Doctoral Thesis

Evaluation of a Multiple Injection Axillary Block Technique by Clinical Assessment and MRI

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This work is dedicated to:


My friend, *Dr. Per Lars Johan Ahlström* (Apr 24, 1953 – Jan 2, 2007)

*From left to right; the author, pointer Tyra and Per*
# Table of Contents

Acknowledgements ........................................................................................................ VI

Abbreviations ................................................................................................................ IX

List of Figures ................................................................................................................ IX

List of Tables ................................................................................................................... X

List of original papers I - IV ........................................................................................ XI

Introduction .................................................................................................................... 1

Regional anaesthesia, the brachial plexus, and peripheral nerve block ....................... 1

Techniques for peripheral nerve localization: ............................................................... 2

Axillary plexus blocks ................................................................................................... 4

MRI (basic principles) ................................................................................................... 5

Background for the studies – why MRI examinations to evaluate PNBs? ....................... 6

Aims of the present thesis and study I – IV .................................................................. 7

Materials ....................................................................................................................... 8

Methods ........................................................................................................................ 10

Axillary Brachial Plexus Block nerve localisation techniques: ..................................... 10

Transcutaneous nerve stimulation (TNS) ..................................................................... 10

Nerve stimulation through a block cannula ................................................................... 10

Transarterial block method ......................................................................................... 12

Combined catheter and transarterial method ............................................................... 13

Block assessment ......................................................................................................... 13

MRI protocol ................................................................................................................. 15

MRI assessment and scoring ....................................................................................... 15

Statistics ....................................................................................................................... 18

Results and summary of the studies I - IV .................................................................. 19

Study I ......................................................................................................................... 19

Study II ......................................................................................................................... 20
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Abbreviations

AXB  Axillary plexus block
LA   Local anaesthetic
MCN  Musculocutaneous nerve
MCA  Medial cutaneous antebrachial nerve
MRI  Magnetic resonance imaging
PhD  Doctor of Philosophy
PNB  Peripheral nerve block
RA   Regional anaesthesia
SD   Standard deviation
TNS  Transcutaneous nerve stimulation
US   Ultra sound

List of Figures

Figure 1 The course of the brachial plexus ................................................................. 2
Figure 2 The brachial plexus; cords and terminal nerves ............................................ 3
Figure 3 Transcutaneous nerve stimulation ................................................................. 11
Figure 4 Axillary block ............................................................................................ 12
Figure 5 Axillary block ............................................................................................ 13
Figure 6 MRI of the right axillary region .................................................................... 16
Figure 7 Axillary cross-sectional view ...................................................................... 17
Figure 8 The axillary four quadrants ........................................................................ 17
Figure 9 MRI cross-sectional view ........................................................................... 22
Figure 10 The MCN exit point .................................................................................. 25
Figure 11 The MCN exit point .................................................................................. 25
Figure 12 Proximal LA distribution .......................................................................... 30
Figure 13 MRI of the axillary sheath distribution ...................................................... 31
List of Tables

Table 1 Materials and Methods ................................................................. 9
Table 2 Block results of study I ................................................................. 19
Table 3 Block results of study III ............................................................... 22
Table 4 Scoring of LA-distribution as observed by MRI from study III ........... 23
Table 5 Proximal and distal LA spread from study III .................................. 24
List of original papers I - IV

The thesis is based on the following papers, which will be referred to by their Roman numerals:


The axillary block

Illustration: Birgitta Kjelstrup
Introduction

*Regional anaesthesia, the brachial plexus, and peripheral nerve block*

Local anaesthetic (LA) injection to a peripheral nerve can provide analgesia or anaesthesia in the corresponding innervated territory. When these regional anaesthesia (RA) techniques are used, surgical procedures can be performed in awake or slightly sedated patients without the need for general anaesthesia.

For a peripheral nerve block (PNB), LA is injected close to a peripheral nerve. A single injection of LA and subsequent removal of the needle is the easiest way to perform a PNB. However, some patients require PNB catheters for pain management after a surgical procedure. PNB techniques are frequently used for surgery of the upper limb.

Compared to the use of general anaesthesia, PNB may provide less psychomotor disturbance, as well as improved pain management and mobilisation after surgery. Therefore, PNBs are often favourable in elderly patients. Additionally, patients with respiratory impairment or unstable cardiac function may benefit from the use of PNB and the avoidance of general anaesthesia. Postoperatively, PNB can reduce opioid consumption and related side effects like nausea, vomiting or respiratory depression.

The brachial plexus is a network of nerves, running from the neck and into the arm (Fig. 1). The brachial plexus can be blocked by PNB at different levels: at the neck in the interscalene region, above or below the clavicle or in the axillary region. A brachial plexus block in the axillary region can be used for anaesthesia during surgical procedures of the elbow, forearm or hand. An axillary plexus block (AXB) may have a lower risk for complications such as nerve injuries or accidental punctures of the lung as compared to the more proximal brachial plexus block techniques.

The brachial plexus develops from the spine and continues into the arm that it innervates (Fig. 1). It is usually formed by the anterior rami of the lower four cervical nerves (C5–C8) and first thoracic nerve (T1). The brachial plexus passes through the cervical canal in the neck and reaches the axilla through the axillary sheath. The nerves are divided into roots, trunks, divisions, cords, and terminal branches (Fig. 2). There are five terminal branches and numerous other pre-terminal or collateral branches that leave the plexus at various points along its length.
Various AXB techniques have been described and there is an ongoing discussion as to how best to perform an axillary block. Further research studies are therefore required. Modern imaging technology may be helpful to compare the different AXB approaches. In this thesis three AXB techniques are evaluated.

**Techniques for peripheral nerve localization:**

The most significant challenge in regional anaesthesia is to identify the target nerves and to place the injection needle in close proximity. Different techniques can be used to find the target nerves.

**Landmarks:**

Without using additional tools, blocks can be performed simply by using anatomical landmarks. The block needle can be positioned and inserted close to a visible or palpable anatomical structure that is situated in a defined position in proximity to the target nerve. These anatomical landmarks include pulsating arteries, superficial or deep bone structures and muscle. The first percutaneous AXB was a landmark based technique, that was
described by Hirschel in 1911. LA was injected at different locations close to the axillary artery which is situated in a central position between the nerves of the axillary plexus.

Figure 2 The brachial plexus; cords and terminal nerves
Red circle: The terminal nerves and cords of the brachial plexus. From a modified version of Gray’s Anatomy of the Human Body.

Paraesthesia:
This technique is based on the principle that the elicitation of paraesthesia indicates that the block needle is in close contact with the nerve. The use of the paraesthesia technique was first described by Kulenkampff in 1911 and has been an essential part of many PNB techniques. Kulenkampff stated that the patient would experience “the same sensation as when striking his crazy bone” (ulnar nerve at the elbow) when the brachial plexus is encountered by the needle.

Transarterial technique:
Peripheral nerves are frequently located in proximity to vascular structures. When the pulsating artery is palpated in the axilla, it can be penetrated by an injection needle. Blood
aspiration indicates an intravascular needle position. When the needle is carefully advanced or retracted and blood is no longer aspirated, it lies just outside the artery and in close proximity to the nerve. The transarterial method does not rely on advanced equipment, and the method has been practiced for decades.\textsuperscript{10-12}

**Nerve stimulator:**
Nerve stimulation was first described by Perthes in 1912.\textsuperscript{13} A nerve stimulator functions via the depolarisation of motor fibres within a peripheral nerve by an electrical current. When the tip of a block needle, connected to a nerve stimulator, is placed close to the nerve, a neuromuscular response (twitching of the corresponding muscle) can be observed. Nerve stimulation as described by Perthes was not continued by others due to the weight and size of the equipment. The introduction of a battery-operated and transportable nerve stimulator by Greenblatt and Denson in 1962 marked the beginning of a new nerve block era with nerve stimulation as a standard tool.\textsuperscript{14} In contrast to paraesthesia techniques, nerve stimulation does not rely on verbal feedback and cooperation of the patient. The method has been used for localization of almost all motor nerves. Modern nerve stimulators have a constant voltage output with an adjustable current level (commonly 0 - 5 Ampere). The impulse duration can be adjusted between 0.1 ms and 1.0 ms. The stimulation frequency is usually between 1 and 2 Hz.

**Ultrasound:**
After the introduction of ultrasound for needle guidance in regional anaesthesia in 1994, this method became increasingly popular for PNB in developed countries.\textsuperscript{15} Ultrasound can be used to identify the nerves and the surrounding anatomy. The needle can then be advanced under continuous visualisation and positioned close to the target nerves. LA injectates can also be identified. The block is assumed to be successful, when the nerve is surrounded by LA. During the last decade, the image quality of ultrasound equipment has improved considerably, making block performance easier and even more precise than ever before. Ultrasound has however, not reduced the frequency of nerve injury complications.\textsuperscript{3} Therefore the concept of dual guidance, using both nerve stimulator and ultrasound simultaneously has been suggested.\textsuperscript{16}

**Axillary plexus blocks**
In 1911 Hirschel described the first percutaneous AXB technique using multiple injections close to the axillary artery.\textsuperscript{8} However, the supraclavicular technique presented by Kulenkampff only a few months later reached much higher popularity, probably due to the
fact that only a single injection was required. After 1970, when Winnie introduced his concept
of the neurovascular sheath, a new interest in using AXB took place.\textsuperscript{17,18}

Winnie proposed that a single injection, within the connective tissue sheath surrounding the
axillary vessels and nerves, could give adequate LA distribution to the brachial plexus and
therefore provide a complete AXB.\textsuperscript{18} The concept of the neurovascular sheath and the
pattern of the LA distribution within that sheath have been repeatedly questioned.\textsuperscript{12,18-23}
Multiple injection techniques have shown better success rates compared with single injection
methods, indicating that free distribution does not always occur.\textsuperscript{24,25} There is also an ongoing
discussion as to whether a selective block of the musculocutaneous nerve (MCN), outside
the axillary sheath, is necessary to achieve a successful AXB with all terminal nerves
blocked.\textsuperscript{26,27}

The AXB primarily targets the terminal nerves of the brachial plexus including the main
branches, the radial, median, ulnar, and musculocutaneous nerves, as well as the medial
cutaneous brachial and medial cutaneous antebrachial nerves. The blocks are typically
performed at the level of the axillary fold. The patient is usually in the supine position with the
arm abducted and flexed at the elbow. The short distance between the skin and the axillary
brachial plexus permits several techniques for peripheral nerve location and block
administration in this region. An axillary PNB catheter can be used for prolongation of the
surgical block and for postoperative pain management.\textsuperscript{17,28}

\textbf{MRI (basic principles)}

Magnetic Resonance Imaging (MRI) uses magnetic fields and radio waves to form images of
body structures. The magnetic field aligns the protons of hydrogen atoms, which are then
exposed to pulses of radio wave energy exciting the protons to higher energy levels. When
the radio frequency pulse is switched off, the protons return to equilibrium state and release
energy. This energy is exchanged with the surrounding tissue (T1 relaxation) and by loss of
phase coherence due to small internal magnetic field variations from neighbouring nuclei (T2
relaxation). T1 and T2 signals are the basis for MR imaging. MRI gives excellent soft tissue
discrimination and excellent differentiation of anatomical structures and pathological
processes in the body. It is obtained without exposure to ionising radiation.

MRI detects LA fluid as a “white sea” on T2-weighted images. These signals are visible for a
prolonged period after injection whereas on ultrasound examination, LA starts fading out
minutes after the injection. Furthermore, MRI gives reproducible images in multiple planes or
in 3D and can have large coverage in the craniocaudal direction. Ultrasound is a valuable tool in RA, but MRI offers better imaging for research purposes.

**Background for the studies – why MRI examinations to evaluate PNBs?**

The axillary region is frequently used for brachial plexus blocks to provide analgesia or anaesthesia for upper limb surgery. Several different axillary methods have been described in the last decades. These different methods have variable efficacy and success rates. The discussion on how to optimize the performance of axillary brachial plexus blocks includes the question of whether multiple injections should be performed and the question of whether a selective block of the MCN is necessary.\(^\text{26,27,29}\)

A few researchers have performed MRI-studies on brachial plexus blocks. Klaastad\(^\text{et al.}\)\(^\text{21,30-35}\) accomplished pioneering work in this field by focusing on anatomical variations, needle approaches and LA distribution with the aid of an open 0.5 Tesla MRI scanner. Their work and thesis\(^\text{36}\) was conducted at The Intervention Centre, Oslo University Hospital, Rikshospitalet where our thesis work and research was performed. In the study of Klaastad et al. on the distribution of LA in AXB, they demonstrated that MRI is a useful tool for the investigation and description of LA spread.\(^\text{21}\)

Stronger magnetic fields, giving a better signal-to-noise ratio, and other technical developments that have taken place in the last few years, have improved the image quality of modern MRI.\(^\text{37}\) For the studies involved in this thesis our research group used a 3.0 Tesla scanner. We expected to visualize more anatomical detail and new relevant information on block performance in the axillary region.

In this thesis, three different AXB methods with a single, double and triple-injection were examined.
Aims of the present thesis and study I – IV

The main aim of this thesis was to investigate three different AXB methods with clinical block assessment and examination of the LA distribution as observed by MRI.

Specific aims:

I. In study I, the aim was to compare the efficacy of a single injection technique through an axillary catheter with a triple injection technique combining the axillary catheter with a double transarterial injection technique.

II. In Study II, an MRI protocol for the scanning of the axillary brachial plexus was developed using a 3.0 Tesla high resolution scanner. The aim of this pilot study was to improve MRI visualisation of the target nerves, surrounding anatomy and the LA. The brachial plexus blocks were performed using the same methods as in study I.

III. In study III, AXB were performed by single, double and triple-injection techniques. The main objective was to investigate whether differences in block success could be explained by differences in the LA distribution as observed by MRI. The single and triple injection techniques were both used in study I and II.

IV. The objective in study IV was to examine the position of the MCN and its relationship to the brachial plexus and the axillary sheath by MRI. This information was used to define how and where the MCN should be blocked when performing AXB.
Materials

The participants were all patients undergoing elective upper limb surgery at the Dept. of Orthopaedics, Oslo University Hospital. The patients for all studies were recruited according to the Helsinki declaration and all patients gave informed consent.

For study I we recruited 51 patients, 32 men and 19 women with a mean age of 43.2 years (SD = 15.1).

For the pilot study II we enlisted 6 volunteers for protocol development and anatomic study. For the LA distribution portion of this study we enlisted 9 patients that were scheduled to receive a nerve block, and who volunteered for an MRI examination ahead of their planned upper limb surgery.

For study III we recruited 45 patients, 33 men and 12 women with a mean age of 45.2 years (SD = 16.9).

The retrospective study IV included the 9 patients in study II as well as the 45 patients in study III, forming one group. Of the 54 patients, 40 were men and 14 were women, with a mean age of 46.3 years (SD = 16.7).

Further study details are seen below in Table 1.
Table 1 **Materials and Methods**: Overview of the studies

<table>
<thead>
<tr>
<th>Study</th>
<th>I</th>
<th>II</th>
<th>III</th>
<th>IV</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Participants</strong></td>
<td>51 patients</td>
<td>6 healthy volunteers, 9 patients</td>
<td>45 patients</td>
<td>Reanalysis of MRI data in 54 patients</td>
</tr>
<tr>
<td><strong>Groups</strong></td>
<td>2</td>
<td>2</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td><strong>Block Methods</strong></td>
<td>1- and 3-deposit</td>
<td>1- and 3-deposit</td>
<td>1-, 2-, and 3-deposit</td>
<td></td>
</tr>
<tr>
<td><strong>MRI</strong></td>
<td>All patients examined with MRI</td>
<td>All patients examined with MRI</td>
<td>MRI reanalysis</td>
<td></td>
</tr>
<tr>
<td><strong>Study Design</strong></td>
<td>Prospective study</td>
<td>Pilot study</td>
<td>Blinded and randomised controlled study</td>
<td>Retrospective study</td>
</tr>
<tr>
<td><strong>Primary Endpoints</strong></td>
<td>Time to successful block: • Analgesia of the median, radial and ulnar nerve</td>
<td>Development of an MRI protocol for the study of the brachial plexus anatomy (group 1)</td>
<td>Rate of successful blocks: • Analgesia of the MCN, median, radial, ulnar and MCA nerve</td>
<td>Position of the MCN and its relation to the axillary sheath evaluated by MRI</td>
</tr>
<tr>
<td><strong>Secondary Endpoints</strong></td>
<td>Block development and block score from 30 min to 50 min</td>
<td>MRI examination of the brachial plexus anatomy after LA injection (group 2)</td>
<td>Difference in block effect explained by difference in LA distribution as observed by MRI</td>
<td></td>
</tr>
</tbody>
</table>

* 1-deposit: single-deposit group (injection through catheter)
* 2-deposit: double-deposit group (transarterial injection lateral and medial to the brachial artery)
* 3-deposit: triple-deposit group (combination of 1-deposit and 2-deposit)
Methods

The AXB’s were performed using the following three techniques:

1. Single-deposit of LA through an axillary catheter
2. Transarterial double-deposit of LA lateral and medial to the artery
3. A combination of 1 and 2 as a triple-deposit of LA

Axillary Brachial Plexus Block nerve localisation techniques:

Transcutaneous nerve stimulation (TNS)

Electrical nerve stimulation can be applied transcutaneously by using a stimulation pen (Stimuplex Pen; B. Braun, Melsungen, Germany) with an electrode on the tip. When the stimulation pen (connected to a nerve stimulator) is placed on the skin precisely above a superficial nerve, the axons within the nerve will be depolarized and a neuromuscular response will be observed. Since the distance between the electrode and the nerve is much greater when compared with nerve stimulation through a block cannula, more energy must be applied for TNS. Therefore the stimulation current must be increased up to 5 mA and longer impulse durations (0.3 - 1.0 ms) must be used. The actual settings depend on the tissue impedance and the distance between the skin and the target nerve. After obtaining a neuromuscular response, the course of a peripheral nerve can be estimated and marked with a colour pen on the skin. TNS can be used to estimate the nerve position under the skin before the cannula is inserted.

The median nerve is typically situated medially and anteriorly to the axillary artery. A mapping of the exact position of the nerve, before the block needle perforates the skin, is of value when performing an AXB. The transcutaneous mapping can especially be helpful when an 18-gauge catheter has to be positioned parallel to the median nerve in proximal direction. In all patients included in our studies, the course of the brachial artery and the position of the median nerve as identified by use of TNS, were marked before inserting the block needle (Fig. 3).

Nerve stimulation through a block cannula

Electrical nerve stimulation was used to place a 45 mm long, 18-gauge block cannula (Contiplex®, REF 4893611, B. Braun, Melsungen, Germany) in proximity to the median nerve in all our patients. The cannula was connected to the cathode of the nerve stimulator (Stimuplex DIG/HNS11; B. Braun) while a skin electrode was connected to the anode.
Figure 3 Transcutaneous nerve stimulation
Mapping of the median nerve that is situated superficially under the skin, with a stimulation pen and a nerve stimulator. The red line indicates the course of the brachial artery as palpated through the skin.

The stimulation current was initially between 1.5 mA to 2 mA and considerably lower than the currents used for TNS. Impulse durations of 0.1 - 0.3 ms and a stimulation frequency of 1 Hz were used. When the needle-tip was advanced in proximity of the target nerve, muscle twitches were observed as the nerve axons depolarised. The current was gradually reduced while moving the needle closer to the nerve.

The Contiplex® is a short catheter with an internal steel cannula. It was inserted one to two cm distal to the lateral border of the pectoralis major muscle. The block needle was first inserted one cm subcutaneous and parallel to the skin at the marked position of the median nerve. It was then raised perpendicular to the skin and advanced towards the fascial sheath, anterior to the brachial artery. After a ‘fascial click’ indicated perforation of the fascial sheath, or when in contact with the nerve, the cannula was tilted tangentially to the skin and advanced parallel to the brachial artery in a proximal direction until stimulation of the median nerve resulted in muscle contractions. The entire 45 mm cannula was inserted along the median nerve under continuous nerve stimulator guidance and observation of motor
response. For the final monitoring of the perineural needle position, a threshold range of 0.2 to 0.8 mA at an impulse of 0.1 ms was accepted. The typical neuromuscular responses of the median nerve are flexion of wrist, fingers or thumb or pronation of the hand. In the final position the internal steel cannula was removed while the catheter was left in the same position (Fig.4).

![Figure 4 Axillary block](image)

Injection via a short catheter positioned parallel to the median nerve.

**Transarterial block method**

The transarterial block method is a technique that is based on penetration of the brachial artery with a needle without using nerve stimulation. We applied a divided transarterial block by performing the first injection lateral (deep) to and the second injection medial (superficial) to the brachial artery. The pulsating brachial artery was palpated through the skin and the position was marked with a colour pen. A standard hypodermic needle (25 G, 0.50 x 25 mm, Sterican; B. Braun) was inserted approximately 1 cm posterior to the insertion site of the Contiplex catheter immediately above the pulsating artery. The needle was then moved perpendicularly to the skin and through the artery. The needle was advanced until blood flow under aspiration ceased, indicating that the needle had penetrated the lateral wall of the artery. In this position, just outside the wall of the artery, a syringe with a 10 cm extension tube was connected. The first injection was set after a negative aspiration test (Fig. 5).
Thereafter the needle was withdrawn to the medial side of the artery where blood flow under aspiration disappeared. In this position a second injection was performed. The axillary artery was compressed for 2 min following the procedure to ensure haemostasis.

**Figure 5 Axillary block**

Transarterial injection lateral to the brachial artery with a syringe, extension tube and hypodermic needle. The needle perforates the axillary sheath and the brachial artery posterior (inferior) to the green catheter.

**Combined catheter and transarterial method**

The author of this thesis has developed the axillary block method using three LA deposits. The method combines an injection through an axillary catheter that is placed parallel to the median nerve, with the double transarterial injection technique as described above. This 3-deposit technique was first described in the publication of study I and later used in the other studies (Table 1).

**Block assessment**

A delta- and C-fibres are responsible for pain and cold sensation (A delta-fibres: sharp pain, C-fibres: dull pain) and belong the same bundle of nerve fibres. Cold sensation tests are therefore frequently used for sensory assessment of PNBs. The ice cube test method has
good patient acceptance and is suitable to quickly access multiple test points. A pinprick test can be used as an alternative to predominantly assess the block effect on A delta-fibres. However, pinprick can interrupt the integrity of the skin and interfere with sterile surgical preparations.

In all our patients, PNBs were assessed by testing cold sensation using ice cubes that were repeatedly applied on predefined points in the sensory area of the peripheral nerves of the brachial plexus. Anaesthesia was defined as a complete loss of sensory perception in the test area. Analgesia was defined as a maintained sensation of touch combined with a loss of cold sensation.

Sensory testing was performed for five terminal nerves of the brachial plexus that innervate the upper extremity. The sensory testing points were as follows: laterally and at the midpoint of the proximal half of the upper arm (axillary nerve), over the brachioradial muscle, 5 cm distal to the elbow joint (musculocutaneous nerve), between the first and second metacarpals on the dorsal side of the hand (radial nerve), between the second and third metacarpals on the volar side of the hand (median nerve), and on the medial side of the fifth metacarpal (ulnar nerve). In addition a sensory testing of the medial cutaneous antebrachial, medial cutaneous brachial and intercostobrachial nerves were included in study II and III.

Two different sensory scoring systems were used in the studies. In study I a scale ranging from 0 to 1.0 was used. A score of 0 represented unimpeded cold sensation while a score of 1.0 indicated a successful block. The patients were asked to describe the degree of their experienced block effect as a percentage compared to the contra lateral side. For example, if the perception of ice (cold sensation) was reduced by 40% compared to the contra lateral arm with normal (100%) sensation, the recorded block score was 0.4. The patient estimated the score subjectively.

In studies II and III a four part scoring system was used. The sensory scoring ranged from 0 to 3 and was defined as follows: 0 - normal sensation; 1 - hypoalgesia, patient had persistent cold sensation but less than on the contra lateral side; 2 - analgesia, patient felt touch but not cold sensation; and 3 - anaesthesia, no feeling at all. In study III, the AXB was defined as successful when all five nerves distal to the elbow (musculocutaneous, radial, median, ulnar, and medial cutaneous antebrachial nerve) had sensory test scores of 2 or 3. We further tested the motor block in the axillary, musculocutaneous, radial, median, and ulnar nerve.
Muscle strength was assessed manually comparing motor function with the contra lateral arm.

**MRI protocol**

An MRI protocol suitable for the high-field 3.0 Tesla resolution scanner was developed using volunteers not receiving an AXB. The anatomic findings from this process are demonstrated in study II. The final and optimised protocol was thereafter used for scanning of the patients, receiving an AXB, in study II and III.

The final MRI settings were:

1. Distal cross-sectional images were acquired using a multislice, angulated, transversal, multishot rapid acquisition with relaxation enhancement (RARE), with echo time (TE) / repetition time (TR) = 65/3193 ms, turbo spin-echo (TSE) factor = 16 (shot length 122 ms, echo spacing = 7.6 ms), acquired 1.11 x 1.11 x 2.5 mm, 20 slices, field of view (FOV) 200 [right-left (RL)] x 242 [anterior-posterior (AP)], bandwidth (BW) = 232.6 Hz and spectral selection attenuated inversion recovery (SPAIR) fat saturation with inversion time (TI) = 100 ms protocol. The scan time was 05:58.

2. Cross-sectional images at the cord level were acquired using a multislice, angulated, sagital, multishot RARE, with TE/TR = 100/3078 ms (two packages), TSE factor = 15 (shot length 122 ms, echo spacing = 8.1 ms), acquired voxel size 1.10 x 1.13 x 2.5, 20 slices, FOV 220 [height of FOV (FH)] x 245 (AP), BW = 217.7 Hz and SPAIR fat saturation with TI = 100ms protocol. The scan time was 06:09.

3. Coronal images were acquired using a multislice, angulated, coronal, multishot RARE, with TE/TR = 65/7983 ms, TSE factor = 16 (shot length122 ms, echo spacing = 7.6 ms), acquired 1.20 x 1.26 x 2 mm, 50 slices FOV 220 (FH) x 202 (RL), BW = 221.7 Hz and SPAIR fat saturation with TI = 100 ms protocol. The scan time was 05:35.

**MRI assessment and scoring**

Initial coronal slices (Fig. 6) were used to determine the region to be cross-sectionally scanned and to examine the extent of the longitudinal LA spread. A cross-sectional view of the neurovascular bundle was obtained via the scanning of two sections perpendicular to the
bundle of nerves and vessels at the cord and terminal nerve levels. To confirm the identity of the terminal nerves, the cross-sectional slices were viewed in a sequence loop.

In study III the distribution of LA to the cords and terminal nerves were examined. The distal and proximal distribution of LA was examined in coronal views (Fig. 6). The cross-sectional distribution of LA was examined in the cross-sectional images (Fig. 7, 8 and 9). The proximity of LA to the cords and terminal nerves was described by the following scores: 0, no contact between local anaesthetic and the nerve; 1, local anaesthetic partly contacts the nerve; and 2, local anaesthetic surrounds the nerve. Furthermore, the distal and proximal distribution of the LA was recorded.

In study IV the position, the course, and the relation to the axillary sheath of the musculocutaneous nerve (MCN) were analysed. The position where the MCN left the axillary sheath and perforated the coracobrachial muscle was defined as the MCN exit point. This point was measured in relation to the axillary four quadrants (Fig. 8), as angles in relation to the axillary artery (Fig. 10) and as a distance to the axillary fold (Fig. 11).

Figure 6 MRI of the right axillary region
Coronal view before cross sectional scanning. The T2-weighted MR images demonstrate the spread and localisation of the LA (appears white). Single-deposit (left), double-deposit (middle) and triple-deposit (right).
Figure 7 **Axillary cross-sectional view**
Cross-sectional view of the right axillary region and the neurovascular sheath. In the T2-weighted MR image the LA appears white.

Figure 8 **The axillary four quadrants**
The axillary sectioning of the neurovascular sheath into four quadrants with the axillary artery at the centre. The typical positions of the terminal nerves are marked. Q₁ = the lateral anterior, Q₂ = the medial anterior, Q₃ = the medial posterior and Q₄ = the lateral posterior quadrant.
Statistics

For statistical analysis SPSS (IBM Corporation, Armonk, New York, USA) was used. $P$-values below 0.05 were considered statistically significant.

In study I, data were tested for normal distribution and presented as mean values and standard deviations. The groups were compared with independent sample t-tests, Pearson’s $\chi^2$ test (Chi-squared test) and Fischer’s exact test to compare variables.

In study III, data were described by mean, standard deviation and counts. The groups were compared with one-way analysis of variance (ANOVA) or the Pearson Chi-square test for continuous or categorical variables as appropriate. Correlating MRI scores with the sensory scores from correspondingly innervated areas, we used cross tabulation and the Gamma test, considering all patients as one group according to the advice from our statistical supervisor. The assessments of the two radiologists in scoring the LA distribution were compared by cross tabulation and the Kappa test.

In pilot study II, statistical analyses were not applied. In study IV the data were expressed using mean, standard deviation, range and counts.
Results and summary of the studies I - IV

Study I

Methods:
In this study we compared the single-deposit with the triple-deposit method. Fifty-one patients were included in a comparative prospective clinical trial and allocated into two groups. All patients had an injection through a catheter, while 26 of the patients had an additional injection lateral and medial to the brachial artery. Each patient received a total of 0.75 ml/kg of a 50/50 mixture of lidocaine 20 mg/ml with 12.5 µg epinephrine/ml and bupivacaine 5.0 mg/ml. We tested the time to block onset during the first 29 minutes after the AXB was performed. In addition, the block progression from 30 to 50 min was recorded.

The primary outcome was the recorded time to achieve a successful block. The secondary outcomes were the block progression and analgesia block scores from 30 min to 50 min.

Results:
At 30 min we found the block to be successful in 52 % of the patients in the catheter group (single-deposit) and in 81% in the triple-deposit group (p<0.05). The mean onset time was 20.8 min and 13.3 min respectively (p<0.05), (Table 2). At 50 min, 68% of the patients in the single-deposit group and 92% in the triple-deposit group had successful blocks (p<0.05).

<table>
<thead>
<tr>
<th>Study I</th>
<th>No. Pat.</th>
<th>Successful blocks after 30 min</th>
<th>Successful blocks after 50 min</th>
<th>Mean time to onset of successful block</th>
<th>Supplemented patients at 50 min</th>
<th>Supplemented nerves at 50 min</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-deposit Group</td>
<td>25</td>
<td>13 (52%)</td>
<td>17 (68%)</td>
<td>20.8 min</td>
<td>8</td>
<td>13</td>
</tr>
<tr>
<td>3-deposit Group</td>
<td>26</td>
<td>21 (81%)</td>
<td>24 (92%)</td>
<td>13.3 min</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>P-value</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td>&lt;0.05</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
The MCN and the radial nerve were better blocked with a higher analgesia score at 30 min in the triple-deposit group (0.95/0.99) compared to the single-deposit group (0.81/0.76), (p<0.05). The radial nerve also had a higher analgesia score at 50 min (0.99 vs. 0.9) respectively (p<0.05).

The success rates improved in both groups from 30 min to 50 min. However, the single-deposit group still had a higher failure rate. Eight patients in the single-deposit group and two patients in the triple-deposit group required peripheral nerve block supplementations.

**Conclusion:**
The combined catheter and transarterial method demonstrated a faster onset and more extensive block than the single injection technique.

**Study II**

**Methods:**
Six healthy volunteers were included in a pilot study to develop an MRI protocol and describe the anatomy of the axillary brachial plexus. To study the effect of LA injections on MRI imaging we examined nine patients who received an AXB prior to a surgical procedure.

The aim of this study was to improve MRI visualisation of the peripheral nerves, surrounding anatomy and the LA.

**Results:**
A new axillary MRI protocol suitable for the high-field 3.0 Tesla MRI scanner was developed. Thereafter the detailed anatomy of the axillary brachial plexus was demonstrated. In the T2-weighted images without fat suppression, fat appears grey-white and blood vessels black. We obtained images of good quality, and both cords and all terminal nerves could be identified. Viewing the images in a sequence loop facilitated the identification of the different nerves.

The patients were examined with T2-weighted fat suppression, where the signals from fat are suppressed and the areas containing LA or liquid appear white. After the injection of LA, neurovascular structures were displaced and the vein was compressed. The displacement of the neurovascular structures, however, made their identification more difficult (Fig. 7).
Conclusion:
The clinical high-field 3.0 Tesla MRI scanner gives good visualisation of the brachial plexus in the axilla. The superior ability to detect local anaesthetics after injection and the multiplanar imaging capability makes MRI a useful tool in studies of the brachial plexus.

Study III
Methods:
45 patients were included in a blinded and randomised controlled clinical trial and allocated into three study groups. Patients in the single-deposit group received an LA injection through a catheter parallel to the median nerve. In the double-deposit group a transarterial block with two deposits was performed. In the triple-deposit group the catheter technique and the transarterial injections were combined. The clinical block assessors were blinded to the block method and MRI images. Two radiologists, blinded for the block method and its clinical effect, independently performed the MRI scoring.

The primary outcomes were sensory block effect and MRI distribution pattern.

Clinical results:
Only patients in the triple deposit group had 100% block success (analgesia or anaesthesia for all five terminal nerves distal to the elbow (Table 3). Supplementary peripheral nerve blocks were only made in the single-deposit group and in the double-deposit group. The MCN was supplemented with additional blocks four times both in the single- and double-deposit group.

MRI findings:
The patients in the triple-deposit group most often had the highest MRI scores (higher LA proximity score, Table 4). For any nerve and cord, at least one of the single-deposit or the double-deposit groups had similarly high MRI score as the triple-deposit group. Considering the cords in the coronal view, the proximal distribution was best in those groups which had LA injections through the catheter (single- and triple-deposit groups) (Table 5, Fig. 6). At the terminal nerve level in the cross-sectional view, the spread to the radial nerve, positioned lateral to the artery, was best in those groups with transarterial injections (double- and triple-deposit group) (Fig. 9).
Table 3 Block results of study III

<table>
<thead>
<tr>
<th>Study III</th>
<th>1-deposit group</th>
<th>2-deposit group</th>
<th>3-deposit group</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Successful blocks</td>
<td>10/15</td>
<td>10/15</td>
<td>15/15</td>
<td>0.04</td>
</tr>
<tr>
<td>Supplemented patients</td>
<td>5/15</td>
<td>5/15</td>
<td>0/15</td>
<td>0.04</td>
</tr>
<tr>
<td>Supplemented nerves</td>
<td>5/75</td>
<td>11/75</td>
<td>0/75</td>
<td>0.058 (1 vs. 3) 0.001 (2 vs. 3)</td>
</tr>
</tbody>
</table>

Successful blocks = number of patients with successful blocks (total 15)  
Supplemented patients = number of patients receiving supplementary nerve blocks  
Supplemented nerves = number of nerves receiving supplementary blocks (total 75)

Figure 9 MRI cross-sectional view

MRI of local anaesthetic (LA) in the right axilla, cross-sectional view. T2-weighted MR images with fat suppression. Typical LA distribution for three axillary block methods, in patients with successful sensory block. The LA appears white. In the triple-deposit group, the artery (black circular structure) is more centrally located within the LA area.
Table 4 Scoring of LA-distribution as observed by MRI from study III

<table>
<thead>
<tr>
<th>Study III</th>
<th>1-deposit group (n=15)</th>
<th>2-deposit group (n=15)</th>
<th>3-deposit group (n=15)</th>
<th>MRI score</th>
<th>MRI score</th>
<th>MRI score</th>
<th>Missing scores</th>
<th>P-values all scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerves</td>
<td></td>
<td></td>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ax</td>
<td>1</td>
<td>3</td>
<td>9</td>
<td>0</td>
<td>1</td>
<td>13</td>
<td>2</td>
<td>0.17</td>
</tr>
<tr>
<td>Mcn</td>
<td>0</td>
<td>1</td>
<td>14</td>
<td>0</td>
<td>3</td>
<td>11</td>
<td>1</td>
<td>0.2</td>
</tr>
<tr>
<td>Rad</td>
<td>0</td>
<td>4</td>
<td>11</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0.012</td>
</tr>
<tr>
<td>Med</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>nc</td>
</tr>
<tr>
<td>Uln</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>0</td>
<td>15</td>
<td>0</td>
<td>nc</td>
</tr>
<tr>
<td>Lat. C</td>
<td>0</td>
<td>3</td>
<td>12</td>
<td>4</td>
<td>5</td>
<td>6</td>
<td>0</td>
<td>0.016</td>
</tr>
<tr>
<td>Post. C</td>
<td>0</td>
<td>4</td>
<td>11</td>
<td>3</td>
<td>6</td>
<td>6</td>
<td>0</td>
<td>0.031</td>
</tr>
<tr>
<td>Med. C</td>
<td>0</td>
<td>4</td>
<td>11</td>
<td>3</td>
<td>3</td>
<td>9</td>
<td>0</td>
<td>0.12</td>
</tr>
</tbody>
</table>

The numbers indicate the counts of patients with an MRI score of 0 - 1 - 2 in the three groups. Score 0 = no local anaesthetic (LA) in contact with the nerve. Score 1 = LA partly contacts the nerve. Score 2 = LA surrounds the nerve. Missing scores = Number of patients without MRI score.


P-value all scores: the calculation of P-values was based on the scores of all patients for each nerve and cord. nc = not calculable P-value - this was the case for both the median and ulnar nerve, both of which had MRI-scores of 2 in all patients of all groups.
Table 5 **Proximal and distal LA spread from study III**

<table>
<thead>
<tr>
<th>Study III</th>
<th>Proximal</th>
<th>Distal</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>1-deposit group</td>
<td>4.5 ± 2.0</td>
<td>14.5 ± 2.6</td>
<td>19.0 ± 3.7</td>
</tr>
<tr>
<td>2-deposit group</td>
<td>1.8 ± 1.5</td>
<td>14.2 ± 2.2</td>
<td>16.0 ± 2.2</td>
</tr>
<tr>
<td>3-deposit group</td>
<td>3.6 ± 2.0</td>
<td>14.5 ± 2.3</td>
<td>18.1 ± 2.9</td>
</tr>
<tr>
<td><em>P</em>-value</td>
<td>0.001 (group 1/3 vs. 2)</td>
<td>0.9</td>
<td>0.026</td>
</tr>
</tbody>
</table>

Longitudinal spread of local anaesthetic from the top of the humeral head in proximal and distal direction. Values are means ± SD in cm. 1-deposit group: catheter injection; 2-deposit group: transarterial injection; 3-deposit group: transarterial and catheter injection.

**Conclusion:**
Distal to the elbow, the triple-deposit method had the highest sensory block success rate. This can be explained by analysis of the MRI distribution patterns.

**Study IV**

**Methods:**
The existing data from the nine patients in study II and the 45 patients in study III were analysed retrospectively. The course of the MCN and the position where the nerve left the axillary sheath and perforated the coracobrachial muscle (MCN exit point) were recorded.

The objective in study IV was to examine the position of the MCN and its relationship to the axillary sheath using MRI.

**Results:**
The MCN was clearly seen in 23, partly in 26 and not identified in 5 of the 54 patients. The MCN exit point was mainly localized in the lateral anterior (Q₁) and the medial anterior (Q₂) axillary quadrant (Fig. 7 and 8). The nerve was localised at a mean angle of 69.4°, ranging from -8.1° to 160.2°, in relation to the axillary artery (Fig. 10). The distance from the insertion point of the block needle in the axillary fold to the MCN exit point had an average of 36.8mm with a range from 0 to 90.5mm (Fig. 11).
**Conclusion:**

There is wide variability as to where the MCN leaves the axillary sheath and enters the coracobrachial muscle. Therefore multiple injection techniques, or the use of a proximally directed catheter, should be used to block the MCN.

**Figure 10** The MCN exit point

The exit points of the musculocutaneous nerve into the coracobrachial muscle in relation to the quadrants and the axillary artery (centre). The four quadrants: \( Q_1 \) = the lateral anterior (0° - 90°), \( Q_2 \) = the medial anterior (90° - 180°), \( Q_3 \) = the medial posterior (180° - 270°) and \( Q_4 \) = the lateral posterior (270° - 360°) quadrant.

**Figure 11** The MCN exit point

The exit points of the musculocutaneous nerve into the coracobrachial muscle in relation to the insertion point of the block needle (arrow) in the axillary fold, and in relation to the centre of the artery.
Discussion

This thesis showed that the triple-deposit technique is preferable regarding the clinically block effect as compared to the single- and double-deposit AXB technique. This is supported by analysis of the MRI distribution patterns.

We found a general correlation between the LA proximity to the nerves and the sensory block scores. Thus a high MRI score typically correlates with a high sensory score. In order to evaluate the block difference between three AXB methods by MRI, this general correlation was of importance.

Validation of single- vs. multiple-deposit block methods

There is a high variability in the block success rate among the various methods of AXB that have been published.\textsuperscript{24,42} The time to onset of a complete and successful nerve block is of great importance to prevent surgical delays. Rapid development of the block and early readiness for surgery can be obtained when LA injections are in close proximity to the nerves.\textsuperscript{43}

Study I and III showed consistent block effect after 50 min for both the single- and the triple-deposit method by clinical assessment. The patients in the triple-deposit group had a block success of 92\% in study I and 100\% in study III. Success rates for the single-deposit groups were 68\% and 67\% respectively. The triple-deposit technique described in this thesis was previously used in another study at the Oslo University Hospital where a similar high success rate of 92\% was achieved.\textsuperscript{44} The clinical block assessment performed in this thesis confirms a superior block effect of the triple-deposit method.

Our clinical results are comparable to those from other studies on axillary blocks where onset time and success rates have been improved by the use of multiple injections.\textsuperscript{11,45,46} Rodriguez et al. had a block success rate of 93.3\% for a triple-injection method and 73.3\% for a double-injection method.\textsuperscript{45} Koscielniak-Nielsen et al. found a multiple-injection technique superior to a double dose transarterial injection method. The multiple-injection group had a success rate of 94\% and the transarterial group 64\%.\textsuperscript{11} The latter is comparable to this thesis’s study III, which demonstrates a 67\% success rate in the double-deposit group.

The clinical results of study I and III support the use of a multiple-injection technique for axillary plexus blocks. Also according to the Cochrane database multi-injection techniques are the method of choice when performing AXB.\textsuperscript{25,47} The authors concluded that the Cochran
review provides evidence that multiple-injection techniques, using nerve stimulation for axillary plexus block, produce more effective anaesthesia than either double or single-injection techniques.

**MRI distribution patterns**
Evaluating LA distribution by MRI in study II and III demonstrates significantly higher proximal LA distribution when a proximal directed catheter was used. LA distribution to the proximal cords and simultaneously to the terminal nerves was demonstrated for the triple-deposit technique (combining a transarterial injection technique with a catheter technique). LA distribution patterns most often had the highest MRI scores in the triple-deposit group. This explains why the triple-injection method had a better block success than the single- and double-injection methods. The combined triple-deposit technique, as described in this thesis, provided LA deposits to the cords and at terminal nerves and was also clinically the most effective technique.

Klaastad et al. observed a lack of block effect despite the close proximity of LA to the nerve. This was also observed in some of the patients in study III. However, if patients had LA contact at both the terminal nerve and corresponding plexus cord level, a sensory block was always observed.

**Block experiences for single nerves**
An effective block of the radial nerve can be a challenging component of the AXB. This was documented in study I in which block failure of the radial nerve occurred eight times in the single-deposit group (32% of the patients), but only one time in the triple-deposit group. In study III, block failures of the radial nerve occurred one time in the single-deposit and three times in the double-deposit group. Although the radial nerve was successfully blocked in all patients within the triple-deposit group, we did not find a statistically significant difference from the other study groups in study III.

In study III the radial nerve had a significantly lower MRI score in the single-deposit group when compared to maximal scores in the double- and triple-deposit groups. This difference in MRI scores (LA proximity to the nerves) did not correlate with clinical assessment, demonstrating a statistically non-significant difference between the groups. Clinical assessment and MRI analysis showed that the posterior positioned radial nerve in some patients lacked contact with the LA. Our MRI findings indicate further that a free LA
distribution in the cross sectional plane, and particularly to the lateral part containing the radial nerve, does not always occur. When a single-injection via the catheter is administered, the reduced cross-sectional distribution should be compensated for with an additional injection to the lateral part of the axillary sheath.\(^{48}\)

In study I, the block success for the ulnar nerve at 50 min was 92% in the single-deposit and 96% in the triple-deposit group. In study III a success rate of 100% was achieved in all study groups. Sia et al. found comparably high success rates of 90% and 92% for successful blocks of the ulnar nerve in a nerve stimulator guided study on AXB with multiple injections.\(^{49}\) The authors could also demonstrate that a selective block of the ulnar nerve in one of the study groups did not increase the block success rate. Tran et al. had comparable success rates in ultrasound guided double-, triple- and quadruple-injection techniques and did not achieve higher success rates for the ulnar nerve when it was selectively blocked.\(^{27}\) Hence, LA distribution to the ulnar nerve can be accomplished with most AXB techniques. Selective blocks for the ulnar nerve are not mandatory for a successful AXB.

In study I and III the MCN was always successfully blocked in the triple-deposit groups. In contrast, four of fifteen patients in both the single- and double-deposit groups of study III had MCN block failures. In study IV the MRI examinations of the course of the MCN, showed high variability as to where the MCN leaves the axillary sheath. According to our results, the use of a triple-deposit technique, that includes a proximally directed catheter, is necessary in order to achieve a successful MCN block. The distance from the axillary fold to the MCN exit point had an average of 36.8mm with a range from 0 to 90.5mm. Short catheters (45 mm, used in this thesis) seem sufficient in order to reach the region where the MCN typically leaves the axillary sheath (Fig. 11).

The results of this thesis indicate that a selective block of the MCN is unnecessary when the triple-deposit technique is performed. Recent studies on ultrasound guided AXB techniques however have supported a selective block of the MCN outside the axillary sheath.\(^{26,27}\) For another double injection technique at the terminal nerve level, a selective MCN block was recomended.\(^{29}\) The selective MCN block is technically easy to perform, but usually an additional injection at a steep needle angle through the coracobrachial muscle is necessary to reach the nerve. If the additional needle pass can be avoided, discomfort for the patients can be reduced.
**The transarterial block method**

In study III the transarterial block method with two deposits lateral and medial to the brachial artery had a low success rate. Only 10 of 15 patients had a successful block of all five terminal nerves distal to the elbow in the double-deposit group. In a study by Cockings et al. however, the transarterial blocks with a double-injection was shown to be more effective with a block success rate of 99%. They did however use a higher volume of LA than we did (50 ml vs 40 ml). Additionally, Cockings directed the transarterial block needle more proximally and towards the cords of the brachial plexus. The transarterial technique, at a distal level with a lower amount of LA, seems to have a higher incidence of block failures and a need for supplemental block injections. This has also been noted by other research groups.

**Axillary catheter**

The interest in axillary catheters and the use of single injection techniques had a resurgence after Winnie’s 1979 work in this field. In study I, II and III of this thesis some of the patients received a single LA injection via a catheter anterior to the brachial artery close to the median nerve. Vester-Andersen et al. demonstrated lack of analgesia most often in the cutaneous area innervated by the axillary, musculocutaneous and radial nerves using a single-injection catheter technique. Providing a block to the posterior section of the axillary sheath seems to represent a challenge to the single-deposit technique in the anterior section.

The high proximal LA distribution as demonstrated with MRI by the catheter injections in study II and III involved the cord level and the infraclavicular region (Fig. 12). The patient received 40 ml of LA injected via a catheter positioned on the median nerve. In the MRI examination we found a high proximal spread to the cord level. Simultaneously a successful block distal to the elbow was recorded.

Blocks of the infraclavicular region have shown high success rates in several clinical studies. In study III, the mean proximal distribution referred to the most proximal point of the humeral head was 4.5 cm in the single- and 3.6 cm in the triple-deposit group (Table 5). This was significantly different to the proximal distribution in the double-deposit group with 1.8 cm. These results demonstrate that an AXB with a proximally directed catheter, with subsequent LA distribution to the cords, can be an alternative to the infraclavicular block.
Figure 12 **Proximal LA distribution**

Right axilla: T2-weighted MR image. A PNB catheter is positioned close to the median nerve. The image demonstrates the proximal distribution of LA to the infraclavicular region and cord level after injection of 40 ml LA via the catheter.

**The axillary sheath. MRI considerations**

Over the years there has been an ongoing discussion about the existence of an axillary sheath and whether free LA distribution occurs within the sheath.\cite{18,20,53} Its existence seems plausible according to the coronal MRI examinations which demonstrate a distal and proximal LA distribution forming a sheath. In order to illustrate the stretching of the axillary sheath during the catheter injection, Fig. 13 demonstrates a successive expansion of the assumed neurovascular sheath.
Figure 13 MRI of the axillary sheath distribution

T2-weighted MR image of the left axillary region. Proximal and distal LA distribution after fractioned injection of 40 ml via a catheter. The images demonstrate a successive expansion of the neurovascular axillary sheath.

MRI-examination

The axillary brachial plexus MRI-protocol for the high-resolution 3.0 Tesla scanner was developed in study II. The anatomic structures and the LA distribution patterns were clearly visible, and in the T2 weighted images with fat suppression the LA appeared as the only white structure. This was beneficial for the challenging MRI scoring of the LA distribution patterns and the LA proximity to the nerves. In a previous study by Klaastad at al., performed at The Intervention Centre in 2002, the terminal nerves were difficult to distinguish from equally sized vessels. Utilising high-resolution images in our research, we could reliably identify all terminal nerves and vessels. A comparable detailed view of the brachial plexus was also demonstrated by other authors when examining the neck and thorax aperture with MRI.

The high-resolution 3.0 Tesla MRI provided a clear visualisation of the LA. As a result it was possible to assess the anatomy and LA distribution in greater detail in study II and subsequently in study III and IV. The high resolution and multiplanar imaging capacity of the MRI made it to a valuable tool for our scientific studies of the anatomy and LA distribution in the axillary region.
Limitations

There are several limitations of the studies included in this thesis. In study I, the lack of randomisation and blinding are a source of potential bias. However, the results from study I are comparable with the results from the randomised and observer blinded study III. This supports the reliability of the results in study I.

In study I, II and III the first author performed all the blocks. When the blocks are performed by a single anesthetist, a standardisation of the technique can be provided. We do not know how the results could have been affected if blocks had been performed by several anesthetists with potentially different levels of block experience. All clinical assessments were performed by only one colleague, also representing a limitation of the study.

Our results are valid for the mixture of LA, volume and concentration used in the clinical studies in this thesis. The volumes injected differ from study I (0.75 ml/ kg) to study III (standardized LA volume of 40 ml). The spread of the LA that was recorded by MRI and clinical assessment are probably dependent on the injected volumes. The comparability between study I and III was further limited by a higher concentration of epinephrine in study I as compared to study III (6.5 µg/ml and 2.5 µg/ml respectively). It is unclear how the epinephrine concentration difference affects the comparability of the results in the two studies.

In study III, the prolonged time interval prior to the block assessment may represent a limitation in the trial. After performing the block and MRI scanning, the average sensory assessment time in study III was 55 minutes. Firstly, the time is not comparable to commonly accepted block onset times in the clinical practice of regional anaesthesia. The onset time for a nerve block and readiness for surgery is typically 20 to 30 minutes. Due to the closed-bore scanner construction, we had no access to the patient during MRI scanning and could not make a simultaneous clinical block assessment. This was in contrast to Klaastad et al. who performed their MRI scanning in an open scanner making block assessments during scanning possible.

In study III, 15 patients were included in each of the three study groups. A larger number of patients would probably have characterised the group differences more strongly, eventually giving more significant differences. Compared to study III, study I had a better data foundation for statistical calculations due to the higher number of patients that were included in the study groups (25 and 26 patients).
MRI is not a practical tool for clinical use in regional anaesthesia. In the MRI suite there is a strong magnetic field. Only MR compatible equipment can be brought into the room, and the patients must not have contraindications for MRI examination. The logistics regarding the magnetic field and the MRI location in distance to the surgical facilities impedes the use of MRI as a research tool for clinical studies. Study II and III were performed with great organisational effort involving many individuals from different departments. Coordination of vacancies at the MRI facility and the availability of colleagues within the surgical program was a challenging process. We therefore spent over two years to carry through study III. The long time period can be seen as a limitation of the study.

MRI measurements are substantially observer dependent. Particularly in study III the discrepancies between the two radiologists in scoring the proximity of LA to the nerves represent a challenge, likely due to the displacement of the neurovascular structures after LA injection. The determination of the MRI scores was sometimes difficult when the rim of LA close to a nerve was narrow. The images were therefore discussed among the two radiologists to reach a consensus agreement. Also in study IV consensus was reached amongst the three observers. The possibility of errors in identifying the nerves or the local anaesthetic’s relation to the nerves had an unknown impact on our results.

**Safety**

The electrical current threshold level accepted for the nerve stimulator in this thesis (0.2 - 0.8 mA at 0.1 ms) was frequently below the actual recommended standard with a minimum current intensity of 0.5 mA.\(^57\) In study I the mean current threshold in the single-deposit group was 0.28 mA and in the triple-deposit group 0.21 mA. In study III we had mean current thresholds of 0.49 mA and 0.46 mA respectively. To avoid accidental intraneural needle placement, an electrical current threshold of at least 0.5 mA is recomended.\(^57\) When we performed our research, a threshold of 0.2 mA was the accepted threshold. The results of recent studies have challenged the application of such low current intensities.\(^58,59\) However, we did not record persisting nerve injury during study I, II and III.

We recorded 4 venous or arterial punctures in study I and one vessel puncture in study III with the Contiplex® cannula. Haematomas or bleeding complications were not recorded. The risk of needle puncture to vital structures in the axillary region is low compared to the infraclavicular, supraclavicular, or interscalene region. Pneumothorax can be a complication of proximal brachial plexus blocks if the block needle is inserted too deep.\(^60\) Additionally if a
haematoma develops in the deep infraclavicular structures after vascular puncture, the ability to provide compression is limited. This is in contrast to the axillary region where the vascular structures are easier to compress.

**Adverse effects**

Performing AXB close to arteries and veins may lead to adverse cardiovascular effects. The transarterial procedure in particular may result in a systemic effect of the LA or vasoconstriction caused by epinephrine injection. In study III three patients experienced tachycardia. Two other patients had pale hands after transarterial block injections. When epinephrine is administered in the LA solution intravascular injection and resultant tachycardia can be detected, allowing the injection to be stopped and the block needle to be redirected. Additionally one patient in study I, in the triple-deposit group (Contiplex® cannula and transarterial injection) and one patient in study III, in the single-deposit group (Contiplex® cannula) had signs and symptoms of systemic LA toxicity: They experienced tachycardia, systemic blood pressure elevation and transient dizziness for several minutes. The rich axillary vascularisation may increase the likelihood of systemic absorption of LA and subsequent systemic toxicity. Thus axillary injections of LA and particularly transarterial deposits should be performed with utmost care particularly when using high doses (as was used in this thesis).

A disadvantage of the transarterial injection method is the high frequency of undesired nerve contact. Nerve stimulation as a tool to avoid close nerve contact or intraneural needle placement cannot be applied with thin and not insulated hypodermic needles that are used for the transarterial method. In study I, one patient experienced paraesthesia (triple-deposit group) and in study III, nine patients experienced paraesthesia (double- and triple-deposit group). However, no patients experienced permanent injury or impairment of the nerves. Permanent nerve dysfunction after needle-nerve contact is exceedingly rare.⁶,⁶¹

Ultrasound (US) guidance is an option to reduce the incidence of PNB related side effects and adverse events. When ultrasound is used, the needle tip and surrounding anatomy can be visualised. Compared with the use of nerve stimulation the incidence of paraesthesia and vessel puncture can be reduced with US guidance.⁶² Additionally ultrasound allows visualisation of free distribution of the injected LA around the nerve and outside of the vascular system. However, the use of ultrasound has not shown to reduce the incidence of complications such as nerve injury in regional anaesthesia.⁶³
Conclusions

The studies included in the thesis demonstrate that an AXB performed with the triple-deposit technique is preferable as compared to the single- and double-deposit AXB with regards to block effect and LA distribution patterns as observed by MRI.

**Study I.** The combined catheter and transarterial triple-deposit block method demonstrated a faster onset and more extensive axillary block than the single-deposit catheter technique.

**Study II.** The axillary MRI protocol for the high-resolution 3.0 Tesla MRI provides detailed visualisation of the cords and terminal nerves. MRI has an excellent ability to detect LA after it has been injected. This, together with the multiplanar imaging capability, makes MRI a useful tool for scientific studies of the brachial plexus and LA distribution in the axilla.

**Study III.** The triple-deposit method as compared to the single- and double-deposit method resulted in a more effective block to all sensory nerves distal to the elbow. The MCN is successfully blocked without the need for supplementary blocks in the triple-deposit method. The more effective sensory block resulting from the triple-deposit method could, to some extent, be explained by analysis of the MRI distribution patterns.

**Study IV.** There is wide variability as to where the MCN leaves the axillary sheath. Therefore multiple injection techniques and the use of a proximally directed catheter should be used to block the MCN.
**Impact of the thesis**

The AXB is a reliable method to block the brachial plexus, and the block is suitable for surgery of the elbow, forearm and particularly the hand. The triple-deposit technique is an appropriate method to achieve this. The AXB with catheter and triple-injections is a somewhat longer procedure, but the advantages of this extra-thoracic technique are a successful block and a low risk of severe adverse reactions. The triple-deposit technique as demonstrated in this thesis makes a selective MCN block superfluous, thus sparing the patient additional and steeper injections in order to achieve contact with the MCN. The knowledge achieved from this thesis can be implemented in clinical practice.

Our MRI findings explain the advantages of the triple-deposit method. The high proximal LA distribution, due to the catheter, results in an axillary block at the cord level. This is synergistic to the effect at terminal level and is obviously beneficial for the effectiveness and speed of onset of the AXB. The triple-deposit method is therefore an alternative to infra-clavicular block techniques that also deposit LA at cord level.

The benefit of the triple-deposit method is that the block can be performed with or without a nerve stimulator and with or without ultrasound guidance. The positioning of the catheter, without nerve stimulator and ultrasound available, must then be performed with a blind perforation technique of the axillary sheath anterior to the artery. Particularly under field conditions with limited equipment, the use of the triple-deposit method should provide the patient with a successful AXB. The technique can be applied in any health care setting and not only in high income countries where ultrasound dominates the field of regional anaesthesia.

**Future directions**

Catheter dislocation is a common problem with brachial plexus nerve blocks. Therefore many anaesthetists prefer single shot techniques without catheter placement. A proximally directed short catheter, as applied in this thesis, is positioned within the axillary sheath and may have a reduced likelihood of dislocation and secondary block failure. The deployment of an AXB catheter is necessary for surgical procedures with long duration or longer lasting postoperative analgesia. The long-term effect and dislocation rate of the proximal directed catheters that were used in this thesis have not been investigated. Future studies should evaluate the various brachial plexus catheters for postoperative pain treatment and continuous LA infusion.
Over time, catheters provide a sympatholytic effect in addition to the analgesic block effect. This sympatholysis results from a block of the nerves regulating the vascular system in the affected arm. The consequence of this sympatholysis is an improved micro-circulation distal to the block. In replantation surgery this can be beneficial for the outcome of a replanted limb. Continuous LA infusion via a stable catheter, as used in this thesis, is a means to ensure this sympatholysis and subsequent improved micro-circulation occurs. The implications of a well functioning AXB catheter on postoperative pain and microcirculation are of scientific interest and will be addressed in future studies.

The future standards for AXB and regional anaesthesia in developed countries will include the use of ultrasound and nerve stimulators. With access to ultrasound, we position the catheter performing dual guidance (nerve stimulator and ultrasound) parallel to the median nerve as in the triple-deposit method. Furthermore, we perform the double LA injections close to the artery, laterally and medially, also applying dual guidance. This corresponds with international recommendations. If ultrasound equipment is not available, the triple-deposit technique with a transarterial injection should still be performed as done in this thesis. The modified ultrasound guided triple-deposit technique will be compared and evaluated in future studies.


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