THERMOCOAGULATION IN DEEP BRAIN STRUCTURES

Modelling, simulation and experimental study of radio-frequency lesioning

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Abstract
Radio-frequency (RF) lesioning is a method utilising high frequency currents for thermal coagulation of pathological tissue or signal pathways. The current is delivered from an electrode with a temperature sensor, permitting control of the current at a desired target temperature. In the brain RF-lesioning can e.g. be used for severe chronic pain and movement disorders such as Parkinson’s disease. This thesis focuses on modelling and simulation with the aim of gaining better understanding and predictability of the lesioning process in deep brain structures. The finite element method (FEM) together with experimental comparisons was used to study the effects of electrode dimensions, electrode target temperature, electric and thermal conductivity of the brain tissue, blood perfusion and cerebrospinal fluid (CSF) filled cysts. Equations for steady current, thermal transport and incompressible flow were used together with statistical factorial design and regression analysis for this purpose.

Increased target temperature, electrode tip length and electrode diameter increased the simulated lesion size, which is in accordance with experimental results. The influence of blood perfusion, modelled as an increase in thermal conductivity in non-coagulated tissue, gave smaller simulated lesions with increasing blood perfusion as heat was more efficiently conducted from the rim of the lesion. If no consideration was taken to the coagulation the lesion became larger with increased thermal conductivity instead, as the increase in conducted heat was compensated for through an increased power output in order to maintain the target temperature. Simulated lesions corresponded well to experimental in-vivo lesions.

The electric conductivity in a homogeneous surrounding had little impact on lesion development. However this was not valid for a heterogeneous surrounding. CSF-filled cysts have a much higher electric conductivity than brain tissue focussing the current to them if the electrode tip is in contact with both. Heating of CSF can also cause considerable convective flow and as a result a very efficient heat transfer. This affected simulated as well as experimental lesion sizes and shapes resulting in both very large lesions if sufficient power compared to the cysts size was supplied and very small lesions if the power was low, mitigating the heat over a large volume.

In conclusion especially blood perfusion and CSF can greatly affect the lesioning process and appear to be important to consider when planning surgical procedures. Hopefully this thesis will help improve knowledge about and predictability of clinical lesioning.
**Abbreviations**

AC  Anterior commissure  
CSF  Cerebrospinal fluid  
CT  Computed tomography  
DBS  Deep brain stimulation  
GPe  Globus pallidus externa  
GPi  Globus pallidus interna  
FEM  Finite element method  
LNG  Leksell® Neuro Generator  
MRI  Magnetic resonance imaging  
PD  Parkinson’s disease  
PET  Positron emission tomography  
PC  Posterior commissure  
RF  Radio-frequency  
SN  Substantia nigra  
SNc  Substantia nigra pars compacta  
SNr  Substantia nigra pars reticulata  
STN  Subthalamic nucleus  
VR  Virchow-Robin
Physical symbols
Scalar symbols are written in italics, e.g. $T$.
Vector symbols are written in italics and bold, e.g. $\mathbf{J}$
Units are written normally, e.g. $\text{kg/m}^3$.

$\eta$ Dynamic viscosity ($\text{N}\cdot\text{s}/\text{m}^2$)
$\rho$ Mass density ($\text{kg}/\text{m}^3$)
$\sigma$ Electric conductivity ($\text{S}/\text{m}$)
$c$ Specific heat capacity ($\text{J}/(\text{kg}\cdot\text{K})$)
$\mathbf{F}$ Volume force ($\text{N}/\text{m}^3$)
$g$ Acceleration of gravity ($\text{m}/\text{s}^2$)
$\mathbf{J}$ Electric current density ($\text{A}/\text{m}^2$)
$k$ Thermal conductivity ($\text{W}/(\text{m}\cdot\text{K})$)
$k_{\text{perf}}$ Thermal conductivity added due to blood perfusion ($\text{W}/(\text{m}\cdot\text{K})$)
$k_{\text{tiss}}$ Thermal conductivity of tissue excluding blood perfusion ($\text{W}/(\text{m}\cdot\text{K})$)
$p$ Pressure ($\text{N}/\text{m}^2$)
$\dot{Q}$ Power density ($\text{W}/\text{m}^3$)
$t$ Time ($\text{s}$)
$T$ Temperature ($^\circ\text{C}$)
$T_{\text{set}}$ Preset electrode temperature ($^\circ\text{C}$)
$u$ Velocity ($\text{m}/\text{s}$)
$V$ Electric potential ($\text{V}$)
List of papers


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1 Introduction
Thermal coagulation of tissue by the use of radio-frequent (RF) currents can be used
to cure or relieve the symptoms for a number of conditions such as bleeding (von
Maltzahn and Eggleston 1995), cardiac arrhythmias (Tungjitkusolmun et al. 2000),
cancer metastases (Goldberg 2001) and severe pain (Cosman 1996). Another suitable
area is symptom relief for movement disorders, in particular Parkinson’s disease
(PD). Here the method is used to block over-active signal pathways in the central grey
parts of the brain and it has been in use since the 1950s (Cosman 1996). Contrary to
what would be expected, the blocking effect caused by the coagulum or lesion
(=wound) can also be obtained by the use of non-heating nerve-stimulating currents
of much lower frequency in the same target, so called deep brain stimulation (DBS)
(Benabid 2003). While DBS has become the more popular method for PD in the
western world due to its reversibility, it is rather expensive and thus not always a
viable option for medical care with limited funds in e.g. developing countries. RF-
lesioning in the brain is thus still an interesting topic to study, especially since
knowledge obtained might be useful in other wider areas of use.

2 Aim
The aim of this study was to investigate RF-lesioning in the brain in order to improve
understanding and predictability of this electrosurgical coagulation technique.
Modelling and simulations using the finite element method (FEM) were used together
with experiments in order to investigate the impact from different factors on the size
and shape of the resulting thermal coagulation lesion. The studied factors were
electrode dimensions, target temperature, physical properties of tissue, blood
perfusion and CSF-filled cavities.
3 Surgical thermocoagulation in the brain

3.1 Tissues of the brain

Grey matter primarily consists of all parts of the neural cell bodies and supporting cells known as neuroglia that provide the neurons with nutrition, a good chemical environment, physical support and protection from microbes. Usually, a small formation of grey matter is called a nucleus in the central nervous system and a ganglion outside it. The brain contains many paired nuclei, which means that there is one nucleus in the left side of the brain and one corresponding nucleus in the right side (Tortora and Grabowski 2000). Paired nuclei are nevertheless usually mentioned in singular form, e.g. the globus pallidus. White matter consists mostly of myelinated axons, which convey signals over longer distances e.g. between different parts of the brain (Tortora and Grabowski 2000). The tissue is rather fatty, with a lipid content of about 18% compared to about 5% for grey matter (Duck 1990). White matter structures of particular interest in stereotactic neurosurgery are the anterior commissure (AC) and posterior commissure (PC) which, together with the corpus callosum, connects the sides of the cerebrum (Tortora and Grabowski 2000). The AC-PC line is a useful imaginary line of about 23-28.5 mm between the two commissures (Lucerna et al. 2002), see Figure 1. Many important structures in the brain, e.g. the nuclei of the thalamus, are visually indistinguishable but the position of the structures in the brain usually relate to the AC-PC line in a fairly predictable manner in different individuals, making it possible to locate an invisible target for neurosurgery (Kaplitt et al. 2003).

![Diagram of the brain showing the AC-PC line and commissures](image)

**Figure 1:** Left: Midsagittal plane of the brain showing the commissural fibres connecting the two halves of the brain: the corpus callosum, the anterior commissure and the posterior commissure. The anterior and posterior commissures form the imaginary AC-PC line, which is useful for navigation in the brain. Right: Lesion created near CSF in a ventricle.

Cerebrospinal fluid (CSF) is a clear liquid that can be found in and around the brain and around the spinal chord. It protects the brain from chemical and mechanical harm as well as providing it with nutrients and removing waste products. Most of the CSF can be found in the subarachnoid space, i.e. between the arachnoid and the pia mater meninges. It can also be found inside the brain in four small cavities called ventricles (= little cavities) (Ransom 2003). CSF consists of 99 % water (Duck 1990) but also
contains ions, proteins, glucose, lactic acid, urea and white blood cells (Tortora and Grabowski 2000). The CSF is mostly produced in the ventricles and circulates around the brain and spinal chord until it drains from the subarachnoid space to the superior sagittal sinus, a venous cavity in the dura mater (Ransom 2003).

The brain uses about 20% of the body’s oxygen consumption at rest, while only making up about 2% of the mass. Most cells in the brain do not receive blood directly as the capillaries in the brain generally are surrounded by a continuous membrane making them much less permeable than those in the rest of the body. Instead the cells and capillaries are connected via a type of neuroglia called astrocytes that selectively pass certain substances between them. This feature is called the blood-brain barrier and protects the brain from many harmful substances. Unfortunately, it also prevents many substances to pass that otherwise could have been used for the treatment of brain disorders. The blood flow in the brain is directed locally so that active neurons and neuroglia receive more blood. (Tortora and Grabowski 2000)

Grey matter has considerably higher blood perfusion with about 70 ml/(100g-min) at rest and maximal perfusion in the cortex of about 300-400 ml/(100g-min) compared to white matter with about 20 ml/(100g-min) at rest (Mellander 1983). A recent Finnish study of cerebral blood flow using magnetic resonance imaging (MRI) on 80 healthy persons gave the results (mean ± standard deviation) 94.2±23.0 ml/(100g-min) for grey matter and 19.6±5.8 ml/(100g-min) for white matter. The authors of that study suspect that some of the values for grey matter are too high due to large vessels in the measured volume (Helenius et al. 2003). A study from France on 27 healthy persons using Positron Emission Tomography (PET) has given the results 47.7±10.9 ml/(100ml-min) for grey matter and 24.7±5.3 ml/(100ml-min) for white matter. The authors of that study note that the poor spatial resolution of PET mixes the grey and white matter, thus probably underestimating the values for grey matter and overestimating the values for white matter (Pantano et al. 1984).

Most of the larger vessels of the brain lie on the surface or in the fissures, i.e. the folds of the brain. Arterioles, i.e. small arteries, enter the brain from the larger surface vessels. The arterioles usually have a diameter of 0.4 mm or less, and are thus not detectable with ordinary clinical MRI (Heier et al. 1989). They are surrounded by CSF-filled spaces called Virchow-Robin (VR) spaces or perivascular spaces (peri- = around, vasculum = tiny vessel (Pickett 2000)). There is some controversy regarding whether these spaces are a part of the subarachnoid space or if they are closed compartments (Edvinsson and MacKenzie 2002). They can increase in size with age and may sometimes become quite large with a volume of several hundred mm³ (Laitinen et al. 2000).
3.2 The basal ganglia, thalamus and associated structures

Despite their name (basal nuclei is a more correct term), the basal ganglia are a group of paired nuclei in the cerebrum surrounding the thalamus. The definition of the basal ganglia varies but nuclei usually included are the caudate nuclei (caud- = tail), the putamen (= shell) and the globus pallidus (globus = ball, pallidus = pale), which is divided into an external part, globus pallidus externa (GPe) and an internal part, globus pallidus interna (GPi). These nuclei are connected to the cerebral cortex and are involved in a number of functions, such as movement control and cognition (Ma 2002). For the purpose of movement control the basal ganglia are also connected with e.g. the substantia nigra, the thalamus and the subthalamic nucleus. The substantia nigra (SN, substantia = substance, nigra = black) is paired nuclei in the midbrain and is responsible for subconscious muscle activity. (Tortora and Grabowski 2000) It consists of two principal parts: the cell-dense substantia nigra pars compacta (SNC) and the net-like substantia nigra pars reticulata (SNR, reticulum = tiny net (Pickett 2000)) (Ma 2002). The thalamus (= inner chamber) consists of a pair of oval volumes of grey matter beneath the third ventricle and takes up the major part of the diencephalon. It is about 3 cm long and contains many smaller paired nuclei that are involved with emotions, awareness, knowledge acquisition, memory and relaying of signals to the cerebral cortex. The subthalamic nucleus (STN) is located in the subthalamus immediately beneath the thalamus. The subthalamus also contains parts of the substantia nigra (Tortora and Grabowski 2000).

![Figure 2: Principal sketch of the basal ganglia and associated structures (approximately frontal section in the middle of the brain).](image1)

3.3 Parkinson’s disease

Parkinson’s disease (PD) is a progressive handicapping disease that is relatively common among older people, in Sweden affecting about 1% of the population over 50 years of age (Midlöv et al. 2005). Other developed countries, as well as China, have a similar prevalence (Zhang et al. 2005). In PD neurons projecting from the substantia nigra to the putamen are lost. This causes disturbances in the neural activity of the basal ganglia and results in a number of movement disturbances. Examples are resting tremor where oscillatory muscle contractions cause the patient to shake, akinesia...
where the patient has trouble initiating movements and bradykinesia where the patient’s movements are slowed and reduced in size. The lost neurons normally release dopamine in the putamen and a therapeutic strategy may thus be to compensate for this. Dopamine itself cannot cross the blood-brain barrier but giving the patient a precursor substance called L-dopa can alleviate the symptoms. (Ma 2002)

L-dopa can in time cause another disabling condition called dyskinesia where the patient instead can suffer from involuntary or poorly controlled movements (Midlöv et al. 2005). This condition can be alleviated by lesioning (pallidotomy) or DBS in the GPi. The procedures can also improve symptoms of the disease itself, especially tremor, but results here have been more inconclusive (Sierens and Bakay 2003; Volkman and Sturm 2003). Lesioning or DBS in the STN can, like L-dopa, reduce the symptoms of the disease and thus allow a lower intake of L-dopa. This in turn may also reduce the dyskinesia caused by the medication (Abosch et al. 2003; Gill et al. 2003). Lesioning (thalamotomy) or DBS can also be performed in the thalamus but these procedures are mostly effective against tremor (Hua et al. 2003). Nuclei in the thalamus can also be the target for treatment of severe chronic pain (Hariz and Bergenheim 1995). Finally, many attempts have been made at implanting dopamine-producing cells of different kinds into the putamen but these tests so far have not been very successful (Koller et al. 2003).

It is not known in much detail how the therapies actually work. Modelling of the impact on excitatory and inhibitory signal pathways based on experiments in nonhuman primates (Figure 3) does not fully explain, and sometimes even contradicts, results on humans. Based on this model it could be suspected that lesioning in the GPi would give similar results as lesioning in the STN or medication with L-dopa, as all procedures should reduce the inhibition of the thalamus. As mentioned however, lesioning in the GPi mainly relieves dyskinetic side effects from the L-dopa. (Ma 2002)

Figure 3: Suggested pathways associated with PD through the basal ganglia. Left: The normal state. Right: In PD loss of projections from SNr causes lack of dopamine release in the putamen resulting in overinhibition of the thalamus and understimulation of the motor cortex. This can be alleviated by administration of L-dopa or lesioning in the STN. Lesioning in the GPi however is effective against dyskinesia induced by L-dopa, which is contrary to what would be expected from the model above. Thin lines represent decreased and thick lines increased activity. Based on (Ma 2002).
3.4 Stereotactic neurosurgery

In order to reach the mm-sized targets in the brain very high precision and accuracy is required. This can be achieved by stereotactic (may refer to taxic = system, or tactus = to touch) techniques, where instruments can be mounted on an adjustable frame firmly attached to the skull or another part of the body. The instrument can then be brought to a well-defined point. For example, the Leksell Stereotactic System® model G (Elekta Intrument AB, Sweden) has a target accuracy of ±1 mm (Lunsford et al. 1996). In order to obtain the target point, imaging of the brain is needed. A box with, for the chosen imaging method, opaque reference lines called fiducials is mounted on a part of the frame which in turn is firmly attached to the patient’s skull. Imaging of the brain is then done through either computed tomography (CT) or magnetic resonance imaging (MRI). The fiducial box is then replaced with the rest of the frame (Figure 4) and the imaging can be used to calculate the desired coordinates in the frame. Examples of clinical applications where stereotaxy can be useful are the already mentioned symptom relief for movement disorders, pain relief, biopsy, tumour resection, aneurysm treatment, diagnosis and treatment of epilepsy, hydrocephalus treatment and psychosurgery. (Maciunas and Galloway(Jr.) 1999)

Figure 4: Left: Prior to surgery a box with opaque fiducials is used in order to determine the position of the target. Right: Leksell Stereotactic System®. The frame can be adjusted so that a point in the brain can be reached from a great range of angles. This allows the surgeon to pick a pathway with minimal risk of serious blood vessel disruption. (Images courtesy of Elekta Instrument AB)

3.5 Radio-frequency (RF) lesioning

In RF-lesioning a high frequency current is used to heat tissue around a small monopolar electrode tip or between the contact surfaces of a bipolar electrode. The oscillating current causes heating of the tissue through collisions between its ions and other molecules. The tissue then heats the tip, which contains a thermocouple that in turn allows the power generator to control the current. For monopolar heating a neutral plate with good electric contact with the body is needed. As the tissue is sufficiently heated to about 60 °C it coagulates and becomes pale and stiff, as the tertiary bonds of its proteins break and the proteins stick to each other (Figure 5)
Around the coagulum in a general thermal injury a zone of stasis with partially damaged tissue and progressively reduced microcirculation emerges and further out a zone of hyperaemia appears where blood flow instead increases. An oedema will also start to form in the zone of stasis (Sjöberg and Östrup 2002). If the tissue is allowed to reach a temperature of 100 °C its water content will vaporise. This is a condition that must be avoided as the tissue then may stick to the electrode (von Maltzahn and Eggleston 1995) and boiling may cause small explosions (van den Berg and van Manen 1962). The lesion is in this thesis defined as the coagulum, though the zone of stasis is also injured and the tissue there may or may not recover after some time (Sjöberg and Östrup 2002).

![Figure 5: Coagulation of tissue as in the case of frying an egg. Heat breaks the tertiary protein bonds. The proteins will then stick to each other and the tissue becomes stiffer and paler.](image)

RF-lesioning is a form of soft coagulation electrosurgery, i.e. the voltage is not high enough to cause sparks between the electrode and the tissue. This gives a slower but more controllable coagulation. The procedure is also known as RF-ablation (ablatus = carry away (Pickett 2000)), although no tissue is actually removed. In this case ablation refers to the removal of function.

The **Leksell® Neuro Generator (LNG)** is a power generator for temperature controlled RF-lesioning in the brain using a current with a frequency of 512 kHz. The temperature of the tip is allowed to rise by a maximum of 6 °C/s and is stabilised at a target temperature determined by the user. The LNG can continuously measure electric impedance between the electrode tip, the neutral plate or between the active surfaces of the bipolar electrode. It also has the capability to deliver stimulation pulses of considerably lower frequencies (20-200 Hz) in order to confirm if the right target position has been reached. The patient is awake during the surgery and if he/she for example experiences visual disturbances during the stimulation the positioning is too close to the optic nerve which may be a risk when lesioning in the GPi (Cook et al. 1998). Typical target temperatures are between 70 and 90 °C and heating time is usually 60 s.
3.6 Other lesioning techniques
Artificial lesions can also be created using a number of other methods. Apart from RF-currents, thermal energy can be delivered by microwave radiation (Wren 2004), laser radiation (Poepping et al. 1999) and ultrasound (Damianou et al. 1995). Lesions can also be achieved by radiosurgery with ionizing electromagnetic radiation (Ohye et al. 1996), cryosurgery where tissue is frozen (Rand 1996) or by the injection of toxic agents such as pure ethanol (Livragi et al. 1995).
4 Physics of electrosurgical thermocoagulation

Electrosurgical thermocoagulation utilises electric currents in order to heat tissue. Equations for electric currents and heat transfer are thus needed in order to model and simulate the process. If fluids like CSF are present some appropriate variant of Navier-Stokes equations is needed to calculate fluid flow and resulting convective heat transfer. These equations are dependent on one another and it is necessary to solve them simultaneously, see Figure 7. See Appendix A for description of the nabla operator $\nabla$, gradient and divergence.

Figure 7: The equations are dependent on one another and need to be solved together. The electric current causes heating but is also affected by the temperature and temperature gradients cause free convection, which in turn causes convective heat transfer.

4.1 Electric currents in tissue

A material’s ability to conduct electric currents is described by its electric conductivity, $\sigma$. Metals have high electric conductivity due to easily accelerated valence electrons. In biological tissue, electric currents are mainly conducted by salt ions solved in water. Solid biological tissue is full of thin cell membranes with very low electric conductivity, effectively working as capacitors. This gives the tissue a very low electric conductivity for low frequencies, while higher frequency currents can pass with much less resistance (Roth 1995). As a consequence biological fluids such as blood and CSF have much higher electric conductivity than more solid tissue such as grey matter or kidney tissue, especially for low frequencies. The electric conductivity increases with temperatures up to approximately 100 °C where vaporisation will cause a rapid decrease in conductivity (Lee et al. 2003).

The equation of continuity for steady currents (Cheng 1989) is commonly used to calculate the electric currents during the lesioning of tissue:

$$\nabla \cdot J = -\nabla \cdot (\sigma(T) \nabla V) = 0 \ (\text{A/m}^3)$$  \hspace{1cm} (1)
Under the assumption of homogeneous and isotropic electric conductivity, this equation reduces to Laplace’s equation (Cheng 1989):

$$\nabla^2 V = 0 \quad (A/m^3) \tag{2}$$

Equation (2) is not used in this thesis however, as homogeneity is not generally a valid assumption for electrosurgical procedures due to the strong temperature dependency of the electric conductivity. Currents in a conductive media will cause resistive (Joule) heating, $\dot{Q}_R$:

$$\dot{Q}_R = J \cdot (\sigma(T) \nabla V) = \sigma(T)(\nabla V)^2 \quad (W/m^3) \tag{3}$$

### 4.2 General heat transfer

Heat within a porous body, e.g. tissue, can be transferred through thermal conduction and thermal convection. How heat is conducted in a body is affected by its mass density, thermal conductivity and specific heat capacity.

Most soft tissues and body fluids have a mass density, $\rho$, of about $1.0 \cdot 10^3$ to $1.1 \cdot 10^3$ kg/m$^3$, slightly higher than water. Hard tissues can be considerably denser. Pure bone tissue has a mass density of about $2.0 \cdot 10^3$ kg/m$^3$ for example. Mass density usually decreases slightly with increasing temperature (Duck 1990). Everything else equal, a denser material will require more energy to heat to a certain temperature than the same volume of a less dense material. It has a greater storage capacity and can thus also deliver more thermal energy to its surroundings. A piece of metal will contain a lot more thermal energy than the same volume of air at the same temperature, for instance. This is one reason to why it is possible to reach into an oven with an air temperature of 200 °C without burning the hand, while touching metal in the same oven can be very painful.

**Specific heat capacity**, $c$, describes how much energy is required to raise the temperature of a unit mass of the material. As with mass density a higher specific heat means slower heating and a higher storage capacity for thermal energy. Common values for soft tissues lie between $3 \cdot 10^3$ and $4 \cdot 10^3$ J/(kg·K) and values for hard tissues typically lie around $1 \cdot 10^3$ J/(kg·K). Water has a fairly temperature independent specific heat capacity of $4.2 \cdot 10^3$ J/(kg·K) between the phase transitions at 0 and 100 °C. Fats on the other hand have considerable and complex temperature dependencies. Phase transitions exist over a range of temperatures and are usually not as abrupt as for water. Furthermore fats often show hysteresis, i.e. the properties are different during heating and cooling. (Duck 1990)

**Thermal conductivity**, $k$, describes a material’s ability to conduct thermal energy, i.e. heat, through conductive heat transfer. Metals have high thermal conductivity for the same reason that they have high electric conductivity: easily accelerated electrons. Gases have very low thermal conductivity, another reason as to why it is possible to reach into a hot oven without burning the hand. Most soft tissues have a thermal conductivity of about 0.5 W/(m·K) slightly lower than water, which has $k = 0.60$ W/(m·K). Fat has lower thermal conductivity, around 0.2 to 0.3 W/(m·K). Thermal conductivity of tissue increases with water content. Ice and frozen tissue with high
water content have a considerably higher thermal conductivity than non-frozen tissue and it increases with decreasing temperature. Thermal conductivity increases moderately with temperature for tissue above 0 °C. Increases of about 0.2 to 1 %/°C have been reported for soft tissues between 3 and 45 °C. (Duck 1990)

While fluids generally have a poor thermal conductivity compared to solids, heat transfer can still be much more efficient thanks to convection, i.e. fluid motion. Here heat is transferred through mass transfer. For instance, the temperature on a cold winter day will be perceived as much colder if a wind is blowing than if the air is still. This is because the body warms air close to the body. If still, this will limit heat loss to the air as it has very low thermal conductivity and the temperature difference between the air and the body is reduced. However, if a wind is blowing the warmed air will be replaced by cooler air, thus increasing heat loss. Heat can also be transferred through electromagnetic radiation such as sunshine. This transfer is not considered in this thesis however.

Thermal transport in a fluid can be described by the thermal transport equation (Chen and Holmes 1980):

$$\rho c \frac{\partial T}{\partial t} + \nabla \cdot (\rho c T \mathbf{u} - k \nabla T) = \dot{Q} \quad \text{(W/m}^3) \quad (4)$$

Where \( \mathbf{u} \) denotes the velocity field (m/s) in the fluid. In solids, where no internal convection occurs, this reduces to the heat conduction equation:

$$\rho c \frac{\partial T}{\partial t} + \nabla \cdot (-k \nabla T) = \dot{Q} \quad \text{(W/m}^3) \quad (5)$$

In this thesis the temperature dependence of mass density \( \rho \), specific heat capacity \( c \) and thermal conductivity \( k \) are assumed to be small enough for relevant temperatures to be approximated as constants. An exception is blood perfusion modelling, see Paragraph 4.4.
Figure 8: Conductive and convective heat transfer. In solid materials, e.g. a slice of meat, the heat transfer is dominated by conduction. Heat transfer can be greatly enhanced by convection as in the case of stirring a stew.

4.3 Free convection

When boiling water, the heating will cause circulation and as a consequence will even out the temperature distribution in the water. This effect is called free convection and is caused by mass density variations as heated water becomes lighter and floats upwards. Important material parameters for convection are mass density, which determines the inertia and gravity force, and dynamic viscosity, $\eta$, which describes the internal resistance to flow through friction. The circulation can be calculated using Navier-Stokes equations with incompressible flow and gravitational (buoyancy) force (Gresho and Sani 1998), (Massoud 2005):

\[
\rho \frac{\partial \mathbf{u}}{\partial t} + \rho (\mathbf{u} \cdot \nabla) \mathbf{u} = -\nabla p + \nabla \cdot [\mathbf{\eta}(T)(\nabla \mathbf{u} + (\nabla \mathbf{u})^T)] + \rho(T)g \quad \text{(N/m}^3\text{)}
\]

The dynamic viscosity of water has a strong non-linear temperature dependency in the range 37-100 °C (Figure 9). While the temperature dependency of mass density is small enough to be ignored in most cases here, it is the driving force for natural convection and must be included in order to cause convection in the simulations.
Figure 9: Left: Free convection is the driving force for the angel chimes Christmas decoration (though here without the chimes themselves). A lit candle beneath the decoration causes the air above it to flow upwards making the wheel and the angels rotate. Middle: Mass density for water as a function of temperature. Heated water will become lighter and flow upwards if beneath cooler water, due to the difference in weight. Right: Dynamic viscosity for water as a function of temperature. As the water is heated the internal friction, and thus the resistance to flow, is reduced. The reduced viscosity of the water also reduces the electric resistance as charged ions can move more easily in the water. The two graphs are based on tabulated data from (Weast 1976).

There is also a strong relation between viscosity and the electric resistance of salt water. Four experiments were performed where the temperature and impedance of a bipolar electrode were measured in a slowly heated water bath. As expected, the experiments showed decreasing impedance with temperature, see Figure 10. A likely explanation is that as the viscosity decreases with increasing temperature the resistance to flow decreases also for the electrically charged salt ions and thus the impedance decreases. If the admittance, which is the inverse of the impedance and if assumed real-valued (conductance) directly proportional to the electric conductivity $\sigma$, is plotted instead a clear linear relation is shown against the temperature. This is the way the electric conductivity is modelled for all tissue in this thesis.
4.4 Influence of blood perfusion

Blood perfusion in living tissue cools heated tissue and can thus cause smaller lesions (Aschoff et al. 2001). Blood perfusion can be modelled as an addition, $k_{perf}$, to the thermal conductivity of the tissue:

$$k_{eff} = k_{tiss} + k_{perf} \quad (W/(m \cdot K))$$  \hspace{1cm} (7)

This model is believed to be appropriate if most of the perfusion in the tissue is through vessels with a diameter of 200 µm or less (Wren et al. 2001). The blood coagulates at about 60 °C and $k_{perf}$ should then become 0 W/(m·K). This relation was introduced in Paper I:

$$k_{eff} = \begin{cases} k_{tiss} + k_{perf} & (T \leq T_{coag}) \\ k_{tiss} & (T > T_{coag}) \end{cases} \quad (W/(m \cdot K))$$  \hspace{1cm} (8)

Alternatively the effect of blood perfusion can be modelled as a heat sink or as a combination of increased thermal conductivity and a heat sink. This approach is thought to be better if macroscopic vessels are present (Wren et al. 2001). An approximation in all these models is that macroscopic direction of the blood flow is disregarded (Arkin et al. 1994). In order to be feasible for numerical solvers steps as in Eq. 8 can be approximated with logistic functions, see Appendix C.
The finite element method (FEM)

The finite element method is a numerical technique for calculating fields that may lack an analytical solution by dividing a complex geometry into simple elements. Solving problems with FEM requires a number of steps. First an appropriate mathematical model is constructed. This model consists of two parts: A geometric model of the studied object and appropriate physical equations e.g. the heat conduction equation or the equation for steady currents described in the previous chapter. Coupled equations may be needed due to variable dependencies, as is the case in this thesis. The physical equations also need defined boundary conditions e.g. a prescribed temperature or heat flow at an edge of the geometric model. Three-dimensional problems may often be reduced in dimension due to symmetry. This can greatly reduce the computational time and requirements though caution is needed as the use of inappropriate symmetry conditions can give gross errors. All models in this thesis have axial symmetry, see Appendix B.

The geometric model is then divided into discrete elements of some simple shape e.g. triangles. The physical equations are then applied to each element and assembled into a huge matrix for the computer to solve. The divided geometry is called a mesh (= net). A fine mesh with many elements gives a smaller numerical error but requires more computational time and power. An appropriate approach to mesh density is to start with a coarse mesh and then test finer meshes to see if the solution is affected considerably. After solving the problem it is important to check if the solution is reasonable. The user may have given incorrect inputs to the software, an inappropriate physical model may have been used, numerical errors may be unacceptably large and the software may contain bugs, see e.g. Paper I for the failure to handle time-dependent boundary conditions in Femlab 2. Known measurements or analytical solutions of similar problems may be of use here. (Cook et al. 2002)

*Figure 11: Mesh for an axi-symmetric model of a 1x4 mm electrode zoomed around the tip. In the finite element method geometries are divided into many smaller elements.*
6 Factorial designs and quadratic regression

The impact of a factor on some result is often dependent on the value of other factors. For instance, some medicines may be rendered useless or give unwanted side effects if taken in combination with each other or with alcohol. Such effects are called interactions and can be found with factorial designs. Studying the effect of one factor at a time while keeping all other factors constant will fail to reveal interactions and may cause the investigator to draw wrongful conclusions. Factorial design was used in Paper I and quadratic regression was used in Papers I and III in order to calculate effects.

6.1 2\textsuperscript{k} Factorial design

The 2\textsuperscript{k} factorial design (Montgomery 1996) is a way to find linear main effects of factors and their interactions. Each factor is given a high and a low level and a number of measurements are made with different combinations of the levels according to a design matrix, \textbf{C}. Factorial effects \( \alpha \) for a 2\textsuperscript{k} factorial design are computed as:

\[
\alpha_j = \frac{\sum_{i=1}^{2^k} y_i c_{ij}}{\sum_{i=1}^{2^k} [c_{ij}]^2}
\]  

where \( y_i \) is the result for measurement \( i \) and \( c_{ij} \) the contrast coefficient for effect \( j \) and measurement \( i \). The contrast coefficient for a high level is +1 and for a low level -1. The contrast coefficients for interaction effects are given by multiplying the coefficients of the main effects. Assume two factors \( A \) and \( B \). The interaction between the factors is given by:

\[
c_{ABi} = c_{Ai} \cdot c_{Bi} \text{ (dimensionless)}
\]  

Example: Two factors at two levels are investigated and the following results, \( y \), are obtained:

<table>
<thead>
<tr>
<th>( c_1 )</th>
<th>( c_2 )</th>
<th>( c_1 c_2 )</th>
<th>( y )</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1</td>
<td>-1</td>
<td>+1</td>
<td>0</td>
</tr>
<tr>
<td>+1</td>
<td>-1</td>
<td>-1</td>
<td>1</td>
</tr>
<tr>
<td>-1</td>
<td>+1</td>
<td>-1</td>
<td>2</td>
</tr>
<tr>
<td>+1</td>
<td>+1</td>
<td>+1</td>
<td>4</td>
</tr>
</tbody>
</table>

\[
\alpha_1 = \frac{-0 + 1 - 2 + 4}{4} = 0.75 \quad \alpha_2 = \frac{-0 - 1 + 2 + 4}{4} = 1.25 \quad \alpha_{12} = \frac{0 - 1 - 2 + 4}{4} = 0.25
\]

A regression model can then be obtained using the calculated effects:

\[
\hat{y} = \bar{y} + \alpha_1 X_1 + \alpha_2 X_2 + \alpha_{12} X_1 X_2 = 1.75 + 0.75 X_1 + 1.25 X_2 + 0.25 X_1 X_2
\]  

where \( \hat{y} \) is the estimated result, \( \bar{y} \) the mean value of the results and \( X_i \) the coded variable for factor \( A \).
The coded variables vary between –1 for the low levels and +1 for the high levels and are thus equivalent to the contrast coefficients. If more variables are included in the design, interactions between three or more variables may be found. These are seldom significant however. The regression model from a $2^k$ design assumes linear main effects from each variable. The appropriateness of this assumption is easy to check by making a measurement with all variables at their mean level. The result should then be approximately $\bar{y}$ if the assumption is good.

A full regression model can become very large if many variables are tested and variables that do not affect the result should thus be omitted. A normal probability plot is an easy way to find the important effects. Unimportant effects here will tend to align in an approximately straight line while important effects will tend to deviate from the normal distribution, see Figure 3 in Paper I.

6.2 Quadratic regression

If a linear model is deemed insufficient then quadratic or higher order terms can be added.

A quadratic regression model omitting interactions between three or more variables can be given as:

$$\hat{y} = \beta_0 + \sum_{j=1}^{k} \beta_j X_j + \sum_{j=1}^{k} \sum_{j' \neq j}^{k} \beta_{jj'} X_j X_{j'} + \sum_{j=1}^{k} \sum_{j' \neq j}^{k} \sum_{j'' \neq j}^{k} \beta_{jj'j''} X_j X_{j'} X_{j''}$$

The regression coefficients $\beta$ are computed as:

$$\beta = (C^T C)^{-1} C^T \mathbf{y}$$

where $C$ is the design matrix for the contrast coefficients $c_{ij}$, see e.g. Table IV in Paper I.
7 Simulation studies

The general geometry of most models in this thesis is an axially symmetric (see Appendix B) model of an electrode surrounded by a sphere of grey matter with a radius of 30 mm (Figure 12). The outer boundary of the sphere is set to a constant temperature of 37 °C and an electric potential of 0 V (ground). When the current is turned on a very localised heating near the electrode tip occurs (Figure 12). Temperature controlled heating during 60 s was simulated and the resulting lesions were assumed to consist of all solid tissue reaching a temperature of 60 °C or more.

![Diagram](image)

**Figure 12:** Left: General geometry of the models. Right: Resistive heating around the electrode. The heating is focussed to the tissue very close to the tip, especially at the rounding and at the sharp edge to the insulation. The heat then spreads outwards to the surrounding tissue and inwards to the electrode tip.

7.1 Impact of tissue characteristics in a homogeneous surrounding with coagulation dependent thermal conductivity

The influence of the surrounding tissue’s electric and thermal conductivity, blood perfusion and the electrode’s target temperature was investigated for an electrode with a diameter of 1 mm and a tip length of 4 mm (Paper I). Blood perfusion was modelled as an added thermal conductivity in non-coagulated tissue. The increase in thermal conductivity due to blood perfusion was set to zero in coagulated tissue and this made the simulated lesion smaller with increasing blood perfusion, as the coagulated tissue became relatively more insulating than the surrounding perfused tissue (Figure 13). The temperature control of the delivered power made the resulting lesion volume relatively independent of the electric conductivity while it increased with increasing thermal conductivity and target temperature (Figure 14).
Figure 13: The impact of coagulation dependent increase in thermal conductivity due to blood perfusion. Left: Here the thermal conductivity is larger in the non-coagulated tissue than in the coagulated tissue and the removal of heat becomes more efficient at the lesion rim than adjacent to the electrode tip. Middle: The temperature field in the same simulation visualised. Right: With no increase in thermal conductivity due to blood perfusion the lesion becomes larger.

Figure 14: Lesion volume as a function of target temperature ($T_{\text{set}}$), thermal conductivity of the tissue ($k_{\text{tiss}}$) and added thermal conductivity due to blood perfusion ($k_{\text{perf}}$).

### 7.2 Required detail of the models

The required detail of the model for the electrode was also studied (Paper II). Here a detailed model of the electrode with inner structures was compared to a simplified model where the electrode had been divided into three parts: a tip, an insulating layer and an upper electrode body. In the simplified model material parameters such as mass density and thermal conductivity were averaged by relative volume in each part of the electrode. The simulations for the simplified model were found to be more than four times faster than those for the detailed one. The results of the simulations were almost identical with differences of 0.4 to 3.3 mm$^3$ compared to lesion volumes of about 30 to 110 mm$^3$. The simplified model was thus deemed better as it gives much faster simulation times with very little decrease in solution accuracy and hence used in Papers III and IV.
7.3 Electrode tip dimensions

Further, the effect of electrode tip dimensions was investigated (Paper III). The tip length and diameter were varied (2-4 mm and 0.5-2.5 mm respectively) and the resulting lesion volumes were used for a regression model. Lesion volume as function of tip length and diameter can be seen in Figure 16.

7.4 Impact of cysts

The influence of CSF-filled cysts in the surrounding tissue was investigated for different geometry and position of the cysts (Figure 17 and Paper IV). The simulations showed considerable convective flow due to the heating in the CSF. This gave very high heat transfer resulting in both larger and smaller lesions when the cyst was in contact with the electrode tip, depending on whether the electrode gave enough power to compensate for the increased heat transfer or not, see Figure 18. Unlike the study in the previous papers the tissue was not homogeneous here and this resulted in focusing of the delivered power to the CSF since it has a much higher electric conductivity than grey matter (Figure 17). Cysts 1 mm away from the tip had little effect on the simulated lesions.
Figure 17: Left and middle: Shape and position of the modelled cysts. Right: Resistive heating with a cyst present. The higher electric conductivity of the CSF focuses the heating to the cyst.

Figure 18: Left: Simulation of lesioning with a large cyst surrounding most of the electrode tip using a target temperature of 70°C. Most of the heat is spread in the CSF and little of the actual grey matter is coagulated so the lesion becomes very small (6.5 mm³). Right: With a higher target temperature, here 80°C, the efficient convective heat transfer may spread heat to a much larger volume and the lesion becomes much larger (189.3 mm³).
8 Experimental studies

It is important to verify that the results from simulations are realistic. For this reason the simulation results were compared to experimental results from an older in-vivo study by Eriksson et al (Eriksson et al. 2002) and new ex-vivo experiments were attempted. Unfortunately, brain tissue is not a material that is easy to work with. It is very soft, deformable and rather sticky making accurate placement of the electrode and cutting out the tissue for subsequent studying of the created lesion difficult.

8.1 Lesion reconstruction from histology

In Eriksson’s study lesions had been made in living porcine central grey tissue using stereotactic neurosurgery (see Paragraph 3.4) and different types of electrodes and target temperatures. The lesions had then been cut out from the brain and cryosectioned into 100 μm-thick slices perpendicular to the electrode path. Four of these slice sets successfully covered most of the actual lesion. Two lesions were created with a 1x4 mm electrode at target temperatures of 70 and 80 °C respectively, one lesion with a 1x2 mm electrode at a target temperature of 80 °C and one with a bipolar electrode with a diameter of 1 mm and contact surface lengths of 2 mm at a target temperature of 80 °C.

![Histology slice with edges marked white. The shape of the lesion is decently but not perfectly regular. The lesion was made with an electrode with a diameter of 1 mm and a tip length of 4 mm at a target temperature of 80 °C.](image)

In order to obtain the lesion volume the lesion area in each slice was now measured and the areas were multiplied with the slice thickness and added together. Some slices were missing or of too poor quality to be measured and in these cases interpolated values between the two closest measurable slices were used instead. For visualisation the radius corresponding to a perfect circle with the same area as the measured lesion slices was also calculated, see Figure 20. Simulations predict a much larger growth of the lesion around the upper active surface of the bipolar electrode compared to what
was actually found in the experimental lesion. Examination of postoperative 3D-MRI revealed that the upper part of the lesion was near a ventricle. Modelling a large cyst in the same way as in Paper IV, i.e. just above the upper active surface, gave a simulation result in much better agreement with the experiment, see Figure 21. The experimental lesions from the monopolar electrodes corresponded well to what is to be expected from the simulations.

Figure 20: Reconstruction of lesion volumes from an older experimental in-vivo study by Eriksson et al (2002). The lines represent the radii of perfect circles with the same areas as the measured areas in the slices. Upper left: Lesion from a 1x4 mm electrode using a target temperature of 80 °C (Volume = 35.4 mm³). Upper right: Lesion from a 1x4 mm electrode using a target temperature of 70 °C (Volume = 15.0 mm³). Lower left: Lesion from a 1x2 mm electrode using a target temperature of 80 °C (Volume = 25.2 mm³). Lower right: Lesion from a bipolar electrode with a diameter of 1 mm and length of active contact surfaces of 2 mm using a target temperature of 80 °C (Volume = 27.2 mm³). The pear shape of the lesion from the bipolar electrode actually differs quite a lot from what is to be expected according to simulations in a homogeneous surrounding, see Figure 21.
Figure 21: Left: The simulated lesion from a 1x2 mm electrode using a target temperature of 80 °C, \( k_{\text{tiss}} \) of 0.5 W/(m·K) and \( k_{\text{perf}} \) of 0.25 W/(m·K). Middle: The simulated lesion from a bipolar electrode with a diameter of 1 mm and length of active contact surfaces of 2 mm using a target temperature of 80 °C, \( k_{\text{tiss}} \) of 0.5 W/(m·K) and \( k_{\text{perf}} \) of 0.5 W/(m·K). This prediction clearly deviates from the actual in-vivo result seen in Figure 20. Right: A CSF-filled ventricle placed just above the upper active surface of the electrode gives much better agreement between experiment and simulation, with a pear shape also for the latter.

8.2 Experiments in ex-vivo brain tissue

Attempts at making lesions in central grey matter of dead porcine brain tissue were also made. The attempts were made in tissue from deceased animals that had been used in other animal studies (approved by the Swedish Board of Agriculture D. No. 38-8269/04) and in tissue obtained from an abattoir (approved by the Swedish Board of Agriculture D. No. 38-6097/05). The expected outcome according to Paper I was that lesions should be bigger for dead tissue since there is no blood perfusion to cool the lesion. Accurate placement of the tip in grey matter without image guiding was unfortunately not successful. As the electric conductivity of grey matter is higher than white impedance (Duck 1990; Laitinen et al. 1966), measurements were used in order to find zones with homogeneous grey matter. The lesions ended up being created in mixed tissue however. Furthermore they shattered when being cryosectioned while surrounding, less thermally damaged, tissue further out held well. This was quite unexpected, as the coagulated zone from the older study had held together well, while tissue surrounding it tended to shatter due to oedema.

While failing to position the electrode in central pure grey matter a lesion that was made in pure white matter showed two interesting characteristics. The blanching of the already whitish tissue gives a lesion that is very difficult to see. With some contrast enhancement of the picture a rather irregular shape can nevertheless be seen in Figure 22. This could be due to the rather strong anisotropy of the white matter. The other notable characteristic was that the impedance of the white matter increased reversibly with a temperature above about 50 °C. This is in contrast to all other tissues that have been tested in this study where the impedance decreases with temperature as
long as the water does not vaporise. The coagulated white matter did not show any considerable tendency to shatter.

Figure 22: Histology section of thermal lesion in white matter. Left: The lesion is very difficult to see compared to lesions in grey matter. Right: By enhancing the contrast of the image a rather irregular contour can be seen. This is likely due to anisotropy of the white matter.

8.3 Experiments in ex-vivo kidney tissue

Kidney tissue is much easier to work with. As it has very similar electrical and thermal characteristics to grey matter it was used in Paper IV as a substitute in order to gain better control of the tissue geometry in the experiments. A hole with a fairly flat bottom surface was cut into porcine kidneys at room temperature. An 1x4 mm electrode was inserted about 3 mm into the tissue and lesions were created without and with saline layers of 1 and 4 mm height above the kidney surface. These experiments do not have the same geometry as real cysts but were made in order to check whether the computer models were realistic.

Figure 23: Lesions with contour marked white in kidney. Left: Lesion made with about 1 mm saline on the kidney surface. Here the high electric conductivity of the saline has focussed the electric power to it and caused a lesion with a top-down pyramid shape. Right: With 4 mm saline above the kidney convective movements in the saline counters this effect by high convective thermal conduction of heat and a resulting cooling of the kidney surface.
9 Discussion

In this thesis modelling, simulation and experiments were used in order to investigate RF-lesioning in the brain with the aim of improving knowledge about and predictability of the process. Studied topics were for example, the impact of tissue characteristics such as thermal conductivity, blood perfusion and the presence of cerebrospinal fluid.

Modelling and simulation is an inexpensive alternative to experiments and can be used to make predictions about devices that have not yet been built or parameters that are difficult or impossible to measure. It is however not reality. Even the most flawless analytical solution can be worthless if underlying physical assumptions or input data are poor. There are a number of uncertainties in the models in this thesis due to the high complexity and variability of biological tissue. The assumption of a homogeneous isotropic surrounding seems sufficiently valid for the cases of the three experimental lesions in living porcine tissue using monopolar electrodes, see Paragraph 8.1. The assumption of homogeneity is much more dubious in the case of the bipolar electrode or for white matter as could be seen in Figure 22. In particular, anisotropy could be interesting to investigate regarding blood flow. The modelling of the impact of blood perfusion as an increase in thermal conductivity (Equation 7) assumes no particular directionality in the flow. This is probably not entirely correct even for microcirculation, but without any knowledge of local directionality of the flow it should be the best approximation. Adding directionality to the blood perfusion will also make simulations more taxing on computer power, as the problem is not axially symmetric unless the direction of the flow is parallel to the electrode. Accurate modelling of inhomogeneities is difficult however. The target area can be visualised using MRI prior to lesioning but the spatial resolution here, with slice thickness about 2-3 mm at reasonable scan times, is unfortunately very coarse compared to the electrode and created lesion sizes.

Another approximation is the use of the 60 °C isotherm as definition of the simulated lesion boundary. In reality tissue damage is not only a function of temperature but also of time which can be accounted for by the use of the Arrhenius equation (Poepping et al. 1999). Similarly the occlusion of the blood vessels is modelled as abrupt at 60 °C but a more gradual occlusion may be more physiologically correct for the zone of stasis. Laser Doppler perfusion monitoring (Nilsson et al. 2003) may be useful for investigation of this in tissue with sufficiently high blood perfusion, as its signal decreases sharply when the tissue coagulates (Antonsson et al. 2006). It may also be possible to use optical detection of the blanching. Optical spectroscopy has, for example, been used by others for the study of thermal damage in the liver (Buttemere et al. 2004). Another uncertainty is how much of the damaged, but not coagulated, tissue in the zone of stasis that will recover and how much of it that will be permanently destroyed.

A reason for making regression models in Paper I is the uncertainty in physical parameters, especially \( k_{\text{perf}} \). Since that investigation I have become very dubious of the large span of values for the thermal conductivity of brain tissue given in (Chato 1985) as all references compiled in (Duck 1990) give values close to \( k_{\text{tiss}} \approx 0.5 \) W/(m-K). To my knowledge there is no reliable reference today for a good value of
\(k_{\text{perf}}\) as measurements of thermal conductivity generally are performed on excised tissue. The blood perfusion in grey matter can also vary considerably in time and space, see Paragraph 3.1. A vision regarding the simulations and regression modelling is that it may be possible to predict resulting lesion size in clinical surgery if \(k_{\text{perf}}\) can be estimated e.g. with the help of laser Doppler perfusion monitoring. The statistical methods used are developed for experimental measurements and it may thus seem somewhat laboured to apply them to simulation studies without any measurement noise. Nevertheless they are useful when a regression model is sought, as they allow the detection of interactions that may be critical to be taken into consideration if reliable predictions are to be made based on the regression. For example, it would be very interesting to see whether the consideration of interactions may explain the discrepancy (Ma 2002) between the Parkinsonian model in Paragraph 3.3 and the result of lesioning in the GPi for dyskinesias.

So far it has not been verified experimentally that blood perfusion actually decreases lesion size in the brain. However it is expected from the simulations in Paper I and also from experimental studies on liver (Aschoff et al. 2001), which has a similar blood perfusion at about 100 ml/(100g·min) (Duck 1990), compared to grey matter at about 50 (Pantano et al. 1984) to 100 ml/(100g·min) (Helenius et al. 2003). Occlusion of blood flow (Aschoff et al. 2001) or pharmacological flow reduction can be used to obtain larger lesions in the liver (Goldberg et al. 1998). The latter method might be suitable for verification of the importance of blood perfusion in the brain too.

The simulated cysts showed a considerable and varied impact on the simulated lesions and thus the cysts may be important to take into consideration during clinical surgery. Other authors have also noted the ability of CSF to shrink (Dieckmann et al. 1965) or expand (Cosman 1996) the lesion growth. An example is the bipolar lesion in Paragraph 8.1 where CSF in a ventricle probably has shrunk the upper part of the lesion. Cysts 1 mm away did not have much impact however and a clinical study of 40 patients by Laitinen et al. found no influence from the presence of cysts and the actual clinical outcome of lesioning in the GPi (Laitinen et al. 2000). It may be possible to detect potentially complicating cysts in contact with the electrode tip through the use of impedance measurements, as CSF has much higher electric conductivity than grey and white matter, see Table 2 in Paper IV. A complicating factor is that the electric conductivity of grey matter is somewhat higher than that of white matter and contact with both white matter and a little CSF may thus give the same impedance as contact with grey matter only. This can make the CSF harder to detect.

In conclusion, blood perfusion and CSF can affect the lesioning process and CSF in the target area should, in particular, be of interest to detect prior to surgery as it can greatly change the size and shape of the created lesion. This work will hopefully help to elucidate the lesioning process and aid improved prediction of the surgical outcome in the future.
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11 Appendix A: Vector analysis

11.1 Gradient
The gradient describes the slope of a function, e.g. the slope of a hill due to difference of height at different positions. For a three dimensional scalar field, \( f \), it is calculated as:

Cartesian coordinates:
\[
\nabla f = \frac{\partial f}{\partial x} \hat{x} + \frac{\partial f}{\partial y} \hat{y} + \frac{\partial f}{\partial z} \hat{z}
\]

Cylindrical coordinates:
\[
\nabla f = \frac{\partial f}{\partial r} \hat{r} + \frac{1}{r} \frac{\partial f}{\partial \phi} \hat{\phi} + \frac{\partial f}{\partial z} \hat{z}
\]

The gradient of a scalar field is a vector field, e.g. the electric field:
\[
\nabla V = -E \quad \text{(V/m)}
\]

The gradient of a vector field is a 2nd rank tensor field.

11.2 Divergence
The divergence describes accumulation, draining, sources and sinks in a field. For a three dimensional vector field, \( A \), it is calculated as:

Cartesian coordinates:
\[
\nabla \cdot A = \frac{\partial}{\partial x} A_x + \frac{\partial}{\partial y} A_y + \frac{\partial}{\partial z} A_z
\]

Cylindrical coordinates:
\[
\nabla \cdot A = \frac{1}{r} \frac{\partial}{\partial r} (r A_r) + \frac{1}{r} \frac{\partial}{\partial \phi} A_\phi + \frac{\partial}{\partial z} A_z
\]

The divergence of a vector field is a scalar field, e.g. for steady state heat conduction:
\[
\nabla \cdot (-k \nabla T) = \dot{Q} \quad \text{(W/m}^3\text{)}
\]

A location in steady state with negative divergence is called a sink and a location with positive divergence is called a source. For time-variable fields negative and positive divergences can also represent accumulation and draining, e.g. for transient heat conduction without sinks or sources:
\[
\nabla \cdot (-k \nabla T) = -\rho c \frac{\partial T}{\partial t} \quad \text{(W/m}^3\text{)}
\]
12 Appendix B: Symmetry

Three-dimensional simulations with FEM are very costly in terms of computational power and time. A lot of computational time and power can be saved if a reduction to two dimensions is possible. This can also allow more complex physics and geometries, as available memory is a limiting factor. Of particular interest here is plane symmetry and axial symmetry. It is important to understand how these symmetries work, as completely erroneous results can be achieved if the symmetry conditions are used in the wrong way.

12.1 Plane symmetry

Plane symmetry can usually\(^1\) be applied if the relevant geometry and physical conditions remain constant enough in one straight direction in a Cartesian coordinate system. This might be the case for e.g. the transverse section of parallel rods with a fairly uniform thickness.

\[\text{Modelled area} \quad \text{No or small changes in this direction} \quad \text{Model} \]

\[\text{Modelled area} \quad \text{Considerable variations in this direction} \quad \text{Model} \]

Left: Geometry with plane symmetry. Right: Geometry without plane symmetry.

12.2 Axial symmetry

Axial symmetry can usually be applied if the relevant geometry and physical conditions remain constant in the rotational direction of a cylindrical coordinate system. This might be the case for e.g. a cylinder.

\(^1\) There are some physical problems, e.g. buckling, where the result is not symmetric despite symmetric geometry and physical conditions Cook RD, Malkus DS, Plesha ME and Witt RJ (2002) Concepts and application of finite element analysis, 4 ed. John Wiley & Sons, Inc.. This can be visualised by compressing a thin (axially symmetric) plastic cup from above.
**Figure 24:** Axially symmetric geometry.

**Figure 25:** Not axially symmetric geometry.
13 Appendix C: The logistic function

The Heaviside step function, $H(x)$, is a convenient way to describe sudden changes, such as coagulation, mathematically:

$$H(x) = \begin{cases} 0 & (x < 0) \\ 0.5 & (x = 0) \\ 1 & (x > 0) \end{cases}$$

The drawback with this function is that it is not differentiable, which can cause problems for numerical solvers. However, the step can be approximated with the sigmoidal (S-shaped) logistic function (Haykin 1999):

$$P(x) = \frac{1}{1 + e^{(-ax)}} \quad a > 0$$

Here $a$ is a constant which describes the steepness of the logistic function. The higher the value of $a$, the closer the logistic function approximates the step function. On the other hand, higher values of $a$ put more strain on the numerical solving.

![Figure 26: The logistic function is a convenient approximation that can be used in order to avoid numerical problems at steps.](image)

$a = 1$
$a = 10$
$a = 100$
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