Visual quantification of motor function during awake brain surgery

Towards a Neuro Research Operating Room

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Preface

This page marks the conclusion of 7.5 incredible years of studying. My journey started in Leiden, passed through Delft and is now concluded in Rotterdam, reflecting the three cities that have been my home for the past years. As soon as I learned about the new study programme of Technical Medicine, I was drawn towards the possibility to combine an interest in the human body with the excitement of new technical innovations. During my studies, I discovered a fascination for the complex interaction between patients, their family, medical specialists, technical innovation and scientific research. In my Master's thesis, I had the opportunity to be on the forefront of this complex interaction, by combining neurosurgical and neuroscientific research and implementing this directly in clinical care. I want to express my gratitude to the big team of medical specialists, technicians and researchers, who made this project possible.

The first two people I would like to thank, are Pieter and Djaina. From my first internship on, you have always supported me to develop myself both academically and personally. I want to thank you for all the opportunities you have already given me and for the fun meetings that sometimes feel more as a 'borrel' than an actual meeting. Pieter, thank you for your infectious enthusiasm and passion to bring the Neuro Research OR one step further. I hope we can share this passion with many more people in the future. Djaina, thank you for being a true example of the medical professional I aspire to be. Your ability to always put the patients first, while finding a way to constantly innovate is really inspiring. Secondly, I would like to thank Arnaud for his never ending stream of new ideas and enthusiasm to immediately put new concepts to action. I very much enjoyed our time in the OR together, and am looking forward to working together in the future.

A special thank you to Stein, for showing me how to make an actual product out of the designs we made. To the Cube lab, thank you for helping me in my technical development and the amazing time you have given me in the lab. To the Na21 crew, thank you for already adopting me as a future PhD student. I am looking forward to spending more time at the 'kantoortuin' with you.

To my family and friends, thank you for all the support and happy memories over the past years. To 217, thank you for all the joy and motivation you have brought me throughout the years. To my -previous- housemates Julia, Noa, Marijn, Edwin and Mathies, thank you for the many fun study sessions at home and all your support during the stressful periods. Marit, thank you for your very valuable ideas and being a listening ear during the -sometimes daily- coffee breaks. In times of stress, these breaks really kept me going. I am very much looking forward to working together in the next years.
To my mum and dad, thank you for your support during the whole course of my studies. You have always encouraged me to go my own path and shown me that the world is full of opportunities. Thank you for creating a home where I am always looking forward to coming home to, even now to finish this thesis.
My dear Sanne, what a joy have all the hot chocolate breaks at the Erasmus been with you. Thank you for always being my role model in life, and sharing your beautiful view on the world with me.
Lastly, I don't know where to start expressing my thanks to Jaro. Besides having been my SolidWorks guru, sparring partner and personal cook, you have been my absolute rock for the past months. Thank you for your endless support, love and for somehow always finding a way to make me laugh.

Let's see what the future brings.

Emma Caroline Gommers
February 2024

Summary

During a brain tumour resection, a neurosurgeon is constantly navigating a delicate balance between resecting as much of the tumour as possible, while avoiding any damage to healthy brain tissue. This challenge is particularly difficult when the tumour is located in a critical functional area, involved in for example language or motor function. For these types of tumours, the awake craniotomy was developed. During this surgery the patient wakes up to perform language and motor tasks, to enable the surgeon to localize these functions inside the brain. In this thesis, we investigate and develop a new quantitative method to monitoring motor function that could potentially improve intraoperative decision making and enables neuroscientific and neurosurgical research.

Chapter 1 provides a background about surgical strategies and technologies that have been developed to aid surgeons' decisions during complex brain tumour resections. We will explain the complexity of robust research in the neurosurgical environment and the need for a dedicated Research Operating Room to create an environment to improve neurosurgical and neuroscientific research.

In **Chapter 2** we make an overview of the possible solutions to quantify motor function before, during and after awake craniotomies and discuss the best solution for the Erasmus MC.

In **Chapter 3** we present a new frame to create a standardized environment inside the operating room for good quality data collection of patient functionality. To design this frame, we identified and interviewed all the important stakeholders and designed three prototypes. The two most promising prototypes were developed. The final prototype was implemented during three awake craniotomies.

This newly developed frame was used in **Chapter 4** to explore video tracking as a new tool to quantify hand motor function. Three patients were followed one day prior to the surgery, during the awake craniotomy, and one day postoperatively. During these three cases, we identified several prerequisites for a reliable recording set-up and explored the potential to detect clinically relevant events during fingertapping and direct electrical stimulation (DES). This showed promising results and underscores the potential for video tracking to be further investigated for quantification of hand motor function.

In **Chapter 5** we put the discussed work into context, discussing it's clinical and scientific relevance and future perspectives. In this thesis, we have demonstrated that it is possible to implement a new quantitative measurement method to monitor hand function in the challenging environment of an operating room. Quantification of visual observations has shown to be low-cost, easily available and implementable in clinical context, because of the fast technological advancements in this field. Video tracking can be used for future research to investigate the relation between intraoperative findings and long-term outcomes, and has the potential to add valuable information for neurosurgical and neuroscientific research.

Contents

1

Background

1.1 Brain tumour resection

Brain tumour resections are very complex surgeries. On the one hand, the surgeon wants to remove as much tumour tissue as possible to improve the survival of the patient. On the other hand, the surgeon also wants to preserve healthy brain tissue involved in important functionality, which is essential for the quality of life of the patient.[1,2] The delicate balance between tumour resection and preservation of functionality is particularly difficult when the tumour is located close to a brain area involved in important functionality like language or motor function, since tumour tissue is often infiltrating surrounding healthy brain tissue.[3] During surgeries to remove these tumours, the surgeon is constantly challenged to make difficult decisions about which tissue can be safely removed and which tissue should be left intact.

To be able to make intraoperative decisions, the neurosurgeon needs to have as much information as possible about the tumour and about surrounding brain tissue. Gathering this information already starts before the surgery with preoperative Magnetic Resonance Imaging (MRI) scans of the brain and functional testing of the patient. This helps the surgeon to make a planning on how to approach the tumour during the surgery and to investigate which functions, like language or sensation, are located close to the tumour. The preoperative data is used intraoperatively to navigate inside the brain, but is currently is not accurate enough to locate and monitor important functional areas inside the brain.[4] Therefore, special surgical strategies have been developed for intraoperative functional testing. One of these strategies is awake brain surgery, also called awake craniotomy.

1.1.1 Awake craniotomy

An awake craniotomy is a special procedure where the surgeon collaborates with the anaesthesiologist, the clinical linguist and the patient. As described before, the surgeon is constantly balancing on the edge between resecting tumour tissue and preserving healthy, functional brain tissue. During an awake craniotomy, the patient wakes up to perform functional tasks to enable the surgeon to map functional brain areas involved in language or speech function, motor function, or sensory function.[5,6] The clinical linguist is constantly monitoring these different functions, while the surgeon uses direct electrical stimulation (DES) to identify cortical and subcortical structures that are related to these functions. If the DES interferes with the patient performing a task, the surgeon knows that the stimulated brain area should be preserved.[7] This is called brain mapping.

Figure 1.1.1: Visualisation of an awake craniotomy. The clinical linguist is sitting next to the patient to monitor functionality. The surgeons and operating assistant are operating on the brain.

1.1.2 Towards a Neuro Research Operating Room

Unfortunately, brain mapping is not as simple as it sounds. Not every intraoperative change in functionality says something about long term outcomes of the patient. Some intraoperative deficits recover immediately postoperatively, or recover in the first weeks.[8] For these deficits, it is not worth leaving tumour tissue behind, as that might decrease the survival of the patient. This shows the importance to present robust evidence about which intraoperative findings are predictive for long term outcomes and should alter surgical intervention.
Providing robust evidence however, is a big challenge in neurosurgery due to the large variability between patients, tumours and surgeons. Every brain is different and every tumour type, tumour location has a varying interaction with surrounding tissue. Moreover, every surgeon has their own surgical preferences and methods. This large heterogeneity between patients and surgeons makes it very difficult to prove that a specific treatment or intraoperative monitoring method is superior to others. Therefore, it is very important to gather preoperative, intraoperative and postoperative data about the relation between tumour type, tumour location, surrounding brain tissue, surgical strategy and a patients functionality. This offers the opportunity to discover trends and relations between intraoperative changes and long-term patient outcomes, that can be supported with quantitative data.

At Erasmus University Medical Centre (Erasmus MC), we therefore aim to establish a special Neuro Research Operating Room (OR), where we create an environment to acquire data about a patients functionality, the brain and the surgeons actions during the procedure. This data will be stored in a large database, from which we conduct neurosurgical and neuroscientific relevant research, see Figure 1.1.2 for reference. Ultimately, this research will lead to new insights to improve surgery for patients with a brain tumour.

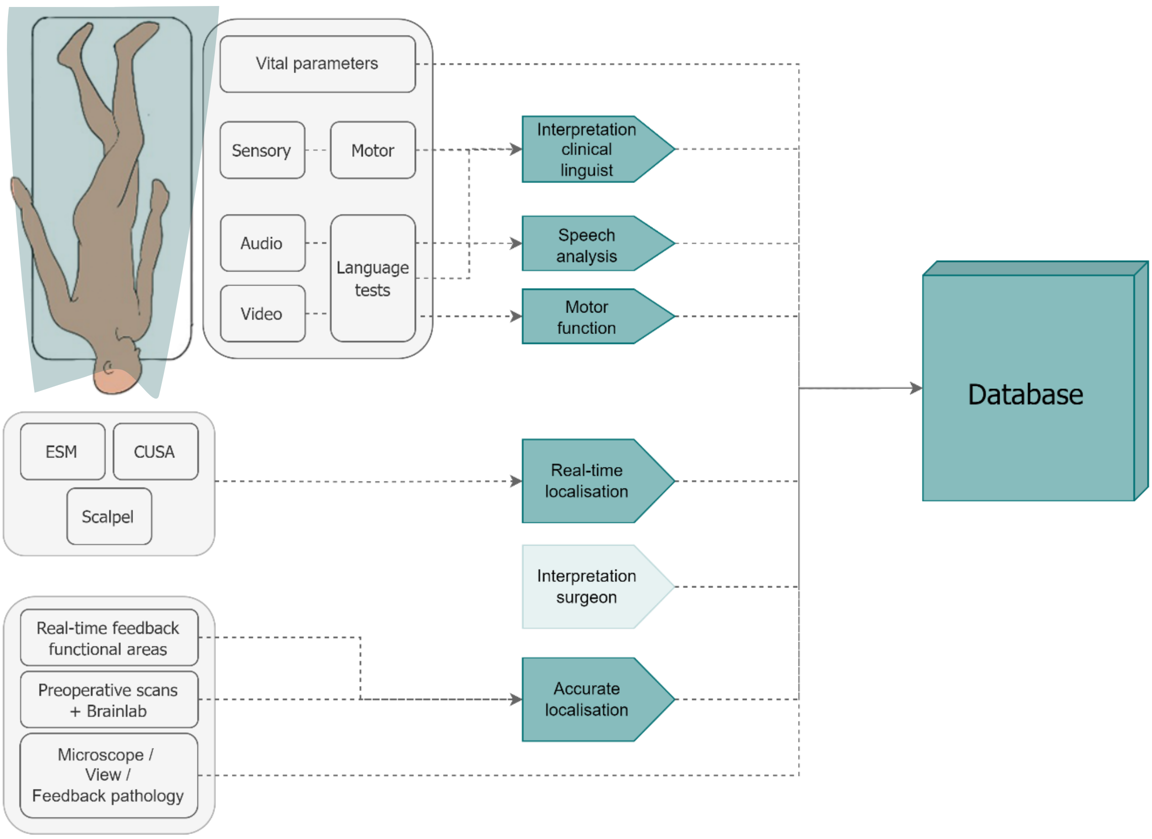

Figure 1.1.2: Visualisation for the future goal to collect intraoperative data about the patient's functionality, the brain and the surgeon's actions. This will be stored in a database to conduct neurosurgical and neuroscientific research.

1.2 Thesis Objective

In this thesis, we will focus on acquiring quantitative data about the patient's functionality. For language and speech function, a whole protocol for intraoperative testing has already been developed.[5,7,9,10] For motor function however, there is still no standardized protocol that shows which intraoperative changes predict long term motor deficits. Therefore, our aim is to find a quantitative motor function monitoring method that can be implemented at the Erasmus MC to acquire reliable preoperative, intraoperative and postoperative data about motor function. To do so, this thesis consists of three parts, with each their own goal.

1. Investigate potential motor function measurement methods and find the most suitable solution for the Erasmus MC. (**Chapter 2**)
2. Create a standardized environment around the patient to enable structural data collection about motor and language function (**Chapter 3**)
3. Explore the use of video tracking as a potential tool to monitor hand function before, during and after awake brain surgery (**Chapter 4**)

The findings of this thesis provide new insights about implementation of a new quantitative method inside the complex environment of an operating room that can be used for future clinical innovations and research purposes.

2

Finding a suitable motor function measurement method

In this chapter, we aim to find a suitable solution to measure motor function for the Erasmus MC. To do so, we will first give a background about motor function. Then, we will give an overview of the different possible solutions. Lastly, we will discuss which solution is most promising and will be further investigated.

2.1 Motor function

2.1.1 Motor control and motor execution

Motor function comprises the whole trajectory of motor control in the brain, the resulting executive function of the controlled muscle and the sensorimotor feedback that is consequently processed in the brain.
A simple first division of this complex system is motor control versus movement execution, see Figure 2.1.1. Motor control contains the whole nervous system involved in the planning, initiation and regulation of motor function. It ranges from the cortical regions in the brain, through the spine to the motoneurons connected to the corresponding muscle, and involves feedback through the sensorimotor neurons. Motor execution is the result of motor control and consists of muscle contraction and the corresponding movement. Motor control can be seen as a system, and motor execution as its output.

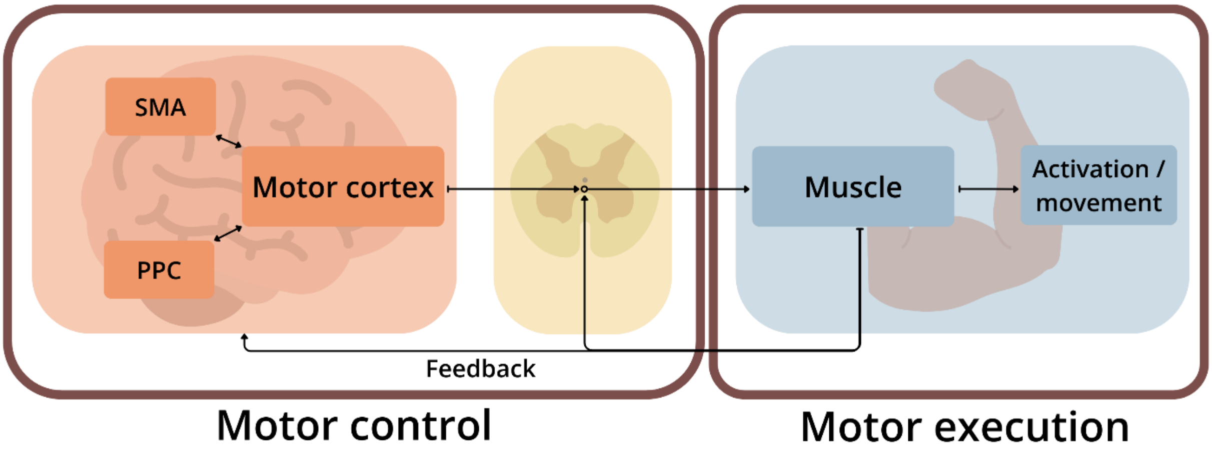

Figure 2.1.1: Motor function described as a motor control system with motor execution as its output. PM: Premotor cortex, SMA: Supplementary Motor Area, PPC: Posterior parietal cortex.

2.1.2 Disruption of the system during or after awake craniotomy

During awake craniotomies, direct electrical stimulation (DES) is used to identify cortical areas and subcortical pathways that are involved in motor, sensory, language and cognitive function. This is called brain mapping. With DES, an electric current is applied to the brain to investigate whether the stimulated brain area is involved in certain functionality by observing its interference on a specific task. In motor tasks, the stimulation can either lead to inhibition of the movement, which is called a negative response, or lead to the activation of a movement or muscle, which is called a positive response.[6] When an eloquent brain area is found, it is marked to avoid resection in this area.

When looking at motor function as described in the previous section, DES, nerve damage or a bleeding can cause a disruption of the motor control system. This disruption can be 1) lesion of one of the brain areas giving input to the motor cortex, 2) damage to the motor cortex itself or 3) impairment of the tracts connecting the motor cortex to the spinal cord, see figure 2.1.2.

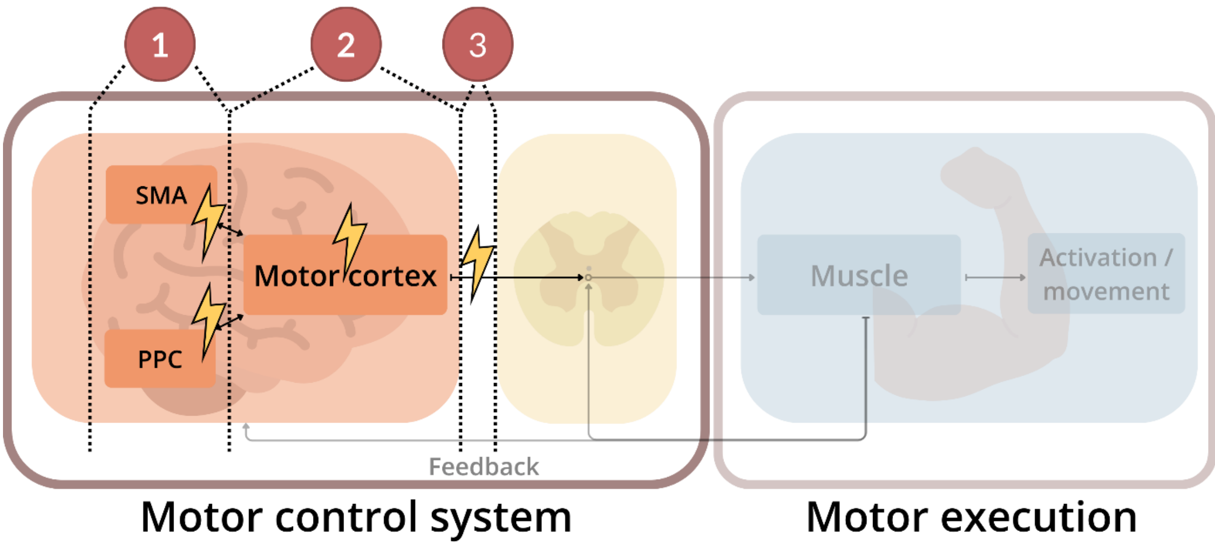

Figure 2.1.2: Different types of disruptions in the motor control system that can be caused by DES, nerve damage or a bleeding. 1: disruption of one of the brain areas giving input to the motor cortex, 2: disruption of the motor cortex itself, 3: disruption of the tracts connecting the motor cortex to the spinal cord.

To detect and measure the type of disruption, either the motor control system itself can be monitored with for example electroencephalography (EEG), or the change in the motor execution as a result of the disruption can be measured. In current practice, intraoperative detection of the disruption is mainly based on measuring the output of the system, the motor execution, while the patient performs a task. This enables the medical team to investigate if the interference of the disruption has an effect on actual functional tasks outside the operating room (OR) and thus not only look at connectivity. Currently, assessment of the performance of the patient is fully based on the visual interpretation by the clinical linguist. Patients are asked to squeeze their hand, or perform a finger tapping test. This is a very subjective method with large interobserver variability. To improve the reproducibility and to enable a more precise monitoring, a quantitative measurement technique is needed to monitor motor execution.

2.2 Quantitative motor function monitoring methods

In previous literature research, we explored recent developments of quantitative motor function measurement methods and their suitability for intraoperative monitoring during awake craniotomies (Supplementary Material A). Six methods were identified: 1) electromyography (EMG), 2) dynamometry, 3) force myography (FMG), 4) markerless optical tracking, e.g. video tracking, 5) marker-based optical tracking and 6) inertial measurement units (IMU). These methods are based on different underlying mechanisms and measure different aspects of motor execution.

2.2.1 Description of six potential solutions

EMG measures electrical activity produced by muscles in contraction.[11] This is a direct reflection of the electrophysiological behaviour of muscle activation. EMG is able to detect muscle activation before there is visible contraction of a muscle. When applying this to awake craniotomy, this means that a stimulation with DES could be detected before this is visible as a muscle twitch.[6] This is similar to EMG currently used for MEPs in asleep surgery. Viganò et al. also showed that positive or negative motor responses can have different underlying muscle activation patterns and a difference in origin of stimulation in the brain, showing its relevance for awake craniotomies.[12] Disadvantages however, include the relatively low signal-to-noise ratio (SNR) and interference of activity from different muscles.[11] Also, a neurophysiologist is needed to interpret the acquired signals real-time. This means that an already complicated surgery including multiple specialists, will take longer and is dependent on one more specialist.

Dynamometry measures force generation using load cells or hydraulics. The most common is the clinically validated Jamar dynamometer, measuring hand grip strength.[13] Different muscle groups can be measured with handheld dynamometers. The main advantage of these devices is their practicality, since they are rather small, simple and have no additional wires. The major disadvantage is the decrease of reliability when the patient has pre-existing weakness.[14] Also, since it is only designed to measure muscle strength, it is not applicable to a wide variety of motions and aspects of motor function.

FMG records volumetric changes resulting from muscle contraction. Volumetric change is measured with force-sensitive sensors placed around for example the arm. The signals from these sensors can be decoded with the help of machine learning to analyse which muscles were active.[15,16] This can even be further decoded to hand gestures. Compared to EMG, FMG electrode placement is easier and FMG has a higher SNR.[16,17] A major disadvantage is that the development of FMG sensors is still ongoing and there are no devices on the market yet.[18] This is a problem for clinical implementation.

Optical motion tracking uses cameras to record and analyse human body movement. Optical tracking can be subdivided into two categories: markerless optical tracking or video tracking, and marker-based optical tracking.
Video tracking records the moving object in its natural form, while marker-based tracking records reflective markers placed on the moving object.[19] These markers are tracked by high-speed infrared cameras. The advantage of video tracking is the simplicity of the technique, since it only needs one or multiple cameras and does not restrict movement.[20] This comes however with a cost in accuracy of the estimated location compared to marker-based tracking.[21,22]

IMUs are composed of an accelerometer and a gyroscope to detect position, acceleration and orientation of the sensor. It can be further equipped with a magnetometer to overcome drifting issues.[23] IMUs have the big advantage that the subject is not required to be within a camera's visual field of view for detection.[24,25] A disadvantage however, is the disturbance of the magnetic field inside buildings and by other equipment, making measurements less reliable.[26]

Table 2.1: overview of quantitative motor function monitoring methods, retrieved from Supplementary Materials A.

Method	Type	Measures	Application	Pros & Cons
Electromyography	Electrophysiology Force Motion	Motor unit depolarization	Diagnosis neuropathies Intraoperative monitoring	+ differentiate underlying mechanisms - noise, complex
Dynamometry	Force	Force	Rehabilitation Stroke	+ clinical validation - applicability
Optical markerless tracking	Motion	Coordinates moving object	Sports & rehabilitation Robotics	+ unconstrained - need patient in view
Optical marker-based tracking	Motion	Coordinates markers	Sports & rehabilitation & stroke Robotics	+ accuracy - interference, complexity
Inertial tracking	Motion	Acceleration and orientation	Sport & rehabilitation	+ small, cost-effective - interference, shift
Force myography	Force Motion	Volumetric changes	Stroke, rehabilitation Robotics	+ small, cost-effective - complex to make

2.2.2 Suitable solution for the Erasmus Medical Center

Based on the research about the different techniques and their advantages and disadvantages, we aimed to find the most suitable solution for implementation in current practice inside the Erasmus MC. We set up a list of requirements together with the neurosurgeon and clinical linguist, see Figure 2.2.1

Requirements for a quantitative motor function measurement method

Hand function

- Measure various motor aspects
- Predicting value
- Non-invasive
- Addition to other tests
- High frequency of measurements
- Versatility

Operating room

- Data acquisition with physical constraints
- No interference with other equipment
- CE mark - adhere to regulations
- Achievable with available specialists
- Low cost
- Reusable

Figure 2.2.1: Overview of the requirements for a quantitative method to measure motor function during awake craniotomies.

Of the six previously described methods, electromyography, dynamometry and markerless optical tracking are suitable for intraoperative application. Force myography is currently not on the market yet, meaning clinical implementation is not possible. Marker-based tracking could interfere with the infrared based neuronavigation, since they both use infrared reflecting fiducials. This interference could pose a significant problem for the neurosurgeon during navigation inside the brain. Inertial measurement units would be interesting in the future, but all the equipment present in the surgery room could interfere with the magnetometer part of the device. This seriously decreases the accuracy of the measurements.
This leaves EMG, dynamometry and video tracking as potential solutions. They each measure different aspects of motor function and all three could give different insights into intraoperative motor changes during tumour resection.
As described before, EMG requires a neurophysiologist to real-time analyse the acquired signals. Due to logistic reasons, this is currently not feasible for the already complex awake craniotomies inside the Erasmus University MC. Therefore, this technique is currently not further investigated but kept in mind for future research.
Dynamometry could be used to quantify one of the current subjective hand grip strength measurement. Patients are asked to squeeze the hand of the clinical linguist, as a measure for hand grip strength. A dynamometer would be a very simple alternative to quantify the hand grip strength. The clinically approved Jamar Hydraulic Dynamometer is however very big and heavy. For patients laying down this weight would be a real problem. Also, the device has been validated in upright sitting position, which is not achievable inside the operating room. Alternatives, like the K-Force Grip developed by Kinvent could be a solution. Due to regulatory constraints, it is not possible to implement this new device inside the operating room during this thesis. Therefore, we

were forced to exclude this method during the pilot study. It would however still be interesting to investigate it’s use in the future.
The third option, video tracking, shows great potential to measure different aspects of motor function. Video tracking could analyse movement initiation, accurate targeting and fine movements. Also, it only needs a camera and a tracking algorithm. With rising healthcare costs, an increasing focus on sustainability and the fast technical advancements, such a simple, versatile tool could be a good solution. On the downside, this limits monitoring possibilities to extremities visible in the view of the camera. Extremities blocked in view by blankets or other equipment, including the torso and legs cannot be monitored. In the awake craniotomy setting, this means that only the hands, part of the arms and the face can be tracked. Despite its shortcomings, video tracking shows promising results to be a simple, low cost, pervasive solution to quantify tasks already performed during awake craniotomies involving the hands and arms. Therefore, we have decided to further investigate the potential of video tracking to monitor motor function before, during and after awake craniotomies.

3

Environment for reproducible measurements

Collecting data about patient functionality is important both intraoperatively as feedback for the surgeon, and postoperatively for research purposes. To be able to do proper research, data should be collected in a standardized manner. The operating room is a challenging environment for standardized data collection, since every patient, tumour and surgical procedure is different. To improve the standardization, a decrease of variability in the surgical set-up is therefore essential. To make a first step, this chapter will focus on improving the frame that separates the sterile and the non-sterile environment around the patient during awake craniotomies. This creates a more stable surgical set-up and enables for new methods to monitor the patient's functionality.

3.1 Approach

To design a new frame, the Double Diamond framework was used, see Figure 3.1.1. This technique can be divided into two diamonds, where the first diamond focusses on defining the problem and the second diamond on finding a solution. Both diamonds consist of a divergent thinking phase, to widen knowledge, and a convergent thinking phase, to narrow down and focus. During the Discover phase, we perform an in depth analysis of current practice by expert consultations and getting firsthand experience. During the Define phase, we focused on defining a clear problem and drawing up requirements. In the Develop phase, we designed various concepts as potential solutions. During the Deliver phase, we converted the most promising concepts into actual prototypes, to test in the operating room. As a last step, we Evaluated the prototypes based on the requirements, and tested the final prototype during three awake craniotomies. Each of the five stages will be discussed below.

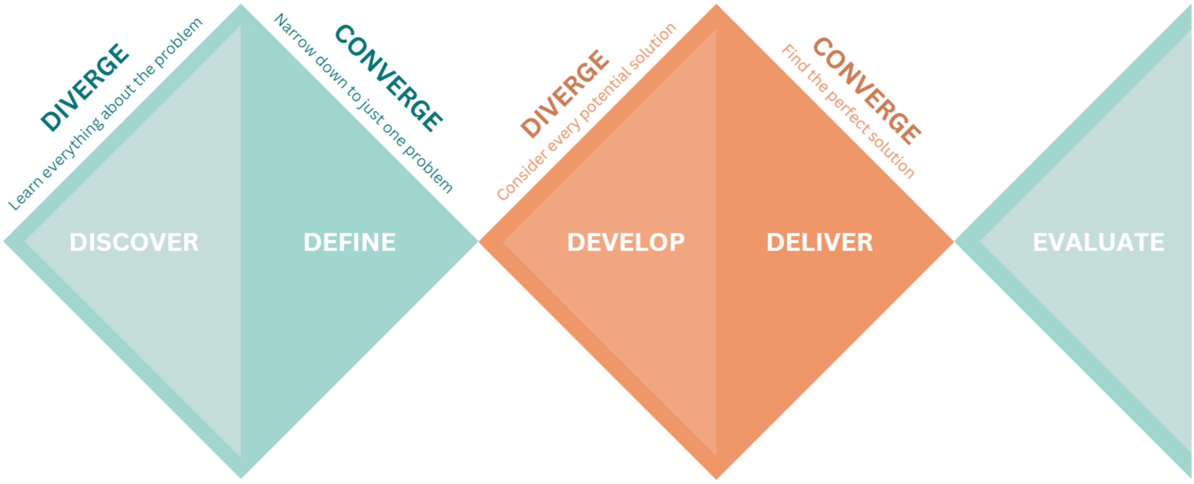

Figure 3.1.1: Design process for the development of an improved environment for patient monitoring during awake craniotomies

3.2 Discover

The first step Discover focusses on learning as much as possible about the problem and the experience of the users. In this step we aimed to identify the stakeholders and their wishes, and map the regulatory side of the Erasmus University Medical Center (Erasmus MC).

3.2.1 Current practice

During awake craniotomies at the Erasmus MC the space around the patient is roughly divided into two sections, see Figure 3.2.1. On one side is the sterile part of the OR, where the surgeon and OR assistant perform the tumour resection. On the other side under the sterile drapes is the non-sterile area, where the anaesthesiologist and clinical linguist communicate with the patient. This non-sterile area under the drapes will from here on be called the ‘tent’. In this tent, the clinical linguist performs language and motor function tasks, like object naming and finger tapping. During these tests, audio and video recordings of the face are made for intraoperative feedback and for research purposes.

The set-up and positioning of the drapes is currently as follows. First, the OR assistant attaches the sterile drapes to the patients head around the craniotomy, to keep the wound sterile. Then, the drapes are unfolded over a frame. Lastly, the tent is set up by the anaesthesiologist to free the face of the patient and create a space for the clinical linguist and anaesthesiologist to sit. This is done by taping the tent to the frame and hanging up the edges with clamps and ropes. See figure 3.2.2 for reference.

Inside the non-sterile side of the tent, audio and video of the patient’s speech and face are recorded. The microphone and camera are attached to another frame, from now on called camera holder, see Figure 3.2.3. This camera holder cannot move in all degrees of freedom, making it difficult to position. Also, it only consists of one arm, which limits it to optimal positioning for only one camera.

Figure 3.2.1: Intraoperative set-up of sterile drapes. Left: sterile side of the tent with the neurosurgeons and OR assistant. Right: non-sterile side with the clinical linguist and patient

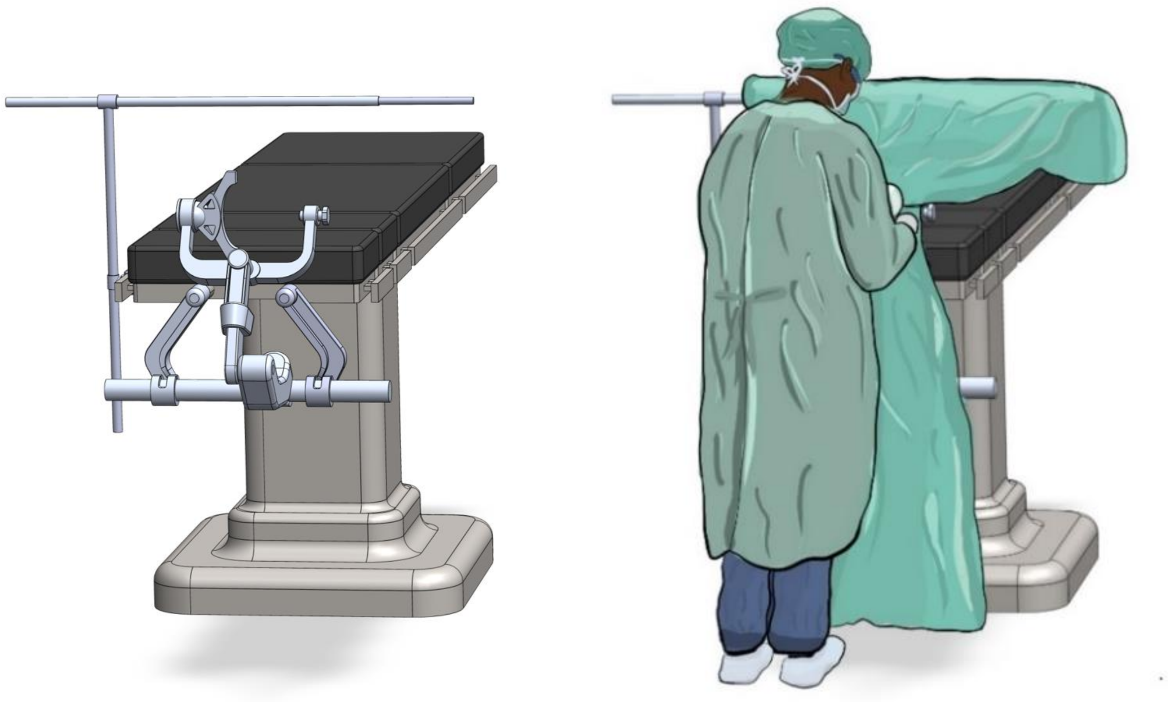

Figure 3.2.2: Current set-up of the sterile drapes, creating a sterile and non-sterile section. The OR assistant

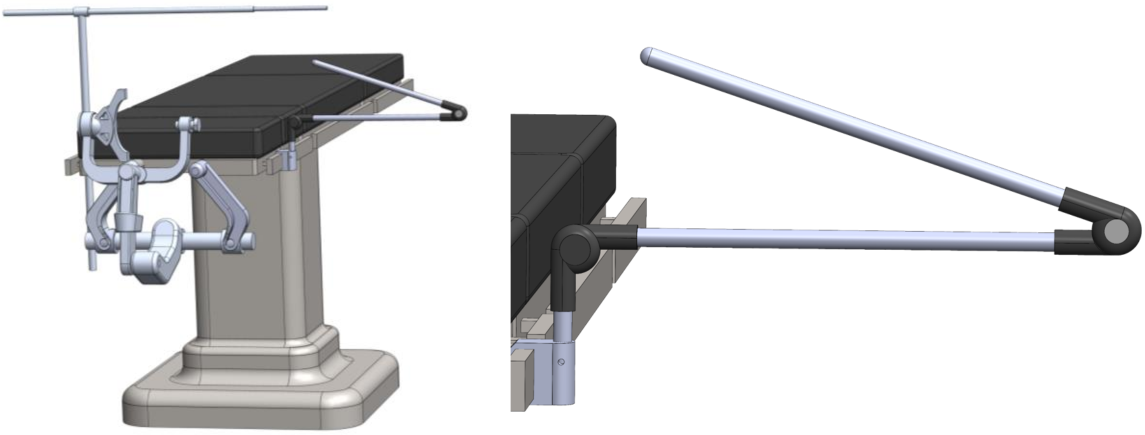

Figure 3.2.3: The existing frame to set up audio and video recordings.

3.2.3 Stakeholders

After mapping the current use of the frame and the tent set-up, we collected information from all the different specialists involved in the setup of the tent, or that work in close contact of the tent. The technical staff of the OR complex and neuroscientists involved in research inside the OR were also interviewed. With their input we will set up a set of requirements, see 3.3.1.
The stakeholders involved inside the OR are the neurosurgeon, the anaesthesiologist, the clinical linguist and the OR assistant. As described and visualized before in Figure 3.2.1, the sterile drapes separate the OR environment in two areas. The surgeon and OR assistant on one side operating on the brain, and the anaesthesiologist and clinical linguist on the other side interacting with the patient.

OR assistant

The OR assistant sets up the sterile drapes, to make sure the skull is exposed and the rest of the patient is covered and kept sterile. Their instrument trays are also placed over these sterile drapes. They hand the instruments to the surgeon over the frame.

The OR assistants shared several wishes and needs for the tent, that mainly focus on the workflow and contact with the surgeon.

1. The sterile area above the sterile drapes should stay accessible to place frequently used instruments.
2. The frame should not be higher than the current design, as this would interfere with handing of the instruments to the surgeon. A higher frame would be ergonomically irresponsible.
3. Arranging the sterile drapes with the new frame should be straightforward.

Anaesthesiologist

The anaesthesiologist sets up the non-sterile part by installing the frame and hanging up the edges with clamps and ropes.
During the interviews, they showed great enthusiasm to improve the current set-up. Setting up the frame, hanging it with tape and clamps and taping it away around the face of the patient to get a clear view is time consuming. It also highly depends on how much time and room there is to free the space around the face. Sometimes, part of the eye of the patient is still covered. After the surgery has started, it is hard to fix this.

Important factors for these specialists are:

1. Improve usability, ease the set up
2. Improve standardization. The new frame should enable a standardized set-up, to guarantee a good view on the patients face and create enough space inside the tent.
3. Keep or increase accessibility to the patient. Both the face and airway should be accessible at all times in case of emergency, but also all the needles and lines for monitoring and drug administration should not be covered.

Clinical linguist

The clinical linguist is the person that sits inside the tent to communicate with the patient during the awake part of the surgery. Currently, there is very limited space inside the non-sterile part of the tent, and the clinical linguist can only sit crouched down. This is both uncomfortable and undesirable for good communication and monitoring.

The main factors discussed to be important for the design of the new frame are:

1. Ensure full view of the patients face for good monitoring and better communication.
2. Create possibilities for video and audio recording of the patients face.
3. Ensure room for a tablet(holder) with intraoperative tests.
4. Increase space inside of the tent for better ergonomics.

Neurosurgeon

The neurosurgeon stands on the sterile side of the tent to operate on the brain. For the surgeon, the biggest concern is that he has as much space to freely move in, to get the best angle to operate on the brain. The new frame should not limit his range of motion. On the other hand, a clear view of the face and proper monitoring is very important for the surgeon to make appropriate decisions about which tissue he can safely remove. Also, as described before a lot about intraoperative monitoring is still unknown. Recording data about changes in the patient's functionality is therefore very important for this field that is constantly in development.

Their main wishes are:

1. The tent frame should not limit movement around the patient
2. The tent should leave enough space for the patient and clinical linguist for optimal monitoring
3. The tent should be flexible for implementation of recording devices or other equipment to monitor patient functionality.

Neuroscientist

The neuroscientist does not have a direct clinical role during neurosurgery. However, the awake craniotomy is a unique setting that creates a window of opportunity to do research on the human brain. The main challenge for neuroscientific research within this setting is reproducibility of intraoperative measurements. Since every patient, surgical strategy and monitoring results are very different, it is even more important to keep the environmental factors as stable as possible. Therefore, the new frame should be adjustable to enable a standard set-up around the patient for reproducible recordings of the patient.

Therefore, their main requirements are:

1. The tent frame should create a standardized space around the patient
2. The tent frame should be adaptable to facilitate multiple measurement methods to monitor the patient, including video and audio recordings

Technical staff OR complex

In the OR complex, there is a technical staff responsible for all the equipment that is used during or around surgeries. This includes all the devices the surgeons are using, but also the OR system of the monitors and screens. One of the technical staff is responsible for the anaesthetic devices. The frame that is currently used fall under his portfolio. During our talks it became clear that they are also designing a new frame for all surgeries. They want this frame to be applicable to all surgeries performed in the Erasmus MC. For this team it is mainly important that there is one standard frame, and that all specialized frames for specific surgeries are attachable to that standard frame. This would mean that the accessory to the frame would be interchangeable between operating rooms.

1. The frame has to be compatible with a standard frame, so that it is interchangeable between different operating rooms
2. The frame should adhere to cleaning regulations

3.3 Define

3.3.1 Problem definition and requirements

After speaking to all the stakeholders, it became clear that the main factors that have to be improved on the clinical side about the tent are: 1) adjustable frame that ensures visibility of the face of the patient, 2) while not decreasing flexibility on the sterile side of the tent and 3) a more user friendly setup. For research it is mainly important to have 1) a stable frame for attachment of recording devices and 2) a solution that creates a standardized environment. This leads to the following design problem:

“ Design a frame that supports the sterile drapes to create a standardized environment around a patient undergoing an awake craniotomy that enables implementation of video recordings to monitor motor and language function ”

To reach this goal, we set up a list of requirements for the design of the frame, see Table 3.

Table 3.3.1: Overview of the main requirements

	Main Product requirements
P.1	The product must support the sterile drapes
P.2	The product must be adjustable for positioning of the patient based on tumou location and patient size
P.3	The product must not create an increased risk of collapsing on the patient
P.4	The product should ensure a clear view of the patient’s face during the entire surgery
P.5	The product should allow for attachment of additional equipment
	Main User requirements
U.1	The product should ease the workflow of the OR assistants and anaesthesiologists compared to the current frame
U.2	The product should not limit movement on sterile side
U.3	The product should create more space inside the non-sterile side of the tent to improve ergonomics of the clinical linguist
U.4	The product should be compatible with a standard frame used inside the surgical centre
	Main Context requirements
C.1	The product must adhere to cleaning regulations for intraoperative frame usage
	Main Technologic requirements
T.1	The product should be compatible with the surgical beds used in Erasmus MC
T.2	The product must resist forces expressed by specialist during the surgery, by experts leaning on the product.
T.3	The product should increase stability and limit movement of the frame, to keep additional equipment stable.

3.4 Develop

During the Development phase we looked at different possible solutions for the defined problem. These solutions focused on either an adaptation of the already existing frame, or the design of a new frame. Each of the solutions will be discussed below.

3.4.1 Concept 1: adaption existing frame with goosenecks

As described before, the current frame is adjustable and crosses over the patient (figure 3.2.2). The first concept focusses on a redesign of that frame to make it suitable for our application while having a smooth and quick implementation. The adjustability of the original frame was kept similar, but the L-shape was changed to a curve to increase the strength and to prevent staff from leaning on the frame, see figure 3.4.1. This is mainly important to keep cameras and other equipment stable, requirement T.3. The terminal end of the frame is equipped with a mounting shaft for the attachment of additional equipment.

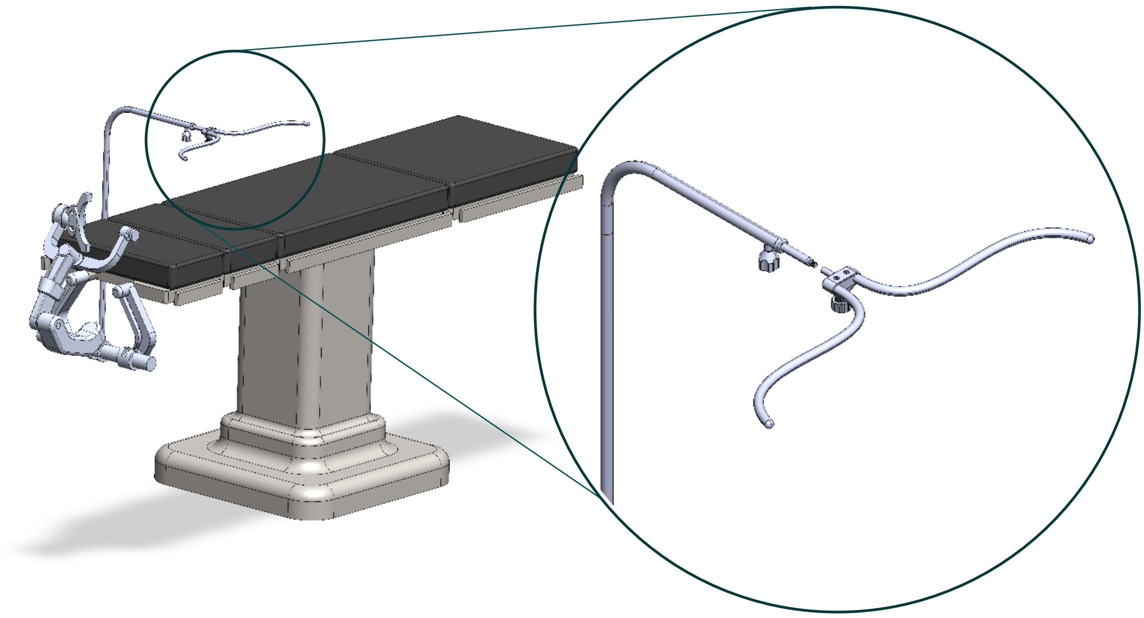

Figure 3.4.1: Visualization of concept 1. The frame is attached to the surgical bed and adjustable according to patient size and positioning. The two gooseneck arms can be bend into the desired position, creating a clear view of the patient.

On this shaft, a connection piece is fixated for the attachment of two goosenecks, i.e. two flexible metal pipes. These goosenecks can be bent to the desired shape, but are stiff enough to stay in position after adaption, see Figure 3.4.2. For cleaning purposes, these goosenecks have to be covered with shrinking tubes. Shrinking tubes are made of plastic and provide a protective layer around for example cables. The tubes are designed to shrink into place and become rigid when heat is applied, making it a durable and protective coating. These shrinking tubes would thus make the goosenecks less flexible, but the rigidity leads to more stability of the frame. A suitable shrinking tube size should be chosen to get a balance between flexibility and stability.

For detailed drawings of this design, see Supplementary Materials B.1 and B.2.

Figure 3.4.2: Left: Example of a gooseneck arm, a flexible metal pipe.[27] *Right: Example of a shrinking tube (black) around a ribbed tube (white)*[28]

3.4.2 Concept 2 : adaption existing frame with articulated arms

The second concept is also an adaption of the currently used frame. This concept uses the same curved frame as a base, shown in figure 3.4.1. For the flexible arms on the mounting shaft, a new design was made.
For the adjustable arms, this design is based on the currently already used Fisso articulated arms inside the OR, see figure 3.4.3. These arms consist of several segments that can rotate in multiple directions, which allows for a wide range of positioning possibilities. One of the applications of these arms is the arms supports used in the Erasmus MC. This means the specialists are already used to working with this equipment. At the end of these arms there is also the possibility to attach extensions or other equipment.

Figure 3.4.3: Fisso articulated arms.[29] *A: shown in three different positions. The red one knob handle simultaneously clamps or releases all three joints. All segments can rotate in multiple directions. B: example of arm support application.*

For this concept frame, two of these arms are attached to the connection piece on the curved frame, see Figure 3.4.4. This makes the design very flexible and stable. At the end of the arm, additional equipment can be attached, like a camera. For detailed drawings of this design, see Supplementary Materials B.3.

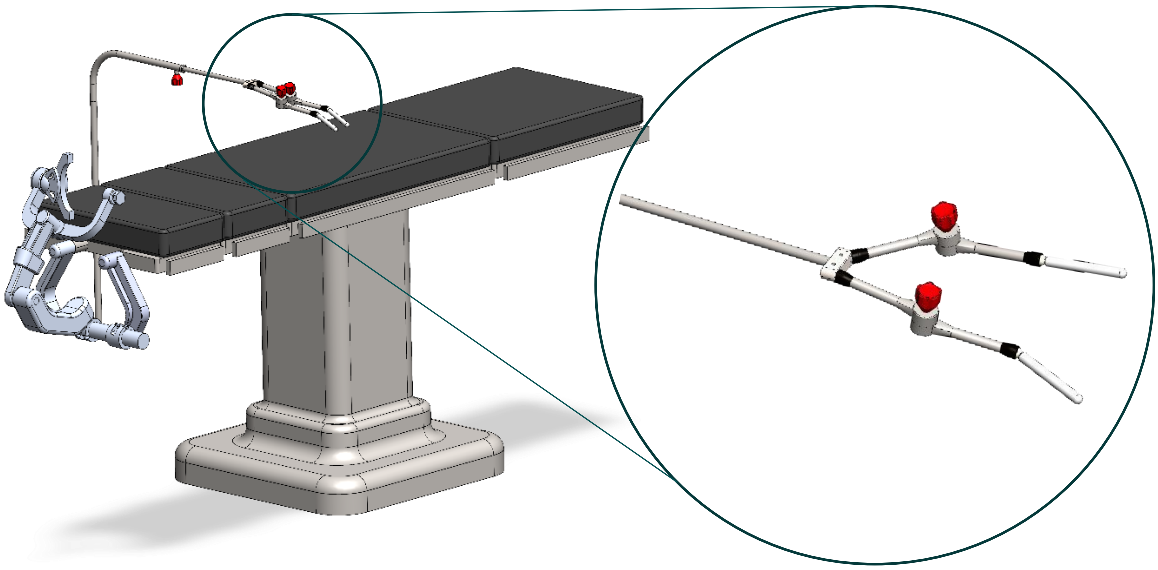

Figure 3.4.4: Visualisation of concept 2. Two Fisso arms are attached to the frame.

3.4.3 Concept 3 : New frame with goosenecks

The third concept is a complete new frame that can be attached to the rail on the side of the surgical bed, see Figure 3.4.5. This design is attached on the opposite side of the regular frame. This means that the design is located next to the patient's face, making it easier to create a clear view. Also, this makes the design less sensible for movement introduced by specialists on the sterile side of the surgery.

In this design, the connection to the surgical bed is similar to the camera holder that is currently used for audio and video recordings of the face, as shown before in Figure 3.2.3. Inside that holder, a frame is placed. Two goosenecks, flexible metal pipes as shown before in Figure 3.4.2 are placed. As described before, goosenecks can be bent into the desired shape, but are stiff enough to stay in position after adaption. In this concept, one of the arms can be bent to keep a clear view of the patients face, while the other can be positioned for camera or microphone placement, or to keep up the drapes. This design can also be expanded into more or longer arms, to match the stakeholders wishes. For detailed drawings of this design, see Supplementary Materials B.4.

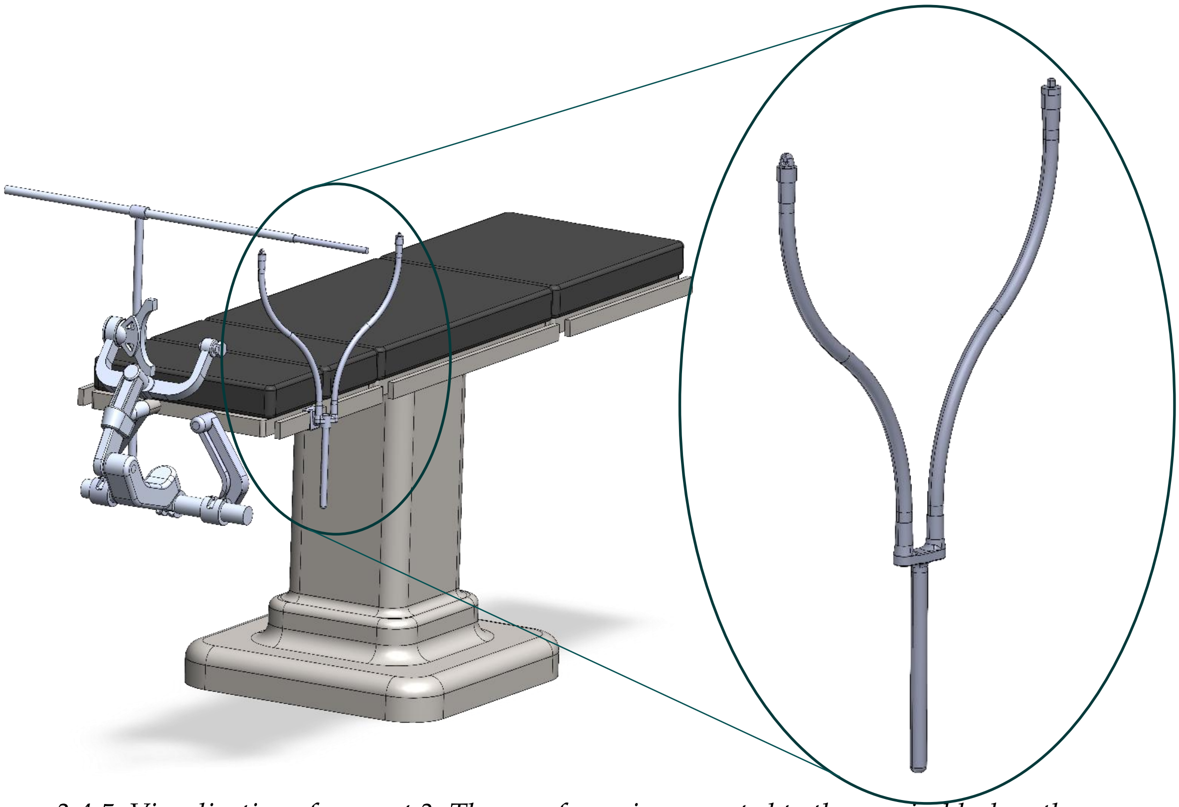

Figure 3.4.5: Visualization of concept 3. The new frame is connected to the surgical bed on the non-sterile side. The two arms can be positioned separately to keep up the drapes or position cameras and microphones.

3.5 Deliver

The Deliver phase focuses on finding a suitable solution for the operating room. In this step we focused on finding a feasible solution that is easy to implement and leaves room for further adjustments in the future.
For this purpose, we first discussed the potential solutions with several stakeholders. Secondly, we tested the two most promising results in the OR environment with as many of the stakeholders present as practically possible. Lastly, we picked the most promising solution and evaluated this prototype during an awake craniotomy.

3.5.1 Expert consultation

The designs of the three concepts were discussed with several stakeholders, including the clinical linguist, the anaesthesiologist and the neuroscientist. The first two experts are involved in the clinical set-up and monitoring inside the tent, while the third expert is involved in research. The combination of these experts gives valuable insides on which concepts to pursue in prototypes and which to exclude for further evaluation. An overview of the results of these expert consultations are shown in Figure 3.5.1. How they relate to the previously determined requirements is collected in a Harris Profile, see Figure 3.5.2.

Results of the expert consultations for the three designed concepts

	1 Concept 1	2 Concept 2	3 Concept 3
Clinical linguist	• Could improve the space inside the tent • Improve monitoring and ergonomics	• High flexibility to position the arms • Could create a very stable, improved tent	• Improvement of existing frame for audio & video • Better flexibility for camera placement
Aneasthesiologist	• Easy implementation as addition to existing frame. • Clear view of the patients face. Less variable set-up	• Easy implementation, Fisso arms are already used. • Major concerns patient safety - risk of collapse	• Independent frame, which eases the set-up • Two frames: timeconsuming & prone to mistakes
Neuroscientist	• Possibility to attach additional equipment • Less variability set-up, improving data acquisition	• Possibility to attach additional equipment • More stability, with the option to clamp.	• Possibility to attach additional equipment • Versatile set-up for future developments

Figure 3.5.1: Results of the expert consultations for the three developed prototypes.

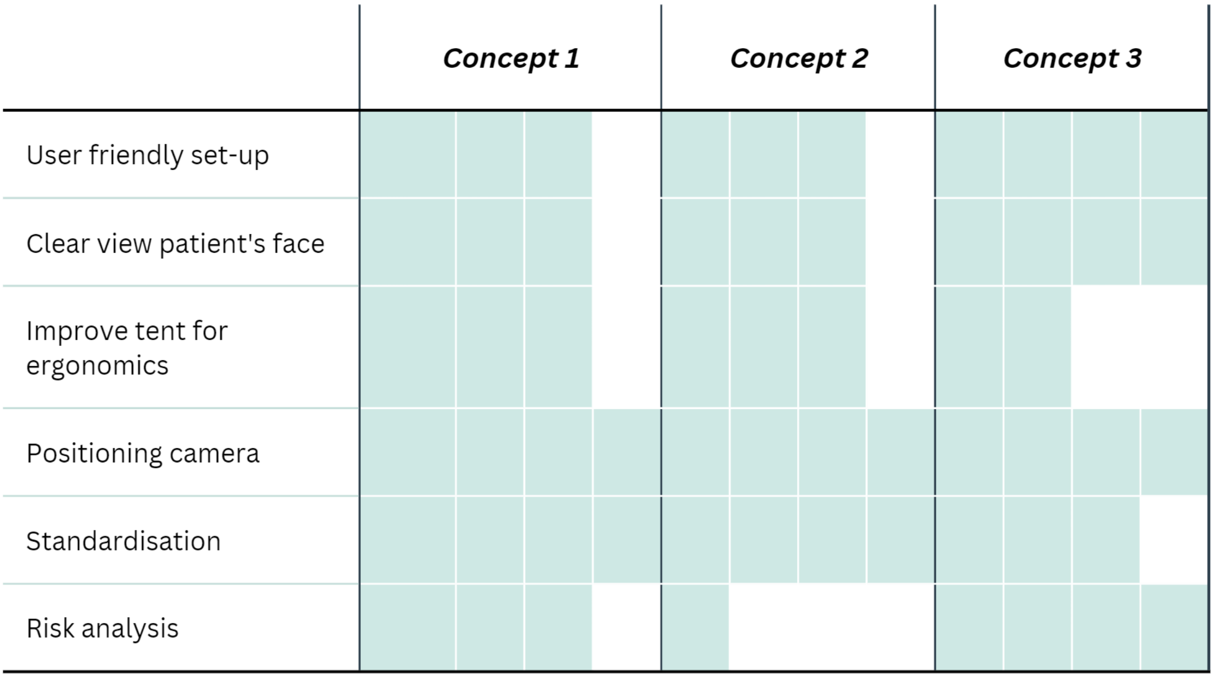

Figure 3.5.2: Harris Profiles of the three concepts

3.5.2 Prototyping for an empty operating room and pre-surgery

With the results from the Harris profiles, the two most suitable concepts were further evaluated. Concept 2 was excluded due to the increased risk of collapsing and injuring the patient when all joints are released, requirement P.3. Concept 1 and 3 were further evaluated for feasibility and usability with prototyping.

Concept 1

To test the principle of concept 1, a prototype was developed that can be attached to the already existing L-shaped frame, see Figure 3.5.1. This prototype was first tested in an empty operating room to test the attachment and adaptivity of the goosenecks. As a second test, the prototype was tested in between surgeries with an asleep patient, to mimic the real circumstances and to get input from several stakeholders, see Figure 3.5.2. The following stakeholders were present: the neurosurgeon, the anesthesiologist, the OR assistant, the clinical linguist and technician of the experimental medical instrumentation (EMI) department.
During the session, several observations were made.

1. The attachment and positioning of the frame is user-friendly, it would ease the set-up of the tent compared to current practice. (U.1)
2. The frame would not limit movement on the sterile side of the surgery. (U.2)
3. The frame does not limit contact with the patient. (P.4)
4. The frame is not stable. This is not due to the L-shape, but the connection to the bed is not tight, resulting in movement of the whole frame. This would be a problem for camera placement. (T.2-3)

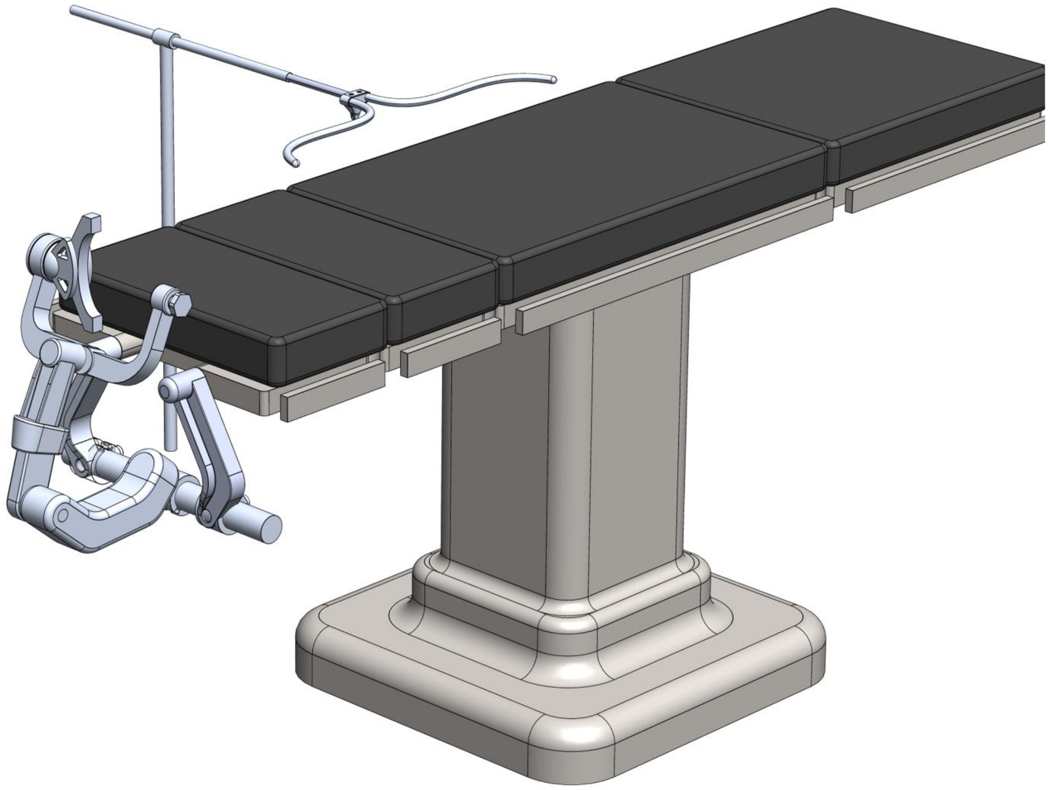

Figure 3.5.1: Visualization prototype concept 1. The standard L-shaped frame is used as a base. Two gooseneck arms are connected to this frame.

Figure 3.5.2: The developed prototype tested inside the operating room

Concept 3

To test concept 3, a prototype was developed that can be attached to the railing on the surgical bed, see Figure 3.5.3. This prototype was first tested in an empty operating room with two biomedical specialists to investigate the positioning of the frame and the possibility to attach a camera, see Figure 3.5.4. The placement of the frame, the drape support and several positions of the camera were tested.

During the session, several observations were made.

1. The attachment and positioning of the frame is user-friendly, it would ease the set-up of the tent compared to current practice. (U.1)
2. The frame does not limit movement on the sterile side of the surgery. (U.2)
3. The frame improves contact with the patient. (P.4)
4. A camera can be placed on both the patient's face and hand (P.5)
5. The two gooseneck arms were screwed into the metal base. Due to the force exerted on the gooseneck arms for positioning, they unscrewed from the base. This makes the prototype instable (T.2-3). To fix this problem, in the next step the arms should be glued into position.

Figure 3.5.3: Prototype of concept 3. Left: concept model, Middle: developed prototype, Right: usage in context.

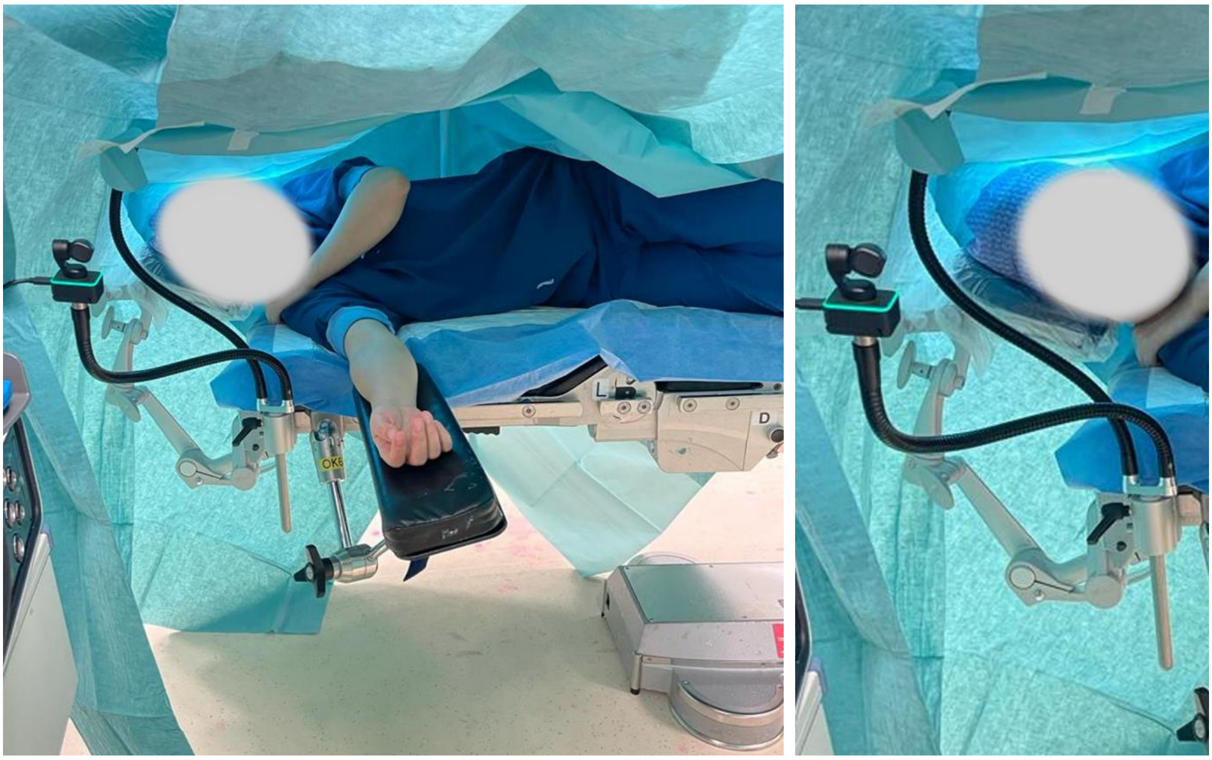

Figure 3.5.4: First test with the prototype of concept 3. Inside an empty operating room, a healthy volunteer is mimicking the position of a patient during an awake craniotomy. The prototype is placed and the arms are positioned for keeping up the drapes and directing the camera at the contralateral hand of the patient.

3.6 Evaluate

3.6.1 Evaluation of Concept 1 and 3

After the first tests with Concept 1 and 3, the most promising prototype for drape support and camera placement was chosen for elaborate testing during two awake craniotomies. This was done with validating the two concepts with the predefined list of requirements, see Table 3.6.1.

Concept 1 fully meets 11 requirements, and does not meet 2 requirements. These 2 requirements include T.1: “The product must resist forces expressed by specialist during the surgery, by experts leaning on the product“ and T.3: “The product should increase stability and limit movement of the frame, to keep additional equipment stable”. This is mainly caused by the instability of the connection to the surgical bed, in which the frame is secured. Due to the long arm of the frame over the patient, a little movement is almost unavoidable, when the equipment also has to be light and easily usable. Also, since the instruments are given to the surgeon over this frame, it will easily move a little. This will be a problem for good measurements with video recording.
Concept 3 fully meets 11 requirements, and partially meets 2 requirements. The two requirements only partially met include product requirement P.1: “The product must support the sterile drapes” and user requirement U.4: “The product should be compatible with a standard frame used inside the surgical centre”. The concept supports the sterile drapes next to the patients face, but does not support the drapes along the full length of the patient’s body. This means that the tent around the face is better defined, but that the rest still needs to be hung up with tape and clamps, as also shown in Figure 2.5.5D. To fully meet this requirement, the concept should be expanded to also cover the other parts of the tent. U.4 is only partly met, because concept 3 is a separate frame from the standard L-shaped frame currently used in all operating rooms. This concept does not replace the L-shaped frame or is in the way of other equipment, so is compatible in the sense that it does not need any adjustments. It does however require an extra frame, which is less feasible.

Table 3.6.1: Validation of Concept 1 & 3 according to the predefined requirements. Legend: V = met, ~ = partially met, X = not met.

	Main Product requirements	Concept 1	Concept 3
P.1	The product must support the sterile drapes	V	~
P.2	The product must be adjustable for positioning of the patient based on tumou location and patient size	V	V
P.3	The product must not create an increased risk of collapsing on the patient	V	V
P.4	The product should ensure a clear view of the patient's face during the entire surgery	V	V
P.5	The product should allow for attachment of additional equipment	V	V
	Main User requirements		
U.1	The product should ease the workflow of the OR assistants an anaesthesiologist compared to the current frame	V	V
U.2	The product should not limit movement on sterile side	V	V
U.3	The product should create more space inside the non-sterile side of the tent to improve ergonomics of the clinical linguist	V	V
U.4	The product should be compatible with a standard frame used inside the surgical centre	V	~
	Main Context requirements		
C.1	The product must adhere to cleaning regulations for intraoperative frame usage	V	V
	Main Technologic requirements		
T.1	The product should be compatible with the surgical beds used in Erasmus MC	V	V
T.2	The product must resist forces expressed by specialist during the surgery, by experts leaning on the product.	X	V
T.3	The product should increase stability and limit movement of the frame, to keep additional equipment stable.	X	V

3.6.2 Utilization and testing during awake craniotomies

After the first tests, concept 3 was further evaluated for drape support and camera placement during two awake craniotomies. As a second test, the improved prototype was used during two awake craniotomies. This frame was used instead of the current used frame for positioning the microphone and camera (Figure 3.2.3). During the surgery, on one of the arms a camera was placed to record hand movement. On the other arm, the standard microphone and camera were placed, see Figure 3.6.1. The goosenecks were covered with sterile ultrasound probe sleeves, to ensure accordance with cleaning regulations. The frame was evaluated with different experts at various timepoints during the procedure: 1) after placement of the frame, before the drapes were drawn up, 2) directly after the drapes were set up and 3) at the end of the surgery. Their feedback was collected and showed valuable inside about the set-up, the resulting tent, camera placement and future usage, see figure 3.6.2.

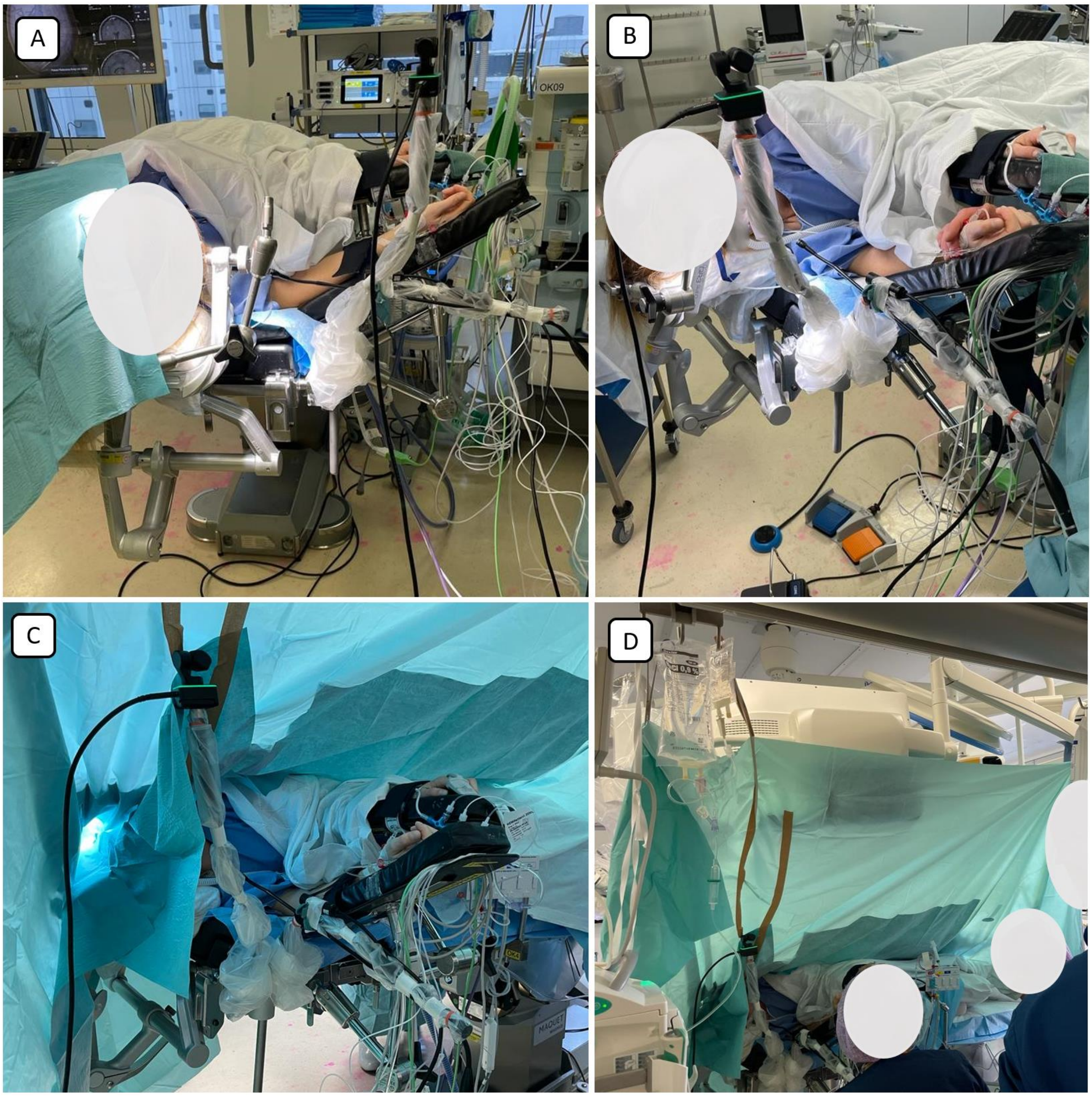

Figure 3.6.1: Intraoperative set-up of the prototype during awake craniotomies. A) set-up from the surgeon's point of view, B) frame set-up from non-sterile side of the tent, C) set-up after drapes are placed, D) full view of the non-sterile side of the tent.

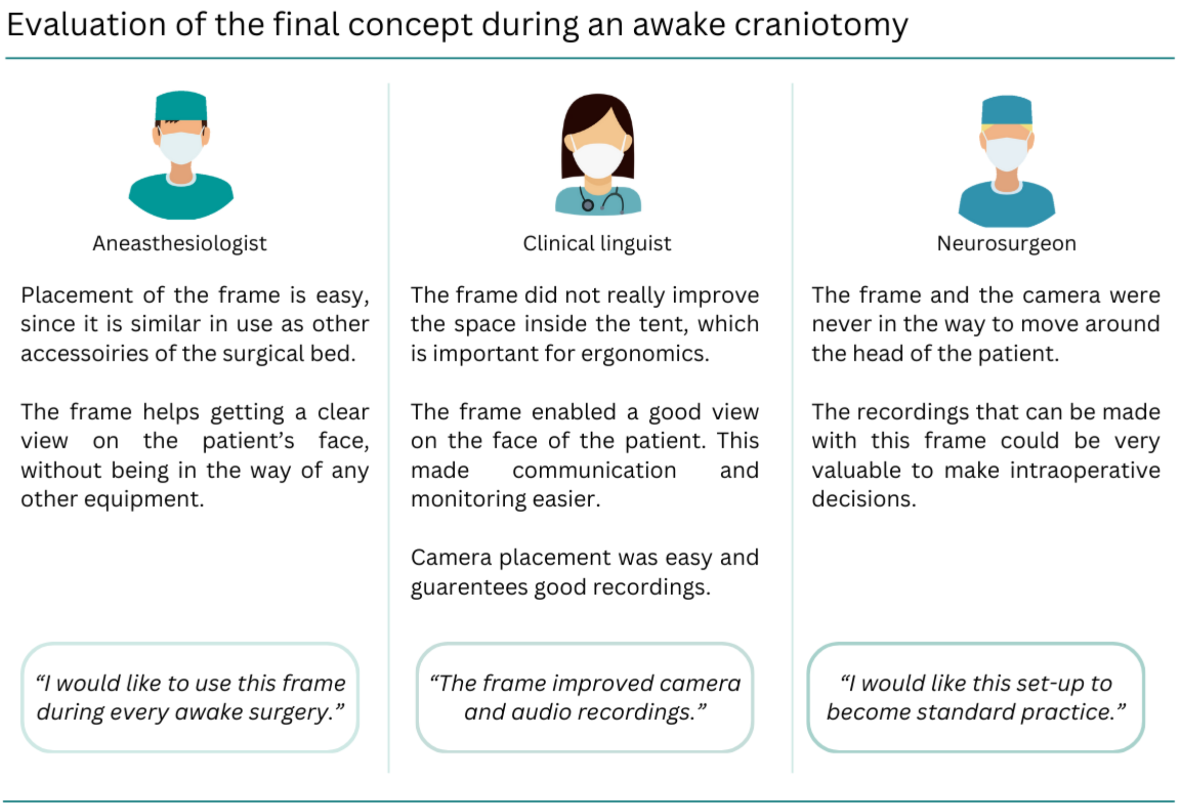

Figure 3.6.2: Feedback of the anaesthesiologist, clinical linguist and neurosurgeon on the final prototype used during awake craniotomy.

3.7 Discussion

In this chapter, we have designed a frame that supports the sterile drapes to create a standardized environment around a patient undergoing an awake craniotomy that enables implementation of video recordings to monitor motor and language function. This goal was established after thorough analysis of current practice and interviews with important stakeholders. With their input we set up a list of requirements and designed three potential solutions. After testing the two most promising concepts, a final prototype was developed and used during three awake craniotomies. Several stakeholders evaluated the prototype at different timepoints. Their main concern was the ability of the frame to improve the space inside the tent for ergonomics of the clinical linguist. On all other points, they expressed considerable satisfaction with the final prototype and would like to structurally implement the new frame.

3.7.1 Strengths & limitations

A big strength of our design approach, is that we involved many different stakeholders. We have already involved them during the prototyping process and during different tests. This enabled us to quickly iterate and design something that the stakeholders really want to use. Also, we immediately started with mapping the regulatory rules inside the Erasmus MC, making sure that our design would adhere to technical and cleaning regulations. This is essential for clinical implementation, especially in a challenging environment like the OR.

A limitation of this approach, is the large list of requirements and multiple goals we wanted to design a solution for. The frame had several needs for clinical use, since it needed to improve the existing set-up, but also had strict requirements for camera placement to ensure reproducible future research. With this wide range of goals and wishes, we mainly focussed on the feasibility and camera placement. Therefore the wish to improve set-up of the whole tent and to create a bigger space for ergonomical reasons, was not met. Despite this shortcoming, we still believe that the board approach with involvement of all the stakeholders has more benefits in the long run, since the designed frame can really be implemented with large stakeholder support.

3.7.2 Recommendations

During the prototyping and testing phase, a lot of feedback and new insights were collected. This has led to several recommendations for further development and implementation of the prototype. These recommendations are supported by the list of requirements and the collected feedback of the several specialists during the whole design process.
The first recommendations focus on further development of the frame. As described in 3.6.2, evaluation of the prototype of concept 3 showed several strong points and several things that have room for improvement. To improve the prototype, the gooseneck arms should be longer than the ones currently used. This makes positioning of the cameras better. Also, the goosenecks should be covered in shrinking tubes, instead of the ultrasound sleeves. These sleeves are both very expensive due to sterility, but are also only suitable for one time use. For sustainability reasons, a more permanent solution has to be found.
The main recommendation for further development of the frame, concerns the requirement that that was only partly met, namely P.1 “keep up the sterile drapes”. Concept 3 does not perform well for this requirement, since it only keeps the drapes up near the face instead of along the whole body of the patient. An additional frame that crosses over the patient should be designed for this specific requirement. Careful consideration is needed to make this second frame easily usable, and that this frame also offers possibilities to attach additional equipment, including a camera.

The second recommendations focus on the design process and implementation of the frame. Firstly, for smooth implementation during the surgery, it is very important to keep all different experts involved that play a role during the surgery. This includes not only the neurosurgeon and anaesthesiologist, but all supporting personnel. They are all crucial for a smooth surgery, and need to be informed about all the different instruments used. Good communication with all stakeholders helps as a good base for implementation, but also for a smoother procedure on the long term. Preferably, involving all these people already starts during the design phase. This remains however a big challenge, due to the limited availability of all the experts outside the surgical setting. This means that most of the tests and discussions have to take place during a surgery, or in between surgeries. To discuss or show a prototype inside this setting, it is essential to involve the technical experts of the OR complex.

With this base of stakeholders support, quick iterations of new prototypes can lead to a feasible design that will structurally be implemented during surgery.

3.7.3 Conclusion

In this chapter, we showed the design process of a frame to keep up sterile drapes and to position video and audio recordings during an awake craniotomy. The developed prototype has shown to be feasible, desirable and usable, as shown by continued use inside the operating room. This was achieved by involving important stakeholders during the design, development and/or testing phase. Further development is needed to develop a sustainable solution that covers all requirements. This solution will play an important role to decrease variability in the surgical set-up, leading to a standardized environment for data collection during awake craniotomies. This will aid neurosurgical research and intraoperative feedback.

4

Exploration of video tracking to monitor hand motor function

Preservation of motor function during brain tumour resections is essential for a patient's quality of life. Monitoring motor function remains a challenge, since it is very complex and consists of many aspects, including motor planning, initiation, coordination and fine movements. These higher motor skills can only be tested when the patient is awake and performing tasks, meaning an awake craniotomy is necessary. There are however no standardized protocols or guidelines describing which intraoperative changes are related to long term motor deficits. To structurally investigate these problems, an objective measurement method is needed.

4.1 Objective

In this chapter, we aim to explore the feasibility and clinical relevance of video tracking to assess hand function of patients undergoing awake craniotomy. This exploration consists of two subgoals: 1) feasibility of implementing video recordings in the clinical course of the patient while ensuring accurate video tracking of these recordings during preoperative, intraoperative and postoperative assessment and 2) an exploration of detecting and quantifying relevant clinical events.

4.2 Methods

A general overview of the proposed methods is shown in Figure 4.2.1. Every part will be discussed separately below.

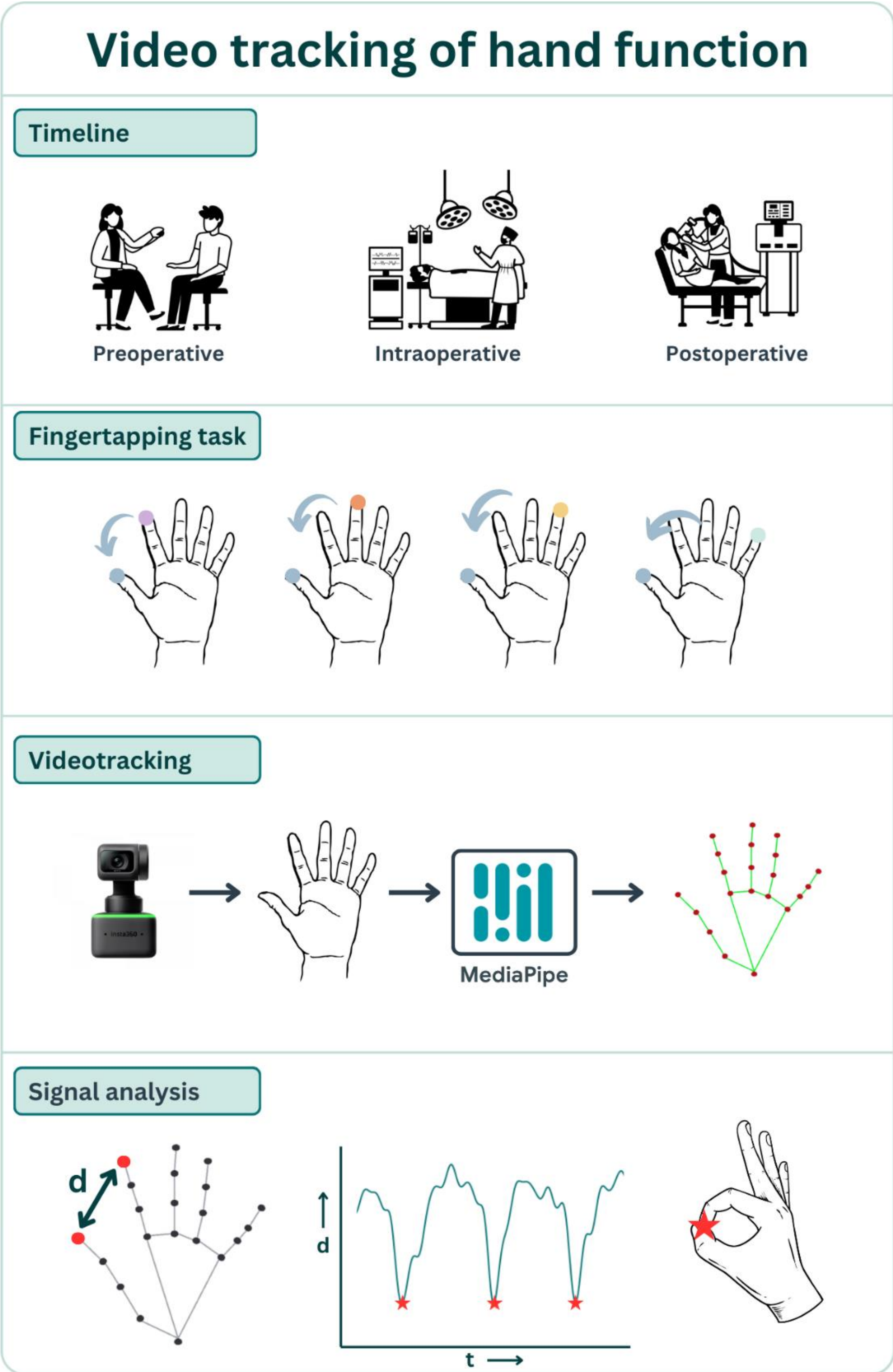

Figure 4.2.4: Overview of the proposed methods for video acquisition and analysis of the fingertapping method. This task will be performed before, during and after the awake craniotomy. Detection of a fingertapping cycle is based on peak detection of the distance between the fingertip in question and the thumb.

4.2.1 Patient selection and experimental design

For this study, we prospectively included patients undergoing awake craniotomies. These patients were monitored at three timepoints: preoperative baseline assessment (T0), intraoperative monitoring (T1) and direct postoperative follow-up (T2). During these three assessments, the patients were asked to perform motor tasks similar to the standard protocol used in the Erasmus University MC. This included finger tapping to test fine finger movement. In this task, the patient performs a recurring pattern of every fingertip touching the tip of the thumb consecutively. The pattern starts with the index finger, follows through the middle finger and ring finger to the pink. Then the patient moves from the pink back to the index finger. This whole pattern will be referred to as one fingertapping cycle, see Figure 4.2.1.
On T0 and T2 each task was performed five times with each hand separately. On T1, the task was performed five times with the extremity contralateral to the tumour location.

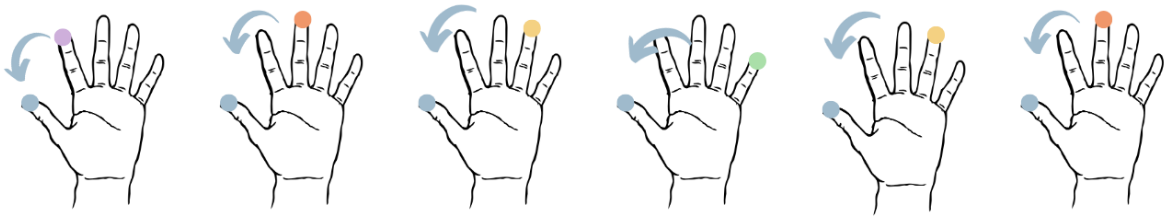

Figure 4.2.1: Fingertapping task, showing one full fingertapping cycle.

4.2.2 Video Data Collection

The participants were recorded with an external webcam (Insta360 Link, 1080x1920 pixels at 30fps, see Figure 4.2.2). This camera has a 3-axis gimbal design, enabling adjustment of the camera to optimally visualise the hand in the field of view. During T0 and T2, the camera was installed on a laptop. On T1, the camera was installed on an intraoperative frame set-up, see Figure 4.2.3. This intraoperative set-up was first tested with healthy participants to investigate the best angle achievable under the practical intraoperative constraints.

Figure 4.2.2: Used camera for video recordings

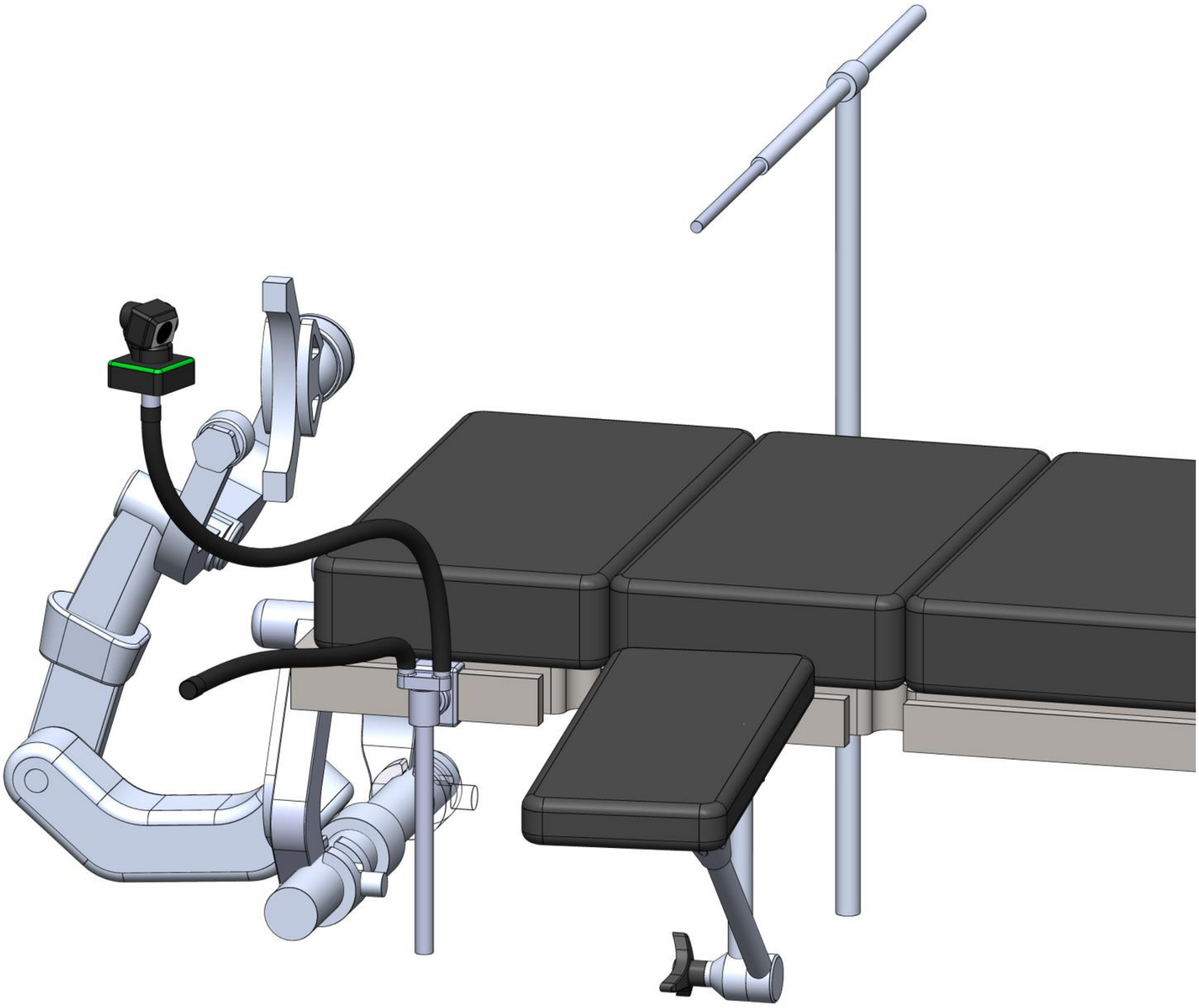

Figure 4.2.3: Intraoperative video recording set-up using the previously developed frame.

4.2.4 Video analysis

Hand landmark tracking

The video frames were processed with MediaPipe Hand Landmark Detection[30] to detect 21 landmarks of the hand skeleton (Supplementary Materials C). All video recordings were horizontally flipped for correct hand labelling and cropped to show only the patient's hand. The accuracy of the algorithm was visually assessed. For every landmark, the algorithm returns the x, y and z coordinates normalized in pixels between 0 and 1. We set the minimum confidence score for hand presence at the default of 0.5.

Hand landmark displacement

To analyse the movement of the hand, the x, y and z coordinates of all the detected hand landmarks were plotted. The displacement of each hand landmark was calculated in normalized pixels in time using the coordinates of two consecutive timepoints, see Formula 1. The magnitude of this displacement in 3D was calculated using the Euclidean distance, see Formula 2.

$$\overrightarrow{\Delta r} = \overrightarrow{r_{i+1}} - \vec{r_i} \qquad (1)$$

$\overrightarrow{\Delta r}$ is the displacement vector, $\overrightarrow{r_{i+1}}$ is the final position vector (x_{i+1}, y_{i+1}, z_{i+1}), and $\vec{r_i}$ is the final position vector (x_i, y_i, z_i)

$$|\Delta\vec{r}| = \sqrt{(x_{i+1} - x_i)^2 + (y_{i+1} - y_i)^2 + (z_{i+1} - z_i)^2} \qquad (2)$$

$\overrightarrow{|\Delta r|}$ is the displacement vector, $\overrightarrow{r_{i+1}}$ is the final position vector (x_{i+1}, y_{i+1}, z_{i+1}), and $\vec{r_i}$ is the final position vector (x_i, y_i, z_i)

Fingertapping

To analyse the fingertapping task, the Euclidean distance between the tip of the thumb and the tip of the index finger, of the middle finger, of the ring finger and of the little finger was calculated (Formula 2). The signals were pre-processed with a low-pass Butterworth filter, to correct for high frequency noise. The cut-off value for this filter was empirically determined.
A decrease of the calculated Euclidean distance relates to a movement of the finger in question towards the thumb. The minimal distance is the moment the fingers touch. These minima were extracted using a peak finding algorithm from the Scipy library, specifically designed to find local maxima by simple comparison of neighbouring values.[31] The time between two peaks of the index finger is the duration of one fingertapping cycle. The mean fingertapping cycle duration of duration was computed to compare the performance of preoperative, intraoperative and postoperative measurements.

Positive stimulation sites

A positive stimulation site elicited by DES of the brain results in a sudden muscle contraction of the arm or hand. This causes the whole hand to jerk. To detect these contractions, the mean displacement of all had landmarks was calculated.

For a full overview of the presented methods, see Figure 4.2.4.

4.3 Results

Three patients were included. All three patients presented with a primary brain tumour and were scheduled for an awake craniotomy. Of each patient, hand function was recorded before (T0), during (T1) and after (T2) the awake craniotomy. An overview of the three cases, their individual research goals and outcomes can be found in Figure 4.3.1 Each case and its analysis will be described separately below.

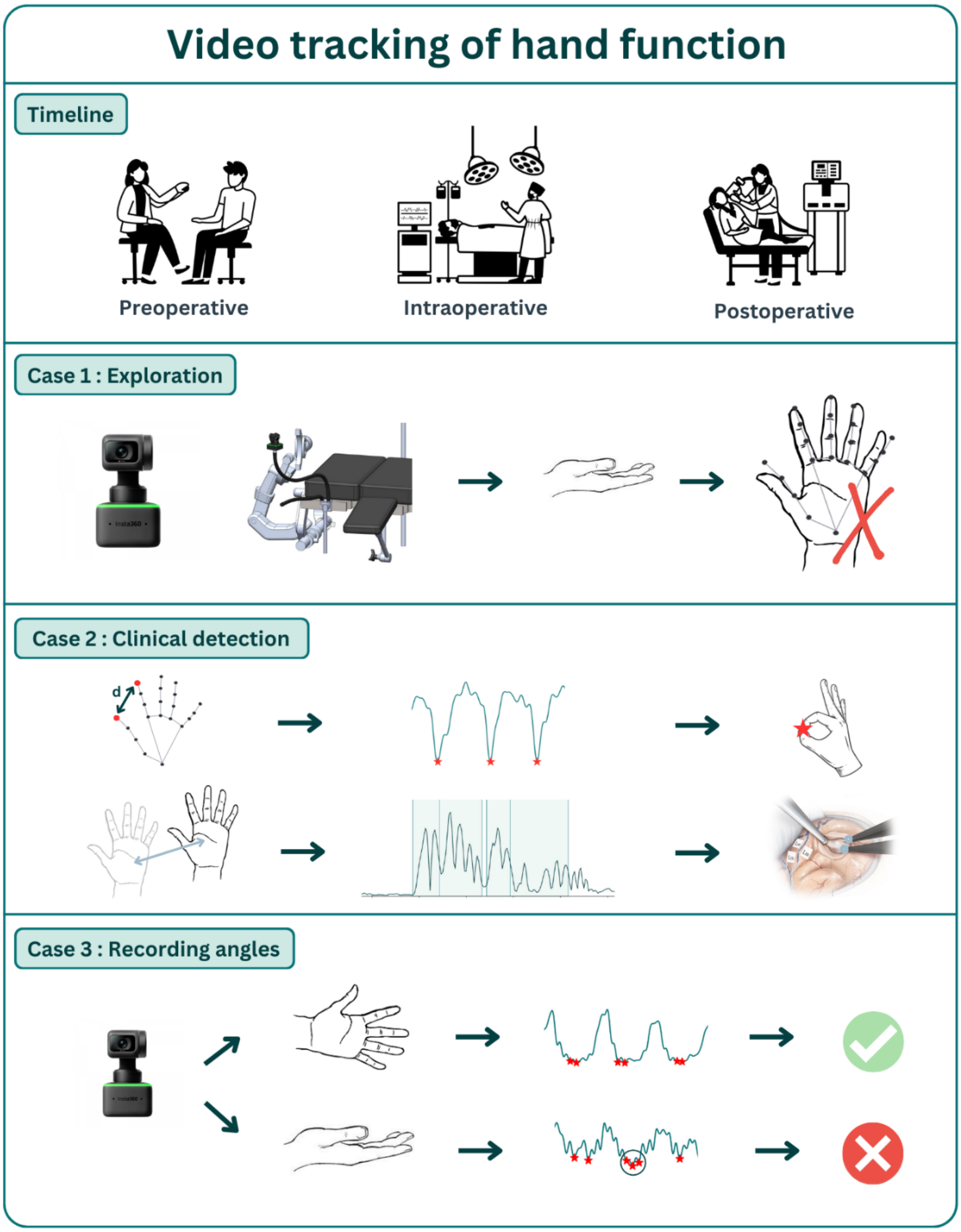

Figure 4.3.1: Overview of the three included cases. In the first case, we explore the video recording set-up and discuss poor video tracking performance due to the angle. In the second case, we show the potential of video tracking to detect clinical relevant events, including the fingertapping task and subcortical stimulation. In the third case, we compare a radial view and a palmar view of the hand in and show that a palmar view shows better results for all fingers in video analysis.

4.3.1 Case 1: exploration

During the first case, we focused on exploring intraoperative camera placement and the accuracy of MediaPipe's hand tracking algorithm.

Clinical Presentation

Our first case was a 43-year-old right-handed patient, diagnosed with a primary brain tumour after an epileptic insult with loss of consciousness. In the first weeks following the insult, the patient reported a headache and experienced difficulties in holding a pen and writing. After a few weeks, the patient showed and reported no symptoms. The MRI scan showed a right frontal lesion, suspected to be a low-grade oligodendroglioma.

Clinical observations motor function

Fingertapping was tested one day prior to surgery (T0), during surgery (T1) and one day after surgery (T2).
Preoperative fingertapping testing showed no deficits.
During the awake craniotomy, the clinical linguist observed no positive stimulation sites. Finger tapping performance was slightly decreased at baseline of the surgery compared to preoperative measurements. The performance during surgery remained stable until the end of tumour resection. Right before closure, the finger tapping performance decreased significantly. This was visually described as a decrease in speed of the task and an increase in hesitations and mistakes when moving from the ring finger to the little finger. Every fingertapping cycle, the ring finger was tapped twice before switching to the little finger.
One day postoperatively, the performance of the fingertapping test recovered to preoperative baseline, without hesitations or double tapping.

Camera set-up and Video tracking

The preoperative and postoperative fingertapping measurements were recorded on a hospital bed at the neurosurgical department. Intraoperative measures were performed with the hand on the armrest and recorded with the camera set-up as shown in Figure 4.3.2.
The positioning of the camera at all timepoints was challenging, leading to video recordings of the radial side of the hand. Not every finger was constantly visible, which was also reflected in poor video tracking results of these fingers, see Figure 4.3.2. The incorrect tracking made further analysis of the fingertapping test unreliable. The clinically detected intraoperative changes were mainly based on hesitations and mistakes of the ring finger and little finger, which showed the poorest tracking results. Therefore, these results were excluded for further analysis.

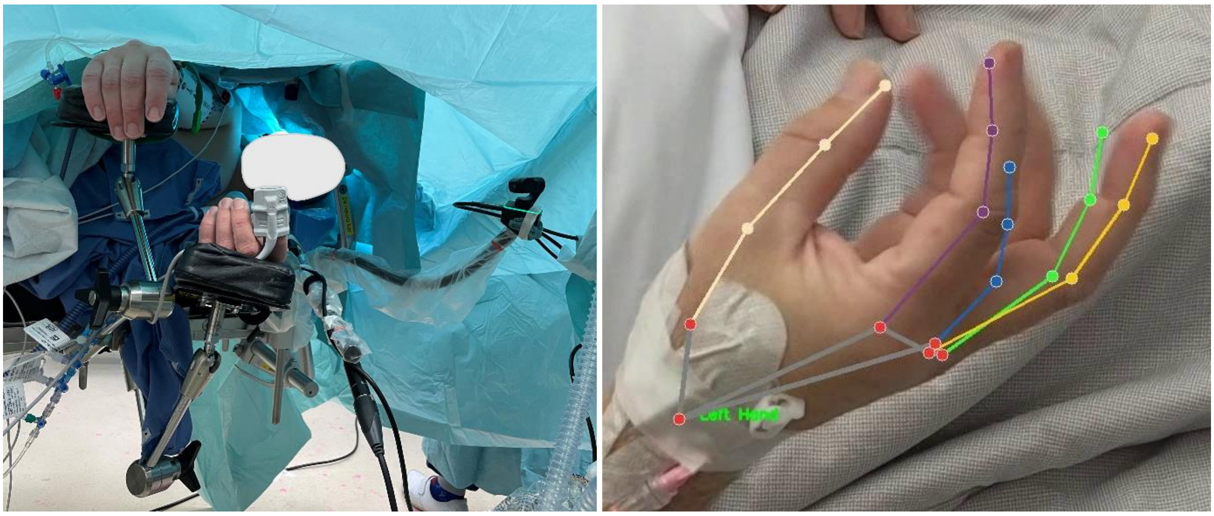

Figure 4.3.2: Camera set-up (left) and postoperative video tracking results (right), showing inaccurate tracking of the pink (blue) and ring finger (green).

Conclusion / Discussion

During this first case, we aimed to explore camera placement and its relation to video tracking results. We discovered that recording form the radial side of the hand was not suitable for video tracking, making further analysis unreliable. A view on the palmar side seems to perform best. These results were taken into account for camera placement in the following patients.

4.3.2 Case 2: Detection clinical observations

In the second case, we investigate the relation between clinical observed changes in hand function and objectively measured patterns in the detected hand landmarks.

Clinical Presentation

The second case involved a 30-year-old patient diagnosed with a primary brain tumour following multiple episodes of language and speech difficulties. The MRI showed a left frontal lesion, suspected of a low-grade astrocytoma. After treatment with levetiracetam, the patient experienced no insults and symptoms.

Clinical observations motor function

Fingertapping was tested 3 days prior to surgery (T0), during surgery (T1) and one day after surgery (T2).
Preoperative fingertapping testing showed no deficits.
Intraoperative baseline performance of the fingertapping task was similar to preoperative findings and remained stable during surgery. During subcortical stimulation, one positive response was detected. While the surgeon was stimulating a specific region, the hand and lower arm showed clear uncontrolled contractions. The location of this positive stimulus is shown in Figure 4.3.3.
Postoperative fingertapping testing showed similar results as preoperative and intraoperative testing.

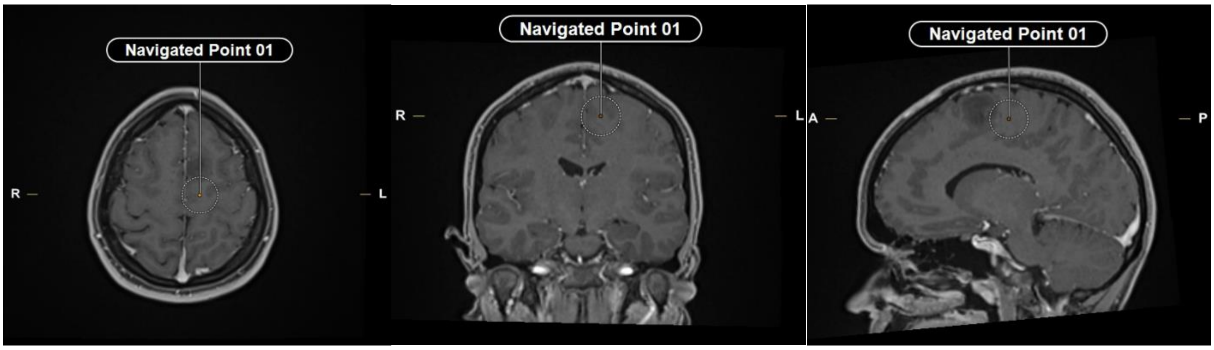

Figure 4.3.3: Positive stimulation site during subcortical stimulation.

Camera set-up and video tracking

Preoperative recordings were performed at the neurosurgical department while the patent was laying in the hospital bed. Postoperative fingertapping was recorded while the patient was sitting at the table in the same room.
During the set-up, the angle of the camera was changed to record the palmar side of the hand. Video tracking using MediaPipe showed good results with the improved set-up, see Figure 4.3.4.

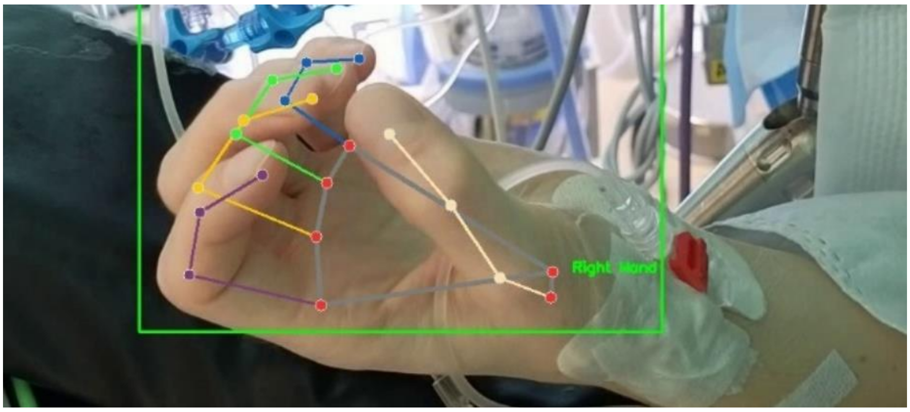

Figure 4.3.4: Results of MediaPipe's Hand Landmarker algorithm. This shows improved tracking results of the ring finger (green) and pink (blue).

Video analysis

Positive stimulus

The involuntary muscle contraction resulting from the subcortical stimulation showed a jerking movement of the whole hand. This was reflected in the coordinates of all the detected landmarks. Mean displacement of all landmarks showed an increase in averaged displacement during involuntary muscle contraction, see Figure 4.3.5. Four separate jerks were visually identified. During the fourth jerk, the clinical linguist was comforting the patient by holding their hand, limiting hand movement. This was reflected in a lower averaged displacement.

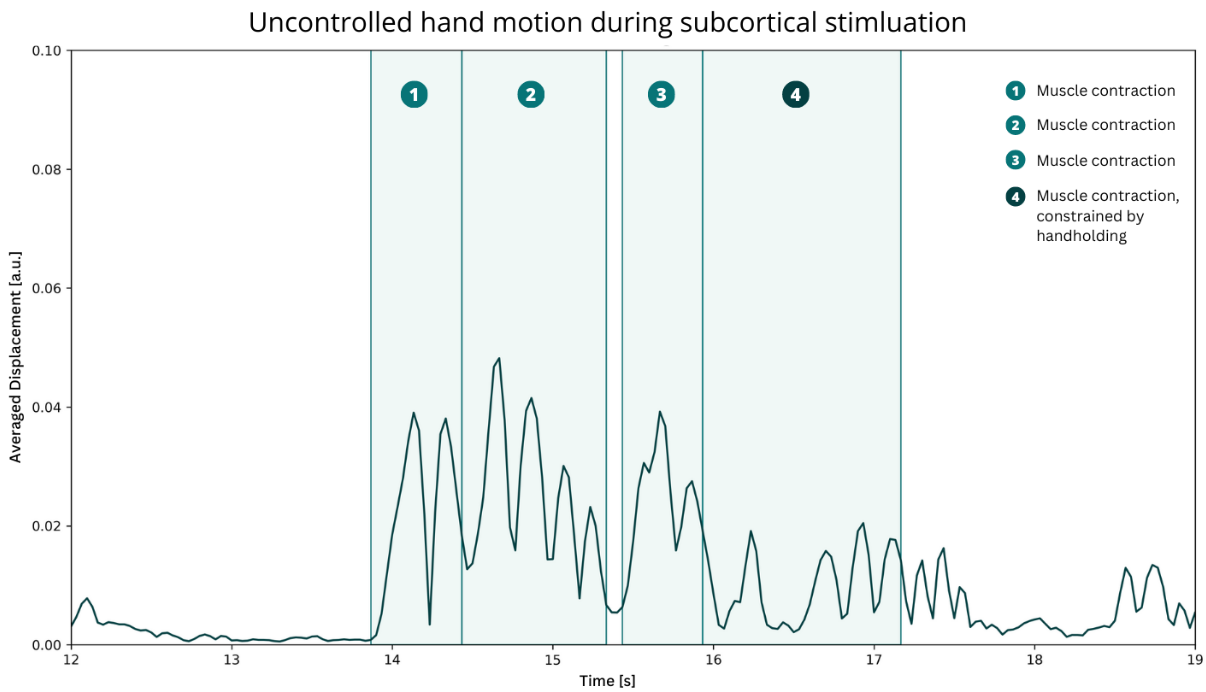

Figure 4.3.5: Averaged displacement of the whole hand during uncontrolled muscle contraction resulting from subcortical stimulation. Four individual jerks were visually identified, which are can be seen as spikes in the averaged displacement. During the fourth jerk, the patient's hand was constrained while the clinical linguist was comforting the patient by holding their hand.

Fingertapping

For fingertapping analysis, the Euclidean distance between the index fingertip and tip of the thumb was calculated. This showed a recurrent pattern for every fingertapping cycle, see Figure 4.3.6.

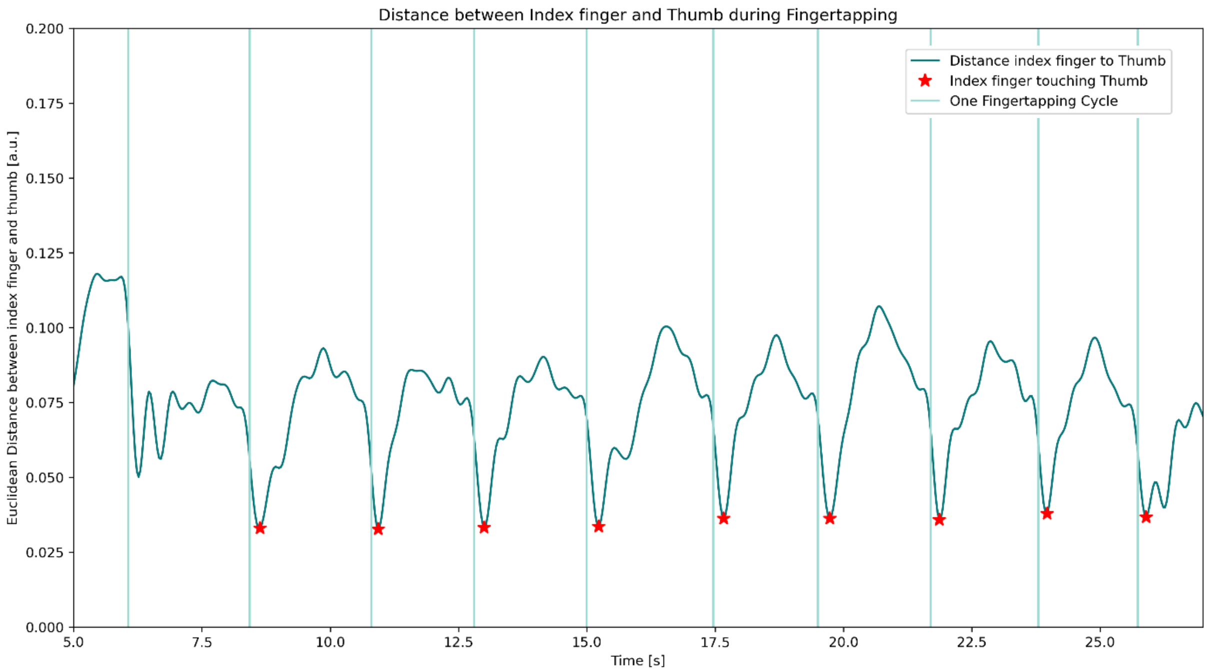

Figure 4.3.6: Intraoperative fingertapping analysis Patient 2. This figure shows the Euclidean distance between the index finger and thumb during the fingertapping task performed during surgery. The vertical lines show the fingertapping cycles. The red stars indicate the moment the index finger touches the thumb, and thus has the lowest distance.

To compare the fingertapping task before, during and after surgery, the mean fingertapping cycle duration was calculated. The start of the cycle was defined as the moment the index fingertip touched the thumb. This showed slight differences between preoperative, intraoperative and postoperative recordings, see Figure 4.3.7.

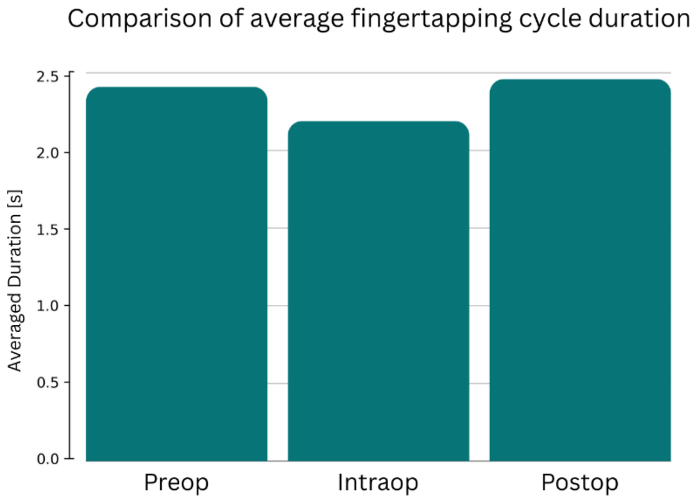

Figure 4.3.7: Comparison of average fingertapping cycle duration before (preoperative), during (intraoperative) and after (postoperative) awake craniotomy.

Conclusion / Discussion

In this case, we explored the potential of video tracking to detect and analyse clinical findings before, during and after surgery. Video tracking and analysis detected the positive stimulus response of involuntary muscle contractions as sudden jerks of the whole hand. Analysis of the fingertapping task showed clear recurring cycles of every finger during an adequate response, with a mean duration in a range of 2.0 to 2.5 seconds. This shows potential to detect a decline in fingertapping performance between different timepoints in future patients.

4.3.3 Case 3: Comparison of different recording angles

During the third case, the influence of different video recording angles was investigated. Also, a follow-up on detection of fingertapping patterns was performed.

Clinical course

The third case involved a 52-year-old patient diagnosed with a primary brain tumour as an incidental finding in 2010. Recently, the patient presented with word-finding problems during fatigue and transient morning sickness, sometimes accompanied with headaches. The MRI showed a slight growth of the orbitofrontal lesion, suspected for a low-grade glioma.

Clinical observations motor function

Preoperative fingertapping assessment was performed 8 days prior to surgery (T0). Postoperative testing was performed on the same day as the surgery (T2).
In this case, the fingertapping task was performed slightly different then described before. Every cycle the index finger was tapped at the start of the cycle and at the end of the cycle, and the pink was tapped twice, see Figure 4.3.8. This resulted in a slightly different pattern than the in the previous patient.
Preoperative fingertapping testing showed adequate motor function of both the right and left hand.
Intraoperative baseline showed no decrease and fingertapping performance stayed stable during the full length of the surgery.
Postoperative testing showed adequate fingertapping performance, similar to preoperative and intraoperative functioning.

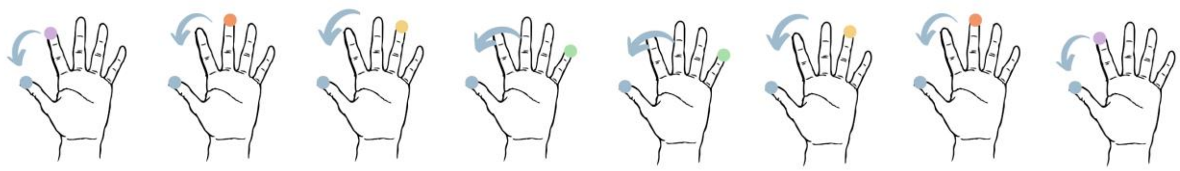

Figure 4.3.8: Alternative fingertapping task that was performed by patient 3.

Camera set-up and video tracking

Preoperative testing was performed in the outpatient clinic with the patient sitting up straight. Postoperative testing was performed at the Post Anaesthesia Care Unit (PACU), while the patient was lying down.
The intraoperative video set-up showed a view on the palmar side of the hand during motor function tasks and stimulation. Postoperative recordings had a radial view of the hand. To improve the postoperative angle and compare the recordings, the patient was asked to repeat the fingertapping task while rotating the hand for a palmar view of the hand.
Mediapipe's tracking showed similar results in both angles for the thumb and middle finger. The index finger, ring finger and pink however showed a big difference between the detected landmarks and the actual finger when recording from the radial side, see Figure 4.3.9. Index finger tracking decreased in accuracy, while ring finger and pink increased.

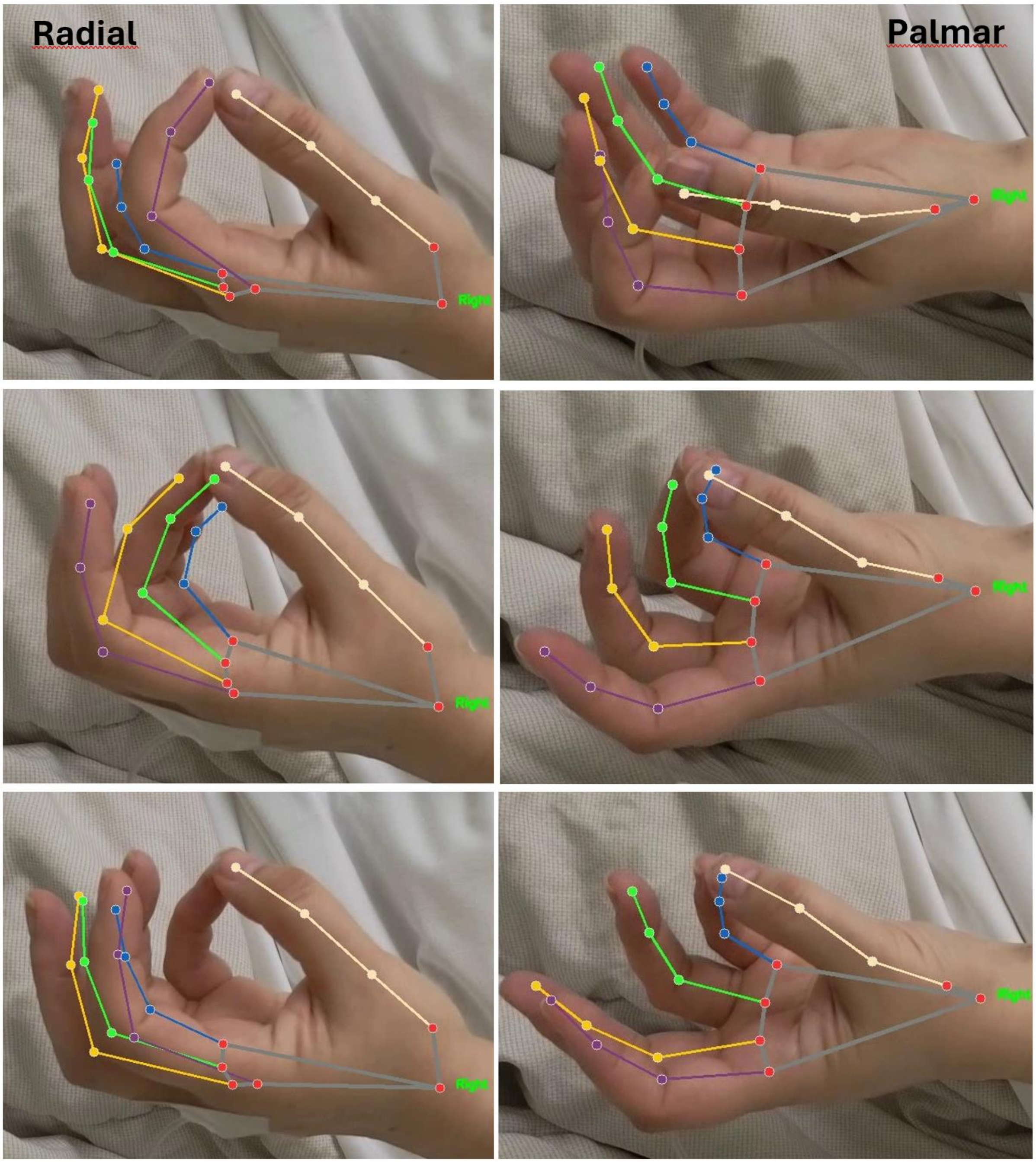

Figure 4.3.9: MediaPipe Video Tracking results from a radial view (left) and palmar view (right) for fingertapping of the index finger, ring finger and pink. A radial view showed better tracking of the index finger (purple), while a palmar side shows better tracking results for the ring finger (green) and pink (blue).

Video analysis

The altered fingertapping task performed by this patient, resulted in a slightly different pattern than the in the previous patient. Fingertapping analysis was performed postoperatively for a recording angle with a radial view and for a recording angle with a palmar view. The palmar view shows a clearer pattern with a higher amplitude during the task, see Figure 4.3.10. This is evident for all fingers, not just the pink and index finger. For the pink, the peak detection makes more mistakes from a radial view.

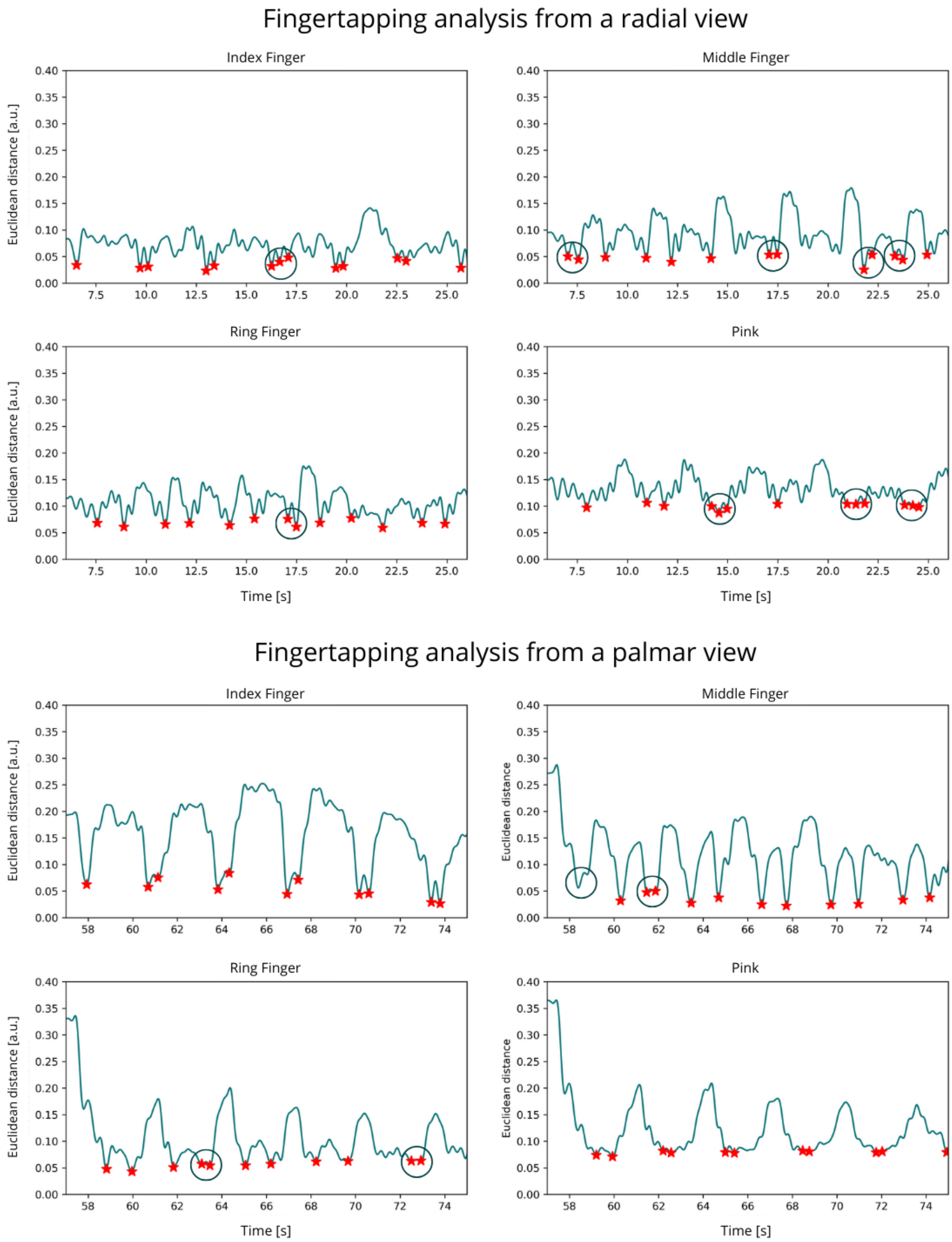

Figure 4.3.10: Fingertapping analysis of both the radial and palmar view. The palmar view shows a clear pattern, while the radial view shows a noisier signal with a lower amplitude. Mistakes are highlighted with circles, showing a bigger number of mistakes for the pink from the radial view.

Conclusion/Discussion

In this case, we aimed to explore the influence of different recording angles on the accuracy of MediaPipe's tracking and the impact on the fingertapping analysis. A radial view of the hand showed good results for tracking the index finger and middle finger but showed poor performance in tracking the ring finger and pink. This was also reflected in the fingertapping analysis, which showed good results for all fingers except the pink when recorded from the radial angle. This shows that analysis of the fingertapping cycle based on the index finger can be performed from both angles, but that a palmar view of the hand is needed for analysis of all individual fingers.

4.4 Discussion

With this pilot study we have made a first step towards quantifying hand function of patients undergoing awake craniotomies with the help of video tracking. We have shown that it is possible to implement video recordings during preoperative, intraoperative and postoperative motor assessments and that with the right angle, video tracking shows potential to track hand movement during cortical stimulation and a fingertapping motor task.

4.4.1 Clinical implementation

Our first aim was to investigate the feasibility of clinical implementation of video recordings in current practice for accurate video tracking of preoperative, intraoperative and postoperative motor function assessments. During the pilot, we implemented video tracking with minimal interference of current practice. Preoperative and postoperative motor tasks were recorded during already existing appointments of the patient with the clinical linguist. The only additional equipment needed was a video camera and a laptop.

Video tracking of the recordings was possible, but the accuracy showed to be highly dependent on the angle of the recording of the hand. This shows the importance of a standardized motor testing protocol with standardized camera placement in a stable environment.

Our approach to record during already existing appointments with very little interference of current practice, is in contradiction with this need. It showed high variability in recording environments. Preoperative and postoperative measurements were conducted in the outpatient clinic, at the neurosurgical department or at the PACU, while the patient was sitting down or lying down.

To improve the inter-recording variability, we made a first step to create a standardized environment inside the OR with the developed frame as described in Chapter 3. A similar approach is needed to create a standardized recording set-up during preoperative and postoperative measurements.

4.4.2 Clinical relevance

Our second goal was to explore whether video tracking could be used to quantify hand function and detect clinically relevant motor changes. We showed that a positive muscle response resulting from direct subcortical stimulation can be detected as a change of displacement of the whole hand over time. We also showed that the fingertapping task can be quantified with signal analysis. The Euclidean distance between the fingertips and the tip of the thumb show clear repetitive patterns that can be quantified to compare preoperative baseline with intraoperative performance and postoperative outcomes.

4.4.3 Strength & Limitations

One of the strengths of this pilot is the application of video tracking during current clinical practice, making the recordings representative for future cases. This shows the potential and advantages, but also the limitations of this method in real practice. We gained direct feedback from clinical experts about feasibility and possibilities for future use, enabling us to also research clinical relevance of quantification.

Another strength of video tracking is its versatility, meaning that it can also be used to monitor a variety of motor tasks and spontaneous movement. Since there is currently still no golden standard for motor function monitoring during awake craniotomies, it is important that a quantitative method can be used in a developing field for various motor tasks. This includes current practice like fingertapping and the hand manipulation test to monitor apraxia[32], but should also should be flexible to test other movements or tasks to research which intraoperative changes are related with long term deficits. Video tracking even has the potential to be expanded to face tracking or tracking of the whole human body.

A limitation of our approach is the variability between the three cases. For every presented case, we had a different objective and the camera position and recording angle was adjusted to the particular situation. This makes it difficult to compare the three cases. It is however also close to reality, since every patient shows different baseline functioning and awake craniotomies can be planned with high urgency. Flexibility in this process is therefore very important. Also, this approach made it possible to quickly iterate to improve the recording set-up and research the potential of video tracking as a monitoring tool for hand function. This matches the phase of investigating a new method.

4.4.4 Future recommendations & challenges

Future research should focus on investigating clinical relevance of video tracking, and on technical improvement of the video tracking algorithm and recording set-up.

To clinically implement video tracking as a standard quantitative measure for hand function and an intraoperative monitoring device, several steps need to be taken.
First of all, the predictive value of intraoperative changes for long term motor deficits has to be researched. Direct feedback to the surgeon of intraoperative motor changes can have an impact on their surgical strategy and the extent of tumour resection. Therefore, it is important to investigate which intraoperative changes have an impact on the long term quality of life of the patient. Only these motor changes should be reported to the surgeon.
For this purpose, the detection of clinically relevant events has to be expanded. During this explorative study, we only monitored the fingertapping task and a positive stimulation site leading to movement of the whole hand. Other motor tasks and other responses to direct (sub)cortical stimulation, like muscle contraction of only (one of) the fingers and inhibition of a movement, should be investigated next. This could include pronation and supination of the hand and the hand manipulation task to monitor apraxia for tumours located (close to) the SMA. Reference values have to be established to determine which changes are different from a healthy population. Also, within a patient the left and right hand can be compared to analyse changes in the affected side. These outcomes should be related to patient-reported motor function performance and activities of daily living (ADL) assessments.
To collect all this data, a motor function testing protocol for patients undergoing awake surgery has to be developed. This testing should be combined with other appointments of the patient, like

the currently combined appointment with the clinical linguist. This limits the number of visits to the hospital.

Furthermore, several technical improvements on the video set-up, tracking results and analysis are necessary.
Currently, MediaPipe's tracking algorithm showed difficulty when multiple hands were present, when part of the hand is occluded and sometimes showed a delay or inaccuracy during hand or finger movement. To improve the tracking results, the recording set-up, the specifications of the camera and preprocessing steps have to be optimized. The best recording angle should be guaranteed with a standardized preoperative, postoperative and intraoperative recording set-up. Also, other work with a higher framerate showed very good tracking results, showing that this should be optimized to detect quick changes.[33] Brightness and contrast enhancements to correct for bad lightning could also help improve performance. To improve depth accuracy, and decrease occlusion of the hand, multiple cameras could be implemented to get a 3D reconstruction of the hand. Also, additional information like the size of the hand could be used in the calculation of 3D positions, to increase accuracy.[34]
To clinically implement intraoperative monitoring, the LiveStream module of MediaPipe's tracking algorithm should be investigated, to enable direct intraoperative feedback to the surgeon.
Relevant features from the fingertapping analysis should be investigated to develop a robust detection algorithm. We explored calculating changes in magnitude of displacement to determine fingertapping cycle length. To investigate the variability of the signal pattern over time, other measurements like autocorrelation of the signal and frequency patterns should be analysed. Also, currently all distances were calculated in normalized values for pixel range. To have a wider range of application for different motor tasks, this should be converted to distance in millimetres with calibration of an element with known dimensions.

Alternatively to direct clinical application of quantified hand function, video tracking could also be an interesting annotation tool. During surgery, video tracking analysis could be used to detect the exact moment a patient is performing motor function tasks and potentially detect positive or negative DES responses. Video tracking can even be expanded to track the face or the whole human body. This can then be synchronized with other modalities, like electrocorticography (ECoG), ultrasound (US) or which instrument the surgeon is using and where in the brain. This could give valuable information about connectivity in the brain and gives the ability to quickly show trends and compare patients.

4.4.5 Conclusion

In this explorative study we showed that video tracking shows potential to visually quantify hand function before, during and after awake craniotomies. We showed that a fingertapping pattern can be recognized and a positive direct stimulation site can be detected from sudden muscle contraction. Future improvement of the hand tracking algorithm, pattern analysis and the motor function protocol should investigate which detected changes are predictive for long term motor outcomes of the patient. This could eventually lead to a new, objective monitoring method to give direct intraoperative feedback to the surgeon and improve long term quality of life of patients undergoing an awake craniotomy.

5

Future perspectives and Conclusions

Brain tumours located in functional areas need special surgical strategies to maximize tumour resection, while preserving healthy brain tissue for a maximal quality of life after the surgery. The neurosurgical field is constantly evolving and investigating new surgical strategies to develop patient-tailored solutions for these complex surgeries. It remains however a big challenge to provide robust evidence about which method has the best long-term patient outcomes due to the high heterogeneity of patients and surgeons. Every brain is different, every tumour is different and is located in a different brain area with a varying interaction with the surrounding tissue. Moreover, every surgeon has their own surgical preferences and methods. This large heterogeneity between patients and surgeons makes it very difficult to prove that a specific treatment or intraoperative monitoring method is superior to others. To be able to investigate which surgical approach and intraoperative monitoring method has the best long term outcomes for a patient, it is important to collect data about tumour characteristics, tumour-brain interaction, surgical strategy and a patient's functionality before, during and after brain surgery. This offers the opportunity to discover trends and relations between intraoperative changes and long-term patient outcomes, that can be supported with quantitative data.

In this thesis, we focus on the part of monitoring patients functionality. We have made two important steps to implement a new quantitative method to measure hand motor function. In **Chapter 2** we present new a frame that aims to create a standardized environment around a patient undergoing an awake craniotomy and to enable implementation of video recordings to monitor motor and language function. We mapped out all the important stakeholders and involved their wishes in the development of a new frame that can be structurally implemented. In **Chapter 3** we explored video tracking as a new tool to quantitatively monitor hand motor function before, during and after awake brain surgery. We identified several prerequisites to acquire good recordings and showed the potential of video tracking to detect clinical relevant events.

A surgical procedure is a complex interaction between the patient, the medical team, the physical environment and technical equipment. Implementing a new technology inside an operating room (OR) that structurally collects reliable data and is applicable for the variability of patients is therefore a serious challenge. From the steps we made during this thesis, we have identified several important factors for future implementations.

- Involving all medical and technical staff inside the operating room is essential to keep a smooth workflow during the procedure. Without creating stakeholder support and ensuring a workable environment for everyone involved, it is impossible to create a standardized environment for data acquisition. Quick iterations that implement the staff's feedback and improve technical outcomes, is essential.
- Due to the dynamic environment in the operating room, flexibility is necessary to acquire reproducible data of every specific patient case.
- Exploration of new quantitative monitoring methods should build on quick iterations, similar to fast prototyping strategies. Quantitative methods should always be combined with professional qualitative observations to create maximum impact.

We have shown that when using these guidelines, it is possible to implement a new quantitative method in the operating room to monitor the patient. Quantification of visual observations has shown to be low-cost, easily available and implementable, because of the fast technological advancements in this field. Video tracking can be used for future research to investigate the relation between intraoperative findings and long-term outcomes, to ultimately improve the quality of life of patients undergoing an awake brain surgery for brain tumour removal. It even shows potential to be implemented in different medical fields inside and outside the operating room.

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Supplementary Materials

A. Motor execution measurement methods for awake craniotomies – a literature research

Introduction

Brain tumors in eloquent areas need special strategies for surgical resection, since impairment of important functionality has a negative effect on both quality of life and on progression free survival.[1,2] For supratentorial tumors that infiltrate (close to) brain areas involved in language, awake craniotomy is well described as the golden standard.[3,4] For tumors invading motor function related areas however, it is still under debate whether asleep or awake craniotomy results in the best outcome.[5]

Asleep surgery under general anesthesia (GA) has the advantage that the primary motor cortex (M1) and the corticospinal tract (CST) can be mapped and continuously monitored during tumor resection using Motor Evoked Potentials (MEPs).[6,7] For this method, cortical strip electrodes are placed on the M1 to record and stimulate the motor cortex. The triggered motor response is measured using electromyography (EMG) by placing surface or intramuscular electrodes on the muscles of interest, including the face muscles and extremities. When the amplitude of the signal decreases >50%[8,9], this is an indication to pause or stop the tumor resection. This allows both for mapping of the motor areas, but also for continuous monitoring of the integrity of the M1 and CST. Also, for patients with pre-existing neurological deficits or inadequate cognition, asleep procedures are a good option.

However, this mapping and monitoring method mainly focusses on the direct connection of M1 through the CST to the muscles and does not include higher motor functions and their correlated areas, like the Supplementary Motor Area (SMA). Damage to the SMA can lead to SMA syndrome, meaning akinesia and mutism. Despite the belief that SMA syndrome is always temporary, several studies have shown that SMA syndrome can actually lead to permanent deficits in many patients.[10,11] Also, monitoring based on the preservation of MEPs is not always an indication for the absence of long-term motor deficits. Giampiccolo et al. (2021) have shown that half of the patients that experienced long-term deficits, had no report of a reduction of MEPs during the surgery, indicating that the motor function should be still intact.[12] These deficits that had no MEP reduction, occurred when supplementary motor areas were resected in conjunction with dorsal premotor regions and the anterior cingulate. This supports the view that GA procedures using MEP monitoring are suitable for tumors close to the premotor cortex and corticospinal tracts, but awake testing techniques are needed for higher motor function monitoring.

In current practice for awake craniotomies, intraoperative assessment of voluntary movement is measured by visual inspection or clinical scales measured by the neuropsychologist, clinical linguist or another team member performing the intraoperative testing. A positive motor response is often defined as 'observed muscle movement' and is thus highly subjective, depending on the experience of the specialist and is performed with a large time-interval. Also, negative motor responses, defined as a complete inhibition of movement without loss of tonus or consciousness, can have different underlying causes when looking at muscle activation. These underlying patterns seem to be involved in the occurrence of SMA syndrome and the permanent deficit in bimanual coordination and fine movements.[11]

Therefore, an objective measurement method is needed to improve motor function mapping and monitoring during awake craniotomies. This method should be able to monitor higher

motor function and be applicable in the complex setting of the operating theater. Since research in awake craniotomies is limited, this search has been expanded to explore and learn from different fields and syndromes, including asleep craniotomies and stroke patients.
In this narrative review we will give an overview of different methods to measure motor function during awake craniotomy. For this purpose, this report is divided in two parts:

1. What is motor function? An approach to subdivide motor function into different aspects and describe which motor deficits occur after awake craniotomies?
2. Which different methods are used to measure motor function? An exploration of new developments and their clinical relevance.

Motor function

Motor control and motor execution

Motor function comprises the whole trajectory of motor control in the brain, the resulting executive function of the controlled muscle and the sensorimotor feedback that is consequently processed in the brain.
A simple first division of this complex system is motor control versus movement execution, see Figure 1. Motor control contains the whole nervous system involved in the planning, initiation and regulation of motor function. It ranges from the cortical regions in the brain, through the spine to the motoneurons connected to the corresponding muscle, and involves feedback through the sensorimotor neurons. Motor execution is the result of motor control and consists of muscle contraction and the corresponding movement. Motor control can be seen as a system, and motor execution as its output.

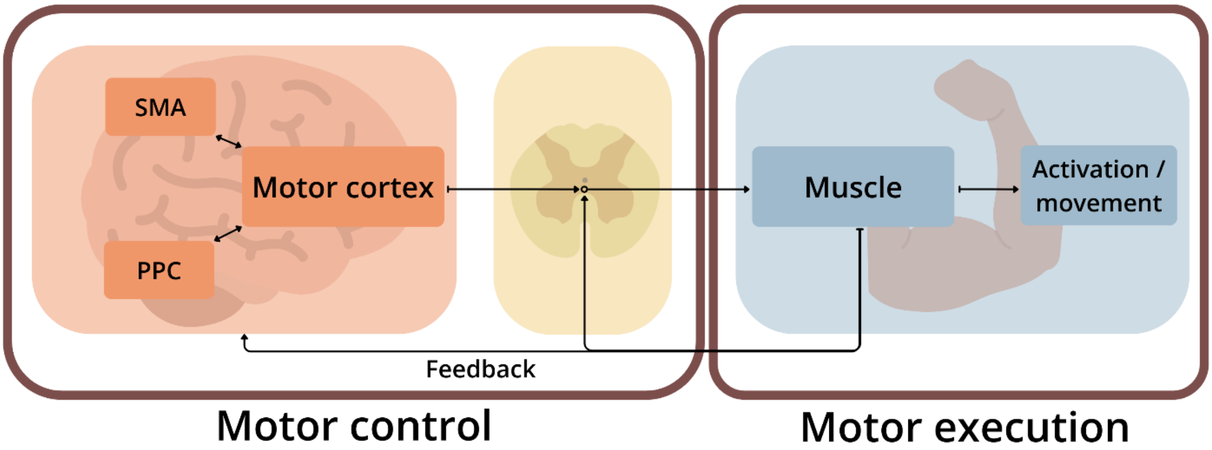

Figure 1: Motor function described as a motor control system with motor execution as its output. PM: Premotor cortex, SMA: Supplementary Motor Area, PPC: Posterior parietal cortex.

Disruption of the motor control system during or after awake craniotomy

Awake craniotomy

During awake craniotomies, direct electrical stimulation (DES) is used to identify cortical areas and subcortical pathways that are involved in motor, sensory, language and cognitive function.[4] This is called brain mapping. With DES, an electric current is applied to the brain to investigate whether the stimulated brain area is involved in certain functionality by observing its interference on a specific task. In motor tasks, the stimulation can either lead to inhibition of the movement, which is called a negative response, or lead to the activation of a movement or muscle, which is called a positive response. When an eloquent brain area is found, it is marked to avoid resection in this area, see Figure 2.

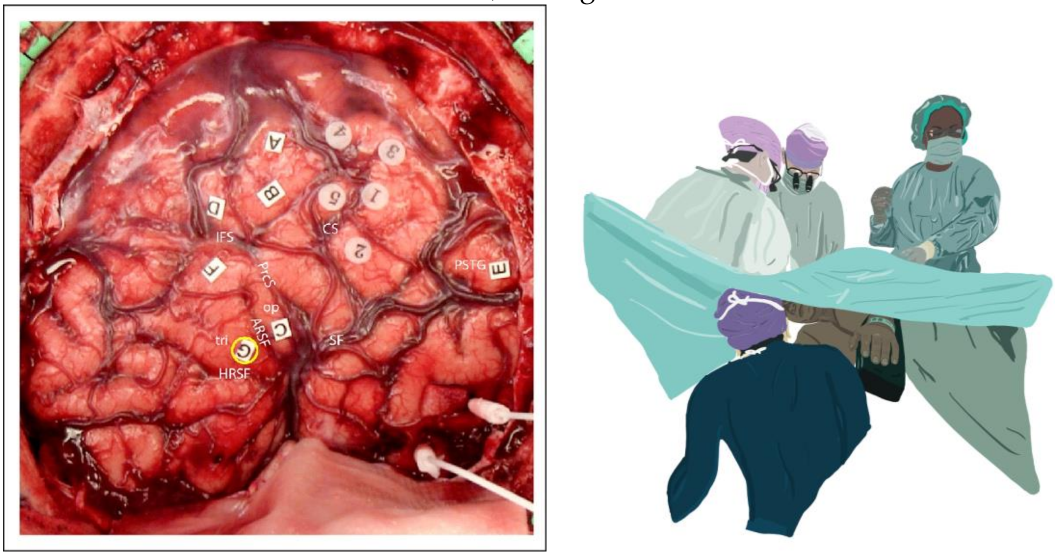

Figure 2: A) Stimulation map showing multiple detected sites as marked with numbers or letters (A-F, 1-5)[13], B) setting of the awake craniotomy with the clinical linguist performing tasks with the patient and the surging stimulating the brain.

When looking at motor function as described in the previous section, DES, nerve damage or a bleeding cause a disruption of the motor control system. This disruption can be 1) lesion of one of the brain areas giving input to the motor cortex, 2) damage to the motor cortex itself or 3) impairment of the tracts connecting the motor cortex to the spinal cord, see figure 3.

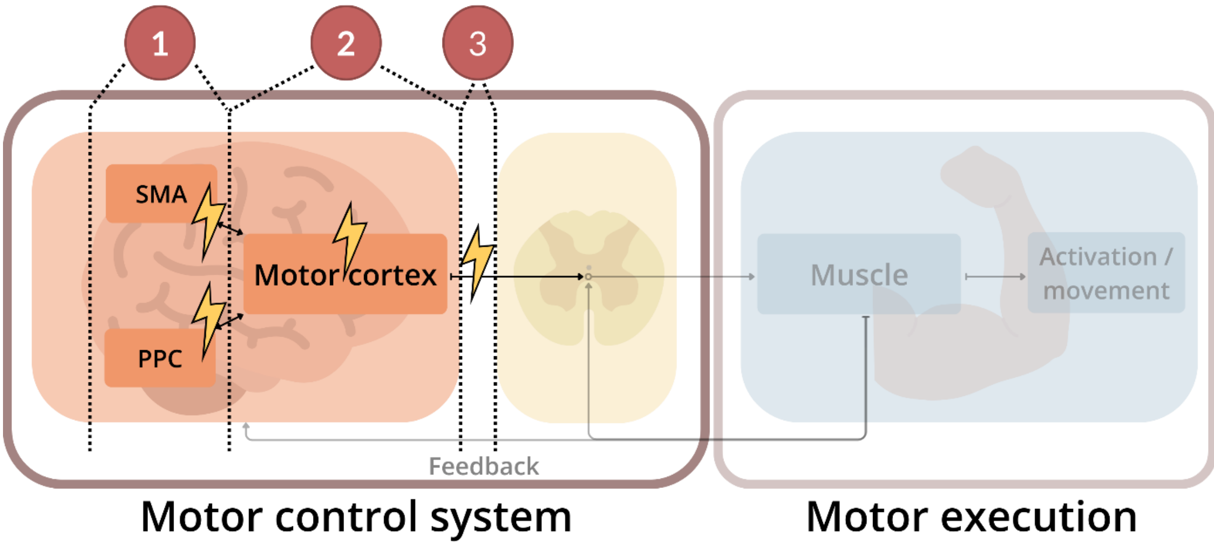

Figure 3: Different types of disruptions in the motor control system that can be caused by DES, nerve damage or a bleeding. 1: disruption of one of the brain areas giving input to the motor cortex, 2: disruption of the motor cortex itself, 3: disruption of the tracts connecting the motor cortex to the spinal cord.

To detect and measure the type of disruption either the system itself can be monitored, with for example electroencephalography (EEG), or the change in the motor execution as a result of the disruption can be assessed. In current practice, intraoperative detection of the disruption is mainly based on measuring the output of the system while the patient performs a task. This enables the medical team to have an idea of the interference of the disruption with actual functional tasks outside the operating room (OR) and not only look at connectivity. Currently, assessment of the performance of the patient is fully based on the visual interpretation of the clinical linguist. Patients are asked to squeeze their hand, or perform a finger tapping test. This is a very subjective method with large interobserver variability. To improve the reproducibility and to enable a more precise monitoring, a quantitative measurement technique is needed to measure intraoperative motor function during awake craniotomies. In this paper, we will investigate several quantitative intraoperative measurements methods of the motor execution as a method to extract the location and type of disruption of the motor control system.

Depending on the location of the disruption, a specific change in the output of the system, the motor execution, is elicited. For example, the connection of the posterior parietal cortex with the ventrolateral premotor area is important for sensory-motor integration of hand movement. A lesion in this connection can lead to apraxia, which causes problems in motor planning for movement or tasks, e.g. tooth brushing..[14] Damage to the motor cortex itself or the connection with the spinal cord leads to symptoms similar to upper motor neuron lesions, presenting as muscle weakness.

When looking specifically at the reported motor symptoms after awake craniotomies, these deficits are divided into transient, short-term deficits and permanent, long-term deficits. Fang et al. reported that 13-25% of all glioma patients undergoing AC experience transient motor deficits, while 0-10.9% have permanent deficits.[15] There are no recent studies dedicated to researching the different types of motor deficits after awake brain surgery, as many studies only report motor symptoms as one of their outcomes while studying other interventions. These mainly include various clinical scales to measure muscle weakness or paralysis[15–17], and only rarely include motor dexterity measures.[12,18] When looking at the motor control system, a muscle weakness is caused by the second or third type of disruption, namely the damage to the motor cortex itself or the connection to the spinal cord, the corticospinal tract. Solely measuring muscle weakness thus does not give full insight in the possible damage an awake craniotomy can do to the motor control system. Currently, there is no clear overview of the different type of which intraoperative changes lead to which types of long-term motor deficits. To our knowledge, no studies have been published to clarify this gap of information. Therefore, it is very important to include motor dexterity, coordination and planning functions in the differentiation of the presented motor deficit, to get a clearer insight into the damaged pathway and its long-term effects.

Motor function measurement methods

As described before, motor function is very complex and consists of many aspects. In this part, we will elaborate on quantitative measurement methods that can be used to describe a change in motor execution during awake craniotomies. The databases of Google Scholar and PubMed were searched for motricity measurements during brain tumor resection with awake craniotomies or under general anesthesia, for stroke assessment or other neurological conditions. These searches included combinations of the following search terms: ""Motor deficit/outcome/impairment/decline", "Functional outcome", "Long-term outcome", "Awake craniotomy/surgery", "Tumour resection", "Stroke [MeSH Terms]", "Neurological disorders" and "Parkinson's Disease [MeSH Terms]". The resulting articles were screened for a description of used methods and for the eligibility of this method to be used in the operating room (OR) environment of the Erasmus University Medical Center. Methods suitable for this OR environment were included in this report.

Motor execution can be measured in various ways. Here we divide the measurement methods in three types: 1) electrical measurement of muscle activity, 2) measurement of force generation and 3) measurement of the movement trajectory. Measurement methods can measure one or a combination of these components. For an overview, see Table 1.

Table 1: Overview of the different motor execution measurement methods

Method	Type	Measures	Application	Pros & Cons
Electromyography	Electrophysiology Force Motion	Motor unit depolarization	Diagnosis neuropathies Intraoperative monitoring	+ differentiate underlying mechanisms - noise, complex
Dynamometry	Force	Force	Rehabilitation Stroke	+ clinical validation - applicability
Optical markerless tracking	Motion	Coordinates moving object	Sports & rehabilitation Robotics	+ unconstrained - need patient in view
Optical marker-based tracking	Motion	Coordinates markers	Sports & rehabilitation & stroke Robotics	+ accuracy - interference, complexity
Inertial tracking	Motion	Acceleration and orientation	Sport & rehabilitation	+ small, cost-effective - interference, shift
Force myography	Force Motion	Volumetric changes	Stroke, rehabilitation Robotics	+ small, cost-effective - complex to make

Electromyography

Background and clinical application

Electromyography (EMG) is a method that measures electrical activity produced by muscles in contraction.[19] The EMG signal results from (multiple) motor units depolarizing, which can be measured as a voltage difference between two electrodes, see Figure 4.[20] There are two types of electrodes that can be used: surface electrodes and needle electrodes. Surface EMG is mostly used in combination with electrical stimulation of the peripheral nerves, while intramuscular EMG is used for the assessment of spontaneous activity for denervation or reinnervation.[21,22]

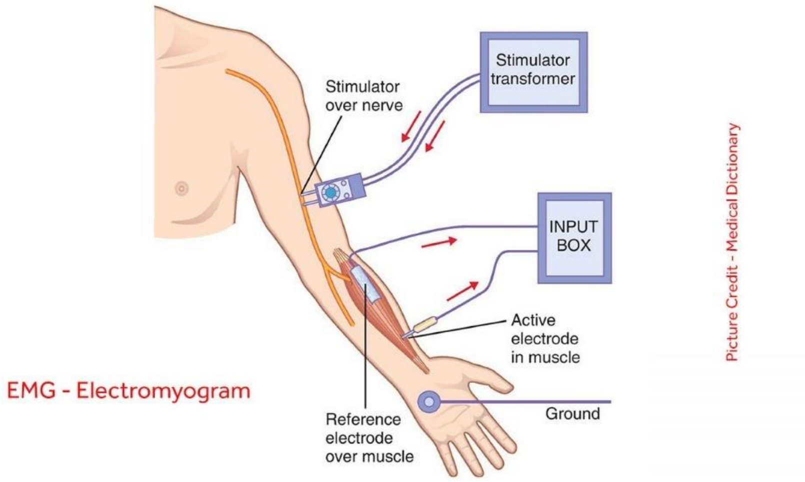

Figure 4: illustration of intramuscular electromyography. After a nerve is stimulated, the motor response can be measured by calculating the voltage difference over two electrodes. By subtracting the noise with use of the ground electrode, a better signal-to-noise ratio is achieved.

EMG is an important tool used for the diagnosis of neuronal pathologies, like carpal tunnel syndrome and neuropathy.[21] With the use of nerve stimulation, the conduction velocity of peripheral nerves can be estimated by measuring the latency. Together with the signal morphology, this can be used to differentiate between various neuropathies.

Besides being a diagnostic tool, EMG is also used for monitoring the integrity of the pyramidal tracts and the primary motor cortex during intraoperative monitoring. As described before, MEPs are used to record the muscle response to cortical or subcortical stimulation.

More recently, EMG has been studied for gesture recognition, hand force recognition and prosthetic limbs.[23–25] By decoding signals from multiple muscles, the orientation of the hand, arm or leg can be determined. This is a big topic in robotics and prosthetic limbs.

Also in awake craniotomies, several research groups are already using electromyography.[17,26] As described before in an example, one of the motor deficits observed after awake craniotomies is apraxia. To monitor ideomotor apraxia, a specific subtype important for the mimicking of gestures, the hand manipulation task (HMt) was developed.[27] In this task the patient's behavior is measured with EMG.

Advantages and disadvantages

Electromyography is the only method that directly measures the electrophysiological behavior of muscle activation. This enables the measurement of muscle activation even when this does not lead to visible contraction of the muscle. When applying this to awake craniotomy, this means that a stimulation with DES could be detected before this is visible as a muscle twitch. This is similar to EMG currently used for MEPs in asleep surgery. Viganò et al. also showed that positive or negative motor responses can have different underlying muscle activation patterns and a difference in origin of stimulation in the brain.[28] This shows a more in depth analysis of changes in muscle activation which is useful for differentiating between several motor control disruptions.

Another advantage is the possibility to measure multiple muscles simultaneously, showing activation patterns of agonist-antagonist pairs and contralateral muscles.

A disadvantage of EMG is the relatively low signal-to-noise ratio (SNR).[19] The EMG signal acquires of noise while traveling through tissues. When using surface electrodes, the distance between the original signal and the electrode recording this can be rather large and thus include a lot of noise. Also, the surface electrodes record the compound muscle unit

depolarization, but are not specific for just measuring one muscle. Interference from other muscles or muscle units leads to another noise source. The quality of the signal is also highly dependent on the electrode-skin contact.
Another disadvantage to use this technique in the OR setting, is the need for application of the electrodes and a neurophysiologist to interpret the acquired signals real-time. This means that an already complicated surgery including multiple specialists, will take longer and is dependent on one more specialist.

Dynamometry

Background & clinical application

For clinical applications, several clinical scales are used to measure force. The most frequently used is the Medical Research Council (MRC) scale to measure muscle strength. For MRC scale, the muscle strength is assessed by the clinician during active contraction by the patient and ranges 0 to 5. Since this scale has a high inter- and intra-rater variability, an objective method using a dynamometer was developed.
The most frequently used and clinically validated dynamometer is the Jamar hydraulic dynamometer. This is a handheld dynamometer that measures hand grip strength, see figure 5A. Recent developments are digital dynamometers or devices that make use of load cells, like the K-Force Grip and handheld dynamometers to measure force of other muscle groups, see figure 5B-C.

Figure 5: Different types of dynamometers. A) Jamar Hydraulic Dynamometer[55], B) K-Force Grip[56], C) handheld dynamometer[57]

Advantages and disadvantages

One of the advantages of dynamometers is the validation in the clinical setting for several target groups.[29] It can accurately measure hand grip strength or strength from other muscle groups with handheld dynamometers. The devices are rather small and have no wires attached, making it easy to apply in several settings. In the limited space available during an awake craniotomy, this is a big advantage.
One of the major disadvantages of the dynamometer is that its reliability decreases when the patient is too weak[30]. Also, it can only measure full hand grip strength and not strength of every individual finger, as this is easily too weak. Especially in patients with pre-existing deficits this can be a problem.
Another disadvantage is that a dynamometer can only measure force. Of course this is what it is designed for, but it is not expandable to measure different aspects of motor function.

Motion tracking systems

To monitor motor changes in movement initiation, coordination and sensorimotor feedback, a larger view than just looking at muscle strength needs to be adopted. Quantification of these processes remains a challenge, but recent developments in motion-tracking systems show promising results to record and analyse motion of (a part of) the whole human. Motor-tracking systems can be based on cameras, wearable sensors or a combination of these. The types of motion-tracking systems that are currently available can be roughly divided into two types: 1) Vision-based optical systems with or without markers and 2) non-vision based inertial systems.[31] Optical systems record (a part of) the human body with cameras, while non-vision based inertial systems use sensors to detect the position, orientation and velocity of the moving body(part). Both types of motion-tracking will be discussed below.

Optical motion tracking systems

Optical motion-tracking systems rely on detection of the moving object with cameras. When recording the moving object in its natural form, this is called marker-less optical tracking. Marker-based tracking on the other hand uses reflective markers that are attached to the human body. These markers are spatially and temporally sampled using high-speed infrared (IR) cameras and their trajectories can be further analysed to give information about the velocity, acceleration, jerk etc.[32]
For both recordings, it is necessary that the object or markers are always visible in the field of view of the used cameras, see Figure 6.

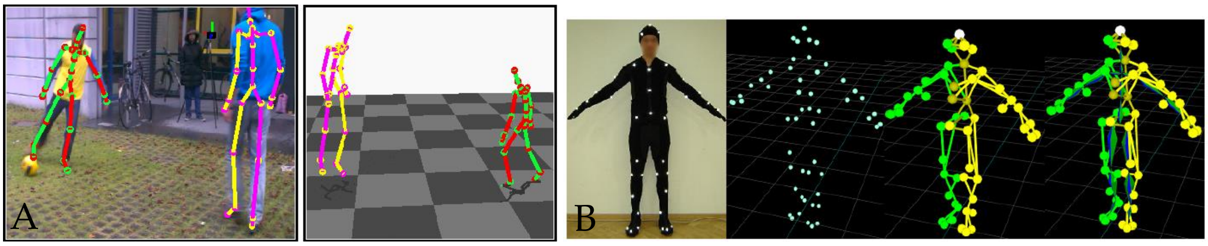

Figure 6: Two optical tracking methods. A): markerless tracking[33], B) marker-based tracking[34].

Markerless optical motion tracking

The recent technical advances in the development of markerless motion tracking has increased its accuracy and possibility to record with accessible cameras, such as webcams or smartphones.[35] Currently, structural application in healthcare is still limited, despite promising results.[36] Most of the research for clinical application study patients with Parkinson's disease or stroke.[36]
Markerless optical motion tracking is currently not used in standard practice for preoperative, intraoperative or postoperative motor function assessment of patients undergoing brain tumour resection. Nakajima et al. (2015) are the first and only group, to the best of our knowledge, to have analysed intraoperative video recordings to investigate motor symptoms and relate these to postoperative outcomes.[18] They mainly focussed on lesions in the SMA and used Brunnstrom's recovery stage (BRS) to measure preoperative and postoperative motor weakness. During the surgery, the patients performed these tests: upper extremity movement, including flexion and extension of the elbow and fingers, and lower extremity movement including flexion and extension of the knee. The following parameters were extracted from the intraoperative recordings:

- Response to DES: measured by negative or positive motor responses
- Motor weakness: presence or absence of the inability to continue the motor task
- Delay of movement initiation: time until movement initiation after patients tried to start the movement or were told to start the movement by the therapist
- Slowness of movement: ratio of the required time for a reciprocal movement of the upper extremity, calculated as the speed at eruption of abnormal motor response divided by speed before SMA resection
- Difficulty in dual task response: success or failure of the dual task in the upper extremity movement and object naming task
- Coordination disturbance: success or failure of coordination movement of upper and lower limb or elbow and fingers

They showed that intraoperative motor symptoms without positive mapping were a predictor for postoperative SMA-syndrome including hemiparesis. This underlines the monitoring of motor functions during not only during stimulation, but also during resection of the tumor. Almost all patients recovered after a few weeks to their preoperative level. This shows that a differentiation between different types of intraoperative motor symptoms is needed to predict short-term versus long-term postoperative motor deficits.

In stroke, symptom assessment using video recordings is more frequently studied for the quantification of movement irregularities to predict and evaluate rehabilitation. One of the parameters that is often quantified is smoothness, since this is improved by learned coordination and decreased by poor motor coordination, muscle weakness and spasticity.[37]

The big advantages of markerless tracking is that the subject can be recorded in a natural setting, without any constraints by wearing markers or sensors, and without the need of a time-consuming marker placement procedure.[36,38] This comes however with a decrease in accuracy of the estimated location.[39,40]

Marker-based optical motion tracking

For marker-based optical tracking two types of markers can be used: passive markers reflecting infrared light, or active markers emitting light. Marker-based tracking is currently frequently used to analyze human motion in research due to its accuracy.[41] The markers are usually attached to anatomical landmarks. This is preferably close to bone, as the skin can move in relation to the landmark, leading to a measurement error.[42]

Applications of research with marker-based tracking systems include stroke and rehabilitation of stroke.[37,43] With the detected coordinates, different aspects of motor function can be assessed with calculations, like curvature or smoothness of the movement..

Disadvantages of marker-based tracking include the time-consuming application procedure and calibration. When looking specifically at the OR setting, marker-based optical tracking also has the disadvantage to potentially interfere with neuronavigational systems. Just like markerless tracking, the subject and its markers need to be fully visible to be able to track the motion.

Inertial motion tracking systems

In contrast to the previously discussed methods, inertial motion tracking systems do not optically track the subject, but use sensors to detect the position, orientation and velocity of the subject, see Figure 7. These sensors are called inertial measurement units (IMU). These IMUs typically consist of accelerometers and gyroscopes. To overcome drifting issues, many IMUs are equipped with a three axis magnetometer to relate the orientation to the local magnetic field.[44]

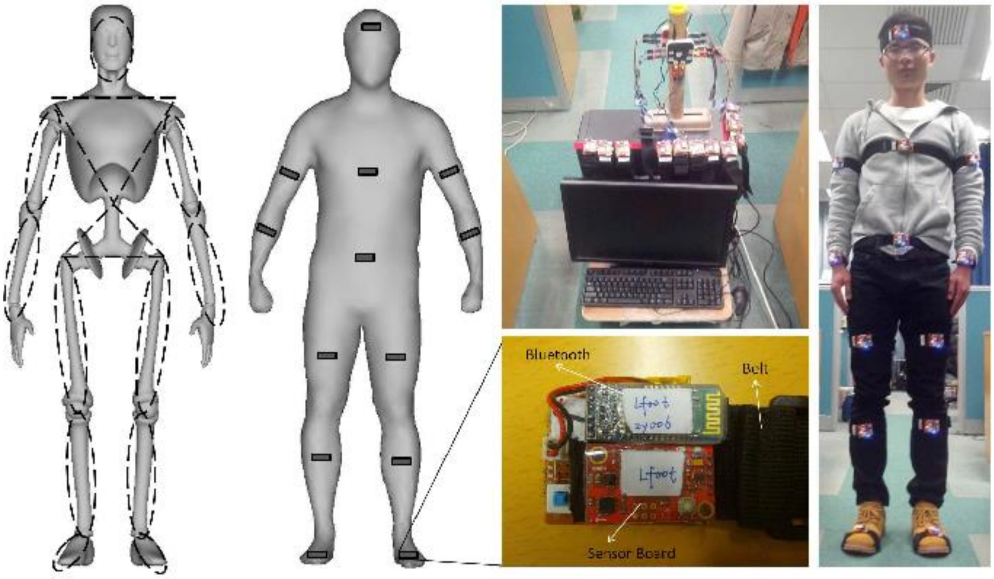

Figure 7: Body position tracking with IMUs.[45]

The interesting thing about the use of IMUs is that the subject does not need to be visible for a camera. This makes it also possible to track in an unconstrained environment.[46,47] Other advantages include that it is a small, cost-effective device[44].

A disadvantage of the magnetometer is that inside buildings the earth's magnetic field is disturbed, which makes it an unreliable reference. Also, other sources can cause magnetic disturbance, leading to orientation errors. Especially in an OR environment this could be a real problem.[48]

Force myography

Force myography (FMG), also called topographic force mapping (TFMs), is a non-invasive technique that records the volumetric change caused by muscle contraction.[49] The volumetric change is measured with force-sensitive sensors, changing resistance according to force application related to a rest-state.[50] When placing many sensors as a band around for example the arm, the combination of these signals can be decoded with the help of machine learning to analyze which muscles were active. This can be converted to the recognition of for example hand gestures. FMG is mainly researched in the context of limb prosthetics and robotics and has currently no clinical applications.

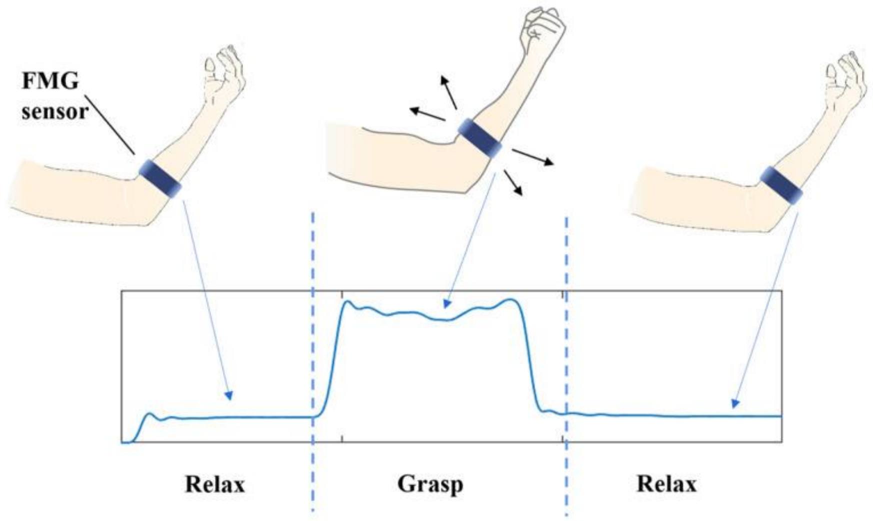

Figure 8: Illustration of Force Myography (FMG)

When comparing FMG to EMG, the big advantages are that FMG does not need extensive skin preparation and specific electrode placement, and is insensitive to sweating.[50] Also, it has a higher SNR and anti-interference ability.[51] Depending on which FMG sensors are used, it can also have a much lower cost than EMG.

A disadvantage of FMG systems is that signal interpretation becomes difficult in episodes where the band with sensors is shifted.[52] Also, as the signals are based on volumetric changes, patients with atrophy would not be suitable for this method. The volume changes in their muscles would be too small to detect. The analysis and decoding of the signals are less complex than that of sEMG to recognize the type of movement, but is more complex than the previously discussed motion tracking options. Lastly, the development of FMG sensors is still ongoing and mostly in a research setting. There are no devices on the market yet. This is also a problem for clinical implementation.[53,54]

Discussion

Preservation of motor functions in an awake surgery setting at long term is of utmost importance for patient's quality of life. Motor function is however a very complex function to monitor, as it consists of many aspects. To properly function, good planning, initiation and coordination is needed. Measuring the motor execution and relating this to the type of disruption in the brain could be essential during surgery to predict if tumor resection can continue or has to be paused to ensure postoperative functionality. In this literature research we aimed to make an overview of various objective, quantitative methods to measure motor execution during awake craniotomies. This is only a preliminary overview of some of the most promising methods to be used in the operating theatre. To investigate which method is best for a specific research question, a more detailed search should be done. In this report we have looked at electrophysiology, force generation and motion detection to monitor a patient during a motor task.

Depending on the goal of the clinician or researcher, the best measurement method should be chosen. If a more in depth analysis of underlying muscle activation patterns is needed to differentiate between different motor control disruptions, EMG could prove to be useful, as also previously described by Viganò.[28] This is however also a more complex method needing an extra specialist and specialized equipment. Also, it is hard to differentiate with EMG between voluntary and involuntary movement. Especially in an awake setting, it is very difficult to determine whether a positive EMG response after DES is caused by the stimulation or by the patient themself. Furthermore, there is currently no proof that EMG is superior in terms of clinical relevance for detecting long term effects.

If a more general analysis of the influence of the motor control disruption on highly skilled movements is the goal, optical or inertial tracking methods would have the preference. EMG and FMG can also be used to decode movement, but this is a rather cumbersome and computational expensive when compared to video tracking or inertial tracking. In the OR, marker based tracking could pose as a problem by interfering with the neuronavigation system which usually also depends on the reflection of fiducials by infrared light. Markerless based tracking would therefore be more feasible. A disadvantage of this method however is the need for total view of the subject. This is often not feasible since the patient is covered for warmth and privacy. Inertial tracking on the other hand could have real issues with shifting since magnetometers will have a large disturbance by other sources and inside a building. Despite depending on the specific surgical set-up, the best option seems to be video tracking.

Whichever method is chosen, it is very important to keep its limitations in mind when interpreting the outcomes. Especially during awake craniotomies, you are only able to measure a change in the specific task that you let the patient perform. This means that you can only monitor the specific functionalities that a patient is performing in that exact moment. If you measure no changes in that specific task, this is by itself no guarantee that there is no deterioration in another function that is not tested. Therefore, it is very important to get a good overview of the different aspects of motor function with different tasks and that these tasks are alternately performed during the surgery. To monitor these tasks, a combination of measuring techniques is needed to relate changes in muscle activation, force generation and movement to disruptions in the motor control system. These intraoperative measurements should -term follow-up of the patients functionality to investigate clinical relevance. A clear standardized protocol to gather these postoperative outcomes should be implemented to distinguish between different motor deficits, as there is currently no clear overview of the motor deficits that occur after awake craniotomies. Even the postoperative ideomotor apraxia as reported by Rossi et al. (2018) during the development of their new task, has never officially been published. This leads to a lack of knowledge about the prevalence of these and other type of motor deficits. For a clinical relevant development of intraoperative motor function testing, this data is absolutely essential. With this data long-term follow-up studies can investigate which intraoperative disruptions in motor control and changes in motor execution are good predictors for long-term patient outcomes. In the future this could lead to a protocol for intraoperative motor function monitoring during awake craniotomies and aiding surgeons to determine which tissue can be safely removed, and which tissue should be preserved.

Conclusion

Measuring motor function during awake craniotomy is essential to ensure good long-term outcomes of the patient. To be able to make predictions based on intraoperative deterioration, several aspects of motor function should be monitored. A combination of multiple techniques, including EMG, FMG, dynamometry and optical motion tracking could be useful to detect changes in motor execution. Future studies will have to look into the relation between intraoperative motor changes, the disruption in the motor control system and their relevance for long term outcomes.

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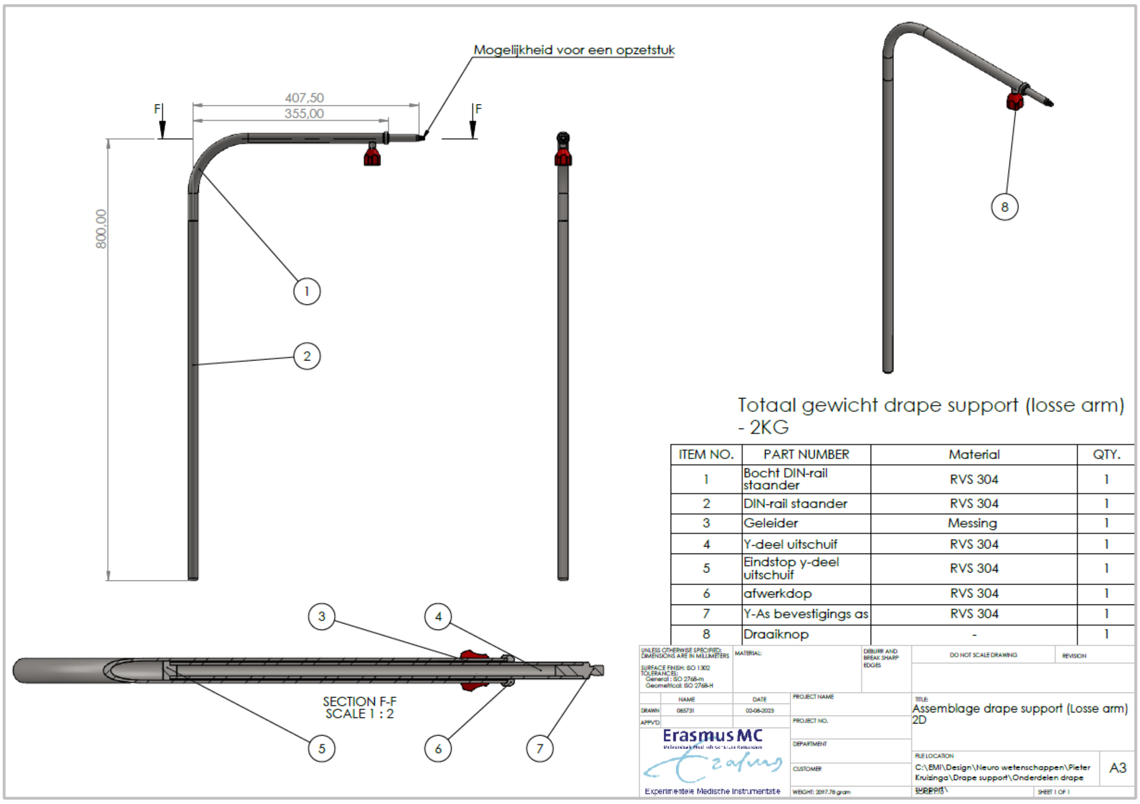
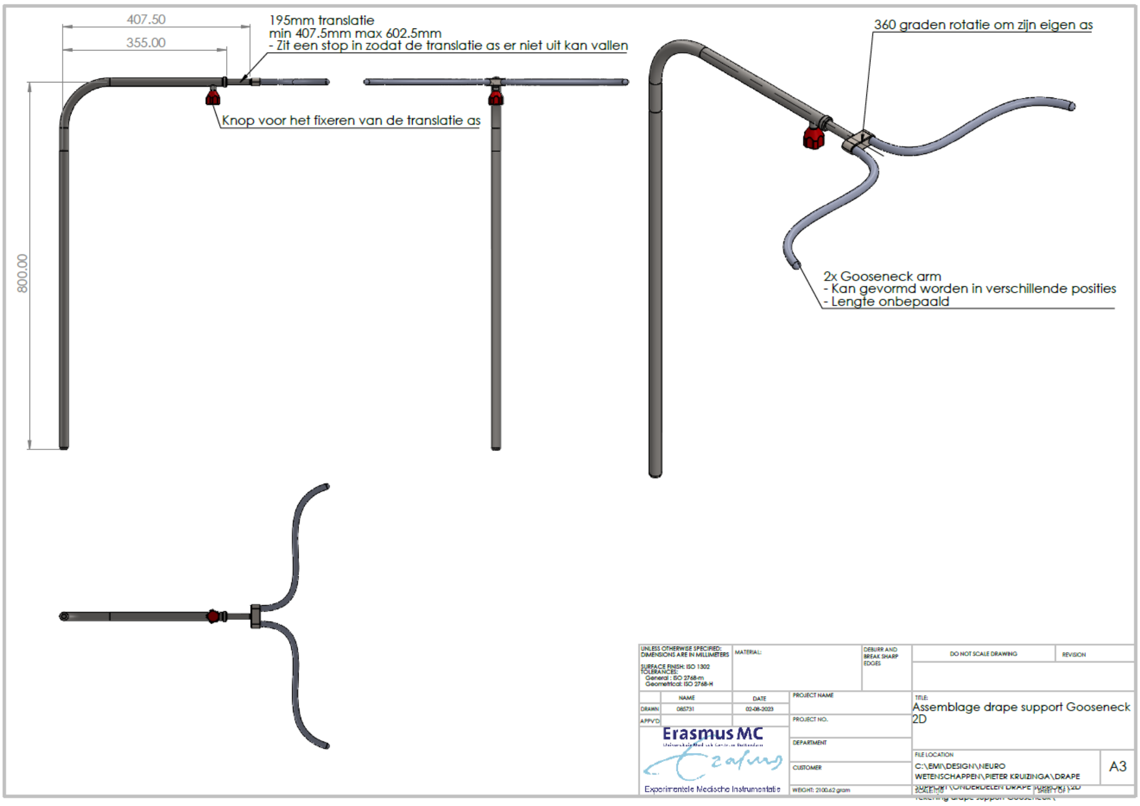
B. Technical drawings of the three concepts

B.1: Technical drawing of the redesigned base frame used in concept 1 and 3

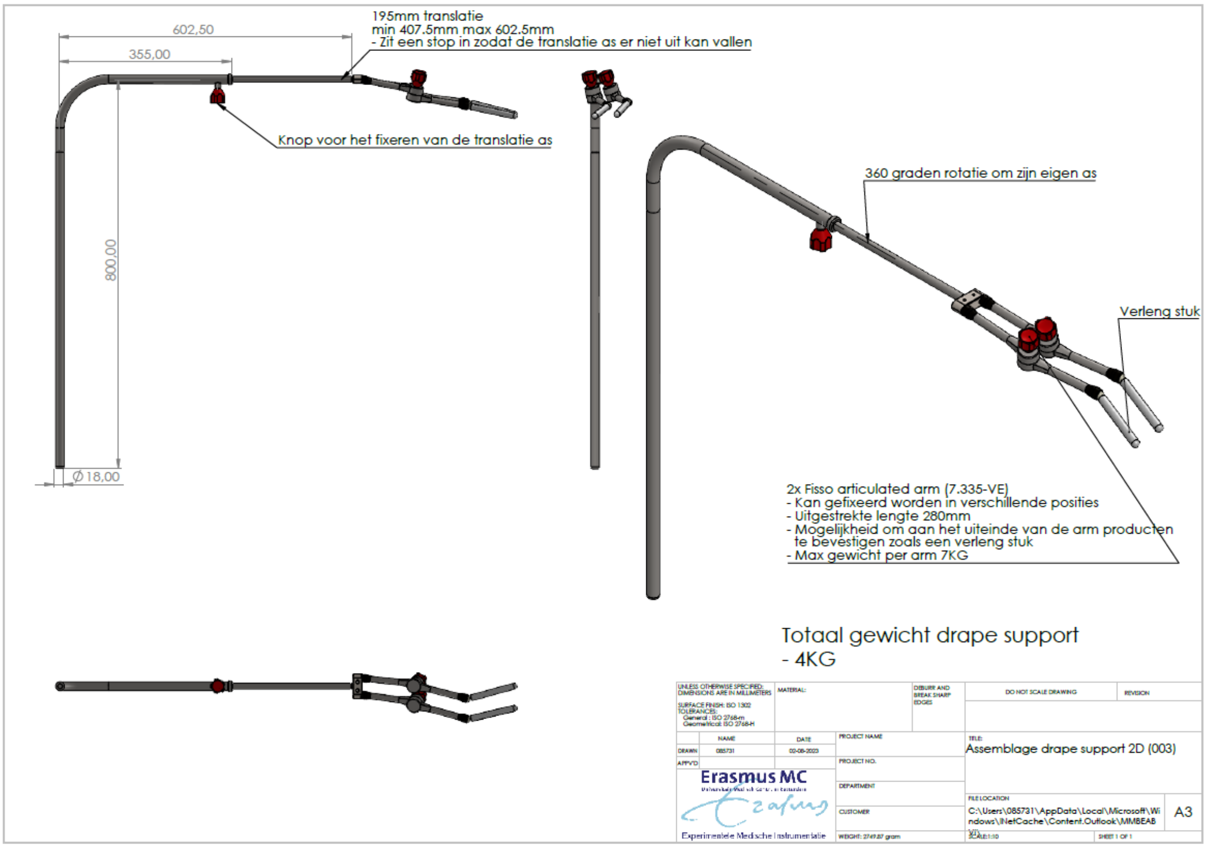


ITEM NO.	PART NUMBER	Material	QTY.
1	Bocht DIN-rail staander	RVS 304	1
2	DIN-rail staander	RVS 304	1
3	Geleider	Messing	1
4	Y-deel uitschuif	RVS 304	1
5	Eindstop y-deel uitschuif	RVS 304	1
6	afwerkdop	RVS 304	1
7	Y-As bevestigings as	RVS 304	1
8	Draaiknop	-	1

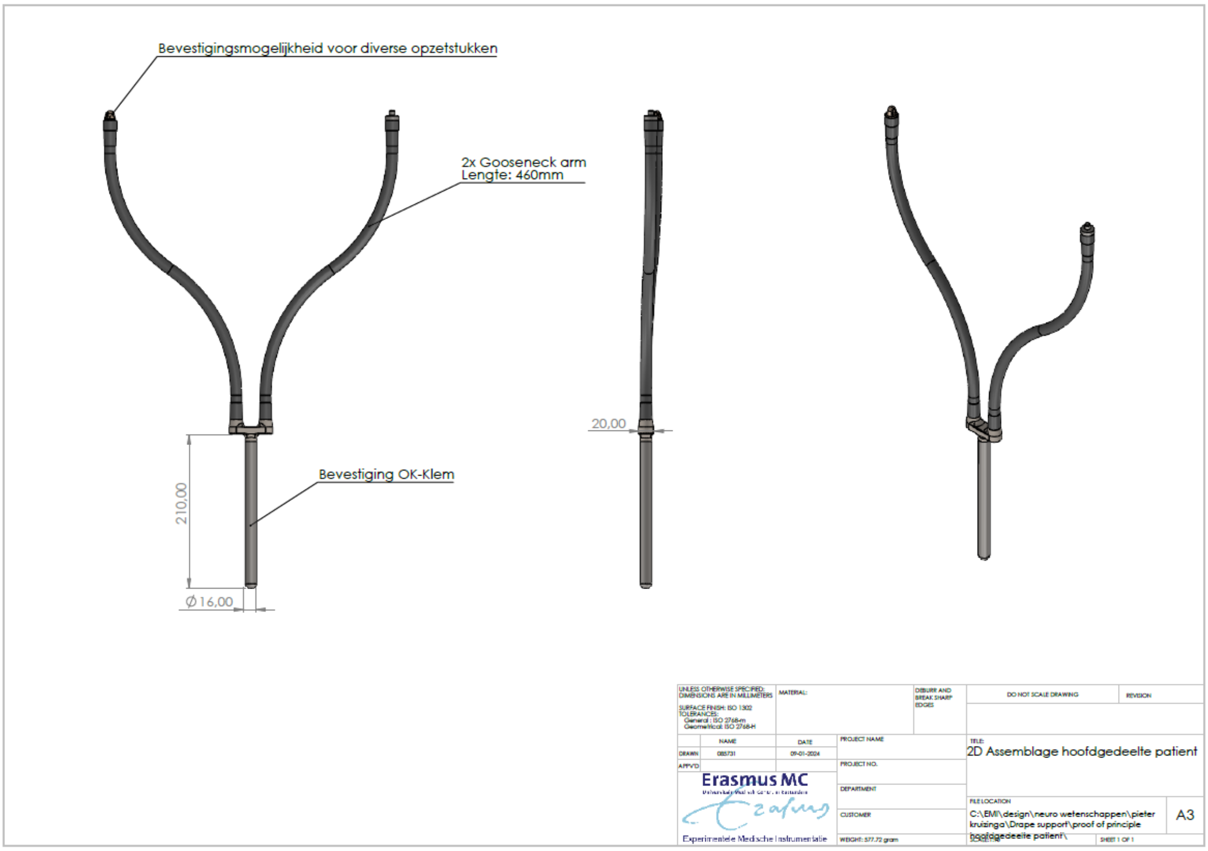
B.2: Technical drawing of concept 1



B.3: Technical drawing of concept 2



B.4: Technical drawing of concept 3



C. Hand Landmarks

MediaPipe’s Hand Landmarker module detects 21 landmarks, see Figure below.