up the instrument after selecting target and entry point coordinates manually from the MRI scan. A sensitivity analysis of the errors in the target and cardan joint coordinates of the instrument due to errors in user input has been done. This shows the importance of accurate read-outs of instrument settings. Although the prototype does not have read-outs accurate enough to ensure sub-millimeter resolution in the target and cardan point, these could easily be added in the form of vernier scales.

Following the sensitivity analysis, FEM analyses have been carried out to determine the instrument stiffness in the cardan point. This point is closest to where the electrode enters the brain; from there the electrode enters the brain unsupported by the instrument. A worst case configuration of the instrument is chosen by maximizing the bending and torsion lengths. The calculated stiffness values are not high in absolute sense. But given the small force required to implant an electrode in the brain, the resulting instrument deflection will remain below 0.1 millimeter in the cardan point. Instrument deformation due to gravitational loading is larger; up to approximately 0.4 millimeter in a worst case scenario. Although this value is small compared to current day electrode placement accuracy (~2.5 millimeters), the MRI targeting procedure still adds an inevitable (larger) error to placement accuracy, dependent on the machine used. One could argue if the material choice for PEEK, with a Young’s modulus a factor of 18 smaller than aluminum and over 50 smaller than steel, is to blame.
Chapter 4:
The aluminum instrument

As a large majority of the DBS practicing centers does not (yet) have an MRI facility in the OR environment, MRI-compatibility of a new instrument would have no added value for them. Justifying the higher (material) cost of an MRI-compatible instrument would, as such, be difficult. A second instrument, made largely from aluminum, has been conceived as an alternative to the PEEK instrument, with MRI compatibility not being a requirement. The resulting freedom in material choice has allowed the use of components in both metal and plastics. The frame of the instrument is made of aluminum, with stainless steel, brass, and bronze being used for various components. The higher Young’s moduli of these materials compared to PEEK allow for smaller wall thickness and feature dimensions, resulting in an overall more finely detailed instrument.

4.1 Instrument design

The design philosophy is not unlike that of the PEEK instrument: connecting system points via members stiff in both bending and torsion. The higher specific stiffness of aluminum (6061 T6) compared to PEEK with a factor of 8.7 (see table 4.1), allows for a more lightweight structure and still improved stiffness.

Table 4.1: Specific stiffness comparison between PEEK and aluminum.

<table>
<thead>
<tr>
<th></th>
<th>density [kg/m$^3$]</th>
<th>Young’s modulus [GPa]</th>
<th>specific stiffness [10$^6$ m$^2$/s$^2$]</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEEK [41]</td>
<td>1320</td>
<td>3.9</td>
<td>3.0</td>
</tr>
<tr>
<td>Aluminum 6061 T6 [42]</td>
<td>2700</td>
<td>69</td>
<td>26</td>
</tr>
</tbody>
</table>

With the insights gained in the realization of the PEEK instrument, the aluminum instrument is designed with a smaller operating range. As the primary targeted ailment is Parkinson’s disease, the location of the electrode stimulation target is typically located in a predefined volume in the skull relative to the adapter disc. Also the preferred approach paths are confined to a sharp bundle limiting the left and right entry point location to a relatively small area. This design choice results in a more compact instrument, further improving stiffness and accuracy.
Two obvious differences with the PEEK instrument are the removal of the upper horizontal translation/rotation stage, and the instrument now reaching over the crown of the head instead of around its side. The instrument is again attached to the back of the patient’s head via the intermediate adapter disc discussed in chapter 3.2. Furthermore, the proposed procedure for use is similar as for the PEEK instrument. Figure 4.2 shows the aluminum instrument with its six DOF indicated.
In figure 4.2, the horizontal tube is used to define translation $x_1$ and rotation $\phi$; the vertical tube for $z$ and $\theta$. The ways in which the translation and rotation are defined, are the same for both.
Figure 4.3: Close-up of the translation and rotation adjustment for $x_1$ and $\phi$.

The translation is achieved with a precision stainless steel spindle which engages in a brass nut pressed into the tube (figure 4.4). Backlash is eliminated with an elastic segment in the nut being compressed radially with a stretched O-ring. The spindle is completely concealed in a housing, which in turn contains a key in a keyway on the tube (figure 4.5).

Figure 4.4: Cross section of the translation and rotation adjustment for $x_1$ and $\phi$. 

Figure 4.5: Translation and rotation adjustment for $x_1$ and $\phi$. 

- translation spindle housing
- SS spindle
- O-ring
- brass nut
- tube
- elastic clamp
- closing lever
- translation spindle knob
- rotation adjustment dial

The precision stainless steel spindle engages in a brass nut pressed into the tube, eliminating backlash with an elastic segment in the nut compressed radially by a stretched O-ring. The spindle is hidden in a housing containing a key in a keyway on the tube.
The rotation is set with a dial via a 1:24 ratio, achieved with a gearbox. Figure 4.5 shows the gearbox in a cross section of the partial assembly; an exploded view of the gearbox is shown in figure 4.6.

An external gear with 96 teeth is placed on an excenter; the former free in rotation around its centerline. It runs in an internal gear with 100 teeth, fixed in its housing. By rotating the rotation adjustment dial (and thereby the excenter), the excenter pushes the external gear in the internal gear, forcing the external gear to rotate by 15 degrees in the opposite direction per revolution of the dial (figure 4.7). The rotation of the external gear is transferred to the translation spindle housing via an Oldham coupling equivalent; the translations of the gear in the plane perpendicular to its centerline are ignored.
Figure 4.7: Axial view on gear set with excenter. The red center cross indicates the center of the external gear (excenter).

After adjusting the translation and rotation $x_1$ and $\phi$ or $z$ and $\theta$, the respective tube (see figure 4.2) can be fixated with respect to the body it runs through by closing the corresponding elastic clamp. A cross section of the clamp for $x_1$ and $\phi$ is shown in figure 4.8. A lever is used to rotate a bolt between two limits, corresponding to the clamp being either opened or closed. A stack of Belleville washers is placed under the bolt head to prevent over-tightening and improve lever feel.

Figure 4.8: Cross section of elastic clamp for $x_1$ and $\phi$.

The instrument head contains the electrode drive which can be adjusted for tilt angle $\psi$ with a spindle $TS$. It is shown in figure 4.9. The stainless steel spindle is supported on a pivot in the instrument head and drives a brass nut attached to the electrode drive housing. This nut contains an elastic section to eliminate backlash by axial pre-tension.
The electrode drive itself consists of a straight guided sled, driven by a spindle $DS$ (figure 4.10). The sled can carry the stimulation electrode or any other equivalent needle-like object. It is coupled to the driving spindle without backlash and straight guided by the spindle and the housing combined.

The backlash free coupling of the sled to the spindle is realized with two mutual axially pre-tensioned nuts (figure 4.11). One of them ($LN$) is of the axial length of the sled; the other ($SN$), shorter than the first, contains an axially compliant section which is stiff in torsion. By
tightening the shorter of the nuts against the sled to a certain extent, its axially compliant section is compressed and axial pre-tension between the two nuts is realized. The shorter nut is then fixated in rotation with respect to the sled.

Figure 4.11: Cross section of part of electrode drive, with detail of backlash free coupling of the sled to the spindle. The different colors of LN and SN are used only to clarify their boundaries; the material is the same for both (brass).

Although the translation spindles and rotation adjustment gearboxes are concealed in housings, it is proposed to cover the instrument with a dedicated surgical drape before use. For use without a drape, the instrument would need to be fully disassembled to allow proper sterilization. This could compromise instrument accuracy upon reassembly, would this not be done by a trained technician.

The surgical drape proposed should primarily isolate the instrument from the surgical site (patient’s skull). Only the implant (electrode) would need to traverse the drape to enter the brain. However, it is common practice in surgery to completely cover non-sterile equipment with a drape, when placed within a sterile field. Because of accessibility of the instrument electrode drive when draped, it is suggested only the instrument head (figures 4.9 & 4.10) is sterilized, with the rest of the instrument covered.
4.2 Instrument kinematics

The instrument kinematics describe how the different DOF of the instrument translate to the coordinates and trajectory of the electrode (tip). As the angular adjustments (φ, ψ, θ) operate in series, the use of coordinate transformation matrices is needed. Figure 4.12 shows the instrument with its DOF and the first order perpendicularity errors within its construction. The instrument kinematics are described based on this figure. For the various DOF, the operating range limits are given in table 4.2.

Table 4.2: Instrument DOF operating ranges lower and upper limits.

<table>
<thead>
<tr>
<th></th>
<th>Lower limit:</th>
<th>Upper limit:</th>
</tr>
</thead>
<tbody>
<tr>
<td>x₁</td>
<td>105 mm</td>
<td>144 mm</td>
</tr>
<tr>
<td>x₂</td>
<td>0 mm (+ offset)</td>
<td>79 mm (+ offset)</td>
</tr>
<tr>
<td>z</td>
<td>115 mm</td>
<td>194 mm</td>
</tr>
<tr>
<td>φ</td>
<td>-60°</td>
<td>60°</td>
</tr>
<tr>
<td>ψ</td>
<td>-30°</td>
<td>30°</td>
</tr>
<tr>
<td>θ</td>
<td>-60°</td>
<td>60°</td>
</tr>
</tbody>
</table>

For the translational adjustments, the absolute values for their limits are given. Whether their contribution to the instrument settings is positive or negative, is taken into account in the vector/matrix-equations describing the kinematics.
Figure 4.12: Aluminum instrument with its DOF and first order perpendicularity errors indicated.
Define:

\[ M_1 = \begin{pmatrix} 1 & 0 & 0 \\ 0 & \cos \varphi & \sin \varphi \\ 0 & -\sin \varphi & \cos \varphi \end{pmatrix}, \quad M_2 = \begin{pmatrix} \cos \theta & \sin \theta & 0 \\ -\sin \theta & \cos \theta & 0 \\ 0 & 0 & 1 \end{pmatrix}, \quad M_3 = \begin{pmatrix} \cos \psi & 0 & -\sin \psi \\ 0 & 1 & 0 \\ \sin \psi & 0 & \cos \psi \end{pmatrix} \]

\[ A_1 = \begin{pmatrix} \cos \theta_{p,1} & \sin \theta_{p,1} & 0 \\ -\sin \theta_{p,1} & \cos \theta_{p,1} & 0 \\ 0 & 0 & 1 \end{pmatrix}, \quad A_2 = \begin{pmatrix} \cos \psi_{p,1} & 0 & -\sin \psi_{p,1} \\ 0 & 1 & 0 \\ \sin \psi_{p,1} & 0 & \cos \psi_{p,1} \end{pmatrix}, \quad A = A_1 A_2 \]

\[ C_1 = \begin{pmatrix} 0 & \cos \varphi_{p,1} & \sin \varphi_{p,1} \\ -\sin \varphi_{p,1} & \cos \varphi_{p,1} & 0 \\ 0 & 0 & 1 \end{pmatrix}, \quad C_2 = \begin{pmatrix} \cos \psi_{p,2} & 0 & -\sin \psi_{p,2} \\ 0 & 1 & 0 \\ \sin \psi_{p,2} & 0 & \cos \psi_{p,2} \end{pmatrix}, \quad C = C_1 C_2 \]

then

\[ \vec{r}_A = \begin{pmatrix} x_1 - r_{x,1} \\ 0 \\ 0 \end{pmatrix} + \begin{pmatrix} 0 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} \varphi \\ \psi \\ \theta \end{pmatrix} \]

which is the coordinate vector of point A (figure 4.12).

Furthermore

\[ \vec{r}_A = \vec{r}_A + \begin{pmatrix} 0 \\ 0 \\ z - r_{x,2} \end{pmatrix} \begin{pmatrix} \theta \end{pmatrix} + \begin{pmatrix} 0 \\ 0 \\ r_{x,2} \end{pmatrix} \begin{pmatrix} \varphi \\ \psi \end{pmatrix} \]

which is the coordinate vector of point C (figure 4.12).

The coordinate vector of point T (target point, figure 4.12) is then defined as:

\[ \vec{r}_T = \vec{r}_C + \begin{pmatrix} -x_2 \\ 0 \\ 0 \end{pmatrix} \begin{pmatrix} \theta \\ \varphi \\ \psi \end{pmatrix} \]

When the perpendicularity error angles all are zero, i.e. \( \varphi_{p,1} = 0, \psi_{p,1} = 0, \theta_{p,1} = 0 \) and \( \psi_{p,2} = 0 \), then matrices \( A \) and \( C \) are identity. It then follows:

\[ \vec{r}_A = \begin{pmatrix} x_1 \\ 0 \\ 0 \end{pmatrix} \]

\[ \vec{r}_C = \begin{pmatrix} -z \sin \varphi \\ x_1 \\ z \cos \varphi \end{pmatrix} \]
\[
\vec{r}_T = \begin{pmatrix}
  x_1 - x_2 \cos \psi \cos \theta \\
  -z \sin \phi - x_2 \cos \psi \sin \theta \cos \phi - x_2 \sin \psi \sin \phi \\
  z \cos \phi - x_2 \cos \psi \sin \theta \sin \phi + x_2 \sin \psi \cos \phi
\end{pmatrix}
\]

(26)

When the desired target and cardan joint coordinates, \( \vec{r}_T = \begin{pmatrix} x_T \\ y_T \\ z_T \end{pmatrix} \) and \( \vec{r}_C = \begin{pmatrix} x_C \\ y_C \\ z_C \end{pmatrix} \), are determined from the MRI scan, the corresponding instrument settings are calculated as follows:

\[
x_1 = x_C
\]

(27)

\[
x_2 = \sqrt{(x_T - x_C)^2 + (y_T - y_C)^2 + (z_T - z_C)^2}
\]

(28)

\[
z = \sqrt{y_C^2 + z_C^2}
\]

(29)

\[
\phi = \arcsin \frac{-y_C}{z} = \arccos \frac{z_C}{z}
\]

(30)

\[
\psi = \arcsin \left( \frac{-\gamma \beta - \delta \alpha}{\sqrt{\gamma^2 + \delta^2}} \right)
\]

(31)

\[
\theta = \arcsin \left( \frac{\alpha + \delta \sin \psi}{\gamma \cos \psi} \right)
\]

(32)

With: \( \alpha = \frac{y_C - y_T}{x_2}, \beta = \frac{z_C - z_T}{x_2}, \gamma = \frac{z_C}{z}, \delta = \frac{y_C}{z} \)

4.2.1 Sensitivity analysis

For the expressions for the target point and cardan joint coordinates, the first order sensitivity to small errors in the instrument settings is calculated. This is done in a similar way as explained in section 3.4.3 for the PEEK instrument.

The expressions for the target point coordinates as defined by the instrument are, as derived in equation (26):

\[
x_T \left(x_1, x_2, \psi, \theta \right) = x_1 - x_2 \cos \psi \cos \theta
\]

(33)

\[
y_T \left(x_2, z, \phi, \psi, \theta \right) = -z \sin \phi - x_2 \cos \psi \sin \theta \cos \phi - x_2 \sin \psi \sin \phi
\]

(34)

\[
z_T \left(x_2, z, \phi, \psi, \theta \right) = z \cos \phi - x_2 \cos \psi \sin \theta \sin \phi + x_2 \sin \psi \cos \phi
\]

(35)

The partial derivatives of these expressions in their constituent variables are listed in table 4.3.
Table 4.3: Partial derivatives of the Aluminum instrument target point coordinate expressions in their constituent variables.

<table>
<thead>
<tr>
<th>( \frac{\partial}{\partial x_1} )</th>
<th>( x_r )</th>
<th>( y_r )</th>
<th>( z_r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>( 1 )</td>
<td>( 0 )</td>
<td>( 0 )</td>
<td></td>
</tr>
<tr>
<td>( -\cos \psi \cos \theta )</td>
<td>( -\cos \psi \sin \theta \cos \phi - \sin \psi \sin \phi )</td>
<td>( -\cos \psi \sin \theta \sin \phi + \sin \psi \cos \phi )</td>
<td></td>
</tr>
<tr>
<td>( 0 )</td>
<td>( -\sin \phi )</td>
<td>( \cos \phi )</td>
<td></td>
</tr>
<tr>
<td>( 0 )</td>
<td>( -z \cos \phi + x_2 \cos \psi \sin \theta \sin \phi )</td>
<td>( -z \sin \phi - x_2 \cos \psi \sin \theta \cos \phi )</td>
<td></td>
</tr>
<tr>
<td>( x_2 \sin \psi \cos \theta )</td>
<td>( x_2 \sin \psi \sin \theta \cos \phi )</td>
<td>( x_2 \sin \psi \sin \theta \sin \phi )</td>
<td></td>
</tr>
<tr>
<td>( x_2 \cos \psi \sin \theta )</td>
<td>( -x_2 \cos \psi \sin \phi )</td>
<td>( -x_2 \cos \psi \cos \phi )</td>
<td></td>
</tr>
</tbody>
</table>

The magnitude of the individual setting errors is chosen as half of the respective scale interval length. These values are listed in table 4.4.

Table 4.4: Magnitude of the instrument setting errors.

<table>
<thead>
<tr>
<th>( \varepsilon )</th>
<th>0.05 mm</th>
<th>0.5 mm</th>
<th>0.05 mm</th>
<th>0.0044 rad</th>
<th>0.0087 rad</th>
<th>0.0044 rad</th>
</tr>
</thead>
<tbody>
<tr>
<td>( \varepsilon_{x_i} )</td>
<td>0.05 mm</td>
<td>0.5 mm</td>
<td>0.05 mm</td>
<td>0.0044 rad</td>
<td>0.0087 rad</td>
<td>0.0044 rad</td>
</tr>
</tbody>
</table>

The expressions for the cardan joint coordinates as defined by the instrument are, as derived in equation (25):

\[
x_c \left( x_i \right) = x_i
\]

\[
y_c \left( z, \phi \right) = -z \sin \phi
\]

\[
z_c \left( z, \phi \right) = z \cos \phi
\]

The partial derivatives of these expressions in their constituent variables are listed in table 4.5.
Table 4.5: Partial derivatives of the instrument cardan joint coordinate expressions in their constituent variables.

<table>
<thead>
<tr>
<th></th>
<th>$x_c$</th>
<th>$y_c$</th>
<th>$z_c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\frac{\partial}{\partial x_1}$</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial x_2}$</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial z}$</td>
<td>0</td>
<td>$-\sin \phi$</td>
<td>$\cos \phi$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial \psi}$</td>
<td>0</td>
<td>$-z \cos \phi$</td>
<td>$-z \sin \phi$</td>
</tr>
<tr>
<td>$\frac{\partial}{\partial \theta}$</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Given the ranges for the instrument settings, the maximum absolute values for the partial derivatives from table 4.3 and 4.5 can be determined. Multiplying these with the respective setting errors from table 4.4, gives a conservative upper limit for the theoretical first order sensitivity of the instrument in the target point and cardan joint coordinates for that specific setting parameter. The results are shown in table 4.6.

Table 4.6: Theoretical absolute first order sensitivity [mm].

<table>
<thead>
<tr>
<th></th>
<th>$x_r$</th>
<th>$y_r$</th>
<th>$z_r$</th>
<th>$x_c$</th>
<th>$y_c$</th>
<th>$z_c$</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\epsilon_x \frac{\partial}{\partial x_1}$</td>
<td>0.05</td>
<td>0</td>
<td>0</td>
<td>0.05</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\epsilon_x \frac{\partial}{\partial x_2}$</td>
<td>0.5</td>
<td>0.4</td>
<td>0.45</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\epsilon_z \frac{\partial}{\partial z}$</td>
<td>0</td>
<td>0.043</td>
<td>0.05</td>
<td>0</td>
<td>0.043</td>
<td>0.05</td>
</tr>
<tr>
<td>$\epsilon_{\psi} \frac{\partial}{\partial \psi}$</td>
<td>0</td>
<td>1.03</td>
<td>1.02</td>
<td>0</td>
<td>0.85</td>
<td>0.74</td>
</tr>
<tr>
<td>$\epsilon_{\theta} \frac{\partial}{\partial \theta}$</td>
<td>0.34</td>
<td>0.66</td>
<td>0.69</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>$\epsilon_{\phi} \frac{\partial}{\partial \phi}$</td>
<td>0.3</td>
<td>0.35</td>
<td>0.3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

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The rotation adjustment for the $\phi$ degree of freedom has the longest arm to the cardan joint. This inherently means the sensitivity of the target point and cardan joint coordinates is largest for deviations in settings of this particular DOF.

As with the PEEK instrument, the kinematics of the instrument are fixed, so the values in table 4.6 can only be altered (i.e. reduced) by altering the magnitudes of the instrument setting errors from table 4.4. It was explained in section 3.4.3 that adding vernier scales to the read-outs of the DOF adjustment settings, increases the resolution with which the user can adjust the settings. Adding vernier scales to the $x_2$, $\phi$, $\psi$, and $\theta$ setting read-outs, could reduce their related sensitivity values by a factor of 10, depending on the choice of scale. The maximum value in table 4.6 would then reduce to 0.1 millimeters.

**4.3 Aluminum instrument stiffness**

As explained in section 3.5, the instrument stiffness is determinative for its accuracy. The force required for electrode implantation in the brain is small, and static instrument deflection due to gravity was identified as the biggest error source for the PEEK instrument in section 3.5.1.

Apart from a difference in design, the biggest difference between the two instruments lies in their materials. Although PEEK has highly favorable mechanical properties when compared to other polymers, it is in another league than aluminum. The specific stiffness of aluminum is a factor of 8.7 higher than for PEEK. Combined with a lower material cost and better availability, aluminum is the better choice of material from a mechanical point of view.

**4.3.1 FEM analysis**

A FEM analysis is used to calculate the instrument stiffness. For the analysis, only the relevant structural parts of the instrument have been modeled. Figure 4.13 shows a subdivision of the instrument; the base and different stages are partly disassembled to show their boundaries more clearly.

![Figure 4.13: Subdivision of aluminum instrument.](image)
The total mass of the instrument is 2160 grams; the masses of the instrument base and stages indicated in figure 4.13, are as follows:

- base: 946 grams
- x1-stage: 770 grams
- z-stage: 444 grams

Again, all irrelevant instrument parts (knobs, spindles, housings, gearboxes et cetera) are removed, the instrument is meshed and boundary conditions are applied. The instrument is configured with the x1 and z degrees of freedom fully extended, providing a worst case scenario for stiffness as all bending and torsion lengths are maximized. A force of 1 newton is applied in the cardan point, consecutively in the x, y, and z directions, to calculate the stiffness in each respective direction. The results of the three analyses are shown in figure 4.14.
4.14a: Instrument x-stiffness in cardan point 1N/0.0037mm = 2.7e5 N/m.

4.14b: Instrument y-stiffness in cardan point 1N/0.0049mm = 2.04e5 N/m.

4.14c: Instrument z-stiffness in cardan point 1N/0.00073mm = 1.4e6 N/m.

Figure 4.14: Nodal displacement in instrument x-direction (4.14a), y-direction (4.14b), and negative z-direction (4.14c), when load force of 1N is applied in said direction in cardan point.

Concluding from the stiffness calculations, the electrode implantation force will not cause any noteworthy instrument deformation. In the worst case scenario of a fully extended
instrument and a load in the instrument’s most compliant direction, the displacement of the cardan point is less than 0.01 millimeters.

Figure 4.15 shows the results of FEM analyses on the instrument deformation under a gravity load, consecutively in x, y, and z directions.

Figure 4.15: Absolute nodal displacement under gravity load in instrument x-direction (4.15a), y-direction (4.15b), and negative z-direction (4.15c).
The instrument components excluded from the FEM analyses add up to a substantial part of the total instrument mass: 1179 grams of the 2160 grams total is not accounted for (55%). This is of no influence on the stiffness calculations represented in figure 4.14; it is however for the analyses represented in figure 4.15. As for the PEEK instrument, the removed components were quite evenly distributed over the instrument. However, the variation in materials used for the various components, makes the estimation of the change in location of the instrument’s center of mass less straightforward. Upon analysis of the simplified model used for the FEM analyses and the complete model, the center of mass of the simplified model turns out to shift 12 millimeters in the z-direction and 6 millimeters in the negative x-direction, compared to the complete model.

Multiplying the cardan point displacement values presented in figure 4.15 by 1.82 (= 1/0.55) would provide an absolute worst case scenario value for the actual displacements under the respective gravity loads. Especially in the scenario shown in figure 4.15b, where torsion of the horizontal tube of the x1-stage contributes to the displacement. For the simplified model, the lever arm with which the gravity force addresses the torsion stiffness of the tube, is longer than for the complete model, as the center of mass lies further away from the tube. All in all, it seems safe to assume the cardan point displacement during surgery, due to gravity, will not exceed 10 micrometer.

4.4 Conclusion
Following the PEEK instrument discussed in Chapter 3, a second instrument, made primarily of aluminum, has been designed and realized. Following the PEEK instrument in time, it can be seen both as an iteration in the design of a new instrument for DBS surgery, and as an alternative when MRI-compatibility is not a requirement.

A similar design philosophy as for the PEEK instrument is followed, namely the connection of system points via members stiff in bending and torsion. The resulting design is more compact and slender, utilizing the higher specific stiffness of aluminum compared to PEEK. Instrument features are more finely detailed, including backlash free spindle drives, and gearboxes.

The adapter disc introduced with the PEEK instrument is used again as intermediate between the patient’s skull and the instrument. Furthermore, the aluminum instrument contains an interface to the head support used currently during surgery.

The instrument kinematics allow a direct translation for target and entry point coordinates to instrument settings. A protocol is provided, prescribing the user how to set up the instrument after selecting the target and entry point coordinates manually from the MRI scan. Following a sensitivity analysis of the errors in the target and cardan joint coordinates of the instrument, due to user input errors, the importance of accurate read-outs of instrument settings is made clear. As with the PEEK instrument, the aluminum instrument prototype could be improved in its accuracy by adding vernier scales to the setting read-outs. This has not been done, but should be considered before the instrument gets used. A first-step increase in read-out resolution with a factor of 10, would bring the maximum worst case sensitivity back to 0.1 millimeter.

FEM analyses have been carried out to determine the instrument stiffness in the cardan point. As was the case for the PEEK instrument, this point is closest to where the electrode enters the brain; from there the electrode enters the brain unsupported by the instrument. A worst case configuration of the instrument is chosen by maximizing the bending and torsion lengths. Loaded with the small force required to implant an electrode in the brain, the
resulting instrument deflection will remain below 0.01 millimeter in the cardan point. Instrument deformation due to gravitational loading, in a worst case scenario, will be of the same order of magnitude (10 micrometer).

One should bear in mind the MRI targeting procedure still adds an inevitable error to placement accuracy, dependent on the machine used. This error will be up to two orders of magnitude larger than the errors introduced by the instrument. It can therefore be concluded the MRI targeting procedure will be decisive for overall procedure accuracy for the aluminum instrument.
Chapter 5:

MRI-compatible actuator

Both the PEEK and aluminum instrument are designed to be operated manually. The settings of the instrument are adjusted only once before surgery, to define the implantation trajectory of the electrode based on the pre-operative MRI planning. As these settings are set and then held for the rest of the procedure, motorization would add weight and cost and at best match accuracy: adding servo stiffness in series to mechanical stiffness reduces system stiffness. The actual electrode implantation is initially also driven by hand: the electrode drive consists of a spindle which is rotated manually to drive a sled carrying the electrode lead. However, this requires the surgeon to be within reach of the spindle knob, and forces other than those needed for solely rotating the spindle could be introduced to the instrument. For these reasons it could be desirable to motorize (only) this particular degree of freedom of the instruments. To maintain full MRI compatibility of the PEEK instrument with a motorized electrode drive, a pneumatically driven actuator has been designed and realized completely in plastics. Figure 5.1 shows the electrode insertion drive of the PEEK instrument, both with manual and motorized actuation.

Figure 5.1: Electrode insertion drive with manual (left) and motorized (right) actuation.
Compressed air is used to operate the drive motor and the motor itself is a mechanically stepping motor. When coupled to the electrode drive, counting the number of steps is sufficient to accurately position the electrode in the brain.

5.1 First version

The motor is shown in figure 5.2a. It has an axial length of 84.4 mm (excluding pneumatic hose connectors) and an outer diameter of 23 mm. The internal working parts are sealed by an enclosure to minimize contamination. A view on these internals is provided in figure 5.2c. The motor is designed to be slender, though still able to provide enough torque to operate the electrode drive. The use of excessively high air pressure is undesirable, so operating pressures are set to not exceed 5 bars. The motor is coupled to the electrode drive via a timing belt (figure 5.1, right); the ratio between the pulleys is 1:1. The electrode drive performs the translation $z_2$ (figure 5.1) via a spindle with a 0.9 millimeter pitch. Combined with the drive motor resolution of 20 degrees, this gives a 0.05 millimeter actuated resolution for $z_2$.

![Figure 5.2: Pneumatic mechanical stepping motor.](image)

Figure 5.2: Pneumatic mechanical stepping motor.
Figure 5.3 shows the motor without its enclosure and with its housing translucent. The top half of the motor, with the red translators, takes care of the clockwise rotation of the shaft (green). The bottom half with the yellow translators, is for counter-clockwise rotation. As both halves operate in a similar way, only the top one is discussed.

The translators (red) can only translate in the motor housing; their rotation is fixed with keys in the housing. The translation is driven pneumatically, using a positive pressure supply for motion towards the corresponding rotor and a soft vacuum supply (= suction) for retraction from the rotor. The rotor (green) is fixed on the shaft.

See table 5.1: when a translator moves towards the rotor, the flanks of three of its teeth will engage with those of three teeth of the rotor. As the translator moves on, the engaged flanks of the translator and rotor will slide relatively, resulting in a rotation of the rotor and shaft. By switching the positive pressure and soft vacuum supplies between the two translators, the rotor will perform a stepping rotation with 20 degree increments. This is realized with a dedicated flow control module, which will be elaborated in section 5.1.1. The indexing accuracy of the operating mechanism is not affected by wear.

For each translator, the air is led from a dedicated connector at one end of the motor, through channels in the housing, to the translator. Whilst one translator pair is in operation, the other pair should remain retracted from its rotor. This is realized by a continuous soft vacuum supply to both translators.
Table 5.1: Operation of the pneumatic mechanical stepping motor; $P_{\text{pos}}$ = positive pressure supply, $P_{\text{sv}}$ = soft vacuum supply.

<table>
<thead>
<tr>
<th>Clockwise rotation</th>
<th>Counter-clockwise rotation</th>
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</table>

The part of the motor enclosure that is clamped when the motor is attached to the instrument, is made eccentrically with respect to the motor / pulley shaft. This allows for adjustment of the belt tension by rotating the motor in the clamp before the clamp is tightened (figure 5.4). An exploded view of the complete motor assembly is shown in figure 5.5.

Figure 5.4: Eccentric fixation of motor in clamp.
Figure 5.5: Exploded view of complete motor assembly:

1. enclosure closing ring
2. enclosure bottom
3. pneumatic hose pillars
4. housing gasket
5. shaft bearing
6. filler ring
7. housing segment
8. rotation lock key for translator
9. translator (counter clockwise)
10. rotor (counter clockwise)
11. shaft
12. rotor lock pin (to shaft)
13. translator (clockwise)
14. rotor (clockwise)
15. enclosure top
16. pulley flange
17. pulley
5.1.1 Flow control module

The first version of the pneumatic actuator requires an alternating supply of positive pressure and soft vacuum for each of the active translators. The inactive translator pair should be supplied with a feed of soft vacuum. Switching the direction of rotation of the motor is achieved by exchanging the air supplies between the two translator pairs.

A flow control module has been designed and realized to operate the pneumatic motor (figure 5.6). It requires two input air feeds, one of positive pressure and one of soft vacuum. The module is used to supply the pneumatic motor with its required feeds. It is designed such that the user can accurately control the motor’s rotation in 20 degree increments, and select clockwise or counter-clockwise rotation.

Switching of the air feeds for the active translator pair is done with a translating piston (figure 5.7). In moving through its housing’s bore, it distributes the incoming air feeds of the flow control module over the respective outputs. Every stroke of the piston results in a switch of the air feeds to the active translator pair, corresponding to an incremental rotation of the motor axis by 20 degrees.
The piston motion is driven by a wave pattern situated on the inner circumference of a ring. This ring is placed inside the rotating handle wheel, chosen as input of the flow control module. To give the user clear control over the indexing of the motor, the input wheel’s rotation is also indexed in 20 degree increments.

The user can select the rotation direction of the motor with a switch on the side of the control module. It operates a cylinder inside the module which can rotate over 90 degrees. This reroutes the internal air passages in the control module such that the two air supply channel pairs for each rotation direction of the motor are mutually interchanged. An exploded view of the flow control module is shown in figure 5.8.
Figure 5.8: Exploded view of flow control module:

1. housing base plate
2. rotation direction switch
3. rot. direct. select cylinder
4. main housing block
5. housing for cylinder (3)
6. housing gasket stack
7. piston housing block
8. piston rotation lock pin
9. handle wheel indexing plunger
10. piston
11. piston seal ring (PTFE)
12. wave ring
13. handle wheel
14. handle wheel bearing
15. bearing fixating disc
16. handle wheel cover
17. handle

Note: 5 is press fit into 7; 14 is press fit into 13.
5.1.2 Motor test

A small test setup is assembled to test the motor in its working and indexing accuracy (figure 5.9). The motor is clamped to a support, and a 360 degree protractor is placed coaxially with the rotor. A thin needle is attached to the rotor, allowing readout of the absolute angular position of the rotor, and deduction of the indexing step sizes (figure 5.10). For both clockwise and counterclockwise rotation, the absolute angular positions the rotor attains when going through a full rotation are noted in table 5.2.

Figure 5.9: Test setup used to test the pneumatic motor and its flow control module.

Figure 5.10: A thin needle attached to the rotor allows readout on the protractor.
Table 5.2: Absolute angular positions of the rotor, together with deduced step sizes, for both clockwise and counterclockwise rotation.

<table>
<thead>
<tr>
<th>Counterclockwise rotation</th>
<th>Clockwise rotation</th>
</tr>
</thead>
<tbody>
<tr>
<td>absolute angle [deg]</td>
<td>step [deg]</td>
</tr>
<tr>
<td>20</td>
<td>22</td>
</tr>
<tr>
<td>38</td>
<td>18</td>
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<td>60</td>
<td>22</td>
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<td>18</td>
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<tr>
<td>340</td>
<td>22</td>
</tr>
<tr>
<td>358</td>
<td>18</td>
</tr>
</tbody>
</table>

Table 5.2 shows the indexing step size for the motor to vary between 18 and 22 degrees for counterclockwise rotation, and between 19 and 21 degrees for clockwise rotation. By design, these should both be 20 degrees. Manufacturing tolerances on the mutual alignment of the translators for each rotation direction are identified as the cause of this. For the counterclockwise translator pair, this tolerance turns out to be 2 degrees from the nominal position for each translator. For the clockwise translator pair, this is 1 degree.

A second finding from the motor test, lies in its behavior when the rotation direction is switched. When the rotation direction switch on the flow control module is operated, the rotor also makes an indexing step. When switching from counterclockwise to clockwise rotation, this step is in the clockwise direction and measures 20 or 23 degrees. When switching from clockwise to counterclockwise rotation, the step is in the counterclockwise direction and also measures 20 or 23 degrees. By design, the indexing step the rotor makes when the rotation direction is switched, should measure either zero or 20 degrees. Herein, the step of 20 degrees should be in the rotation direction towards which is switched.

A combination of the aforementioned mutual rotor alignment tolerances per pair, combined with a minute relative misalignment between the rotor pairs for the two rotation directions, results in the step of 20 or 23 degrees when the rotation direction is switched. On second thought, a step of either 20 or 23 degrees is preferable over either zero or 20 degrees. This is because the smaller difference between 20 and 23 (3 degrees) allows a better estimation beforehand of the actual behavior. Furthermore, the fact that the step takes place at all, and is in the direction towards which the switch in rotation direction was commanded, introduces a safety feature.
When the motor is coupled to the instrument electrode drive with a spindle pitch of 0.9 millimeters, the counterclockwise motor rotation steps of 18 and 22 degrees result in a drive sled progression (i.e. a motion towards the target) of 0.045 and 0.055 millimeters per step respectively. For the clockwise rotation with steps of 19 and 21 degrees, this is a sled retraction (i.e. a motion away from the target) of 0.048 and 0.053 millimeters per step respectively. When the rotation direction of the motor is switched, the resulting step is either 0.05 or 0.058 millimeters.

Finally, a test of the motor, coupled to the electrode drive of the PEEK instrument, shows it sometimes does not complete a step. This is likely because the motor output torque is only just enough to rotate the spindle. Any small increase in torque required to rotate the spindle, can lead to the motor missing a step. It is therefore crucial that the spindle is kept clean and is properly run in to ensure as small a variation as possible on the operation torque required over the complete travel of the sled. Would the user only count the steps he or she dictates with the flow control module, this could lead to the microdrive sled not progressing as far as intended. This makes it necessary to always verify the actual progress of the electrode drive sled, which can be difficult when operating in a confined space.

5.1.3 Suggestions for improvement

The motor and control module have been realized and tested. Both work as intended, with the following insights gained in the process:

1. The choice for a working mechanism of the motor based on supplies of positive pressure and soft vacuum is not optimal. Although gaskets are applied on all mating surfaces in the internals of both the motor and control module, internal leakage does occur. This quickly contaminates the soft vacuum, drastically reducing the efficiency of the system. A reduction in motor output torque is the result.

2. The flow control module is designed to be placed on a horizontal surface (e.g. a table top) when it is operated. Upon using the controller it is found however, that users prefer holding the controller in one hand whilst rotating the handle wheel with the other.

3. The rotating handle wheel of the flow control module wrongly suggests the motor’s direction of rotation is linked to the rotation direction of the wheel. Rotating the wheel in any direction leads to an ongoing rotation of the motor, and thereby an ongoing progression of the electrode drive in one direction (when the motor is coupled to said drive). This could pose a safety concern, when rapid retraction of an electrode is required after it has erroneously been inserted too deep in the brain. In such situation the user might intuitively rotate the wheel in the opposite direction, thereby progressing the electrode even further in the undesired direction. The motor rotation direction is only dictated by the position of the dedicated switch.

Redesigns have been made for both the motor and flow control module, based on the insights given above.
5.2 Second version

5.2.1 Actuator
The second version of the pneumatic actuator is shown in figure 5.9a. It has an axial length of 93.3 mm (excluding pneumatic hose connectors) and an outer diameter of 27 mm. Again, the internal working parts are sealed by an enclosure to minimize contamination. A view on these internals is provided in figure 5.9c. The working principle is similar to that of the first version (see figure 5.10 and table 5.3/), however now requiring two supplies of positive pressure (for example 2 and 5 bar of pressure).

Figure 5.9: Second version of the pneumatic mechanical stepping motor.
Figure 5.10: Rotation of motor shaft (green): red translator pair for clockwise, yellow translator pair for counter-clockwise rotation.

Table 5.3: Operation of the second version of the pneumatic mechanical stepping motor.

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<tr>
<th>Clockwise rotation</th>
<th>Counter-clockwise rotation</th>
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The motor now has five pneumatic hose connectors instead of four. One connector is for the continuous low pressure air supply to the air spring orifices. The other four feed on/off high pressure air to their respective translators, corresponding to the motor’s rotation.
PTFE sealing rings are added along both the outer and inner circumference of all translators. These are intended to eradicate the leakage of air past the translators, whilst minimizing the increased friction of the translators along the housing wall and shaft. An exploded view of the complete motor assembly is shown in figure 5.11.
The design of the teeth patterns on the rotors and translators is again chosen such, that the rotor will perform a stepping rotation with 20 degree increments when the motor is operated.

5.2.2 Redesigned flow control module

The air supplies required for the second motor design, are a continuous feed of low pressure air, and a feed of high pressure air alternating over two lines corresponding to the translators driving the motor rotation. The low pressure air supply is connected directly to the motor; the alternating high pressure air supply is realized with the redesigned flow control module shown in figure 5.12. A change in rotation direction is achieved by switching the set of lines over which the alternating feed of high pressure air is sent (each translator pair corresponds to one set of two lines).

Figure 5.12: Redesigned flow control module.

Alternating the high pressure air feed is achieved with a translating piston (figure 5.13). In moving through its housing’s bore, it switches the high pressure air feed over the two channels of each output pair. The piston motion is driven by a wave disc, which in turn is rotated with the handle wheel. To ensure the piston follows the wave profile, it is preloaded against the disc with a coil spring. The piston is located in the handgrip which allows the user to conveniently hold the module with one hand, whilst rotating the handle or handle wheel with the other hand.
When the rotation direction of the handle wheel is changed from clockwise to counterclockwise (or vice versa), the output pair over which the air is sent to the motor is switched accordingly. A lever, placed coaxially with the wave disc, operates two pairs of needles which can slide in the air channels inside the handgrip. Figure 5.14 shows the lever and needles in more detail. Starting from a neutral position, sliding a needle slightly further into its channel will block the airflow running from the piston towards the air output. When the needle is retracted slightly from its channel, the airflow mentioned will be freed up completely. The two extreme positions of the needle are distinguished by a rotation of 18 degrees of the lever (plus and minus 9 degrees starting from a neutral position).
Figure 5.14: Air output selection lever operation. The red dashed rectangles indicate blocked air channels; the black dashed rectangles indicate open air channels.

The rotation of the wave disc, and therewith the handle wheel, is indexed with a spring plunger which is integrated in the air output selection lever. When the lever is in either of its extreme positions and the wave disc is rotated further in the corresponding direction, the spring plunger provides indexing of the rotation. When the wave disc is now rotated in the other direction, the spring plunger will lock the rotation of the lever to that of the disc, until the lever reaches its other extreme position. From there on, the spring plunger will again index the rotation of the wave disc and handle wheel.

Switching the output pair over which air is sent to the motor, changes which translator pair in the motor is provided with the alternating high pressure air. This effectively changes the motor’s rotation direction. An exploded view of the redesigned flow control module is shown in figure 5.15.
Figure 5.15: Exploded view of flow control module (redesign):

1. handgrip end
2. gasket
3. piston preload spring
4. piston seal ring (PTFE)
5. piston
6. cam follower bearing
7. air channel needle
8. handgrip / housing
9. piston rotation lock pin
10. wave disc bearing
11. wave disc
12. air output selection lever
13. indexing spring plunger
14. wave disc bearing cover
15. handle wheel
16. handle

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5.3 Conclusion
A fully MRI-compatible actuator has been designed and realized. It is driven pneumatically and operates as a mechanically stepping motor. Combined with a dedicated flow control module, it allows for remote operation of the PEEK instrument described in chapter 3. The motor has been designed to be compact and slender, integrating with the instrument design to form a complete package, when utilization of the instrument under real-time MRI is desired. The motor has been designed with a stepping resolution of 20 degrees. When coupled to the electrode drive spindle, this results in an actuated resolution on the implantation depth of 0.05 millimeters.

Upon realization of the first motor and flow controller designs, the prototypes have been tested in their working and indexing accuracy. Slight deviations from the intended stepping resolution of 20 degrees have been measured, leading to a maximum deviation of 5 micrometers from the actuated drive spindle resolution of 0.05 millimeters. These deviations are attributed to manufacturing tolerances in the alignment of some internal parts of the motor. Furthermore, a few insights have been gained by which the designs could be improved.

Taking these insights into account, a second version of the motor has been designed, together with a redesigned flow control module. Where the first motor design was based on air supplies of both positive pressure and soft vacuum, the second version only requires positive pressure air supplies at two different pressure levels. The working principle is less sensitive to internal air leakage, and rotation steps should be more distinct. Furthermore, the rotation direction of the handle wheel of the redesigned flow control module is directly linked to the rotation direction of the motor. This was not the case for the first design, which required an additional switch for the user to select the desired motor rotation direction. All in all, the redesigned flow control module improves upon the first version by a greater ease of use.
Chapter 6:

Prospect on future applications

From the beginning of the project, deep brain stimulation has been the target application of the new instruments described in Chapters 3 and 4. Although this is a very specific application, the instruments perform a general task. They define a straight-lined trajectory for a needle-shaped object, based on target and starting point coordinates. These coordinates are, for now, chosen by hand from MR images, in which a structural part of the instruments (the adapter disc) acts as a reference.

There are more surgical procedures where an instrument which can perform such tasks could be of value. This chapter elaborates upon how the instruments designed could be used during these procedures. As it is preferable to be able to use the instruments without the need for any major changes, the focus will lie on surgical procedures to the head.

The following applications are considered:
- removal of intracranial hematoma;
- biopsies of brain tissue;
- internal ultrasound;
- placement of external ventricular drain;
- administering of brachytherapy seeds.

6.1 Intracranial hematoma

Hematoma is a general term for a localized collection of blood, outside the blood vessels. A hematoma can be caused by both disease and trauma. A common example of a trauma induced hematoma is a bruise, which can even be seen through the skin. Usually a hematoma dissolves naturally over time. However, when internal bleeding continues, the hematoma will remain or might even increase in size.

Within the skull there are several types of hematoma distinguished from one another. Moving from outside to in, there first is the epidural hematoma (figure 6.1a). This results from bleeding between the skull and dura mater. Symptoms include headache, confusion, vomiting, and paralysis. Second, there is the subdural hematoma (figure 6.1b), where blood gathers between the dura mater and arachnoid mater. The bleeding results from tears in bridging veins which cross the subdural space, and can cause compression of brain tissue. Third, the subarachnoid hematoma is located between the arachnoid mater and surface of the brain (figure 6.1c). Symptoms include headache with rapid onset, a decreased level of consciousness, vomiting, fever, and neck stiffness.

Furthermore, there can be bleedings within the brain. These are typically not called hematomas, as they usually involve acute, ongoing bleeding. By the time such bleedings
would have developed into hematomas, the patient would be majorly disabled or dead. Two of such bleedings typically distinguished, are:

- intraparenchymal hemorrhage (figure 6.2), where the bleeding takes place inside the brain tissue;
- intraventricular hemorrhage, where blood flows into the ventricular system and circulates through the subarachnoid space.

Especially intraparenchymal hemorrhage quickly leads to compression of surrounding brain tissue, followed by neurological dysfunction.

6.1.1 Surgical removal of hematoma

Common surgical removal of hematomas involves a craniotomy to gain access to the brain and subsequently the hematoma. In case of a small epidural hematoma, surgery via a burr hole (also called trepanning) is sometimes performed. The goal of surgery is to remove the collection of blood and stop the bleeding would this still be ongoing. The blood forming the hematoma can be either liquid or coagulated, and is removed by suction and irrigation. In case of ongoing bleeding, hemostasis is achieved by means of electrocautery, gel foam, or other means.
Performing a craniotomy is an invasive process. It is effective when quick access to the brain is required in an emergency situation. Removal of the bone flap already relieves pressure from the brain, after which the hematoma itself can be removed less hastily.

In less urgent cases, the ability to remove a (deep-lying) hematoma via a small burr hole in the skull based on pre-operative MRI data, could provide a less invasive and more accurate alternative to removal via craniotomy.

A suction needle could be inserted in the brain accurately, along a predefined trajectory, using one of the new instruments. The procedure required would be very similar as for implanting a DBS electrode. Using the adapter disc as a reference in the pre-operative MRI scan, the suction needle could be inserted accurately into the hematoma. After removal of the hematoma, a hemostatic agent could be injected to stop possible ongoing bleeding. Trauma to surrounding brain tissue would be minimized, with less risk on complications during and after surgery. Since the procedure would only require a burr hole instead of a craniotomy, the patient recovery time would be reduced as well.

### 6.2 Biopsies

A brain biopsy involves the removal of a small piece of brain tissue for diagnosis of a possible pathology. It can be used to diagnose tumors, infection, and Alzheimer’s disease, amongst others. The biopsy is typically performed using a stereotactic frame for accuracy. As the new instruments have been suggested as alternatives to the stereotactic Leksell frame for DBS surgery, they could also be used for biopsy surgery using the same reasoning.

![Figure 6.3: Schematic representation of brain biopsy procedure [47].](image)

When a biopsy needle can be positioned accurately in the region of interest, a small tissue sample is sufficient for diagnostic analysis. This is because in that case, one can be certain all tissue stems from the suspect region. A small needle can be used, requiring only a small burr hole.

Figure 6.4 shows a typical needle used for brain biopsies.
Figure 6.4: Brain biopsy needle [48].

The needle can be loaded into the instrument much like a DBS electrode lead. Localizing the target area by means of MRI can easily be enriched by attaching the adapter disc to the patient’s skull for reference. From here on the procedure for inserting the biopsy needle is analogous to the procedure for implanting a DBS electrode. After insertion however, the biopsy is taken by operating the needle, after which the needle (with the tissue sample) is removed.

Based on the diagnosis, and if further treatment on the same or following day is possible, the adapter disc could be left in place on the patient’s skull. In case of brachytherapy for example, the instrument could be used to implant the radio-active seeds (section 6.5).

6.3 Internal ultrasound

Magnetic resonance imaging and computed tomography are both often used when high quality images of the skull’s internals are required. Their versatility and reliability make them both invaluable in current day diagnostics. However, they both also have their drawbacks. MRI for example is an expensive and time-consuming imaging method. Furthermore, it does not provide clear distinction between adjacent structures with similar consistency (e.g. different nuclei in brain tissue). CT, on the other hand, uses x-rays to create images, leading to a radiation load on the patient and medical personnel.

Medical ultrasound provides another means to see soft internal body structures. It requires less intricate equipment, and is more often used for qualitative rather than quantitative analysis. However, its potential in imaging resolution is large, especially when higher frequencies are used. The drawback for these higher frequencies lies in their absorption by the tissue being imaged.

Medical ultrasound is not used to image the adult brain, as it is enclosed by the skull which effectively blocks the sound waves. However, the availability of a relatively easy to use imaging method for accurately locating specific brain structures, could prove useful when extreme positional accuracy is required.

As explained in section 1.4.3, different functional regions in the brain can have the same physical consistency, making them hard to distinguish using MRI. An idea has been formed to combine large-scale MRI with local ultrasound: based on a pre-operative MRI scan, a slender ultrasound transducer is inserted in the brain to accurately determine the relative
position of the target area with respect to the transducer tip. When the position of this transducer tip is known with respect to an outside reference, the same holds indirectly for the location of the target area.

Figure 6.5 shows an ultrasound probe used for endobronchial ultrasound. Although this application, which involves internal imaging of a bronchus, is very different from internal imaging of brain tissue, similar hardware could be used.

![Endobronchial ultrasound probe](image)

Figure 6.5: Endobronchial ultrasound probe [49].

### 6.4 Ventricular drain placement

An external ventricular drain is used to relieve elevated intracranial pressure by draining cerebrospinal fluid. This can be needed when the normal flow of cerebrospinal fluid in the brain is obstructed; for example in patients with hydrocephalus. When an external ventricular drain is placed, it allows for monitoring and control of the intracranial pressure. It typically forms a temporary solution to the problem at hand, which sometimes needs to be addressed by other surgical means.

The drain consists of a slender plastic catheter, which is placed inside one of the brain ventricles with its distal end. Two potential complications which can occur due to inaccurate drain placement, are bleedings and misplacement of the catheter tip. When one of the new instruments would be used for placing the drain, these complications could be omitted.

The trajectory along which the drain should be placed, could be planned accurately before surgery, using the adapter disc as reference in the MR images used. Blood vessel crossings could be avoided, and entry of the brain on a gyrus could be assured, both minimizing the risk of bleedings. Furthermore, the location of the ventricles could be accurately determined on the MR images, and targeted with the instrument.

The geometry of a typical ventricular drain is similar to that of a DBS electrode lead wire. The drain itself is stiffened with a removable stylet upon insertion in the brain. Placement of the drain could therefore be performed completely analogous to implantation of a DBS electrode lead. Figure 6.6 shows two typical ventricular drains with a stylet.
6.5 Brachytherapy

Brachytherapy is a form of radiotherapy, where small radioactive seeds are placed inside a tumor with the aim of destroying it. It is, amongst others, used for the treatment of brain tumors. The tumor can be subjected to a relatively high dose of radiation, whilst the radiation load on surrounding healthy tissue remains small. The seeds can be either removed later on, or left in place after decay.

Accurate placement of the radioactive seeds is crucial. After determining the exact location of the tumor on MR images, one of the new instruments could be used to implant the radioactive seeds exactly where the surgeon wants them to be. For this, the instrument needs to be loaded with a hollow needle through which the seeds can be guided to the target. With a typical diameter of less than 1 millimeter, this needle will be of similar outer diameter as a DBS electrode lead wire. Figure 6.7 shows typical cylindrical radioactive seeds with a length of 4.5 millimeters and a diameter of 0.8 millimeters.

The hollow needle, filled with a stylet, should be inserted in the brain along the chosen trajectory, to the chosen depth. The stylet can then be removed, and the radioactive seeds fed through the needle.

As stated in the beginning, we have constrained our thoughts to brain surgery. However, the same principles as used in the instrument, can be used for other parts of the body as well, with adapted interfaces. We will leave this for now for future research.
Concluding remarks

In the final chapter of this thesis, insights gained over the course of the project are shared for their recommendative value with respect to possible future projects in the field of medical technology.

Technical conclusions
The goal of the PhD project described in this thesis was to increase DBS treatment efficacy by increasing implantation accuracy and optimizing the surgical procedure. This has been realized by designing and developing two new surgical instruments for DBS electrode implantation, together with a redefinition of the surgical procedure.
In the design of the new instruments, the main goal was to achieve unambiguous translation of target and entry point coordinates to instrument settings. This has been realized by introducing an adapter disc which gets fixated with screws to the back of the patient’s skull, before the MRI scan for targeting is made. It serves as both a visual reference for imaging and a structural reference for the instrument.
The first instrument prototype is completely made from PEEK. This material ensures full MRI compatibility, allowing for implantation under real time MRI, would this be desired. For the second prototype, the requirement for MRI compatibility is left behind. The freedom in material choice is exploited in the design, together with experience gained from the PEEK instrument. The resulting prototype is more compact and dedicated to DBS surgery, although in the same style as the PEEK instrument.
Next to the two instrument prototypes, an MRI compatible actuator has been designed and realized. It is required for the possible application of the PEEK instrument in the confined environment of an MRI scanner. Only the straight lined insertion of the electrode needs to be motorized, as the other instrument settings are adjusted before attaching the instrument to the patient’s head. The goal of the design process was to keep the drive as compact as possible, in line with the limited forces at play during electrode insertion in the brain.
Moving the scope of this thesis broader than only DBS, surgery to the brain is intrinsically characterized by elevated risk and the requirement for precision. As all burr hole surgery to the brain can be complicated by brain shift, a small device is proposed to prevent this shift from occurring. It could be used in conjunction with the new instruments to further improve electrode positioning accuracy, or the positioning accuracy of specific tools for other treatments which could benefit from the new instruments. Some of such treatments are discussed in the final part of this thesis.

Valorization
Upon review of the currently used stereotactic frames, the first things that came to notice were their archaic appearance and their general lack of stiffness in bending and particularly
torsion. Although functional, these instruments require extensive user experience to achieve really satisfactory results. Given the small scale on which DBS surgery currently is being performed, this user experience is often accounted for. The neurosurgeons performing DBS electrode implantation generally perform outstanding work, with a large improvement in patient quality of life as result. Over the years of performing the surgery, they have mastered all peculiarities of the instrument and the procedure.

A new instrument will not be accepted readily by these current day performers, who already achieve the maximum possible accuracy by replicating the MRI scan resolution [52]. Their experience and skill have led to routine and routine should necessarily not be changed for the sake of changing. Finding a demand for a new instrument or approach amongst these ranks is therefore probably not the way to go in search of valorization.

With the large potential of DBS as a means to drastically improve patient quality of life, numerous patients could benefit from the treatment, who at this moment do not qualify for it. Pharmacological treatment is used first, and only if this is or becomes ineffective, DBS is considered. However, patients are confronted with medicine side effects and undergo the strain of increasing dosage over time.

A causality dilemma between the offer and demand for DBS surgery is certainly at play. Given the constraint of a limited number of neurosurgeons, of which only a few perform DBS surgery today, enabling any neurosurgeon to perform the surgery successfully by means of a new instrument seems a valid cause. The availability of DBS surgery could be increased without the need for a large investment in the form of years of surgeon training to gain the necessary experience. Whether the demand for surgery rises, depends on patients, general practitioners, and even neurosurgeons being aware of the availability of an improved DBS procedure. Dealing with the means to influence this lies outside the scope of this thesis and should be addressed with commercialization of the instrument.

Design philosophy

Upon initiation of the PhD project described in this thesis, no specific end goal was set. The stereotactic frames used were remarked on their archaic appearance and the desire for a more contemporary alternative was expressed. Thoughts of a robotic system were briefly examined, but soon deemed to result in a system too complex for merely the implantation of a needle-shaped object in the brain. A purely mechanical instrument was decided to be the most feasible alternative to the stereotactic frames.

With designing a new instrument, it is often desirable to be able to start with a ‘clean slate’. The design can be completely new and does not need to build upon, or be compatible with, what is already available. When only (clearly defined) design goals are set, this gives the designer the freedom to reach these goals as he or she sees fit.

However, a design is often intended as replacement for an already available device; a redesign. The designer typically knows this device, which almost unavoidably influences the design philosophy of the new instrument: it can force the new design to be ‘in the same direction’ as the available device, or steer it completely away from it. The challenge lies in being able to critically evaluate what is already there, take note of its strengths and weaknesses, and build upon this with one’s own knowledge and skill. This will result in the new device being better than the old.
**User involvement**

A mechanical designer, by default, gets assigned with the task to design a device for an application from a different specialism. In the case of medical technology, this specialism is a medical one (for this project: neurosurgery). The intended user of the device (i.e. a surgeon) will typically see this application from a different perspective than the designer. It is therefore crucial that the designer gets familiar with this application, and translates the request of the surgeon into a technical design task.

It is sometimes quoted that in this translation, the designer should note what the surgeon would have asked, would he or she have really thought over the problem thoroughly. When this is interpreted as ‘listening in between the words spoken’, this could be a true statement: the process of getting familiar with a new application often involves getting used to new jargon terms and different ways of work. However, the designer should not completely redefine the surgeon’s requests in such a way, that the device he or she ends up designing, is completely different from what the surgeon had in mind, in both shape and functionality. Each specialist involved should be encouraged to think outside his or her own field, but not as much as to overthrow the input from another in his or her respective specialism.

**Project evaluation**

Looking back on this PhD project, several aspects come to mind which could have been done differently.

In gathering information about the procedure of DBS electrode implantation, too little time was spent on talking to different specialists from the field. Not only surgeons known for their liberal-minded approach towards new developments should have been interviewed, but also the more conservative ones with extensive experience and confidence in the current surgical procedure. The goal of developing a new surgical instrument should not be to improve the confidence the design engineer has in the procedure, but to improve upon it from a medical point of view. The technical implementation in the form of a new instrument should only be a means to achieve this goal.

This approach could shift the focus, from development based on what is technically possible and what the engineer thinks the surgeon should want, to development based on a demand from surgical practice. As specialists from either the engineering field or surgical practice typically cannot fully comprehend the possibilities and limitations of the other specialism, frequent and open dialogue is key to achieve satisfying results.

A clear example of the above, which can be found in the work described in this thesis, is blindly dropping the center-of-arc principle [53] which is such a highly praised characteristic of the currently used stereotactic frames. From an engineering point of view, this principle seems just a way to achieve the function of defining a straight trajectory towards a chosen target point. Decoupling the way in which the surgical instrument defines the target point and the trajectory is not necessary to get a functioning instrument. It does however allow the user to intuitively make small changes to the trajectory without altering the target point coordinates. Would the user want to make these same changes using an instrument (like the ones designed) with more complex kinematics, he or she should re-run the instrument setup calculation protocol for the altered trajectory. Although DBS involves a strictly scripted procedure, the surgeon’s ability to fully comprehend the way in which the instrument’s kinematics translate settings to target point coordinates and trajectory, could prove crucial in whether he or she would like to work with the instrument. However, a nicely designed training procedure and device could be an answer to this challenge.
As the workings of deep brain stimulation continue to be understood better, the number of ailments for which it can provide symptom relief keeps increasing. Furthermore, ongoing research in neurophysiological diseases will reveal more brain regions where electrical stimulation could have desirable effects.

It is known from possible stimulation side effects in Parkinson’s disease, that stimulation of certain regions in the brain can cause changes in behavior and character of the patient. Such effects might trigger a curiosity about the possibilities of deep brain stimulation in deliberately altering human characteristics. Whether research in such possibilities is ethical, is up to the reader to decide.
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A new instrument for Deep Brain Stimulation surgery

Deep brain stimulation (DBS) surgery is a surgical procedure which dates back to the 1990’s. Its goal is the implantation of a ‘pacemaker system’ for the brain. An electrode is implanted in the brain and connected to a pacemaker which is usually placed under the patient’s collarbone. DBS can provide symptom relief for various neurophysiological diseases, like Parkinson’s disease and epilepsy. The location of the stimulation target depends on which disease is being treated. Unfortunately, physically determining the stimulation target in the patient’s brain, as decided based on fused MRI and CT scans, proves to be challenging and full of risk.

After the surgeon has located the stimulation target on an MRI scan of the patient’s brain, the surgeon is faced with the difficult task of accurately placing the stimulation electrode in the target. This often concerns the deep-seated subthalamic nucleus (STN), which measures only 8 by 4 millimeters. The electrode has to be placed in the STN-part that controls movement. If the electrode ends up elsewhere, the electrical stimulation will result in undesirable side effects, and the surgery will be considered a failure. Furthermore it is important that the electrode does not damage any delicate structures in the brain, which would lead to surgical complications.

In the current day surgical procedure, the surgeon uses a special instrument called a stereotactic frame (which looks a bit like a bow sundial) to implant the electrode along the chosen trajectory, based on the MRI scan of the patient’s brain. This scan does not include a frame reference, as the frame cannot go in the MRI-scanner with the patient because of the strong electromagnetic fields of the scanner. To link the MRI coordinates of the stimulation target to the frame, an additional CT scan is made, with part of the frame attached. After this, the CT and MRI scans are fused and the MRI-derived coordinates can finally be translated to frame settings. The fusion of the MRI and CT scan introduces an error of up to several millimeters to the initial imaging accuracy. Combined with the inherent limited stiffness in the stereotactic frame, this leads to only highly experienced surgeons being able to implant the stimulation electrode accurately.

In order to also enable less experienced surgeons to perform this surgery, this PhD thesis describes two new surgical instruments for implanting DBS electrodes in the brain. First I focused on how to achieve an unambiguous translation of target (location in physical brain) and skull entry point coordinates to instrument settings. I came up with an adapter disc which gets fixated with three small surgical screws to the back of the patient’s skull. This is less painful and more comfortable than the currently used frame, which is clamped on the head.
with four pins forced into the skull bone. The adapter disc serves both as a visual reference in the MRI scan, and as a structural reference for the instrument.

After this, I started with the design of the first prototype of the new instrument. As it would be nice to allow for electrode implantation under guidance of real-time MRI, I chose to make the prototype MRI-compatible. This led me to the decision to design the instrument completely in plastics; mostly PEEK, because of its rigidity and high melting point. Upon realization of this PEEK prototype, it became clear that the material choice implied higher cost and a more bulky design than would be the case when MRI-compatibility would not be required. This led to the design of the second, non-MRI-compatible prototype, in which I exploited the freedom in material choice, together with all the experience I had gained from the PEEK instrument. The result is a more compact instrument, although conserving the same style as the PEEK instrument.

Alongside the two instrument prototypes, I have developed an MRI-compatible actuator, which is controlled by the surgeon. It is required for the possible application of the PEEK instrument in the confined environment of an MRI scanner. Since the other instrument settings are adjusted before attaching the instrument to the patient’s head, only the straight lined insertion of the electrode needs to be motorized. The goal of the design process was to keep the drive as compact as possible, in line with the limited forces at play during electrode insertion in the brain.

The goal of both instruments is to enable all neurosurgeons to perform successful DBS surgery; not only the highly experienced ones. Furthermore, the instruments permit a reduction in preparation time, risk and cost, compared to the current-day procedure. This could eventually lead to more patients receiving the treatment and in an earlier stadium of their disease.
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*Att fly är livet, att dröja döden*
Curriculum vitae

Marc Janssens was born in Roosendaal on the 18th of May, 1988. He finished secondary school in 2006 at the Gertrudiscollege in Roosendaal, after which he started studying mechanical engineering at the Eindhoven University of Technology in 2007. He graduated (cum laude) within the Constructions & Mechanisms group in November 2012. His graduation work, titled ‘Design of a short stroke reluctance actuator support structure for WS450’, was awarded with the ‘Wim van der Hoek constructeursprijs’ by the Dutch Society for Precision Engineering in 2013.

Marc started his work as a PhD student within the Control Systems Technology group at TU/e in April 2013. The PhD project, presented in this thesis, is focused on the design and development of a new instrument for deep brain stimulation surgery.

In the period from February 2016 until April 2017, Marc worked part-time at the VDL Enabling Technologies Group in Eindhoven as a design engineer, next to a part-time continuation of his PhD research.

Over the course of the PhD project, two instrument prototypes have been realized. Further valorization of these instruments is under investigation.
Appendix: instrument photos