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Peripheral Nerve Blocks for Analgesia after Elective Total Hip Arthroplasty

PhD dissertation

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PREFACE

The present PhD thesis is based on the results of research performed from September 2015 to June 2018 while I was employed first as scientific assistant at the Faculty of Health at Aarhus University and since April 2017 as clinical assistant at the Elective Surgery Centre at Silkeborg Regional Hospital. The Medical University of Innsbruck, Austria was venue for Study I. Elective Surgery Centre, Silkeborg, Denmark was venue for Study II. Department of Radiology at Aarhus University Hospital, Denmark was venue for Study III.

Front page: *Transverse ultrasonogram (curved array transducer) of the left hip joint and overlaying tissues. A nerve block needle is inserted in-plane from the lateral (right) side of the image. The tip of the needle is in the iliopsoas plane – just right for injection of local anaesthetic for the novel iliopsoas plane block.*

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For Randi – my love.

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Aarhus, December 2018

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ABBREVIATIONS

95CI	95 % Confidence Interval
AIIS	Anterior Inferior Iliac Spine
AIIS-IP	AIIS-originated iliopsoas muscle
ASA	American Society of Anesthesiologists physical status classification score
ASIS	Anterior Superior Iliac Spine
CAS	Cumulated Ambulation Score
FICB	Fascia Iliaca Compartment Block
FNB	Femoral Nerve Block
GCP	Good Clinical Practice
HOA	Hip OsteoArthritis
IPB	Iliopsoas Plane Block
IQR	Inter-quartile range
IV	intravenous
LFCB	Lateral Femoral Cutaneous nerve Block
LIA	Local Infiltration Analgesia
lig.	ligament/ligamentum
LPB	Lumbar Plexus Block
m.	muscle *(when part of a muscle's name)*
MRI	Magnetic Resonance Imaging
n.	nerve *(when part of a nerve's name)*
NSAID	NonSteroidal Anti-Inflammatory Drug
OME	Oral Morphine Equivalents
ONB	Obturator Nerve Block
QLB	Quadratus Lumborum Block
SD	Standard Deviation
THA	Total Hip Arthroplasty
VAS	Visual Analogue Scale

1 - Introduction

1.1 Overview

Patients for total hip arthroplasty (THA) are typically in their late sixties or older. A substantial subgroup suffers from moderate or severe postoperative pain.[1,2] Providing postoperative analgesia after THA can be challenging as the patients must be able to ambulate early – preferably on the day of surgery – in order to avoid postoperative complications.[3] To that end, systemic analgesic regimens that include opioids are far from ideal because of the well-known adverse events of opioids including sedation, nausea and vomiting, cognitive dysfunction, delayed ambulation and aspiration pneumonia.[4]

Regional anaesthesia has proven effective to significantly diminish the opioid consumption after major surgery of other joints,[5-7] but regional anaesthesia of the hip is challenging, as the joint is innervated by multiple mixed sensory-motor nerves that follow multiple paths from the lumbosacral plexus.[8] The nociceptors in the hip joint capsule and the intraarticular structures are probably predominantly innervated by the femoral and the obturator nerves.[8-11]

We aimed to investigate the effect of an obturator nerve (n.) block (ONB) on pain after THA – and to examine if the ONB affected the patients' ability to ambulate on the day of surgery. As a femoral n. block (FNB) is known to increase the risk of fall,[12,13] we developed a new nerve block – the iliopsoas plane block (IPB). Theoretically the IPB would anaesthetize the hip articular sensory branches of the femoral n. without blockade of any motor branches. We examined this novel nerve block in a cadaver study as well as a study on healthy volunteers.

1.2 Epidemiology and background

The prevalence of hip osteoarthritis (HOA) is difficult to estimate due to discrepancy between clinical symptoms and radiological findings.[14,15] However, osteoarthritis has a severe impact on patients quality of life and is a significant economical burden for the society.[16,17] In Denmark the estimated annual additional cost of patients due to osteoarthritis was 2.3-3.1 billions DKK (320-420 millions €) in 2003.[18]

Treatment of HOA aims to relieve pain and regain function which is achieved by lifestyle interventions, pharmacologic treatment and surgical intervention in the form of THA.[14] THA have revolutionized the treatment of end-stage HOA since its introduction in the 60's.[19] It is an efficient and cost-effective intervention as it both relieves pain and improves function of patients who often have severe preoperative pain and reduced quality of life.[20]

In Denmark, approximately 9.700 patients undergo THA annually corresponding to 170 per 100.000 citizens. About 1.000 of those are operated at the Elective Surgery Centre in Silkeborg. Danish patients for THA had – in 2015 – a mean age of 69 years and approximately 60 % were women.[1] The incidence of comorbidities among these patients is increasing.[21,22]

1.3 Anatomy of the hip

The hip joint is a simple ball-and-socket joint between the acetabulum and the head of femur (Figure 1). The acetabular articular surface is covered by a crescent shaped hyaline cartilage surrounding the acetabular fossa except for a distal opening (the acetabular notch, Figure 1D). From the inferior part of the fossa the ligamentum (lig.) teres is spanning the articulation to the head of femur, to which it carries the arterial blood supply (Figure 1C). The articular socket is widened by the labrum – a fibrocartilaginous ring extending from the acetabular rim. The joint is enclosed by the hip capsule that is reinforced by the strong capsular ligaments: The ilio- and pubofemoral ligaments anteriorly and the ilio- and ischiofemoral ligaments posteriorly. The capsular ligaments stabilize the joint and with their spiralling course around the neck and head of femur functions by further tightening the joint when the femur is extended (Figure 1A-B).[23]

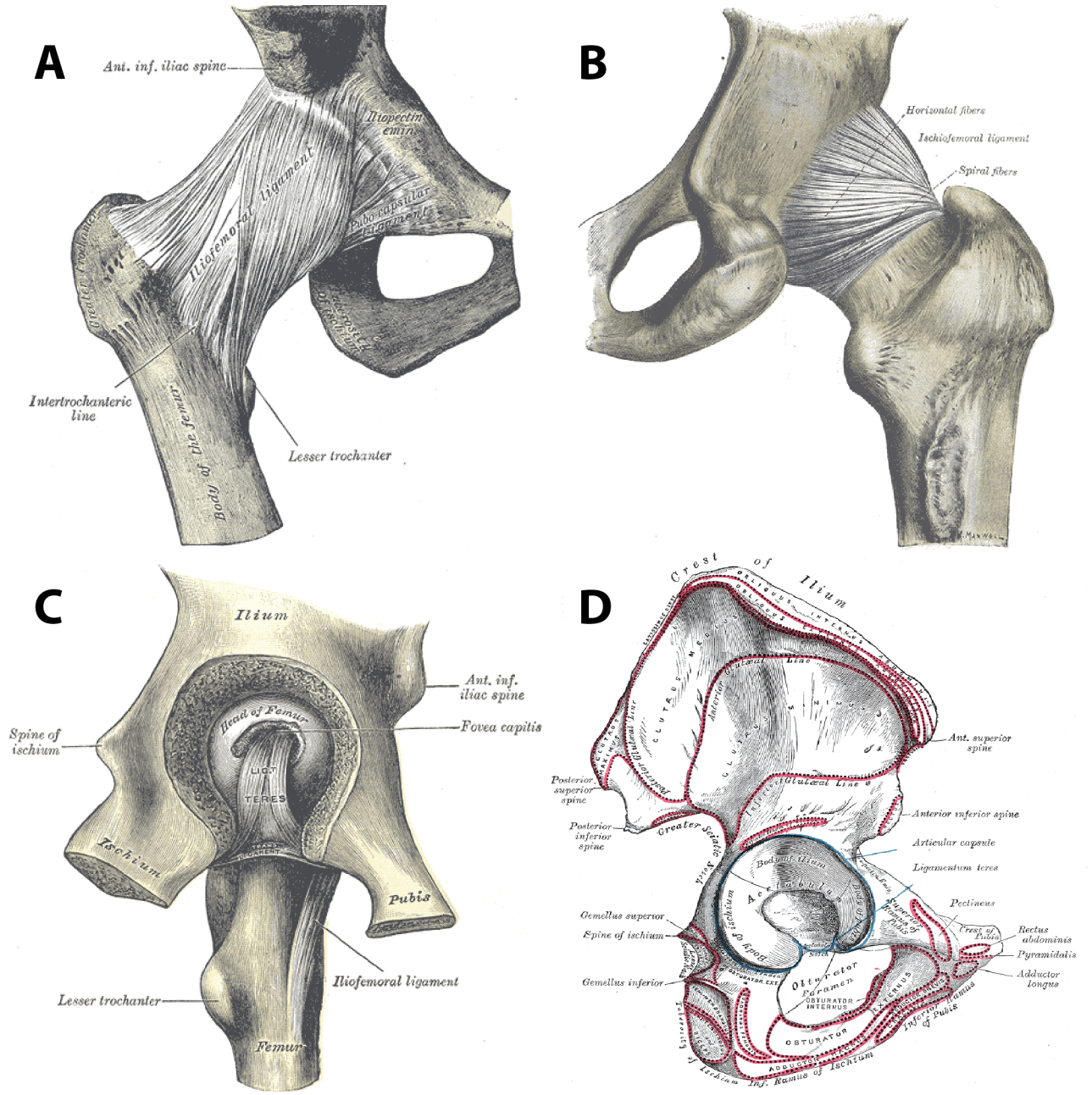

Figure 1. Bones and ligaments of the hip joint. ***A:*** *Right hip-joint, anterior view.* ***B:*** *Right hip-joint, posterior view.* ***C:*** *Left hip-joint, medial view, opened by removing the floor of the acetabulum from within the pelvis to reveal the ligamentum teres and its insertion on the head of femur.* ***D:*** *Right Hip Bone, lateral view. Insertion of the hip joint capsule is outlined in blue. Modified excerpt from Henry Grays Anatomy of the Human Body (1918).*[24]

The muscles surrounding the hip (Figure 2) are divided into four compartments: The gluteal musculature (extension and external rotation of the hip joint), the anterior compartment (flexion, abduction and external rotation of the hip joint), the medial compartment (adduction, external rotation and some extension of the hip joint) and the posterior compartment (extension and both external and internal rotation of the hip joint). The anterior and medial compartments will be reviewed in more depth in the following.

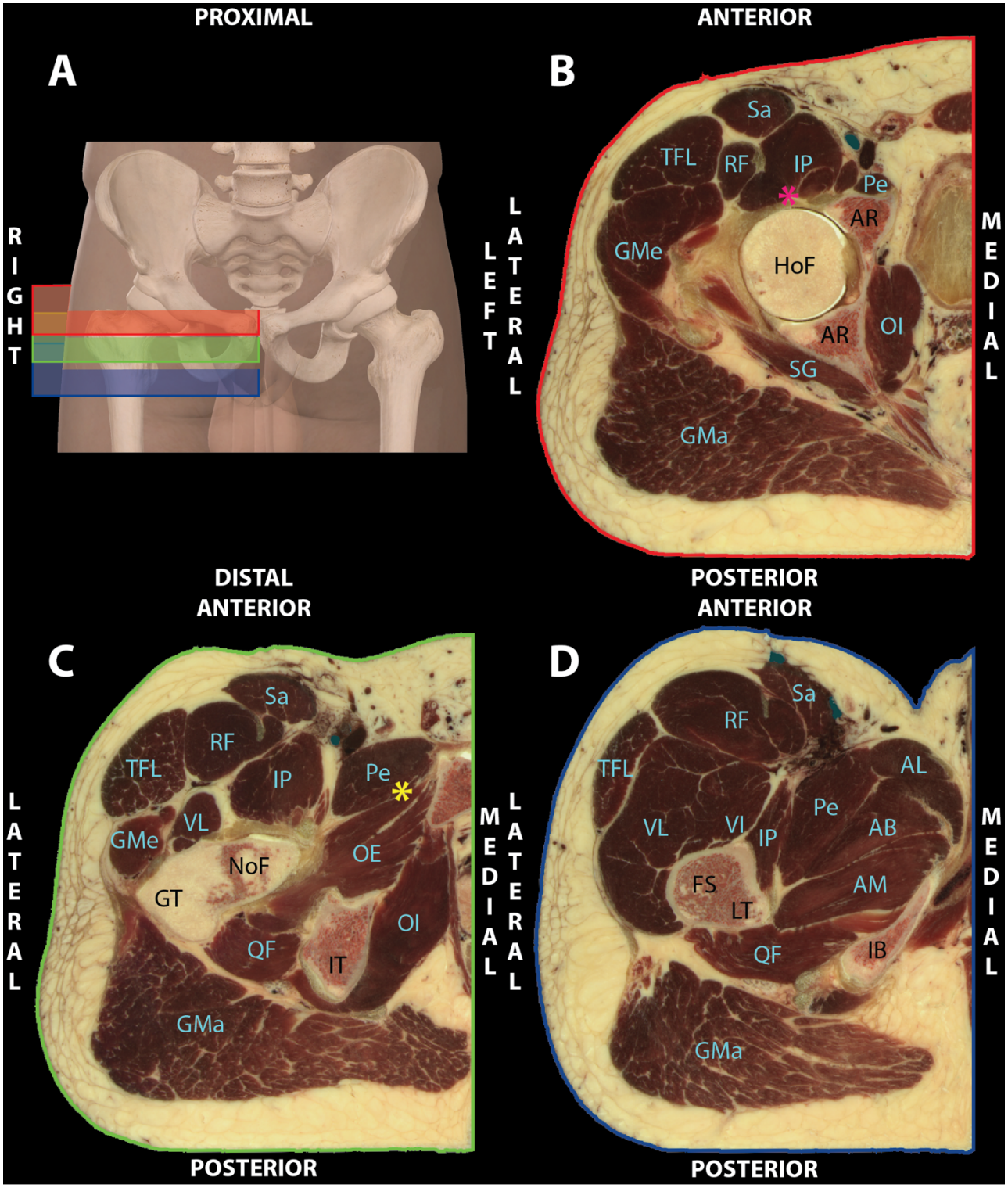

Figure 2. Transverse dissection planes showing the muscles surrounding the hip joint. ***A:*** *Overview. Red plane through head of femur just proximal to the greater trochanter (corresponding to B). Green plane through the greater trochanter and the neck of femur (corresponding to C). Blue plane through the lesser trochanter (corresponding to D).* ***B:*** *Pink asterisk marks target of injection for iliopsoas plane block.* ***C:*** *Yellow asterisk marks target of injection for subpectineal obturator nerve block. Sa: Sartorius muscle (m.); TFL: Tensor fasciae latae m.; RF: Rectus femoris m.; IP: Iliopsoas m.; Pe: Pectineus m.; GMe: Gluteus medius m.; HoF: Head of femur; AR: Acetabular rim; SG: Superior gemellus m.; OI: Obturator internus m.; GMa: Gluteus maximus m.; VL: Vastus lateralis m.; OE: Obturator externus m.; GT: Greater trochanter; NoF: Neck of femur; QF: Quadratus femoris m.; IT: Ischial tuberosity; VI: Vastus intermedius m.; FS: Femoral shaft; LT: Lesser trochanter; AL: Adductor longus m.; AB: Adductor brevis m.; AM: Adductor magnus m.; IB: Ischial bone.*

1.3.1 Anterior muscular compartment

The anterior muscular compartment consists of the sartorius, iliopsoas, and quadriceps femoris muscles.

The sartorius muscle (m.) originates from the anterior superior iliac spine (ASIS) and takes an oblique course across the anterior thigh before inserting on the proximal medial tibia in the pes anserinus. The muscle is innervated by the femoral n.[25]

The iliopsoas m. is formed by the psoas major m. and the iliacus m., as they join in the strong iliopsoas tendon that inserts on the lesser trochanter. The iliopsoas tendon is separated from the pubis and the hip joint capsule by the iliopectineal bursa. The psoas major m. originates from a complex attachment to the anterior surfaces and transverse processes of all five lumbar vertebrae. The psoas major m. is innervated by the ventral rami of the lumbar spinal nerves L1-L3. The iliacus m. originates from the iliac crest and the cranial 2/3 of the iliac fossa. The iliacus m. is innervated by branches of the femoral n.[25] A minor extrapelvic posterolateral component of the iliopsoas m. originates from the anterior inferior iliac spine (AIIS) and courses distally in close relation to the rectus femoris tendon to insert on the lesser trochanter.[26] This part of the muscle is in the following denoted the AIIS-originated iliopsoas m. (AIIS-IP; Figure 5B, p. 25).

The quadriceps m. consists of four parts; rectus femoris, vastus medialis, vastus intermedius and vastus lateralis. The rectus femoris m. originates from the AIIS and the superior part of the acetabulum from a common rectus femoris/AIIS-IP tendon. The rectus femoris m. is the only part of the quadriceps femoris m. that affects the hip joint. The vastus medialis m. originates from the proximal anteromedial femur, the vastus intermedius m. originates from the proximal anterior femur and the vastus lateralis m. originates from the proximal anterolateral femur. All four parts of the quadriceps m. insert on the proximal patella and are innervated by the femoral n.[25]

1.3.2 Medial muscular compartment

The medial muscular compartment consists of the gracilis, pectineus, adductor longus, adductor brevis, and adductor magnus muscles.

The gracilis m. arises from an aponeurosis from the pubic body, the pubic ramus and the adjoining part of the ischial ramus. It descends along the inner thigh and ends in a

rounded tendon that attaches to the upper part of the medial surface of the tibia. The muscle is innervated by the obturator n.[25]

The pectineus m. originates from the superior pubic ramus, runs along the medial border of the iliopsoas and inserts on the lesser trochanter just distal to the iliopsoas. The pectineus m. is innervated by the femoral n. and the accessory obturator n. when present. It can furthermore receive a branch from the obturator n.[25]

The adductor longus m. is the most superficial of the three adductor muscles. It originates by a tendon from the anterior aspect of the pubic body and inserts into the linea aspera on the middle third of the posterior femur. The adductor longus is innervated by the obturator n. [25]

The adductor brevis m. originates from the pubic body and inferior pubic ramus and courses distal and lateral deep to the pectineus and adductor longus before inserting on the posterior femur along the pectineal line and the proximal part of the linea aspera. The adductor brevis is innervated by the obturator n.[25]

The adductor magnus m. originates from the inferior pubic ramus, the ischial ramus and the ischial tuberosity, from where the muscle fibres fan out in their lateral and distal course towards the insertion on the linea aspera and the medial supracondylar line on the femur. The muscle is innervated by the obturator n. as well as by the tibial part of the sciatic n. – the latter innervating the medial (ischiocondylar) portion of the muscle. [25]

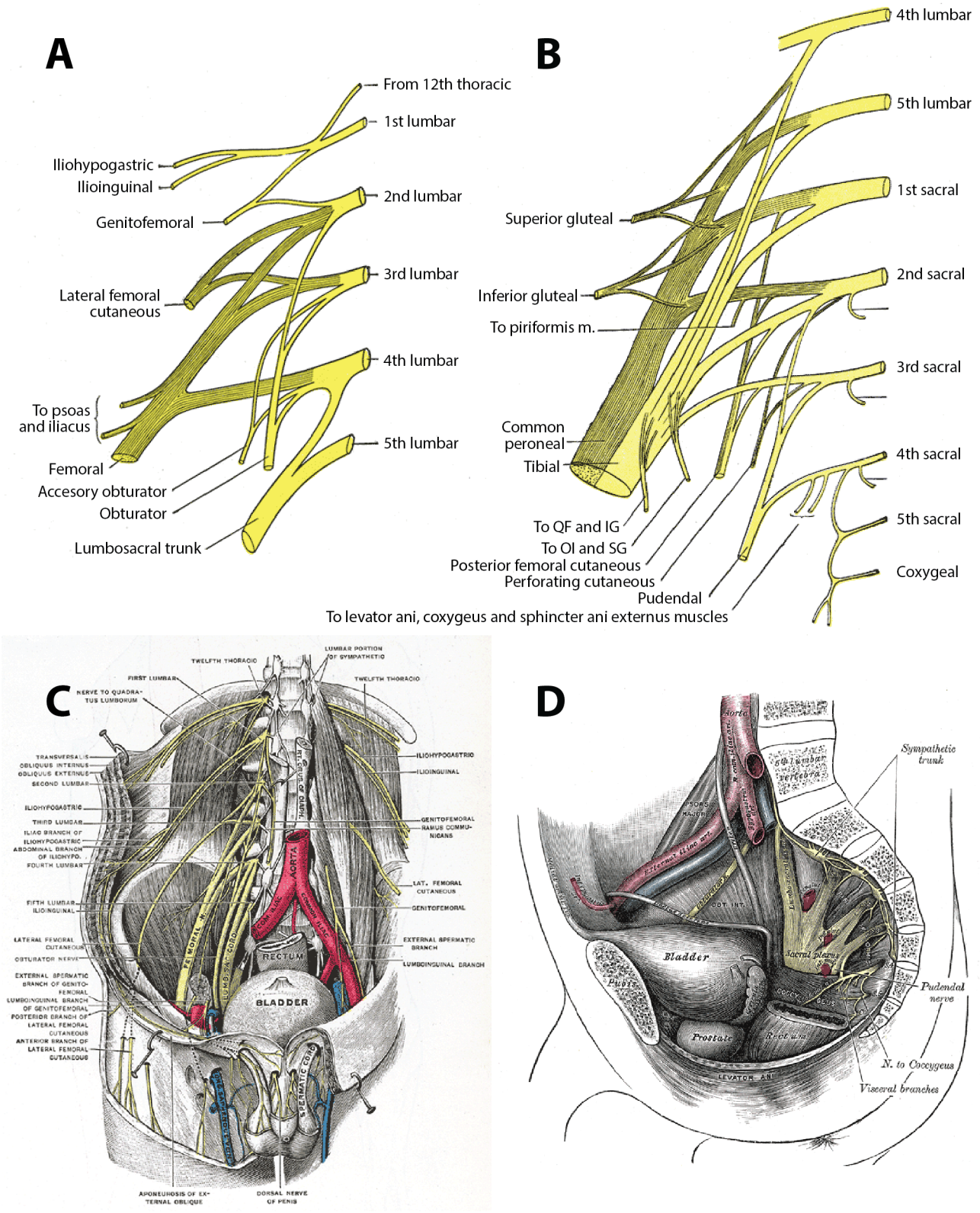

Figure 3. The lumbosacral plexus. ***A:*** *Schematic drawing of the lumbar plexus and associated peripheral nerves.* ***B:*** *Schematic drawing of the sacral (and pudendal) plexus and associated peripheral nerves.* ***C:*** *The lumbar plexus with the psoas major muscle (m.) dissected (left) and in situ inside the psoas major m. (right) anterior to the transverse processes of the lumbar vertebrae.* ***D:*** *The sacral plexus in situ on the posterior wall of the pelvis. Modified excerpt from Henry Grays Anatomy of the Human Body (1918).[24] QF: Quadratus femoris m.; IG: Inferior gemellus m.; OI: Obturator internus m.; SG: Superior gemellus m.*

1.3.3 Neural innervation of the hip

The innervation of the hip and lower extremity is derived from the lumbosacral plexus, that is formed by the ventral rami of the lumbar and sacral spinal nerves (Figure 3). The three major nerves from the lumbar plexus are the lateral femoral cutaneous, the femoral, and the obturator nerves. The nerves from the lumbar plexus mainly innervate the anterior parts of the hip and thigh including the anterior parts of the knee joint. The major nerve from the sacral plexus is the sciatic n. formed by the common peroneal component from the dorsal part of the sacral plexus and the tibial component from the ventral part of the sacral plexus. The nerves from the sacral plexus mainly innervate the posterior aspects of the hip and femur as well as the crus and foot.[25] The posterior parts of the knee joint is innervated by the obturator n. and the tibial component of the sciatic n. that form the popliteal plexus.[27,28]

The anterior section of the hip joint capsule is innervated by the femoral n. and the obturator n. – as well as the accessory obturator n. when present.[8,29] This section of the capsule contains both mechanoreceptors and nociceptive free nerve endings.[9,10] The posterior part of the hip joint capsule is innervated by the superior gluteal n., the n. to the quadratus femoris as well as branches directly from the sciatic n.[29] This section of the capsule contains practically no nociceptors and the nerves innervating this section are thought to be primarily involved in proprioception.[9,10]

Kampa et al. in a 2007 dissection study described a lateral sparsely innervated *"internervous safe zone"* between the areas innervated by the femoral and the superior gluteal nerves.[30] This finding has, however, not been supported by more recent histological studies by Haversath et al. and Gerhard et al.[9,10]

Dee in '69 published the results of his studies on the innervation of the hip joint – predominantly achieved by dissection of 37 cats supplemented by histological studies of excised tissue from five humans.[31] Dee – in contrast to the more recent studies by Haversath et al. and Gerhard et al.[9,10] – observed a predominant occurrence of nociceptors in the posterior and inferior parts of the hip joint capsule.[31] Unfortunately it is difficult, when assessing Dees article, to discern which results originate from human tissue and which originate from the feline studies. Furthermore, the results of the more recent studies

are probably of a higher validity as the authors had access to advanced techniques such as immunohistochemical markers of nociceptors and computer-assisted picture analysis.

The intracapsular structures containing neural end organs are the acetabular labrum, lig. teres and the transverse acetabular lig.[9,10,32,33] The innervation of these organs is not fully understood (see section 1.3.4.2), but the obturator n. and maybe the n. to the quadratus femoris have been reported to be involved.[8,11,33]

The skin covering the anterior and lateral hip areas is innervated by the iliohypogastric n. and the lateral femoral cutaneous n.[34] The most cranial part of the surgical incision for THA via the posterior approach is innervated by the superior cluneal nerves.[35]

1.3.4 Neural pathways to the hip

The femoral n., the obturator n. and the accessory obturator n. all arise from the lumbar plexus where they are formed by branches of the ventral rami of the lumbar nerves.[25] As these nerves are the targets of the nerve blocks investigated in this thesis, their course from the lumbar plexus to the hip joint will be described below.

1.3.4.1 Femoral nerve

The femoral n. is formed by contributions from the dorsal branches of the ventral rami of the second to fourth lumbar nerves. The nerve is formed in the posterior part of the psoas major m. where the major part of the lumbar plexus (from the anterior rami of L2-L4) is enclosed. The femoral n. traverses the psoas major m. during its descent towards the pelvis and emerges from the lateral edge of the muscle at the approximate level of the fifth lumbar or first sacral vertebrae. The nerve continues its distal course deep to the fascia iliaca and exits the pelvis deep to the inguinal lig. – lateral to the femoral artery.[25,36]

The hip articular branches of the femoral n. can leave the nerve both proximal and distal to the inguinal lig.[37] The branches either penetrate the iliopsoas m. or courses laterally and distally around the lateral margin of the muscle to return towards the hip taking a proximal course between the iliopsoas m. and the hip joint capsule.[29,37] The branches terminate in the anterolateral part of the capsule,[29,37] which it supplies with both nociception and mechanoreception.[9,10] In contrast to the above Wertheimer in his study

from ’52, did not find any *“direct branches from the femoral nerve or from its branches to the capsule”*.[8]

1.3.4.2 Obturator nerve

The obturator n. is formed by contributions from the ventral branches of the ventral rami of the second to fourth lumbar nerves. The obturator n. originates – like the femoral n. – from the lumbar plexus inside the psoas major m., but exits the muscle at the posteromedial aspect of the muscle at the approximate level of the fifth lumbar vertebrae. The nerve descends posterior to the common iliac vessels and continues in the angular space between the external iliac vein and the internal iliac artery, it courses over the obturator internus m. to leave the pelvis via the obturator canal. Near the external foramen of the obturator canal the nerve divides into an anterior and a posterior branch.[25,36]

According to Short et al. hip articular branches from the obturator n. branch off the obturator n. proximal to or within the obturator canal (62 %) and/or from the obturator n.’s posterior branch (69 %).[37] Birnbaum et al. and Wertheimer observed articular branches from both the anterior and posterior branches as well as the trunk of the obturator n.,[8,29] while Grays Anatomy claims that the hip articular branches leave the anterior branch of the obturator n.[25] The branches either course directly to the hip joint, or form a plexus that innervates the capsule with both proprioception and nociception.[9,10,37] According to Wertheimer and Rüdinger the obturator n. often sends twigs that penetrate into the acetabular notch – apparently to supply intraarticular innervation.[8,11] Alzaharani et al. suggest in their histological study of the acetabular labrum, that innervation of the labrum *“primarily comes from a branch of the nerve to the quadratus femoris as well as the obturator nerve.”* [33] The reference to this claim, however, is a histological study in Japanese by Hosokowa published in ‘64.[38] According to the English abstract of Hosokowas article, the neural innervation of the intracapsular structures have not been examined in the study, why the claim by Alzaharani et al. probably should be considered with some caution.

1.3.4.3 Accessory obturator nerve

The reported frequency of occurrence of the accessory obturator n. varies greatly in the literature - from 4 to 54 % of cadaver sides.[8,37] In a big study including 500 cadavers

Katritsis et al. found the presence of an accessory obturator n. in 13 % of cadaver sides.[39] When present, the accessory obturator n. is formed from the ventral branches of the ventral rami of the second to fourth lumbar nerves.[39] The distal course of the accessory obturator n. is parallel to the obturator n. along the posteromedial aspect of the psoas major m. The accessory obturator n. leaves the obturator n. to cross anterior to the superior pubic ramus and continue deep to the pectineus m. (sometimes making anastomoses with the obturator n.) to terminate in the hip joint capsule.[25,37,39]

1.4 Surgical techniques for total hip arthroplasty

Three different surgical approaches for THA are commonly used: The direct anterior approach,[40] the direct lateral approach,[41] and the posterior approach.[42] Each approach is associated with advantages as well as shortcomings, but no approach can claim superiority compared to the others.[43] The posterior approach is the most commonly used internationally and is also the procedure used in our clinical trial (Study II), why it will be reviewed in more detail below.[44]

Posterior THA can be performed in either general or spinal anaesthesia as well as in peripheral blockade of the lumbosacral plexus in special cases.[45,46] The patient is positioned in the lateral decubitus position and the extremity for surgery is draped so the limb can be moved freely. A surgical incision is initiated 5 cm distal to the greater trochanter and continued proximally to the tip of the greater trochanter where the incision is curved posteriorly and continued 6 cm towards the posterior superior iliac spine. The fascia lata is incised and the underlying gluteus maximus is split bluntly separating the muscular fibres. After identification and protection of the sciatic n. the short external rotators (obturator internus, and superior and inferior gemellus muscles) and the piriformis m. are tenotomised at their insertion onto the greater trochanter exposing the posterior hip joint capsule. The capsule is incised and the head of femur is posteriorly dislocated to allow a femoral neck osteotomy. Following removal of the excised head and neck of femur the labrum, lig. teres and the transverse acetabular lig. are excised and the acetabulum is prepared for embedding by reaming and lavage. The acetabular component of the prosthesis is embedded and the hip is flexed, internally rotated and slightly adducted to expose the proximal femur. The femur is prepared for insertion by reaming and lavage and the femoral component of the prosthesis is inserted into the proximal

transsected end of the femur. The prosthetic joint is now aligned and the capsule is closed. The short external rotators are reinserted onto the proximal femur followed by skin closure and bandaging.[43,47]

1.5 Postoperative management

Contemporary postoperative management after THA follows the fast-track principles.[48] Fast-tracking – also known as enhanced recovery – has succeeded in reducing postoperative morbidity and mortality during the last decades, shortening hospital stay and time until complete return to normal function as well as increasing patient satisfaction after surgery.[49] The mean to these aims has been a multimodal approach in the pre-, intra- and postoperative phases that include patient information, reduction of surgical stress, pain relief, fluid therapy and early ambulation.[3] Early ambulation is an important element of enhanced recovery, but ambulation on the day of surgery is conditioned by effective pain control without opioid-induced dizziness or motor blockade of the postural muscles.[3,50,51]

1.6 Postoperative pain

The mean postoperative pain following THA is only mild, but a substantial subpopulation of the patients experience moderate to severe pain during the first postoperative days.[52-54] In a large Danish questionnaire study 37 % of patients reported moderate or severe acute pain following the intervention; this was associated to an increased risk of developing chronic hip pain.[2]

Postoperative pain following THA can theoretically originate from the surgical incision through the cutis and subcutis, from the manipulation and incision of the muscles surrounding the joint, from the incision through and manipulation of the hip joint capsule, from the excision of intraarticular connective tissue, and from the reaming and implantation into the hip bone and femur. The neural innervation of these structures is summarized in Table 1.

Structure		Innervation
Cutis and subcutis		Lateral femoral cutaneous n.[34] Iliohypogastric n.[34] Superior cluneal nerves[35] Probably middle cutaneal nerves and posterior femoral cutaneous n.
Fascia lata		Probably same as overlying cutis and subcutaneous tissue.
Gluteus maximus m.		Inferior gluteal n.[25]
Obturator internus m		N. to obturator internus[25]
Gemellus superior m.		N. to obturator internus[25]
Gemellus inferior m.		N. to quadratus femoris[25]
Piriformis m.		Branches from spinal nerves S1 and S2.[25]
Hip joint capsule	Anterior	Femoral n.[29] Obturator n.[8,29]
	Posterior (no nociception)	Superior gluteal n.[9,29] N. to quadratus femoris[9,29] Sciatic n.[9,29]
Intraarticular connective tissue		Obturator n.[8,33] N. to quadratus femoris*[33]
Acetabulum		Obturator n. [55,56] Femoral n. [55,56] Sciatic n. (tibial component) [55,56]
Head and neck of femur		Obturator n. [55,56] Femoral n. [55,56] Sciatic n. (tibial component) [55,56]

*Table 1. Neural innervation of the structures affected by total hip arthroplasty through the posterior approach. *Alzaharani et al.[33] claims that "labral innervation primarily comes from a branch of the nerve to the quadratus femoris as well as the obturator nerve." Valid references to this claim have, however, not been specified (see section 1.3.4.2).*

1.7 Postoperative analgesia

Traditional pain management strategies after THA include both systemic analgesia, central or peripheral nerve blocks as well as local infiltration analgesia (LIA).[57-60] The systemic analgesia regimens often include paracetamol, nonsteroidal anti-inflammatory drugs

(NSAID), opioids and sometimes gabapentinoids.[57,61] Oftentimes, systemic analgesia is insufficient to provide postoperative analgesia after THA primarily because of intolerable side effects of opioids.[59,60]

Previously epidural analgesia has been employed for postoperative analgesia after THA, as an epidural provides superior pain control compared to a regimen based on systemic opioids.[62,63] However, epidural analgesia has numerous serious side effects including arterial hypotension and urinary retention compared to analgesia regimens based on systemic opioids or peripheral regional analgesia.[64,65] Furthermore, the prolonged motor blockade following epidural analgesia impedes early ambulation.[66]

LIA is gaining popularity for postoperative analgesia after total knee and hip arthroplasty despite very limited – or absent – evidence of effect.[67,68] A recent systematic review concluded that *"LIA* [after THA] *provided no additional analgesic effect when combined with a multimodal analgesic regimen consisting of acetaminophen, celecoxib, and gabapentin."* This finding was in part due to the relative low average pain scores in both groups.[69] The role of LIA in the subgroup of patients with moderate to severe postoperative pain after THA remains to be examined.

Postoperative analgesia based on peripheral nerve blocks is described in the following section.

1.8 Peripheral nerve blocks

Peripheral nerve blocks with potential to provide analgesia after THA are reviewed below.

1.8.1 Lumbar plexus block

The aim of a lumbar plexus block (LPB) is to anaesthetize the femoral, lateral femoral cutaneous and obturator nerves by targeting these nerves inside the intramuscular compartment between the major anterior lamina and the minor posterior lamina of the psoas major m. (known as the psoas compartment). Even though the iliohypogastric and ilioinguinal nerves also originate from the anatomical lumbar plexus (L1),[70] a LPB will not anesthetize these two nerves as they are not contained inside the psoas compartment.[71] A LPB is a deep peripheral nerve block adjacent to the neuraxis and is as such associated

with potental serious complications. It is only employed by expert regional anaesthesiologists.[72]

Multiple approaches exist to block the lumbar plexus – both with[73-77] and without[78-80] ultrasound guidance. The relatively deep target (7-8 cm) combined with the proximity to the lumbar vertebrae complicates ultrasonographic visualisation of the target lumbar plexus.[71,75]

Both single-injection and continuous LBP provides pain relief and reduces opioid consumption after THA.[79,81] Nevertheless, the LPB carries significant risks of adverse events and serious complications that limits the applicability of the LPB: LPB carries a risk of retroperitoneal hematoma in patients with coagulopathy, and it is therefore subject to the same contraindications as central nerve blocks regarding therapeutic anticoagulation;[82,83] LPB can cause spread of local anaesthetic to the epidural space causing a central bilateral nerve block with the accompanying risk of arterial hypotension and urinary retention;[79,84] A French survey found 5 serious adverse events (cardiac arrest, respiratory failure, seizures and death) caused by epidural or intrathecal diffusion of local anaesthetics in 394 cases of posterior LPB (1.3 %).[85]

Given the risk of severe adverse events and the failure of a LPB to provide superior analgesia after THA when compared to a continuous fascia iliaca compartment block (FICB – see below),[13] a LPB for postoperative pain after THA should probably be a second-choice exclusively performed by experts on special indications.

1.8.2 Lateral quadratus lumborum block / transversalis fascia plane block

Both the lateral quadratus lumborum block (termed QLB1) and the transversalis fascia plane block (TFPB) target the iliohypogastric, and the ilioinguinal nerves (and in some cases also the subcostal nerve) by injecting local anaesthetic in the corner of the pararenal fat compartment between the transversus abdominis aponeurosis and the lateral margin of the quadratus lumborum m.[86-88] This results in cutaneous anaesthesia of the lateral hip region which is the region of surgical incision.[34] Recent case studies report good postoperative pain relief from QLB1 after THA, but the effect has not been confirmed in a blinded randomized clinical trial.[89-91]

1.8.3 Fascia iliaca compartment block

The aim of the FICB is to induce anaesthesia of both the femoral and the lateral femoral cutaneous nerves by injection of local anaesthetic deep to the iliac fascia.[92,93]

The FICB has been shown to reduce morphine consumption after THA compared to no block.[94] Furthermore, it can be claimed that the FICB has a safety advantage over the FNB, as the target of injection is further away from the femoral n.[56,95] Despite the ability of the FICB to provide pain relief after THA, the accompanying weakness of the quadriceps femoris m. (due to anaesthesia of the femoral n.) impedes enhanced recovery and early ambulation.

1.8.4 Femoral nerve block

The FNB is a classical basic nerve block, with a potential effect on pain after THA.[96] Compared to the FICB the FNB is associated with an increased theoretical risk of nerve injury, since the target of injection is in close proximity to the main trunk of the femoral n. Furthermore, the inherent motor blockade of the quadratus femoris m.,[97] increases the risk of fall and impairs the patients ability to ambulate.[12,13] Thus, as with the FICB, the FNB is not indicated for patients scheduled for early ambulation after THA.

1.8.5 Lateral femoral cutaneous nerve block

The lateral femoral cutaneous nerve is a purely sensory branch of the lumbar plexus that innervates the skin covering the lateral thigh – including parts of the surgical incision from the posterior approach for THA.[25,34,98] In contrast to the above-mentioned nerve blocks, a selective lateral femoral cutaneous n. block (LFCB) do not cause motor-blockade. However, the effect of a standalone LFCB on pain after THA has only been assessed in two trials: A randomized clinical trial found no difference in pain-related outcomes after THA in subjects who had a LFCB compared to subjects who had a sham block.[99] Unfortunately the nerve blocks were not tested, which makes it impossible to estimate the frequency of missed blocks. In patients with moderate to severe pain after THA (visual analogue scale (VAS) > 4) the mean [with 95 % confidence interval (95CI)] effect on pain measured on a VAS was just 17 [4-31] mm.[100]

A LFCB covers part of the surgical incision for THA via the posterior approach in 8 of 20 subjects (40 %),[34] but appears only to have a limited effect on postoperative pain. as a

standalone nerve block. Further randomized blinded clinical trials are needed to examine the effect of a LFCB combined with additional nerve blocks to provide analgesia of the surgical incision after hip surgery.

1.8.6 Obturator nerve block

Branches to the hip joint from the obturator n. originate from the anterior branch or the posterior branch or the main trunk.[8,29,37] Furthermore, the accessory obturator n. supplies innervation of the hip joint in approximately 13 % of cases as described above (section 1.3.4.3). It is therefore essential, that a proximal approach to an ONB is used, if one aims to anaesthetize the innervation of the hip joint from the obturator n. A proximal injection of 15 mL between the pectineus and external obturator muscles (Figure 2C) has been shown to spread to all branches from the obturator n. as well as the accessory obturator n. when present.[101] It is unknown, whether a standalone ONB reduces postoperative pain after THA.[56,102]

1.8.7 Combinations of cutaneous nerve blocks

The area of surgical incision for the posterior approach to THA is innervated by multiple cutaneous nerves.[35] A recent volunteer trial from our research group has shown that a transversalis fascia plane block combined with a LFCB only offers partial coverage of the incision for posterior THA in 14 of 20 subjects (70 %) - in the remaining 6 subjects the incision was not covered at all.[34] The addition of a novel nerve block that anaesthetizes the superior cluneal nerves provided complete coverage of the surgical incision for posterior THA in 8 of 20 subjects (40 %), while 9 (45 %) only had partial coverage and 3 (15 %) had no coverage at all.[35] It remains to be clarified which nerves innervate the remaining part of the field of surgical incision needed to provide complete anaesthesia after posterior THA. The middle cluneal nerves and posterior femoral cutaneous n. are probably contributing substantially to the innervation of this region.

Clinical trials are warranted to elucidate the relevant clinical role of cutaneous nerve blocks after THA.

1.9 Research questions

Postoperative analgesia after THA with systemic multimodal analgesia and regional anaesthesia has previously been investigated with respect to LPB, FICB and FNB. However, these nerve block techniques generate motor blockade of the postural musculature which impedes ambulation and increases the risk of fall. The aim of the present research project was to investigate methods for postoperative analgesia after THA with no or limited impact on the ability to ambulate.

The sensory branches from the femoral n. to the hip joint either pierce the iliopsoas m. or wind around its lateral border towards the joint capsule.[29,37] An injection of local anaesthetic in the anatomical plane between the iliopsoas m. and the iliofemoral lig. of the hip joint capsule (Figure 2B) was hypothetized to selectively anaesthetize the sensory articular nerve branches from the femoral n. without affecting any motor branches.

As described above, the obturator n. innervates significant parts of the hip joint (section 1.3.4.2), but the effect of an ONB on postoperative pain after THA has not been sufficiently examined (section 1.8.6). Even though the obturator n. innervates the majority of the hip adductor muscles, a study from our group has shown, that patients can ambulate after total knee arthroplasty despite an active ONB.[5]

The above considerations lead to the following three research questions:

1.9.1 Research question 1

Does the injectate spread selectively to all sensory hip articular branches of the femoral n. by injection between the fascia of the iliopsoas m. and the iliofemoral lig.?

1.9.2 Research question 2

Does a proximal ONB decrease opioid consumption after THA – and does it impair postoperative ambulation compared to a sham block?

1.9.3 Research question 3

Does an IPB affect muscle strength of the quadriceps m. due to spread to motor branches of the femoral n.?

2 - Aims and hypotheses

2.1 Study I

In the first study we aimed to assess the spread of dye injected in the iliopsoas plane between the iliopsoas m. and the iliofemoral lig. in cadavers.

The hypothesis was that 5 mL of dye injected in the iliopsoas plane would spread to all hip articular sensory branches of the femoral n. without spreading to any motor branches.

2.2 Study II

In the second study we aimed to investigate the effect of a proximal ONB on the postoperative consumption of opioids after THA performed with the posterior approach in patients.

The hypothesis was that an ONB would reduce the postoperative opioid consumption compared to placebo.

2.3 Study III

In the third study we aimed to assess the effect of an IPB on the muscle strength of the quadriceps femoris m. and to track the spread of injectate using magnetic resonance imaging (MRI) in volunteers.

The hypothesis was that the IPB would have no effect on the muscle strength of the quadriceps femoris m. and that the injectate would spread exhaustively and exclusively inside the iliopsoas plane.

3 - Materials and Methods

The materials and methods section refer to the materials and methods sections of the attached Articles I-III (p. 57).

3.1 Methodological considerations

3.1.1 Development of the iliopsoas plane block

The method for the IPB was developed after studying relevant literature[8,9,11,29,33] and examining embalmed dissected cadavers at the Department of Anatomy, Faculty of Health, Aarhus University. Based on these preliminary studies we generated the research idea, that an injection of a relatively small volume in the iliopsoas plane – the potential space between the iliopsoas m. and the iliofemoral lig. – would spread exclusively to the hip articular sensory branches of the femoral n. Since the IPB is an interfacial plane block a certain volume of injectate is needed to secure spread to all relevant nerve branches.[103] However, after having performed test injections on cadavers and volunteers we settled on injecting 5 mL, as larger volumes tended to cause spread beyond the iliopsoas plane.

During development of the IPB as well as in Study I we used a sagittal orientation of the transducer and a needle insertion just distal to the transducer with an in-plane advancement of the nerve block needle (Figure 4). Based on the results of Study I we altered the method for Study III to use a transverse orientation of the transducer (Figure 5A) as discussed in section 3.1.4.

3.1.2 Study I

To answer the first research question (section 1.9.1) we performed a cadaver study.[104-106] A cadaver study offers the opportunity of assessing the spread of injectate inside the human body with a higher degree of detail and resolution compared to MRI imaging of living humans. Due to the small size of the target hip articular sensory branches of the femoral n. they would not be visible with neither computed tomography nor MRI. Furthermore, a cadaver study is a suitable first step of assessing the patterns of spread of the injectate with a new nerve block technique for safety reasons.

3.1.3 Study II

The second research question (section 1.9.2) concerned postoperative pain, which mandated a clinical trial. The high efficacy of spread of injectate to all hip articular branches from the obturator n. with the proximal sub-pectineal ONB (Figure 6) had previously been established in cadavers.[101] Opioid consumption was selected as primary outcome, as it is a well-established surrogate endpoint for postoperative pain in clinical trials.[5,107-109]

A secondary endpoint in Study II was the subjects' ability to ambulate on the day of surgery. In previous trials the cumulated ambulation score (CAS) had been used,[5,110,111] but originally the CAS was not developed to assess early ambulation (on the day of surgery).[112,113] In cooperation with Lone Ramer Mikkelsen, a physiotherapist and senior researcher at the Elective Surgery Centre, I drafted a new ambulation score for assessment of the ability to early ambulation after major lower limb surgery. After consulting physiotherapists specialized in early ambulation after THA, as well as senior researcher and physiotherapist Morten Tange Kristensen, who is one of the originators of CAS, we developed the ambulation score used in Study II. The design of the new score is similar to CAS, but it employs exercises that are more relevant for assessment of the ability of early ambulation after prosthetic hip surgery. The manual for the ambulation test is presented in Appendix 4 (p. 95).

3.1.4 Study III

The answer to the third research question (section 1.9.3) was designed as a randomized volunteer trial. A volunteer trial allowed meticulous testing of the motor effect of the IPB, and thereby pre-clinical assessment of safety (ie. risk of fall) and interference with ability of ambulation. The spread of injected local anesthetic with added contrast was assessed with MRI. The hypothesis was that an IPB would not impair maximal isometric force of the quadriceps femoris m. Consequently, the study was designed as a non-inferiority trial.

Study I showed that the local anesthetic was sometimes unintentionally injected in the iliopectineal bursa when the transducer was oriented sagitally. In cadavers, injection in the iliopectineal bursa was associated with spread of injectate to the motor branches of the femoral n. For the purpose of Study III, we modified the orientation of the transducer to

transverse (Figure 5), to facilitate injection lateral to the iliopsoas tendon in order to avoid injections in the iliopectineal bursa.

3.2 Study designs and overview

	Study I	Study II	Study III
Design	Observational cadaveric study	Randomized triple-blinded controlled clinical trial	Randomized double-blinded controlled paired volunteer trial
No. of groups	1	2 (independent)	2 (paired)
Subjects	15 cadaver sides (from 8 cadavers)	60 patients	20 volunteers
Intervention	IP injection	ONB vs. sham	IPB vs. sham
Outcomes	Patterns of spread of injectate *postmortem*	Opioid consumption Ability to ambulate Pain and nausea	Muscle strength Patterns of spread of injectate *in vivo*
Publication	Article I (p. 58)	Article II (p. 64)	Article III (p. 70)

Table 2. Overview of study design, interventions and selected outcome parameters. IP: Iliopsoas Plane; IPB: Iliopsoas Plane Block; ONB: Obturator Nerve Block.

3.3 Ethics

3.3.1 Study I

The cadavers were donated to the Department of Anatomy of the Medical University of Innsbruck for scientific purposes. According to Austrian and Tyrolean law ethical approval was not requested for individual studies.

3.3.2 Study II and III

Studies II and III were conducted in accordance with the Declaration of Helsinki[114] and the EU-directive on good clinical practice (GCP). Adherence to the latter was monitored by the GCP unit at Aalborg and Aarhus University Hospitals. The trials were approved by the Ethics Committee of the Central Denmark Region, the Danish Medicines Agency, and the Danish Data Protection Agency. Both trials were registered prospectively in the EudraCT

database. In addition, Study II was registered in the ClinicalTrials.gov database. The registrations were carried out and approved prior to starting screening for eligibility.

3.4 Study participants

3.4.1 Study II

For the randomized clinical trial we included patients aged ≥ 18 years with an American Society of Anesthesiologists physical status classification score (ASA) of I-III who were scheduled for THA in spinal anaesthesia. Exclusion criteria were inability to cooperate or communicate in Danish, anticipated discharge from the hospital on the day of surgery, neuropathy in the lower extremities, contraindications to NSAID or dexamethasone, chronic pain treated with opioids, pregnancy, allergy towards the investigational drugs, or current treatment with amiodarone, verapamil or corticosteroids.

3.4.2 Study III

For the randomized volunteer trial, we recruited healthy men and women aged ≥ 18 years with ASA I-II. Exclusion criteria were inability to cooperate or communicate in Danish, neuropathy in the lower extremities, chronic pain treated with opioids, weekly alcohol-consumption ≥ 14 units for females and ≥ 21 units for males, obesity (body mass index > 25 kg m^{-2}), claustrophobia, pregnancy, allergy towards the investigational drugs and daily consumption of medicine except oral contraceptives.

3.5 Interventions

3.5.1 Iliopsoas plane block

In Study I and III we examined the novel IPB. The aim of the IPB was to inject local anaesthetics in the iliopsoas plane – a potential interfascial space between the fascia of the iliopsoas m. and the iliofemoral lig. as well as between the minor posterolateral part of the iliopsoas m. originating from the AIIS and the major anteromedial part of the iliopsoas m. of supra- and intrapelvic origin. The iliopsoas plane was identified ultrasonographically using a curvilinear transducer (Figure 4A,C). In Study I a sagittal orientation of the transducer was used and the needle was inserted distal to the transducer and advanced in-plane (Figure 4C-D). In Study III we used a transverse orientation of the transducer to

secure injection in the iliopsoas plane lateral to the iliopectineal bursa. The needle was inserted lateral to the transducer and advanced in-plane (Figure 5A).

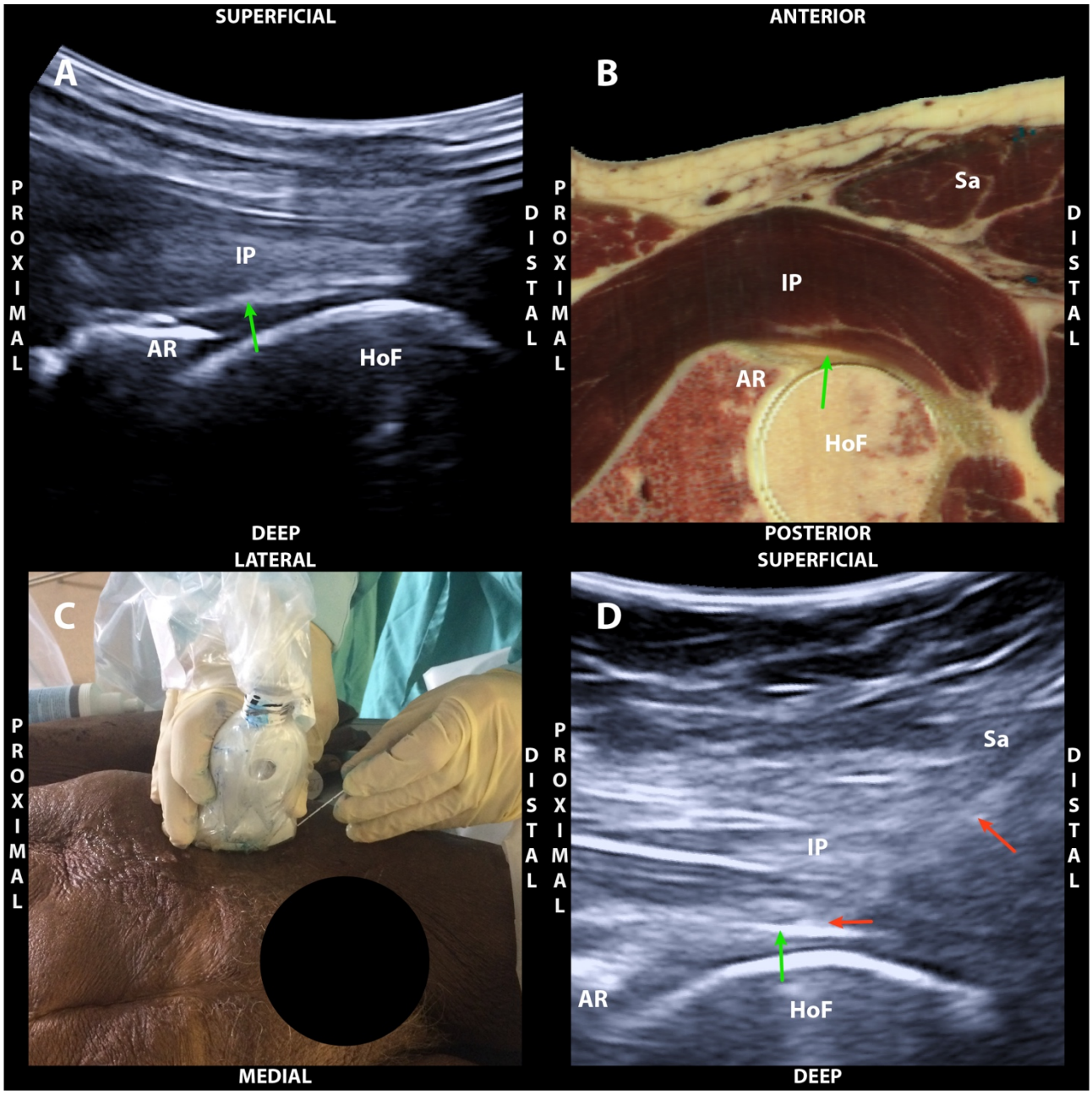

Figure 4. Iliopsoas Plane Block (subject's left side) as used in Study I. ***A:*** *Sagital ultrasonogram identifying the iliopsoas plane between the iliopsoas muscle (IP) and the iliofemoral ligament (green arrow). The underlying head of femur (HoF) diving below the acetabular rim (AR) is an important ultrasonographic landmark.* ***B:*** *Sagittal section corresponding to A. The sartorius muscle (Sa) overlays the IP.* ***C:*** *Ultrasound scan corresponding to A. The nerve block needle is inserted in-plane with a steep angle just distal to the transducer.* ***D:*** *Ultrasonogram like A, but with needle (red arrows) inserted until the tip is located in the iliopsoas plane. Modified excerpt from Article I.*

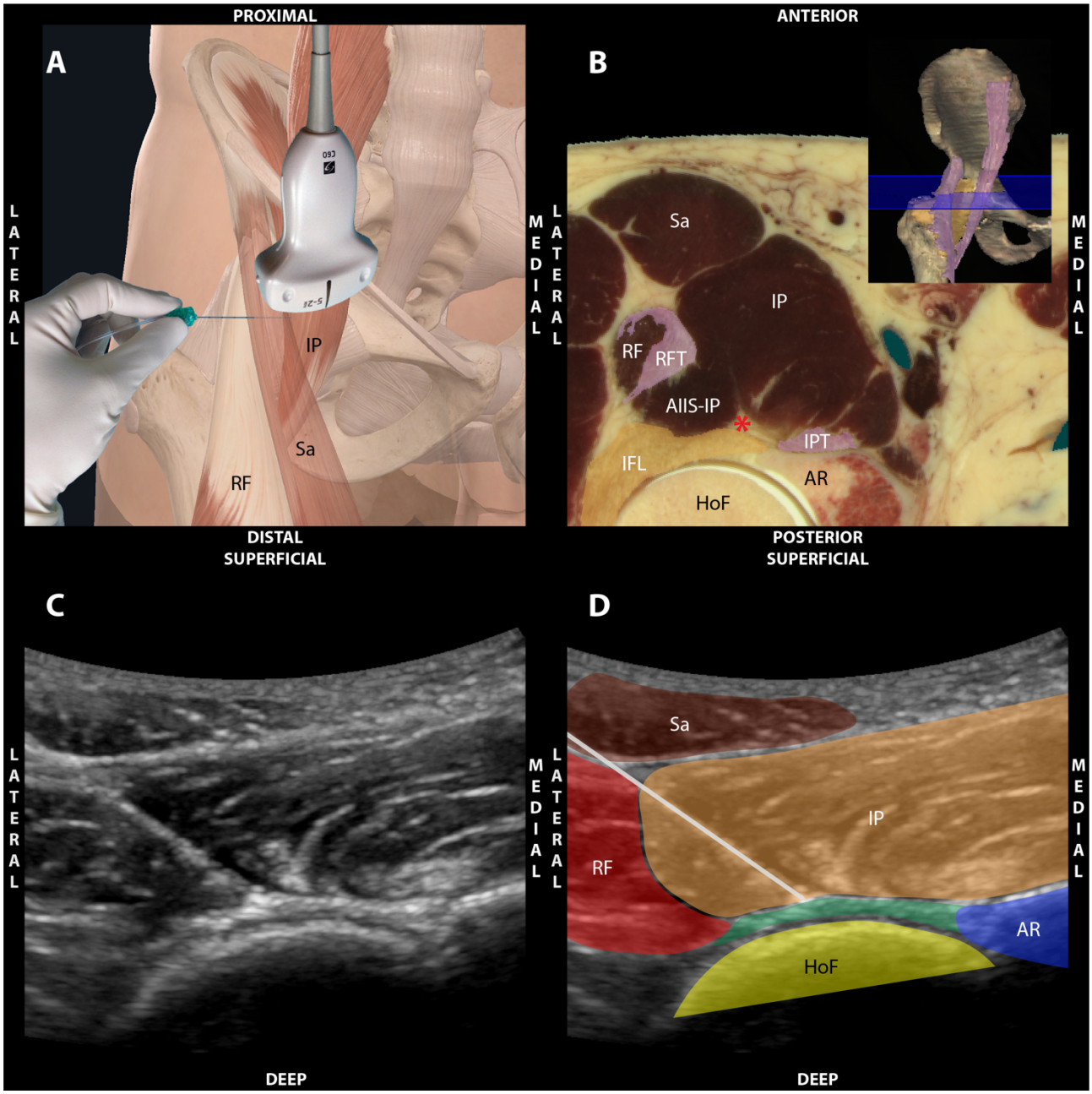

Figure 5. Iliopsoas Plane Block (subject's right side) as used in Study III. ***A:*** *Positioning of the probe and insertion of the needle for the iliopsoas plane block. The needle trajectory pierces the sartorius (Sa) and iliopsoas (IP) muscles. The target is deep to the IP medial to the rectus femoris muscle (RF). Modified excerpt from Complete Anatomy '19 with permission from 3D4Medical (www.3d4medical.com).* ***B:*** *Transverse section of the target area (red asterisk) between the IP and the iliofemoral ligament (IFL; yellow). The deeper lying head of femur (HoF) and acetabular rim (AR) are important ultrasonographic landmarks. The lateral spread of injectate is limited by the rectus femoris muscle (RF), its tendon (RFT; purple) and the part of the iliopsoas muscle that origins from the anterior inferior iliac spine (AIIS-IP). The medial spread is limited by the iliopsoas tendon (IPT; purple) and the underlying iliopectineal bursa. Insert showing level of section as well as IFL (yellow), IPT (right, purple), and the RFT (left, purple). Modified excerpt from VH Dissector with permission from Touch of Life Technologies Inc. (www.toltech.net). Built on real anatomy from the National Library of Medicines Visible Human Project.* ***C:*** *Ultrasonogram with needle insertion for iliopsoas plane block.* ***D:*** *Same as C with explanatory labels: The head of femur (yellow) dives deep to the acetabular rim (blue). The nerve block needle (white) pierces the sartorius (brown) and iliopsoas (orange) muscles until the tip is superficial to the iliofemoral ligament (green) and medial to the rectus femoris muscle (red). Modified excerpt from Article III.*

3.5.2 Obturator nerve block

In Study II we examined a proximal/sub-pectineal ONB approach. [5,101,115] With the subject supine a linear ultrasound transducer was placed in the inguinal groove with an approximately transverse orientation. The femoral artery and vein were identified, and while the tail of the probe was tilted distally the pectineus and adductor longus and brevis muscles were identified medial to the femoral artery and vein. A nerve block needle was inserted in-plane from the lateral end of the transducer, and advanced until the tip of the needle was in the interfacial plane between the fascia of the pectineus m. and the fascia of the obturator externus m. (Figure 6) At this location 15 mL of project medication was injected and spread between the two muscles was observed.

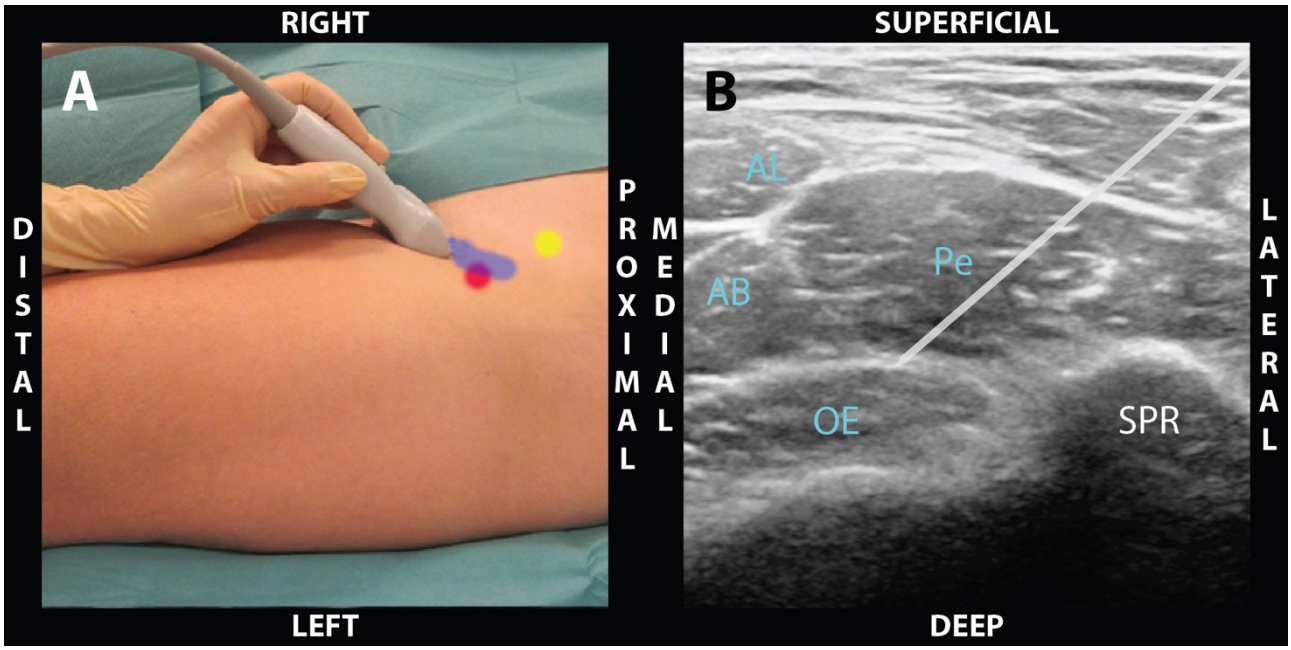

Figure 6. Sub-pectineal obturator nerve block (subject's left side) as used in Study II. ***A:*** *The transducer is oriented in the transverse plane, placed in the inguinal groove (purple line) distal to the anterior superior iliac spine (yellow dot) and tilted approximately 45° (tail in distal direction) to visualize the target (B). The needle is inserted lateral to the transducer (red dot) and advanced in-plane. Modified excerpt from Runge et al.[5]* ***B:*** *Ultrasonogram corresponding to A. The needle (white line) is advanced through the pectineus muscle (Pe) which is seen superficial to its origin from the superior pubic ramus (SPR). The target of injection is between the Pe and the obturator externus muscle (OE) (Figure 2C). The adductor longus and brevis muscles (AL resp. AB) are important landmarks seen medial to the Pe.*

3.5.3 Study I

Needle insertion for an IPB was performed in 15 embalmed cadaver sides as described above (section 3.5.1) using a sagittal orientation of the transducer. When the tip of the needle was in the target iliopsoas plane 5 mL of methylene blue was injected and spread was observed between the iliopsoas m. and the iliofemoral lig. All injections were performed by an experienced regional anaesthesiologist (Thomas Fichtner Bendtsen).

After performance of injections the cadavers were dissected and the course of the hip articular sensory branches of the femoral n. as well as the spread of the injected dye was meticulously assessed by two reputed anatomists (Romed Hörmann and Bernhard Moriggl).

3.5.4 Study II

Sixty patients for THA completed the randomized clinical trial. The subjects had oral administration of analgesia with paracetamol (acetaminophen) and ibuprofen two hours before surgery complying with standard care. Spinal anaesthesia was carried out with 10 mg bupivacaine. Dexamethasone 8 mg intravenous (IV) was administered as prophylaxis against postoperative nausea and vomiting after which THA was performed using the posterior approach (section 1.4).

Within 1 hour after surgery all subjects were randomly allocated to active or placebo ONB as described above (section 3.5.2) with either 15 mL bupivacaine-epinephrine (5 mg/mL + 5 µg/mL) or normal saline (placebo). A portable medical infusion pump was connected to an IV catheter for patient-controlled analgesia with bolus doses of IV morphine (0.05 mg/kg). If subjects experienced intolerable morphine related side effects oral oxycodone (5 mg) was administered.

Five hours after surgery the patients ambulated assisted by physiotherapists, who were blinded to the random group allocation. The physiotherapists used a standardized ambulation test for assessment of the ability to ambulate as well as the muscular control of the operated leg (Appendix 4, p. 95).

Intensity of pain and nausea was assessed at regular intervals during the first 24 postoperative hours by anaesthesiologists and physiotherapists, who were blinded to the random group allocation.

3.5.5 Study III

Twenty healthy volunteers were recruited for the trial. Baseline measurements of isometric force of knee extension (innervated by the femoral n.) and hip adduction (mainly innervated by the obturator n.) were performed bilaterally. Sensitivity on the lateral thigh (innervated by the lateral femoral cutaneous n.) as well as proximal to the patella (innervated by the femoral n.) was assessed.

The volunteers were positioned supine and IV access as well as monitoring of vital parameters was established. An IPB was performed bilaterally as described above (section 3.5.1) with blinded random allocation of active vs. placebo IPB and using a transverse orientation of the transducer. According to the randomization lidocaine-epinephrine (18 mg/mL + 5 µg/mL) was injected either on the right or the left side. Placebo (isotonic saline) was injected on the contralateral side. Additionally, both injections contained diluted gadoteric acid (1,75 mg/mL) – an MRI contrast agent. All injections were made by an experienced regional anaesthesiologist (Thomas Fichtner Bendtsen).

The volunteers were transferred to an MRI scanner and both T1 and T2-weighted MRI sequences were performed in order to be able to assess spread of the injectate.

Assessment of isometric force and sensibility was repeated 1 hour after completion of IPB.

3.6 Outcome parameters

3.6.1 Study I

The primary outcome parameter of Study I was a binary estimate of the frequency of staining of all hip articular sensory branches of the femoral n. after injection of 5 mL methylene blue in the iliopsoas plane.

Secondary outcome parameters were (a) a binary estimate of the frequency of staining of one or more motor branches from the femoral n., (b) a binary estimate of the frequency of sonographic visibility of the iliopsoas m. as well as the iliofemoral lig., (c) the mean vertical distance from the skin surface to the target iliopsoas plane, (d) the mean vertical distance on the skin surface from the needle insertion point to the transverse plane intersecting the ASIS, (e) the mean horizontal distance on the skin surface from the needle insertion point to the sagittal plane intersecting the ASIS, (f) the mean length of the needle trajectory, (g) a binary estimate of the frequency of injection in the iliopectineal bursa.

3.6.2 Study II

The primary outcome of Study II was the mean cumulated opioid consumption – converted to oral morphine equivalents (OME) – during the first 12 postoperative hours after THA.

Secondary outcome parameters were (a) mean cumulated opioid consumption (as OME) during 12-18 hours after surgery, (b) mean time until the first opioid request, (c) median pain score (NRS) at rest and during passive hip flexion at 1, 2, 5, 7 and 24 hours after surgery, (d) median nausea score (NRS) at the same time points, (e) frequency of episodes of vomiting and cumulated consumption of ondansetron as well as droperidol during the first 18 postoperative hours, (f) mean time interval (minutes) from end-of-surgery to discharge from the post-anaesthesia care unit, (g) mean time interval (hours) from surgery to discharge from hospital, (h) mean duration of spinal anaesthesia after surgery (minutes), (i) quality of sleep during the first night after surgery assessed using a 3-point ordinal scale, (j) median ambulation score according to the standardized ambulation test (Appendix 4, p. 95) performed 5 hours after surgery, and (k) median level of muscle control of the operated leg assessed by a physiotherapist during the ambulation test.

3.6.3 Study III

The primary outcome parameter of Study III was the mean difference of maximal isometric force of knee extension from baseline to one hour after nerve block.

Secondary outcome parameters were (a) mean difference of maximal isometric force of hip adduction from baseline to one hour after nerve block, (b) mean difference of maximal isometric force of knee extension from baseline to one hour after nerve block performance in the blocked leg compared to the non-blocked leg, (c) mean difference of maximal isometric force of hip adduction from baseline to one hour after nerve block performance in the blocked leg compared to the non-blocked leg, (d) frequency of normal sensitivity of pinprick in the dermatomal skin territory of the femoral n. one hour after nerve block, (e) frequency of normal sensitivity of pinprick in the dermatomal skin territory of the lateral femoral cutaneous n. one hour after nerve block, (f) frequency of spread of injected MRI contrast in the iliopsoas plane, (g) frequency of spread of injected MRI contrast between the iliopsoas m. and the iliofemoral lig., (h) frequency of spread of injected MRI contrast to the area of the obturator n. between the pectineus and the obturator externus muscles, (i) frequency of spread of injected MRI contrast to the area of the femoral n. on the superficial aspects of the iliopsoas m., (j) frequency of intraarticular spread of injected MRI contrast, (k) frequency of spread of the injected MRI contrast to the posterior aspect of the hip joint

between the greater and lesser trochanter and (l) frequency of spread of the injected MRI contrast to the iliopectineal bursa.

3.7 Randomization and blinding

3.7.1 Study I

No randomization was applied in Study I. The anatomists who performed the dissections were not present when the injections were carried out, and the regional anesthetist who carried out the injections did not attend the dissections or the assessment of spread of injectate.

3.7.2 Study II

Subjects were block randomized (in blocks of six with an 1:1-ratio) in order to receive either an active ONB or a sham ONB (placebo). Randomization was performed by the Hospital Pharmacy of Aarhus University Hospital using permuted block randomization.[116] The pharmacy delivered the project medication in blinded vials leaving investigators, staff and subjects blinded to the random group allocation. Statistical inference was made prior to unblinding the groups.

3.7.3 Study III

Subjects were randomized (in a 1:1-ratio) to receive an active IPB either on the left or the right side. On the contralateral side the subjects received a sham IPB with isotonic saline. Randomization was performed by a sub-investigator without further connection to the trial using STATA software (version 14.2, StataCorp, College Station, Texas, USA).[117] Two other sub-investigators without further connection to the trial produced project medication in blinded syringes securing that both investigators and subjects were blinded to random group allocation. The group allocation was unblinded before statistical inference was made.

3.8 Data collection

Data was captured using REDCap electronic data capture tools for all three studies.[118] Data was collected by anaesthesiologists, physiotherapists and assistants using case report forms on paper or by entering data directly into the REDCap database using a tablet

computer or a laptop. When data was collected on paper, it was entered into the electronic database by the primary investigator as soon as possible. Data was transferred automatically to the database by a secure connection to two mirrored REDCap servers hosted at different locations at the Department of Clinical Medicine at Aarhus University. Accuracy of data capture from studies II and III was assessed by an external GCP monitor from the GCP unit of Aarhus and Aalborg University Hospitals.

3.9 Statistical analysis

3.9.1 Sample size estimation

As Study I was a descriptive study estimation of sample size was not relevant. The sample size of 15 cadaver sides was based on feasibility and was similar to the traditional range of sample size in comparable dissection studies.

The sample size calculation for Study II was based on results from a non-blinded non-randomized pilot study. Aiming for a power of 80 % and a 2-tailed α-error of 5 % we calculated a required sample size of 28 subjects for each group using STATA software (version 14.2). In order to avoid lack of power due to sampling error we included 30 subjects per group.

Study III was a noninferiority study. In a previous unpublished pilot study from our research group, we estimated the standard deviation (SD) of the primary outcome measure. The estimated non-inferiority level was 40 N. We aimed for a power of 90 % and a 2-tailed α-error of 5 %. Using the web-based sample size calculator Sealed Envelope (www.sealedenvelope.com) we calculated a minimum sample size of 18 subjects. To account for dropouts, we decided to include 22.

3.9.2 Statistical analysis

Statistical analysis was performed using STATA software (version 14.2). Normal distribution of data was evaluated using QQ plots and histograms. Normally distributed continuous data were presented as mean with SD or 95CI and groups were compared using Students *t*-test. Skewed continuous data were presented as median with inter-quartile range (IQR) and independent groups were compared with the Mann-Whitney *U* test. Paired groups with skewed continuous data were compared using the Wilcoxon signed-

rank test. Ordinal independent data were presented as number of subjects with percentage of group and intergroup comparisons were made using the Mann-Whitney *U* test. Paired categorical data were presented as number with percentage of the group and groups were compared using McNemars test. Time-to-event data were presented as Kaplan-Meier plots and intergroup comparisons were made using the log-rank test. A *P* value below 0.05 was considered statistically significant. For *P* values below 0.05 in repeated measurements the Bonferroni correction was applied.

4 - RESULTS

The results are reported in detail in Article I – III (p. 57). A summary of the key findings is presented below.

4.1 Study I

In 10 of 15 dissections (67 % [95CI: 38-88 %]) the injected dye did spread in a well-defined compartment between the iliopsoas m. and the iliofemoral lig. where it stained all hip articular sensory branches of the femoral n. to the hip joint (Figure 7). In four of 15 dissections (27 % [95CI: 8-55 %]) the dye was unintentionally injected into the iliopectineal bursa. This caused a rather unpredictable spread reaching the motor branches of the femoral n. in all four cases. In one dissection (7 % [95CI: 0.2-32 %]) pre-existing adherences between the iliopsoas m. and the iliofemoral lig. limited the spread of injectate which spared some hip articular sensory branches from staining.

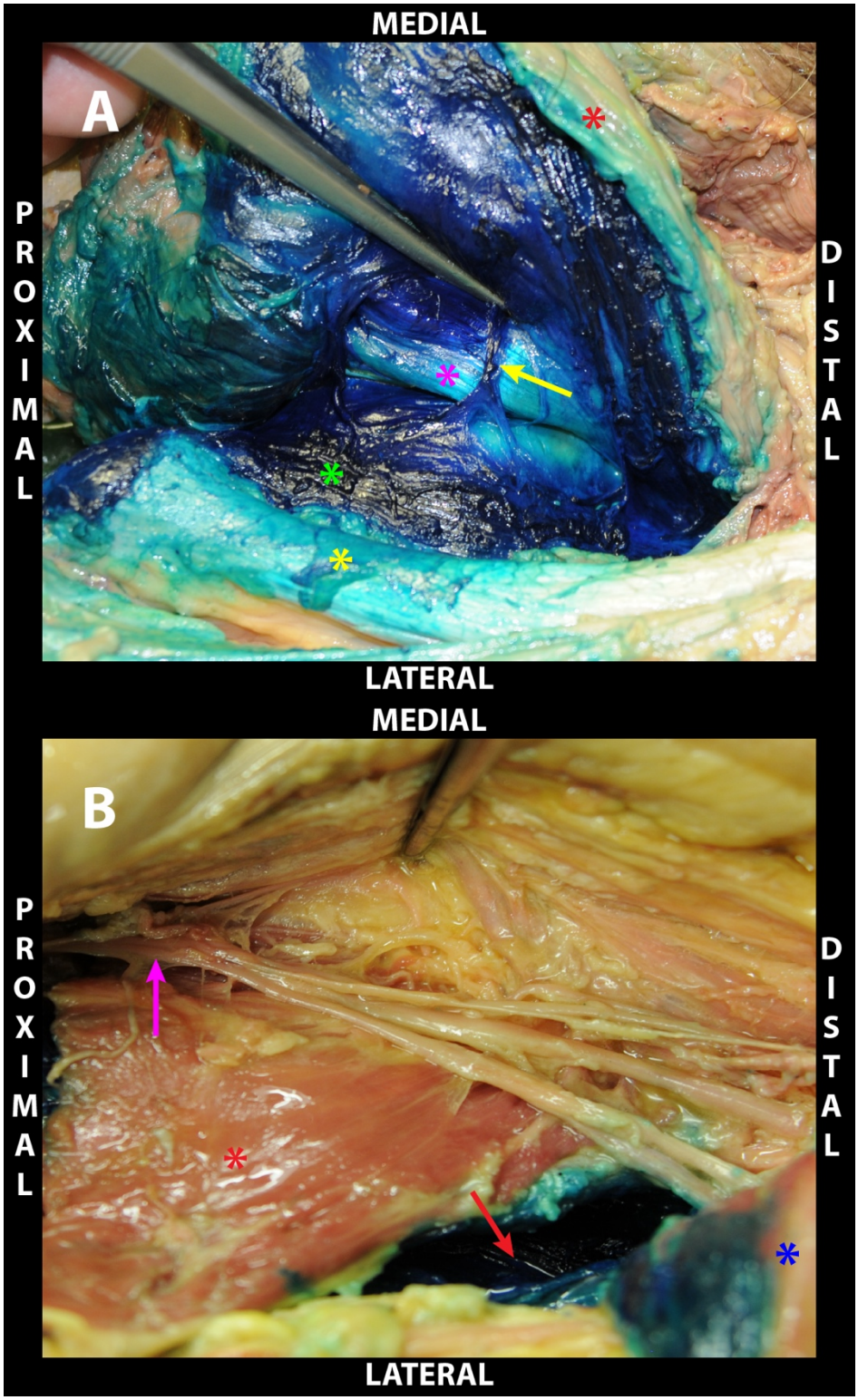

Figure 7. ***A:*** *Spread of dye in the compartment between the iliopsoas muscle (red asterisk) and the iliofemoral ligament (green asterisk) colouring a branch from the femoral nerve to the hip joint (yellow arrow). The iliopsoas muscle is cut proximally and flipped medially. The iliopsoas compartment is bordered laterally by the rectus femoris muscle (yellow asterisk) and medially by the iliopectineal bursa deep to the tendon of the iliopsoas (magenta asterisk).* ***B:*** *The femoral nerve (magenta arrow) and its major mixed sensory and motor branches are not dyed after injection in the iliopsoas plane, as the iliopsoas muscle (red asterisk) obstructs the spread of dye (red arrow). The sartorius muscle (blue asterisk) is cut from its origin and flipped laterally. The faint staining of the distal branches of the femoral nerve is an artefact of the dissection. Modified excerpt from Article I.*

4.2 Study II

Subjects who had an active ONB had a consumption of (mean [SD]) 39.9 [22.3] mg opioid (OME) during the first 12 hours after surgery. Subjects in the placebo group had a consumption of 40.5 [30.5] mg opioid (OME) during the same period. The difference of 0.6 mg opioid (OME) between groups was clinically and statistically insignificant (P = 0.93). Opioid consumption during 12-18 hours after surgery (median [IQR]) was 12.5 [0 - 17.0] mg OME in the active ONB group and 10.1 [0 - 17.3] mg OME in the placebo group (P = 0.34).

An active ONB did not affect time to first opioid request (Figure 8). Neither did it affect pain at rest or during passive flexion of the hip, as well as nausea at 1, 2, 5, 7 and 24 hours after surgery (Figure 9).

Median [IQR] ambulation score was 6 [4.5 - 8] in subjects who had an active ONB and 7 [6 - 8] in subjects who had a sham ONB (P = 0.13). The range of the ambulation score was 0-8: 0: Subject unable to ambulate from supine to sitting position; 8: Subject could perform all exercises without human physical support. Subjects who received an active ONB had a reduced median [IQR] muscular control score during ambulation 5 hours after surgery compared to the placebo group (2.5 [2 - 3] vs. 3 [2.5 - 3]) (P = 0.026). The range of the muscular control score was 0-3: 0: Subject were unable to ambulate from supine to sitting position; 3: Subject had good muscular control of operated leg during all exercises.

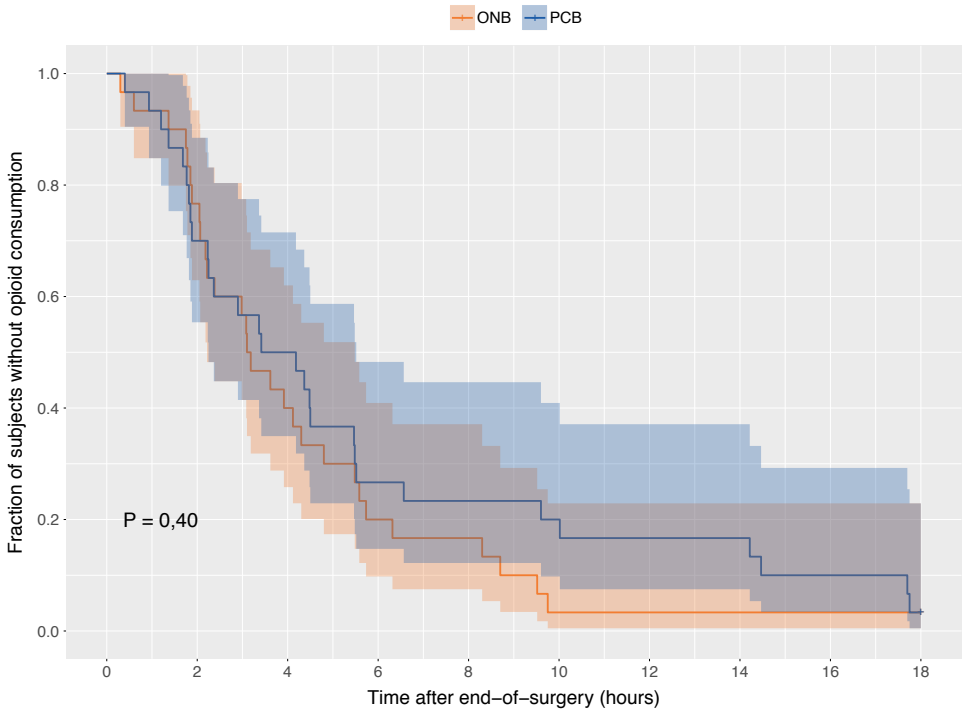

Figure 8. Kaplan-Meier survival plot of time from surgery to first opioid request (with 95 % confidence intervals). Groups are compared using the log-rank test. ONB: Obturator nerve block (orange). PCB: Placebo (blue). Excerpt from Article II.

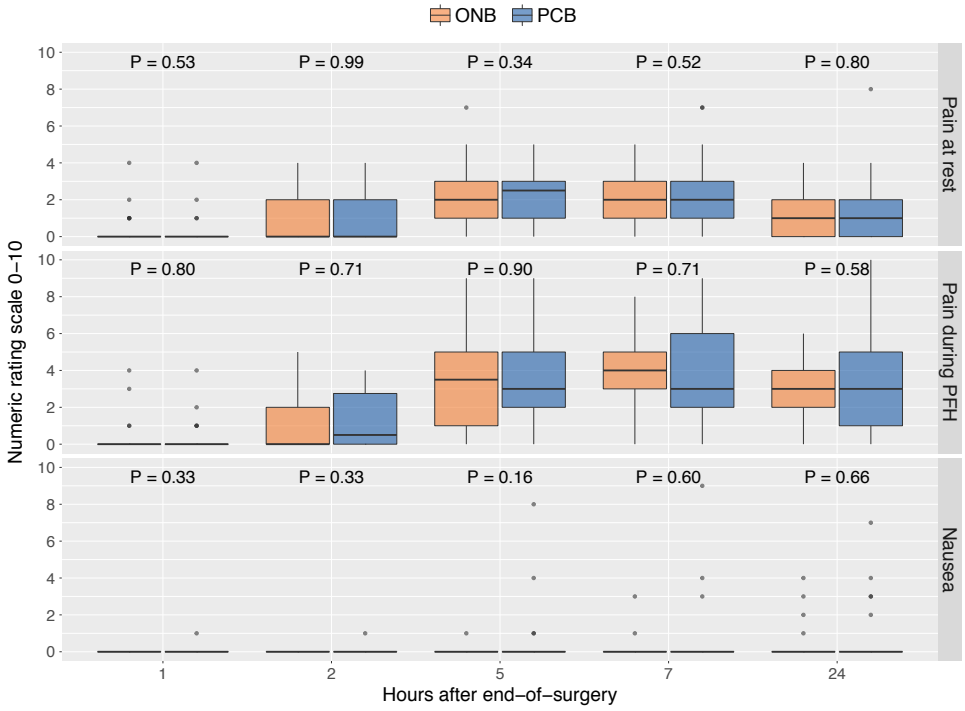

Figure 9. Pain at rest and during passive 90 degrees flexion of the hip (PFH) as well as intensity of nausea at 1, 2, 5, 7 and 24 hours after total hip arthroplasty. Groups are compared using the Mann-Whitney U test. Numeric rating scale 0-10 (0: No pain/nausea; 10: Worst pain/nausea imaginable). ONB: Obturator nerve block (orange). PCB: Placebo (blue). Modified excerpt from Article II.

4.3 Study III

Active IPB generated a mean reduction of maximal force of knee extension (mean [95CI]) of -9.7 N [-22, 3.0] from baseline to one hour after nerve block performance (p = 0.12). The mean maximal force on the side of active IPB compared to the non-blocked side (mean (CI)) was -8.1 N (-18, 2.5) (p = 0.12) (Figure 10). The mean maximal force on knee extension at baseline was (mean [95CI]) 354 N (299, 409). Only 14 of 20 subjects contributed to the primary endpoint as the remaining six subjects performed a maximal force of knee extension at baseline that exceeded the scale of the dynamometer.

The injectate spread consistently in the iliopsoas plane between the iliofemoral ligament and the iliopsoas m. as well as between the AIIS-IP and the iliopsoas muscles major component (Figure 11).

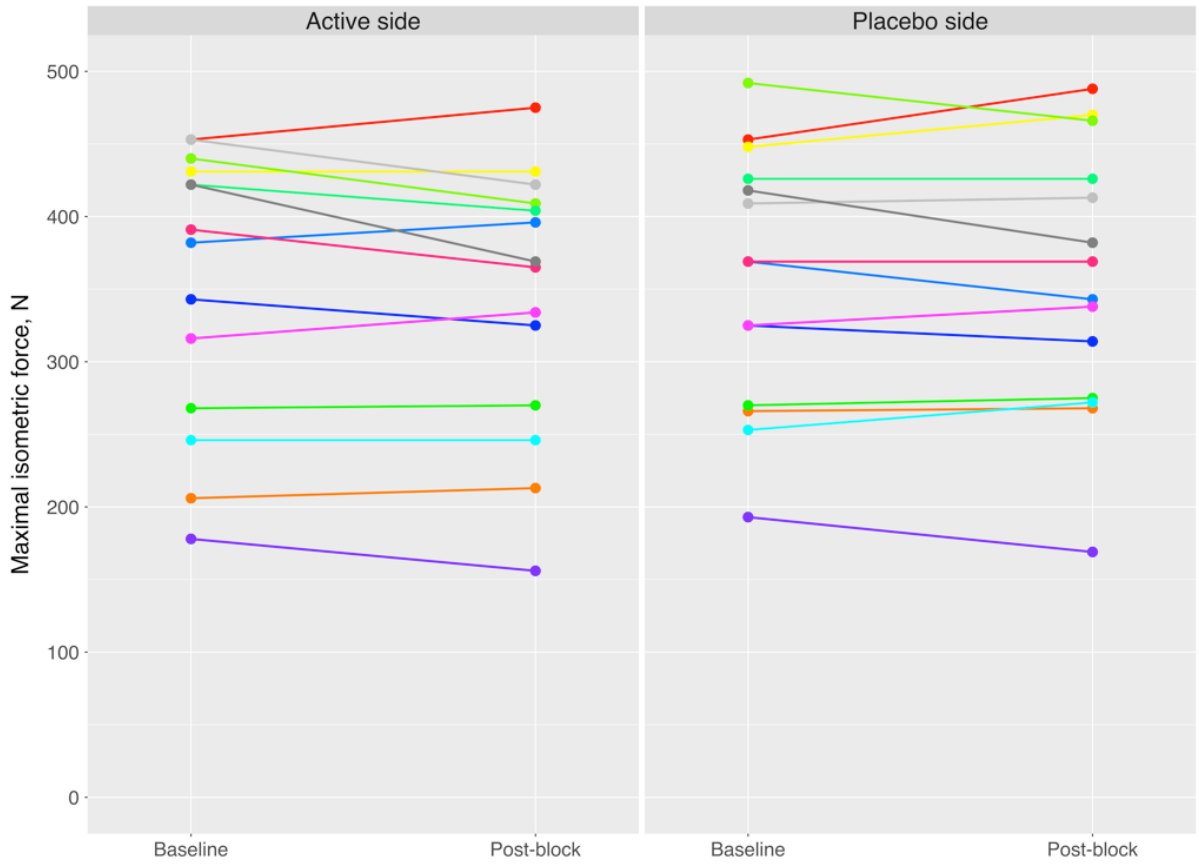

Figure 10. Maximal isometric force on bilateral knee extension (N) before (Baseline) and one hour after (Post-block) performance of iliopsoas plane block (IPB) in 14 volunteers. Subjects were randomly allocated to active IPB in left vs. right side with a contralateral sham IPB (Placebo). Each individual subject is represented by similar colour on both sides of the figure. Excerpt from Article III.

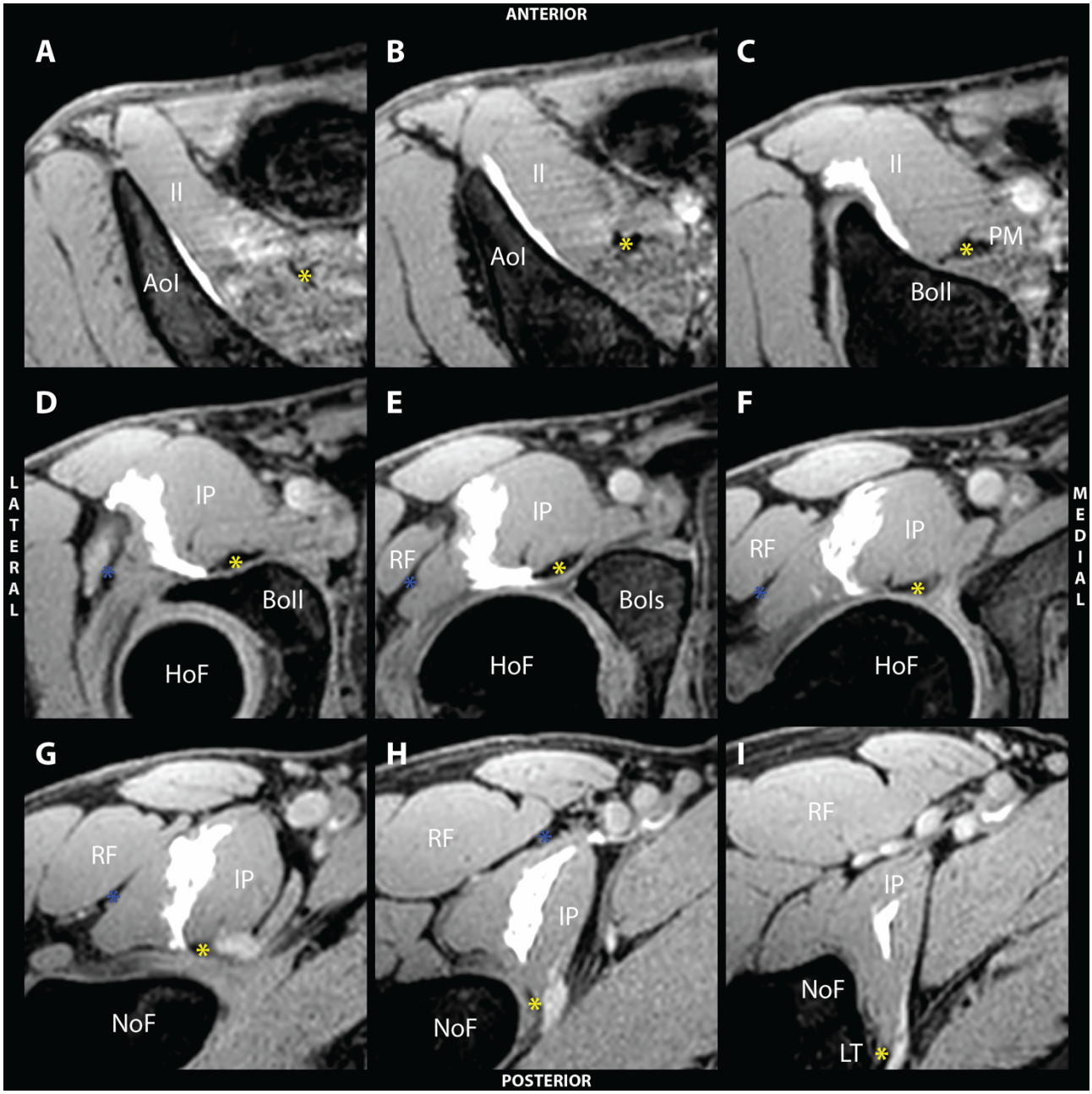

Figure 11. Typical pattern of injectate spread in a single subject visualized on transverse T1-weigthed MRI slices. The distance between slices is 13 mm. ***A****: Most proximal slide. 55 mm proximal to the greater trochanter.* ***B-H****: Intermediate slides.* ***I****: Most distal slide. 48 mm distal to the greater trochanter. Il: Iliacus muscle (m.); AoI: Ala of Ilium; PM: Psoas Major m.; BoIl: Body of Ilium; IP: Iliopsoas m.; HoF: Head of Femur; RF: Rectus Femoris m.; BoIs: Body of Ischium; NoF: Neck of Femur; LT: Lesser Trochanter. Blue asterisk: rectus femoris tendon; Yellow asterisk: iliopsoas tendon. Excerpt from Article III.*

5 - Discussion

The three studies (I-III) are discussed in detail in Articles I-III (p. 57). A brief summary of the discussions are presented below. The conclusions are presented in Chapter 6 (p. 44) and the perspectives are discussed in Chapter 7 (p. 45).

5.1 The obturator nerve block

5.1.1 Major findings

In our randomized clinical trial (Study II) an ONB had no clinically relevant or statistically significant effect on postoperative pain after THA through the posterior approach. Despite an active ONB subjects were able to ambulate when tested 5 hours after surgery, but had a reduced muscular control of the operated leg compared to controls. Our trial is the first to investigate the effect of a sole ONB on postoperative pain after THA.

5.2 The iliopsoas plane block

5.2.1 Major findings

In the cadaver study (Study I) the injectate spread to all hip articular branches of the femoral n. in 10 of 15 cadaver sides (67 % [95CI: 38-88 %]). The 5 missed injections were due to unintentional injection in the iliopectineal bursa (4 of 15 (27 % [95CI: 8-55 %])) and adhesions between the iliopsoas m. and the iliofemoral lig. (1 of 15 (7 % [95CI: 0.2-32 %])).

In the randomized volunteer trial (Study III) we found no significant decrease of maximal force on knee extension as a result of the IPB. The injectate from the IPB consistently spread in the iliopsoas plane between the minor posterolateral component of the iliopsoas m. (AIIS-IP) and the main component of the iliopsoas m. as well as between the iliopsoas m. and the iliofemoral lig.

5.2.2 Previous studies

The IPB is a new technique and it has not been presented previously, as the nerve block technique was developed by our research group during the course of my PhD study. Other authors have, however, examined the effect of an FNB or a selective blockade of the hip articular branches of the femoral n. on pain originating from the hip.

An FNB reduces hip fracture pain,[119] but only few studies have assessed the effect of a sole FNB on pain after THA. A 2014 nonblinded pilot study find a reduced pain score in patients who received an FNB compared to a regimen based on non-opioid analgesics.[96] However, another randomized clinical trial did not find an effect of a FNB on postoperative pain after THA – possibly because the study was underpowered.[120] A "3-in-1" block reduces the opioid consumption and delays the first opioid request.[121-123] However, since the "3-in-1" block – in addition to anaesthetizing the femoral n. – has potential to anaesthetize the lateral femoral cutaeous n. the observed effect cannot necessarily be attributed solely to anaesthesia of the femoral n. Similarly, an FNB in combination with an LFCB provides analgesia after THA,[124,125] but the effect of the FNB cannot be distinguished from a potential analgesic effect of an LFCB, in these studies. Furthermore, the internal validity and sample sizes are limitations of the studies cited above.

As discussed in the introduction (section 1.8.4) an FNB is associated with an increased risk of fall. A 2010 metaanalysis assessed the effect of FNB or LPB on risk of fall after total hip and knee arthroplasty. The authors found zero falls (95CI: 0-5 %) in the control group compared to 7 % (95CI: 3-15 %) in the nerve block group (P = 0.013).[12] A randomized clinical trial from 2015 examined the effect of an FNB on risk of fall after hip arthroscopy compared to placebo.[126] Of the 27 patients with FNB, 6 had an incidence of fall during the first 24 postoperative hours (22 %) compared to zero in the control group (P = 0.025).

A peripheral nerve block that selectively and exclusively targets the hip articular sensory branches of the femoral n. – such as the IPB – could theoretically provide postoperative analgesia after THA without any associated risk of fall.

Most of the hip articular sensory branches of the femoral n. branches off cranial to the inguinal ligament.[37] Thus, there is a theoretical risk that these branches will not be anaesthetized by a conventional ultrasound guided FNB, as this block is performed at the level of the inguinal ligament.[127] In contrast, an injection in the iliopsoas plane – as used in the IPB – reach all hip articular branches of the femoral n. as shown in Study I.

To my knowledge, the only other study of a nerve block that aim to target the hip articular sensory branches of the femoral n. selectively and exclusively is by Girón-Arango et al., who described the novel PEricapsular Nerve Group (PENG) block in a brief technical

report published in July 2018. The target of the PENG block is an injection of 20 mL local anaesthetic on the anterior aspect of the iliopubic eminence, from where it is hypothesized to spread to the high articular branches of the femoral n. (branches that leave the femoral n. proximal to the inguinal lig.) as well as the accessory obturator n. when present. The brief technical report presents a case series of 5 patients who had a PENG block in order to relieve significant pain after a hip fracture. The patients all reported a significant pain reduction during both rest and activity – from a median [range] NRS score at rest of 5 [4-8] at baseline to 0 [0-1] 30 minutes after the block. None of the patients experienced severe quadriceps weakness although this was not systematically assessed.[128] There is a certain similarity between the PENG block and the IPB as the target of the PENG block is injection on the deep side of the iliopsoas m. just a few centimeters proximal to the target of the IPB. However, the target of the PENG block is between the tendon of the iliopsoas m. and the superior pubic ramus and is thus probably inside the iliopectineal bursa. This is in contrast to the IPB, where the target of injection is more lateral in the iliopsoas plane in order to avoid injection into the bursa. The originators of the PENG block speculate that the injectate might spread to the hip articular sensory branches of the obturator n. as well as the hip articular sensory branches of the femoral n. and the accessory obturator n. However, this theory is somewhat contradicted by the results from our studies (Study I and III) as no injections – even when inadvertently injecting the iliopectineal bursa – did spread to the space deep to the pectineus muscle. Thus, the injectate did not reach the obturator n. Another potential limitation of the PENG block is that it probably does not spread to the low hip articular sensory branches of the femoral n. These nerve branches leave the femoral n. distal to the inguinal lig. and either pierce the iliopsoas m. or course around its lateral margin to the iliopsoas plane. As shown in our cadaver study (Study I) these branches are reached by an IPB. Further studies are needed to assess the spread of injectate from the PENG block, as well as to assess its analgesic effect in a randomized blinded trial. We have addressed the above issues in a letter-to-the-editor published in *Regional Anesthesia and Pain Medicine* (Appendix 5, p. 98).

5.3 Limitations

5.3.1 Obturator nerve block

The sample size of Study II was based on results from an unblinded pilot study where the control group did not receive sham blocks (placebo). The results from the pilot study – as well as our clinical experience – lead us to believe that there was a substantial effect of an ONB on postoperative pain after THA. Therefore, the trial was not powered to detect small differences in opioid consumption between the groups. For example, statistical detection of an intergroup difference of 10 mg OME would require a sample size of at least 200 patients. Such a large study of a minor effect would not be clinically relevant.

Even though an ONB does not seem to have an effect on postoperative pain after THA through the posterior approach, this may not be the case when THA is performed through the anterior approach, as the anterior approach to the hip goes through the anterior part of the hip capsule which is in part innervated by the obturator n.[8,29] The effect of an ONB on postoperative pain after THA with an anterior approach remains to be investigated in a clinical trial.

The ambulation test used in Study II was developed for the purpose of the particular study and was not tested for measurement error prior to use. The intra- and interrater variability of the ambulation and muscular control scores is therefore unknown. In addition, it is unknown whether a reduction in ambulation and muscular control scores would translate into a clinically relevant effect on morbidity, mortality or length of stay in hospital. Nevertheless, we chose to develop and use the test, as none of the existing ambulation tests such as the timed up and go test, CAS, self-paced walk test, or the stair climb test were targeting early ambulation after major hip surgery.[113,129]

5.3.2 Iliopsoas plane block

Since the IPB is a selective and exclusive sensory nerve block that solely anaesthetizes the hip articular sensory branches from the femoral n. its analgesic properties cannot be assessed in volunteers without hip pain. While the cadaver study (Study I) has shown that the injectate from a successful IPB reaches all hip articular sensory branches of the femoral n. and the volunteer trial (Study III) has shown the IPB to be void of motor blockade a

clinical trial is necessary to assess the effect of an IPB on postoperative pain after major hip surgery.

The lack of motor blockade and spread of injectate in living humans after the IPB has only been assessed in young and healthy volunteers with normal body weight. This population is not representative of most typical THA patients, who are frequently older, obese and comorbid. This should also be considered in a future clinical trial.

A theoretical risk of infection is associated with the IPB as the local anaesthetic is injected close to the surgical field. The risk of infection after peripheral nerve blocks is generally extremely low, and almost exclusively associated with the use of perineural catheters.[130,131] The risk of early (< 3 months) deep infection after THA is also low – approximately 0.1-0.2 %.[132] However, there is a theoretic risk that the accidental introduction of dermal bacteria around the hip joint could lead to postoperative infection of the prosthesis. This small risk could probably be eliminated or reduced significantly by the use of sterile precautions during block performance similar to epidural and intrathechal blockade techniques.

6 - Conclusions

The results of the present thesis improve our understanding of the effect of peripheral nerve blocks targetting the hip joint for analgesia after elective THA.

6.1 Obturator nerve block

A proximal ONB has no significant effect on pain after elective primary THA through the posterior approach. The ONB induced no severe adverse effects, and subjects were able to perform postoperative ambulation despite a subjective experience of a reduced muscular control of the operated leg.

6.2 Iliopsoas plane block

In cadavers, 5 mL of injectate in the iliopsoas plane – lateral to the iliopectineal bursa – spreads to all hip articular branches of the femoral n. In volunteers the IPB did not result in muscular weakness. The injectate from the IPB did spread consistently in the iliopsoas plane between the AIIS-IP and the main component of the iliopsoas m. as well as between the iliopsoas m. and the iliofemoral ligament.

7 - Perspectives and future research

7.1 Obturator nerve block

Based on the results from our clinical study (Study II) an ONB is unsuitable for postoperative analgesia after posterior THA, as a contingent analgesic effect of ONB – if any – is very small and most unlikely clinically relevant. Further trials should explore the potential effect of an ONB on pain after THA through the anterior approach.

The effect of an ONB on pain prior to hip fracture surgery as well as pain after hip arthroscopy also remains to be examined further in soundly blinded randomized clinical trials.

If an ONB is found to have an analgesic effect on hip-derived pain, future efforts should be put into the development of a novel nerve block that selectively targets the hip articular branches of the obturator n. This would provide the opportunity to relieve perioperative pain without impairing muscle control of the operated leg.

7.2 Iliopsoas plane block

Despite the rather successful pre-clinical testing of the IPB, this nerve block still needs to be examined in a clinical setting, to determine its potential analgesic effect on postoperative pain after THA as well as other types of chronic or acute pain related to the hip.

7.3 Cutaneous nerve blocks

As mentioned in the introduction (section 1.6) postoperative pain after THA can originate from the surgical transcutaneous incision, bony surgery and implantation of the prosthesis. The innervation of the cutis, subcutis and deep fascia of the surgical incision for posterior access to the hip is often covered by different nerves - the lateral femoral cutaneous, the iliohypogastric and the superior cluneal nerves.[35] It remains to be examined

whether one blockade or a combination of nerve blocks targeting these nerves can offer clinically significant analgesia after posterior THA.

8 - ENGLISH ABSTRACT

A significant subgroup of patients suffer from moderate or severe pain after total hip arthroplasty (THA). Regional analgesia has the potential to reduce postoperative pain and thereby spare patients from opioids, but regional analgesia of the hip is complicated as the area is innervated by multiple nerves. However, the nociceptors of the hip joint are primarily innervated by the obturator and femoral nerves. The effect of an obturator nerve block (ONB) on pain following THA has never been investigated. A femoral nerve block is known to reduce pain after THA, but is unfortunately accompanied by an increased risk of fall. We have developed a novel nerve block – the iliopsoas plane block (IPB) – that has the potential to anaesthetize the hip articular sensory branches of the femoral nerve without causing motor blockade.

The aims of the thesis were:

I) To assess the spread of injectate from the IPB in a cadaver model.
II) To assess the effect of an ONB on postoperative pain after THA.
III) To assess whether an IPB induces muscle weakness of the thigh.

In Study I we demonstrated that dye injected using the IPB technique did spread to the relevant nerve branches in 10 of 15 cadaver sides. The incomplete patters of spread were due to unintended injection in the iliopectineal bursa (4 of 15) and adherences (1 of 15). Study II revealed that an ONB had no effect on postoperative pain after THA; subjects with an ONB had an opioid consumption of (mean [SD]) 39.9 [22.3] mg opioids (oral morphine equivalents) during the first 12 postoperative hours. The corresponding dose in controls was 40.5 [30.5] mg (P = 0.93). In Study III we found that an IPB did not induce muscle weakness in volunteers. The injectate did consistently spread in the iliopsoas plane.

In conclusion, an IPB has the potential to provide analgesia after THA without inducing muscle weakness, but this hypothesis has to be tested in a clinical trial. An ONB does, on the other hand, not appear to provide postoperative analgesia after THA through the posterior approach.

9 - Dansk resumé

Danish abstract

En betydelig undergruppe af patienter lider af moderate eller svære smerter efter total hoftealloplastik (THA). Regionalanæstesi har potentiale til at reducere postoperative smerter og dermed skåne patienterne for opioider, men regionalanæstesi af hoften er kompliceret da området er innerveret af flere forskellige nerver. Nociceptorerne i hofteleddet er imidlertid hovedsageligt innerveret af nervus obturatorius og nervus femoralis. Det er aldrig tidligere undersøgt, om et obturatoriusblok har effekt på smerterne efter THA. Det er derimod vist, at et femoralisblok reducerer smerterne efter THA. Desværre medfører et femoralisblok en øget risiko for fald. Vi har udviklet et nyt nerveblok – iliopsoas plane blok (IPB) – der har potentiale til selektiv bedøvelse af nervegrenene fra nervus femoralis til hofteleddet uden samtidig at paralysere lårets muskler.

Formål med afhandlingen:

I) Vurdering af spredningen af injektatet ved IPB i en kadavermodel
II) Vurdering af effekten af et obturatoriusblok på smerter efter THA
III) Vurdering af, om IPB forårsager paralyse af lårets muskler

I Studie I viste vi, at farvestof indsprøjtet ved brug af IPB teknikken spredte sig til de relevante nervegrene i 10 af 15 kadaversider. De fejlslagne blok skyldtes uintenderet injektion i bursa iliopectinea (4 af 15) og adhærencer (1 af 15). Studie II viste, at et obturatoriusblok ikke har effekt på postoperative smerter efter THA; forsøgspersoner med et obturatoriusblok fik (gennemsnit [standarddeviation]) 39,9 [22,3] mg opioider (peroral morfinækvivalent) i løbet af de første 12 postoperative timer. Den tilsvarende dosis i kontrolgruppen var 40,5 [30,5] mg (P = 0,93). I Studie III fandt vi, at et IPB ikke medførte muskelsvaghed hos frivillige forsøgspersoner. Injektatet spredte sig konsistent i iliopsoas planet.

Det kan konkluderes, at IPB har potentiale til effektiv postoperativ smertelindring efter THA uden at medføre muskelsvaghed. Denne hypotese skal efterprøves i et klinisk studie. Et obturatoriusblok lindrer ikke postoperativ smerte efter THA via den posteriore adgang.

10 - REFERENCES

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ARTICLES

The dissertation is based on the following attached articles.

Article I p. 58

Nielsen ND, Greher M, Moriggl B, Hoermann R, Nielsen TD, Børglum J, Bendtsen TF.
Spread of injectate around hip articular sensory branches of the femoral nerve in cadavers.
Acta Anaesthesiol Scand. 2018;62(7):1001–1006. DOI: 10.1111/aas.13122

Article II p. 64

Nielsen ND, Runge C, Clemmesen L, Børglum J, Mikkelsen LR, Larsen JR, Nielsen TD, Søballe K, Bendtsen TF.
An Obturator Nerve Block does not Alleviate Postoperative Pain after Total Hip Arthroplasty – a Randomized Clinical Trial.
Reg Anesth Pain Med. Epub ahead of print 23-01-2019. DOI:10.1136/rapm-2018-100104

Article III p. 70

Nielsen ND, Madsen MN, Østergaard HK, Bjørn S, Pedersen EM, Nielsen TD, Søballe K, Børglum J, Bendtsen TF.
The Iliopsoas Plane Block: Selective Sensory Blockade of the Hip Articular Branches of the Femoral Nerve – a Blinded and Randomized Trial in Healthy Volunteers.
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ORIGINAL ARTICLE

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Spread of injectate around hip articular sensory branches of the femoral nerve in cadavers

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Background: Anatomical knowledge dictates that regional anaesthesia after total hip arthroplasty requires blockade of the hip articular branches of the femoral and obturator nerves. A direct femoral nerve block increases the risk of fall and impedes mobilisation. We propose a selective nerve block of the hip articular branches of the femoral nerve by an ultrasound-guided injection in the plane between the iliopsoas muscle and the iliofemoral ligament (the iliopsoas plane). The aim of this study was to assess whether dye injected in the iliopsoas plane spreads to all hip articular branches of the femoral nerve.

Methods: Fifteen cadaver sides were injected with 5 mL dye in the iliopsoas plane guided by ultrasound. Dissection was performed to verify the spread of injectate around the hip articular branches of the femoral nerve.

Results: In 10 dissections (67% [95% confidence interval: 38-88%]), the injectate was contained in the iliopsoas plane staining all hip articular branches of the femoral nerve without spread to motor branches. In four dissections (27% [8-55%]), the injection was unintentionally made within the iliopectineal bursa resulting in secondary spread. In one dissection (7% [0.2-32%]) adhesions partially obstructed the spread of dye.

Conclusion: An injection of 5 mL in the iliopsoas plane spreads around all hip articular branches of the femoral nerve in 10 of 15 cadaver sides. If these findings translate to living humans, injection of local anaesthetic into the iliopsoas plane could generate a selective sensory nerve block of the articular branches of the femoral nerve without motor blockade.

1 | INTRODUCTION

Providing postoperative regional anaesthesia for major hip surgery patients is challenging, as the hip joint is innervated by multiple nerves. The anterior aspect of the hip joint is innervated by the femoral and obturator (and accessory obturator) nerves all originating from the lumbar plexus.[1,2] The posterior aspect of the hip joint is innervated by the superior and inferior gluteal nerves from the sacral plexus as well as a sacral plexus branch via the nerve to the quadratus femoris and in some cases branches directly from the sciatic nerve.[1,2] However, the nociceptors of the capsule are mainly situated in the anterolateral and anteromedial part of the capsule,[3,4] which is innervated by the femoral and obturator nerves as well as the accessory obturator nerve when present.[2,5]

A femoral nerve block is known to provide some degree of analgesia after total hip arthroplasty.[6] However, a femoral nerve block for pain relief after hip surgery is controversial, as it is associated with an increased risk of fall,[7,8] as well as an hindrance to early mobilisation.

The sensory branches of the femoral nerve to the hip joint either penetrate or innervate the iliopsoas muscle or wind around the lateral margin of the muscle before innervating the anterolateral part of the hip joint capsule.[2,5] All sensory hip branches of the femoral nerve must thus pass through the anatomical plane between the iliopsoas muscle and the iliofemoral ligament—the so-called iliopsoas plane. We suggest, that an injection of local anaesthetic in this plane, will provide regional analgesia of the sensory articular branches from the femoral nerve to the hip joint without spread to any motor branches.

The primary aim of the study was to assess the spread of injectate in the iliopsoas plane in a cadaver model and to assess if the sensory branches from the femoral nerve to the hip joint were stained by the injectate without staining of the motor branches.

Editorial Comment

Selective blockade of hip articular sensory branches of the femoral nerve would be advantageous for post-operative analgesia after hip arthroplasty, where one wants to try to preserve motor function. In this cadaver dye study, the authors showed that it is possible in this model to get spread of injectate in the iliopsoas plane to achieve this goal.

2 | METHODS

Cadavers were donated to the Division of Clinical and Functional Anatomy at the Medical University of Innsbruck for scientific and educational purposes.[9] Ethical approval was not necessary according to Austrian law. The cadavers were preserved by arterial injection of an ethanol-glycerol solution followed by 1-3 months of immersion in diluted phenolic acid.[10,11]

We performed ultrasound-guided injections of 1% methylene blue between the iliopsoas muscle and the hip joint capsule on both sides of 8 cadavers except in 1 cadaver side that was unsuitable for injection due to the postmortem excision of the hip joint. Fifteen cadaver sides were thus included in the study.

The ultrasound-guided injections were performed using an 8-1 MHz curved array probe with a Esaote MyLabSeven ultrasound system (Esaote SpA, Genoa, Italy). All injections were performed by one of the authors (TFB). The dissections were carried out by two other authors (BM and RH), who were not present during the injection of the dye.

The outcomes were (1) the frequency of staining of all hip articular branches of the femoral nerve (2) the frequency of staining of some of the motor branches of the femoral nerve (3) the frequency of ultrasonographic identification of the iliopsoas muscle and the iliofemoral ligament (4) the distance from the skin to the target iliopsoas plane (5) the distance from the point of needle insertion to the horizontal plane intersecting the anterior superior iliac spine (ASIS) (6) the distance from the point of needle insertion to the sagittal plane intersecting the ASIS (7) the length of the needle trajectory (8) the frequency of injection in the iliopectineal bursa.

2.1 | Injection procedure

The cadaver was positioned supine and the probe was oriented in the transverse plane and placed at the level of the inguinal crease to identify the femoral nerve lateral to the femoral vessels. The lateral margin of the femoral nerve was marked on the skin to avoid piercing the nerve. The probe was then oriented in the sagittal plane across the ASIS, and slided medially along the inguinal ligament until the anterior aspect of the head of femur was identified, where it enters the acetabulum (Figure 1A). The iliofemoral ligament was identified as a hyperechoic structure extending from the rim of the acetabulum and superficial to the head of femur (Figure 1A,D). An 80 mm, 22-gauge Ultraplex needle (B.Braun, Melsungen, Germany) was inserted from the distal end of the probe (and lateral to the skin marking indicating the femoral nerve) with the bevel facing downwards and advanced in-plane until the needle tip reached the anatomical plane between the iliopsoas muscle and the iliofemoral ligament (Figure 1C,D). At this location, 5 mL of methylene blue was injected, and the spread of dye was observed between the iliopsoas muscle and the iliofemoral ligament.

After completing the injection, we gauged the target depth (distance from skin to the iliopsoas plane on the ultrasonogram), the length of the needle trajectory, as well as the distance from the ASIS to the point of needle insertion in the sagittal as well as the transverse plane.

2.2 | Dissection procedure

The following procedure was employed in all 15 cadaver sides. Two initial incisions were made through all epimuscular tissue layers including the strong fascia lata: The first incision was extended from a point three fingerbreadths lateral to the superficial inguinal ring from where it was continued cranially and parallel to the inguinal ligament to be terminated laterally above the ASIS. The second incision was extended obliquely from above the ASIS approximately following the sartorius muscle to the medial side of the thigh. The resulting tissue flap was raised and reflected medially to expose the muscular boundaries of the iliopsoas muscle. If necessary, the incisions were extended slightly. The hip joint was flexed and the iliopsoas muscle was mobilised and lifted to allow identification of the hip articular branches of the femoral nerve in their path through the iliopsoas plane. In some cadaver sides the iliopsoas muscle was cut —after careful registration of the staining of the articular branches— for better photo-documentation.

2.3 | Statistics

Continuous data are presented as mean and range. Proportions are presented as number with percentage of all 15 cadaver sides and a

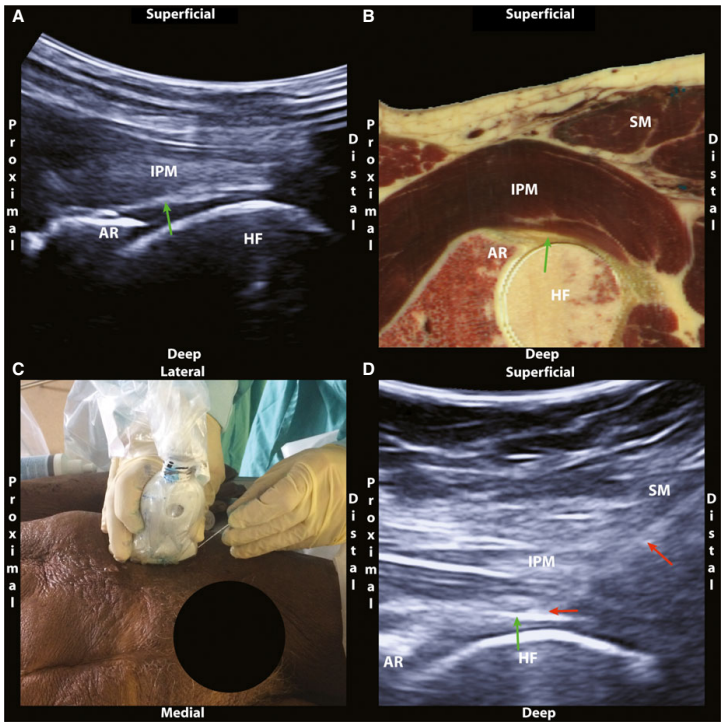

FIGURE 1 A, Sagittal ultrasonogram showing the head of femur (HF) as it dives into the acetabulum. The iliofemoral ligament (green arrow) is visualised as a hyperechoic structure extending from the acetabular rim (AR) deep to the iliopsoas muscle (IPM). B, Sagittal section at the approximate level of A. The Sartorius muscle (SM) overlays the IPM. C, Sagittal ultrasound scan with a curved array probe at the approximate level of A. The needle is inserted in-plane at a steep angle from the distal end of the probe. D, Sagittal ultrasonogram showing the needle (red arrows) positioned for injection of dye between the IPM and the iliofemoral ligament (green arrow). Modified excerpt from VH Dissector with permission from Touch of Life Technologies Inc (www.toltech.net). Built on real anatomy from the National Library of Medicine's Visible Human Project [Colour figure can be viewed at wileyonlinelibrary.com]

95% two-sided confidence interval. For proportions on 100% a 97.5% one-sided confidence interval is reported.

3 | RESULTS

Eight cadavers (7 females and 1 male) with an age range from 81 to 98 years were used for this study. Ultrasonographic identification of the iliofemoral ligament, the iliopsoas muscle, and the iliopsoas plane was feasible in all 15 investigated cadaver sides.

The distance from the skin to the target iliopsoas plane was 2.5 (*1.4-3.5*) cm (mean (*range*)). The point of needle insertion was 9.8 (*6.0-12.0*) cm distal and 1.7 (*0-4.5*) cm medial to the horizontal and sagittal planes intersecting the ASIS. The length of the needle trajectory was 4.4 (*2.0-6.0*) cm.

In all 15 dissections (*100% [97.5% one-sided confidence interval (97.5CI): 78-100%]*), the branches from the femoral nerve to the hip joint were identified. In all 15 dissections (*100% [97.5CI: 78-100%]*), some or all branches from the femoral nerve pierced the iliopsoas muscle to reach the iliofemoral ligament and the hip joint. In four dissections (*27% [95% two-sided confidence interval (95 CI): 8-55%]*), we identified femoral nerve branches that winded around the lateral margin of the iliopsoas muscle and reached the hip joint capsule by crossing the iliopsoas plane.

In 10 dissections (*67% [95 CI: 38-88%]*), the spread of the injected dye was contained in a well-defined anatomical compartment deep to the iliopsoas muscle and superficial to the iliofemoral ligament. The compartment was delimited laterally by the rectus femoris muscle and its tendon and medially by the iliopectineal bursa, which was consistently tightly adherent to the iliofemoral ligament as well as to the tendon of the iliopsoas muscle. Five milliliter of dye injected into this compartment resulted in staining of all articular branches from the femoral nerve without staining any motor branches (Figure 2). In all 10 dissections, we observed spread of dye deep to the iliopsoas muscle and cranial to the inguinal ligament, but without staining of any intrapelvic nerves.

In one dissection (*7% [95 CI: 0.2-32%]*), the lateral part of the iliopsoas muscle was found to be firmly adherent to the iliofemoral ligament. The hip articular branches of the femoral nerve that pierced the iliopsoas were stained, but the adherence limited the lateral spread of dye and thereby prevented the staining of articular branches that winded around the lateral margin of the iliopsoas.

In four cadaver sides (*27% [95 CI: 8-55%]*), the dye was injected into the iliopectineal bursa. This resulted in rupture of the bursa: In three dissections (*20% [95 CI: 4-48%]*), the dye reached all the articular sensory branches and some of the motor branches of the femoral nerve. In one dissection (*7% [95 CI: 0.2-32%]*), the dye spread

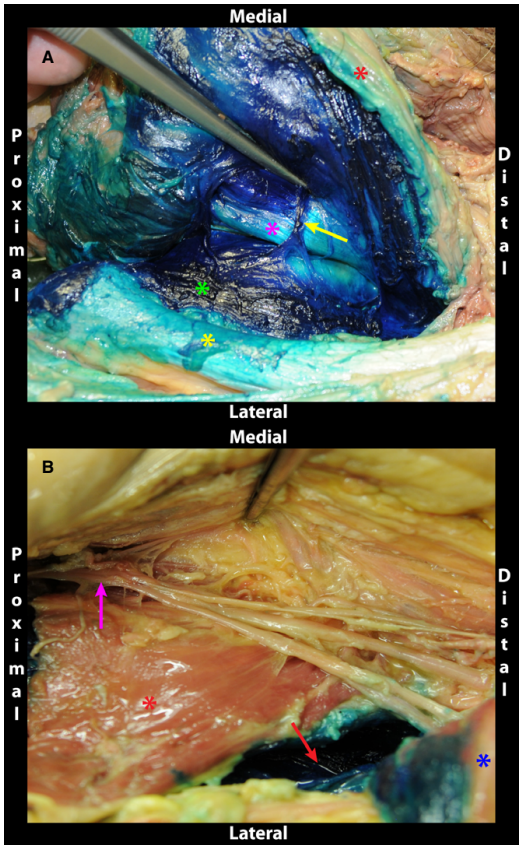

FIGURE 2 A, Spread of dye in the compartment between the iliopsoas muscle (red asterisk) and the iliofemoral ligament (green asterisk) colouring a branch from the femoral nerve to the hip joint (yellow arrow). The iliopsoas muscle is cut proximally and flipped medially. The iliopsoas compartment is bordered laterally by the rectus femoris muscle (yellow asterisk) and medially by the iliopectineal bursa deep to the tendon of the iliopsoas (magenta asterisk). B, The femoral nerve (magenta arrow) and its major mixed sensory and motor branches are not dyed after injection in the iliopsoas plane, as the iliopsoas muscle (red asterisk) obstructs the spread of dye (red arrow). The sartorius muscle (blue asterisk) is cut from its origin and flipped laterally. The faint staining of the distal branches of the femoral nerve is an artefact of the dissection [Colour figure can be viewed at wileyonlinelibrary.com]

laterally and reached some of the articular sensory branches as well as a small motor branch to the rectus femoris muscle.

4 | DISCUSSION

The present cadaver study demonstrated that 5 mL of dye injected in the iliopsoas plane between the iliopsoas muscle and the iliofemoral ligament exclusively stained all sensory branches from the femoral nerve to the hip joint in 10 of 15 injections. The employed technique entailed injection into the iliopectineal bursa (medially in the iliopsoas plane) in four of 15 injections, causing spread of dye to sensory branches as well as some of the motor branches of the femoral nerve. The sole unsuccessful injection, with spread to only some of the sensory branches of the femoral nerve, was due to adherences between the iliopsoas muscle and the iliofemoral ligament, which could not be explained by disease or previous surgery of the deceased.

Hip capsule nociceptors are almost exclusively located anterolaterally and anteromedially.[3,12] The anterolateral area of the capsule is innervated by the femoral nerve, while the anteromedial area is innervated by the obturator nerve, and the accessory obturator nerve—when present.[5,13,14] The majority of intracapsular nociceptors are located in the synovium and the labrum.[15,16] These structures are innervated by the obturator nerve and a branch from the nerve to the quadratus femoris (from the sciatic nerve).[16] It can be speculated that selective regional anaesthesia of the sensory branches from the femoral and obturator nerves innervating the hip joint, will alleviate most pain after total hip arthroplasty originating from the hip joint and its capsule.

We have previously demonstrated that a sub-pectineal obturator nerve block will reach all branches from the obturator nerve to the hip joint, including the accessory obturator nerve when present.[17] The only muscles innervated by the obturator nerve are hip adductors, and our research group has demonstrated that total knee arthroplasty patients with an obturator nerve block has the same ability to ambulate as control patients despite hip adductor paralysis due to obturator nerve blockade.[18] Femoral nerve block—on the contrary—increases the risk of fall after hip as well as knee arthroplasty[7,19] and thus prevents early ambulation. If regional anaesthesia were to be used for postoperative analgesia after total hip arthroplasty, it would be imperative to be able to block the sensory branches from the femoral nerve to the hip joint without causing motor blockade.

To the best of our knowledge, this is the first study to demonstrate that the spread of injectate in the plane between the iliopsoas muscle and the iliofemoral ligament effectively reaches all sensory hip branches of the femoral nerve without spread to the motor branches. These encouraging results leads us to hypothesise, that it might be possible to achieve blockade of all sensory branches from the femoral nerve to the hip joint with an injection of local anaesthetic in the iliopsoas plane. This nerve block could probably relieve pain from the hip joint without causing any motor blockade. We have coined this novel peripheral nerve block *the iliopsoas plane block*.

This study has certain limitations. First, postmortem changes might cause a different pattern of the spread of injectate compared to the living. Second, it is possible, that the dissection by itself has caused artefactual spread of methylene blue. This is always a potential bias in dissection studies. We endeavoured to minimise accidental spread of dye by meticulously performing the dissection as

described in the Methods section. Third, 27% of the injections were unintentionally made into the iliopectineal bursa. The iliopectineal bursa cannot be visualised with ultrasound under normal circumstances—not even in the living.[20] Our results indicate that an injection into the bursa entails spread not only to hip sensory branches from the femoral nerve but also spread to some of the motor branches, which would work against the intention of exclusive sensory blockade in the living patient of this technique. A possible alternative approach to avoid bursal injection would be to use a transverse orientation of the ultrasound probe combined with an insertion of the needle in the lateral aspect of the iliopsoas plane just deep to the lateral part of the iliopsoas muscle, which is lateral to the iliopsoas tendon and medial to the rectus femoris tendon.[21] This would minimise the risk of injecting into the iliopectineal bursa, as the iliopectineal bursa is consistently located between the iliopsoas tendon and the iliofemoral ligament in the most proximal and medial part of the space between the capsule and the muscle (ie the iliopsoas plane). Finally, this was an observational study without any blinding or randomisation.

Further studies are warranted to investigate an improved injection technique as described above, to demonstrate the spread of injectate in the iliopsoas plane in living humans, to confirm the lack of motor blockade from the iliopsoas plane block, as well as to confirm that the block indeed provides sensory nerve blockade of the hip joint in patients after hip surgery.

5 | CONCLUSIONS

This study demonstrates that dye injected in the anatomical plane between the iliopsoas muscle and the iliofemoral ligament—the iliopsoas plane—can spread to all articular sensory branches from the femoral nerve to the hip joint. The employed technique, however, caused 4 of 15 injections to be accidentally made into the iliopectineal bursa. One of 15 injections into the iliopsoas plane lateral to the bursa did not reach all branches from the femoral nerve due to fibrous adhesions. Assuming that these findings in cadavers translate to living humans, injection of local anaesthetic into the iliopsoas plane could provide sensory nerve blockade of the articular branches of the femoral nerve without any motor blockade. We have coined this nerve blockade the iliopsoas plane block.

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CONFLICTS OF INTEREST

The authors declare no conflicts of interest.

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Original article

An Obturator Nerve Block does not Alleviate Postoperative Pain after Total Hip Arthroplasty: a Randomized Clinical Trial

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ABSTRACT

Background and objectives A substantial group of patients suffer from moderate to severe pain following elective total hip arthroplasty (THA). Due to the complex innervation of the hip, peripheral nerve block techniques can be challenging and are not widely used. Since the obturator nerve innervates both the anteromedial part of the joint capsule as well as intra-articular nociceptors, we hypothesized that an obturator nerve block (ONB) would decrease the opioid consumption after THA.

Methods Sixty-two patients were randomized to receive ONB or placebo (PCB) after primary THA in spinal anesthesia. Primary outcome measure was opioid consumption during the first 12 postoperative hours. Secondary outcome measures included postoperative pain score, nausea score and ability to ambulate.

Results Sixty patients were included in the analysis. Mean (SD) opioid consumption during the first 12 postoperative hours was 39.9 (22.3) mg peroral morphine equivalents (PME) in the ONB group and 40.5 (30.5) mg PME in the PCB group (p=0.93). No difference in level of pain or nausea was found between the groups. Paralysis of the hip adductor muscles in the ONB group reduced the control of the operated lower extremity compared with the PCB group (p=0.026). This did, however, not affect the subjects' ability to ambulate.

Conclusions A significant reduction in postoperative opioid consumption was not found for active versus PCB ONB after THA.

Trial registration number NCT03064165 and 2017-000068-14.

INTRODUCTION

Patients frequently suffer from moderate to severe postoperative pain in the days following total hip arthroplasty (THA).[1] The pain is often alleviated by a multimodal regimen that includes paracetamol, non-steroidal anti-inflammatory drugs, and opioids.[2] However, the use of opioids is associated with an increased risk of postoperative complications, an increased cost of admission as well as an increased length of stay.[3 4] Furthermore, orthostatic hypotension and dizziness, induced by opioids,[5] may impair early postoperative ambulation, which is crucial in order to avoid postoperative complications.[6]

Peripheral blockade of the nerves that innervate the hip joint offers the potential for a reduced postoperative opioid consumption, but such nerve blocks might be conceived as challenging, as the hip joint is innervated by several nerves from the lumbosacral plexus.[7] However, the nociceptors of the hip joint capsule are primarily located in the anterior part of the capsule.[8 9] The anterolateral part of the hip capsule is innervated by the femoral nerve while the anteromedial part is innervated by the obturator nerve—and the accessory obturator nerve when present.[10] The majority of intra-articular nociceptors are found in the acetabular labrum.[9] These are innervated by the obturator nerve as well as a branch from the nerve to the quadratus femoris.[11] An obturator nerve block (ONB) could thus provide relief of postoperative pain after THA.

A femoral nerve block may reduce postoperative pain after THA,[12] but is also associated with increased risk of fall and delayed ambulation.[13] However, the effect of an isolated ONB has not previously been investigated for this procedure. We hypothesized that an ONB would decrease the opioid consumption during the first 12 hours after THA. We aimed to test our hypothesis in a randomized clinical trial in patients scheduled for primary THA.

METHODS

Ethics

This triple-blinded randomized clinical trial was conducted in accordance with the Declaration of Helsinki. The trial was monitored by the Good Clinical Practice Unit at Aalborg and Aarhus University Hospitals and was prospectively registered in ClinicalTrials.gov (NCT03064165, date of registration: 24 February 2017) and EudraCT (2017-000068-14, date of registration: 24 May 2017). Written informed consent was obtained from all subjects before inclusion. The investigational drug (bupivacaine-epinephrine) is approved for perineural administration by the Danish Medicines Agency.

Patient population

We included patients aged ≥18 years with ASA I–III status who were scheduled for primary THA in spinal anesthesia at the Elective Surgery Center, Silkeborg Regional Hospital, Silkeborg, Denmark. The Elective Surgery Center annually performs approximately 1000 total hip arthroplasties.

Exclusion criteria were inability to cooperate or communicate in Danish, scheduled discharge

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on the day of operation, neuropathy in the lower extremities, contraindications to non-steroidal anti-inflammatory drugs or dexamethasone, chronic pain treated with opioids, pregnancy, allergy towards the investigated medicinal products or current treatment with amiodarone, verapamil or corticosteroids.

Randomization and blinding

Subjects were randomized in blocks of 6 in a 1:1 ratio for postoperative analgesia with an ONB (ONB group) or placebo with a sham block (PCB group). Randomization was performed by a computer algorithm using the method of randomly permuted blocks. The hospital pharmacy of Aarhus University Hospital performed the randomization before initiation of the trial and delivered the project medication in blinded vials leaving investigators, staff and subjects blinded to group allocation. Subjects who were excluded after inclusion were replaced by new ones.

After completion of the last subject, the pharmacy released an anonymized randomization list revealing only the subjects' group allocation but not the assigned treatment of the groups. Statistical inference was thereby made on blinded groups. Only after intergroup statistical testing of all endpoints the groups were unblinded.

Interventions

Preoperative and intraoperative treatment followed a standard protocol which included peroral paracetamol 1 g and ibuprofen 400 mg 2 hours prior to surgery. Spinal anesthesia was induced with 2 mL isobaric bupivacaine 5 mg/mL. Dexamethasone 8 mg was administered intravenously at the beginning of surgery as a precautionary measure against postoperative nausea.

THA was performed by one of four orthopedic surgeons, who all used the posterior approach without injection of local infiltration analgesia.[14] Within 1 hour after end of surgery an ultrasound-guided proximal ONB was performed as previously described.[15] A linear transducer (X-Porte, Fujifilm SonoSite, Bothell, Washington, USA) was oriented in the transverse plane and placed in the inguinal crease. The tail of the transducer was tilted distal in order to visualize the pectineus muscle (medial to the femoral vessels) at its insertion at the superior pubic ramus superficial to the external obturator muscle. An 80 mm nerve block needle (SonoPlex, PAJUNK Medizintechnologie, Geisingen, Germany) was inserted in-plane from the lateral end of the transducer and advanced until the tip of the needle was inside the interfascial plane between the pectineus and the obturator externus muscles. The risk of intraneural needle tip placement was minimized by applying electrical nerve stimulation with a fixed current of 0.2 mA (Stimuplex HNS 11, B Braun, Melsungen, Germany).[16] In case of muscle twitches of the hip adductors, the needle was retracted until the twitches were not present. Fifteen milliliters of either bupivacaine 5 mg/mL with epinephrine 5 µg/mL or isotonic saline—depending on random group allocation—was injected in the interfacial plane between the pectineus and external obturator muscles.

Postoperative pain was treated with peroral paracetamol 1000 mg four times daily and peroral ibuprofen 400 mg three times daily. A mobile infusion pump (Rythmic Evolution, Micrel Medical Devices, Athens, Greece) was connected to an intravenous catheter for patient-controlled analgesia with bolus doses of morphine 0.05 mg/kg without background infusion. Lockout was 10 min and a maximum of four boluses per hour was allowed. Subjects were instructed to evaluate their pain on an 11-point numeric rating scale (as described below under outcome measures) and administer a bolus when experiencing pain above 3 at rest or above 5 during activity. Peroral oxycodone 5 mg was administered according to the same criteria if subjects had intolerable side effects of intravenous morphine. Nausea was treated with intravenous ondansetron 4 mg which was repeated after 30 min if necessary. Subjects with persistent nausea despite two doses of ondansetron were treated with intravenous dehydrobenzperidol 0.25 mg.

Pain at rest and during passive 90° flexion as the hip, as well as nausea was assessed 1, 2, 5, 7, and 24 hours after surgery. Five hours after surgery the subjects were ambulated by a physiotherapist using the ambulation test described below.

All subjects were interviewed by a medical doctor on the day after surgery, where any adverse events were assessed. After discharge from hospital the electronic health record was screened for additional adverse events. Adverse events were reported to the Danish Medicines Agency.

Data were collected by anesthetists and physiotherapists who were blinded to group allocation. Collection, management and storage of data were performed using REDCap electronic data capture tools hosted at the Department of Clinical Medicine, Aarhus University.[17]

Outcome measures

The primary outcome measure was cumulated opioid dose during the first 12 hours after surgery. Secondary outcome measures included cumulated opioid dose during 12–18 hours after surgery, time to first opioid request, pain score at rest and during passive 90° flexion of the hip as well as intensity of nausea at 1, 2, 5, 7 and 24 hours after surgery, number of episodes of emesis as well as cumulated dose of ondansetron and droperidol during the first 18 hours after surgery, time to discharge from the postanesthesia care unit (PACU) and time to discharge from the hospital, duration of the spinal anesthesia, quality of sleep during the first night after surgery, the ability to ambulate 5 hours after surgery as well as the level of muscular control of the operated leg during ambulation.

Opioid consumption was primarily recorded using a mobile infusion pump (Rythmic Evolution, Micrel Medical Devices) with morphine. Data were extracted using the monitoring software of the pump. Consumption of other opioids was collected from the electronic health record. Opioid consumption is reported as peroral morphine equivalents (PME).[18] Duration of spinal anesthesia was assessed using repeated pinpricks (Neurotips/Neuropen, Owen Mumford, Oxford, UK) on the anterior aspect of the mid-thigh of the operated leg every 15 min. The end of spinal anesthesia was defined as the time a subject could feel sharp pain at this location. Pain and nausea were recorded using an 11-point numeric rating scale from 0 (no pain/nausea) to 10 (worst pain/nausea imaginable). Episodes of emesis, doses of oxycodone, ondansetron and droperidol, as well as time of end of surgery and discharge from PACU and hospital were collected from the electronic health record. Sleep quality was assessed by the subject the day after surgery using a 3-point ordinal scale (1: sleep not interrupted; 2: sleep interrupted but not by pain; 3: sleep interrupted by pain). The ability to ambulate was assessed by physiotherapists using a standardized ambulation test developed for this trial based on the Cumulated Ambulation Score.[19] The test consisted of four consecutive activities. The first activity was ambulation from supine position (with the head of the bed elevated to 30°) to sitting position on the bedside. The second activity was ambulation from sitting to standing position. The third activity was walking at least 10 m supported by a high walker on wheels. The fourth activity was walking at least 10

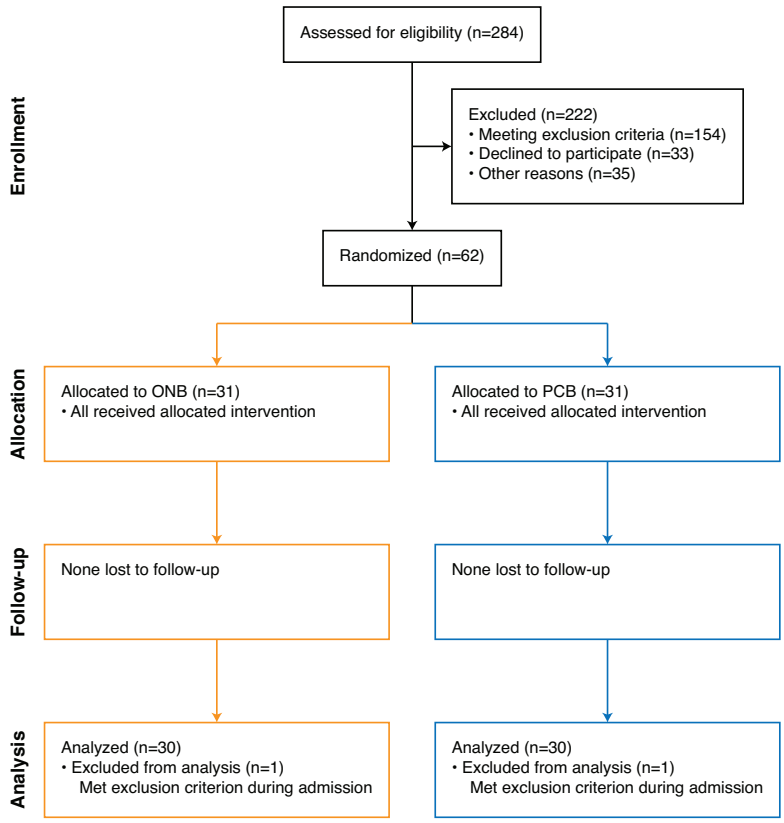

Figure 1 Consolidated Standards of Reporting Trials (CONSORT) flow diagram. ONB, obturator nerve block (orange); PCB, placebo (blue).

m supported by elbow crutches. For each activity, the physiotherapist evaluated the ability to perform the activity with or without physical support (0–2 points) as well as the muscular control of the operated leg (1–3 points). If the subject could not perform an activity, the test was terminated and the reason(s) for termination was noted. Each test produced two scores: an ambulation score and a muscular control score. The ambulation score was the sum of ambulation scores of all performed activities. The range of the ambulation score was thus 0–8 (0: subject was unable to ambulate to sitting position; 8: subject could walk with elbow crutches without personal physical support). The muscular control score was the median of muscular control scores of the completed activities. The range of the muscular control score was thus 0–3 (0: subject was unable to ambulate to sitting position; 3: subject had good muscular control of the operated leg during all activities). The test manual is found in the online supplementary material 1.

Sample size estimation and statistical analysis

Sample size was estimated using STATA software (V.14.2, StataCorp, College Station, Texas, USA). We aimed to show a significant difference in opioid consumption during the first 12 hours after surgery. Based on data from a non-blinded pilot study we estimated the mean opioid consumption (SD) to be 32 (31) mg PME in the ONB group and 56 (31) mg PME in the control group. The required sample size was thus 28 subjects per group with 80% power and a two-tailed α error of 5%. We recruited 30 subjects per group to provide a safety margin.

Statistical analysis was performed using STATA software (V.14.2, StataCorp). Normal distribution was assessed using quantile-quantile plots and histograms. Continuous data that followed a normal distribution were presented as mean (SD) and comparisons between groups were made using the Student's t-test, while skewed continuous data were presented as median (IQR) and intergroup comparisons were made using the Mann-Whitney U test. Ordinal data were presented as number of subjects (percentage) and compared between groups using the Mann-Whitney U test. Time-to-event data were presented as Kaplan-Meier plots and groups were compared using the log-rank test. A p value below 0.05 was considered statistically significant. For repeated measurements the Bonferroni correction would be applied in the case of p values below 0.05. Data were plotted using RStudio (V.1.0.143, RStudio, Boston, Massachusetts, USA) and the ggplot2 package (V.2.2.1, RStudio).

RESULTS

Sixty-two patients were included between September 2017 and June 2018. Two subjects were excluded after administration of project medication as they were unable to cooperate due to senile confusion not manifest prior to surgery. The trial was ended when 60 included subjects had completed follow-up. All 60 subjects were analyzed for the primary outcome (figure 1).

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Table 1 Demographic variables and perioperative characteristics

	ONB (n=30)	PCB (n=30)
Age (years)	68 (8.1)	72 (12.1)
Sex, F/M	14/16	11/19
BMI (kg/m^2)	27 (3.9)	26 (3.4)
ASA score I/II/III	8/21/1	5/23/2
Charlson Comorbidity Index	0 (0–0)	0 (0–0)
Surgeries per surgeon	13/3/1/13	12/4/0/14
Duration of surgery (min)	40 (12)	39 (13)

Values are mean (SD), count or median (IQR) as appropriate.
ASA, American Society of Anesthesiologists; BMI, body mass index; F, female; M, male; ONB, obturator nerve block; PCB, placebo.

Demographic variables and perioperative characteristics were similar in the study groups (table 1).

The mean (SD) opioid consumption during the first 12 postoperative hours was 39.9 (22.3) mg PME in the ONB group and 40.5 (30.5) mg PME in the PCB group (p=0.93). Further secondary endpoints are presented in tables 2 and 3. Time to first opioid request was similar in the two groups (p=0.40) (figure 2). No differences were observed in pain scores between the study groups at any time during follow-up (figure 3).

No severe adverse events occurred in either group.

DISCUSSION

In this triple-blinded randomized clinical trial we found that an ONB did not effectively reduce postoperative opioid consumption after THA. The only significant difference between subjects who received a postoperative ONB and PCB was a reduced muscular control of the operated leg during ambulation. However, that did not impair the subjects' ability to perform the standardized ambulation test 5 hours after surgery.

This is—to our knowledge—the first trial investigating the effect of an ONB as a single intervention on postoperative pain after THA. Other trials have previously investigated the effect of an ONB on other painful conditions in the hip joint: ONB guided by CT provided pain relief in 11 of 15 patients with osteoarthrosis, femoral head necrosis, developmental dysplasia, as well as pain following hip arthroplasty in a prospective observational study.[20] Another retrospective observational study found pain relief in patients with chronic hip pain after nerve blocks of the articular branches of both the obturator and the femoral nerves. However, the contributions to pain relief from each of the two different nerve blocks were not assessed.[21] An ONB as well as an ONB combined with a lateral femoral cutaneous nerve block has been shown to provide superior analgesia after hip fracture surgery compared with parenteral analgesia alone.[22] The same research group found that peripheral nerve blockade with either ONB combined with a lateral femoral cutaneous nerve block or a fascia iliaca compartment block provided better analgesia after hip fracture surgery than parenteral analgesia alone.[23] However, these trials employed landmark-guided nerve blocks, which today should be considered obsolete. Furthermore, the trials were non-blinded, which reduced the internal validity of the studies significantly. In addition, in hip fracture surgery with internal fixation technique, all the intra-articular nociceptors innervated by the obturator nerve remain as opposed to THA, where these intra-articular nociceptors are excised.

Table 2 Postoperative endpoints after total hip arthroplasty

	Hours after surgery	ONB (n=30)	PCB (n=30)	P value
Opioid consumption (mg PME)	12–18	12.5 (0–17.0)	10.1 (0–17.3)	0.34
Nausea (NRS11)	1	0 (0–0)	0 (0–0)	0.32
	2	0 (0–0)	0 (0–0)	0.32
	5	0 (0–0)	0 (0–0)	0.16
	7	0 (0–0)	0 (0–0)	0.59
	24	0 (0–0)	0 (0–0)	0.65
Emesis (frequency)	0–18	0 (0–0)	0 (0–0)	0.97
Cumulated dose of ondansetron (mg)	0–18	0 (0–0)	0 (0–0)	0.68
Cumulated dose of droperidol (mg)	0–18	0 (0–0)	0 (0–0)	–
Ambulation score (range: 0–8)	5	6 (4.5–8)	7 (6–8)	0.13
Muscular control score (range: 0–3)	5	2.5 (2–3)	3 (2.5–3)	0.026
Length of stay in PACU (min)	–	106 (38)	123 (49)	0.13
Length of stay at hospital (hour)	–	28 (26–29)	28 (26–29)	0.66
Duration of spinal anesthesia (min)	–	152 (38)	167 (44)	0.17

Values are mean (SD) or median (IQR) as appropriate. Length of stay and duration of spinal anesthesia begin at end of surgery.
NRS11, 11-point numeric rating scale (range: 0–10); ONB, obturator nerve block; PACU, postanesthesia care unit; PCB, placebo; PME, peroral morphine equivalents.

Table 3 Quality of sleep during first night after surgery

	ONB (n=30)	PCB (n=30)
Sleep undisturbed (%)	6 (20)	5 (17)
Sleep disturbed but not by pain (%)	21 (70)	18 (60)
Sleep disturbed by pain (%)	3 (10)	7 (23)
P value	0.28	

Self-reported quality of sleep during the first postoperative night after total hip arthroplasty. Count (with fraction of group). Comparison by Mann-Whitney U test.
ONB, obturator nerve block; PCB, placebo.

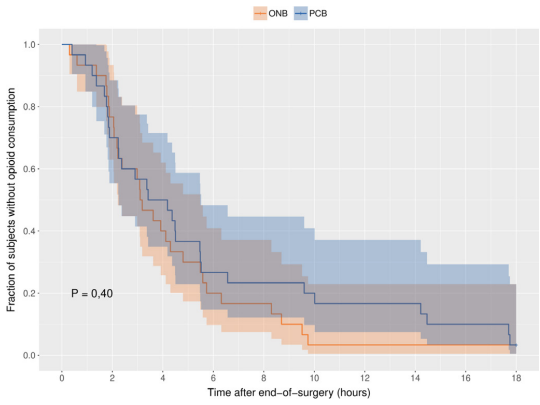

Figure 2 Kaplan-Meier plot of time from end of surgery to first opioid request (with 95% confidence intervals). Groups are compared using the log-rank test. ONB, obturator nerve block (orange); PCB, placebo (blue).

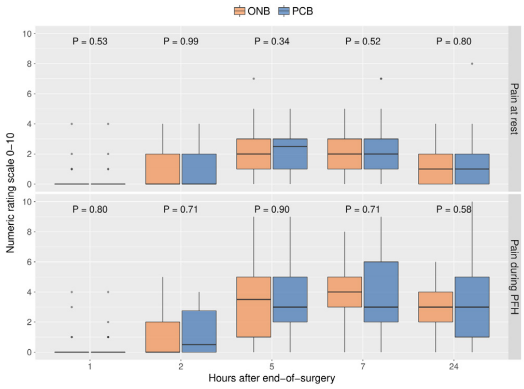

Figure 3 Pain at rest and during passive 90° flexion of the hip (PFH) at 1, 2, 5, 7 and 24 hours after total hip arthroplasty. Groups are compared using the Mann-Whitney U test. Numeric rating scale 0–10 (0: no pain; 10: worst pain imaginable). ONB, obturator nerve block (orange); PCB, placebo (blue).

The vast majority of intra-articular nociceptors in the hip joint are located in the acetabular labrum and the ligamentum teres, which as mentioned are innervated by the obturator nerve.[8] Since these structures are removed during THA, any postoperative pain mediated by the obturator nerve would be either acute neuropathic pain or nociceptive pain from the anteromedial part of the hip joint capsule. This makes the pain mechanism for postoperative pain after THA different compared with other painful conditions of the hip and other surgical procedures.

The lack of blinding in the previous studies, as well as the combination of multiple nerve blocks in some studies makes it difficult to assess if a single ONB indeed has an effect on hip-derived pain. Furthermore, the pain mechanisms in chronic hip pain and in postoperative pain after hip fracture surgery with internal fixation are different from that in postoperative pain after THA. Based on our results, the use of an ONB should probably not be applied as a standard for postoperative analgesia after THA with a posterior approach. As the anterior part of the hip joint capsule is incised with the anterior approach to THA, in close proximity to the area innervated by the obturator nerve, an ONB could be speculated to provide pain relief after this approach. This should be an aim for further clinical trials. Whether an ONB could be useful for pain relief in selected patients with persistent deep postoperative hip pain after posterior THA or preoperatively in hip fracture patients remains to be investigated in randomized clinical trials.

In order to provide effective regional anesthesia for patients undergoing THA further trials are needed to determine which nerves are involved in the mediation of postoperative pain. In our opinion, future studies should focus on the hip articular sensory branches of the femoral nerve that innervate the anterior hip joint capsule as well as the lateral femoral cutaneous nerve, the iliohypogastric nerve, and possibly the superior cluneal nerves that innervate the area of the surgical incision.[24 25] A combination of peripheral blocks that anesthetize these nerves could possibly alleviate postoperative pain after THA and thus minimize the need for opioid treatment.

This trial has some limitations. First, since the nerve blocks were performed after surgery, while the subjects had active spinal anesthesia, it was not possible to test the effect of the ONB (decreased strength of hip adduction) immediately after nerve block performance. We deliberately chose not to assess the ONB after cessation of the spinal anesthesia in order to reduce the risk of unblinding subjects in the ONB group as well as to avoid the risk of hip luxation theoretically associated with testing of hip adductor strength. The significant reduction of motor control in the ONB group indicates that a significant fraction of subjects in the ONB group indeed had an ONB, although the motor control score was not intended as an assessment of the nerve block. Moreover, we used the exact same robust easy-to-perform method for ultrasound-guided subpectineal ONB as in a previous trial, where the efficacy of the technique was documented.[15] Second, even though we took meticulous precautions to keep patients and staff blinded, some subjects may have become aware, that they had received an active ONB due to paralysis of the hip adductors. Despite this risk of unblinding, we found no difference between the groups in any relevant endpoints. Third, the study was not powered to detect small reductions in opioid consumption as a result of an ONB. However, as the mean difference (with 95% confidence interval) in opioid consumption during the first 12 postoperative hours was only 0.6 mg PME (−14.4 to 13.3) a clinically significant effect of an ONB on pain relief after THA with a posterior approach is unlikely.

In conclusion, we found no effect of an ONB on pain after THA with a posterior approach. Future clinical trials regarding peripheral nerve blocks for this procedure may profitably focus on motor-sparing blockade of the hip articular sensory branches of the femoral nerve as well as blockade of the nerves that innervate the area of the surgical incision.

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Contributors Conception or design of the work: NDN, CR, LC, JB, LRM, JRL, TDN, KS, TFB. Data collection: NDN, CR, LC. Data analysis and interpretation: NDN, CR, JB, TDN, TFB. Drafting the article: NDN. Critical revision of the article: CR, LC, JB, LRM, JRL, TDN, KS, TFB. Final approval of the version to be published: NDN, CR, LC, JB, LRM, JRL, TDN, KS, TFB.

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Disclaimer The content is solely the responsibility of the authors.

Competing interests None declared.

Patient consent for publication Not required.

Ethics approval Ethics Committee of the Central Denmark Region (1-10-72-90-17), Danish Medicines Agency (2017-000068-14), Danish Data Protection Agency (1-16-02-182-17).

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The Iliopsoas Plane Block: Selective Sensory Blockade of the Hip Articular Branches of the Femoral Nerve – a Blinded and Randomized Trial in Healthy Volunteers

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Conflicts of Interest:

The authors declare no conflicts of interest.

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ABSTRACT

Background and objectives

A femoral nerve block relieves postoperative pain after total hip arthroplasty, but its use is controversial due to motor paralysis accompanied by an increased risk of fall. Assumedly, the iliopsoas plane block (IPB) targets the hip articular branches of the femoral nerve without motor blockade. However, this has only been indicated by a cadaver study. Therefore, we designed the present volunteer study.

Methods

Twenty healthy volunteers were randomly allocated to blinded paired active vs. sham IPB. The primary outcome was reduction of maximal force of knee extension after IPB compared to baseline. Secondary outcomes were reduction of maximal force of hip adduction, frequency of cutaneous anesthesia of the thigh, and the pattern of injectate spread.

Results

Mean (confidence interval (CI)) change of maximal force of knee extension from baseline to one hour after IPB was -9.7 N (-22, 3.0) (p = 0.12). Mean (CI) change of maximal force of hip adduction was 0.75 N (-12, 14) (p = 0.91). No subjects had cutaneous anesthesia after IPB. The injectate was consistently observed in an anatomically well-defined plane between the intra- and extrapelvic components of the iliopsoas muscle anterior to the hip joint.

Conclusions

We observed no significant reduction of maximal force of knee extension after IPB in volunteers. The injectate was consistently contained in a fascial compartment previously shown to contain sensory branches from the femoral nerve to the hip joint. Further clinical trials are needed to assess the postsurgical analgesic properties of the IPB in patients.

INTRODUCTION

A femoral nerve block can relieve postoperative pain after total hip arthroplasty,[1] but its use is controversial, as it impedes ambulation and increases the risk of fall due to motor paralysis.[2,3] The sensory branches of the femoral nerve that innervates the hip joint leave the nerve either proximal or distal to the inguinal ligament.[4] At this level the femoral nerve is located superficial to the the iliopsoas muscle and deep to the iliac fascia. To reach the hip joint the articular branches of the femoral nerve either pierce the iliopsoas muscle or wind around its anterolateral margin before innervating the anterolateral part of the hip joint capsule.[4-6]

In a cadaver study, we have shown, that injection of 5 mL of dye in the iliopsoas plane between the iliopsoas muscle and the hip joint capsule - just lateral to the iliopsoas tendon and the iliopectineal bursa - will spread throughout the iliopsoas plane to all sensory branches of the femoral nerve innervating the hip joint.[7] This indicates that injection of local anesthetic in the iliopsoas plane - an iliopsoas plane block (IPB) - will selectively target the sensory femoral nerve branches innervating the hip joint thereby avoiding quadriceps femoris motor blockade. The aim of the present study is to assess whether the novel IPB causes motor blockade in living humans. Further, we aimed to assess the pattern of injectate spread in the living using magnetic resonance imaging (MRI).

METHODS

Ethics

This double-blinded randomized volunteer trial was conducted in accordance with the Declaration of Helsinki and approved by the Central Denmark Region Committees on Health Research Ethics (1-10-72-167-18), The Danish Medicines Agency (2018-000089-12), and the Danish Data Protection Agency (1-16-02-83-18). The trial was monitored by the Good Clinical Practice Unit at Aalborg and Aarhus University Hospitals and was prospectively registered in EudraCT (2018-000089-12, date of registration: 24/04/2018). Written informed consent was obtained from all subjects prior to inclusion. Experimental off-label use of perineural administration of MRI contrast (gadoteric acid) was approved by the Danish Medicines Agency.

Subjects

The primary investigator (NDN) recruited healthy volunteers ≥ 18 years with an American Society of Anesthesiologists physical status classification score (ASA) I-II from a Danish website dedicated to recruit volunteers for research.

Exclusion criteria were inability to cooperate or communicate in Danish, lower limb neuropathy, chronic opioid use, weekly alcohol-consumption ≥ 14 units for females and ≥ 21 units for males, obesity (body mass index > 25 kg m^{-2}), claustrophobia, pregnancy, allergy to the investigational drugs and daily consumption of medicine except oral contraceptives.

Interventions

The trial was performed at the Department of Radiology, Aarhus University Hospital. After informed consent, two physiotherapists performed baseline motor and sensory tests. Pain sensation was tested bilaterally by repeated standardized 40-gram pinpricks (Neurotips/Neuropen, Owen Mumford Ltd., Oxford, UK) in the sensory territories of the lateral femoral cutaneous nerve of the thigh as well as the anterior femoral cutaneous nerves from the femoral nerve (the proximal medial edge of the patella).[8] Normal sensation was defined as sharp pain elicited by pinprick repeated maximally 5 times.

Maximal isometric force of knee extension was tested with the volunteer sitting on the edge of an examination table. A broad band fixed both thighs to the table. A circular broad band around each lower limb – one at a time – 10 cm above the ankle was stretched by knee extension thereby applying force against a dynamometer (PowerTrackII/Commander, JTech Medical Industries, Salt Lake City, Utah, USA) fixed between the other end of the circular band and the frame of the examination table.[9] Maximally 5 seconds of isometric contraction was followed by 30 seconds of rest and repeated 4 to 10 times until the maximal force was

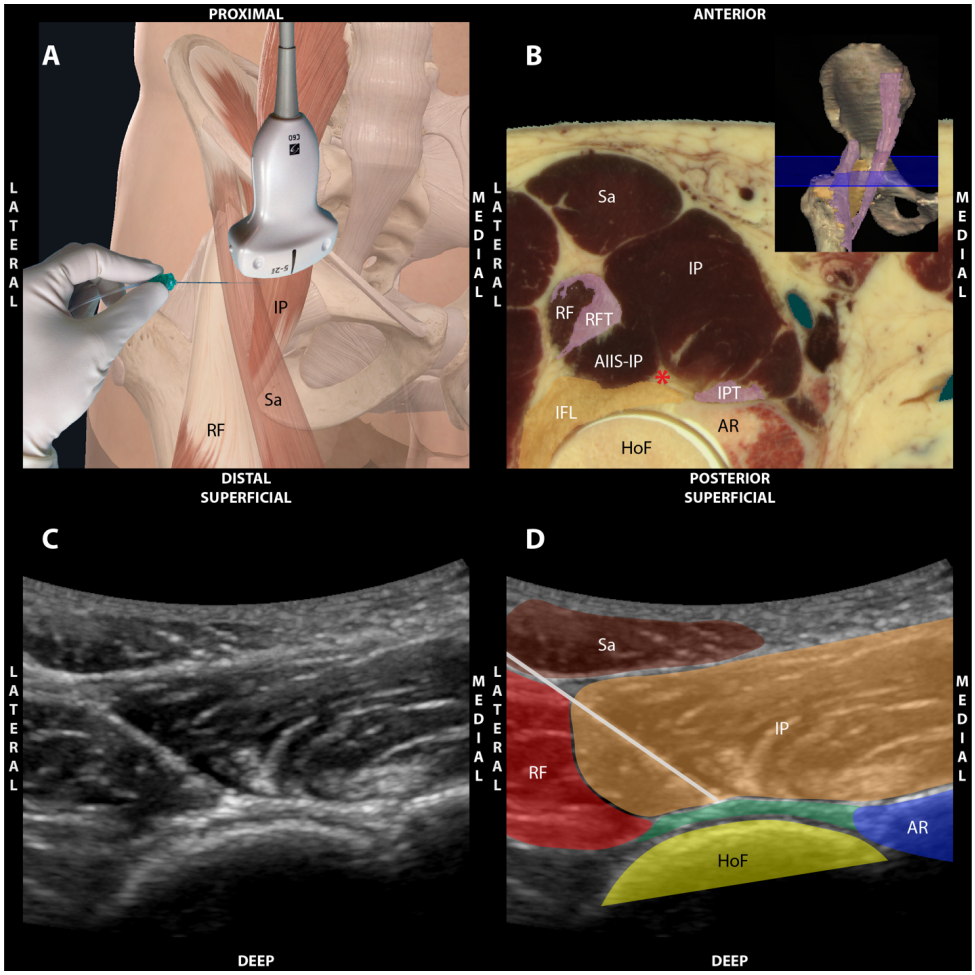
reduced compared to the preceding measurement. Standardized performance was endeavored by playing a recorded audio instruction for the volunteers during each session.

Maximal isometric force of hip adduction was tested with the volunteer supine. The examiner kept the handheld dynamometer immobile against the leg 5 cm proximal to the medial malleolus.[10] Maximal isometric force of hip adduction was determined as described above.

The volunteers were placed supine on an MRI compatible table. Intravenous access was established and vital signs were monitored with three-lead electrocardiogram, pulse oximetry, and non-invasive blood pressure measurement.

All nerve blocks were performed by a regional anesthesia expert (TFB). Blinded bilateral (active vs. placebo) iliopsoas plane blocks were randomly allocated to left or right. The nerve blocks were guided by ultrasound (X-porte ultrasound system, Fujifilm Sonosite, Bothell, Washington, USA). A curvilinear 5-2 MHz transducer (C60XP, Fujifilm Sonosite, Bothell, Washington, USA) was oriented in the transverse plane just caudad to the anterior superior iliac spine. The transducer was then rotated 20-30 degrees counterclockwise on the right side and clockwise on the left side, and parallel shifted along the inguinal ligament until the hip joint was identified where the head of femur dived deep to the acetabular rim (Figure 1). The skin was disinfected and an 80 mm, 22-gauge nerve block needle (Ultraplex, B.Braun, Melsungen, Germany) was advanced in-plane from the lateral side, until the tip of the needle was located in the iliopsoas plane between the iliopsoas muscle and the iliofemoral ligament just lateral to the iliopsoas tendon (Fig. 1C-D). Project medication was injected in the iliopsoas plane and appropriate spread of injectate deep to the iliopsoas muscle was verified in real-time by ultrasound. The study drug was 5 mL of lidocaine-epinephrine 18 mg/mL + 5 µg/mL mixed with gadoteric acid 1,75 mg/mL randomly allocated to either left or right side. Five mL of gadoteric acid 1,75 mg/mL was administered on the contralateral side.

Figure 1



A: Positioning of probe and insertion of the needle for the iliopsoas plane block. The needle trajectory traverses the sartorius (Sa) and iliopsoas (IP) muscles. The target is deep to the IP medial to the tendon of the rectus femoris muscle (RF). Modified excerpt from Complete Anatomy '19 with permission from 3D4Medical (www.3d4medical.com). B: Transverse section of the target area (red asterisk) between the IP and the iliofemoral ligament (IFL; yellow). The deeper lying head of femur (HoF) and acetabular rim (AR) are important ultrasonographic landmarks. The lateral spread of injectate is limited by the rectus femoris muscle (RF), its tendon (RFT; purple) and the part of the iliopsoas muscle that origins from the anterior inferior iliac spine (AIIS-IP). The medial spread is limited by the iliopsoas tendon (IPT; purple) and the underlying iliopectineal bursa. Insert showing level of section as well as IFL (yellow), IPT (right, purple), and the RFT (left, purple). Modified excerpt from VH Dissector with permission from Touch of Life Technologies Inc. (www.toltech.net). Built on real anatomy from the National Library of Medicines Visible Human Project. C: Ultrasonogram with needle insertion for iliopsoas plane block. D: Same as C with explanatory panels: The HoF (yellow) dives deep to the AR (blue). The nerve block needle (grey) is advanced through the Sa (brown) and IP (orange) until the tip is above the iliofemoral ligament (green) medial to the RFM (red).

The subjects were transferred to a 3T MRI scanner (Philips Achieva 3.0T dstream, Koninklijke Philips Electronics, Eindhoven, The Netherlands), where 3D gradient echo T1-weighted (in-phase, out-of-phase, water and fat mDixon images) and T2-weighted turbo spin echo sequences were obtained.

Finally, sensory-motor testing was repeated as described above at one hour after nerve block performance.

Before being discharged the volunteers were assessed for adverse events.

Outcome measures

The primary outcome measure was reduction of maximal force of knee extension one hour after IPB compared to baseline. Secondary outcome measures included the following clinical measures: Reduction of maximal force of hip adduction one hour after IPB compared to baseline, and maximal force for active vs. sham one hour after IPB for knee extension as well as hip adduction, anesthesia for pinprick on the lateral thigh and the proximal medial corner of patella one hour after IPB compared to baseline. Furthermore, the pattern of spread of injectate was assessed on MRI scans as binary outcomes as follows: Spread of injectate inside the iliopsoas plane, spread of injectate between the iliofemoral ligament and the iliopsoas muscle, spread of injectate to the interfacial plane between the pectineus and the external obturator muscle, spread of injectate to the superficial surface of the iliopsoas muscle, intraarticular spread of injectate in the hip joint, spread of injectate to the posterior side of the hip joint capsule, and spread of injectate to the iliopectineal bursa. All MRI-related outcomes were evaluated independently by two observers. In case of disagreement an experienced MRI-radiologist made the final decision.

Randomization and blinding

Subjects were randomized in a 1:1-ratio for active IPB on either the right or left side; on the contralateral side a sham IPB was performed. The randomization sequence was generated using STATA software (version 14.2, StataCorp, College Station, Texas, USA) by an investigator without further involvement in the trial. Project medication was prepared in blinded syringes by two investigators without further connection to the trial leaving subjects, investigators, and assistants blinded to allocation.

The group allocation of MRI scans remained blinded until the statistical analysis was completed.

Sample size estimation and statistical analysis

The study was designed as a non-inferiority-study. In a previous non-published pilot study, we found a standard deviation for the primary outcome measure (reduction of maximal power of knee extension from baseline to after block) of 40 N. The non-inferiority-limit was arbitrarily set to 40 N based on data from said pilot study. To rule out a difference greater than the non-inferiority limit with a power of 90 % (1 - β) and a level of significance (α) of 0.05 a sample size of 18 subjects would be needed.[11] To avoid decreased power due to dropouts we chose a sample size of 22 subjects.

Statistical analysis was performed using STATA software (version 14.2, StataCorp, College Station, Texas, USA). Normal distribution was assessed using quantile-quantile plots. Continuous data that followed a normal distribution were presented as mean (confidence interval (CI)), and comparisons between groups were made using the Student *t*-test, while skewed continuous data were presented as median (inter-quartile range (IQR)), and intergroup comparisons were made using the Wilcoxon signed-rank test. Paired categorical data were presented as number (percentage of all subjects) and were compared using McNemars test. Data regarding spread of MRI contrast were presented as number (percentage of all injections). No statistical inference was made regarding the MRI data. A *p*-value below 0.05 was considered statistically significant. Data were plotted using RStudio (version 1.0.143, RStudio inc., Boston, Massachusetts, USA) and the ggplot2 package (version 2.2.1, RStudio inc., Boston, Massachusetts, USA).

RESULTS

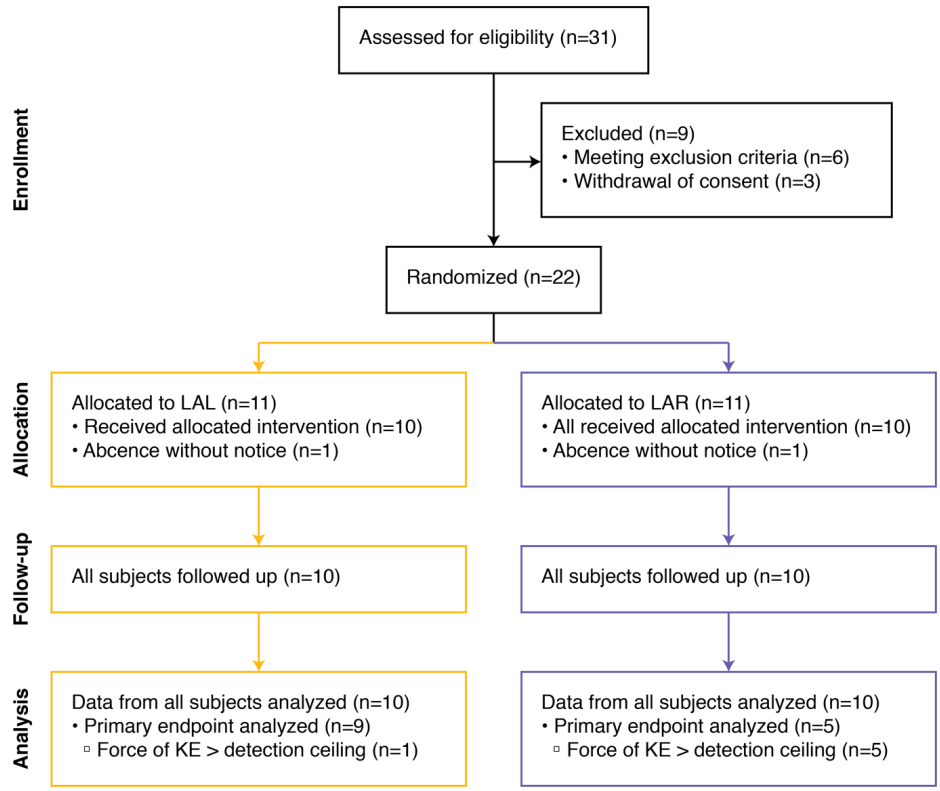
Twenty-two volunteers were enrolled in the study. Two enrolled volunteers did not show up on the day of trial and were excluded. The 20 remaining volunteers completed the trial per protocol on the 9th and 10th of June 2018. The trial ended as scheduled per protocol. Six volunteers performed maximal force of isometric knee extension that exceeded the scale of the dynamometers (≈ 500 N) at baseline. Four of these volunteers also performed a maximal force of isometric knee extension above the detection limit one hour after IPB, one subject performed a measurable maximal force of isometric knee extension (below the detection ceiling) bilaterally one hour after IPB and one subject only performed a maximal force of isometric knee extension below the detection ceiling on the side with active IPB. The data of these six subjects did not contribute to the comparison of maximal force of knee extension before and after IPB. Fourteen subjects were thus analyzed for the primary outcome (Fig. 2). Demographic variables are presented in Table 1.

Table 1. Demographic variables

	Volunteers (n = 20)
Age, years, median (range)	25 (20-62)
Sex, F/M, count	9/11
BMI, kg/m^2, mean (CI)	22.1 (21.2, 22.9)
ASA-score, I/II, count	17/3

Demographic variables for volunteers. M: male; F: female; BMI: body mass index; CI: 95 % confidence interval.

Figure 2

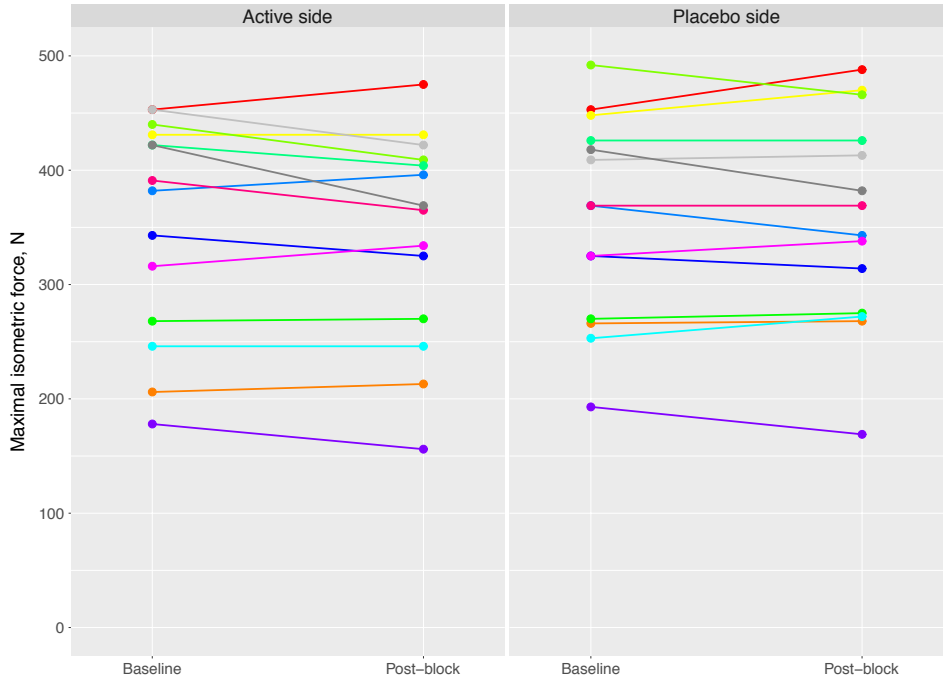


CONSORT (CONsolidated Standards Of Reporting Trials) flow diagram. LAL: Local Anesthetic Left side (yellow); LAR: Local Anesthetic Right side (purple); KE: Knee Extension.

The mean (CI) paired difference of maximal force of knee extension between baseline and one hour after active IPB was -9.7 N (-22, 3.0) (p = 0.12) (Figure 3). The mean (CI) paired difference between active and sham IPB was -8.1 N (-18, 2.5) (p = 0.12). The mean (CI) maximal force of knee extension (n = 14) was 354 N (299, 409) at baseline. Thus, the size of the statistically insignificant mean reduction from baseline to one hour after IPB was 2.7%.

The mean (CI) paired difference of maximal force of hip adduction from baseline to one hour after active IPB was 0.75 N (-12, 14) (p = 0.91). The mean (CI) paired difference between active and sham IPB was 3.3 N (-7.4, 14) (p = 0.53). The mean (CI) maximal force of hip adduction was 120 N (102, 138) at baseline.

Figure 3



Maximal isometric force of bilateral knee extension (N) before (Baseline) and one hour after (Post-block) performance of iliopsoas plane block (IPB) in 14 volunteers. Subjects were randomized to receive an active IPB on either left or right side along with a contralateral sham IPB (Placebo). The individual subjects are identified by colors.

All subjects had intact bilateral sensibility for pin-prick on the lateral thigh and proximal to the medial corner of the base of patella one hour after IPB.

The observed patterns of spread of injectate are presented in Table 2. Typical patterns of spread are presented in Figures 4 and 5. Both injections in one volunteer did present minor spread to the anterior surface of the iliopsoas muscle, with an observed reduction of maximal force of knee extension of 18 N (4.3 %) from baseline to one hour after active IPB. Intra-articular spread of injectate was observed two times, but was not accompanied by adverse events.

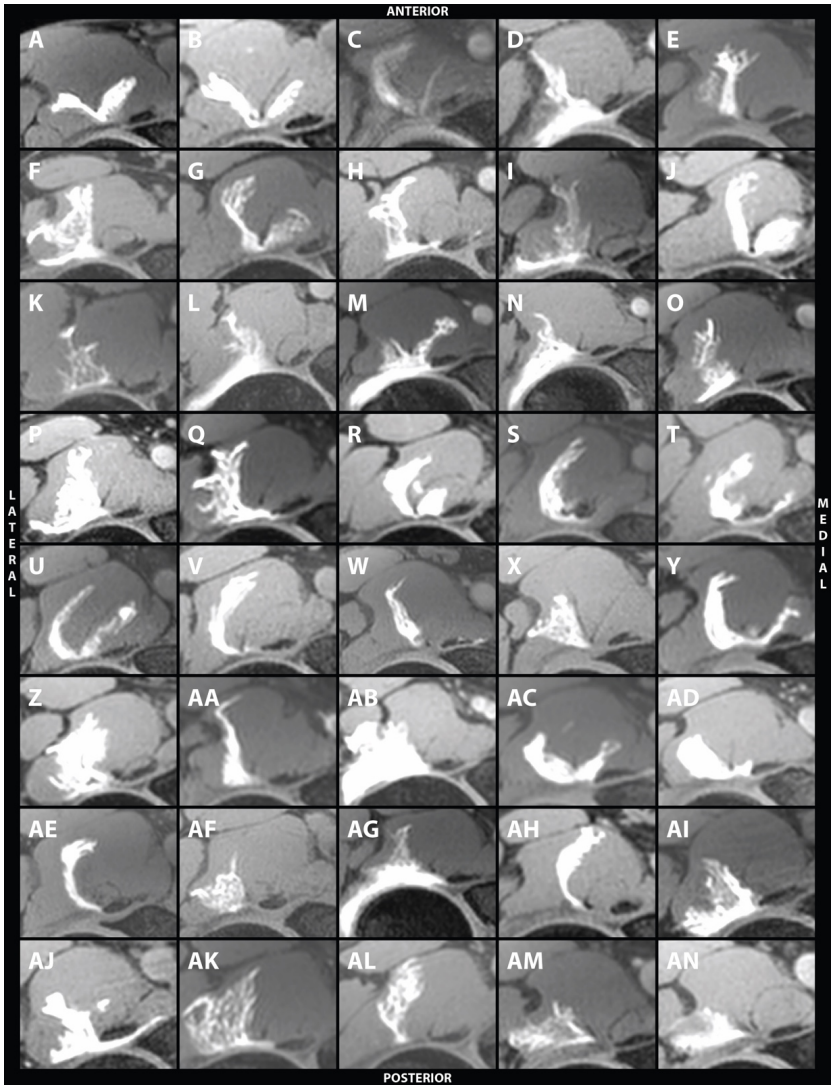
No subjects experienced severe adverse events during the trial.

Table 2. Spread of injectate.

	All injections (n = 40)
Spread inside the iliopsoas plane	40 (100 %)
Spread between iliopsoas muscle and iliofemoral ligament	13 (33 %)
Spread to iliopectineal bursa	11 (28 %)
Medial spread – between pectineus and external obturator muscles.	0 (0 %)
Superficial spread – to the superficial surface of the iliopsoas muscle.	2 (5 %)
Intra-articular spread – deep to the hip joint capsule	2 (5 %)
Deep spread – posterior to the hip joint but outside the hip joint capsule	0 (0 %)

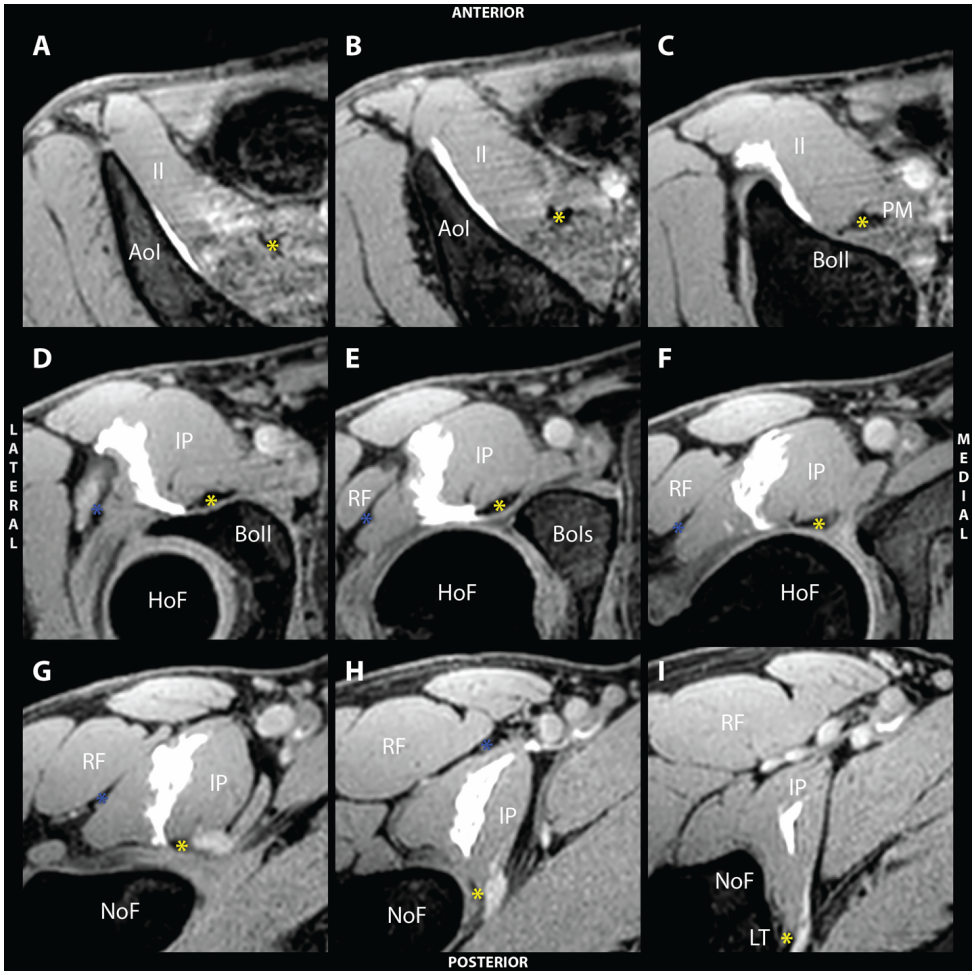
Spread of injectate following injection for iliopsoas plane block. Count (percentage of all injections).

Figure 4



Patterns of injectate spread from bilateral iliopsoas plane blocks in 20 volunteers visualized on transverse T1-weighthed MRI slices at the approximate level of the center of the head of femur. Anatomy corresponding to Fig. 1B. Injectate spread patterns from the right and left side from each volunteer is presented in pairs (A and B, C and D etc.). Left side slices (B, D etc.) are mirrored horizontally for ease of comparison. A-AN: In all subjects the injectate did spread up through the iliopsoas muscle between the lateral smaller component of the iliopsoas muscle (originating from the anterior inferior iliac spine) associated with the tendon of the rectus femoris muscle and the iliopsoas muscle's medial main component of intrapelvic origin. Medial spread was in most cases limited by the iliopsoas tendon. D, F, I, L, N, P, AB, AI, AJ, AK, AM, AN: Spread of injectate between the iliopsoas muscle and the hip joint capsule. T, AJ: Spread of injectate through the iliopectineal bursa deep to the iliopsoas tendon to the medial aspect of the iliopsoas muscle. M, AG: Intra-articular spread of injectate.

Figure 5



Typical pattern of injectate spread inside the iliopsoas plane in a single subject (corresponding to Fig. 4AL) visualized on transverse T1-weighthed MRI slices. The distance between slices is 13 mm. A: Most proximal slice. Fifty-five mm proximal to the greater trochanter. B-H: Intermediate slices. I: Most distal slice. Fourty-eight mm distal to the greater trochanter. Il: Iliacus muscle (m.); AoI: Ala of Ilium; PM: Psoas Major m.; BoIl: Body of Ilium; IP: Iliopsoas m.; HoF: Head of Femur; RF: Rectus Femoris m.; BoIs: Body of Ischium; NoF: Neck of Femur; LT: Lesser Trochanter. Blue asterisk: rectus femoris tendon; Yellow asterisk: iliopsoas tendon.

DISCUSSION

In this double-blinded randomized volunteer trial, no significant reduction of maximal muscle force of knee extension was observed after IPB. Accordingly, no subjects experienced lower limb weakness when standing up from sitting position one hour after IPB performance.

Intraarticular spread of injectate was observed in 5% of IPB injections (2/40). Thus, it can be speculated that application of IPB in prosthetic hip surgery would require sterile precautions similar to e.g. subarachnoid or epidural injections.

The injectate from the IPB consistently spreads in a well-defined fascial plane extending from the anterior inferior iliac spine (AIIS) to the minor trochanter (Fig. 4 and 5). We have coined this the "iliopsoas plane": The anteromedial wall is the extrapelvic part of the IlioPsoas muscle with IntraPelvic origin (IP-IP). Above the level of the AIIS, the posterolateral wall of the iliopsoas plane is the ala and corpus of ilium (Fig. 5A-C). Between the AIIS and the lesser trochanter, the posterolateral wall of the iliopsoas plane is made by the part of the IlioPsoas muscle that originates from AIIS (AIIS-IP) as well as the iliofemoral ligament of the hip joint (Fig. 5D-I). The AIIS-IP extends from the AIIS to the lesser trochanter.[12]

In a recent cadaver dissection study from our research group, we observed that spread of injectate with the IPB technique was confined to the iliopsoas plane and consistently stained all sensory branches from the femoral nerve to the hip joint.[7]

Since we published our first description of the IPB, another interesting nerve block has been proposed with the aim of anesthetizing the hip articular sensory branches of the femoral nerve; the novel PENG block, which was presented in a brief technical report along with a case series of five patients scheduled for hip fracture surgery.[13] The target of the PENG block is to inject 20 mL between the iliopsoas tendon anteriorly and the superior pubic ramus between the AIIS and the iliopubic eminence posteriorly. However, injection deep to the iliopsoas tendon is probably not ideal when targeting the hip articular branches of the femoral nerve as the iliopectineal bursa is located at the target of injection between the iliopsoas tendon and the underlying bone and hip joint capsule.[7,14] Furthermore, the PENG block is probably solely targeting the branches that leave the femoral nerve cranial to the inguinal ligament (high branches),[4] while the low branches that leave the femoral nerve distal to the inguinal ligament will most likely not be reached by the PENG block. However, further trials are needed to assess the efficacy of the PENG block regarding effect and spread of injectate.

The present study has some limitations: First, the IPB selectively anesthetizes the sensory hip articular branches of the femoral nerve. Consequently, the analgesic effect cannot be assessed in healthy volunteers without hip pain. That would require relevant clinical studies with patients. Second, we excluded six volunteers from the analysis of the primary outcome due to supramaximal performance of force before IPB that exceeded the range of the utilized dynamometers. This inherently increases the risk of type II error. However, the difference in maximal force before and after IPB in the remaining volunteers was relatively small (2.7%) and considered to be without clinical relevance. All of the six excluded volunteers subjectively assessed no difference in motor control between the limbs after IPB as well as before vs. after IPB. Third, most of the volunteers were young and healthy and had normal BMI in contrast to many patients scheduled for major hip surgery. Clinical trials are required to assess the efficacy of the IPB in older, obese, comorbid patients after surgery.

In conclusion, we found no statistically or clinically significant reduction of force of knee extension due to the IPB. The block resulted in spread of injectate throughout the iliopsoas plane previously shown to contain all sensory femoral nerve branches innervating the hip joint. Clinical trials are warranted to assess the effect of the IPB on postoperative pain after major hip surgery.

ACKNOWLEDGEMENTS

The authors would like to thank Jennie Maria Christin Strid, MD, PhD, for her help with randomization and blinding.

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APPENDICES

The following documents are attached as appendices.

- **Appendix 1:** Declaration of co-authorship, Article I (p. 89)
- **Appendix 2:** Declaration of co-authorship, Article II (p. 91)
- **Appendix 3:** Declaration of co-authorship, Article III (p. 93)
- **Appendix 4:** Test manual for the ambulation test used in Study II.
  Published as supplementary digital content with Article II (p. 95)
- **Appendix 5:** Letter-to-the-editor regarding comparison of PENG block and IPB.
  Accepted for publication in Regional Anesthesia and Pain Medicine. (p. 98)

Appendix 1 - Declaration of co-authorship, Article I (1/2)

AARHUS UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Niels Dalsgaard Nielsen

This declaration concerns the following article/manuscript:

Title:	Spread of injectate around hip articular sensory branches of the femoral nerve in cadavers
Authors:	Nielsen ND, Greher M, Moriggl B, Hoermann R, Nielsen TD, Børglum J, Bendtsen TF

The article/manuscript is: Published ☒ Accepted ☐ Submitted ☐ In preparation ☐

If published, state full reference: Acta Anaesth. Scand. 2018; 62(7):1001–1006. DOI: 10.1111/aas.13122

If accepted or submitted, state journal:

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution
F. N/A

Element	Extent (A-F)
1. Formulation/identification of the scientific problem	C
2. Development of the method	C
3. Planning of the experiments and methodology design and development	B
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	C
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	A
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

Appendix 1 - Declaration of co-authorship, Article I (2/2)

AARHUS UNIVERSITY

Signatures of first- and last author, and main supervisor

Date	Name	Signature
15/10-18	Niels D. Nielsen (first author)	
21/10-18	Thomas F. Bendtsen (last author and supervisor)	

Date: 15/10-18

Signature of the PhD student

Appendix 2 - Declaration of co-authorship, Article II (1/2)

AARHUS UNIVERSITY

Declaration of co-authorship concerning <u>article for PhD dissertations</u>

Full name of the PhD student: Niels Dalsgaard Nielsen

This declaration concerns the following article/manuscript:

Title:	An Obturator Nerve Block does not Alleviate Postoperative Pain after Total Hip Arthroplasty – a Randomized Clinical Trial
Authors:	Nielsen ND, Runge C, Clemmesen L, Børglum J, Mikkelsen LR, Larsen JR, Nielsen TD, Søballe K, Bendtsen TF

The article/manuscript is: Published ☐ Accepted ☒ Submitted ☐ In preparation ☐

If published, state full reference:

If accepted or submitted, state journal: Regional Anesthesia and Pain Medicine

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution
F. N/A

Element	Extent (A-F)
1. Formulation/identification of the scientific problem	C
2. Development of the method	B
3. Planning of the experiments and methodology design and development	B
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	B
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	A
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

Appendix 2 - Declaration of co-authorship, Article II (2/2)

AARHUS UNIVERSITY

Signatures of first- and last author, and main supervisor

Date	Name	Signature
15/10-18	Niels D. Nielsen (first author)	
21/10-18	Thomas F. Bendtsen (last author and supervisor)	

Date: 15/10-18

Signature of the PhD student

Appendix 3 - Declaration of co-authorship, Article III (1/2)

AARHUS UNIVERSITY

Declaration of co-authorship concerning article for PhD dissertations

Full name of the PhD student: Niels Dalsgaard Nielsen

This declaration concerns the following article/manuscript:

Title:	The Iliopsoas Plane Block: Selective Sensory Blockade of the Hip Articular Branches of the Femoral Nerve – a Blinded and Randomized Trial in Healthy Volunteers.
Authors:	Nielsen ND, Madsen MN, Østergaard HK, Bjørn S, Pedersen EM, Nielsen TD, Søballe K, Børglum J, Bendtsen TF

The article/manuscript is: Published ☐ Accepted ☐ Submitted ☒ In preparation ☐

If published, state full reference:

If accepted or submitted, state journal: Regional Anesthesia and Pain Medicine

Has the article/manuscript previously been used in other PhD or doctoral dissertations?

No ☒ Yes ☐ If yes, give details:

The PhD student has contributed to the elements of this article/manuscript as follows:

A. Has essentially done all the work
B. Has done most of the work (67-90 %)
C. Has contributed considerably (34-66 %)
D. Has contributed (10-33 %)
E. No or little contribution
F. N/A

Element	Extent (A-F)
1. Formulation/identification of the scientific problem	B
2. Development of the method	B
3. Planning of the experiments and methodology design and development	B
4. Involvement in the experimental work/clinical studies/data collection/obtaining access to data	C
5. Development of analysis plan and preparation of data for analysis	B
6. Planning and conducting the analysis of data	A
7. Interpretation of the results	B
8. Writing of the first draft of the manuscript	A
9. Finalization of the manuscript and submission	B

Appendix 3 - Declaration of co-authorship, Article III (2/2)

AARHUS UNIVERSITY

Signatures of first- and last author, and main supervisor

Date	Name	Signature
11/12-18	Niels D. Nielsen (first author)	
4/1-19	Thomas F. Bendtsen (last author and supervisor)	

Date: 11/12-18

Signature of the PhD student

Appendix 4 - Test manual, ambulation test (1/3)

Ambulation score

Test manual

Developed by Niels Dalsgaard Nielsen[a], Morten Tange Kristensen[b] & Lone Ramer Mikkelsen[a]

Overview

The ambulation score is an adaptation of the Cumulated Ambulation Score[1] (CAS). The test is developed to assess early ambulation (on the day of surgery) after total hip arthroplasty but can be applied on patients after all types of major lower limb surgery. The test consists of 4 activities:

- Ambulation to sitting position in bed
- Ambulation to standing position from bed
- Walking with a high walker on wheels
- Walking with elbow crutches

For each activity, it is assessed whether the patient can perform the activity (if required with personal physical support) as well as the level of muscular control with the operated leg. If the patient is unable to perform an activity the test is terminated without attempts of performing any remaining activities.

Activities

Ambulation to sitting position in bed

Getting from supine position in bed (with the head of the bed elevated 30 degrees) to sitting position on the edge of the bed. The patient turns to the same side of the bed as (s)he is operated.

Ambulation to standing position from bed

The height of the bed is adjusted, so the upper edge of the mattress (without compression from patient) has a height corresponding to the distance from the sole of the foot to the joint line of the knee + 10 cm (3,9 in). The patient is getting from sitting to standing position.

Walking with a high walker on wheels

The patient is walking a minimum of 10 m (33 ft) with a high walker on wheels.

Walking with elbow crutches

The patient is walking a minimum of 10 m (33 ft) with elbow crutches.

Ambulation score

For every completed activity the patient's ability to ambulate is assessed according to the following:

A score of 2 is assigned if the activity is performed independently. The patient must perform the activity without any kind of personal physical support. Verbal support and assistive devices are allowed.

A score of 1 is assigned if the activity is performed using personal physical support. Assistive devices are allowed.

A score of 0 is assigned if the activity cannot be performed despite substantial help from one or more persons and assistive devices.

---

[1] *Kristensen MT, Andersen L, Bech-Jensen R, Moos M, Hovmand B, Ekdahl C, Kehlet H. High intertester-reliability of the Cumulated Ambulation Score for the evaluation of basic mobility in patients with hip fracture. Clinical Rehabilitation 2009; 23: 1116-1123*

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Appendix 4 - Test manual, ambulation test (2/3)

Muscular control score

For every completed activity the patient's ability to control the operated leg is assessed according to the following:

A score of 3 is assigned if control with the operated leg is good. Good control means, that the patient can use the operated leg efficiently during ambulation. Muscular control is only slightly affected compared to the non-operated leg.

A score of 2 is assigned if control with the operated leg is fair. Fair control means, that the patient can use the operated leg to some extent during ambulation but muscular control is considerably affected compared to the non-operated leg.

A score of 1 is assigned if control with the operated leg is poor. Poor control means, that the patient has difficulties using the operated leg during ambulation, and muscular control is almost insufficient to perform the ambulation.

A score of 0 is assigned if the patient cannot perform the first activity.

Termination of test

If the test is terminated (e.g. if the patient is unable to walk with elbow crutches) the reason(s) is stated according to the following:

- Pain
- Nausea or vomiting
- Dizziness or indisposition
- Insufficient motor control to ambulate safely
- Drainage from the surgical wound that preclude further ambulation
- Other reasons (reasons noted)

Results

The test produces two scores:

- An **ambulation score** (0-8): The sum of ambulation scores from the performed activities.
- A **muscular control score** (0-3) The median of muscular control scores from the completed activities. If first activity (ambulation to sitting position) cannot be performed the score is 0.

Furthermore, the patient is evaluating the intensity of the worst hip related pain in the operated side during ambulation on a 11-point numeric rating scale where 0 is *no pain* and 10 is the *worst pain imaginable*.

Appendix 4 - Test manual, ambulation test (3/3)

Score sheet for ambulation score

Please refer to the detailed manual before using the score.

Patient name		Time, end of surgery	
Date		Time, ambulation	

Circle the two relevant scores for each activity. Mark the highest category that applies.

Activity 1: Ambulation to sitting position in bed

Head of the bed elevated to 30 degrees. Legs to the operated side.

Ambulation		**Muscular control**	
2	Performs independently (incl. assistive devices)	**3**	Good control
1	Performs with personal physical support	**2**	Fair control
0	Cannot perform step	**1**	Poor control
		0	Cannot perform step

Activity 2: Ambulation to standing position from bed

Height of bed adjusted to distance from the sole of the foot to the joint line of the knee + 10 cm (3,9 in).

Ambulation		**Muscular control** *(only if activity is completed)*	
2	Performs independently (incl. assistive devices)	**3**	Good control
1	Performs with personal physical support	**2**	Fair control
0	Cannot perform step	**1**	Poor control

Activity 3: Walking with a high walker on wheels

Walking at least 10 m (33 ft).

Ambulation		**Muscular control** *(only if activity is completed)*	
2	Performs independently	**3**	Good control
1	Performs with personal physical support	**2**	Fair control
0	Cannot perform step	**1**	Poor control

Activity 4: Walking with elbow crutches

Walking at least 10 m (33 ft).

Ambulation		**Muscular control** *(only if activity is completed)*	
2	Performs independently	**3**	Good control
1	Performs with personal physical support	**2**	Fair control
0	Cannot perform step	**1**	Poor control

Reason for termination

Check reasons for termination if test terminated before activity 4:

- ❑ Pain
- ❑ Dizziness or indisposition
- ❑ Drainage from the surgical wound
- ❑ Nausea or vomiting
- ❑ Insufficient muscular control
- ❑ Other reasons (note reasons)

Pain during ambulation

Worst hip related pain during ambulation (circle patients response):

No pain **0** **1** **2** **3** **4** **5** **6** **7** **8** **9** **10** Worst imaginable pain

Appendix 5 - Letter-to-the-editor (1/1)

PostScript

LETTER TO THE EDITOR

Motor-sparing regional analgesia for hip-derived pain

To the Editor:

We wish to congratulate Girón-Arango *et al* from the PEricapsular Nerve Group (PENG) with their excellent report on the novel PENG block for treatment of acute pain after hip fracture.[1] Their results show great promise for a future approach to motor-sparing regional analgesia for the hip.

Yet, we would like to make a few comments regarding the PENG block and its applicability, as it bears great similarity to the iliopsoas plane block (IPB) that was recently developed and described by our group.[2]

As described both in the recent beautiful anatomical study by Short *et al*[3] and by ourselves,[2] approximately 30% of dissected specimens have femoral nerve branches leaving the femoral nerve below the inguinal ligament (dubbed '*low femoral branches*' in the Short paper) to either pierce the iliopsoas or course around its lateral margin. It is—in our opinion—unlikely that these branches will be covered by the injection from the PENG block. All the hip articular branches from the femoral nerve as well as the accessory obturator nerve do, however, cross a well-defined compartment in the iliopsoas plane sandwiched between the iliopsoas muscle and the iliofemoral ligament.[2–4] In our study, we observed that this well-defined anatomical compartment was delimited laterally by the rectus femoris muscle and its tendon and medially by the iliopectineal bursa, which was consistently tightly adherent to the iliofemoral ligament as well as to the tendon of the iliopsoas muscle. The iliopectineal bursa obstructed spread of injectate to the obturator nerve branches innervating the inferomedial part of the hip capsule.[2] To anesthetize all the hip articular branches from the femoral nerve—possibly along with the branches from the accessory obturator nerve—an injection in the iliopsoas plane would thus be ideal, while anesthesia of hip articular branches of the obturator nerve would require a separate subpectineal injection.[5] As we have described in our cadaveric study, the ultrasonographic landmarks for an IPB in order to anesthetize all the femoral hip articular nerve branches are easily identifiable (figure 1). The injectate spreads to *all* hip articular branches of the femoral nerve as long as injection into the iliopectineal bursa is avoided.[2]

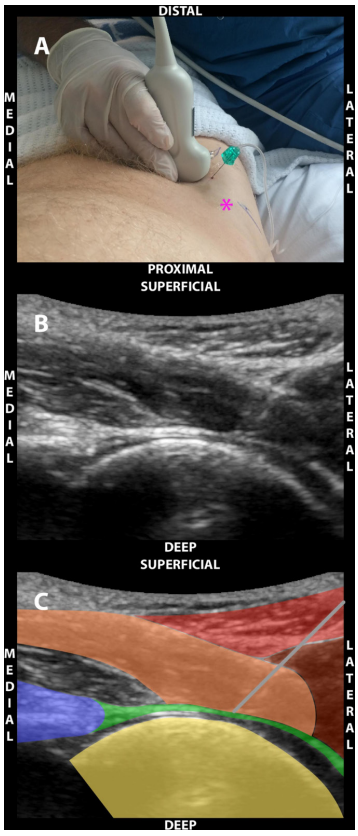

Figure 1 (A) Positioning of ultrasound probe above the hip joint and point of injection for the iliopsoas plane block. The probe is rotated approximately 20° clockwise from the transverse plane. The needle is inserted in a steep in-plane trajectory from the lateral end of the probe. The anterior superior inguinal spine is marked with a pink asterisk. (B) Ultrasonogram corresponding to A. (C) Same as B, but with explanatory panels: the head of femur (yellow) dives deep to the acetabular rim (blue). The nerve block needle (gray) is advanced through the sartorius (red), the rectus femoris (brown) and the iliopsoas (orange) muscles until the tip is just above the iliofemoral ligament (green). Local anesthetics are injected between the iliopsoas muscle and the iliofemoral ligament.

We are looking forward to read further explorations from the PENG group regarding the spread of injectate as well as randomized clinical data comparing their novel nerve blockade to our IPB.

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