Analysis of the neuronavigation market for development of a new technology: need validation and market aspects

ELIN MIGNÉRUS

Master of Science Thesis in Technology and Health
Stockholm 2014
This master thesis project was performed in collaboration with KTH, Unit for Neuronic engineering.

Analysis of the neuronavigation market for development of a new technology: need validation and market aspects

Analys av marknaden för neuronavigation för utveckling av en ny teknik: behovsvalidering och marknadsaspekter

ELIN MIGNÉRUS

Master of Science Thesis in Technology and Health
Advanced level (second cycle), 30 credits
Supervisor at KTH: Johnson Ho
Examiner: Dmitry Grishenkov
School of Technology and Health
TRITA-STH. EX 2014:80

Royal Institute of Technology
KTH STH
SE-141 86 Flemingsberg, Sweden
http://www.kth.se/sth
Abstract
Neuronavigation is the technology used during brain surgery to verify the location in which the surgeon is working in terms of depth and width. Despite being considered to be helpful, the technology lacks when it comes to the consideration of brain shift, the dynamic changes of the brain during surgery. The purpose of this report was to verify the suspected need of an additional tool and investigate the market size and dynamics.

The thesis work mainly followed the method of Biodesign – The process of innovating medical technologies, which covers all steps in the innovation process. To fit the specific purpose, the method was partly amended.

The results of the report are divided into two categories – need and market. A need statement was developed and the market was mapped in terms of size and other players in the market space. The conclusions drawn are that there is a need for technology development in order to safely account for brain shift during tumour resection surgery, but that it is likely to be hard to enter the market due to other researchers who have made more progress in the area.
Sammanfattning

Examensarbetet följde främst metoden som presenteras i *Biodesign – The process of innovating medical technologies*, som täcker alla steg i innovationsprocessen. För att passa det specifika syftet med rapporten anpassades metoden i enlighet med målet.

Rapportens resultat är uppdela i två kategorier – behov och marknad. En behovsformulering utvecklades och marknaden kartlades beträffande storlek och andra aktörer på marknaden. De slutsatser som dras är att det finns ett behov för teknikutveckling för att säkert kunna ta hänsyn till brain shift under tumörresektioner, men att det troligtvis är svårt att träda in på marknaden då det finns andra forskare som har kommit längre inom området.
Preface
The report is written within the course HL204X, Technology and Health, and is a thesis project at the master’s program in Medical Engineering at KTH Royal Institute of Technology.

I would especially like to acknowledge those who have helped during the preparation of the report; interviewees for taking the time to discuss the subject, Lund University Hospital for allowing me to observe during surgery and my supervisor, Johnson Ho (KTH), for guidance during the process.
Contents

1 Introduction .................................................................................................................. 1
  1.1 Background .............................................................................................................. 1
    1.1.1 Status report .................................................................................................... 1
  1.2 Project definition .................................................................................................... 3
    1.2.1 Thesis objectives .............................................................................................. 3
  1.3 Limitations ............................................................................................................. 3
2 Method .......................................................................................................................... 4
  2.1 Biodesign ................................................................................................................ 4
    2.1.1 Needs finding ................................................................................................... 4
    2.1.2 Needs screening ............................................................................................... 4
  2.2 Interviews .............................................................................................................. 6
  2.3 General search ....................................................................................................... 6
  2.4 Method discussion ................................................................................................. 6
3 Result ............................................................................................................................. 8
  3.1 Need ....................................................................................................................... 8
    3.1.1 Need statement ................................................................................................. 8
  3.2 Market ..................................................................................................................... 9
    3.2.1 Disease state fundamentals ............................................................................. 9
    3.2.2 Treatment options .......................................................................................... 11
    3.2.3 Stakeholder analysis ...................................................................................... 13
    3.2.4 Market size ..................................................................................................... 16
    3.2.5 Market dynamics ............................................................................................ 18
4 Discussion ..................................................................................................................... 29
  4.1 Regulatory .............................................................................................................. 30
  4.2 Reimbursement ..................................................................................................... 30
  4.3 Business strategy ................................................................................................. 31
5 Conclusion ................................................................................................................... 32
References ......................................................................................................................
List of tables
Table 1 Need analysis ........................................................................................................... 8
Table 2 Treatment landscape............................................................................................... 13
Table 3 Stakeholder analysis ............................................................................................... 15
Table 4 Summary of market forces ...................................................................................... 26

List of figures
Figure 1 Porter's Five-Force model ....................................................................................... 5
Figure 2 Statistics of intracranial surgery on tumours, 2007-2012 ........................................ 9
Figure 3 Prevalence of intracranial surgery on tumours, 2007-2012 ............................... 10
Figure 4 Top-down economic evaluation, focus: surgery ..................................................... 16
Figure 5 Top-down economic evaluation, focus: radiation therapy ................................. 17
Figure 6 Market evaluation, Western Europe ...................................................................... 18
Figure 7 Revenue trend, Medtronic, Inc. ............................................................................ 20
Figure 8 Revenue trend, BrainLAB AG ............................................................................... 22
Figure 9 Revenue trend, Stryker Corp. ................................................................................ 23
Figure 10 Overview of strategic actions in Western Europe, 2002-2012 ................................. 24
Figure 11 Strategic activities per company, 2002-2012 ......................................................... 25

List of appendices
Appendix A – Interview guides (Swedish)
1 Introduction

1.1 Background

Neuronavigation is a tool used during brain surgery to locate where in the brain the surgeon is actually working, i.e. intraoperative orientation. (Ganslandt, et al., 2002) The navigation is based on preoperative MR images, which are merged to build a 3D view that is displayed on a computer-workstation. The preoperatively collected information is calibrated against the patient in the surgical setting using a coordinate system, which makes the images on the workstation point-to-point maps corresponding to the patient’s brain. (Ganslandt, et al., 2002)

Brain shift is the name for deformation of the brain during surgery, which can occur due to several reasons including gravity, intraoperative position of the patient, the volume of a resected tumour and loss of cerebrospinal fluid (CSF). (Liebenthal, 2011) Studies have shown that the brain deforms around 1.2-20 mm in the direction of gravity during surgery, with displacement taking place in both superficial and deep structures. (Zhuang, et al., 2011)

The problem with brain shift, from a navigation perspective, is that the preoperative images used in navigation planning are no longer representative for the brain’s real-time anatomy; hence, the preoperative planning is no longer as accurate. This leads to that the surgeon has to do his own estimation of how much the brain has deformed as the surgery continues which introduces the aspect of subjectivity. When objectivity decreases as there are no real-time data to rely on, the human factor is introduced, and the risk increases due to potential mistakes in judgement. (Bjartmarz, 2014)

1.1.1 Status report

Today, no Swedish hospital uses intraoperative image updating during neurosurgery, although several clinics are looking into the area. There are currently several different ways to account for brain shift during brain surgery: intraoperative image update, biomechanical models etc.

1.1.1.1 Intraoperative image update

There are different imaging methods that can be used intraoperative: magnetic resonance imaging (MRI), computed tomography (CT) and sonography. Although being more time effective, CT and sonography are not commonly used since the method provides low image resolution (Zhuang, et al., 2011), which is a disadvantage when trying to achieve accuracy in the navigation. Although having lower resolution, ultrasound images can be fused with preoperative MR images to achieve an idea of how much the brain has shifted, relative to the start. This method can be used in the training of how to interpret ultrasound images of the brain, which then can be used for intraoperative updating. (Bjartmarz, 2014)

1.1.1.2 Biomechanical models

Today, there is no biomechanical model that is used for neurosurgery in a clinical setting; however, finite element models (FEM) are currently used in different medical areas, such as analysis of bone tissue response (Trabelsi, et al., 2011), dental care and several areas of research. (Soares, et al., 2012) Several researchers have looked into biomechanical models for
prediction of brain deformation during neurosurgery and the most recent testing has been done on non-linear FEM, as linear modelling does not represent the tissue mechanics well enough; only very small deformations are considered to have a linear elastic response.

In one study, the researchers used hexahedron-dominant finite element meshes and non-linear finite element formulations (Wittek, et al., 2007); the information that was put into the model was collected from surface displacement, which could be done with already existing technology, e.g. ultrasound or intraoperative MR. Results showed that the non-linear model can complement image processing techniques in non-rigid registration.

Another study, where researchers used the Total Langrangian Formulation\(^1\) of FEM together with Dynamic Relaxation\(^2\) (Joldes, et al., 2009), they showed that, with the proposed termination criteria, the model was accurate and computationally efficient when predicting brain deformation. They also discussed that one of the main parameters of Dynamic Relaxation can be computed pre-operatively, which shortens the time for intraoperative update.

In 2010, Wittek et al. used non-linear FEM procedures for testing in six brain shift cases, with very accurate results. The biomechanical model, using over 50,000 degrees of freedom, was compared to intraoperative MR images to validate the results. (Wittek, et al., 2010) Later on, the same research group have introduced the discussion on the importance of accounting for brain-skill interface, with the results showing that this is of importance when modelling brain shift. (Zhang, et al., 2013) (Mazumder, et al., 2013)

Testing has also been done on layer-by-layer brain phantoms (Ma, et al., 2010), with applied forces taken into account. The testing was done with x-ray markers to measure the displacement and computation was performed with non-linear FEM. Researchers showed good agreement between modelling and experiment results, which they consider highlights the predictive power of such biomechanical models.

**1.1.1.3 Other methods**

Aside from biomechanical modelling, other methods for brain shift compensation have been researched. One of these methods is fluorescence-guided resection in combination image guidance (Valdés, et al., 2010) which was conducted by letting the patient consume a biomarker before surgery where after a blue light was used to illuminate the brain tissue. Under the blue light, tumour tissue, which has a quicker glucose breakdown, showed a red fluorescence, helping the surgeon to distinguish between healthy and diseased tissue. The results showed a better accuracy when using biomarkers than for surgeries where only image update was used.

---

\(^1\) Refers the stress and strain at time \(t\) to the original configuration at \(t_0\); effective when there are large displacement, large rotation or small strain

\(^2\) Numerical method where the aim is to have internal and external forces in equilibrium
1.2 Project definition

The incentive to this study is a supposed need for a navigation tool which can account for brain shift caused by tumour resection during neurosurgery. Even if the suspected need is proven, there are still questions that could hinder the start of an innovation process for a solution to the problem; the solution should preferably be commercially viable in order to raise investment for the project. An effective way to determine whether or not the project is worth proceeding with is by doing a market analysis, which helps the innovator determine several aspects. (Yock, et al., 2009)

There are several reasons to why it is important to determine the market before starting the product development (PD) process: a pre-PD market analysis helps the innovator/developer to determine how much resources can be put in, i.e. if the PD is financially motivated; by evaluating the market dynamics, a forecast of the market reception of the product can be performed; information on existing competitors can help the innovator with the product identification, both in a differentiation point-of-view and the freedom to operate. The market research should be performed early in the innovation process, to avoid unnecessary large costs.

1.2.1 Thesis objectives

From the above stated facts, the following objectives were developed

1. Investigate the need for an additional surgical planning tool, to be used in addition to existing technology when planning tumour removal.

2. Map the market dynamics for surgical planning tools used in brain surgery.

1.3 Limitations

Validation testing of the suspected need was based on the opinions of Swedish surgeons. One of the interviews with surgeons were performed via telephone, due to the wide spread of neurosurgical clinics. However, to equalise the conditions as much as possible, the interviews were performed in the same method as if they were held in person.

Observations were only made during one surgery due to limited access and the geographical spread of the clinics.

The general structure of an innovation team incorporates different competencies that are relevant for the project; normally, the team could include scientists and subject experts as well as people with commercial knowledge. For this thesis work, the “innovation team” only consists of one person, why the knowledge is therefore not as extensive and subject expertise is missing.
2 Method
Because of the diverse nature of the different parts of the thesis, several methods were used. The main method used was parts of Biodesign: The Process of Innovating Medical Technologies (Yock, et al., 2009), which incorporates the steps of identifying a need and determining a market. Aside from this, interviews were held and a general search approach was used. Further descriptions of the methods are found below.

2.1 Biodesign
Biodesign: The Process of Innovating Medical Technologies (hereafter referred to as “Biodesign”) describes a method of making innovation happen, which is developed and used at the Stanford Biodesign Program. The process is divided into three main phases namely identification, invention and implementation. For this thesis, focus will lie on the first phase which incorporates needs finding and needs screening. As the incentive for this project already focuses on a specific idea, the Biodesign method was amended accordingly.

2.1.1 Needs finding
The needs finding consists of three steps: deciding on strategic focus, observation and problem identification and need statement. As the strategic focus was predefined, the goal was to perform the other two activities; however, since there was already a suspected problem, the problem identification was used to validate the initial idea.

2.1.1.1 Observation and problem identification
Activities performed during this step was a study during a brain tumour resection to observe how surgeons used and relied on the neuronavigation system before and during the surgery. In addition to observation, interviews were held; the method and design of the interviews is described in section 2.2.

2.1.1.2 Need statement development
The need was analysed and stated as a result of the findings from observations and interviews. It was important to be thorough when creating the need statement; the output from the need statement development phase was a stated need which was carefully composed to not include a solution or be too wide or too narrow.

2.1.2 Needs screening
Originally, in the Biodesign process, the innovator has several needs to screen through; however, as this project only handles one need, the screening was performed for that. For this thesis, the screening was performed through four steps, as follows.

2.1.2.1 Disease state fundamentals
For the disease state fundamentals, anatomy, pathophysiology, clinical presentation and economic impact etc. were researched for the disease in question, which in this case was brain shift. Data was collected through literature that describes and discusses brain shift.

2.1.2.2 Treatment options
Current treatment options were looked into from a clinical, economic, utility and emerging point of view; both technological and unconventional options were considered.
2.1.2.3 Stakeholder analysis
The stakeholder analysis was performed by considering all the stakeholders who would be affected by a solution. The analysis was limited to Swedish stakeholders.

2.1.2.4 Market analysis
In the market analysis, potential market segmentation, size, dynamics and needs were investigated. The market size was estimated with a top-down approach.

The market dynamics was evaluated by using Porter’s five-force model, which is a technique for analysing industries and competitors by stating the following facts:

1. Degree of existing rivalry
2. Threat of potential entrants
3. Bargaining power of suppliers
4. Bargaining power of buyers
5. Threat of substitutes

The use of the five-force model describes the market situation without focusing on a company or competitor in particular.

![Figure 1 Porter's Five-Force model](image_url)

In addition to the five-force model, a SWOT-analysis (Strengths, Weaknesses, Opportunities and Threats) was performed to evaluate other players on the market. The SWOT analysis discusses both positive and negative internal (strengths and weaknesses) and external (opportunities and threats) aspects of a company, to evaluate the position in relation to the current market situation. The SWOT analysis also helps to evaluate what could be the competitive advantage of a company or product, thereby helping the inventor determine the strategic focus.
2.2 Interviews

As stated in section 2.1.1.1, interviews were held to obtain data during the problem identification phase, to support the need statement. Semi-structured qualitative interviews were held with three neurosurgeons, representing different clinics throughout Sweden. The goal with the interviews was to get a differentiated view of how surgeons work at different clinics, which was the basis for selection of interviewees.

When designing the interview guide, the focus was to have different types of questions that could encourage the interviewee in different ways (Bryman & Bell, 2005). The first few questions were direct to get some relevant background information; other questions were either open ended or the interviewee was asked to give a “mini-tour”, where a situation was to be explained. The choice of performing semi-structured interviews was made since it allows for pre-defined subjects, or general questions, but the interview guide still has space for spontaneity depending on the development of the interview.

In Sweden, there are six different neurosurgical clinics, half of which were represented in the interviews. Interview guides are found in Appendix A.

2.3 General search

To be able to perform the stakeholder analysis, a general search has been conducted in order to gather relevant information on companies and current methods. The search has been performed through the use of

- Generic search engines (Google, etc.) have been used to gather information about companies that are active on the market for neuronavigation. In order to find relevant information, terms such as “neuronavigation”, “virtual reality” and “neuronavigation + company name” have been used.
- The search for scientific articles to support the underlying incentive and background information was performed using search engines PubMed, KTH Library search and Google Scholar. Search terms such as “brain shift”, “neuronavigation”, “virtual reality” and “intraoperative image update + neurosurgery” have been used.

2.4 Method discussion

The Biodesign method was chosen since it incorporates all parts of an innovation process, and has been proved to work in projects at Stanford University and Centre for Medicine, Technology and Health (CTMH). Although there were guidelines for how to perform the method, some specifics were decided on separately. The opinion is that the weakness of the biodesign method lies in the fact that it is hard to separate results from analysis, since some facts require interpretation.

---

3Collaboration between KTH, the Karolinska Institute and Stockholm County Council
What speaks for the biodesign method is the support gained from other innovation processes. Although biodesign is applied to the innovation of medical technologies, it follows a general innovation scheme that is supported by other sources. (Morris, 2011)

The scope of this thesis does not incorporate intellectual property (IP) landscaping, which is an important issue to address before continuing the innovation process. A suitable next step after identifying the market dynamics and deciding whether the market is attractive to enter, would be to investigate if developing an idea would infringe on existing IP protection.

Interviews were decided to be held semi-structured, in order for interviewees to have the possibility to reflect and discuss different questions. It also made space to interpret and give more comprehensive answers. However, the interviews were held with a varying degree of understanding of the technology and might therefore not be comparable straight off. When interpreted in the results, the interviews laid the basis for a general perception of current and future technology, and the specifics should therefore not influence the results too much. Structured interviews were only held with three interviewees, the number of which should be increased to be able to conclude a general opinion amongst the interviewees. Only one observation was made during surgery; however this well showed the area of use of the technology.

When performing the general search on companies and research, the span of information that is found is very wide. Since the results incorporated companies and papers that have closed down, or are no longer relevant, the focus was put on the three main providers of navigation systems; these have the largest impact on the market space, and constitute the companies that are represented at the Swedish neurosurgical clinics4.

The scientific article search was narrowed down as interviews and the observation provided input and understanding of the area under development; the search would be more efficient in a case where the innovator is a part of the market research team. The findings were based on top results in the searches, and might therefore exclude papers from less cited researchers or papers where the title does not match the search terms although the contents covers the area. When translating the scientific articles into the results, the focus was on the main principles of the articles. The current research should be evaluated further by someone with deeper technological understanding.

---

4 Two out of three systems are represented
3 Result

3.1 Need

The result from the observation and the interviews held confirms that there is a gap in the current technology regarding brain shift. Although there are technologies for intraoperative image update available on the market, the Swedish clinics are far from using these in the everyday operations as they are expensive or put demands on operation rooms etc.

3.1.1 Need statement

According to Kotler and Keller (2009), a need can be distinguished among five types, displayed in Table 1, which have been applied to the identified problem.

<table>
<thead>
<tr>
<th>Need</th>
<th>Explanation</th>
<th>What has been found</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stated</td>
<td>What is expressed</td>
<td>A method to account for brain shift</td>
</tr>
<tr>
<td>Real</td>
<td>What the customer really means</td>
<td>A real-time intraoperative image update method to account for brain shift</td>
</tr>
<tr>
<td>Unstated</td>
<td>What is expected, but not expressed</td>
<td>Easy to use; not prolonging time of surgery</td>
</tr>
<tr>
<td>Delight</td>
<td>What is not necessary, but would delight the customer</td>
<td>No extra, bulky, instruments or additional features to existing instruments</td>
</tr>
<tr>
<td>Secret</td>
<td>What the customer secretly want out of using the product</td>
<td>Comprehensible technology; easy to incorporate</td>
</tr>
</tbody>
</table>

Table 1 Need analysis

Looking at the needs that have been identified during the need identification, the stage in which technology is needed is different from the suspected need; surgeons express a need for an updating technique to be used during surgery, rather than in surgical planning which they don’t put much time explicitly into. From this information, the following need statement have been developed:

*An easy-to-use, time- and cost effective, intra-operative real-time image updating method that accounts for brain shift in intracranial tumour resection.*

To clarify what type of need the innovator is dealing with, it was classified as one of the following three types (Yock, et al., 2009)

- Incremental need: improvement of existing solutions
- Blue-sky need: a solution that is differentiated from existing ones
- Mixed need: a mix of the above

Since there have been research performed on biomechanical methods for prediction of brain deformation, but there are currently no solutions on the market, the need is classified as a **mixed** need.
3.2 Market
Determining the market and market dynamics is a crucial activity that needs to be performed before starting any product development. An innovator planning to enter the market should strive to find a market place that is favourable to start-ups; a desirable industry has the properties of being young which indicates less competition, not having a dominant design and where advertising and branding is of less importance. (Abrams, 2013)

When innovating medical technologies, it is also important to gather information on the disease that will be treated, since the figures on the disease could state whether there is a viable market or not. The following chapter includes the results of research on the disease, treatment options, stakeholders and market dynamics.

3.2.1 Disease state fundamentals
As stated in the introduction, brain shift is the deformation of the brain due to forces and actions performed during brain surgery; brain shift is affected by gravitational force, hence the position of the patient, loss of fluids, resection of brain tissue etc. (Liebenthal, 2011). Besides the “normal” displacement, the brain is further affected by tumour resection as the edges from which the tumour is detached collapses due to gravity and loss of elasticity. This can lead to remaining diseased tissue “hiding” behind healthy tissue, which lessens the efficiency of the surgery. (Bjartmarz, 2014)

3.2.1.1 Incidence
As brain shift occurs during all tumour resection surgeries, the incidence is estimated to be the same as the incidence of intracranial tumour surgeries, the trend of which is portrayed in Figure 2. In Sweden, the number of intracranial tumour surgeries is about 1400 per year (Socialstyrelsen, 2014), which gives an approximation of 1400 cases of brain shift per year.

![Intracranial surgery on tumours](image-url)
Figure 2 also displays the average time hospitalised when going through brain tumour resection.

3.2.1.2 Prevalence

The prevalence describes how large part of the population suffers from the disease in question. As the covered disease is in fact a state during a surgery, the prevalence only puts the incidence into perspective by comparing it to the current population. The calculation of the prevalence in Sweden is done by dividing the incidence per year with the population of that time (Statistiska centralbyrån, 2014) according to

\[ P = \frac{I}{p} \times 100 000 \]

where \( P \) represents prevalence, \( I \) represents incidence and \( p \) represents population. The result is presented in Figure 3.

![Intracranial surgery on tumours](image)

**Figure 3 Prevalence of intracranial surgery on tumours, 2007-2012**

The prevalence has slightly increased over the last two years according to statistics; although it is still low compared to other diseases.\(^5\)

3.2.1.3 Mortality

Since there is no commonly used method for measuring brain shift intraoperative, the surgeon always has to estimate how much the brain has deformed; the evaluation made by the surgeon reflects on the overall situation of the surgery, not brain shift explicitly (Lindvall, 2014). Therefore, it is hard to state the number of deaths that have occurred as a direct result of brain shift. However, a correlation between extent of tumour removal and survival has been found (Orringer, et al., 2012), suggesting that better management of brain shift could decrease the mortality rate.

\(^5\) Pacemaker insertion has a prevalence of 65-75 people per 100 thousand
3.2.1.4 Economic impact
A potential consequence of brain shift is the risk of tumour residues after resection; therefore, when looking at the economic impact of brain shift, one can study the cost of a possible second surgery to remove tumour residues. The cost for brain tumour removal is suggested to be approximately $26,500 (Healthcare Bluebook, 2014), corresponding to approximately SEK 173,000 (currency as of April 29th, 2014). No explicit data was found on how many cases of tumour residues lead to reoperation, but looking at the cost it is clear that it has an economic impact because of the large cost per person.

3.2.2 Treatment options
The term treatment options might in this case be misleading, since the potential solution would not have treating functions in itself. However, when looking at the stated need, the treatment options comprise current methods used to account for or measure brain shift during tumour removal. Except for already existing methods, the methods that are currently in research were also considered. Information on current research is found in the status report in section 1.1.1.

Each treatment option has been evaluated according to pros, cons and cost range, which can be used to identify the gap on the market.

3.2.2.1 Surgical estimation
Although not requiring technology, the intraoperative estimation made by the surgeon is considered to be an option that meets the need.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>Cost range</th>
<th>Companies/research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quick</td>
<td>Subjective</td>
<td>No cost; cost of prolonged operation duration is marginal</td>
<td>-</td>
</tr>
<tr>
<td>Surgeons are used to assess the situation along the surgery</td>
<td>Depends on experience</td>
<td>No sustainable data to back-up decision</td>
<td>-</td>
</tr>
</tbody>
</table>

3.2.2.2 Biomechanical models
Biomechanical models are under development by several researchers over the globe, in the search for a new way of accounting for brain shift during tumour resection.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>Cost range</th>
<th>Companies/research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real-time update</td>
<td>Not developed enough to be used in clinical setting</td>
<td>-</td>
<td>Wittek et al. most successful</td>
</tr>
<tr>
<td>Accurate images</td>
<td>Needs large data capacity</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Requires fast computations of intraoperative data into model</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The cost range for biomechanical models is hard to state, since it would depend on what computer capacity is needed etc., versus what hospitals already use.

### 3.2.2.3 Intraoperative MR
Intraoperative MR is viewed as a very reliable intraoperative imaging method, and is commonly used as reference data in studies of other methods. MR is also used as the preoperative imaging modality, the images of which surgeons base their surgical plan.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>Cost range</th>
<th>Companies/research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Detailed images</td>
<td>Time consuming – increasing operation duration</td>
<td>High; cost-benefit ratio under active investigation</td>
<td>BrainLAB, Medtronic</td>
</tr>
<tr>
<td>Real-time data</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Same modality as preoperatively</td>
<td>Expensive; requires adapted operation rooms (ORs) and equipment</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3.2.2.4 Intraoperative ultrasound
Intraoperative ultrasound is not a commonly used modality but has good potential of increased usage (Tisell, 2014).

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>Cost range</th>
<th>Companies/research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real-time data</td>
<td>Image quality</td>
<td>Low; ultrasound is a cheap modality with high presence in hospitals</td>
<td>BrainLAB (ultrasound integration), Medtronic (SonoNav), SonoWand Invite</td>
</tr>
<tr>
<td>Can be fused with preoperative images</td>
<td>Interpretation of images, especially for less experienced surgeons</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### 3.2.2.5 Intraoperative CT
CT is another option of receiving updated images during surgery; however, since CT is based on ionising radiation, it is not as efficient in displaying soft tissues and difference in soft tissue structures. CT is not commonly used for intraoperative image update in tumour resection surgeries.

<table>
<thead>
<tr>
<th>Pros</th>
<th>Cons</th>
<th>Cost range</th>
<th>Companies/research</th>
</tr>
</thead>
<tbody>
<tr>
<td>Real-time data</td>
<td>Displaying of soft tissue structures (tumour vs. healthy tissue)</td>
<td>Moderate; CT is expensive, but C- and O-arms have high presence in hospitals</td>
<td>Medtronic (O-arm), BrainLAB (Airo-Mobile Intraoperative CT), etc.</td>
</tr>
<tr>
<td>Image quality</td>
<td>Ionising radiation</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time effective examination</td>
<td>Prolonging operation duration</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Requires immediate image processing and transfer</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
3.2.2.6 Other options

Except for those mentioned above, there are other imaging modalities that are used in neurosurgery.

**Positron emission tomography (PET)** is a functional imaging technology that displays the activity of the brain (Liebenthal, 2011), i.e. it can locate a tumour because of the higher activity of the tumour cells. In order to locate the activity relative to the anatomy, PET can be combined with either CT or MRI. Although PET combined modalities deliver detailed images, the technology combinations would still carry the cons of stand-alone CT or MRI, in addition to increasing in price. However, if solutions would become more integrated, this could be a future option.

**Functional MRI (fMRI)** is another functional neuroimaging procedure, which measures activity based on changes in blood flow. (Liebenthal, 2011) As well as PET, fMRI should be combined with an anatomical image to provide extensive information, and the technology is not widely used in the clinical setting; however, this is one technology that can be used in multimodal neuroradiological images that can be useful in neuronavigation. (Wakabayashi, et al., 2009)

3.2.2.7 Comparison of treatment options

After considering the treatment options one-by-one, a comparison was made to clearly identify where there is space for innovation. Five different benefits were reflected on in the comparison, which is presented in Table 2.

<table>
<thead>
<tr>
<th>Objective</th>
<th>Surgical estimation</th>
<th>Bio-mechanical models</th>
<th>iMRI</th>
<th>Intraop. Ultrasound</th>
<th>iCT</th>
<th>Innovation space</th>
</tr>
</thead>
<tbody>
<tr>
<td>Easy-to-use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Time effective</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High resolution</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cost effective</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Table 2 Treatment landscape, ○= poorly met, □= moderately met, ▲= met

As viewed in the comparison of methods, there is market space that has not yet been filled, which means that there is room for innovation. From the comparison, it also becomes clear what would be the some of the competitive advantages for a product containing these benefits.

3.2.3 Stakeholder analysis

Before analysing how the stakeholders are affected by the need, and a new solution, they have to be identified. To properly identify the different stakeholders is especially important in the life science field, since the customer and the payer might not be the same person; therefore, it is also important to identify and consider the reimbursement system of the healthcare system which is primarily targeted.

- **Patients** – patients are not consciously affected by the need, since they do not interact with any of the current treatment options. Patients are however highly affected, since
it is their treatment that could be improved. The stakeholder category patients include people undergoing tumour resection surgeries.

- **Physician** – it is primarily the surgeon who is affected by the stated need, since he/she is the one performing the surgery. However, tumour residues can indirect affect other physicians such as the oncologists, who are planning the continued treatment.

- **OR personnel** – the OR personnel, such as operation nurse, are affected by the need since their workflow is dependent on the technology used in the OR.

- **Facilities** – facilities such as the OR, storage space, etc. are affected since technology solutions like MR or ultrasound requires that the facilities meet certain criteria (physical space, air flow etc.).

- **Potential partner** – since neuronavigation systems are already in use, an additional service would either have to be compatible with all systems, or sold together with one of the existing systems, the owner of which would become a partner company.

- **Payer** – it is important to be able to show a positive health economic result to convince the payer of the use of the product. Who the payer is will vary throughout different reimbursement systems, which means that different payers are affected at different levels; however, the payer will ultimately be affected through the cost of the product. In the Swedish healthcare system, the payer is the 20 different county councils.
<table>
<thead>
<tr>
<th>Stakeholder</th>
<th>Primary benefits</th>
<th>Primary costs</th>
<th>Assessment of net impact</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Patients</strong></td>
<td>Safety of decisions made by surgeon during surgery</td>
<td>Longer surgery</td>
<td><strong>Positive</strong>: Decisions made during surgery would be more reliable, decreasing the risk of surgery</td>
</tr>
<tr>
<td></td>
<td>Improved clinical outcome</td>
<td>Higher cost of surgery(^6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Physician</strong></td>
<td>Data for decision making</td>
<td>Learning of new technology</td>
<td><strong>Positive</strong>: Neurosurgery is an innovative surgical area, with surgeons used to adapt to new technology</td>
</tr>
<tr>
<td></td>
<td>Intra-operative, real-time update of the brain dynamics.</td>
<td>Potentially more equipment</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Possibility to virtually perform the surgery in advance</td>
<td>Adapt workflow to new technology</td>
<td></td>
</tr>
<tr>
<td><strong>Other OR personnel</strong></td>
<td></td>
<td>Adapt workflow to new technology</td>
<td><strong>Negative</strong>: OR personnel who are not involved in the decision making will only be affected by the adapted workflow or prolonged operation duration</td>
</tr>
<tr>
<td><strong>Facilities (dependent on treatment option)</strong></td>
<td>Possibly no additional physical space/OR amendments needed (biomechanical models, ultrasound)</td>
<td>Additional IT capacity</td>
<td><strong>Positive</strong>: It is easier to procure new IT than remodel the hospital premises</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Possible amendments of physical space/ORs</td>
<td></td>
</tr>
<tr>
<td><strong>Potential partner</strong></td>
<td>Competitive advantage</td>
<td>Economic cost of in-licensing/collaboration</td>
<td><strong>Positive</strong>: By partnering, a larger company does not have to put in-house efforts into development and should instead in-license expertise</td>
</tr>
<tr>
<td></td>
<td>No cost of in-house development</td>
<td>Less control of technology development</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Quick adaption of technology; no development time</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Payer</strong></td>
<td>Decreasing risk of additional treatment; lower cost for total treatment</td>
<td>Higher cost per single treatment</td>
<td><strong>Negative</strong>: No economic winning through “soft values”</td>
</tr>
<tr>
<td></td>
<td>Delivery of safe treatment</td>
<td>Cost of buying</td>
<td></td>
</tr>
</tbody>
</table>

Table 3 Stakeholder analysis

To get another view of different stakeholders, they are identified in three different spheres: professional, market and government. The three spheres have different structures in the sense that the stakeholders have different values; the structures are normative, cognitive and regulative respectively (Hidefjäll, 2014). In this case, the classification would be

- **Normative**: physicians, who decide what is used in the daily practice
- **Cognitive**: existing neuronavigation providers, who sets the standard for technology to function with

\(^6\) Depending on reimbursement system
- Regulative: regulatory institutions such as the FDA or regulatory bodies, who controls market approval etc.

### 3.2.4 Market size

A study has shown that intra-operative image update leads to better patient outcome in terms of complete tumour resection (Senft, et al., 2011). The authors found that complete tumour resection was accomplished in 96% of the surgeries with intraoperative image updating, compared to 68% for the control group. If these results are generalised, there is a 28 percentage-points higher chance of complete tumour resection when using intraoperative image updating.

Figure 4 and 5 shows an estimation of how much money can be saved if reoperation and increased radiation therapy, respectively, occurred in 10% of the cases where the tumour removal is incomplete, i.e. a health economical evaluation of different scenarios.

![Figure 4 Top-down economic evaluation, focus: surgery](image)

As seen in Figure 4, the economic benefit from using an additional technology is not very high; however, there is a positive result which generates opportunity for closer evaluation of the cost of using a technology.

A common treatment that is used in combination with surgical tumour removal is radiotherapy, i.e. to kill or slow down tumour cells by using ionising radiation. One aspect of the radiation dose planning is the size of the cancer, indicating that a higher dose would be used when there is a large amount of tumour residues (Cancer Research UK, 2014). Whether additional radiation is possible to give depends on the location of the tumour, previous radiation dose, type of tumour and age of the patient (Texas Oncology, 2014).
Radiation therapy costs are approximated to SEK 25,000\(^7\) per patient (Socialstyrelsen, 2014). Compared to the evaluation of reoperation, this economic benefit is smaller.

If instead looking at market forecasts, the surgical navigation systems (SNS) market is growing throughout several geographical markets. In Western Europe, the SNS market is forecasted to grow to $372.7M by 2018, at a compound annual growth rate (CAGR) of 5.2\% (Frost & Sullivan, 2013). The corresponding numbers for image-guided surgery\(^8\) in the Asia-Pacific region are $110.9M at a CAGR of 10.2\%, where Japan is the fastest growing market (Frost & Sullivan, 2014). The US SNS market is forecasted to reach $195M by 2016 at a moderate growth rate (Millenium Research Group, 2012).

Although the SNS market includes more than neuronavigation, the before mentioned forecasts still indicates a strong trend of a growing acceptance for surgical navigation systems. Frost & Sullivan (2013) determines that there is a high and increasing need for innovation and that one of the market drivers is acceptance, which is estimated to increase over time. They also state improved outcomes and shortened hospital stays as strong motivators to the market increase; as seen in Figure 2, the average time hospitalised has been relatively stable over the past years, which could indicate that a large change is needed for this metric to improve.

In Western Europe, neurosurgery represented 15.2\% of the SNS market in 2011, corresponding to a market size of $39.9M (Frost & Sullivan, 2013). If neurosurgery were to follow the same growth rate as SNS in general, the following market size will be obtained (displayed in Figure 6).

---

\(^7\) Cost is estimated from cost of breast cancer radiation therapy. Both treatments have a radiation dose of ~50Gy.

\(^8\) Includes SNS
The estimation in Figure 6 is based on the capturing of the Scandinavian market, which is forecasted to be the second smallest market in Europe by 2018 (Frost & Sullivan, 2013). To only reach one market is however highly unlikely, as all of Western Europe follow the same regulatory framework; that said, if one reaches the market with a diversified product in the neuronavigation area, it is likely to capture a larger part of the European market even if Scandinavia would be the first point of entrance.

Even though the market is expected to grow, there are some restraints that companies have to face during the upcoming years. First of all, healthcare systems are bootstrapping because of the growing population, and the impact will increase over time. This will slow down the technology adoption as hospitals have a higher barrier for buying new technology. Secondly, the introduction of a new technology requires learning by healthcare personnel, which also speaks against technology adoption. (Frost & Sullivan, 2013) This has also been expressed by surgeons, who state that the handling of technology needs to be quick and easy, since they don’t have time to work a long time with software (Bjartmarz, 2014). However, surgeons also consider the neurosurgical area to have come far in technology development and adoption (Tisell, 2014).

3.2.5 Market dynamics
Determining the market dynamics is an important step before deciding whether to go into a market or not, since it will give an estimation of the chance of succeeding in that market. The market dynamics takes into account the current players on the market, as well as the starting position of the company that considers a market entrance.

The market dynamics analysis is divided into three parts: a SWOT analysis of the current situation, a competitive analysis of the existing competitors and an analysis of market forces that sums up the industry situation.
3.2.5.1 SWOT

The following SWOT analysis is based on the possibilities of the research group at the unit for neuronic engineering at KTH Royal Institute of Technology in Stockholm, Sweden.

Strengths
The research group have previously developed technology that has shown successful results, indicating that there is a strong base to work from. Good experience with biomechanical models increases the chance of succeeding with a new application area.

Because of the connection to the Karolinska University, there are good relationships between KTH and personnel at the university hospital. This strengthens the possibility of developing a technology that could be clinically useful, because of the input from potential users in the role of medical advisors etc.

Weaknesses
By being located in Sweden there is a small home market, with only six neurosurgical institutions to reach. For the product to reach a larger mass of customers, it would be necessary to go international early on, which requires intellectual property (IP) protection and regulatory alignments for more than one market.

Opportunities
Since no other research group has launched a clinically viable product, there is room for innovation on the market. By being the first player in the market, a company has the opportunity to set a market standard for the product, and thereby be a part of how the market space will develop.

Even if a company is not the first to enter the market, there is still opportunity to gain success. If there is another player entering the market before, that company could face the challenge of market acceptance – by entering afterwards, it will be easier to reach out to the general mass of customers straight away instead of just the early adopters.

Threats
The threats on the market place consist of possible competitors who could enter the market, and thereby gain a first mover advantage. This could give rise to problems with IP, freedom to operate, a more saturated market space and put demands on pricing strategies.

Another threat is lack of sources of funding; for the technology to be turned into a scalable business idea there is a need for funding. The available funding on the Swedish, and Nordic, market is limited with only a few venture capitalists and limited amounts of soft money. Funding is especially hard to get in the seed stage\(^9\) (Tillväxtanalys, 2013), which could lead to problems with scaling the business and make market expansion unavailable.

Connected to the small home market, there is also a threat in having to overcome international legislation. Although there are globally harmonised initiatives regarding quality etc., individual states are encouraged to draw up national guidelines and regulations (World Health

---

\(^9\) Only 3% of invested capital 2012
Organization, 2014) that has to be followed by companies that enter those markets. This could become a capital requiring activity, depending on the level of harmonisation.

3.2.5.2 Competitive analysis

The competitive analysis incorporates several aspects to map the features of the main competitors. This analysis can help reveal gaps on the market, and indicate what strategies should be adopted if entering the market.

There are three primary competitors in the SNS market (Frost & Sullivan, 2013), namely Medtronic, Inc., BrainLAB AG and Stryker Corporation. According to Frost & Sullivan (2013), the market concentration\(^\text{10}\) for the total image-guided systems and robot-assisted surgery market is over 70%, which indicates that the market concentration is high within the SNS market as well; this means that, when discussing navigation systems for tumour removal surgeries, the mentioned companies are the ones to primarily focus on investigating.

The following paragraphs present the analysis of the three main competitors working in the SNS market, focusing on a few main aspects.

Medtronic

Medtronic, Inc. is an American medical device company that operates worldwide, with the largest markets in Western Europe, US and Japan. Medtronic’s neuronavigation system is called StealthStation; in addition to StealthStation, Medtronic also provides intraoperative MR, ultrasound and intraoperative CT, which can be used together with the navigation system.

The company reports revenues divided into different areas; neurosurgical navigation is included in the surgical technology category. Medtronic have during recent year experienced increasing revenues which is displayed in Figure 7, and explains the increase in revenues from “sales of capital equipment”, including StealthStation. Their stated primary competitors include BrainLAB and Stryker, which is in accordance with other market statistics. (Medtronic, Inc., 2013)

![Figure 7 Revenue trend, Medtronic, Inc.](image)

\(^{10}\) Percentage of the market held by the top three competitors
Looking at Medtronic’s total revenue, the geographic revenue mix shows that the US is the largest market by far and stands for over half of the total revenue (55%). Other top markets are Western Europe and Canada (24%) and Asia Pacific (11%). (Medtronic, Inc., 2013)

**Strengths**  
Medtronic is an established company; in 2013 they passed the number of 4000 StealthStation systems installed worldwide. The company have a strong brand image and a large portfolio, which increases the chances that customers have come across Medtronic devices before.

**Weaknesses**  
While being the world’s largest medical device company, Medtronic offers a wide range of products within a few different product categories. This leads to a large budget where resources need to be carefully allocated to make sure that the company makes smart investments within relevant R&D areas; this might lead to lack of investment in certain areas that are not as economically beneficial, depending on the company’s strategy. Also, from being a publically traded company, it is important for Medtronic to deliver good results to keep the size of the market capitalisation.

**Opportunities**  
Medtronic has a strong financial position, and has the ability to acquire smaller companies and/or IP to increase the product portfolio. Besides buying competence, Medtronic has an increasing trend (CAGR 4.3% 2009-2013) regarding investment in research and development, making it possible to develop new and current technologies. Medtronic has also relocated the R&D activities to new regions such as India and China, which opens up for cost-savings and therefore releasing more capital. (Trefis Team, 2014)

**Threats**  
During 2013, the return to shareholders decreased compared to 2012 after going up for several years. If this is the start of a downward trend, this could affect the company’s position on the market and its ability to attract shareholders.

A possible threat for future operations is if Medtronic cannot capitalise on previous and/or future acquisitions; inefficient strategic moves can be costly for the company, and would have to be compensated for in order to not lose too much economic resources.

**BrainLAB**  
BrainLAB AG is a German medical device company that is privately held. BrainLAB offers a wide range of products; within the neurosurgical area, the BrainLAB neuronavigation constitutes the product offering together with intraoperative MR and ultrasound.

BrainLAB is a private company, and therefore doesn’t provide official company performance reports. However, the company shares general information, which gives an indication on the market position. BrainLAB presents a revenue of $144,3M (€105,5M) for the surgical area in the fiscal year of 2012; the total revenue increased with 9% from the previous year, with the two revenue streams *product sales* and *services*, displayed in Figure 8. (BrainLAB AG, 2012)
Looking at the current trend, the revenues gained through services have increased more from 2011 to 2012, compared to product sales. This would indicate that additional services to existing hardware are an increasing market; however, it generates less money than product sales.

Despite originating from Europe, BrainLAB experiences the highest revenue from North America, which represented 44% of total revenue in 2012; this was followed by Europe and RoW (31%) and Asia (25%).

**Strengths**
BrainLAB have a strong distribution network and operates worldwide. The company is one of the main competitors in both Western Europe and Asia-Pacific (Frost & Sullivan, 2013). Furthermore, BrainLAB is a company who originally focused on software, and therefore have a good basis for future development in the software area.

**Weaknesses**
BrainLAB has experienced product recall from the FDA at several occasions (U.S. Food and Drug Administration, 2014), which indicates that there is a lack of control over the products that reaches the market and that substantial testing might not be in place.

**Opportunities**
The company has engaged in several strategic partnerships to strengthen its global market position. Through the partnerships the company gains opportunities through complementary technology, know-how and distribution channels. There is also an opportunity in software upgrades because of a matured market for neurosurgery; if this opportunity is captured, this means a chance of a stronger business. (BrainLAB AG, 2012)

Since BrainLAB is a privately held company, they have an opportunity in going public to raise capital if needed.
**Threats**
The above mentioned product recalls can harm the brand image even though the neurosurgical application has not been recalled. If customers believe that BrainLAB lack in safety, there is a risk that the company will not be considered when choosing a navigation system.

**Stryker**
Stryker Corporation is an American medical device company that is available in over 100 countries through local distributors and direct sales forces. Stryker has its main market in the US, which represented 66.3% of the total revenue in 2013. (Stryker Corporation, 2014) The neuronavigation system offered by Stryker is called *iNtellect Cranial* and is an integrated hardware and software solution.

Stryker divides the revenues into three main areas, which are divided further into product categories. The neuronavigation system falls under the *Instrument* category, the revenue trend of which is displayed in Figure 9.

![Figure 9 Revenue trend, Stryker Corp.](image)

As seen in the revenue trend, sales revenues have been increasing; however, the segment has not grown significantly over the past years.

**Strengths**
Stryker manufactures both hardware and software in-house, which means that they have control over the technology development, and thereby can justify the products. The company has a long history in the neurosurgical navigation field, with presence since 2000, and therefore has the experience needed to develop good products. (Stryker Corporation, 2006)

**Weaknesses**
The company is currently (2013) involved in the defence of product liability issues; as well as for BrainLAB, this could affect the overall brand image and thereby affect the business and revenues.

As mentioned above, Stryker performs all development in-house, which also could be a weakness. If problems occur with the technology, there is an in-house problem which could be harder to solve than an external solution.
Opportunities
Stryker has over the past year increased its investment in research and development, with a percentage increase of 13.8% from 2012 to 2013. (Stryker Corporation, 2014) This suggests that the company puts focus on the development of new and existing products, which furthermore could strengthen the market position.

Threats
Even though the company has seen increase in revenues, there has only been a small change in the instruments sector. As competitors continue to grow their businesses, Stryker should generate a higher increase in revenue to keep up with the market.

Strategic actions
Since the three main competitors in the SNS market currently don’t use biomechanical model to complement their navigation systems in neurosurgery, it is of relevance to look at their previous strategies to assess if it could be of interest to initiate collaboration.

Figure 10 displays the strategic actions that were undertaken during the last decade in the image-guided systems and robot-assisted surgery market. The primary reason for creating alliances was technology development, while acquisitions were, in all cases but one\textsuperscript{11}, completed to expand the companies’ range of products (Frost & Sullivan, 2013).

![Figure 10](image)  
Figure 10 Overview of strategic actions in Western Europe, 2002-2012

As seen in Figure 10, Medtronic have focused on acquisitions while BrainLAB have entered more alliances during the past decade; Stryker have been passive in the mergers and acquisitions activities. As the compilation above does not account for any specifics of these strategic activities, the company specifics are stated in Figure 11.

\textsuperscript{11} Medtronic acquired Ventor Technologies (IL) as a part of a market expansion
As seen in Figure 11, Medtronic have made 1-3 yearly acquisitions during 2007-2011, and the only recent alliance was introduced over ten years ago. This would indicate that Medtronic, as a leading medical device company, rather acquire smaller companies than engaging in collaborations to develop their technology. Unlike Medtronic, BrainLAB have focused more on strategic alliances, only introducing acquisitions in 2012. Most of the activities have taken place during recent years, which indicates strive for technology development by leveraging on collaborations and joint ventures.

Research groups
Research within the area of brain shift in combination with image guided surgery has primarily focused on the use of biomechanical models, based on the finite element method (FEM), to predict brain shift during tumour removal. A team that has published several articles on the subject is the research team at University of Western Australia (UWA), who previously have worked on biomechanical modelling of the brain.

Strengths
The UWA team is strong and have experience in the biomechanical models area. The team have produced several publications with good progress in the area of brain shift modelling.

Weaknesses
Research is taking place in Australia, who does not operate according to the teacher’s exemption, therefore any IP that is generated will belong to the university which makes it harder to commercialise a product that was generated from research.

The home market for this research group is not the most lucrative; hence it would be necessary to reach international markets quickly, which puts higher demands on IP and regulatory work.

Opportunities
Since the team have already started testing the model, and therefore are well into development, they have an opportunity of getting to market first, if they manage to develop a product that is clinically approved.

Although IP ownership could be weakness by decreasing the chances of commercialisation, the fact that IP belongs to the university could also be an opportunity, if the product makes it
to the market. A university has a better financial starting point which can be useful both for filing for IP and if a product would infringe on another patent.

**Threats**
The threat towards a university research group, if trying to commercialise, is if more established companies decide to go into the same market; without a large budget it is hard to drive technology development in the same pace as larger, well-funded companies.

3.2.5.3 *Porters five forces*
Porter’s five forces (P5F) is a market analysis model that determines the industry attractiveness with a specific firm’s external environment in focus. Unlike the SWOT analysis, P5F only focuses on how external forces affect the specific firm relative to other companies.

As with the previous SWOT analysis, the analysis of P5F is based on the possibilities of the research group at the unit for neuronic engineering at KTH Royal Institute of Technology in Stockholm, Sweden. A brief overview of the forces and impacts is presented in Table 4.

<table>
<thead>
<tr>
<th>Force</th>
<th>Market situation</th>
<th>Degree of risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Existing rivalry</td>
<td>Research – several research groups working in the field</td>
<td>High</td>
</tr>
<tr>
<td>Threat of potential entrants</td>
<td>Research – researchers have already been performing trials; could potentially be entering market</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Existing navigation companies – large companies, high R&amp;D investments</td>
<td>Moderate</td>
</tr>
<tr>
<td>Supplier power</td>
<td>Potentially used material is assessed to not be very specific; the ability to negotiate good terms is estimated to be good</td>
<td>Low</td>
</tr>
<tr>
<td>Buyer power</td>
<td>Acceptance by healthcare system; not only customers, but also reimbursement systems that have to be taken into consideration</td>
<td>High</td>
</tr>
<tr>
<td>Threat of substitutes</td>
<td>Surgeons are more familiar with more traditional imaging modalities.</td>
<td>Moderate</td>
</tr>
<tr>
<td></td>
<td>Incorporating existing imaging modalities could require capital, remodelling of ORs, prolonging of operation times etc.</td>
<td></td>
</tr>
</tbody>
</table>

Table 4 Summary of market forces

1 Degree of existing rivalry
Since there is neither any current product development of biomechanical models nor any products placed on the market, the existing rivalry consists of other research groups who are working in the area.

There are several researchers who have published within the area, although the group who are leading in this area is the research group at the University of Western Australia. This
concentration of successful research groups stretches the market into a monopoly; however since there are other players in the market space, it is not literally monopolistic.

As stated in the status report, the articles published up until today are not highly differentiated from each other, i.e. most researchers are following the same ideas of non-linear finite element modelling. A lower degree of differentiation increases the rivalry between existing research groups.

2 Threat of potential entrants
Since neuronavigation has been developed during the last couple of decades (Stryker Corporation, 2006), it is still an innovative area where more can be developed. These properties make it more likely that there will be new entrants in the area of solving neuronavigation despite brain shift.

The entry barriers for this market are quite high for start-ups, which lowers the threat of potential entrants. Since there is no current biomechanical model that is clinically approved, a new entrant would have to perform clinical trials to validate the safety of the product, which increases the economic cost of entering the market. Furthermore, the first mover on the market has to tackle the issue of regulation and reimbursement systems.

What on the other hand increases the threat is growth potential of this market segment. As there is no product that has set a dominant design, there is a large opportunity for a first mover to capture a large market share, and thereby also be profitable.

The potential entrants are

- Research – if researchers manage to develop technology that is viable in a clinical setting, there is an opportunity to enter the market
- Existing neuronavigation systems providers – the large players on the SNS market is currently focusing on connecting their devices with intraoperative technology such as MR. However, if they decide to go into the biomechanical models market as well, they are a threat to other potential entrants

3 Bargaining power of suppliers
The supplier power is determined by the number of suppliers and the amount bought from them. Since it, before planning the product development, is hard to determine which suppliers a firm would have to have, it is also hard to determine what amount of power they would have. However, since the idea of biomechanical models does not require specific material such as raw material, the power of potential suppliers is estimated to be low.

4 Bargaining power of buyers
The bargaining power of buyers is decided by to what degree a company is reliant on a few customers, i.e. the fewer the customers, the higher bargaining power do the customers have. Since the customer is included in the healthcare system, this is not as simple as it would be for a regular consumer product. The bargaining power is not only dependent on the customer, but the reimbursement system as well.
Furthermore, there are a few factors that will adjust the bargaining power of buyers

- Whether the product can be included in the reimbursement system – if a company can convince buyers that the product is viable health economically, there is a larger chance of product acceptance
- Key opinion leaders (KOLs) – if KOLs are “recruited” or not will affect the power of buyers
- Who is targeted – if the goal is to sell to each hospital there are a significantly larger amount of customers than if the target segment is SNS providers

Although there are several things to be taken into consideration, the bargaining power of buyers is still high since there is a need for acceptance by the healthcare system.

5 Threat of substitutes
Substitutes are defined by technologies and/or companies that are not competitors, but fulfil a strategically equivalent role for customers (Kotler & Keller, 2009); in this case, this means other solutions that provide the surgeon with intraoperative image updating. Whether these solutions constitute a threat or not is influenced by function, relative price, ease of use etc.

The possible substitutes for a biomechanical model of the brain are the ones stated in treatment options, i.e. iMR, iCT and intraoperative ultrasound. These are technologies that have already reached the market, and are currently in use.

Currently, the threat of hospitals introducing iMR as a standard when performing tumour resection is relatively low, since MR is very expensive and would prolong operation times. Also, it puts requirements on the design of ORs, which might not be fulfilled already. iCT, which could consist of a C-arm that is commonly used in hospitals today, does not provide detailed information about the tissue changes, and is therefore not likely to be a serious threat.

Something that could compose a larger threat is intraoperative ultrasound if it became more widely spread. Ultrasound is a relatively cheap imaging modality, and if surgeons learn how to interpret the information provided from the ultrasound measurements, this could be a cost- and time effective solution to intraoperative image updating.
4 Discussion

The purpose of this thesis was to investigate the market need, size and dynamics for a suspected need for a new technology to be used in neurosurgical planning. The results were collected through several different methods, including observations, interviews and studying of market dynamics and existing companies on the market.

The first part of this thesis work was to validate the suspected need. After collecting information from the actual healthcare setting, by performing an observation and interviews with surgeons, the need had to be rephrased to instead incorporate image updating during surgery. When getting a new perspective on the usage of current technology and the gap in the product offering, the remaining thesis work and analyses were amended to support the new focus. Due to the fact that the validation process did not prove the suspected need to be right, but rather put light on the actual need that is experienced by the target users, the analysis becomes more accurate relative to the end setting in which a solution would end up in. This also proves the value of investigation prior to product development and how, by working according to this process, the product development process becomes more efficient.

Secondly, the market size and dynamics were to be determined by studying disease state fundamentals, stakeholders and current players on the market. The results showed that, depending on the development of current research, there is an innovation space that could be filled. However, results also showed that the technology might not be financially motivated, although the market is estimated to grow annually during the upcoming years.

When the market size was estimated in terms of the health economic analysis, the calculations were based on a single report which stated statistics on the correlation between complete tumour resection and survival. Although this makes the calculation very generalised, it could still indicate of which magnitude the economic savings could be. The result showed a relatively low economic impact from the “disease” when looking at Sweden and if the estimation is accurate the financial argument of this technology is weakened, and it should therefore be backed up by other benefits that would be obtained.

The SNS markets show good forecast, especially the Asia-Pacific (APAC) region, where the CAGR exceeds 10%. In general, APAC are emerging markets with a large population, and will therefore continue to be an upcoming market that advantageously could be targeted. The focus target market for this analysis was instead the Scandinavian market, since it would be the home market for a company generated from KTH; the Scandinavian neurosurgical navigation systems market only shows a forecast of about $2M, which is relatively low if a company cannot capture a very high market share. However, as stated in the results it is not likely to only capture the Scandinavian market if a clinically approved product was launched as an addition to the SNS field. One of the market attitudes that was found was the focus on the patient, which would be good for the kind of product in mind, since it could decrease the influence of the economic cost/benefit argument.

Looking at the market dynamics investigation, the treatment option analysis shows that there is room for innovation; however, since there are researchers already working in the field, the
development of their models will determine whether there will be an empty market space or not. The fact that there is technology under development lowers the accuracy of the analysis, which is an important part of deciding if one should enter the market. Another treatment option that has potential of growing stronger is ultrasound, if promoted correctly. The possible increase of use of another treatment option also affects the potential entrance negatively.

Other possible entrants on the biomechanical models market are the current SNS providers, i.e. Medtronic, BrainLAB or Stryker. Even if it is possible that one or more of these companies would enter the market, it would seem unlikely when looking at their mergers and acquisition trends; almost all strategic collaborations or acquisitions was made to expand the technology offering, which indicates that the companies might not put in-house effort into the development of this specific application.

From the results there are several areas that should be discussed before concluding whether it would be viable to continue the product development process. Following are the areas to be considered.

4.1 Regulatory
As stated, there is currently no clinically accepted product on the market, which would affect the product development process regulatory wise. Assuming that the first step in regulatory compliance would be to receive a CE mark, the inventor would have to perform a risk analysis to assure the safety of the product; this could either be done through clinical trials or by proving similarities to previously accepted products. Since the latter option is not available, there is only one choice.

Clinical trials have the disadvantage of being expensive and require human capital, both for setting up and managing the trial and the test persons who will participate. The trial process also takes time, and requires a place to perform the trial which preferably would be a neurosurgical institution since there is a need for the test setting to include a reference system.

4.2 Reimbursement
I the medtech industry there is a high focus on the reimbursement system in which a new product will be placed, and that the products that are developed are reimbursable. If looking at Sweden, in order to get a reimbursement code, health economic data is needed. The economic analysis conducted in this thesis indicates that there should be financial winning for the healthcare funders if a solution to intraoperative image update was introduced. The study of the economic impact in this thesis is not very thorough, and if an innovator decides to enter the market, a more comprehensive study should be made to try to prove the economic benefit of using intraoperative imaging update that accounts for brain shift.

That a product is reimbursable is decisive for the sales potential, a question to be asked is however if it is possible to get around the reimbursement codes by targeting SNS providers as the customers. If, by offering a program for image updating as an additional service to existing neuronavigation technology, that is a reason to choose the target segment to be one or more SNS providers.
4.3 Business strategy

There are several aspects to consider when deciding what marketing and business strategy should be chosen for a business idea. The main choices are

- **Partnering with SNS provider.** A partnership or strategic collaboration would be effective in the matter of getting an existing customer base and be able to leverage on those relationships. Starting collaboration could also speed up the time to market and reduce the costs, since the need for sales force decreases. The disadvantage with partnering is the one has to share the revenues, which means less net income for the inventor.

- **No partnering.** The strategy could instead be to develop a product that is applicable to all neuronavigation systems, and sell it directly to the clinics. This would mean a larger amount of customers, since all neurosurgical clinics do not use the same systems; however, this puts pressure on the company sales and the reimbursement plan for the product.

- **Looking for exit.** A third strategy would be to not enter the market, or to only target a smaller segment before looking to exit the market through a sales deal. In order for this to work, the inventor has to have increased the valuation in the company for it to be attractive and get a good valuation, which can be costly since valuation is mostly increased by actual assets such as IP, sales etc. However, a plan to exit means less maintenance of the product sales or collaboration partnership.

If looking at the current SNS providers’ strategic history, BrainLAB has a trend of entering strategic partnerships, which suggests that this could be a good company to initially target if the strategy is to stay on the market and continue development in a collaboration. Medtronic has instead a history of acquisitions which, together with the spread of their system, makes them attractive for an exit. To decide on how to target the company, one should look into the previous acquisitions to see what strategy Medtronic has had during those. Stryker seems to be the smallest of the three market leaders, which could be a positive thing; if choosing to collaborate with Stryker, the partnership could benefit both companies, since Stryker should aim for a larger market share and therefore need to strengthen their competitive advantage. However, the disadvantage is that the technology is not as widely used today, which means a smaller existing customer base, but could on the other hand open up for a more lucrative deal.

If the aim is to exit within 5 years for example, the pressure on the company increases since the valuation has to be quite high in order to get a good deal. Valuation is, as said, increased by assets such as IP, which in turn requires capital since international IP is expensive to acquire.

**Sustainable competitive advantage**

Since the researchers working in the area are looking at similar things, an innovator has to find a sustainable competitive advantage if deciding to enter the market. Even if one is the first mover, the value proposition must include something that is hard to take after in order to prevent future competitors from taking market share.
A good and differentiated sustainable competitive advantage might be hard to decide on; since the users want a simple product, the possibility of adding to the product is limited. A competitive advantage could lie in a pricing strategy – if it is possible to set a sales model that is hard to copy, that would increase the chances for a company to outlive future competitors. The sales model could incorporate several revenue streams, with continuous revenue through hospital subscription or similar, where customers are under contract.

5 Conclusion
The questions to answer in this thesis were whether there is a clinical need for an additional product in neurosurgery and whether the market is attractive to enter considering the market size and dynamics.

The need was identified and validated during observations of a tumour resection surgery, where the navigation tool was heavily used but only on historic images. The need was not in planning, as suspected, but rather in the intraoperative setting. It was also validated through interviews where all interviewees spoke on the need for image updating and a more objective way of making decisions.

By looking at the market size and dynamics, the conclusion is that there is a market space and a financial winning for this product; however, the health economic data will likely not be a motivator for this product, and if the decision is to enter the market, this argument has to be backed by other benefits. There are research groups that are already working within the field, and the research is not highly differentiated. Through the analysis of Porter’s five forces, the conclusion is that it would most likely be hard to enter the market before another research group, since they are well on their way with development and published tests. However, if the aim of the other research groups is not to commercialise, this could help a new entrant, who could also look at their previous work as a source of open innovation.

If entering the market, there are several strategic pathways that could be chosen, with different SNS companies in mind accordingly. The conclusion is that the best strategy is to target one or several SNS providers for either a strategic collaboration or an exit, since they already have an existing customer base and growing sales. The challenge would be to increase valuation.

A final conclusion is that the decision to enter this market is dependent on the capability to raise capital and invest time for development and further industry investigation. If one has the capital, it is possible to enter the market with a new, innovative product that could help save lives and drive the technology development forward.
References


BrainLAB AG, 2012. *Consolidated financial statements for the fiscal year from 01.10.2011 to 30.09.2012 (originally in German),* Feldkirchen: BrainLAB AG.


Medtronic, Inc., 2013. 2013 Annual Report, s.l.: Medtronic, Inc..


Soares, C. et al., 2012. Finite Element Analysis - From Biomedical Applications to Industrial Developments. s.l.:InTech.


Appendix A

**Intervjuperson:** Magnus Tisell, sektionschef/överläkare Sahlgrenska Universitetssjukhuset

**Plats:** Arlanda flygplats

**Datum:** 2014-02-28

**Intervjutid:** ca 11.00–11.35

**Inledande**

- Hur länge har du arbetat som neurokirurg?
- Hur ofta har ni tumöroperationer?
- Vilket navigeringssystem? / Vilken leverantör?
- Kan du beskriva hur du använder teknik från preoperativ planering till operationens genomförande?
  - När man läser om Medtronics teknik står det att de räknar med för brain shift, är det något ni använder er av?
- Använder ni idag någon teknik för att uppdaterabilderna intraoperativt?
  - Hur mycket upplever du att du tar stöd av tekniken?

**Tidsåtgång**

- Hur lång tid läggs i genomsnitt på preoperativ planering?
  - Tycker du att det är en rimlig tidsåtgång i förhållande till hur mycket tekniken används vid operationstillfället?
- Upplever du att tidsförloppen (planering → post-op) skulle kunna förkortas om du hade tillgång till annan teknik än det som erbjuds?

**Om operationen**

- Hur definierar du brain shift?
  - Hur är det med ändringar av dynamiken som beror på att man avlägsnar vävnad under en operation?
- Tror du att svårighetsgraden att hantera brain shift är kopplat till
  - Erfarenhet?
  - Fall till fall?
- Har du varit med om något fall där det har hänt något pga brain shift?
- Anser du att den teknik du jobbar med är ett tillräckligt bra komplement för att räkna in brain shift i planering/genomförande?
  - Varför/varför inte? Utveckla

**Navigeringssystem/VR**

- Ser du att det finns något gap i pre-/intraoperativ teknik som används idag?
  - Teknikerna för uppdatering av bilder inne i op.sal? (iMRI, iCT, C-båge etc.)
Hur ser du på virtual reality? Att jobba med beräknade modeller av hjärnan?
  o För att visualisera möjliga händelser?
  o Vad är det som känns bra/obekant?
    ▪ Tror du att man skulle behöva uppdatera en sådan modell kontinuerligt under operationen för att räkna med alla förändringar som görs?
  o Pärligt?

Avslutande

- Finns det något mer du vill berätta om/tillägga?
  o Men skulle du säga att neurokirurgin överlag är innovativ?

- Hur ser överföringen från neuro till onkologen ut?
  o Tror du att det skulle kunna vara en idé att använda en ”VR-bild” för överföringen av information? Genom att till exempel ”efterregistrera” hur operationen gick?
Intervjuperson: Hjalmar Bjartmarz, neurokirurg Skånes Universitetssjukhus, Lund
Plats: Lunds universitetssjukhus
Datum: 2014-03-21
Intervjutid: ca 10.00–10.35

Inledande
- Hur länge har du arbetat som neurokirurg?
- Hur ofta har ni tumöroperationer?
- Vilket navigeringssystem? / Vilken leverantör?
- Kan du beskriva hur du använder teknik från preoperativ planering till operationens genomförande?
  o Upplever du att du tar mycket stöd av tekniken trots att du inte lägger så mycket tid på det?

Tidsåtgång
- Hur lång tid läggs i genomsnitt på preoperativ planering?
  o Tycker du att det är en rimlig tidsåtgång i förhållande till hur mycket tekniken används vid operationstillfället?
- Om man tar med brain shift i diskussionen, hur gör du för att använda navigering (djup, placering) i och med att det är historiska bilder?
  o Hur ser du på iUL?
    ▪ Menar du att man då ser hur UL-bilden förhåller sig i relation till MR-bilden?
    ▪ Kan man fokusera på övriga delar av hjärnan för att uppskatta brain shift, istället för att titta på UL-bilden i sig?
- Upplever du att tidsförloppen (planering → post-op) skulle kunna förkortas om du hade tillgång till annan teknik än det som erbjuds?

Om operationen
- Hur definierar du brain shift?
- Tror du att svårighetsgraden att hantera brain shift är kopplat till
  o Erfarenhet?
  o Fall till fall?
- Anser du att den teknik du jobbar med är ett tillräckligt bra komplement för att du ska kunna kompensera för brain shift i planering/genomförande?
Navigeringssystem/VR

- Ser du att det finns någotgap i pre-/intraoperativ teknik som används idag?
  o Men det tar även tid att få fram exempelvis MR-bilder
- Hur ser du på virtual reality? Att jobba med beräknade modeller av hjärnan?
  o Pålitligt?

Avslutande

- Finns det något mer du vill berätta om/tillägga?
**Intervjuperson:** Peter Lindvall, överläkare Norrlands Universitetssjukhus

**Plats:** Telefonintervju

**Datum:** 2014-04-09

**Intervjutid:** ca 10.10–10.30

**Inledande**

- Hur länge har du arbetat som neurokirurg?
- Hur ofta har ni tumöroperationer?
  Vilket navigeringssystem? / Vilken leverantör?
- Kan du beskriva hur du använder teknik från preoperativ planering till operationens genomförande?
  o Hur mycket upplever du att du tar stöd av tekniken?

**Tidsåtgång**

- Hur lång tid läggs i genomsnitt på preoperativ planering?
  o Tycker du att det är en rimlig tidsåtgång i förhållande till hur mycket tekniken används vid operationstillfället?

- Upplever du att tidsförloppen (planering → post-op) skulle kunna förkortas om du hade tillgång till annan teknik än det som erbjuds?
  o Vart anser du att det brister?

**Om operationen**

- Hur definierar du brain shift?
- Tror du att svårighetsgraden att hantera brain shift är kopplat till
  o Erfarenhet?
  o Fall till fall?

- Anser du att den teknik du jobbar med är ett tillräckligt bra komplement för att räkna in brain shift i planering/genomförande?

- Har du varit med om något fall där det har hänt något pga brain shift?

**Navigeringssystem/VR**

- Ser du att det finns något gap i pre-/intraoperativ teknik som används idag?
  o Ja, hur ser du på teknikerna för uppdatering av bilder inne i op.sal? (iMRI, iCT, C-båge etc.)

- Hur ser du på virtual reality? Att jobba med beräknade modeller av hjärnan?
  o Vad är det som känns bra/obekant
Avslutande

- Finns det något mer du vill berätta om/tillägga?
- Skulle du säga att neurokirurgin är ett innovativt område, som är villigt att testa nya tekniker?