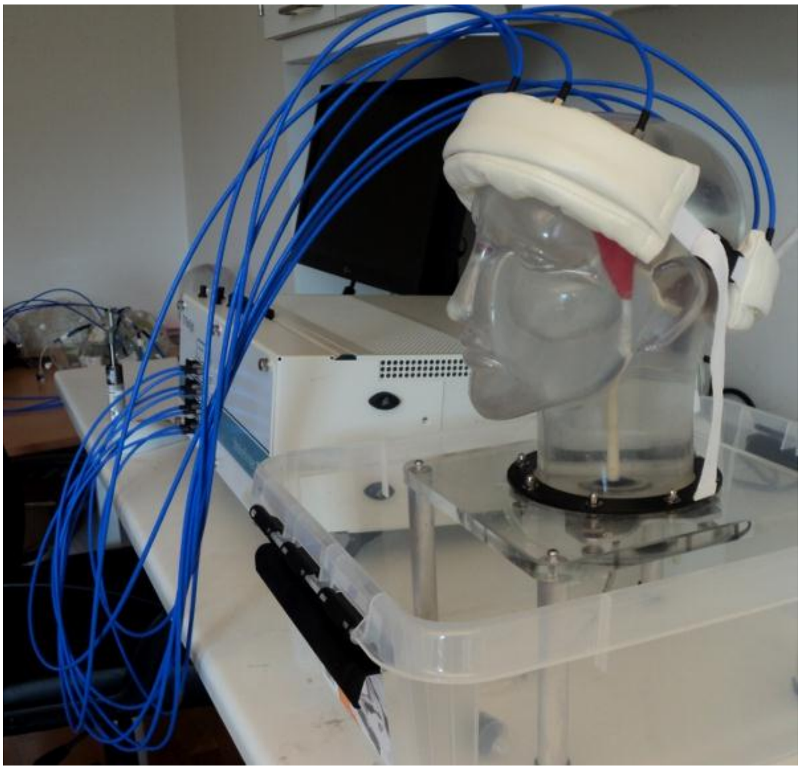

Design and Development of Stroke Cap for Monitoring of Transient Ischemic Attacks

Clinical planning, design and evaluation
Master of Science Thesis

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Preface

This project has been carried out as a Master of Science Thesis for Medfield Diagnostics AB and the Biomedical Electromagnetics group at Chalmers University of Technology. The work began in September 2011 and ended in April 2012 and was mostly situated at Medfield Diagnostics.

Acknowledgements

I am grateful to Stefan Kidborg for his invaluable guidance and support throughout the thesis. I would also like to thank Patrik Dahlqvist – CEO at Medfield Diagnostics AB, professor Mikael Persson, for giving me the opportunity to contribute to their important work of improving stroke diagnostics and my examiner Andreas Fhager

Martina Johansson

Abstract

DESIGN AND DEVELOPMENT OF STROKE CAP FOR MONITORING OF TRANSIENT ISCHEMIC ATTACKS

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Stroke refers to hemorrhage or infarction of the brain and when treating this condition, it is of great importance to determine the extent and nature of the damage. Trombolytic treatment can save the life of a person with a brain infarction, but will be devastating for a person with hemorrhage. Medfield Diagnostics have spent several years on developing a stroke diagnostic device that can investigate the brain damage after a stroke quickly, with the help of microwaves.

The stroke helmet and strokefinder R10 is in clinical use as research equipment. This thesis project carried out the task to design and optimize the appearance and function of the next generation M100.

One important and basic task is to design and optimize the appearance and function of the helmet or cap. Strokefinder R10 is a plastic helmet, which works well for fixed positions. The interior of the plastic helmet is covered with water filled bags, to facillitate antenna-head connection and to enable change of circumference to fit different head sizes. The aim of the project is to develop a helmet or cap for M100, a design that is comfortable to wear, easy to put on and economically efficient. Further issues that are highly important is however the cap should be possible to sleep with (sleep monitoring of the brain for proactive stroke treatment), what kind of materials are suitable (regarding both comfort and economical aspects) and however it should be recyclable or disposable. The design should also optimize the position of measuring devices on the head, taken into consideration that the patients will have different head size.

Night surveillance can be crucial for patients that have suffered from several strokes or are prone to TIA (Transient Ischemic Attacks) which means that there is a transient episode of neurologic dysfunction caused by ischemia (loss of blood flow) without acute tissue death.

If a patient suffer from a TIA, there is increased stroke risk for the next couple of days. This report are mainly focused on the development of a cap that is suitable for TIA monitoring. In

the end of this report, the area of animal studies will also be addressed as a future aid in the development of stroke diagnostics equipment.

KEYWORDS: diagnostic applications, stroke, medical devices, clinical trial

Sammanfattning

DESIGN AND DEVELOPMENT OF STROKE CAP FOR MONITORING OF TRANSIENT ISCHEMIC ATTACKS

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Stroke innebär blödning eller blodpropp i hjärnan och när man behandlar detta tillstånd är det av största vikt att snabbt bedöma utbredning och typ av skada. Trombolytisk (propplösande) behandling kan rädda livet på en person som drabbats av en blodpropp, men vara förödande för en person som redan har en blödning. Medfield Diagnostics har ägnat flera år till att utveckla diagnostisk utrustning för att snabbt kunna undersöka hjärnskador efter en stroke, med hjälp av mikrovågor.

Den diagnostiska utrustningen, Strokefinder R10 är bland annat en hjälm med antenner som sänder mikrovågor genom hjässan, vilken används kliniskt som testsutrustning. Detta projekt utfördes med syfte att designa och optimera utseende och funktion för nästa generation Strokefinder M100.

Strokefinder R10 är en plasthjälm som fungerar väl för fasta positioner. Insidan är täckt av vätskefyllda påsar för att underlätta förbindelsen mellan huvud och antenn och möjliggöra justering av omkretsen för att passa olika huvudstorlekar. För M100 behöver flera parametrar tas hänsyn till, till exempel huruvida hjälmen ska gå att sova med (för sömnövervakning under förebyggande strokebehandling), vilken typ av material som är aktuella (ur både ekonomiskt- och bekvämlighetsperspektiv) och huruvida materialen ska vara återvinningsbara eller engångsartiklar.

Designen måste också optimera positionen av antennerna på hjässan, och ta hänsyn till att patienterna har olika huvudstorlek (som typiskt varierar mellan 50 till 60 cm)

Nattövervakning kan vara nödvändigt för patienter som har lidit av flera stroke-attacker och/eller är benägen att få TIA (Transienta Ischemiska Attacker) vilket innebär en transient episod av neurologisk dysfunktion orsakad av hämmat blodflöde, utan akut vävnadsdöd.

Om en patient erfar en TIA är risken för en riktig strok förhöjd under de nästkommande dygnen. Den här rapporten är i huvudsak fokuserad på utvecklandet av en mössa för TIA övervakning. I slutet av rapporten, tas även frågor rörande djurstudier upp, som ett led i framtida utveckling av stroke diagnostisk utrustning.

NYCKELORD: diagnostisk teknik, stroke, medicinska apparater, klinisk prövning

Contents

Terminology

CT Computer Tomography

MRI Magnetic Resonance Imaging

EEG Electroencephalograph

TIA Transient Ischemic Attack

NIHSS National Institute of Health Stroke Scale

Chapter 1

Introduction

In this section purpose and background of the project are given and potential benefits of microwave technology in the treatment of acute stroke are presented as well as the ideas behind the development of the stroke cap.

1.1 Background

Early, fast and accurate diagnosis of acute stroke is important in order to improve the patient's chances of proper treatment and recovery. Stroke is the third largest cause for acute death and first cause for health costs in the western world. About 40% of the survivors are left with impairment[1]. Improved techniques for diagnosis have the ability to significantly lower costs for health care. Thrombolytic treatment of acute stroke became internationally approved in 2000, introducing a successful method for treatment of ischemic stroke. But if the treatment is given to patients suffering from hemorrhagic stroke, the results are devastating. Moreover, treatment must be given within three to four hours of the first symptoms, according to regulations, else the risk of causing a bleeding is large. The sooner the treatment is introduced the less brain tissue will be damaged. Therefore, quick diagnosis of stroke type is in high demand. Medfield Diagnostics AB is currently in a product development phase with the aim to develop microwave based techniques for diagnosis of acute stroke. The long-term goal is to improve the diagnostic and treatment procedures for patients with brain injuries and acute stroke by introducing new imaging technologies. Clinical trials are ongoing in collaboration with Sahlgrenska University Hospital and Chalmers University of Technology. The aim of the trial is to illustrate the ability of microwave technology to distinguish between stroke caused by clot or bleeding. Microwave based stroke diagnosis equipment have several benefits. The equipment can be made small enough to fit into emergency rooms and ambulances which would thereby enable earlier diagnosis compared to existing technologies.

As the title of this report suggest, monitoring of transient ischemic attacks (TIAs) are also in high demand. The reason for that is that TIAs could be an important warning sign that a real stroke is likely to occur. In fact, often times a real stroke will occur just a couple of days after a TIA, which will be described in more detail below. If a patient could have his or her brain monitored just before a preceding stroke, no damage would have to come about which in turn would save tremendous money, suffering and lives.

Electromagnetic radiation in the microwave band is non-ionizing and therefore nearly non-hazardous[2]. Complementing imaging technologies such as computer tomography use ionizing radiation, which is possibly carcinogenic[3] and a completely different technique.

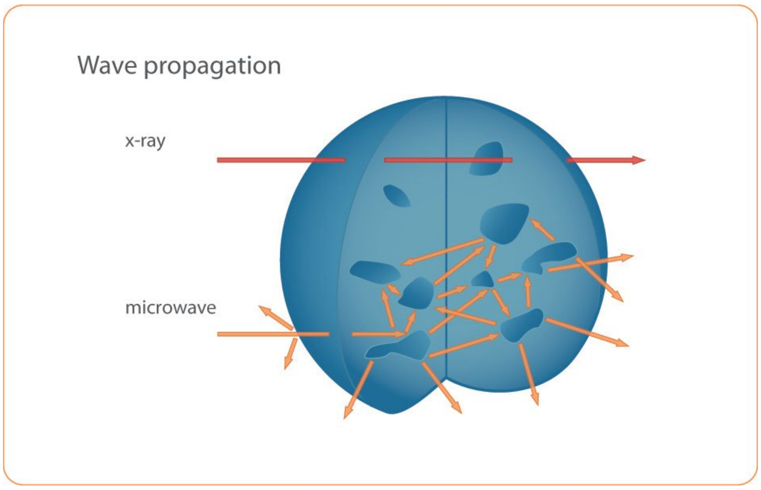

figure 1.1 comparison of x-ray versus microwave propagation [4]

Ionizing radiation is radiation composed of particles that individually can liberate an electron from an atom or molecule producing ions. These tend to be especially chemically reactive, and the reactivity produces the high biological damage caused per unit of energy of ionizing radiation.[5] Non-ionizing radiation refers to any type of electromagnetic radiation that does not carry enough energy per quantum to ionize atoms or molecules—that is, to completely remove an electron from an atom or molecule.[6]

The propagation of microwaves in biological tissue is dependent on the dielectric properties of the tissue and therefore interfaces between tissues with differences in dielectric properties provide high spatial contrast. These are the primary reasons why microwave based diagnosis is a promising technology to solve the acute stroke diagnosis need. Several articles have been published proving this statement, especially from the department of Signals and Systems at Chalmers University of Technology [7][8]. Figure 1.1 illustrates how microwaves propagate in biological tissue, and also how it differs from x-ray radiation.

The technical aspects are as crucial as challenging to develop, but another important aspect is the design, function and evaluation of the actual stroke cap that is going to be used both for research and clinical use.

The demands on a product like this is important to consider carefully, as the pick of materials can interfere with microwave propagation, contribute to sources of error or improve and decrease uncertainty parameters. The cap must fit all patients and have to be hygienic, safe, comfortable and economically efficient.

1.2 Purpose

The long-term aim of Medfield Diagnostics is to develop a stroke diagnosis instrument for the acute stroke care, thus improving patient life and lowering overall costs. The first steps towards this goal is to attempt to distinguish between Intracerebral Hemorrhage (ICH) and Ischemic Stroke (IS), besides brain monitoring during and after a TIA. The purpose of this master thesis project has primarily been to develop and evaluate a stroke cap that can be used in the process of stroke diagnosis, night monitoring and pre-stroke surveillance.

Some temporary designs have been made to be able to conduct the development of the microwave interpretation and strokefinder equipment, however this thesis is pointed towards the development of the stroke cap alone and especially one that can function well during night monitoring. The thesis withholds the practical progress of the stroke cap design as well as evaluation and ideas for future work, animal studies, ethical aspects and so on. The first section sheds a light on different type of stroke, the previous stroke cap designs and some product requirement. Section 2 will present the different design ideas and evaluation. Section 3 takes a look at the pre-clinical testing, section 4 covers animal studies and ethical aspects and section 5 withholds discussion, summary and outlook. Ideas and proposals for future work are added to the last chapter as a closure.

1.3 Stroke

This section sheds light on some general important aspects of stroke: types, statistics, diagnosis and treatment. There are two primary types of stroke, caused by blood clot or a bleeding (ischemic and hemorrhagic), where the first is treatable in the acute phase with excellent outcome,[1]. However, the treatment is harmful to patients with stroke caused by bleeding and therefore it is crucial to make the correct diagnosis.

The known types of stroke can be divided into some categories, presented here with a short description.

1.3.1 Transient Ischemic Attack - TIA

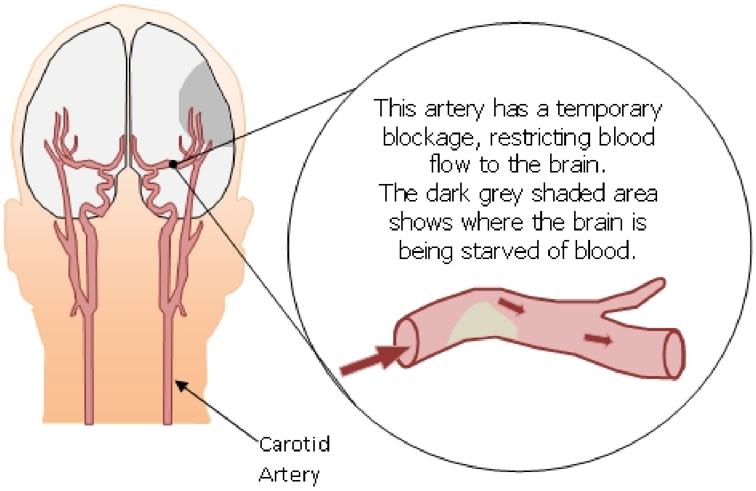

figure 1.2 Illustration of TIA [9]

A transient ischemic attack (TIA) is an acute episode of temporary neurological dysfunction resulting from focal cerebral ischemia not associated with permanent cerebral infarction. The clinical symptoms of TIA typically last less than an hour, but prolonged episodes can occur. While the classical definition of TIA included symptoms lasting as long as 24 hours, advances in neuroimaging have suggested that many such cases represent minor strokes with resolved symptoms rather than true TIAs.

The definition of TIA is as follows: A transient episode of neurological dysfunction caused by focal brain, spinal cord, or retinal ischemia, without acute infarction. The figure shows how a clot is blocking an artery, causing a temporary blockage of blood flow to parts of the brain. A patient that has suffered from a transient ischemic attack runs an elevated risk to suffer from a real stroke within the next few days. [10]

To carefully investigate onset, duration, fluctuation, and intensity of symptoms is of highest importance, whereof night surveillance of high risk patients are of great interest. This is also important to prevent and reduce the risk of a following infarction.

1.3.2 Ischemic stroke – IS

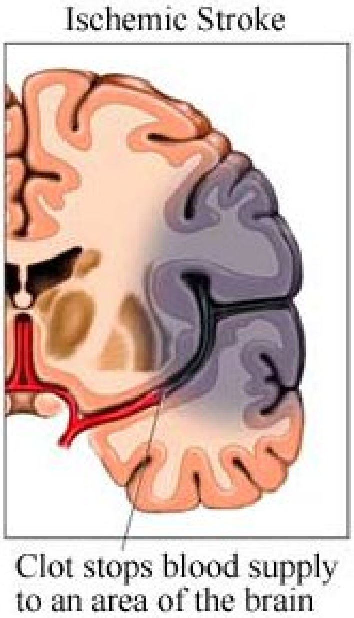

figure 1.3 Ischemic stroke[11]

A blood clot or other artifact particle not belonging in the blood circulatory system get into a too narrow artery, get stuck and thus blocks the pathway, typically causing loss of oxygen supply to the surrounding area. The illustration above typically shows how this event look like. Hemorrhages (bleedings) can appear as a secondary symptom due to increased pressure and can, if left unchecked, lead to permanent brain damage or death. Ischemic stroke can have permanent and transient symptoms, where the definition transient stroke means that the symptoms disappear within 24 hours. A transient type of stroke (TIA) is usually a certain sign of an impending stroke of more severe degree[12].

1.3.3 Intracerebral hemorrhagic stroke – ICH

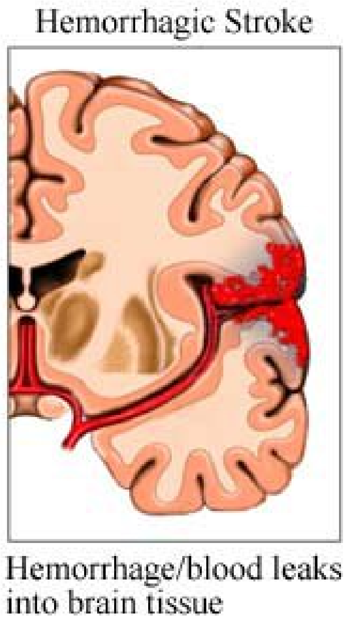

figure 1.4 Intracerebral hemorrhagic stroke [13]

As the figure shows, an artery or vein can rupture, spawning leakage of blood inside the brain causing the surrounding brain area to malfunction due to increased pressure, loss of oxygen or other side-effects. If the bleeding is intracerebral it means that the bleeding occurs inside the brain as opposed to for example subarachnoid which corresponds to a a bleeding between the skull and brain[14]

1.3.4 Other types

There are several other less common types of stroke such as hybrids of blood clots and bleedings. A hybrid stroke may start as an ischemic block which evolves to hemorrhagic/ischemic hybrid due to pressure buildup caused by the blockage in the circulatory system. Regardless of the stroke type, the sufferers are often times quite aged and frail and it is then of highest importance that the diagnostics can be performed as free of discomfort as possible. The stroke cap must be securely positioned on the patients head not to cause any measurement errors. As we can see from the above stroke types, stroke can occur in a number of ways which also is important to be aware of when designing the cap and determine the antenna position.

1.3.5 Stroke – Statistics

Stroke is held to be one of the main causes of death in the world[1], causing about 10% of total death toll in the world yearly (numbers generated in 1999). In a study by Harraf. et. al,[15] performed in the UK in 2002 with 22 participating hospitals it was found that 55% of the suspected stroke cases in the study suffered an ischemic stroke, 14% suffered from transient ischemic stroke (TIA), 7% suffered an intracerebral hemorrhage, 1.5% suffered a subarachnoid hemorrhage, 21% suffered from other types of stroke or non-stroke symptoms and finally in 1.5% of the cases no diagnosis was established. Note that the study sported 739 subjects with a median age of 75 years of age.

One particular study[16], made use of data collected in the former Oxford region of Great Britain and the study points out that the fatality rates of stroke and how it has improved since the late 70's. For the period 1978-1987 the combined mortality rate was 39.7% up to 30 days and 56.9% at one year after admission. For the period 1988-1997 the corresponding numbers were 32.9% and 48.9% respectively, showing and improvement. But still, the numbers show that in general a lot if people die from stroke even though they are admissioned to hospitals, which clearly points out that a lot of improvement can be done in terms of effectiveness of the hospital organization and treatment procedures to improve statistics.

1.3.6 Stroke – Diagnosis

Stroke in general yield symptoms like impaired speech, numbness in limbs, immobilization of limbs, visual impairment (partial or full loss of sight) and many other observable symptoms. When in the pre-treatment stage of stroke, time is of essence. If the subject qualifies for thrombolytic treatment, common policy is that treatment has to be started within three hours. Once the subject has reached a hospital it is common to run a CT scan and/or MRI scan[17] [18] to determine the stroke type. The classification process builds upon exclusion where treatment is type specific (see 1.4). There exist both medical diagnostic criteria[19], and layman observable criteria[20], for quickly determining stroke symptoms. The NIHSS is also used as clinical stroke assessment tool to evaluate stroke-related neurologic deficit. The NIHSS was originally designed as a research tool to measure baseline data on patients in acute stroke clinical trials. Now, the scale is also widely used as a clinical assessment tool to evaluate acuity of stroke patients, determine appropriate treatment, and predict patient outcome. One interesting aspect would be to couple the NIHSS to the graphical results of the microwave scanning of the brain of patients that has suffered or are suffering from stroke symptoms.

1.3.7 Stroke – Treatment

Ischemic Stroke

Several methods for treating ischemic stroke are being used for different time windows and are well described in the literature. The most common treatment is thrombolytic treatment which reduces the risk of death and persisting effects but with a small probability of intracranial hemorrhage. Thrombolytic treatment involves breakdown of blood clots. Another method of decreasing death rate and post-hospital dependency is treatment with aspirin[21]. A Canadian study[22] , suggests that thrombolysis is the preferred alternative provided that the subject qualifies. In that study 36.8% of the participants returned to pre-stroke level of functioning. The statistics were collected on 1135 stroke patients of 2.5 years.

Intracerebral hemorrhagic stroke

For this type of stroke the treatment depends on the location and severity of the stroke. The possible treatments will be explained in order of severity of the stroke. If severity is low, the hemorrhage is left to heal by itself. Treatment is aimed to find the cause of the stroke and trying to apply countermeasures. If the severity increases it can be treated by surgery, where the area is drained of the misplaced liquids and the artery is patched up and reinforced to withstand similar problems in the future[23]. Both cases above have in common that the patient needs some kind of rehabilitation due to brain damage and the associated loss of function. It has been shown[24], that specialized caring units (stroke units) improve the outcome of patient rehabilitation and resettlement at home post-hospital time.

1.3.8 Clinical trials

When it comes to evaluation of the stroke cap there are a lot of parameters that need to be considered, some of them is however the cap is possible to wear during a prolonged period of time and how stable it is.

The patient must be able to move and change position during surveillance without it affecting measurement results.

The stroke cap is going to be used both for research, as a research cap and for acute stroke diagnosis as well as for overnight surveillance. There is a possibility that several different caps will be used, to fulfill the different demands on each area. When evaluation is done, all the necessary parameters stated in section 1.6 need to be considered and one easy way to do this is simply to try on different prototypes and analyze the comfort, price, antenna positioning and design.

It is also of importance that the demands are clearly motivated and well structured, and that no demand or design idea, jeopardize the microwave propagation or measurement results.

The evaluation of the final caps will involved pre-clinical testing both in home environment and in the lab. However, all of the evaluation procedures might not fit into this report.

1.3.9 Night Surveillance

Night surveillance might be essential due to severely increased stroke risk in some patients, such as patients that have been suffering from TIAs or even several real infarctions. To be able to monitor the brain night time can give a good head-start in both stroke treatment and alleviation of possible complications.

To carry out successful surveillances night time, when the patient is at sleep, some important parameters needs to be taken into consideration. Firstly a stable, yet comfortable set-up is of highest importance. Secondly, the data acquired must be frequently monitored and instantly interpreted in case of a sudden stroke episode.

To develop a set-up that works well for night surveillance, pre-clinical tests were performed during night time.

Generally, some restrictions are given to the patient prior to the event of night surveillance, such that the patient should be awake 24 hours before the monitoring. However, when it comes to night surveillance for stroke risk patients, no such restrictions can be given. This is because the surveillance must be performed several days in a row, and the patient group are often elderly and quite frail. Focus must be on increased life quality and the possibilites of increased health and longevity must clearly surpass any inconvenience of the surveillance.

1.4 Previous Designs

figure 1.5 Strokefinder R10 complete set-up, in use both on phantom heads, healthy volonteers and actual stroke patients.

The figure illustrates the set-up currently in use with the Strokefinder R10 which is described extensively in the background section. It is a very fixed set-up, suitable for daytime monitoring, but not ideal for night surveillance. It is also quite sensitive for patient movements and the waterbags may have contributed to some source of error. Some improvements are needed when it comes to both comfort and stability.

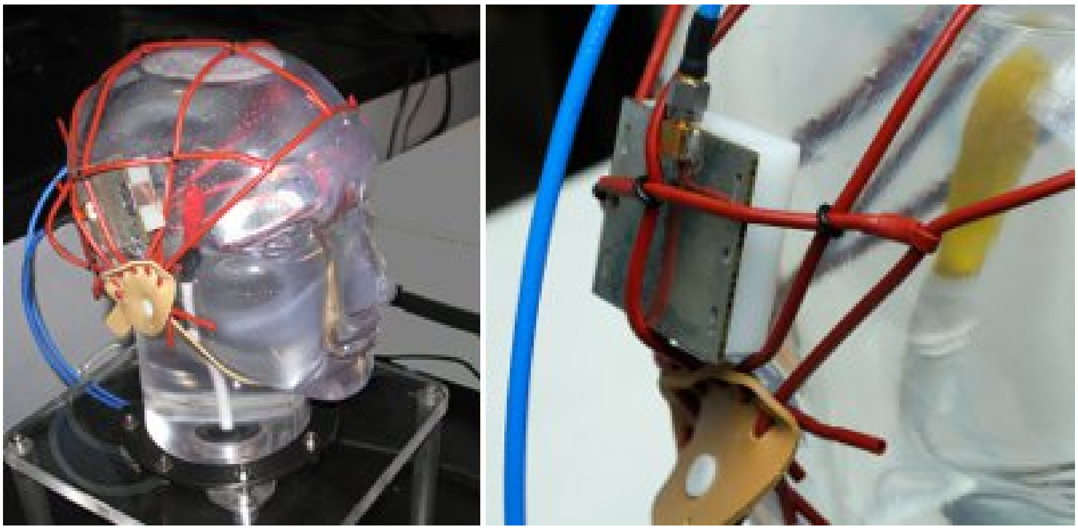

figure 1.6 test cap for antenna testing. Simple design just to be able to attach numerous antennas in various places. Suitable for fixed positions on phantom heads.

This is a prototype model with elastic rubber bands formed as a net that covers the head. The advantages are the adjustable size, and that the antennas just needs to be positioned beteen the cords. Simple and smart, but not suitable for night time monitoring. Worked well when measuring and testing on the phantom head.

1.5 Product requirements

The following list conducts the product requirements.

→ Price worthiness

→ Comfort

→ Suitability for night surveillance

→ Hygiene

→ Fitting

→ Adaptable antenna positioning

→ Adaptable number of antennas

It is important that the stroke cap has a relatively low price since it is only going to be manufactured in very small quantities and might need further design changes for optimal functioning. Additives such as neck pillows, protective caps or other protection materials needs to be disposable and therefor manufactured in larger quantities. All cap gadgets needs to be economically justifiable.

Except for costs, the comfort is the most important aspect of the entire helmet. The target group for this product are usually above sixty five years of age, and often times allready suffer from aches and comorbidity. The comfort is especially important during night surveillance because the patient must be able to sleep like normal. Another aspect of night surveillance is the fitting, since it needs to allow some sleep movements. If the antennas move out of place it will create uncertainties and even plain errors in the measuring results. The last requirements focus on the antennas, both positioning and the amount. Too few antennas and poor positioning will give uncertain results, so to consider these two parameters carefully is of highest importance for a well functioning and safe product.

figure 1.7 Antennas that transmits and receives microwaves and are used for stroke detection.

The figure above shows the antennas currently in use, approximately 4 cm wide and 2 cm thick with a sharp metallic plate attached to them. As we can see, these types of antennas might cause a great deal of discomfort whem placed on the head of the patient. It is important that the antennas are as close to the head as possible, without causing any harm or pain.

1.5.1 Ethical boards

Permission from a human ethical committee is needed to conduct tests on humans in general and patients in particular. For pre-clinical trials with non-hazardous equipment on healthy volonteers, no permission needs to be granted. However, if the tests are being conducted on actual stroke patients approval must be given.

The stroke diagnostics procedure is completely harmless and painless but still need to be supervised and approved by a liable medical doctor. The same goes for healthy volonteers. However for further sophistication of the stroke finder, animal testing might be required which needs approval from an animal testing ethics committee that weighs benefits against suffering.

The stroke cap needs testing and evaluation on humans only, but the strokefinder might be objective for animal testing.

This implies several types of new issues such as what kind of animals to use, where the animal testing should take place and wheter or not the benefits weigh up the possible suffering. In excess of these questions, the committee also needs to aprove of the study in its whole.

Chapter 2

Prototype Design

This section will present all the test prototypes. Several different ideas laid the foundation of the final model. Many aspects was taken into consideration, especially proper microwave propagation, ultimate comfort and low cost.

2.1 Specific product criteria

The materials used need to be non-allergenic, soft, elastic and airy and not too sweaty against the skin. It has to be comfortable to wear close to the face. When it comes to usage, it needs to be easy to take on and off, nonslip and stably positioned on the head. It is important to eliminate as many sources of errors as possible, which implies that the design must be properly thought through. It is also of importance that the cap does not put pressure on neck and temples, cover the ears or restrict eye seight . It needs to allow some movement from the patient since it is going to be worn for several hours both day time and night time. The antennas must be securely in place.

Two other important aspects to consider are hygiene and price. The product is going to be worn directly on skin and hair, and therefor needs to be sanitary. Custom made high tech solutions are very expensive to manufacture, especially when it comes single samples. Therefor the product also have to be price worthy. Protective caps and other possible additives are being manufactured in larger quantities and have less demands.

2.2 Presentation of the prototype candidates

2.2.1 Test cap 1 - Fabric cap

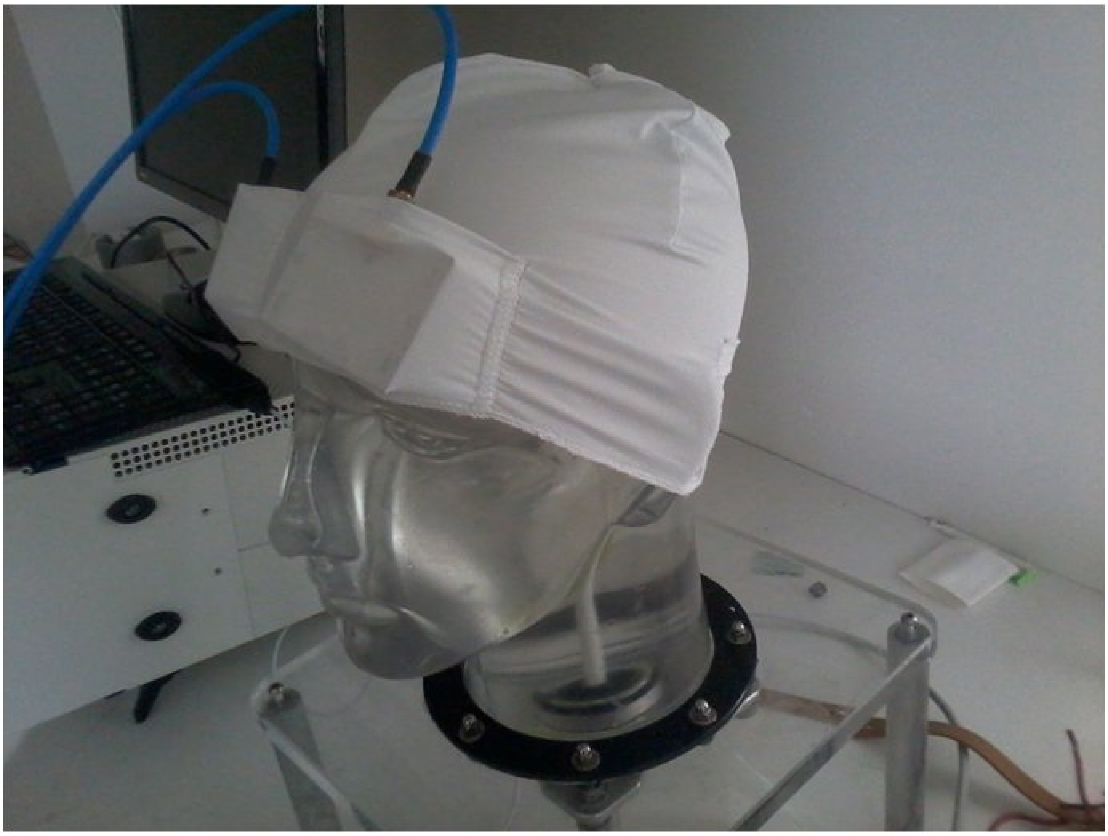

figure 2.1 First cap prototype

This is the first prototype in the quest of developing a stroke cap suitable for stroke diagnostics, and proactive surveillance for patients with elevated stroke risk. The cap is manufactured in an airy stockinet material to avoid sweat and discomfort. There are a total of four antenna pockets, two in the front and two in the back to cover forehead and back of the neck. Some measurements have been made with this setup but it is uncertain if the amount of antennas are enough, preferably eight to twelve antennas are sufficient to cover the entire head area. The antenna pockets are a little too wide to hold the antennas in place and the cap a bit too mismatched. When wearing the cap with antennas mounted, it slides down towards the eyes causing discomfort. As the picture shows, the cap also covers the ears which is uncomfortable and triggers a claustrophobic sensation. The lightness of the material is great for the antenna signal, it can pass through the material with ease. The disadvantage here is that the fabric doesn’t provide any support, so metallic sharp edges of the antennas have direct contact with the head. This is acceptable when standing but as soon as the patient is laying down, the antennas puts a lot of pressure on the head. This is a question of comfort, it might be ok for the patient a short period of time, but hardly for over-night surveillance or even when sitting down in a chair with the head against the headrest. The antenna measurements are 4,5x5,0x1,5 cm and if the antennas could be made smaller and thinner, it would provide room for a different design, more similar to an EEG cap.

EEG caps have small circular electrodes, which differs a great deal from antennas, but the small size makes it easier to cover the whole head without causing too much discomfort. It is quite common with over-night EEG which calls for a comfortable setup. However, to change the shape and size of the antennas is not part of this project and calls for deepened knowledge about the functioning and properties of antennas.

Some improvements for this first prototype could be a more dynamic and anatomic design. Many people find it unpleasant when the fabric covers the ears, and the antennas in the back of the head causes discomfort when laying down. It is absolutely crucial that the antennas are as close to the skull as possible, but some kind of pads around or in between the antennas could make it more comfortable. Another important thing is to keep the antennas in place, and a chin strap could be a nice solution for this. A soft teasel strap along the temples and attached either to the point of the chin, or just under the chin. In conclusion one could say that the first prototype constitutes a very nice basis for further evaluation and development. The fabric is excellent and it is easy to see where improvements need to be made. It is also important to see that even though the idea of a cap with antenna sockets on is easy, it might require tricky and somewhat advanced design work to fulfill all necessary criteria.

2.2.2 Test cap 2 - Extensive fabric cap

figure 2.2 First model revised with extra features

This is the second model. The idea started out as a regular cap, similar to a bathing cap with some extra features such as antenna cases and a chin strap. The material is a very soft, stretchy fabric, similar to the one used in sport clothes. Since there is a border along the edge of the cap it is easy to change the position and number of antennas, but it also has the disadvantage of instability. Another disadvantage of the model was the lack of comfort. The thin fabric provides no support for the hard and pointed edges of the antennas, which makes it impossible to sleep with and even quite uncomfortable to wear when laying down. However, the low manufacturing price makes one consider the simple design for short clinical trials, or as a research cap, perhaps for one or two hours when the patient is in an upright position. The comfort obviously needs to be improved and the antennas need more secure cases to ensure their exact position. The idea to add pads and even a pillow for support of the back of the head, arised from the drawbacks of the first and second model. The first model however, was still good enough to follow up with a second version. This second fabric cap, does not cover the ears and does not slip since the fabric is a little more rough than the first one. The fabric is covered with tiny holes to provide air flow and the chin strap makes the prototype more stable.

2.2.3 Test cap 3 - Cap with neckpillow

figure 2.3 Cap with neck pillow attached to it and soft inner coating.

This is the second version of the second prototype. The border around the edge, function as antenna holder with room for approximately eight antennas closely packed as a crown around the head.

The new features are the pillow in the back and thin stripes of foam rubber on the inside. The pillow unburdens the pressure from the antennas, and the foam stripes makes it overall softer to wear. The pillow in combination with the stripes provides a quite satisfying support for the edgy and hard antennas. There is also a removable and padded chin strap for increased comfort.

When laying down, the neck pillow provides sufficient support and actually offloads the rest of the head a great deal. The disadvantage is that the support only is sufficient when patient is laying down on the back, and only allows for a quite fixed set-up. However, night surveillance need to allow some sleep movements.

Many patients that are prone to acute stroke, are above seventy five years of age. This elderly group of people usually have many other types of conditions already, many suffer from bedsores that can get really severe and even end in amputation. There is in other words a real need for the patient to be able to move a bit, especially when it comes to night surveillance or TIA surveillance. To be completely still during long periods of time can even cause blood clots to form, so to be completely still during long hours of surveillance would be extremely counterproductive.

Possible improvements for this kind of cap is limited due to the design. More antenna cases can be added and the type of fabric might be considered, although the requirements only specify a thin and stretchy material. Head sizes differ between 50 cm and 60 cm in general, although it is a very stretchy fabric it might not be elastic enough for a larger head.

Some kind of buckle might be added to be able to adjust the circumference in a secure and stable way.

The evaluation of the first and second prototype, resulted in the idea of a completely different design, namely the fourth test cap.

2.2.4 Test cap 4 - The skeleton helmet

figure 2.4 basic plastic construction with parts from a bicycle helmet.

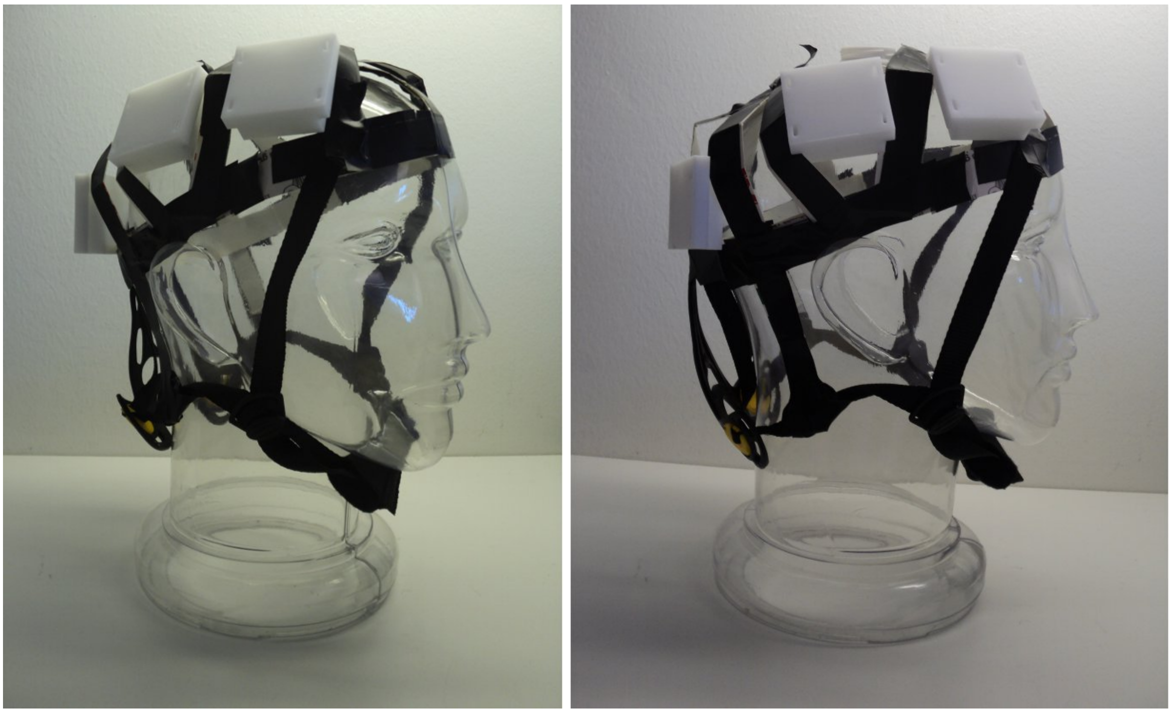

figure 2.5 Thin plastic material with the antennas roughly positioned

This fourth prototype is constructed only of the supporting parts of a helmet, leaving room for antennas inbetween the spaces.

The advantages of this design is that it has a very stable and smart construction that really takes the load and pressure of the antennas, even though the structure is quite soft and thin.

The back of the head has an outer construction of plastic and an inner support of foam rubber. Thin stripes of foam rubber covers the inner lining of the plastic skeleton that makes up the helmet. On the outside, plastic spikes are attached along the straps where the antennas can be securely mounted. A buckle is attached to the front to adjust the circumference.

This test helmet has the benefits of being both stable and comfortable at the same time. There is still some room for improvement when it comes to the antenna holders, even if the antennas are quite fixed in this design. They dont slip and the design also allows for some movement. The plastic is hygienic since it is easy to wipe off with a sterile cloth. An inner, very thin disposable cap might be added to improve this part.

The drawback of this model is possibly the economic aspect, since advanced, custom made technical solutions are quite expensive to manufacture, especially in small quantities.

Even though all other parameters of this third design is favourable, the costs may surpass the advantages and other options must be considered. The model also needs to be tested extensively for night surveillance.

2.2.5 Test cap 5 - The water cap

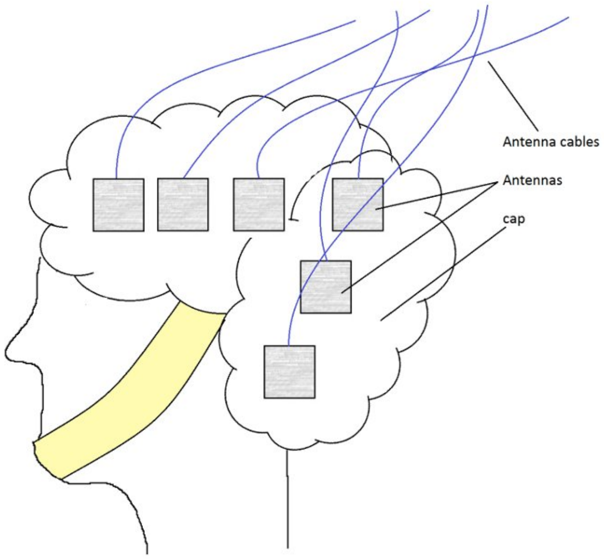

figure 2.6 A sketch of the design idea at the top and the actual result below.

The fifth prototype is an attempt to experiment with dielectric properties and different materials. The Strokefinder R10 has water filled pads covering the inside of the helmet, to be able to adjust the fitting without loosing the antenna-head connection. Focus was on wheater it was possible or not to create a cap that was impeccably comfortable.

The idea was also that the source of error might be some what smaller, if the entire helmet was built like a waterfilled cushion.

It provides great comfort and is suitable for overnight surveillance since it does not disturb the sleep at all. It is also very hygienic and easy to just wipe of with a sterile cloth. An additional chin strap is added for extra support. The chin strap is made of a soft cotton fabric, but might aswell be made of waterfilled plastics just as the rest of the helmet. The antennas can be easily attached to bits of teasel glued to the plastic surface, and can therefor be moved around freely to change both position and number of antennas.

To secure everything, a thin cap is put over the plastic cap to keep the antennas in place and hold everything together. This solution was so comfortable to sleep with that no extra pillow was needed, but unfortunately the model lacked too much in terms of price, stability and error sources.

2.2.6 Test cap 6 - The head band designs

Head band design 1

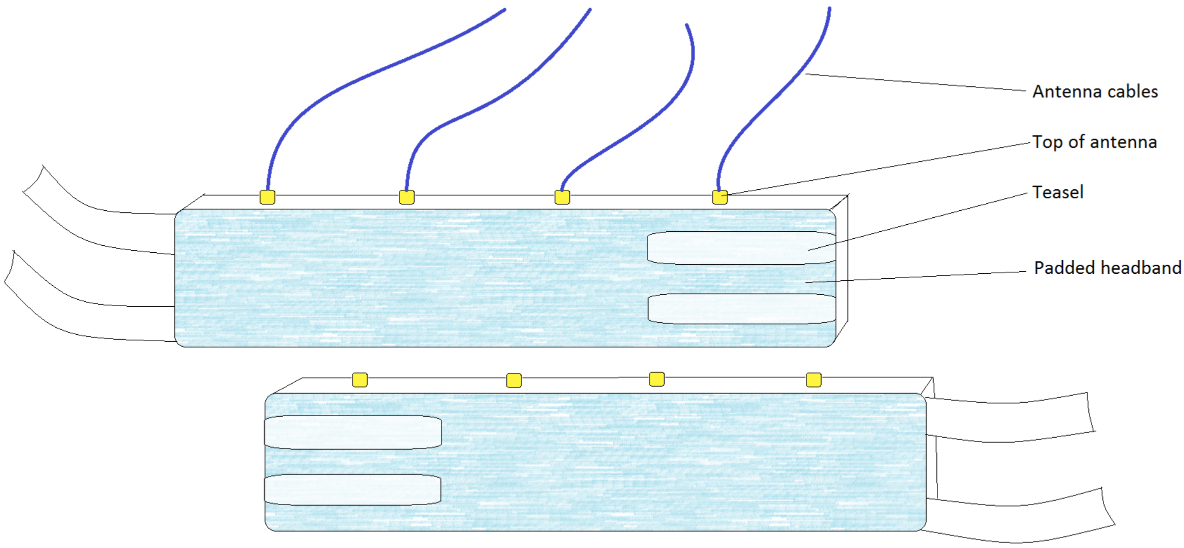

figure 2.7 The first sketch of the head band designs

The sixth cap is the final model, and the idea was rising from the third prototype with the neck pillow. To add a pillow to a cap was a bit unhandy, but to remove the cap completely and extend the neck pillow to a head band was a better solution. The head band could then be stuffed with padding and antennas, and the circumference could be adjusted with buckles or just a stretchy material.

Considering that the number of antennas should be approximately 8 – 12, it is sufficient to place them around the head like a crown, just like the two first test caps suggest. Considering this, a merge of cap design 1, 2 and 3 could be the ultimate solution – namely, a padded headband with openings for the cords and antenna plates, and some kind of adjustable straps along the head.

This prototype was not only comfortable but also simple to make, low in manufacturing cost and easy to use. Three types of headbands was created to be able to optimize the size adjustments and comfort. The first headband prototype was the most complex one, made in two pieces with adjustable buckles on each side of the head.

The fabric of choice was first a thick tricot material, but later on white galon to optimize the hygienic aspect.

Head band with teasel straps

figure 2.8 One-piece headband with padding

The second headband design was a one piece band with teasel straps on the sides. This made it possible to quickly adjust the circumference, but had the disadvantage that the antennas got different position depending on the head size.

The teasel straps might get stuck in the patients hair but, if replaced with a buckle, it might cause discomfort when laying down. Some kind of padded protection might be added to the fastener. The antennas are placed in protective, plastic, pockets.

Stretch band

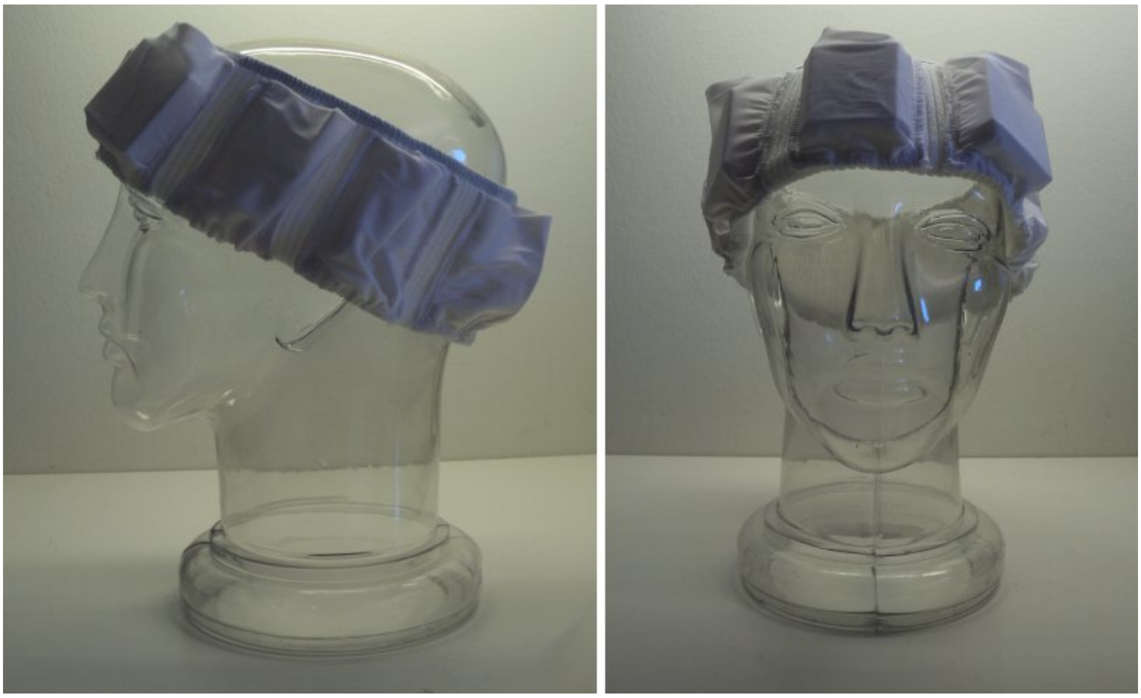

figure 2.9 Connected headband without padding

The third design was made in a simple, thick and elastic fabric with pockets in a thin material attached to it.

The idea here is to simplify the first models because the fitting got better with a headband instead of a cap. It is not particularly comfortable but easy to put on with the advantage that the antennas have the same relative position regardless of head size.

This could be a nice research cap since it is easy to use, quick to put on, it does not slip and is also cheap to manufacture in large scale quantities.

2.3 The protection cap

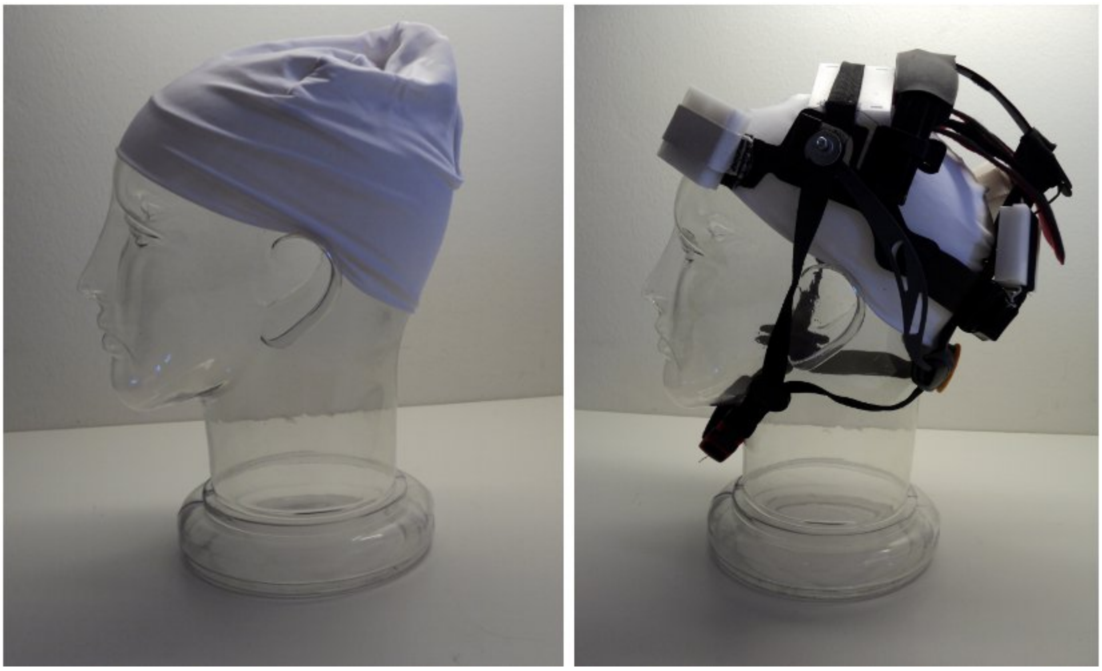

Figure 2.10 The protection cap is worn underneath the stroke cap for increased hygiene and safety

All the stroke cap designs are used directly on skin and hair which makes it non-hygienic. To avoid manufacturing many stroke caps, just because of this reason, a simple and disposable protection cap will be used.

The protection cap is made of a thin tricot fabric similar to the ones used in sport clothes. It is designed as a normal cap but might have an opening in the top for air flow and extra comfort.

2.4 Test chart

Here is a quick evaluation of the test caps, presented in table 2.1 below.

Maximum and minimum score for each feature is 10 and 0 respectively. 0 means that the criteria is not met at all, and 10 means that the criteria is fully met. Scores inbetween are somewhat arbitrary with respect to the relative qualities of the different test caps.

The product requirements are abbreviated as follows:

Night Suitabillity for night surveillance

Position Adaptable antenna positioning

Number Adaptable antenna number

etc.

The last row gives an overall score summary that gives a hint on which prototype to choose. Some test caps that got a high score might not be suitable anyway because of other types of draw backs.

Table 2.1

Caps	1. Fabric cap	2. Extensive Fabric	3. Neck pillow	4.Skeleton	5. Water pads	6. Headband
Criteria						
Price	10	10	7	3	2	7
Comfort	1	1	6	8	10	8
Night	1	1	6	8	10	8
Hygiene	0	0	0	6	8	8
Fitting	2	3	6	10	2	8
Size	0	0	0	10	2	10
Position	0	5	5	0	5	2
Number	0	5	5	5	5	5
Sum	14	25	35	50	44	56

Total maximum score is 80.

None of the designs reach maximum score since it is difficult to create a perfect model and still meet the criteria of being price worthy and fairly cheap to manufacture. On the contrary side it is also challenging to create an economically efficient design that meets the criteria of comfort and adjustment in size, number of antennas and hygiene.

Therefor a compromise was made, with the choice of a cheaper model together with a protective cap worn either on top or underneath.

The top designs was further refined and tested.

2.5 Refinement of the final designs

2.5.1 Head band prototype

The head band design was professionally manufactured and refined with galon fabric and extra padding.

figure 2.11 Complete set-up with 8 antennas

The illustration above shows a phantom head with the headband and antennas plugged into the Strokefinder. As we can see, the antennas are thick and stiff and affect the flexibility of the set-up.

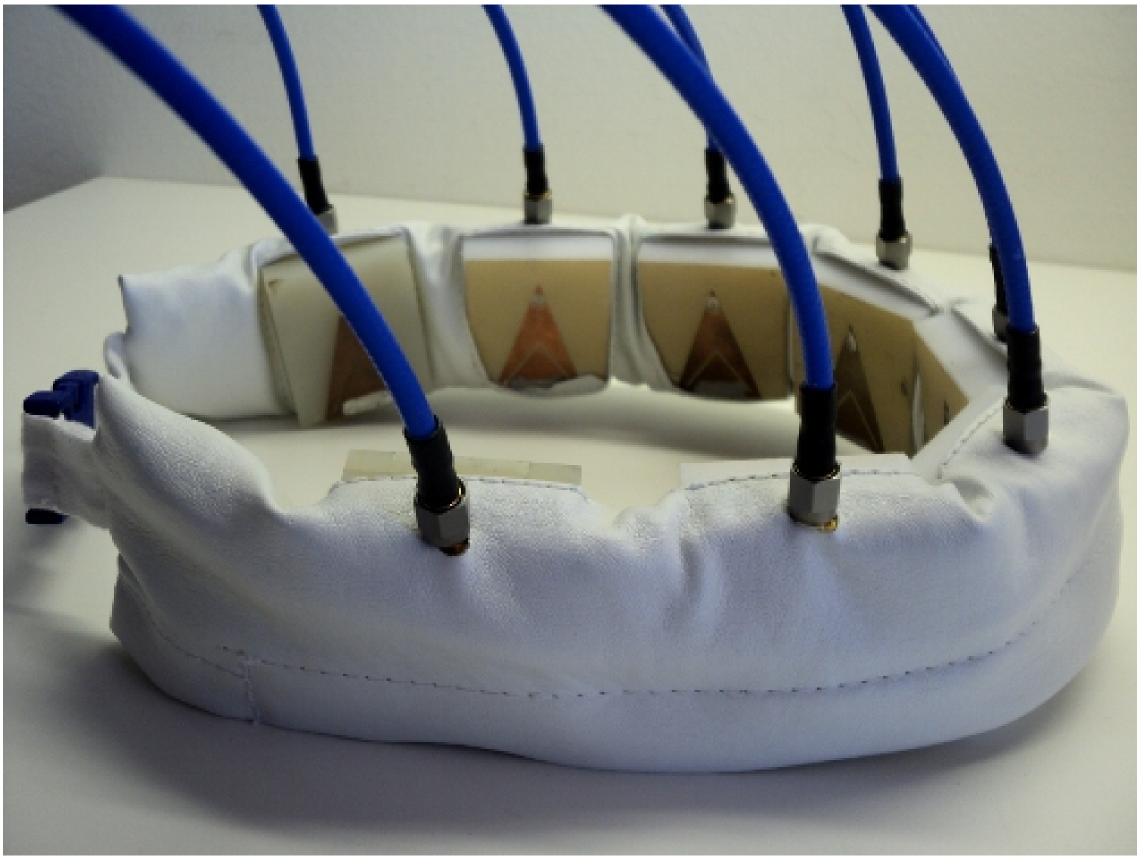

figure 2.12 Headband seen from above

The antennas were put in plastic covers to further soften the edges and protect the antennas. The illustration shows a close up on the headband with the attached antenna cables.

2.5.2 Skeleton helmet

The stroke helmet, also called skeleton helmet, from section 2.2.4 was refined with a more stable material. The prototype is made up by a construction helmet, a bicycle helmet and padding with antenna holders created from elastic straps. A chin strap and two control knobs in the back regulates the circumference easily without changing the antenna position.

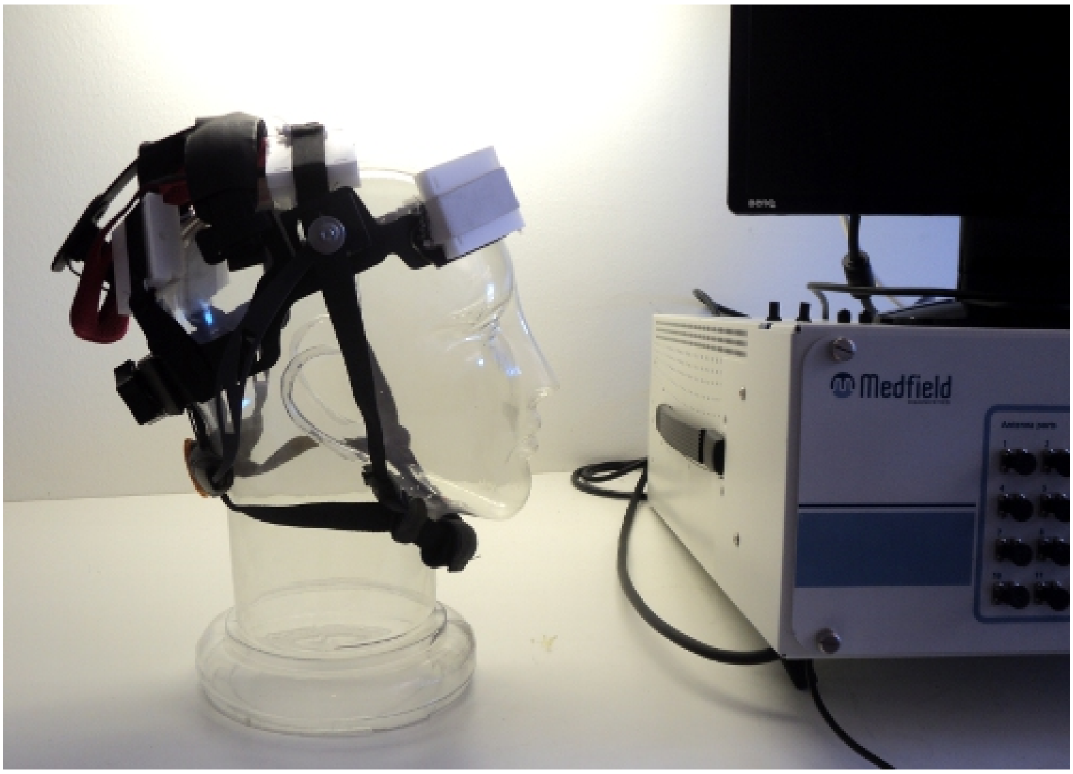

figure 2.13 Skeleton helmet

Above is a side view of the skeleton helmet placed on the phantom head.

figure 2.14 Skeleton helmet front and back

It is highly hygienic, stable and safe to use. It is also suitable for night surveillance as it allows movement from the patient.

Both the head band and the helmet are well functioning prototypes, but furder testing is needed to know which one will be the final design. Above is two pictures of the helmet from the front and back, the two control knobs are clearly visible.

Chapter 3

Verification and pre-clinical tests

This third chapter conducts the final part of the cap evaluation and construction. During the manual manufacturing of the test caps, limited testing was conducted. All the prototypes was tested by a small group of people (6-10) and analyzed according to the eight parameters in section 1.5

All the test caps was tried on during night time to test the possibility of usage for night surveillance.

3.1 Pre-clinical tests

figure 3.1 One of the many testings with the complete set-up, here with the headband design.

Pre-clinical trials implies all the alpha-testing of the prototypes with no patients involved. The tests were performed in the lab and in home environment during night testing. All the test caps was tried on by 6-10 people and the two final designs was testet extensively several days in a row.

The realization came that the cap alone was completely different to wear with and without antenna cables. The antenna cables increased the demands on the cap severly by increasing the instability a great deal. The cables are thick, quite stiff and must not be bent. They put a lot of pressure on the cap, even when laying down, causing it to slide. The helmet design could take the pressure, but on the other hand is it too clumsy in general to fit with the general idea of a smooth and lightweighted product. This provides a new dilemma. The design should be easy to use, hygienic, safe, simple and cheap but still be able to hold the pressure from the cables without causing it to slide off the patient.

3.1.1 Testing results

The most important aspect to consider is the suitability for TIA night monitoring which means that the stability and comfort must be in focus.

The primary advantage of the skeleton helmet is the stability. When just wearing the helmet in an upright position it is very comfortable to wear, even with the cables attached to it. During the night testing, half of the group could sleep as normal and the other half thought it was too disturbing. The helmet has a chin strap but it did not provide enough support during the sleep test. The helmet structure in general is a bit too clumsy for night monitoring but overall the most stable design. The idea is that the patient should be able to sleep as normal, the whole night, without disturbance but even if the helmet is comfortable and stable, it might be a bit too big and unhandy. An important general idea for the Strokefinder M100 is for it to look modern, high-tech and professional, this is one reason to choose the less stable headband prototype instead. The advantage of the headband is that it is neat, light-weighted and made of washable galon fabric. The padding hides the edgy antennas and makes it somewhat comfortable to wear when laying down. However, when the cables are attached to the cap, it puts a lot of pressure on it causing it to slide a bit. It is possible to sleep with the headband but the fastening device in the back creates an uneven gap between the antennas depending on the patient's head size. Possible improvements are for example to increase the padding, add a chinstrap and devide the headband in two pieces to even the antenna distribution. Another idea is to add some extra support on top of the head such as a sparse net or something similar to the first version of the skeleton helmet.

3.2 Revision of the headband

figure 3.2 Revised two-piece headband design with chin strap for extra stability and safety

The idea with extra padding, a chin strap and to devide the headband in two was tried out, due to the new demands of stability. The chin strap is a stretchy piece of fabric with a whole in the middle were the chin can fit, providing non-slip. All the fastening appliances are made of teasel because it makes it easy to adjust and remove. Teasel is not optimal though, due to that it can get stuck in the patients hair or clothes, but it is softer and smoother than buckles. The new design provided more stability when attached to the antenna cables, however it was still not as stable as any helmet design. Further improvements needed to be thought about. One idea was to add stability straps to the neck and on top of the head. That however, would condradict the product aim that the cap should be easy and simple.

figure 3.3 Stretchy net cap covering the head band

When EEG measurements are conducted, the EEG cap with antennas and cables are all covered with the stretchy net cap with a 'built in' chin strap to keep everything in place during night monitoring. These net caps are available in different sizes, it is a disposable product bought in large quantities and very cheap. This combination would provide a very easy and simple design, together with the new improved headband.

figure 3.4 Stretchy net cap

The net cap above is size large, but all different sizes are available. This size however, seemed to be suitable for covering the whole headband without causing discomfort. To handle the antenna cables, a hole can be cut on the top.

figure 3.5 The final head band design

All drawbacks from the different head band designs was corrected and the whole design was renewed. The illustration above shows a professionally manufactured stroke cap in the latest model. It lacks loose pieces, everything is securely in place and it is both washable and wipeable with a sterile cloth. All the bits of teasel have been removed and replaced with buckles. The buckles are easier to keep clean, and since they are positioned on the side of the head, they wont put any pressure on the head while lying down.

figure 3.6 Close-up details of the headband

As we can see from the close-up, there are no free pieces of foam rubber. Everything is covered with galon fabric, and a zipper i added to makes it easier to remove and replace the antennas.

figure 3.7 Close-up details of the headband

Each antenna cage are properly covered with stuffed pieces of galon, making the whole construction incredibly soft and comfortable.

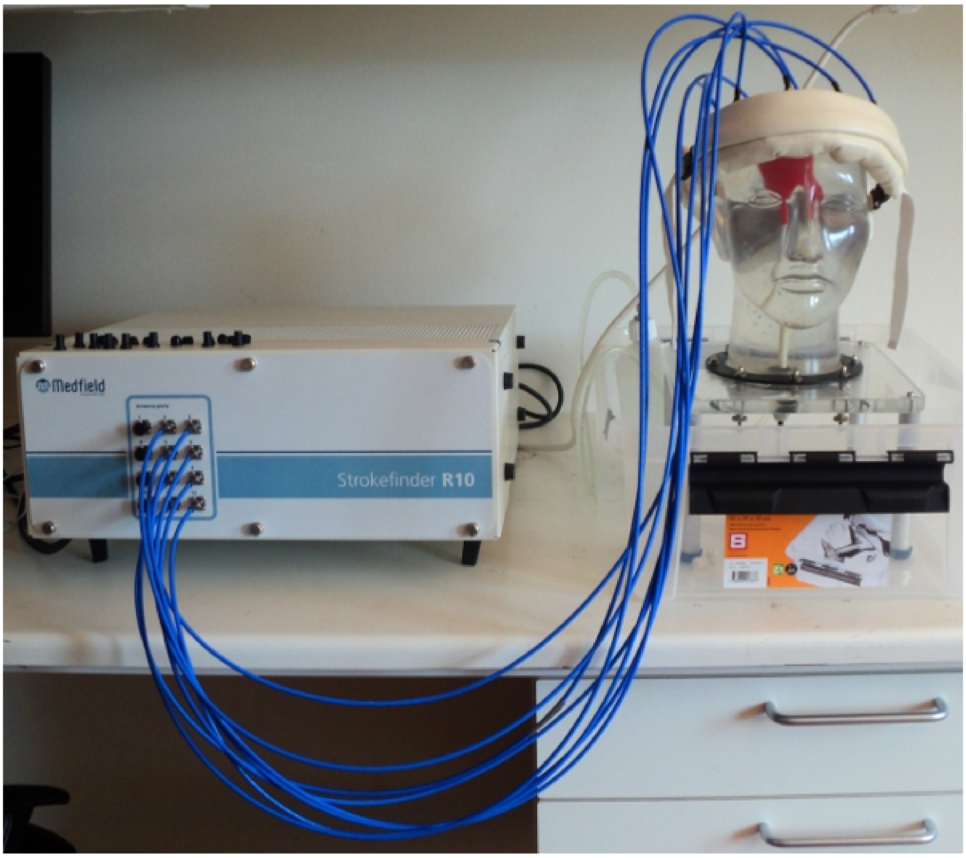

figure 3.8 The final set-up, front view

The latest design with antennas attached and everything plugged in is shown in the figure above. This is the final result of the developement and design of the stroke cap, and it will be used for clinical, and pre-clinical trials and Sahlgrenska University Hospital.

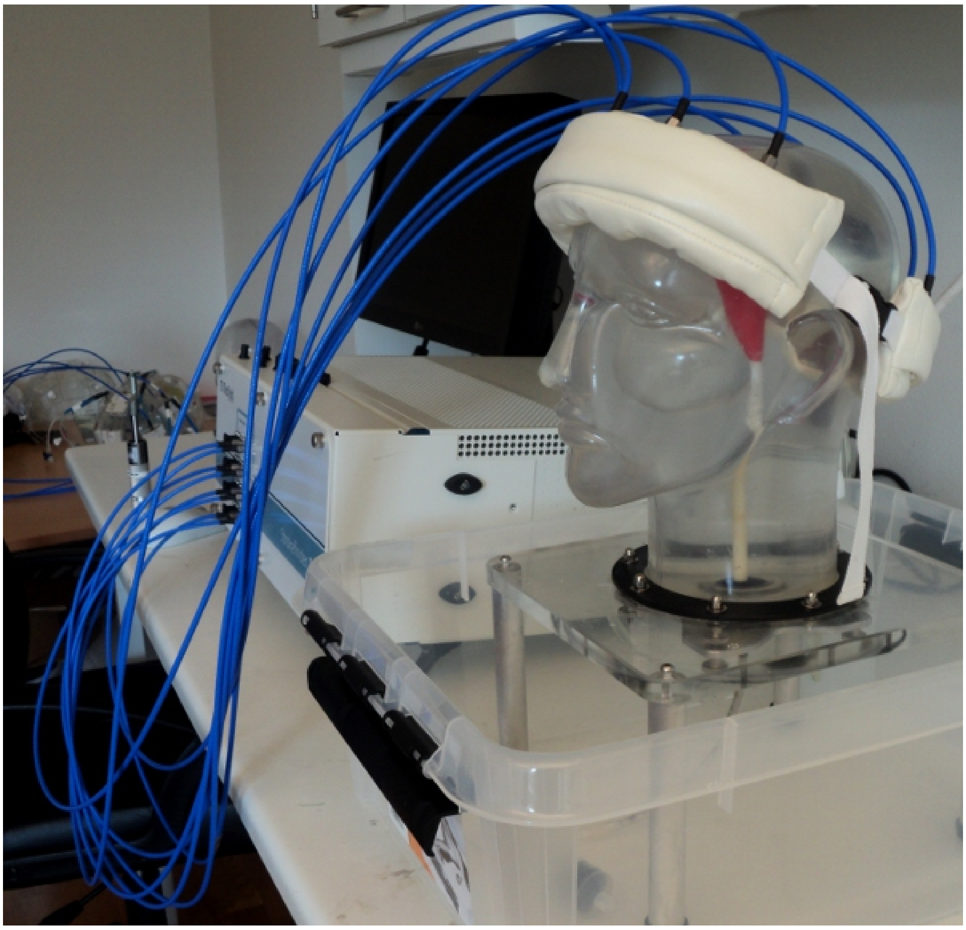

figure 3.9 The final set-up, side view

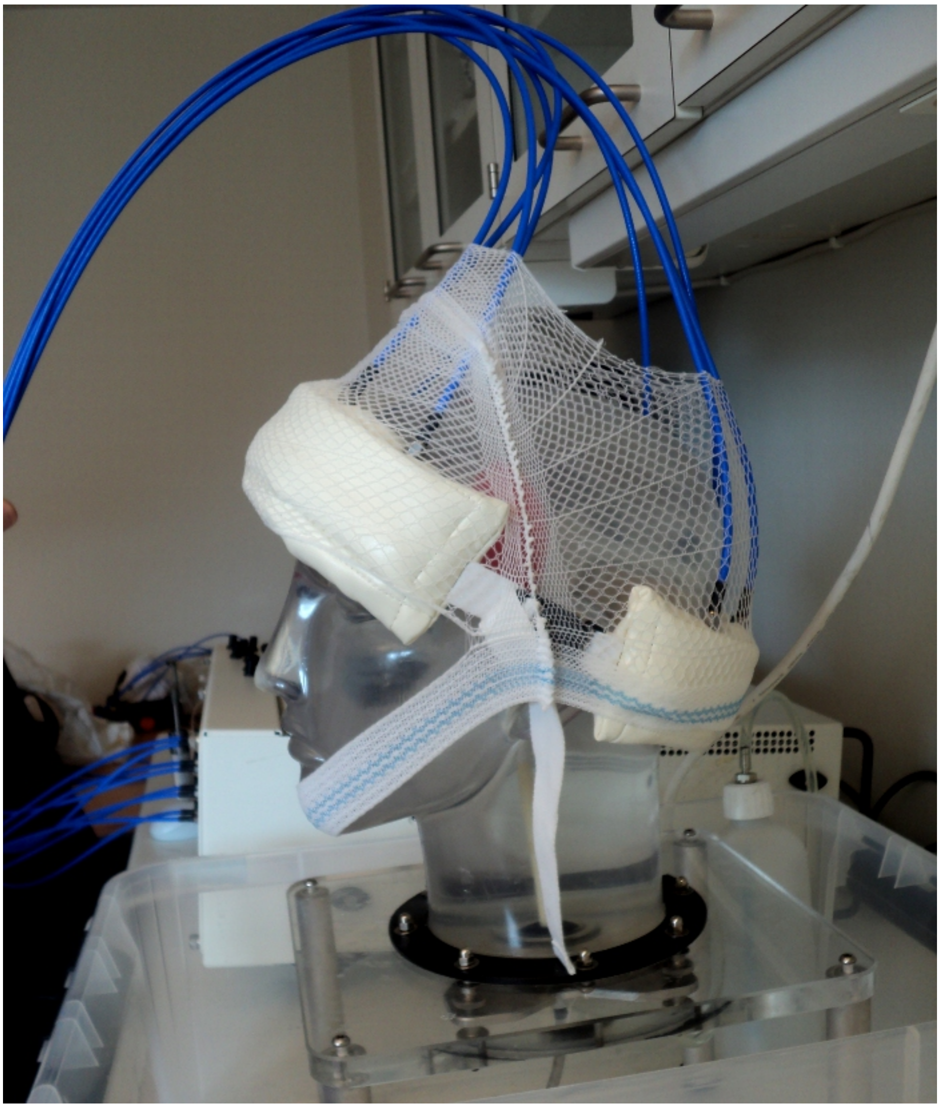

fig 3.10 Complete set-up with net cap

3.3 Summary

Several different ideas was tried out during this master thesis project. This chapter conducts the testing and improvements of the head band design which seems to be the best solution so far. A trade off between stability and lightness was made in the earlier steps, that resulted in a simple head band were the antennas are placed around the head like a crown. For night- and TIA monitoring, a light and easy design is needed for comfort and to allow some movements by the patient. When the cap with antennas was plugged in to the strokefinder, a whole new problem occured. The head band was not stable enough to bear the load from the cables. The eight antennas and eight cables put a strong pressure on the head and cap, causing both discomfort and the cap to slide off. Another problem was the difference in antenna distribution depending on head size, since the circumference was adjusted in the back. The buckle was also too hard and needed to be covered or softened in some way. One head band design had teasel straps instead of a buckle, but the teasel got stuck in hair and clothes and is also difficult to keep clean. The last issue to deal with was the hygiene aspect. Hygiene have been an important aspect all the way, but the demands are increasing in Swedish healthcare and everything needs to be anticeptic either by being washable or wipeable with a sterile cloth. Loose parts of foam rubber, teasel or cotton is not acceptable. It is desirable that the cleaning process is as effective and safe as possible, for the sake of the patient and to fulfill the hospital demands.

When the final cap was manufactured, all these aspects was taken into consideration. The antenna distribution was optimized, the buckles covered and the loose parts removed. Better coverage for the antenna edges was also managed.

The future antenna cables are much thinner and lighter and there is also a possibility that other types of antennas can be manufactured. This however, cannot be taken into consideration because the goal is to have a functioning set up right away. With the current prerequisites given.

The final cap meets the criteria and is ready for clinical trials.

3.3.1 Final Results

6 - 10 healthy volunteers tried out the different caps in the different stages of the testing procedure. The main focus during the testing was comfort, stability and how it felt to sleep with the cap on. The different head band designs and the professionally manufactured skeleton helmet was tried out in this way. In summary, the helmet was comfortable and stable, but too clumsy. The headband was light and comfortable, but not stable enough. Regardless of the instability issue, the head band got to be the winning design because it was the easiest design to keep clean and also it was most in alignment with the image of a modern, medical diagnostic device. However, the instability issue was solved with the net cap in figure 3.4 which was surprisingly efficient in keeping everything in place, both cap and cables. In this way two items are used. One disposable net cap and one recyclable head band. This is the most economically efficient solution at the moment, and at the same time the most stable, easy and comfortable.

Chapter 4

Animal Testing

figure 4.1 2D image of a mouse brain [25]

This chapter conducts the principles for animal testing and the possible application of clinical trials in the development of Strokefinder M100.

4.1 Animal testing in stroke research

Some ways to induce a stroke in animal models are for example through hypotension or artery occlusion, to create human like stroke events. Different species also vary in their susceptibility to the various types of ischemic insults. One example are gerbils, who does not have a Circle of Willis and stroke can be induced by common carotid artery occlusion alone. Different species provide different results, therefor a variety of animal models are used. Mice, rats, rabbits and even primates. It would be theoretically feasable to design a set up that could work for larger animals with the current antenna size. Practically however, a lot of steps needs to be taken.

This kind of procedures are performed by the Stroke Research group at Sahlgrenska Hospital University, but mostly with smaller species such as rats and mice. This obstructs the use of the current designs since it is adapted to a head with a cicumference of 50 to 60 cm. However, if needed, a prototype consisting of only two antennas is possible to manufacture with the current antenna model. For really small animal models, such as mice, a completely different set up is required with a different antenna type.

Animal testing is important for drug development and further understanding of different types of stroke. Transferability of animal results to human stroke is however much more complicated than desired. Although multiple therapies have proven to be effective in animals, only very few have done so in human patients. There are for example many side effects of highly potent neuroprotective drugs that restrict the use of effective dose in patients. In animal studies, the exact time for the stroke event is known and therapy can be started early - this is however a dilemma with human stroke patients, that the time of incidence onset is unknown. Other problems are the morphological differences between the brain of humans and animals, and evaluation of efficiacy. In animals, treatment effects are mostly measured as a reduction of lesion volume, whereas in human studies functional evaluation (which reflects the severity of disabilities) is commonly used. Thus, therapies might reduce the size of the cerebral lesion (found in animals), but not the functional impairment when tested in patients.[26]

4.2 Ethical Dilemmas

Stroke models are carried out on animals which inevitably suffer during the procedure.There is a lot of stress during single or multiple animal caging, transport, animal handling, food deprivation, pain after surgical procedures, neurological disabilities etc. Thus, according to general consensus, these experiments require ethical justification. The following arguments can be produced to give reason for the conduction of animal experiments in stroke research: Stroke is very frequent in humans. Stroke is the third leading cause of death in the developed countries. Stroke is the leading cause of permanent disability in the developed countries. Yet there is no effective treatment available for the majority of stroke patients. Currently there are no in vitro methods that could satisfactorily simulate the complex interplay of vasculature, brain tissue, and blood during stroke, and thus could replace the greater part of animal experiments.

During animal experimentation the following prerequisites have to be fulfilled to maintain the ethical justification ("the three Rs"): Reduction: Animal numbers have to be kept as little as possible (but as high as necessary - to avoid underpowered studies -) to draw scientific conclusions. Refinement: Experiments have to be well planned and to be conducted by trained personnel to minimize the suffering of animals and to gain as much knowledge as possible. Replacement: Whenever possible animal experiments have to be replaced by other methods (e.g. cell culture, computer simulations etc.).

As we can see, the ethical dilemmas are directly linked to the investigation of stroke lesions and neuroprotective drugs, and not specifically to the possible testing of Strokefinder M100. The first rule of ethical justification is about reducing the number of animals used for studies, and by fusing the testing and analysis of stroke hit animals with the testing of the Strokefinder, this could be effectivly achieved. [27]

4.3 Steps of procedure

4.3.1 Ethical committees

Sweden has since 1979 had a system where all the animals in research must be approved by a ethical committee, which is jointly composed of scientists and lay people (which includes representatives of animal protection organizations), with a lawyer as chairman. Those wishing to use animals in their research writes an application to the Board where the carefully described both what to do with the animals and the areas where these experiments is to answer.

The Committee must then weigh the benefits of animal experiment in terms of increased knowledge, better treatments, etc. against the animal suffering.

National Board for Laboratory Animal Science gomes under the Scientific Council for Medicine, and there are seven boards in Sweden. Every board consists of representatives of researchers at the University who work with animals. The boards job is to be the research community's policy organs in laboratory animal issues, provide information to the public and researchers, administer health surveys in laboratory animals and implement national meetings and seminars.

Department of Agriculture

Who decides who gets to do animal testing? The actual condition for engaging in animal experiments issued by the Department of Agriculture. When a permit is granted appointed a manager and a veterinarian who shall ensure that operations are conducted according to Animal Welfare

Act. Premises where animal testing is done must be approved and no animals other than those bred for the purpose - may be used.

The process

But to apply for animal testing is in fact a lengthy process, allowing researchers to submit an application to the animal experimentation ethics committee. The group prepare requests, checks if they are complete and tells the researcher who submitted them if there are serious problems. In most cases this leads to a discussion between the researcher in charge and the board. After some while, the board have come to a resolution which is final even if it is possible to appeal in theory. The whole process from application to final permission might take several month of procedure. According to statistics, almost all applications gets approved in Sweden. [28]

→ The current application form is attached in appendix [29]

4.4 Ethical requirements

What is covered by the requirement for ethical review?

The requirement for ethical reviews covers mammals, birds, reptiles, amphibians, fishes and cyclostomes. Although embryos can be covered, it is determined from case to case. Ringing of birds need not be examined, nor feeding trials conducted in conjunction with conventional livestock. Application for ethical review Applying for ethical review is done via a special form (Appendix) The form is forwarded to the relevant animal ethics committee. Which board to consider the issue depends on the animal experiment performed.

All types of experiments that involve animals, invasive or non-invasive require a permit. [30]

4.5 Moral issues

Is it morally right to use animals? If the board approves the trial, the benefits of the experiment assessed weigh up and thus is morally right. Further, the permission also stated the point that the animals are not subjected to unnecessary suffering.

4.6 Economical aspects

The costs regarding animal testing are often sponsored by the government and therefor payed by with tax money. The research animals are expensive and need special compartments and staff that are experts in animal handling. Companies, however usually pay their animal experiments by themselves but might have shared animal handling with a university. Smaller animals like gerbils reproduce easily and are not too expensive, approximately 100 SEK per animal. Larger animals such as primates or dogs cost several thousand swedish crowns per animal. One thing to take into consideration is that the start up cost is larger than the maintenance because most animal research labs have their own small scale breeding. Especially when it comes to rabbits, rats and mice. Depending on the intensity of the animal studies the costs can be quite large. The use of 500 primates á 5000 SEK gives a total cost of 2.5 million crowns, while the same number of gerbils á 100 SEK is 50000 crowns. Here a trade off needs to be made, between expected results, medical insights and progress and ultimately - cost. Often times, small gerbils are excellent for studying human phenomena even if their physiology is a bit different.

Chapter 5

Conclusions, discussion and future outlook

5.1 Discussion and summary

At first, the course of action for this thesis was a bit unclear. There was allready a functioning stroke cap in use for clinical testing of the Strokefinder R10. It is an advanced helmet design that function well for short time monitoring and fixed positions. However the demands changed when the testing should include night surveillance for TIA patients. It was no longer fixed positions, and not measurements during a few hours daytime. To be able to perform clinical trials on actual stroke patients, night time, a whole different set up was needed. The new cap had to meet a new set of criterias such as comfort, antenna distribution and positioning, better size adjustment, extended lightness, cleanliness etc. The new stroke cap began to take form with a soft and elastic fabric, just to create something different from the helmet in use. The first model was just a simple cap with pockets, and then got extended with pillows in the back and other softening materials. It was obvious that just a fabric cap would be insuffiecient to meet all the needs of a medical device. Many aspects needs to be taken into consideration, not only cost or comfort. Also the type of fabric must be chosen carefully. Cotton fabric have the advantage of being easy to wash, but galon is easier to wipe off with anticeptics. A helmet with different bits and pieces is difficult to keep clean, especially if there is padding or such close to the patients hair or skin. Even the later designs with galon fabric head band had some draw backs when it came to hygiene. Stability is important not only because instability causes discomfort, but because instability causes sources of error which is unacceptable in stroke diagnostics. No system is perfect, but it is still of high importance to eliminate all apparent error sources and not contribute with any new ones. The current antennas and antenna cables are thick and hard, but it is impossible to optimize all aspects of a product at once. To be able to create a cheap, simple and usable stroke cap is just one part of the entire product. It is not the most important, technical part but is crucial that it function well during clinical testing. If the stroke cap suffer from too many drawbacks, it will affect the technical set up negatively. Everything put together - Strokefinder, antennas, cables and cap provides an entirety should function well together. The improvements of the stroke cap affect the entire device, small steps towards a product that can be in clinical use and replace all other methods for stroke diagnosis. Further improvements can be made along the way, as soon flaws are detected. However, not everything can be made at once for several reasons. The economic aspect is one, but everything also needs to be approved and tested. It needs to be safe. When it comes to clinical testing, actual stroke patients are involved which makes it highly important that the product is safe and don't cause any harm.

The final stroke cap in this master thesis project still have some flaws and drawbacks but it is absolutely good enough to be approved for clinical use, and it meets all the necessary requirements for a medical device. The time was limited and not all desirable testings could be performed. The design and evaluation of the cap took several month to perform, since every step of the way had to include testing, evaluation and analysis. As soon as a model seemed to be what was sought for, it was recreated professionally which was quite time-consuming and somewhat costly. However, this step could not be skipped. The whole process of evaluation, problem solving in medical design and manufacturing was necessary to come up with a final product with high standards. To be able to meet all the critera that was set up in section 2, the designs had to be reviewed several times. Even designs that was too simple or too complex was given one or two extra chances, to be sure no possible solution was neglected. One wild shot, was a stroke cap entirely made of waterfilled pads with antennas glued to the surface. It was theoretically a nice idea because it provided both comfort and eased the microwave propagation through the head. However, a model like that could not be manufactured professionally without costing too much. The more complex model, the more expensive to manufacture in small quantities. The skeleton helmet was a desire to not abandon the original Strokefinder R10 helmet completely. A helmet with soft interior and several regulators is indeed comfortable and stable but lacks too much in all other areas. The other designs are all on the same track - soft and simple. However, they all lacked stability as their main flaw. With the help of the disposable net cap, it could easily be solved, and the padded head band could finally be a winning design. Not because it is perfect, but because it is the solution that meet the most demands without being clumsy, expensive or too complex. Generally, it is always a good idea to keep it simple. Especially in medical design because the product is going to be used by different people, in different stages of the testing process and on several different patients. With that aspect taken into consideration, the head band is the most natural evolvement of the original stroke helmet. It is suitable for the next generation of Strokefinder, M100.

Section 4 took a look at animal testing in stroke research, and there is a posibility that a device like the Strokefinder could be used in this area of research. Both for testing and development of the strokefinder, and for better understanding of stroke events. However, this is clearly an area for the future and will perhaps not be possible for several years, and when it is - it might not be needed. However, the aspect of animal studies cannot be neglected. It is an important tool in all medical research to be able to use animal models for better understanding of drugs, general physiology and diagnostic devices. If the strokefinder will come into contact with animal testing is not clear yet, but to take a look at costs, moral and ethical issues, performance and practical steps is still of high value. Depending on the costs and the progress of the development of the Strokefinder, issues like this might be valid sooner than expected. That is why application procedure and approval for animal testing is included in this report, to provide extensive evaluation of the product in its whole. The focus point for this master thesis project was medical design, and to develop a functional stroke cap that could meet high demands - and be a part of a highly sofisticated medical, diagnostic tool. In conclusion, this is also the result of the project with extensive information and discussion added, regarding future aspects both when it comes to further testing and future applications.

5.2 Future applications

The use of the Strokefinder in early diagnosis and post-stroke evaluation.

5.2.1 NIHSS

The National Institute of Health Stroke Scale (NIHSS) is a standardized method used by physicians and other health care professionals to measure the level of impairment caused by a stroke.

The NIHSS serves several purposes, but its main use in clinical medicine is during the assessment of whether or not the degree of disability caused by a stroke merits trombolytic treatment. Another important use of the NIHSS is in research, where it allows for the objective comparison of different stroke treatments and rehabilitation interventions.

NIHSS measures several aspects of brain function, including consciousness, vision, sensation, movement, speech, and language. A certain number of points are given for each impairment uncovered during a neurological examination. A maximal score of 42 represents the most severe and devastating stroke. Current guidelines as of 2008 allow strokes with scores greater than 4 points to be treated with trombolytica.

The level of stroke severity as measured by the NIHSS scoring system:

→ 0= no stroke

→ 1-4= minor stroke

→ 5-15= moderate stroke

→ 15-20= moderate/severe stroke

→ 21-42= severe stroke [31]

5.2.2 NIHSS Chart

Category	Score/Description		Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials	Date/Time Initials
1a. Level of Consciousness (Alert, drowsy, etc.)	0 = Alert 1 = Drowsy 2 = Stuporous 3 = Coma						
1b. LOC Questions (Month, age)	0 = Answers both correctly 1 = Answers one correctly 2 = Incorrect						
1c. LOC Commands (Open/close eyes, make fist/let go)	0 = Obeys both correctly 1 = Obeys one correctly 2 = Incorrect						
2. Best Gaze (Eyes open - patient follows examiner's finger or face)	0 = Normal 1 = Partial gaze palsy 2 = Forced deviation						
3. Visual Fields (Introduce visual stimulus/threat to pt's visual field quadrants)	0 = No visual loss 1 = Partial Hemianopia 2 = Complete Hemianopia 3 = Bilateral Hemianopia (Blind)						
4. Facial Paresis (Show teeth, raise eyebrows and squeeze eyes shut)	0 = Normal 1 = Minor 2 = Partial 3 = Complete						
5a. Motor Arm - Left **5b. Motor Arm - Right** (Elevate arm to 90º if patient is sitting, 45º if supine)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement X = Untestable (Joint fusion or limb amp)	Left					
		Right					
6a. Motor Leg - Left **6b. Motor Leg - Right** (Elevate leg 30º with patient supine)	0 = No drift 1 = Drift 2 = Can't resist gravity 3 = No effort against gravity 4 = No movement X = Untestable (Joint fusion or limb amp)	Left					
		Right					
7. Limb Ataxia (Finger-nose, heel down shin)	0 = No ataxia 1 = Present in one limb 2 = Present in two limbs						
8. Sensory (Pin prick to face, arm, trunk, and leg - compare side to side)	0 = Normal 1 = Partial loss 2 = Severe loss						
9. Best Language (Name item, describe a picture and read sentences)	0 = No aphasia 1 = Mild to moderate aphasia 2 = Severe aphasia 3 = Mute						
10. Dysarthria (Evaluate speech clarity by patient repeating listed words)	0 = Normal articulation 1 = Mild to moderate slurring of words 2 = Near to unintelligable or worse X = Intubated or other physical barrier						
11. Extinction and Inattention (Use information from prior testing to identify neglect or double simultaneous stimuli testing)	0 = No neglect 1 = Partial neglect 2 = Complete neglect						
	TOTAL SCORE						

INITIAL	SIGNATURE	INITIAL	SIGNATURE	INITIAL	SIGNATURE

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figure 5.1 [32] NIHSS chart

5.2.3 NIHSS and Strokefinder M100

Microwaves spread when they penetrate tissue. And the image field, and its dependence on brain tissue and any bleeding, is highly complex.

Since Stroke Finder is based on 4-12 antennas, and each transmitting and receiving microwaves at 400 different frequencies. The data involved is gigantic. From these data sets, the patient is diagnosed with the use of algorithms.

When the brain is scanned with the microwave tomography technique, one antenna at a time transmits while the other ones recieve. This is repeated in the frequency range of 100MHz to 3GHz, until all the antennas have transmitted its signal. During the scanning process, a graph of the microwave propagation through the brain is gradually reconstructed on a monitor. The graph tells the position and size of the clot or bleeding in the brain, by using both amplitude and phase to calculate the dielectrical constant.

An interesting but yet plausible use for the setup, is to map the scanning results to the NIHSS.

The damage of the brain after a stroke might include a much more extensive area than just the position of clot or bleeding, due to the reduced blood flow. If the NIHSS and the microwave tomography results can be synched, the damaged areas of the brain can be easily targeted and a better understanding of the patients difficulties could be acquired.

For example could the NIH stroke evaluation be performed while the Strokefinder is running, to give instant notification of damaged brain areas and a graphical illustration of the impairment.

5.2.4 Strokefinder and graphical interphase

Both for the integration of NIHSS and for a more user friendly orientation a graphical user interphase is going to be implemented in the later stages of development.

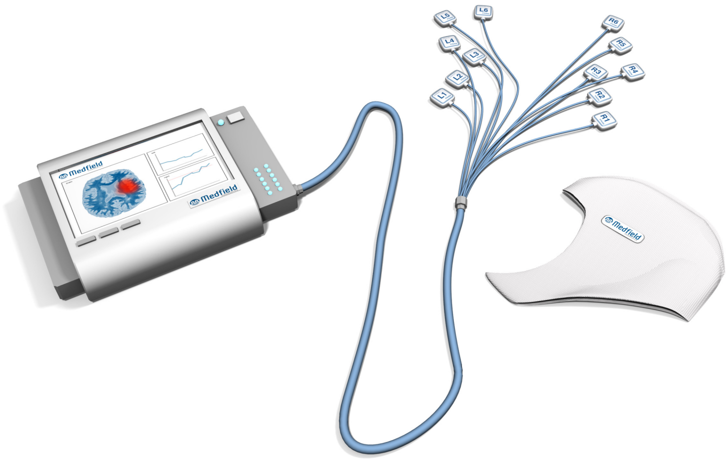

Figure 5.2 Strokefinder future design with graphical interphase. [33]

5.3 Future development of the stroke cap

The current stroke cap have antennas of the size 4 x 4 x 2 cm and if the antennas could be made smaller it would give room for other cap designs with even more antennas. This would also give room for better animal testing potentials. Currently, the more antennas, the more data is conducted and the more advanced mathematical algorithms need to be used. However, more antennas might not be needed, only thinner. This is an issue of cost, since specialized high-tech solutions are extremely costly even though they are feasible.

Figure 5.1 Example of a possible future design [34]

The figure above illustrates a future stroke cap design. This requires other antennas and antenna cables. The current antenna cables are stiff and must not be bent, each cable is also approximately 4mm in diameter. The illustration suggests an overall more neat and flexible solution.

5.4 Future outlook of the Strokefinder

The goal of the Strokefinder equipment is to decrease the overall size to make it more portable and usable in ambulances. It is allready smaller than other imaging devices such as CT but could be further improved in that area. Ideally the Strokefinder will have the size of a mobile phone, and several research groups are currently working on that aim.

5.5 Future development of the testing procedure

Before the Strokefinder can be used just as frequently as todays CT technique, extensive clinical trials need to be conducted. The Strokefinder must be proven to work just as well, or better than the CT, to be authorized for standard usage.

Clinical trials with actual stroke patients is crucial aswell as healthy volunteers. Another possibility to improve the procedure of ensuring the function, security and excellence of the Strokefinder is animal testing. A lot of animals are used in the development of stroke drugs and there might be a posibility to fuse those experiments with testing of the Strokefinder.

5.6 Economical aspects

Since stroke is one of the most common death causes in the world it is also very costly, several billion swedish crowns is needed only for treatment and rehabilitation every year. With early diagnosis and especially TIA surveillance many lives can be saved and also improved, since the stroke event can be treated much earlier. People that suffer from stroke often get permanent disabillities and need long-term rehabilitation. With TIA surveillance, a pending stroke could be treated before it causes any damage and therefor increase the economical efficiency in health care. This is an important issue both for the health care sector and for the national economy. If more people can be treated earlier with less complications for less money, millions can be saved every year. The importance of TIA surveillance is that it can predict possible stroke events and prevent them from occuring by pro-active treatment. With implemented TIA surveillance on a regular basis, for high-risk patients, thousands of lifes can be saved and improved.

Chapter 6

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Jordbruksverket

ANSÖKAN
-etisk prövning av djurförsök

Datum

____

Denna blankett är fastställd av Centrala försöksdjurs-nämnden (CFN) den 28 september 2001.
Vägledning för att fylla i blanketten finns att hämta på Jordbruksverkets webbplats (www.sjv.se).
Ansökan lämnas till den djurförsöksetiska nämnd inom vars verksamhetsområde det planerade djurförsöket ska utföras.

☐ I ansökan bör med motivering anges vilka uppgifter som enligt sökanden kräver **sekretess**

Uppgifter om sökanden (försöksledaren)

Namn		
Institution, avdelning eller motsvarande		
Telefonnummer (även riktnr)	Faxnummer (även riktnr)	E-mail
Adress		Postadress

Ansökan är en fortsättning av tidigare prövade försök

Diarienummer

☐ Försöket avser framställning av genetiskt modifierade djur

☐ Försöket avser användning av genetiskt modifierade djur

Försöksledarens klassificering av försökets svårighetsgrad (endast ett alternativ skall anges)

☐ Ringa svårighetsgrad ☐ Måttlig svårighetsgrad ☐ Avsevärd svårighetsgrad

Uppgifter om det planerade djurförsöket

Sidorna 1-4 i ansökningsblanketten fylls i av den sökande. OBS! Vid uppgiftslämnandet skall ett enkelt språk användas.
Viktigt är också att tillräckliga uppgifter lämnas för den djurförsöksetiska nämndens bedömning av försöket.

1. Projektets titel

Diarienummer

2. Syftet med djurförsöket och eventuell redovisning av tidigare resultat

3. Andra metoder än den valda

Uppgifter skall kortfattat lämnas om det finns andra metoder, med eller utan användning av djur, för att uppnå syftet med försöket

4. Dokumentationskrav

Om nationella eller internationella dokumentationskrav genom djurförsök föreligger, skall uppgifter som styrker behovet av försöket anges

Diarienummer

5. Valet av djurart, ras och stam

Djurart	Totalt antal djur
Motivering för val av djurart med karaktärisering av djuren	

6. Försökets tids- och genomförandeplan

Försöket beräknas påbörjas	Försöket pågår t o m
Beskrivning av försökets uppläggning och genomförande skall göras med tyngdpunkt på de ingrepp som görs, olika moments varaktighet m m	

7. Vård och förvaring

Uppgifter skall lämnas dels om djurens vård och förvaring omedelbart före, under och omedelbart efter försöket, dels om vid vilken institution eller klinik förvaringen sker och var försöket skall utföras

Diarienummer

8. Djurens situation och försökets slutpunkt

Beskrivning skall göras av den påverkan på djuren som väntas, eventuella komplikationer, smärtupplevelser, beteendeförändringar m m. Vidare skall motivering för klassificering av försökets svårighetsgrad lämnas (jämförs s. 1)

9. Anestesi- och avlivningsmetoder

Användning av narkosmedel, bedövningsmedel, smärtlindrande medel och lugnande medel skall anges liksom avlivningsmetod som skall användas

Underskrift sökande

Datum	Underskrift
	Namnförtydligande

Underskrift ansvarig föreståndare enligt 20 § djurskyddslagen har utan erinran tagit del av det planerade djurförsöket

Datum	Underskrift
	Namnförtydligande

Diarienummer

Kompletterande uppgifter till ansökan

OBS! Om nya eller kompletterande uppgifter tillförs under ärendets beredning skall
Dessa antecknas nedan genom beredningsgruppens försorg eller av den djurförsöksetiska nämnden

Beredningsgruppens förslag till nämndens ställningstagande

Datum	Underskrift	Namnförtydligande
Datum	Underskrift	Namnförtydligande
Datum	Underskrift	Namnförtydligande
Datum	Underskrift	Namnförtydligande

Diarienummer

Den djurförsöksetiska nämndens beslut (Om inte annat sägs i beslutet gäller detta under tre år från dagen för beslutet)

☐ Godkänns ☐ Avslås

☐ Godkänns med följande villkor:

Datum	Ordförandens underskrift
	Namnförtydligande

Motivering och ev avvikande mening, se protokollet. I förekommande fall hur man överklagar, se bilaga