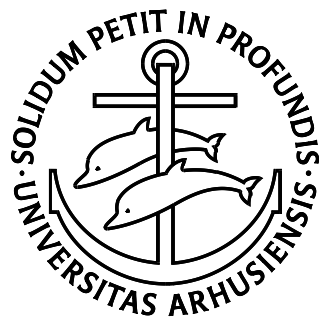


# Cerebral Palsy in Orthopaedic Surgery

Perspectives on pain and seating performance related to hip reconstruction

PhD dissertation

Line Kjeldgaard Pedersen



Health  
Aarhus University  
2016

---

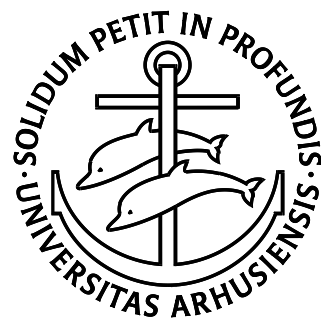


# Cerebral Palsy in Orthopaedic Surgery

Perspectives on pain and seating performance related to hip reconstruction

PhD dissertation

Line Kjeldgaard Pedersen



Health

Aarhus University

Department of Children's Orthopaedics

---

## **Supervisors**

Bjarne Møller-Madsen MD DMSc Professor  
Dept. Of Children's Orthopaedics  
Aarhus University Hospital  
Nørrebrogade 44, 8000 Aarhus C  
Denmark

Ole Rahbek MD PhD Associate Professor  
Dept. Of Children's Orthopaedics  
Aarhus University Hospital  
Nørrebrogade 44, 8000 Aarhus C  
Denmark

Lone Nikolajsen MD DMSc Associate Professor  
Danish Pain Research Center  
Aarhus University Hospital  
Nørrebrogade 44, 8000 Aarhus C  
Denmark

## **Evaluation committee**

Unni Narayanan, MBBS, M.Sc., FRS(C)  
Paediatric Orthopaedic Surgeon  
The Hospital for Sick Children  
Toronto, Canada

Deborah Eastwood, MB, FRCS  
Paediatric Orthopaedic Surgeon  
Great Ormond Street Hospital  
London, United Kingdom

John Rosendahl Østergaard, MD, DMSc, Professor (Chairman of the committee)  
Centre for Rare Diseases, Department of Pediatrics  
Aarhus University Hospital  
Aarhus, Denmark

## **Defence**

The defence is public and takes place 8<sup>th</sup> of February 2017 at 15.00 in "Samfundsmedicinsk auditorium", Bartholins Allé 4, Aarhus Universitet, 8000 Aarhus C.

# Preface

This PhD thesis is based on five studies carried out while I was employed as a PhD student at Department of Children's Orthopaedics at Aarhus University Hospital between 2010 and 2015 and while receiving my orthopaedic specialist training. This PhD would not have been possible without the funding received from the Elsass Foundation.

I have found the PhD process to be exiting, interesting and challenging. It takes a lot of work, but the results are worth it. I did not come to reach for the PhD degree on my own, but was encouraged through a small research project at the Department of Children's Orthopaedics that I earlier on worked on. This project was just scratching the surface of pain management in children with cerebral palsy and it became obvious that more research on the subject was needed.

Recently I had the experience of climbing the Kilimanjaro Mountain in Tanzania. Since then, I have actually realized that completing a PhD study is much like climbing a mountain with all its ups and downs resulting in being "on top of the world". You start out with the best intentions and plan the perfect climb. But you will always encounter rocks blocking your way, forcing you to find a way around it. Exactly like research. During the 6 days I spend on the mountain, the road ahead of me changed from the paved path to almost invincible climbs combined with the always lurking altitude sickness. I am convinced that reaching Uhuru Peak would not have been possible without the help and support of a number of people. The same goes for the PhD study. I could not have completed either without the help and support from my family and friends.

First of all, I want to thank all the children and their parents, who were willing to participate in the clinical studies during their hospital stay and extensive surgery. Their willingness to aid in this research will help us improve the treatment of many children in the future.

My deep gratitude goes to my supervisors: Bjarne Møller-Madsen, Ole Rahbek and Lone Nikolajsen, who encouraged me to start this process and supported me during my studies. Your help guided to me to find a way around the rocks that turned up along the way. Your spirit helped me to keep trying - even when the reviewers gave me a hard time. Your advice helped me to manage my projects - even when they acted up. You read and commented on all my long manuscripts and your guidance led me to succeed in getting my research published.

A special thank is needed for my family. They have supported me all the way. It has been invaluable for me, from time to time, to have been able to completely relax and recharge my batteries in their loving company.

Last, (but especially not least) I would not have been able to complete this PhD without the research group at the Children's Orthopaedic Department. The

always available ping-ponging of ideas or problems with these colleagues have given me so much in-put and solutions to obstacles. Not only have the scientific discussions been rewarding, also the general ambiance and social connections at our office have been priceless.

Even though this thesis concludes my PhD studies, I plan to be involved in future research at the Department of Children's Orthopaedics. Research is like a contagious virus with no cure. Now I've got the "research".

Line Kjeldgaard Pedersen  
Aarhus, 2016





## **This thesis is based on the following papers:**

- I. Assessment of pain in children with cerebral palsy focused on translation and clinical feasibility of the revised FLACC score. **Scandinavian Journal of Pain 9 (2015) 49-54 [1].**
- II. The revised FLACC score: reliability and validation for pain assessment in children with cerebral palsy. **Scandinavian Journal of Pain 9 (2015) 57-61 [2]. \***
- III. Epidural analgesia is superior to local infiltration analgesia in children with cerebral palsy undergoing unilateral hip reconstruction. **Acta Orthopaedica 2016; 87 (2): 176-182 [3].**
- IV. Definition and intra-variability of outcome measures of seating performance in 65 healthy children. **Submitted to Gait & Posture. \*\***
- V. Hip reconstruction improves functional seating performance in children with cerebral palsy. **Submitted to Journal of Pediatric Orthopaedics. \*\*\***

\* Presented at The Annual Meeting for The Danish Orthopaedic Society, Copenhagen 2014 as an oral presentation and at the 34<sup>th</sup> Annual Meeting of the European Paediatric Orthopaedic Society, Marseille, France April 2015 as an e-poster.

\*\*Presented at The Annual Meeting for The Danish Orthopaedic Society, Copenhagen 2013 as a poster and nominated for best poster and at The Annual Meeting for The Danish Orthopaedic Society, Copenhagen, October 2015 as an oral presentation.

\*\*\*Presented at the 32<sup>nd</sup> Annual Meeting of the European Paediatric Orthopaedic Society, Athens, Greece April 2013 as an oral presentation and at the 4<sup>th</sup> International Cerebral Palsy Conference, Pisa, Italy, October 2012 as a poster presentation and at The Annual Meeting for The Danish Orthopaedic Society, Copenhagen, October 2015 as an oral presentation.



## Abbreviations

AI;	Acetabular Index
AUH;	Aarhus University Hospital
BoNT;	Botulimum Neurotoxin
CA;	Crohnbach's Alpha
CHEOPS;	Children's Hospital of Eastern Ontario Pain Scale
CoF;	Center of Force
COSMIN;	COnsensus-based Standards for the selection of health Measurements INstruments
CoV;	Coefficient of Variation
CP;	Cerebral Palsy
DESS;	Echelle Douleur Enfant San Salvador
FAU;	Factor Analysis Uniqueness
FLACC score;	Face, Leg, Activity, Cry and Consolability score
GMFCS;	Gross Motor Function Classification System
GMFM;	Gross Motor Function Measure
HD;	Hip Dislocation
HR-PRO;	Health Related – Patient Reported Outcome
ICC;	Intra Class Correlation
ICU;	Intensive Care Unit
INRS;	Individualized Numeric Rating Scale
ITB;	Intrathecal Baclofen
LIA;	Local Infiltration Analgesia
MAPS;	Multidimensional Assessment of Pain Scale
MP;	Migration Percentage
NAPI;	Nursing Assessment of Pain Intensity
NB;	Normal Back position
NCCPC;	Non-Communicating Children's Pain Checklist
NCCPC-PV;	Non-Communicating Children's Pain Checklist-Postoperative Version
NRS;	Numerical Rating Scale
PPP;	Paediatric Pain Profile
PROM;	Patient Reported Outcome Measure
RCT;	Randomised Controlled Trial
r-FLACC score;	Revised Face, Leg, Activity, Cry and Consolability score
SD;	Standard Deviation
SDR;	Selective Dorsal Rhizotomy
SPARCLE;	Study of PARticipation of children with Cerebral palsy Living in Europe
UB;	Up-right back position
VAS;	Visual Analogue Scale
VAS-OBS;	Observer Visual Analogue Scale

# Contents

1. English summary.....	13
2. Danish summary .....	14
3. Overview of studies .....	15
4. Introduction.....	16
Cerebral Palsy (CP) .....	16
Epidemiology and aetiology.....	16
Non-orthopaedic management of CP.....	17
Orthopaedic surgery in children with CP .....	17
Pain.....	18
Core pain behaviours.....	18
Characteristics of pain in children with CP .....	18
Pain assessment tools.....	19
Local Infiltration Analgesia (LIA) and epidural analgesia.....	20
Pain management in children with CP .....	21
Translation and validation of Patient Reported Outcome Measures (PROMs).....	21
Translation.....	21
Psychometric properties.....	21
Reliability.....	22
Validity.....	22
Seating performance .....	22
Anatomy and biomechanics .....	22
Seat interface pressure .....	23
Pelvic tilt and seating asymmetry .....	23
Assessment of seating performance .....	25
Seating difficulties in CP .....	25
5. Aim of the thesis.....	27
6. Materials & methods.....	28
Hypotheses.....	28
Study designs.....	28
Patient characteristics .....	29
Ethical issues .....	30
Methodological considerations .....	31
Hip reconstruction and anaesthesia .....	31
Local infiltration analgesia.....	32
Radiographic evaluation .....	32
Pain assessment .....	32
Measurement of seating performance.....	33
Basic measures .....	34
Outcome measures of seating performance .....	35
Statistical considerations .....	37
Sample sizes .....	37
Statistics .....	37
7. Results.....	39
Study I.....	39
Outcome 1: Danish translation of the r-FLACC score .....	39

Study II.....	40
Outcome 1: Reliability measurement properties. ....	40
Outcome 2: Validity measurement properties. ....	41
Study III .....	42
Outcome 1: Pain measurements. ....	42
Outcome 2: Opioid consumption. ....	42
Study IV .....	43
Outcome 1: Reproducibility of seating parameters.....	43
Outcome 2: The 5 parameters of seating performance .....	43
Study V.....	44
Outcome 1: Seated pelvic tilt in children with CP .....	44
Outcome 2: Radiological parameters in children with CP .....	45
Outcome 3: Seating performance of normal children versus children with CP ..	45
8. Discussion.....	46
Key findings .....	46
Interpretation and limitations .....	46
Clinical feasibility and translation .....	46
Psychometric properties.....	47
Postoperative analgesia for children with CP.....	49
Seating performance in normal children .....	50
Seating performance in children with CP.....	53
Generalisability .....	56
9. Conclusion.....	57
Pain.....	57
Seating performance .....	57
10. Perspectives and future research .....	58
Pain.....	58
Seating performance .....	58
11. References.....	59
12. Appendices.....	66
Tables .....	66
Figures.....	69
Papers I-V .....	72



# 1. English summary

Present thesis concerns cerebral palsy in orthopaedic surgery and further enlightens the perspectives on pain and seating performance. The centre of the thesis is the hip reconstructive procedure that many children with cerebral palsy undergo due to progressive dysplasia and subluxation of one or both hips. The studies in this thesis all relate to the hip reconstruction procedure and stems from concerns or difficulties we previously have encountered.

The hip reconstructive surgery is, among others, performed to avoid pain and to improve mobility and sitting function in these often severely disabled children. In the early postoperative period, during the hospital stay we have seen that it has been difficult to adequately manage the postoperative pain after hip reconstruction, hence *study III* was planned in order to test the efficacy of both epidural analgesia, local infiltration analgesia and an approximated placebo treatment in children with cerebral palsy undergoing unilateral hip reconstruction. We found that epidural analgesia is superior to both LIA and placebo with significantly lower pain scores and lower opioid consumption postoperatively and may be considered as first choice in children with CP.

No validated Danish pain assessment tools have been available for pain assessment in children with cerebral palsy. A literature search on the topic revealed that the r-FLACC pain score seemed valid and clinically feasible, though it only was developed in English. *Study I* is focused on the translation and clinical feasibility of the r-FLACC score and in *study II* a reliability and validation process following the COSMIN guidelines was undertaken.

Seating performance was evaluated using a Tekscan CONFORMat sensor. The Tekscan equipment has previously been used to assess plantar pressure of the feet in standing and walking persons; but the technical development now gives the possibility of measuring seated pressures and balance. In *study IV* the reproducibility of the parameters of seating performance of the CONFORMat sensor was determined in 65 healthy children and 5 appropriate measures of seating performance were defined including 3 measures for pelvic tilt. These measures were used in *study V*, where the seating performance of children with cerebral palsy undergoing unilateral hip reconstruction was evaluated before and after surgery. Results showed that unilateral hip reconstruction improves seated pelvic tilt but this was not correlated to supine radiographic pelvic tilt concluding that radiographic and interface pressure pelvic tilt are discrepant assessment methods that are not directly comparable.

## 2. Danish summary

Denne PhD afhandling omhandler cerebral parese i relation til ortopædkirurgi og belyser forskellige perspektiver af smerte og siddestilling. Omdrejningspunktet for afhandlingen er den hofte rekonstruktions operation mange børn med cerebral parese får foretaget på grund af tiltagende dysplasi og sublaxation af et eller begge hofter. Studierne i denne afhandling relaterer sig alle til denne hofte rekonstruktions operation og udspringer fra bekymringer og problemer vi har oplevet i denne forbindelse.

Hofte rekonstruktionen udføres blandt andet for at forebygge og behandle smerter, bedre hoftemobiliteten samt at forbedre siddestillingen hos disse ofte svært handicappede børn. I den første tid efter hofte rekonstruktions operationen, under indlæggelsen, har vi tidligere haft problemer med at give børnene tilstrækkelig smertedækning. Derfor planlagde vi *studie III*, for at undersøge den smertestillende effekt af henholdsvis rygmarsbedøvelse, lokal bedøvelse og tilnærmet placebo hos børn med cerebral parese der gennemgik hofte rekonstruktion af den ene hofte. Vi fandt at rygmarsbedøvelse er overlegen i forhold til både lokal bedøvelse og tilnærmet placebo, med signifikant lavere smertescores og morfika forbrug og vurderes derfor for førstevalg hos børn med CP.

Der findes ingen validerede danske smerte målingsredskaber til børn med cerebral parese. En litteratursøgning på emnet afslørede at r-FLACC smertescoren virker valid og klinisk anvendelig; men den er kun udviklet i en engelsksproget udgave. *Studie I* fokuserede derfor på oversættelse og klinisk anvendelighed af r-FLACC scoren og i *studie II* blev den danske version testet med hensyn til reliabilitet og validitet ved hjælp af COSMIN vejledningen.

Siddestilling blev evalueret med Tekscan CONFORMat udstyret. Tekscan udstyr har tidligere været brugt til at evaluere fodens tryk mod underlaget hos stående og gående personer; men den tekniske udvikling har nu åbnet op for muligheden for at måle siddende tryk og balance. I *studie IV* blev intra-variabiliteten for siddestillings parametre målt med CONFORMat udstyret bestemt hos 65 raske børn og 5 siddestillings parametre blev defineret. Disse parametre blev brugt i *studie V*, hvor siddestillingen hos børn med cerebral parese der gennemgik hofterekonstruktion blev evalueret før og efter operationen. Resultaterne viste at ensidig hofterekonstruktion forbedrede bækken kipningen; men at dette ikke var korreleret til de liggende røntgenbilleder. Herfra kan konkluderes at bækken kipning målt med henholdsvis røntgen og siddetryk er forskellige målemetoder der ikke er direkte sammenlignelige.

### 3. Overview of studies

	Question	Patients	Methods	Results	Interpretation
<b>Study I:</b> Assessment of pain in children with cerebral palsy focused on translation and clinical feasibility of the revised FLACC score. <i>Scand J Pain 9 (2015) 49-54</i>	How does the r-FLACC pain score perform compared to other pain scores and can it be valid translated into Danish?	No patients included.	Literature review on pain assessment tools and clinical feasibility. 10-step translation of the r-FLACC using back-translation.	The Danish version of the r-FLACC pain assessment tool.	The r-FLACC pain score has superior clinical feasibility and can assess pain in Danish children with CP.
<b>Study II:</b> The revised FLACC score: reliability and validation for pain assessment in children with cerebral palsy. <i>Scand J Pain 9 (2015) 57-61</i>	Does r-FLACC pain score maintain its psychometric properties after translation?	27 children, age 3-15 yrs with tetraplegic CP unable to self-report pain, GMFCS II-IV.	Reliability: Internal consistency inter- and intra- rater reliability. Validity: Content, construct and criterion validity.	Excellent internal consistency and intra-rater reliability and good inter-rater reliability. Validity was established.	The Danish r-FLACC is valid and reliable for postoperative pain assessment in children with CP.
<b>Study III:</b> Epidural analgesia is superior to local infiltration analgesia in children with cerebral palsy undergoing unilateral hip reconstruction. <i>Acta Orthopaedica 2016; 87 (2): 176-182</i>	Does epidural analgesia provide more effective analgesia than LIA after unilateral hip reconstruction in children with CP?	18 children with CP, GMFCS III-V undergoing unilateral hip reconstruction.	6 ptt.: Epidural analgesia. 6 ptt.: LIA, 6 ptt.: Placebo. Outcome measures were postoperative pain (r-FLACC) and opioid consumption.	Epidural analgesia is superior to both LIA and placebo with significantly lower r-FLACC scores and lower opioid consumption postoperatively.	Epidural analgesia may be considered as first choice in children with CP.
<b>Study IV:</b> Definition and intra-variability of outcome measures of seating performance in 65 healthy children. <i>Submittet to Gait &amp; Posture.</i>	Are basic measurements of seating performance reproducible in normal children and can parameters of seating performance be defined?	65 normal children included from a Danish primary school.	The Tekscan CONFORMat seat interface pressure mat was used for 30 sec. measurements with relaxed and up-right back position.	Basic measures showed good to excellent reproducibility and 5 parameters of seating performance were defined.	Seating performance can be assessed with 5 outcome measures including 3 measures for pelvic tilt.
<b>Study V:</b> Hip reconstruction improves seating performance in children with cerebral palsy. <i>Submittet to Journal of Pediatric Orthopaedics.</i>	Does hip reconstruction in children with CP improve seating performance?	18 children with CP, GMFCS III-V undergoing unilateral hip reconstruction	The Tekscan CONFORMat seat interface pressure mat was used pre- and postoperatively.	Unilateral hip reconstruction improves seated pelvic tilt but this is not correlated to supine radiographic pelvic tilt	Radiographic and interface pressure pelvic tilt are discrepant assessment methods that are not directly comparable.

# 4. Introduction

## Cerebral Palsy (CP)

### Epidemiology and aetiology

Cerebral Palsy (CP) is the common name for non-progressive impairments due to insults to the developing brain. It was reported by William John Little in 1843 as Little's Disease [4;5]. In 1887 sir William Osler published the book "The Cerebral Palsies of Children" and this nomenclature has persisted. Winthrop M. Phelps published the first major publication on orthopaedic treatment of CP in 1862 and introduced the holistic approach and stated that children with CP should be helped to achieve their full potential as individuals [4].

Several epidemiological definitions have been proposed in the description of CP. In 2005, a panel of internationally recognized experts agreed on a definition and classification of CP; though much debate still exists regarding the accuracy of the definition [4;6]:

*"Cerebral palsy (CP) describes a group of permanent disorders of the development of movement and posture, causing activity limitations that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, cognition, communication, perception, and/or behavior, by epilepsy, and/or by a seizure disorder. [6]"*

The incidence of CP is between 2-3 per 1000 live births, though exact estimation is not possible since the diagnosis of CP cannot be confirmed before the child reaches 4-7 years of age [4;7-9]. The cause of CP is not fully understood with risk factors and possible causes of CP present at different periods. Prenatal causes include intrauterine infections, toxins (including alcohol, smoking and drugs), intrauterine growth restriction, metabolic or genetic syndromes and multiple-birth pregnancies. Perinatal factors include neonatal asphyxia, preterm/extreme preterm birth and low birthweight. Postnatal causes include infections, hyperbilirubinemia with kernicterus, cerebral anoxia or trauma. The diagnosis of CP is primarily made through clinical examination; but neuroimaging may be confirmatory. While the brain lesion in CP is static, the clinical manifestations are progressive [4;10].

Several classification systems are used due to the heterogeneity of symptoms and aetiology. The topographical classification is widely used in orthopaedic evaluations and classifies the children according to limb involvement. Hemiplegia requires spastic upper and lower limbs on the same side, diplegia requires major spasticity of the lower limbs and minor involvement of the upper limbs and tetraplegia or total body involvement requires spasticity of all four limbs [4]. The physiological classification addresses six types of movement disorders in CP: 1) Spasticity, 2) Dyskinesia (tension type, dystonia, chorea, ballismus or rigidity), 3) Ataxia, 4) Tremor, 5) Atonia, 6) Mixed spasticity and dystonia. Lastly, the Swedish classification is known for its simplicity by only consisting of four groups: spastic (70%), dyskinetic (10%), ataxic (10%) and mixed (10%) CP. This classification is used in many epidemiological studies [4;11].



Children with CP might have cognitive and/or motor impairments due to non-progressive cerebral damage. The severity of the cognitive impairments range from no impairments at all to learning disabilities to severe mental retardation [4]. The functional capability of children with CP is classified according to the Gross Motor Function Classification System (GMFCS) (range I-V). Children with GMFCS I may have no functional impairment, GMFCS II may need assistive devices, GMFCS III need assistive devices for ambulation, GMFCS IV has limited self-mobility and often require a wheel-chair and GMFCS V are always wheelchair bound and lack head control [10].

### **Non-orthopaedic management of CP**

Treatment of CP is multidisciplinary aimed at associated features such as feeding difficulties, drooling, intellectual impairment, seizures, impaired vision and hearing, abnormal pain, bladder and bowel dysfunctions [9]. The focus in management differs according to the GMFCS level and the consequences of cognitive and motor impairments. A constant increased muscle tone or spasticity is a cause of pain, muscle spasms, reduced mobility, contractures, hip dislocation and problems with activities of daily living [12;13]. Treatment of spasticity has improved with Botulinum Neurotoxin (BoNT) and intrathecal baclofen (ITB) as the main treatment modalities [7]. In children with spasticity Selective Dorsal Rhizotomy (SDR) may reduce spasticity [14]. Muscle contractures can be treated by splinting, stretching, physical therapy, BoNT, orthopedic lengthening or spasticity reduction [14].

### **Orthopaedic surgery in children with CP**

The primary manifestations in CP include loss of motor function and balance in combination with muscle tone abnormalities, all of which might result in musculoskeletal secondary manifestations. Orthopaedic treatment of children with CP aims at correcting dysfunction, preventing deformity progression, and optimising overall function. Since spastic CP is the predominant type of CP many children develop spasticity caused contractures of the major joints (hip, knee, ankle, elbow, and wrist) [4;10;11].

The muscular imbalances in children with CP might result in subluxation and acetabular dysplasia of the hips, with the incidence related to the GMFCS level of the child. The estimated prevalence of total hip dislocation is 10-15% and the prevalence of hip subluxation is 25-60% in children with CP [7]. Increased muscle tone and imbalance of the hip flexors (iliopsoas), adductors and hamstrings leads to muscle shortening and contractures around the hip joint, which consequently leads to progressive hip subluxation and, if untreated, hip dislocation. The dislocation of the femoral head is usually in the postero-supero-lateral direction [4;7;10;15]. The progressive hip subluxation is commonly treated with soft tissue surgery (adductor-and iliopsoas lengthening or release) or hip reconstruction. The total hip dislocation is a severe complication with long-term consequences in children with CP; though it is preventable by early surgical intervention. Therefore close hip surveillance is necessary for identifying hips at risk. Elkamil et al [7] showed that the CP follow-up programme (CPUP) has significantly reduced the number of hip dislocation in Swedish children with CP and it is now being implemented in Denmark (CPOP) [4;7;10;16].

# Pain

## Core pain behaviours

In 1998 McGrath et al [17] conducted a qualitative study to ascertain the pain behaviours of non-verbal children with CP. The results are still the basis in developing pain assessment tools. Through interviews with caregivers to non-verbal and cognitively impaired children with CP, 31 core behaviours were classified into 7 categories: Vocal; Eating/Sleeping; Social/Personality; Facial expression of pain; Activity; Body and limbs; and Physiological. These categories and 26 of the pain behaviours were used in developing the first pain assessment tool for children with CP, the Non-Communicating Children's Pain Checklist (NCCPC) [18]. A revision for postoperative use omitted the Eating/Sleeping category (Non-Communicating Children's Pain Checklist - Postoperative Version (NCCPC-PV)) [19].

Children with cognitive impairments (CI) often elicit behavioural limitations and idiosyncrasies masking the expression of pain. Behaviours known to be typical pain indicators in normal children are inconsistent and difficult to interpret in children with CI. Atypical pain behaviours in children with CI include laughing, singing, clapping of hands, anger, aggressiveness and self-injury and increase the risk of inaccurate pain assessment. Expression of core pain behaviours and atypical pain behaviours is inconsistent; hence assessment of pain needs to be individualised [17;20;21].

## Characteristics of pain in children with CP

Several pain assessment tools exist for normal children relying on self-report, and characterized as the gold standard of pain assessment. However, children with cognitive impairments i.e. severe CP might not be able to self-report pain increasing the risk of unrecognized and untreated pain. An observational and behavioural pain assessment tool is needed for children with CP not able to self-report [17;22;23].

Pain in children not able to self-report can be assessed by parents or health-care professionals. Penner et al [23] evaluates the presence of pain, causes and the effect on quality of life in children with CP. Only fair agreement between the physician's pain assessment and the parent's assessments was found, in contrast to an excellent agreement between the children self-reporting pain and their parents. Studies show that parents tend to overestimate their child's level of pain, especially in severely impaired children or if the parent was stressed [24;25]. Nevertheless, in children not able to self-report pain, a proxy report is recommended [25].

Chronic pain, daily day pain, postoperative pain and procedural pain need to be differentiated. The SPARCLE2 study found that 75% of children with CP experience pain and in therapeutic procedures such as physical therapy 50% experiences procedural pain [24]. Breau et al [22] found that common daily day pain arose from accidental pain or non-accidental pain such as musculoskeletal pain, infection pain, gastrointestinal pain, recurrent pain or common childhood pain. CP is associated with painful conditions such as contractures, spasticity and spasms, which might contribute to the daily day pain experienced by many children with CP [26]. Penner et al [23] reports that physicians reported pain in 38% of children with CP and for the non-ambulatory children (GMFCS IV-V) hip dislocation/subluxation, dystonia/spasticity and constipation were the most common causes. Ramstad et al [25] conclude that musculoskeletal pain is the dominating cause of daily day pain in

children with CP, the pain increases with age and pain sites are multiple, but maximum pain was located in the lower extremities (including hips). Postoperative pain management is challenging in children with CP and is assessed more infrequently than in cognitive normal children resulting in lower analgesia use [22;24;27]. In addition children with CP often experience a prolonged rehabilitation period after surgery characterized by continued pain [28].

### **Pain assessment tools**

Several pain assessment tools exist for children with CP. They vary on some levels, and are similar on other. We evaluate pain assessment tools using these questions:

- Is the pain assessment tool based on core pain behaviours?
- Is pain assessment based on self-report, behavioural observations or physiological measurements?
- Is the pain assessment tool developed for use in a daily day setting, procedural pain setting or postoperative setting?
- Is pain assessed by parents, health-care professionals or both?
- Is the pain assessment tool standardized, individualised or does it have the possibility for adding individual behaviour?
- Is the score developed for use in children or adults?
- Have the psychometric properties been evaluated?
- Does the pain assessment tool have good clinical feasibility?

The psychometric properties of a pain assessment tool are important; but for translation from research into clinical use, the feasibility or clinical usefulness of the tool needs evaluation [29;30]. Voepel-Lewis et al [30] concludes that poor pragmatic properties of a pain assessment tool decreases the clinical usefulness, which slows its implementation despite excellent psychometric properties. Several studies have evaluated clinical feasibility of pain assessment tools for children with CP by use of questionnaires and interviews with health-care professionals [20;30;31].

The NCCPC-PV is elaborate and based on core pain behaviours with 6 standardised categories and 27 items based on observations by parents and health-care professionals with no possibility for individualisation. Only variable validity and reliability were found for the NCCPC-PV, though it is generally acclaimed for being very accurate. The NCCPC-PV requires 10 minutes observation contributing to low clinical feasibility. The NCCPC-PV has lower clinical feasibility compared to the r-FLACC and NAPI, but higher compared to the DESS [19;20;30;32-34].

The FLACC (Face, Legs, Activity, Cry and Consolability) score was developed for postoperative pain in normal children. A revision (r-FLACC) included core pain behaviours of children with CP and added of an open-ended descriptor leaving the possibility for individualisation. The psychometric properties of the r-FLACC show excellent agreement in all of the 5 categories. The r-FLACC have been compared to the NCCPC-PV, the NAPI, the INRS and the PPP regarding clinical feasibility and was found superior due to its ease of use, lower time requirements and flexibility regarding individualisation [19-21;30;31;35].

The Nursing Assessment of Pain Intensity (NAPI) [36], developed for children with CP was adapted from the CHEOPS (Children's Hospital of Eastern

Ontario Pain Scale) developed for normal children [37]. The NAPI have acceptable inter-rater reliability and better clinical feasibility than the NCCPC-PV [30].

The Paediatric Pain Profile (PPP) is developed for everyday pain assessed by the parents. It consists of 20 pre-set behavioural items developed through interviews with health care professionals and parents. The PPP was found to be valid and reliable. Two recent feasibility studies included the PPP and found it inferior when compared to the r-FLACC. In addition nurses preferred the r-FLACC over the PPP due to lower time to read and complete scores [20;31;38].

The numerical rating scale (NRS) has been revised into the Individualized Numeric Rating Scale (INRS) for postoperative pain in children with CI by stratifying each child's individual pain behaviour to a number on the scale. The child's behaviour, vocalisation, expression and other physical changes are linked to a number (1-10). The INRS may be used by both parents and health-care professionals and have good psychometric properties. Clinical feasibility has only been assessed by comparison to the NCCPC-PV, the r-FLACC and the PPP showing superiority of the r-FLACC [20;39].

The Multidimensional Assessment of Pain Scale (MAPS) has 5 items, scored 0-2 including behavioural and physiological postoperative parameters. The assessments can only be made by health-care professionals since parameters such as blood pressure and heart rate are included. Good clinical feasibility and acceptable validity was found, though not validated for children with CI [29].

The Echelle Douleur Enfant San Salvador (DESS) consists of 10 items and some are similar to the core pain behaviours described by McGrath et al [17]. It is developed for multi-handicapped neurologically impaired patients of all ages with no possibility for individualisation. Adequate psychometric properties were found; but regarding clinical feasibility it is found inferior to the NCCPC-PV [34;40].

The Visual Analogue Scale (VAS) is a validated and commonly used for children and adults able to self-report. It is called the Observer Visual Analogue Scale (VAS-OBS) when assessment is done by a proxy, i.e. parent or health-care professional. It consists of a line with "no pain" and "most pain" marked at each end. The patient or observer marks the level of pain. Crellin et al [41] reviews the psychometric properties of the VAS-OBS and finds that concurrent validity cannot be established due to only moderate correlations between a child's self-reported pain and the parents VAS-OBS scores. De Jong et al [42] found the VAS-OBS to be unreliable, hence abstained from reporting their clinical feasibility results [41-43].

None of these pain assessment tools have been translated into Danish and no consensus on which score is preferable for pain assessment in children with CP are agreed on. After reviewing the evidence regarding pain assessment tools the r-FLACC appear to be superior on several aspects especially regarding its ease to use in a postoperative setting, its use of core pain behaviours, its possibility for individualisation, its psychometric properties and its clinical feasibility.

### **Local Infiltration Analgesia (LIA) and epidural analgesia**

Kerr et al [44] have documented the positive effect of high-volume local infiltration analgesia (LIA) in adults after arthroplasty. The original LIA consisted of ropivacaine, ketorolac and adrenaline, which was infiltrated in the surgical field in addition to postoperative bolus injections. LIA has been investigated extensively in

adult arthroplasty surgery [45-47]. Only a few studies have investigated the effect of LIA in children. No studies have investigated LIA in children with CP [48].

Epidural analgesia is commonly seen as a first choice in postoperative pain management. However, adverse effects might limit its use in children with CP [11]. General side effects are urinary retention, unevenly distributed motor block, inadequate analgesia, hypotension, nausea, sedation, pruritus and epidural haematoma or infection, which all might be difficult to monitor and treat in children with CP [49]. In addition, children with CP often have scoliosis or ITB pumps, causing safety concerns or problems when inserting an epidural catheter [50-53].

### **Pain management in children with CP**

Postoperative pain includes surgical pain, spasticity and spasm related pain and pain related to casting. Children with CP react to postoperative pain with i.e. hypothermia, nausea, seizures, desaturations and muscle spasms. Inadequate pain management or casting-related muscle-stretching might increase spasms through spinal reflexes, which further inflicts pain. ITB and BoNT have been shown to decrease spasticity and spasms and consequently postoperative pain [5;11;54].

Long et al [55] found that CP children receive less intraoperative opioid compared to normal children [55]. Moore et al [56] found that children with CP undergoing SDR have lower postoperative pain and reduced muscle spasms when treated with epidural analgesia compared to systemic analgesia [56]. Nemeth et al [57] supplemented epidural analgesia with baclofen and found that epidural baclofen do not alter the pain-spasm cycle significantly. However, the study used surrogate measures for narcotic consumption instead of measuring postoperative pain [57]. Muthusamy et al [52] found lower pain scores in children with CP treated with a pain pump with bupivacaine compared to oral analgesics only [52].

Spasticity and spasm induced postoperative pain in children with CP is common. Epidural analgesia seems to be effective in managing pain and spasms. It is suggested that local analgesics as either pain pumps or LIA may have similar effects, though only a few studies have evaluated this. Hence, it is found relevant to compare the effect of LIA and epidural analgesia.

## **Translation and validation of Patient Reported Outcome Measures (PROMs)**

### **Translation**

Clinical trials often include a Patient Reported Outcome Measure (PROM) as primary or secondary output. The production of an accurate and culturally linguistic usable translation is essential for correct data processing [58]. Due to a previous lack of consistency in the methods of translations of PROMs the Translation and Cultural Adaptation group (TCA Group) was initiated in order to review the literature and existing guidelines. Wild et al [59] report the consensus agreed upon and discuss the strengths and weaknesses of the different methods [59].

### **Psychometric properties**

The quality of a measurement instrument, as for example the r-FLACC score, is determined by its psychometric properties as for example its reliability and validity. Standardised criteria for evaluation of this are described in detail in the COSMIN

guidelines [60-62]. COSMIN stands for COnsensus-based Standards for the selection of health Measurements INstruments.

### **Reliability**

Reliability describes the consistency of the measurements if the same results are produced from different samples or if the same results are produced each time it is measured the same way in the same subjects. *Internal consistency* measures if each item is sufficiently correlated and measures the same construct. *Reliability* measures difference over time (intra-rater) and with different raters (inter-rater) by using tests and retests. *Measurement error* evaluates the absolute amount of measurement error [60-64].

### **Validity**

External validity describes if results are generalizable to a population and internal validity describes if the instrument actually measures what it is designed to measure. *Content validity* is a subjective assessment of whether the content of the instrument adequately reflects what the instrument is supposed to measure. *Construct validity* evaluates if the scores of the instrument are consistent with predefined hypotheses on relationships (internal and external) to other instruments or expected differences in scores between relevant groups. *Structural validity* is included in construct validity and evaluates the dimensionality of the construct. *Cross-cultural validity* evaluates whether the translation of an instrument has included back and forward translations. *Criterion validity* evaluates whether the scores of an instrument are comparable to another "Gold Standard" instrument with known good validity. If no gold standard instrument exists criterion validity cannot be assessed [41;60-64].

## **Seating performance**

### **Anatomy and biomechanics**

Normal sitting function is perceived instinctly in healthy people, though many biomechanical aspects are present in the process of sitting. The bony base of support in sitting is formed by the ischial tuberosities, sacrum and coccyges [65], which are the frame in the interface between the body and support (Fig. 1).

The three-dimensional position of this framework is defined by the pelvic tilt/pelvic obliquity (Antero-Posterior (AP) pelvic tilt, Left-Right (LR) pelvic tilt and pelvic rotation) [4]. The soft tissue base of support in sitting is formed by the buttocks and thighs. The amount and quality of this soft tissue surrounding the bony framework of the seating area plays a role in pressure distribution [66;67].

Several muscles are involved in sitting, hip movement and pelvic tilt. The *iliopsoas muscle* is a powerful flexor of the hip and facilitates anterior pelvic tilt. The *hip adductors* (pectineus, adductor longus, adductor brevis, adductor magnus and gracilis) function as hip adductors and may be contract in children with CP causing pelvic tilt [68]. The *rectus femoris muscle* acts as a hip flexor, a knee extensor and may play a role in pelvic anterior tilt. The rectus femoris, adductors and iliopsoas muscles are released during the hip reconstruction procedure. Lastly, *the hamstrings* (biceps femoris, semitendinosus and semimembranosus muscles) acts as a hip extensor, knee flexor and may play a role in pelvic posterior tilt. Functionally the hamstrings and rectus femoris are antagonizers and stabilize the sagittal plane pelvic tilt [4;69;70].



*Figure 1 Bone-model illustrating the bony base of support in the seated position seated on the CONFORMat. All photos of the pelvic bone model are made in collaboration with the clinical photographer at AUH.*

### **Seat interface pressure**

The pressure between two surfaces is commonly known as interface pressure and the seat interface pressure is the pressure between the entire seating area of a person and the support surface (chair, cushion etc.) [71]. The larger the area of weight distribution is, the lower the interface pressure is. Cushions or supports may be designed to distribute the weight over a large area, such as alternating pressure seat supports and recline or tilt wheelchairs [72]. Yu et al [72] describes three factors that influence seat interface pressure and interact in a complex and dynamic way: (1) the cushion features (shape, material, structure etc.), (2) the overall body (posture, built, activities etc.) and (3) localized body features (anatomic formation, soft-tissue properties, composition etc.)

Measurement of interface pressure can be used to evaluate the risk of development of pressure ulcers [73]. An exact seat interface pressure threshold for tissue damage is difficult to specify due to differences in the internal bone and soft tissue mechanical stress concentrations. Bouten et al [74] refers to the traditionally quoted value for capillary closure pressure of 32 mmHg depending on local pressure gradients across the vessel wall and states that seat interface pressures well above capillary pressures can be supported by the soft tissues before blood flow is seriously impaired. The pressure threshold for ulceration varies in different body areas and the risk areas with low pressure threshold are commonly the prominent body parts such as the coccyges, sacrum and ischial tuberosities [72].

### **Pelvic tilt and seating asymmetry**

Several causes of AP pelvic tilt exist. Iliopsoas contracture increases the anterior pelvic tilt and consequently increases the lumbar lordosis, which might be painful [4]. Posterior pelvic tilt with a decreased lumbar lordosis is seen in severely hypotonic children or after scoliosis surgery. Posterior pelvic tilt results in a more

vertically placed sacrum causing painful sitting and possible ulcers over the sacro-coccygeal area. Hamstring and rectus weakness, inadequate lengthening or spasticity may cause affected AP pelvic tilt (Fig. 2) [75].

LR pelvic tilt is defined by either right or left pelvic obliquity or a level pelvis. Obliquity is common in children with tetraplegia with total body involvement with contractures above and/or below the iliac crest. An asymmetrical adduction contracture or presence of scoliosis of the spine might cause LR pelvic tilt (Fig. 3).

Pelvic rotation is primarily seen in relation to scoliosis (Fig. 4).



**Figure 2** Bone-model illustrating AP pelvic tilt in the seated position. Left: Pelvic anterior tilt. Right: Posterior pelvic tilt.



**Figure 3** Bone-model illustrating LR pelvic tilt in the seated position. Left: Level pelvis. Right: High one-sided pelvic tilt.



**Figure 4** Bone-model illustrating pelvic rotation in the seated position. Left: Level pelvis. Right: Pelvic rotation.



Scoliosis, pelvic tilt and hip deformity are associated to an asymmetrical seating position (Fig. 5). Normal variations in seat load are seen with up to 60% of the total load placed on one side of the midline; hence asymmetry has previously been described as more than 60% of the total body load on one side. The center of force (CoF) is located near the midline and in front of the perineum [65]. In non-ambulatory paraplegic patients Drummond et al [76] found a risk for pressure sores if 30% or more of the total body weight was distributed under one ischium or if 11% or more of the total body weight was distributed to the sacral and coccygeal area. In addition, if more than 30% of the total seated pressure is near the sacral and ischial area, skin breakdowns might occur [65;71;76].

### **Assessment of seating performance**

Seating performance can be assessed by pressure mapping. Different pressure mapping equipment has been investigated and a large variation in the type of outcome is seen. Most pressure mapping systems have numerical output (CONFORMat, FSA, Clinseat, XSensor, Pliance-X); but have also been analysed with semi-quantitative methods (visual ranking). Only in some types of equipment have all the psychometric properties been evaluated [65;77-79]. The present available interface pressure mats consists of a number of arrays of sensels with different capabilities and materials [8;68;78;79].

A few studies have used interface pressure to determine seat load characteristics; but no consensus has been made as to the most appropriate outcome measures. For example, controversy exists whether average or peak pressure is the best descriptor of interface pressure [80]. Gutierrez et al [81] reports basic outcomes such as maximum pressure, contact area, mass, active area of the highest 75% of the maximum pressure and distance from each side's peak pressure location to the CoF. A formula for calculating asymmetry indices was proposed. Nielsen et al [65] further investigate seat load characteristics by use of peak pressure and contact area of the entire and the maximum pressure surface and three asymmetry indices were calculated using the formula proposed by Gutierrez et al [81]. Miller et al [78] used both quantitative (average and maximum pressure and number of high load pressure sensors in the sacral area) and semi-quantitative (visual ranking of the pressure map) outcome measures. Fradet et al [8] used tuber pressure and evaluated pelvic tilt in all 3 planes.

### **Seating difficulties in CP**

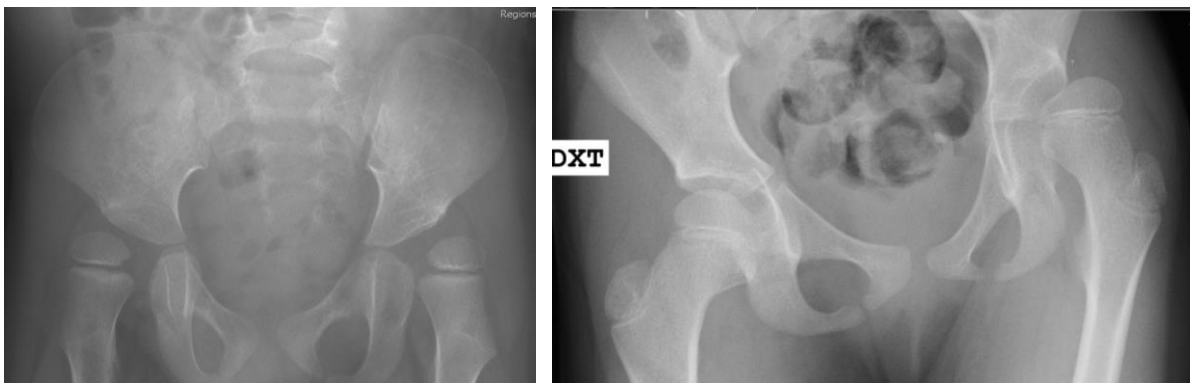
Optimal seating is critical in non-ambulatory children. Impaired seating position increases the risk of deformities, asymmetries, pain, pressure ulcers, cardiovascular or respiratory insufficiencies, postural control, participation impairments and decreased quality of life (Fig. 5). Seating correction aims for a perpendicular, upright position minimizing the risk of pressure ulcers, prevention of deformity progression and enablement of the child to participate in daily activities with use of both arms [68;70].

Inappropriate seating positions increase the risk of contractures and progressive deformities such as scoliosis or hip dislocation. Children with GMFCS IV-V are unable to change position while seated and the long time they spend in an abnormal position increases the risk of contractures [82]. They are passive sitters and rely entirely on supportive seating measures adjusted to manage sitting disabilities

such as spasticity, hypotonia, dystonia, ataxia and musculoskeletal deformities [70]. Asymmetrical lying positioning can also increase postural deformities [8].

Chronic pain in children with CP might originate from an impaired seating position or due to secondary effects such as deformities, infections or pressure sores [22;23;33]. Immobilisation or motor impairments might hinder pressure-relieving movements and result in pressure sores [83].

Knowledge of balance and postural control in the seated position in children with cognitive, sensory or motor impairment, are key elements in improving rehabilitation, participation and independence including optimization of upper-extremity function [8;84]. Hence, a valid assessment of seating performance is a core element in optimising a range of aspects in the life of children with CP.



*Figure 5 Preoperative radiographs from study III. a) Bilateral subluxated hips. No pelvic obliquity. b) Unilateral hip subluxation on the high side of a coronal plane pelvic obliquity.*

## 5. Aim of the thesis

- I. To evaluate pain assessment tools for children with CP and to choose a suitable score for translation into Danish. Furthermore the study aims to document the process of translation of the r-FLACC pain score using a standardised guideline.
- II. To evaluate the psychometric properties of the Danish version of the r-FLACC score by testing reliability and validity using the COSMIN checklist as a guideline.
- III. To test the efficacy of epidural analgesia and LIA for the management of early postoperative pain in children suffering from CP.
- IV. To determine the intra-variability of the basic measures of seating performance in 65 healthy children and to further define appropriate measures of seating performance.
- V. To assess the change in seated pelvic tilt in children with CP after hip reconstruction and to correlate the radiological hip status with seating performance.

# 6. Materials & methods

## Hypotheses

**Study I:** The r-FLACC pain score can be translated into Danish with approved techniques, creating a high quality and clinically feasible pain assessment tool for Danish children with CP.

**Study II:** The r-FLACC pain score maintains its psychometric properties after translation into Danish and is valid and reliable for measuring postoperative pain in children with CP not able to self-report.

**Study III:** Epidural analgesia is superior to local infiltration analgesia for early postoperative pain management in children with cerebral palsy undergoing unilateral hip reconstruction and spica casting.

**Study IV:** The basic measures of seating performance in healthy children have low intra-variability assessed with the Tekscan CONFORMat interface pressure mat. The basic measures can be further evolved into appropriate measures of seating performance.

**Study V:** Hip reconstruction improves seated pelvic tilt and the radiological hip status is correlated with seating performance.

## Study designs

The translation process of *study I* comply with the international 10 step guideline set up by the Translation and Cultural Adaptation Group [59].

*Study II* is a validation study of the r-FLACC pain score. The study was designed as a prospective observational cohort study including children with CP not able to self-report pain and planned for orthopaedic surgery at department of children's orthopaedics at AUH. All children were exposed to surgery and with a predefined hypothesis that the level of pain increases after orthopaedic surgery, the postoperative level of pain was assessed using the r-FLACC. Effect modification was minimized by including all types of orthopaedic surgery from minor procedures to extensive bony reconstructions, since the magnitude of surgery might modify the effect on postoperative pain. Other causes of pain in children with CP might confound the effect of the exposition, meaning that the level of pain measured on the r-FLACC score postoperatively may not be entirely due to the surgery. However for present study, this effect is primarily relevant when evaluating construct validity.

*Study III* was designed as a two-part study. The first part was a prospective randomized controlled trial with randomization to either LIA or placebo analgesic treatment after the hip reconstruction in addition to intravenous or oral analgesia. Furthermore, a bolus administration of the randomized treatment at 8 and 20 hours postoperatively was given. If necessary the pain management was supplemented with epidural analgesia as described in paper III [3]. In the second part of the study, children undergoing hip reconstruction were consecutively included for postoperative pain management with epidural analgesia in addition to

intravenous or oral analgesia (Fig. 6). For all 3 groups, the study period ended 21 hours postoperatively and pain assessments were made at 4 hours, 9 hours and 21 hours postoperatively. The opioid consumption was assessed in the period of anesthesia, last 30 min of anesthesia, during the first 4 postoperative hours, from 4-9 hours and from 9-21 hours.

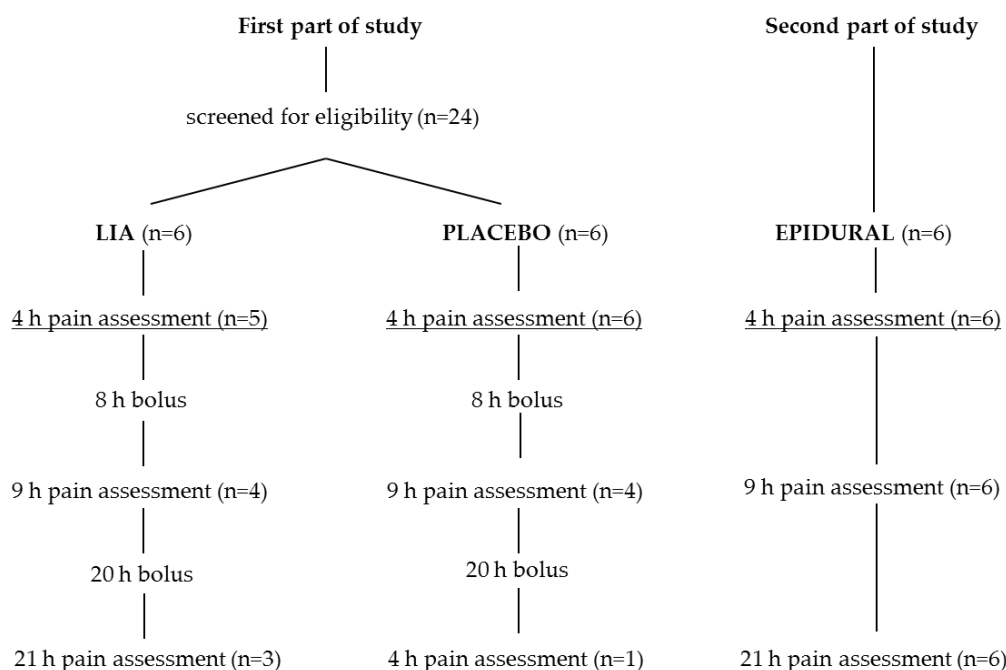


Figure 6 Time-line of study III

Study IV was designed as a cross-sectional observational cohort study. Permission for contacting the parents of the children of 4 school grades was obtained from the principal at Strandskolen in Aarhus. Afterwards written study information was distributed to all children and parents in a first, third, fifth and seventh grade. Only the children, whose parents had given written consent, were included in the study. If the parent indicated on the consent form that the child had been or was being evaluated for an orthopaedic condition, the child was excluded from analysis.

Study V was designed as a prospective observational cohort study. Inclusion criteria were planned unilateral hip reconstruction with relevant soft tissue procedures in children with CP. Exclusion criteria were bilateral surgery. When the decision was made that unilateral hip reconstruction was necessary, the parents were informed of the study and invited to participate. The preoperative assessment of seating performance was done in the outpatient clinic after informed parental consent was obtained. The postoperative assessment of seating performance was done when the child came in for clinical postoperative follow-up (>3 months postop).

## Patient characteristics

Study I is a translation study, hence no patients were included in the study.

In Study II, 27 children 3-15 years old (11 girls and 16 boys) were included. All the included children had tetraplegic CP and were not able to self-report pain. GMFCS scores ranged from II-IV (Table 1). Inclusion criteria were children with CP who were not able to self-assess pain and planned orthopaedic surgery at the Department of Children's Orthopaedics, AUH. The surgical procedure

varied in severity from minor tendon surgery to major bony orthopaedic surgery. Twenty children underwent pelvic and femoral osteotomy, 4 children underwent tendon or soft tissue surgery, 1 child underwent calcaneal osteotomy, 1 child underwent epiphysiodesis of the distal femur and 1 child had femoral plates removed.

In *Study III*, 18 children were included at the Department of Children's Orthopedics, AUH, from Sept 2009 to Nov 2014. Inclusion criteria were planned unilateral femoral and pelvic osteotomy; planned postoperative hip spica casting and age above 18 years. Exclusion criteria were previous surgical interventions in the same anatomical region, multi-level surgery, known allergy/intolerance to study drugs or implanted intrathecal baclofen pump. In the first study period, 12 children with CP with varying levels of cognitive impairment were included and randomized for either LIA or placebo treatment. In the second study period, 6 children were consecutively included for epidural analgesia postoperatively. Demographic and surgical variables were similar between the 3 groups. Demographics are presented in table 1, for specifics see paper III [3].

In *study IV* 66 normal children were included. One child had reports of a mild conservatively treated scoliosis and was excluded from data analysis. Demographics from the 65 children who underwent data analysis are presented in table 1 and paper IV (appendix).

In *study V* 18 children with CP were included at the Department of Children's Orthopaedics at AUH from 2010-14. 10 children had unilateral hip dislocation (HD) and 8 children had bilateral HD. All children underwent unilateral hip reconstruction. 6 children had an ITB pump implanted for management of spasticity (Table 1).

Some of the children were eligible for inclusion and subsequently included in more than one of the studies. However, this did not change any part of the studies. The children and their parents were informed of the studies separately and were informed to give consent to each study. 10 children were included in both *study III and V* and 17 children were included in both *study II and III*.

	Study II	Study III	Study IV	Study V
No. Of children (n)	27	18	65	18
Age/years (SD)	9 (3-15)	8 (3-13)	11 (7-14)	7 (4-10)
Sex (M/F)	16/11	10/8	33/32	8/10
GMFCS (range)	II-IV	III-V	n.a	III-V
ITB pump (no.)	n.a	0	n.a	6

**Table 1** Baseline demographics for study II-V. Values are median (range). Demographics in detail are listed in paper II-V, Appendix.

## Ethical issues

For all five studies oral and written informed consent was obtained from the parents of the children, and the study was carried out in accordance with the principles of the Helsinki Declarations

*Study I and II* was approved by the Committee on Health Research Ethics, Central Denmark Region (M-20100189) and the Danish Data protection Agency (1-16-02-97-10).

*Study III* was approved by the Committee on Health Research Ethics, Central Denmark Region (M-20080207), the Danish Medicines Agency (EudraCT. no

2008-006913-26) and the Danish Data Protection Agency. It was registered at clinicaltrials.gov (NCT00964639), conducted in accordance with the guidelines for Good Clinical Practice (GCP), and monitored by the GCP unit at Aarhus University Hospital.

For both *study IV and study V* the local ethical committee of the Central Denmark Region assessed that no ethical approval was necessary since no interventions were done in the studies.

## Methodological considerations

### Hip reconstruction and anaesthesia

In *study III and V* all children underwent unilateral hip reconstruction. On the ileum, the osteotomy was either the innominate osteotomy of Pemberton or Salter using a modified Smith-Peterson approach combined with a shelf augmentation [85;86]. The femoral osteotomy was made just below the trochanter minor through a standard lateral incision and the necessary shortening, derotation and varisation was performed. The femoral osteotomies were internally fixed using either the LCP Pediatric Hip Plate 3.5/5.0 for varus osteotomies (DePuy Synthes), Richards Intermediate Compression Hip Screw (smith&nephew) or the Integra Surfix Paediatric Plate (Allegra) (Fig. 7).



**Figure 7** Commercial illustrations of the LCP Pediatric Hip Plate 3.5/5.0 for varus osteotomies (DePuy Synthes), Richards Intermediate Compression Hip Screw (smith&nephew) and the Integra Surfix Paediatric Plate (Allegra) and radiographics of implants used in study V.

All patients underwent additional adductor release through a small medial groin incision, rectus femoris release through the modified Smith-Peterson incision at the ileum and iliopsoas release at the level of the trochanter minor through the lateral femoral incision after femoral osteotomy was performed. All surgeries were performed by two surgeons (OR, BMM).

All hip reconstruction procedures were performed with the child under general anaesthesia using propofol and/or sevoflourane and remifentanil. For *study III*, all included children had an epidural catheter inserted and tested in case they needed supplemental epidural analgesia. In the epidural group a continuous epidural infusion with bupivacaine 2.5 mg per ml was maintained for the first 2-3 days postoperatively (continuing after end of study). All children were transferred to the intensive care unit postoperatively where standard pain treatment consisted of paracetamol 15 mg/kg x 4 p.o. or rectally, fentanyl 0.5-1µg/kg i.v. or morphine 0.05-0.1 mg/kg i.v.

## Local infiltration analgesia

In *study III* both the LIA and placebo group received intraoperative infiltration. In the LIA group the dosage was ropivacaine 2 mg/kg and epinephrine 5µg/ml as infiltration and ropivacaine 0.5mg/kg as bolus. The concentration of ropivacaine was 2 mg/ml and for a child of 30 kg the dosage amounts to a volume of 30 ml to be infiltrated. Identical volumes were used of isotonic saline in the placebo group. All infiltrations were performed by the same surgeon (OR) using the “moving needle” technique described by Kerr and Kohan [44]. Details on infiltration and the process of randomization and blinding are described in in paper III [3].

## Radiographic evaluation

In *study III and V* a radiographic evaluation of the hips were performed using plain anterior-posterior radiographs of the hips. No specific study-related method for obtaining the radiographs was used. All radiographs were taken at the radiology department at AUH by trained personnel. The radiographs need to show a perfect horizontal view of the pelvis with the legs in neutral position. A hip adduction might result in a false high MP and a hip abduction in a false low MP [87].

The measurements used were the migration percentage (MP) and the acetabular index (AI). Chan et al [10] reports that in children with CP, MP is within acceptable limits if it is below 30%. In adults the AI is considered normal when it is less than 20°; but in children below 5 years of age an AI of 25° is considered normal [10]. Hägglund et al [87] analysed the radiographs of 272 children with CP in a standardised follow-up and found that measurement of MP alone was sufficient in screening for hip dislocation and recommended that hips with a MP of 33-40% should be surgical treated or receive intensified observation and if above 40% should receive surgical intervention [87]. In *study V* the children were stratified into a preoperative unilateral or bilateral group, where unilateral was defined as only one hip with MP > 30% and bilateral was defined as both hips with MP > 30%. In present study, MP was calculated as the width of the femoral head placed lateral of Perkins' line divided by the total width of the femoral head multiplied by 100 [88].

The assessments were all done by the same person (LKP) and in 12 hips the measurements were repeated after 2 weeks to test reproducibility. The mean coefficient of variation (CoV) proved very good reproducibility of the measurements (CoV, MP: 2.5%; CoV AI: 2.5%). Other studies have found high measurement errors of inter-rater measurements of MP, hence these studies recommended that only one investigator for radiographic measurements was used [7;87;88].

## Pain assessment

Available pain scores for children not able to self-report pain were reviewed in *Study I* and the r-FLACC was selected for translation into Danish based on superior clinical feasibility. The translation followed the guideline published by Wild et al [59].

The r-FLACC score consists of 5 subgroups (Face, Legs, Activity, Cry and Consolability) in which the patient can be assigned 0,1 or 2 points related to specific pain reactions, resulting in a total score between zero and ten, where 0 reflect no pain and 10 reflects the maximum level of pain (Fig. 1, appendix). The r-FLACC score has the possibility of including the child's own pain behaviours. Before use the child's individual pain behaviors are added to the open-ended descriptor in each



subgroup. An example of the parent-reported individual pain behaviours of a child with CP is presented in paper 1 [1].

The VAS-OBS was used for simultaneous pain assessment by the parents in order to assess criterion validity. Since no other pain assessment tool for children with CP not able to self-report was available in Danish, the VAS-OBS was chosen acknowledging its questionable psychometric properties [41;42].

In both studies the r-FLACC score was assessed through a standardized 2 minutes video-recording including a close-up of the face, the legs and the full body of the child. The parents or primary caregivers were asked to try to console the child if they found it necessary while recording. The video recordings were viewed in a randomized order and assigned an r-FLACC score by a registered nurse (RN) experienced in the care and pain management of children with CP. The RN was blinded to the treatment allocation and independently assigned an r-FLACC score, after having read the child's individual pain behaviours. In addition to the r-FLACC pain assessment, the Observational Visual Analog Scale (VAS-OBS, range 0-10) [89] was used at the bedside in both *study II and III*. The parents or primary caregivers estimated the pain intensity of the child during the same 2 minutes as the video-recording was done.

In *study II*, internal consistency was evaluated in all 27 children. Inter-rater reliability of the r-FLACC score was evaluated in 20 children with 2 RNs independently assigning r-FLACC scores. Intra-rater reliability was evaluated by one of the RNs reviewing 10 of the recordings 1 year later. Ten children had both a preoperative and postoperative video-recording done in order to assess construct validity of the r-FLACC score. Criterion validity was evaluated by comparing the r-FLACC and VAS-OBS scores in all 27 children.

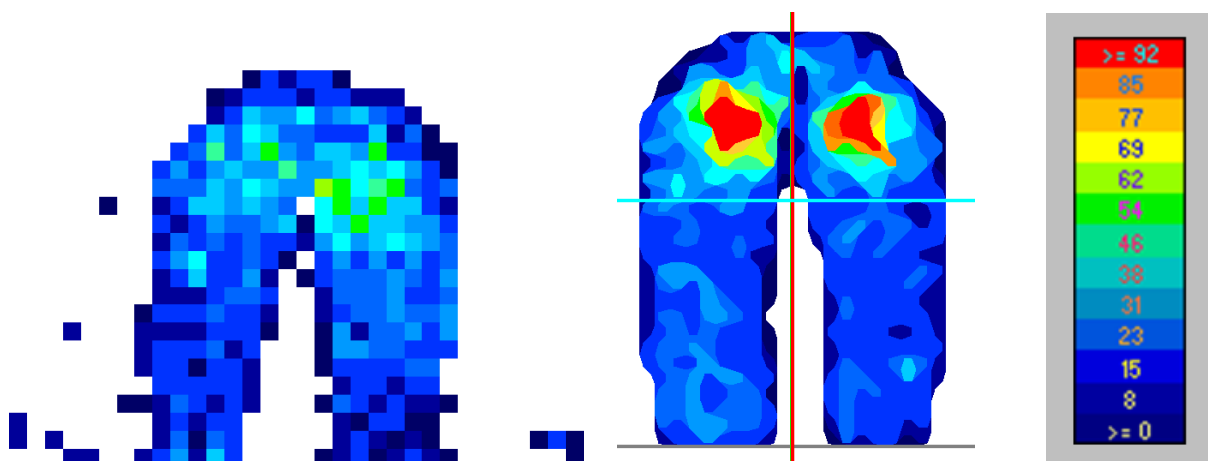
In *study III*, all 18 included children had a video-recording and a VAS-OBS assessment done preoperatively, at 4 hours postoperatively, at 9 hours postoperatively and at 21 hours postoperatively unless they had been excluded prior to the assessment time. Complete pain questionnaires for the r-FLACC were returned for sixteen children. A secondary outcome was the mean opioid consumption corrected for body weight (fentanyl equivalent dosages per kg) during the study period.

### **Measurement of seating performance**

In *study IV*, each child completed six measurements of seating position and all received identical instructions. The instruction was to sit with unsupported feet, hands placed on the thighs looking straight forward. The pressure sensor was placed on the same examination bed for all measurements to maintain identical underground properties. The measurements were done without undressing the child, unless if the child wore trousers with big buttons. Three recordings of 30 seconds were done seated in a normal back position, followed by three recordings with the child in an up-right back position. Between measurements the children were encouraged to stand up and move or shake their legs. All measurements were conducted with minimum disturbances. The 2000 frames of each recording were averaged using Tekscan F-Scan Research software and for analysis the 2-D display was chosen and the colour scale was set to display maximum pressure as red at 100 mmHg. An edit file for each recording was created; deleting sensors with loadings not related to the child's seating area as well as the distal two rows (Fig. 8).

In *study V*, seating performance was assessed in 18 children with CP undergoing hip reconstruction. These children were all classified as GMFCS III-V, indicating inadequate postural control for independent sitting. A standardized algorithm for manual support during the measurement of seating performance was necessary [67]. All persons supporting the children received identical instructions. The child was to sit on the pressure sensor with unsupported feet and a back inclination of approximately 90 degrees with the person supporting the child standing in front of the child, having one hand on each side of the thorax giving just the amount of support needed for the child not to fall over. Due to the constant movements of a child with CP the support needed to be dynamic rather than static.

The sagittal midline and a transverse line between the buttocks and the thigh areas were defined using the following guidelines (Fig. 8). Midline: 1) Equal amount of sensor columns loaded on the right and left side. 2) Equal amount of sensors loaded between the peak pressure areas to the midline on each side. 3) The CoF should be close to the midline. Transverse line: 1) Placed posterior to the point where the blue-tone colors of the thighs gets light-blue indicating higher pressure. 2) One unloaded sensor should be present between the legs posterior to the line. A re-test of line placement by another rater was performed on 12 recordings for assessment of reproducibility (3 children from each grade in *study IV*). A Coefficient of Variation (CoV) showed very good reproducibility of both midline and transverse line placement (CoV, midline: 0.004; CoV transverse line: 0.026).



**Figure 8** Left: Averaged 2-D display with sensor loadings not related to the child. Middle: 2-D contour displayed averaged recording with the midline and transverse line depicted. Right: Color scale.

### Basic measures

*Study IV* analyses the following basic measures of seating performance and aim to establish reproducibility hereof before proposing appropriate outcome measures based on the basic measures. The basic measures are illustrated in figure 9.

**Average pressure** is defined as the average pressure loaded onto the sensors for the total contact interface and for the right and left side.

**Peak pressure/tuber pressure** is defined as the average pressure in a 2x2 sensor area and is located by the Tekscan software. The peak pressure is assessed for the right and left side. In this thesis, the assumption is made that peak pressure for each side equals tuber pressure.

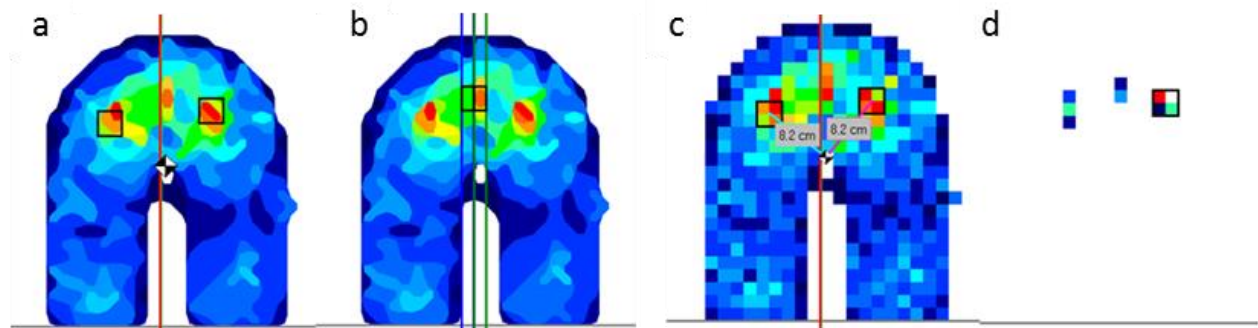
**Sacral pressure** is not given by the software; hence a definition has been set up. The peak pressure (2x1 sensor) in the column of sensors on each side of the

midline was analysed by manual placing of an analysis box in the Tekscan software and averaged to sacral pressure (2x2 sensors).

The **distance from CoF to tuber pressure** can be used to evaluate pelvic rotation. The distance is measured manually in the Tekscan software by placement of a line from the centre of tuber pressure to the CoF (Fig 9 and 10).

**Area** is defined as the area of the loaded sensors calculated by the Tekscan software. This is assessed both for the total contact area and for each side (right and left side of the contact area)

**Area with 25% of maximum peak pressure:** The peak pressure of the total seating interface is measured. The software is set to only display the area loaded with the highest 25% pressure. For example, if peak pressure is 155 mmHg, the maximum 25% of peak pressure is between 116 mmHg and 155 mmHg. The area with this pressure range is large if the pressure is well redistributed and small when the highest pressure is put on a limited area.



**Figure 9** a) The midline (vertical red line), center of force (CoF) (diamond-mark) and peak pressures (left: 86 mmHg; right: 121 mmHg), b) The two columns flanking the midline with sacral pressure, c) The distance from the two sides' peak pressures to the CoF, c) The area (10.85 cm<sup>2</sup>) with the maximum 25% of the peak pressure (121 mmHg - 25% of peak pressure = 91 mmHg).

## Outcome measures of seating performance

### 1) Pelvic LR tilt

Pressure and peak pressure asymmetry index for measuring coronal plane pelvic tilt.

### 2) Pelvic AP tilt

Sacral pressure for measuring sagittal plane pelvic tilt.

### 3) Pelvic rotation

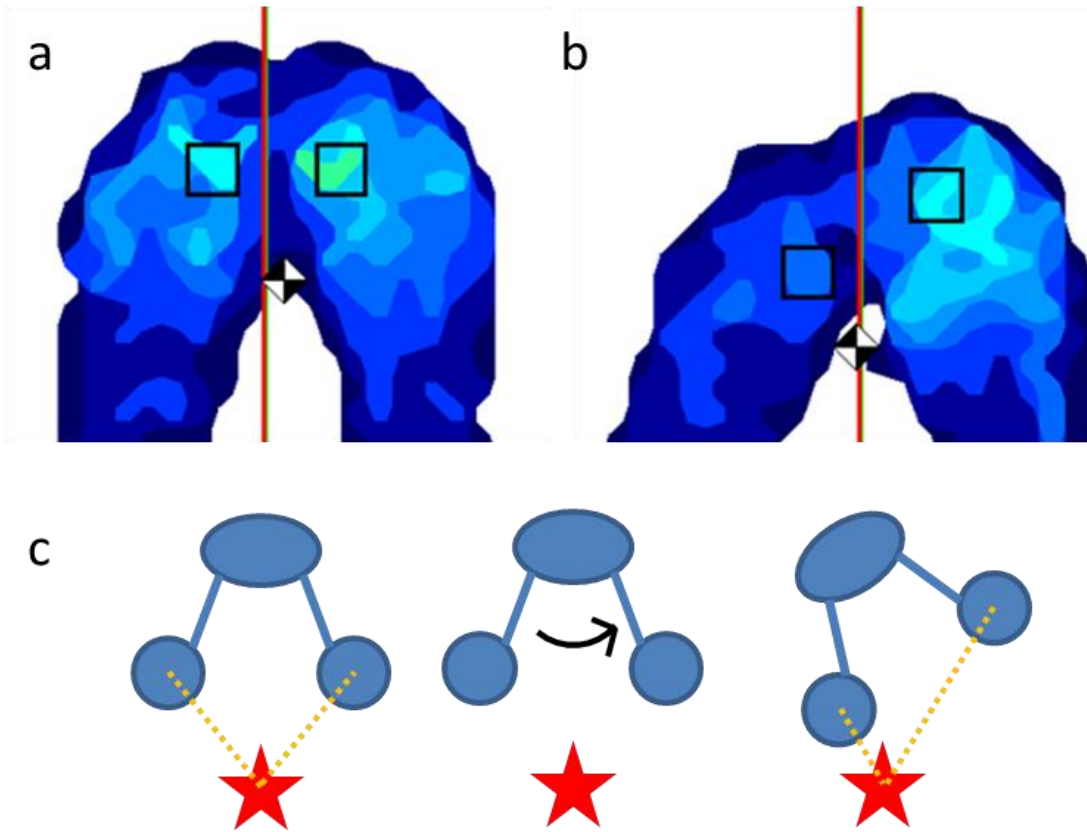
Distance asymmetry index for measuring transverse plane pelvic tilt (Fig 10).

### 4) Soft tissue quantity

Area asymmetry index for assessment of soft tissue quantity.

### 5) Pressure ulcer risk

The area with 25% of the maximum pressure for assessment of the loading area and risk of pressure sores.



**Figure 10** a) Interface pressure map of seating performance of a child seated in normal position. Black square: Peak pressure/ tuber pressure. Diamond: CoF. The distances from tuber pressure to CoF are 7.1 cm and 7.6 cm respectively equivalent to a distance asymmetry index (pelvic rotation) of 0.0, b) Interface pressure map of seating performance of the same child seated with maximum rotational position. The distances from tuber pressure to CoF are 9.8 cm and 5.2 cm respectively equivalent to a distance asymmetry index (pelvic rotation) of 0.31, c) Illustration of distance asymmetry index as a measure of pelvic rotation. The spine (blue oval) is the mechanical centre of rotation and the distances to the tubera (blue circles) does not change by rotation of the pelvis. The location of the CoF (red star) is not determined by the rotation of the pelvis. When the pelvis rotates, the distance from one side's tuber to CoF (yellow line) decreases as the other side's distance from tuber to CoF (yellow line) increases.

## Statistical considerations

### Sample sizes

For *study I*, no sample size calculation was needed. *Study II* evaluates the psychometric properties of the r-FLACC score, but no standards for sample size calculations exist regarding analyzing such a measurement instrument. Terwee et al. [64] report the COSMIN guidelines and recommend including 4-10 subjects per item in the score if factor analysis is used. Since the r-FLACC has 5 items we chose a sample size of 25 children. Final sample size was 27 children adjusting for possible drop-outs. Acknowledging that a formal factor analysis would also require > 100 children to be included only Factor Analysis Uniqueness (FAU) was evaluated.

For the first part of *study III*, a sample size calculation was made based on an expected difference between the LIA and the placebo group of 5 points on the r-FLACC score (SD 3). With 80% power ( $\alpha = 0.05$ ,  $\beta = 0.2$ ) a sample size of 12 children in total was required. In the second part of the study identical assumptions were made between the epidural and the LIA group resulting in an equal sample size of 12 children in total.

In *study IV* 65 normal children were included and in *study V* 18 children with CP undergoing hip reconstruction were included. Since the used outcome measures were developed by these studies no meaningful standard deviation was available for sample size calculations. Post-hoc power analyses were not assessed to be indicated, since the null-hypotheses were in fact rejected using appropriate significance levels. This is in accordance to Knapp [90], who states that “a statistically significant effect based on a small sample is more impressive than a statistically significant effect based on a large sample, since large-sample sizes can “buy” effects that are not scientifically important [90-92].

### Statistics

For all statistical analyses STATA 11 (StataCorp LP, Texas, USA) was used. Before the parametrical statistical analyses data were plotted with QQ-plots and SD-tests to assess normal distribution. A p-value of <0.05 was considered to be significant for all five studies.

Analysis of the r-FLACC scores and VAS-OBS scores in *study II and III*, the opioid consumption in *study III* and parameters of seating performance in *study IV and V* were carried out with use of the 2-sample Students t-test with equal variances (un-paired) for normal distributed data.

The psychometric properties in *study II* is evaluated using statistics proposed by the COSMIN checklist [60-62]. The assumption of unidimensionality of the r-FLACC is tested by FAU and a result < 0.6 is interpreted as indicating unidimensionality and hence structural validity [63]. A complete factor analysis with rotation of factors and their loadings was not performed since the FAU was assessed as being adequate for testing the assumption of unidimensionality before establishing the internal consistency. Internal consistency is assumed if Cronbach's Alpha (CA) is between 0.70 and 0.95 [63]. Sholtes et al [63] states that the preferred statistics for measurement error is by evaluating the standard error of measurement (SEM) and the smallest detectable change (SDC). In *study II*, though, measurement error is evaluated visually by use of the Bland-Altman plots of both intra and inter-rater measurements as proposed by Martinkevich et al [93], in which mean

differences close to zero indicate low bias and small intervals between the results indicate low limit of agreement, thus low measurement error. In the plots the differences between pairs of measurements are plotted against the average of each pair in combination with the mean difference and the upper and lower limits of agreement.

Reliability is for categorical data evaluated by kappa statistics and for continuous data by intra-class correlation (ICC) or Pearson or Spearman correlation coefficients [63]. The r-FLACC outcome and the numerical output of assessment of seating performance are considered as continuous data.

Intra and inter-rater reliability in *study II* and intra-variability in *study IV* are evaluated by a one-way analysis of variance ICC - type 1,1 [94]. ICC ranges from 0 to 1 and is interpreted using the following criteria: 0.00-0.39 poor, 0.40-0.59 fair, 0.60-0.74 good and 0.75-1.00 excellent [95;96]. As stated by Müller et al [97], the terms reliability, reproducibility and repeatability have been used inconsistently for assessing intra and inter observer consistency, which might confuse the interpretation of ICC. In *study IV*, the biologic variation with-in the individual child is assessed, hence the term intra-variability is used.

Floor and ceiling effects of the r-FLACC assessments are assessed by evaluation of the percentage of minimum and maximum pain scores with 30% being the cut-off point for acceptance [93].

When both the outcome instrument and the gold standard instrument are continuous scores, as the r-FLACC and VAS-OBS are, a Pearson's correlation coefficient >0.70 indicates criterion validity, which is used in *study II* [63].

The reproducibility of the radiological measurements in *study III and V* are evaluated by a Coefficient of Variance (CoV), which is the ratio of the SD to the mean. A value below 10% is commonly considered to show good reproducibility.

In *study IV and V*, an asymmetry index is calculated for the parameters of seating performance using the following formula proposed by Gutierrez et al [81]:

$$Asymmetry = \frac{max - mean}{mean}$$

The asymmetry index measure the percent difference from each side to their mean and result in a number between 0 and 1, where 0 represents perfect symmetry and 1 represents total asymmetry [81].

# 7. Results

## Study I

### Outcome 1: Danish translation of the r-FLACC score

An evaluation of pain assessment tools for children with CP ranked the r-FLACC pain score high; hence it was chosen for translation. The Danish version of the r-FLACC pain score is the end result of this part of the study (fig. 11).

All ten standardised steps for translation were followed. Details on each step are presented in paper 1 [1].

r-FLACC score til bestemmelse af smerter hos børn med cerebral parese	
<b>Face / Ansigt:</b>	
0 point:	Neutralt udtryk eller smil
1 point:	Lejlighedsvis grimassering/panderynken; tilbagetrukket el. uinteresseret; <i>virker ked af det eller bekymret</i>
2 point:	Vedvarende grimassering eller panderynken; hyppig/konstant dirrende hage, sammenbidte tænder; <i>stresset ansigtsudtryk; udtrykker frygt eller panik</i>
<i>Individuel adfærd:</i>	
<b>Legs / Ben:</b>	
0 point:	Normal eller afslappet stilling; <i>normal muskelspænding &amp; bevægelse af ben</i>
1 point:	Urolige, rastløse, anspændte; <i>lejlighedsvis rystelser</i>
2 point:	Sparkende, eller benene trukket op; <i>markant øget spasticitet, konstante rystelser eller spjæt</i>
<i>Individuel adfærd:</i>	
<b>Activity / Aktivitet:</b>	
0 point:	Ligger stille, normal stilling, bevæger sig frit; <i>regelmæssig rytmisk, vejrtrækning</i>
1 point:	Vrider sig, flytter sig frem og tilbage, <i>anspændte el. forsigtige bevægelser; let agiteret (f. eks bevæger hovedet frem og tilbage, aggression); overfladisk, indtrækninger, lejlighedsvis suk.</i>
2 point:	Kroppen spændt som en bue, stiv eller spjættende; <i>svær agitation; slår med hovedet; skælven (ikke kulderystelser); holder vejret, gisper el. skarpe vejrtrækninger, svære indtrækninger</i>
<i>Individuel adfærd:</i>	
<b>Cry / Gråd:</b>	
0 point:	Ingen gråd/ udtrykker sig ikke i ord om smerte.
1 point:	Støn el. klynk; lejlighedsvis klagen; <i>lejlighedsvis verbale udbrud eller stønnen</i>
2 point:	Græder vedholdende, skriger eller snøfter, hyppige klager; <i>gentagne udbrud, konstant stønnen</i>
<i>Individuel adfærd:</i>	
<b>Consolability / Trøstbarhed:</b>	
0 point:	Veltilpas og afslappet
1 point:	Beroliget ved lejlighedsvis berøring, knus el. ved at blive talt til. Kan afledes.
2 point:	Svær at trøste eller få til at føle sig tilpas; <i>skubber plejepersonale og pårørende væk, modsætter sig omsorg el. tiltag for at opnå veltilpashed</i>
<i>Individuel adfærd:</i>	

**Figure 11** The Danish version of the r-FLACC score for pain assessment in children with cerebral palsy. Revisions from the original FLACC score are noted in italics [1].

## Study II

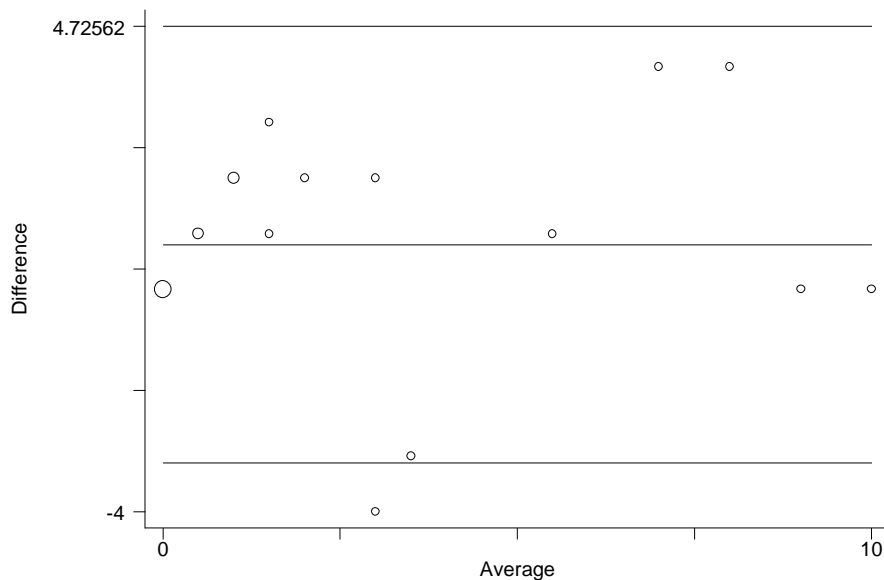
### Outcome 1: Reliability measurement properties.

Internal consistency of the r-FLACC pain score was established using Cronbachs Alpha (CA) and factor analysis. CA for rater 1 was 0.9023 and for rater 2 was 0.9758. The CA values for each subgroup are listed in Table 2. A factor analysis of the 5 subgroups showed low FAU indicating unidimensionality (FAU face: 0.55; FAU legs: 0.25; FAU activity: 0.31; FAU cry: 0.25; FAU consolability: 0.19).

	CA Rater 1 (n=27)	CA Rater 2 (n=20)
Face	0.9147	0.9756
Legs	0.8777	0.9729
Activity	0.8763	0.9744
Cry	0.8697	0.9630
Consolability	0.8618	0.9630
Total	0.9023	0.9758

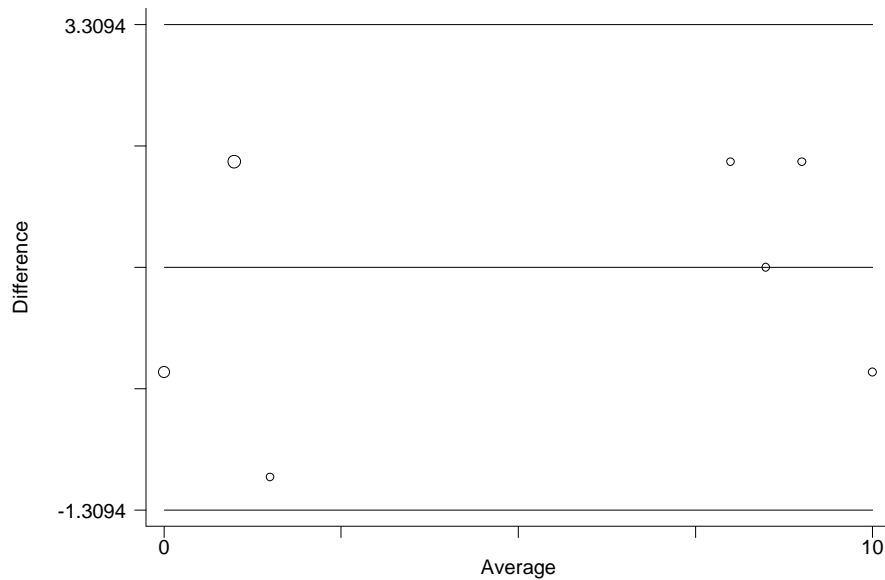
**Table 2** Internal consistency illustrated by Cronbachs Alpha (CA) for both raters for each of the 5 subgroups in the r-FLACC pain score [2].

Intra-rater reliability was excellent measured by test-retest of the r-FLACC score resulting in an ICC of 0.97530. Inter-rater reliability between rater 1 and 2 was good with an ICC of 0.74576. The measurement error of both intra and inter-rater reliability are illustrated by Bland-Altman plots (Fig. 12, Fig. 13).



**Figure 12** Agreement (inter-rater reliability) illustrated by Bland-Altman plot (n=20) with comparison between rater 1 and rater 2. The differences between the pairs of measurements on the vertical axis are plotted against the average of each pair on the horizontal axis. The middle horizontal line reflects the mean difference (0.8 (95% CI: -0.119; 1.719) and the upper and lower line the limits of agreement (-3.126; 4.726) [2].





**Figure 13** Agreement (intra-rater reliability) illustrated by Bland-Altman plot (n=10) with comparison between the first r-FLACC scores from rater 1 and the re-test scores after 1 year. The differences between the pairs of measurements on the vertical axis are plotted against the average of each pair on the horizontal axis. The middle horizontal line reflects the mean difference (1.0 (95% CI: 0.174; 1.826)) and the upper and lower line the limits of agreement (-1.309; 3.309) [2].

No floor or ceiling effects were observed and the entire range of the r-FLACC score was used with a minimum r-FLACC score of zero in 30% of the children and a maximum score of ten in 7% of the children.

## **Outcome 2: Validity measurement properties.**

Content validity was tested by the originators of the r-FLACC and is transferable through translations.

Construct validity was supported by a significant increase in r-FLACC scores following surgery compared to preoperative assessments (n=17; difference 2.23; p=0.0397).

Criterion validity was evaluated by Pearson's Correlation Coefficients, when comparing the r-FLACC scores of the two raters and the VAS-OBS scores. In rater 1 a coefficient of 0.76 (n=27) was found and in rater 2 a coefficient of 0.59 was found (n=20).

## Study III

### Outcome 1: Pain measurements.

The primary outcome of *study III* was the level of pain 4 hours postoperatively. In the children treated with epidural analgesia lower both r-FLACC ( $p=0.01$ ,  $p=0.01$ ), and VAS-OBS ( $p=0.02$ ,  $p=0.00$ ) scores were found compared to the LIA and the placebo group, respectively (Table 3).

	LIA	p-value *	Epidural	p-value **	Placebo	p-value ***
<b>4 hours postoperatively</b>						
Number of patients	5		6		6	
Opioid consumption ( $\mu\text{g}/\text{kg}$ )	6.3 (2.8)	<b>0.00</b>	0.5 (0.7)	<b>0.00</b>	7.8 (3.1)	0.42
r-FLACC score (range 0-10)	4.8 (3.0)	<b>0.01</b>	0.7 (0.8)	<b>0.01</b>	5.2 (3.3)	0.85
VAS-OBS score (range 0-10)	5.2 (3.3)	<b>0.02</b>	0.6 (0.9)	<b>0.00</b>	6.5 (2.4)	0.47
Supplemental epidural analgesia (no) (a)	0		n.a.		0	

\*Between LIA and epidural values. \*\*Between epidural and placebo values. \*\*\*Between placebo and LIA values.

**Table 3** Postoperative pain and opioid consumption. All values are mean (SD). One patient in the LIA group was excluded immediately after surgery. (a) Supplemental analgesia given at 4 hours postoperatively.

All 5 subgroups of the r-FLACC score were significantly lower in the epidural group compared to the placebo group. When comparing the epidural group to the LIA group 4 subgroups had significantly lower values (legs, activity, cry and consolability). No difference between the LIA and the placebo group was found.

At 9 and 21 hours postoperatively, the same trend was seen, though not significant due exclusion of patients in the LIA and placebo group lowering the patient number. Two of 5 children in the LIA group met the criteria for supplemental epidural analgesia and 5 of 6 children in the placebo group met the criteria for supplemental epidural analgesia.

In the LIA group, one child received epidural analgesia though not needing it and was excluded from data analysis. In the epidural group, the parents of 1 child were not able to use the VAS-OBS score and the child's VAS-OBS data was excluded. No serious adverse effects from local infiltration analgesia or epidural analgesia were observed and after end of the study period 4 patients accidentally removed the epidural catheter but reinsertion was not found necessary.

### Outcome 2: Opioid consumption.

Both perioperatively and during the last 30 minutes of anesthesia, the mean opioid consumption were lower in the epidural group, compared to the LIA and placebo group ( $p=0.01$ ,  $p=0.29$  and  $p=0.09$ ,  $p=0.03$ ), since the epidural group received continuous epidural infusion during surgery. No significant differences in perioperative opioid consumption between the LIA and placebo group were found.

Both during the first 4 postoperative hours and from 4-9 hours postoperatively, the mean opioid consumption was lower in the epidural group compared to both the LIA group ( $p=0.00$ ,  $p=0.00$ ) and the placebo group ( $p=0.00$ ,  $p=0.00$ ).

## Study IV

### Outcome 1: Reproducibility of seating parameters

Basic parameters of seating performance of the 65 healthy children establish a normal material and consist of area, pressure, peak pressure, 25% max area and distance measures. These basic parameters are tested for reproducibility and are subsequently utilized in the calculation of the 5 parameters of seating performance. The basic measures are presented in table 1, appendix.

A one-way analysis of variance Intra-Class Correlation (ICC) was calculated for each of the basic parameters of seating performance and is presented in table 4. The ICCs for each grade are presented in table 2 (Appendix). For the 65 children included, all parameters of seating performance in both NB and UB showed ICC values ranging between 0.67-0.99 indicating good to excellent reliability. The ICC values for each grade shows that the first grade has lower ICCs than the third, fifth and seventh grades.

	NB	95% CI	UB	95% CI
Right area	0.99	0.99-1	0.99	0.99-1
Left area	0.99	0.99-1	0.99	0.99-1
Right pressure	0.92	0.88-0.95	0.92	0.89-0.95
Left pressure	0.93	0.91-0.96	0.92	0.89-0.95
Right tuber pressure	0.95	0.92-0.97	0.94	0.91-0.96
Left tuber pressure	0.91	0.88-0.95	0.87	0.82-0.92
25% max pressure areal	0.71	0.60-0.81	0.70	0.60-0.80
Right distance	0.70	0.60-0.80	0.67	0.56-0.78
Left distance	0.75	0.66-0.84	0.77	0.69-0.85

*Table 4* ICCs for the basic measures of seating performance with normal position (NB) and up-right back position (UB). ICC > 0.60: good and excellent reliability.

### Outcome 2: The 5 parameters of seating performance

Seated pelvic obliquity in all 3 dimensions (Pelvic AP tilt, Pelvic LR tilt and Pelvic rotation), soft tissue quantity and pressure ulcer risk for normal children are presented in table 5. Stratification into grades are presented in table 3, appendix.

A significant decrease in sacral pressure per kg is seen when NB is changed to UB ( $p=0.00$ ), reflecting an anterior pelvic tilt and elevation of the sacrum. Sacral pressure decreased significantly for all grades (fig 1, appendix). The area with 25% of the maximum pressure significantly decreased when NB was changed to UB ( $p=0.02$ ).

	NB	UB	Diff <sub>mean</sub>	95% CI*	P-value**
AP pelvic tilt (mmHg/kg)	1.6	1.3	0.4	0.2-0.5	<b>0.00</b>
LR pelvic tilt (index)	0.04	0.04	0	-0.01-0.01	1
Pelvic rotation (index)	0.08	0.07	0.01	-0.01-0.03	0.32
Soft tissue quantity (index)	0.02	0.02	0	-.01-0.00	0.34
Pressure ulcer risk (cm <sup>2</sup> )	26.3	22.5	3.7	0.6-7.0	<b>0.02</b>

\*95% CI for Diff<sub>mean</sub>

\*\* Students t-test testing NB=UB.

*Table 5* Seating performance for normal children with normal back position (NB) and up-right back position (UB).

## Study V

### Outcome 1: Seated pelvic tilt in children with CP

Basic parameters of both preoperative and postoperative interface pressure maps used for calculation of the parameters of pelvic tilt are presented in table 4 (appendix). No significant differences are seen between pre- and postoperative pressure measurements on both the side of the hip reconstruction and the contralateral side.

A significant improvement in seated LR pelvic tilt was seen ( $p=0.04$ ) for the 18 children with CP undergoing unilateral hip reconstruction. The LR pelvic tilt measured with peak pressure asymmetry index also significantly decreased ( $p=0.00$ ). In addition a trend toward a seated anterior pelvic tilt with a reduced sacral pressure pr. kg ( $p=0.49$ ) and a trend toward improved pelvic rotation was seen ( $p=0.54$ ), (Table 6).

TOTAL	Preop	Postop	Diff <sub>mean</sub>	95% CI*	P-value**
LR pelvic tilt, mean*** (index)	0.12	0.08	0.04	0.00-0.08	<b>0.04</b>
LR pelvic tilt, peak**** (index)	0.25	0.10	0.15	0.06-0.24	<b>0.00</b>
AP pelvic tilt (mmHg/kg)	4.2	3.7	0.5	-1.0-1.9	0.49
Pelvic rotation (index)	0.24	0.20	0.03	-0.07-0.13	0.54

\*95% CI for Diff<sub>mean</sub>

\*\* Students t-test testing preoperative=postoperative.

\*\*\* Mean pressure asymmetry index.

\*\*\*\* Peak pressure asymmetry index.

*Table 6 Pelvic tilt for CP children preoperatively (Preop) and postoperatively (Postop).*

For the unilateral group, with unilateral hip involvement, changes in pelvic tilt were insignificant. (LR pelvic tilt improved ( $p=0.28$ ;  $p=0.09$ ), AP pelvic tilt increased ( $p=0.73$ ), pelvic rotation decreased ( $p=0.19$ ). For the bilateral group, with bilateral hip involvement and unilateral hip reconstruction, LR pelvic tilt significantly decreased ( $p=0.05$ ;  $p=0.02$ ), but no significant changes were seen regarding AP tilt and rotation. (AP pelvic tilt increased ( $p=0.74$ ), pelvic rotation increased ( $p=0.50$ ), (Table 7). No correlations between pelvic tilt and age, weight, implant type were found.

	Preop	Postop	Diff <sub>mean</sub>	95% CI*	P-value**
<b>UNILATERAL GROUP (n=10)</b>					
LR pelvic tilt, mean*** (index)	0.10	0.07	0.04	-0.04-0.11	0.28
LR pelvic tilt, peak**** (index)	0.21	0.09	0.12	-0.02-0.27	0.09
AP pelvic tilt (mmHg/kg)	3.8	3.3	0.5	-1.3-2.3	0.52
Pelvic rotation (index)	0.25	0.16	0.09	-0.06-0.24	0.19
<b>BILATERAL GROUP (n=8)</b>					
LR pelvic tilt, mean*** (index)	0.14	0.09	0.05	0.00-0.10	<b>0.05</b>
LR pelvic tilt, peak**** (index)	0.30	0.13	0.18	0.04-0.31	<b>0.02</b>
AP pelvic tilt (mmHg/kg)	4.7	4.3	0.4	-2.5-3.4	0.74
Pelvic rotation (index)	0.21	0.26	-0.05	-0.21-0.11	0.50

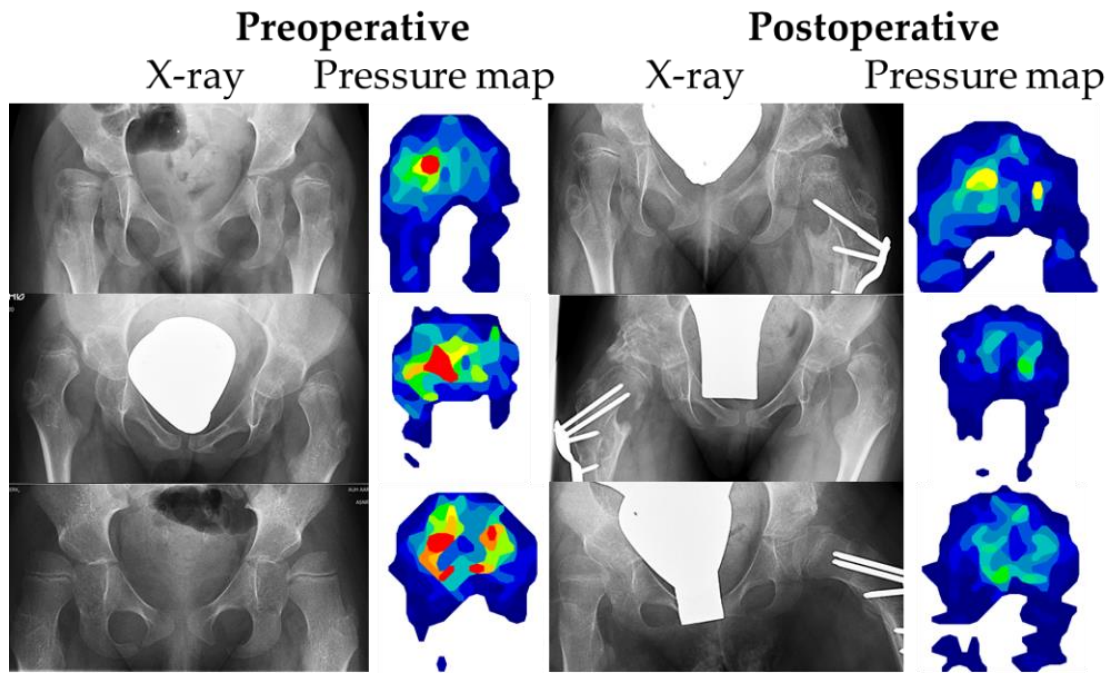
\*95% CI for Diff<sub>mean</sub>

\*\* Students t-test testing preoperative=postoperative.

\*\*\* Mean pressure asymmetry index.

\*\*\*\* Peak pressure asymmetry index.

*Table 7 Three-dimensional pelvic tilt for CP children preoperatively (Preop) and postoperatively (Postop) stratified into a unilateral and bilateral group.*



**Figure 14** Pre- and postoperative x-rays and pressure maps of 3 children undergoing unilateral hip reconstruction. Preoperatively they all have bilateral HD with low MP index and high seated LR pelvic tilt. Postoperatively, MP index markedly increases and seated LR pelvic tilt is improved.

### Outcome 2: Radiological parameters in children with CP

In all children migration percentage (MP) and acetabular index (AI) were evaluated on both pre- and postoperative radiographs. Results for AI are presented in table 4, (Appendix). The MP on the operated side significantly decreased after surgery ( $p=0.00$ ) and did not change on the not operated side ( $p=0.15$ ). The MP asymmetry index significantly increased ( $p=0.01$ ). When divided into groups, the MP asymmetry index for the unilateral group did not change ( $p=0.66$ ) but the MP asymmetry index for the bilateral group increased from 0.15 to 0.94 ( $p=0.00$ ), (Table 8, Fig. 14).

No correlation was seen between preoperative LR pelvic tilt and preoperative MP index ( $p=0.91$ ) or for postoperative LR pelvic tilt and postoperative MP index ( $p=0.49$ ). In addition no correlations were seen between LR pelvic tilt and MP index when divided into the unilateral and bilateral group.

	Preop	Postop	Diff <sub>mean</sub>	95% CI*	P-value**
MP <sub>op</sub> (%)	69	1	68	58-78	<b>0.00</b>
MP <sub>non-op</sub> (%)	31	34	-3	-7-1	0.15
MP index <sub>total</sub>	0.46	0.86	-0.40	-0.69- -0.11	<b>0.01</b>
MP asymmetry index <sub>unilateral</sub>	0.71	0.80	-0.09	-0.53-0.35	0.66
MP asymmetry index <sub>bilateral</sub>	0.15	0.94	-0.78	-0.94- -0.61	<b>0.00</b>

**Table 8** Radiological results for CP children preoperatively (Preop) and postoperatively (Postop).

### Outcome 3: Seating performance of normal children versus children with CP

The 5 parameters of seating performance were compared between normal children and CP children (Table 5, Appendix). LR pelvic tilt and pelvic rotation were significantly higher in children with CP and the pelvis was significantly more posteriorly tilted. LR pelvic tilt and soft tissue quantity was compared on only seat pressure defined by the transverse line between the buttocks and the thighs. This was due to inconsistencies in thigh pressure, most likely due to spasticity and increased thigh movements in the children with CP.

# 8. Discussion

## Key findings

In *study I* known pain assessment tools for children with CP were evaluated and subsequently the r-FLACC score for assessment of pain in children with CP was chosen for translation due to its good reported validity, reliability and clinical feasibility. The translation into Danish was done according to the guideline proposed by the Translation and Cultural Adaptation Group, increasing the quality of the Danish version of the r-FLACC score.

The psychometric properties of the Danish version of the r-FLACC score was evaluated in *study II* and both reliability and validity was established.

*Study III* used the r-FLACC pain score to evaluate early postoperative pain in children with CP undergoing unilateral hip reconstruction and found that epidural analgesia is superior to both LIA and placebo with significantly lower r-FLACC scores and lower opioid consumption postoperatively. Furthermore, a high proportion of children in the LIA and especially the placebo group needed epidural analgesia for adequate pain management.

In *study IV* the basic measures of seating performance were evaluated for reproducibility in 65 normal children. All ICCs indicated good to excellent reproducibility, hence the basic measures were used for calculating 5 appropriate outcome measures for seating performance. Pelvic AP tilt was defined as the magnitude of the sacral pressure, which significantly decreased with a back-position change from normal to up-right defining an anterior pelvic tilt. Pelvic LR tilt was proposed defined as the asymmetry index between average pressure of the right and left side of the seat interface. Pelvic rotation was proposed defined as the asymmetry index between the distance between the peak pressure point and the CoF. Soft tissue quantity is proposed defined as area asymmetry index. The risk of pressure ulcer is proposed defined as the area containing the maximum 25% of peak pressure.

*Study V* finds hip reconstruction to improve seated pelvic tilt in children with CP. For all 18 children the functional seated pelvic tilt after hip reconstruction showed significant improvement in LR pelvic tilt but this decrease was mainly seen in children with preoperative bilateral subluxated hips. The seated pelvic tilt was not correlated to the radiographic pelvic tilt. This indicates that this method assesses the clinical useful functional seated pelvic tilt in contrast to the commonly used supine radiographic pelvic tilt.

## Interpretation and limitations

### Clinical feasibility and translation

In *study I* a pain assessment tool relevant for children with cognitive impairments was chosen for translation. Many properties need to be evaluated, among others reported psychometric properties, individualization vs. standardization and clinical feasibility. Six different pain assessment tools for children with cognitive impairments were evaluated. The r-FLACC score was chosen, among others, due to its good clinical feasibility and validation for use in a postoperative setting. However, the background evidence for the r-FLACC was more extensive than some

of the other scores, hence could have biased the choice of the r-FLACC as the preferred pain assessment tool. If all evaluated tools had had the same testing, the choice could have been made more educated [20;30;34;98].

The international translation guidelines were made for securing sound translations and analysis of cultural and linguistic differences and establishing cross-cultural validity. *Study I* adheres to the ten steps of translation as proposed by Wild et al [59]. This increases the quality of the Danish version of the r-FLACC score. Even though international guidelines were followed, some methodological concerns might be raised [59]. The developers of the r-FLACC gave permission for translation; but declined to be involved in the process creating potential imprecisions or misinterpretations in the forward translation. Furthermore the harmonisation was not completed due to other language translations of the r-FLACC not being present. One study has translated the original FLACC score into Brazilian Portuguese with use of back-translations [99], but due to the differences between the FLACC and the r-FLACC, harmonisation of the back-translations is not possible. Present translation has been published [1] making harmonisation possible in future r-FLACC translations. Two et al [58] report a method for harmonisation of a global translated PROM to countries that share a common language but have cultural linguistic differences. This method may be used if the r-FLACC was to be translated to i.e. Swedish and Norwegian resulting in the possibility of obtaining reliable and pertinent assessment of pain in children with CP in Nordic trials.

### **Psychometric properties**

In *study II*, the psychometric properties of the translated r-FLACC score was assessed using the COSMIN checklist as a guideline. The COSMIN Checklist is developed for Health-Related Patient-Reported Outcomes (HR-PROs), which are complex instruments aimed to measure not directly measurable, multidimensional constructs. These instruments are often elaborate questionnaires measuring complex constructs as for example, quality of life or treatment outcomes. The r-FLACC score is not a classical HR-PRO, since it is not patient-reported and pain, as a construct, is not regarded as complex as other constructs measured by a HR-PRO. However, we choose to use the COSMIN checklist as a guideline in testing the psychometric properties of the r-FLACC, knowing that some elements would not be applicable. On the other hand the study benefits from the systematic and evidence-based approach.

In *study II and IV* reproducibility parameters (ICCs) are used instead of agreement parameters (kappa statistics) in accordance with the COSMIN checklist. This approach is often used in medical science [39] increasing the comparability of results. The discussion is continued by de Vet et al [100], who state that agreement parameters may be more illustrative than reproducibility parameters. However present studies also used the Bland-Altman plots for visually illustrating intra- and interrater reproducibility, which effectively illustrates both reproducibility and agreement parameters.

In *study II*, the measurement errors were illustrated through Bland-Altman plots rather than calculated measures. This approach visually depicts how far the differences of measurements are from their mean and effectively shows measurement errors. Construct validity evaluates if scores are consistent with predefined hypotheses [63] and in *study II* it is hypothesized that surgery will increase the level of pain in children with CP, showing an increased r-FLACC score.

Malviya et al [21] demonstrated a decrease of r-FLACC scores after administration of analgesics also establishing construct validity.

The validity and reliability of the translated r-FLACC score were established in a postoperative setting in children with CP not able to self-report pain. Some differences from the original validation study by Malviya et al [21] may be discussed. The inclusion criteria for present study included only cognitively impaired children with CP not able to self-report pain. Opposite, the original study included both a group of children able to self-report and a group not able to self-report pain. The r-FLACC was constructed only for observational use in children not able to self-report, which could limit the original study; but opposite it benefited from a larger study population and the inclusion of both bedside and video assessments.

Since pain is not as complex a construct as other measured by a HR-PRO, the r-FLACC may be considered more unidimensional with all 5 items of the score being highly correlated. This would likely result in a high internal consistency and unidimensionality. This was, in fact, the case with *study II* finding excellent internal consistency for both raters and for each item in the score. According to Scholtes et al [63], CA values between 0.70-0.95 establishes internal consistency, but if the CA is above 0.95 the measurement instrument may be comprised of too many items assessing the same construct. *Study II* result in a CA of 0.90 and 0.98 (two raters), which supports internal consistency, and further illustrates that the r-FLACC measures pain as a very specific construct compared to other HR-PROs. In addition, it is noteworthy that of the 5 items in the r-FLACC, the consolability item may be considered a more complex construct than the face, legs, activity and cry items, which is also demonstrated by the consolability item having the lowest CA value, though still well above the accepted range.

*Study II* shows excellent intra-rater reliability; but only good inter-rater reliability with a large interval of agreement as seen on the Bland-Altman plots. The same trend is seen in other studies on psychometric properties of pain assessment scores. The range of ICCs for inter-rater reliability were similarly wide for both the INRS (0.65-0.87) [39], for the NCCPC-PV (0.78-0.82) [19] and for the PPP (0.74-0.89) [38], which indicates that pain assessment of a child with CP not able to self-report will be more exact when done by the same person.

The most important limitation to *study II* is the low criterion validity. Only acceptable criterion validity could be established in rater 1 and for rater 2 it could not be established at all. This was established through comparison to another gold standard instrument as the COSMIN Checklist instructs [60-62]. No perfect gold standard pain assessment tool for children with CP exists in Danish, hence, acknowledging this limitation, the VAS-OBS was chosen for this study, since it is the mostly used validated pain score [41;42]. A range of consequences of low criterion validity may be discussed. According to Scholtes et al [63], if comparison to another gold standard instrument is flawed, it is impossible to know which instrument is invalid when the criterion validity is low. The VAS-OBS and r-FLACC scores differ in several ways, which could influence the comparison. It varies whether pain assessment is performed by parents or a RN and whether the assessment is performed bedside or by use of a video-recording. If the r-FLACC score had low criterion validity when compared to a perfect gold standard instrument, it could be discussed whether the r-FLACC actually measured pain as a construct. On the other



hand, *study II* did find acceptable criterion validity for rater 1 and the original r-FLACC validation study by Malviya et al [21] did establish criterion validity by comparison to the NAPI, which is a better gold standard pain assessment tool than the VAS-OBS. When considering both the differences between the r-FLACC and the VAS-OBS and the original version validity, the assessment is that the r-FLACC score actually do measure pain in children with CP not able to self-report.

Even though being a limitation regarding criterion validity, the uses of video-recordings for pain assessment are considered an advantage regarding reliability-testing. Reliability investigates if changes in scores for a patient, who have not changed remains the same. By video-recording the child the pain reactions of the child on the tape are unchanged and the true test-retest result can be obtained.

### **Postoperative analgesia for children with CP**

*Study III* is designed in two parts. The first part is randomized and double-blinded and the second part is a prospective consecutive cohort design. The initial hypothesis was that postoperative pain management in children with CP could be adequately managed by LIA. Hence, the first part was designed as a RCT between LIA and an approximated placebo. If a design with randomization between LIA and epidural had been chosen, it would have been a non-inferiority study between 2 established treatments with a need for a very large study population. This would not have been possible to complete during a reasonable time-frame due to the very heterogenic study population. It is a limitation to the study, that the LIA and epidural group are compared as two consecutive cohorts and not by RCT. On the other hand, the study did show a significant difference between the two groups.

*Study III* adheres to a 3-arm study design proposed by Dahl et al [101]. This design evaluates a new versus an established intervention with a third group called an 'approximated placebo control'. The placebo group acts as an approximated placebo control since the children are given oral or intravenous analgesia (paracetamol, opioids) both routinely and when needed as opposed to a no treatment approach with no analgesic treatment, which would be both unethical and decrease the assay sensitivity.

Epidural analgesia in children with CP is controversial since it might have unwanted side effects and be technically challenging to insert in children with scoliosis or intrathecal baclofen pumps [49]. In addition adverse events such as epidural hematoma or infection are difficult to diagnose in children with CP [50-53]. Nevertheless, epidural analgesia is considered first choice in postoperative pain management in children with CP because of its good effect on pain and spasticity [11]. Similar to present study Moore et al [56] found lower pain scores in an epidural analgesia group compared to a systemic fentanyl and diazepam group after SDR in children with CP and spasticity. As Nolan et al [11] states, epidural analgesia in children with CP appears to reduce spasticity due to the prevention of muscle spasms by a pain-induced spinal reflex. Brenn et al [49] conclude that epidural analgesia lowers the level of pain and spasms with few side effects in children with CP following orthopaedic surgery. In accordance to these studies present study finds a decreased level of pain in the epidural group, which may be partly caused by a decreased amount of muscle spasms causing pain.

Immobilization in a cast is hypothesized to increase the amount of muscle spasms and subsequently pain in children with CP, which would favor

epidural analgesia over LIA as postoperative pain management. Opposite to present point of view Lubicky et al [54] argue that casting does not increase spasms and pain.

LIA is widely used in hip and knee replacement surgery in adults [54;102;103], where several RCTs have analysed the effect of LIA on postoperative pain, though using different study designs and modifications from the original LIA technique [45;47;103;104]. LIA has never been investigated in relation to orthopaedic surgery in children with CP, but the analgesic effect should be transferable in theory. This study finds LIA inferior compared to epidural analgesia, which might be due to the muscle spasms in children with CP not being as effectively treated with LIA as with epidural analgesia. In addition, a higher dosage of ropivacaine than used for LIA in *study III* would most likely be safe and more efficient, though no consensus has been made internationally regarding the safe dosages for children.

The results of *study III* might be limited by a too low dose of ropivacaine per infiltration site, though known dosage recommendations have been used. The hip reconstruction is extensive and combined with a low bodyweight of the children resulting in a low volume of ropivacaine, the analgesic effect of LIA might have been reduced. Furthermore, the medial adductor release site was not infiltrated with LIA, possibly affecting the level of pain, though this site it is not assessed as painful as the extensive bony and soft tissue procedures performed on the ileum and femur.

### **Seating performance in normal children**

In *study IV*, the Tekscan CONFORMat interface pressure mat was chosen over other available mats due to its high sensor resolution and high test-retest reliability [8;68;78;79]. An interface pressure mat need to be sensitive enough to document small quantitative changes in pressure distribution [65]. The older version, the Tekscan Clinseat, has more sensels than the CONFORMat; but the COMFORMat seems to have better pliability. Pipkin et al [79] investigated the interface pressure between a buttocks model and a cushion in four different interface pressure mats (Tekscan Clinseat, Tekscan CONFORMat, FSA and XSensor) and found that all four had high test-retest reliability with ICCs>0.9 (not including peak pressure). Furthermore the presence of the individual mats influenced medial pressure magnitude mostly for the Tekscan Clinseat and the FSA mats, indicating that the CONFORMat and XSensor mats had better capability to envelop the curvature of the model with less pressure redistribution due to the presence of the mat. The FSA and Pliance-X are lower resolution interface pressure mats and have been found to have too low sensor resolution for assessment of tuber pressure in children [8;79]. Field et al [77] reviewed the psychometric properties for 19 clinical tools or functional tests for assessment of seating performance in children with motor impairments and found that none met all criteria for a well-developed measure. Gutierrez et al [81] found good repeatability of the Tekscan Clinseat by having 2 healthy persons make 19 seating measurements in 10 days. The measurement repeatability was assessed by the deviations of the Standard Deviation (SD) for each parameter.

Three sources of inconsistencies are present in relation to interface pressure mapping and are difficult to distinguish from one another. Methodological inconsistencies might arise from measuring errors from the mat itself, from intra- or inter rater differences in the analysis of the output or from the biologic variation with-in the subject assessed for seating performance. Measurement inconsistency from the mat itself is often reported as reliability. Intra- and inter observer

consistency have inconsistently been addressed as reliability, reproducibility or repeatability [97]. In *study IV*, the primary outcome is the biologic variation, called intra-variability, of basic seating outcomes in normal children through triple measurements. The reliability of the CONFORMat itself is high according to Pipkin et al [79] who eliminated the biologic variation by use of a standardized buttocks model, hence it is assumed that measurement error from the mat itself is minimized in *study IV*. However, this effect cannot be quantified and is a limitation to the study. In *study V*, we did not perform repeated measurement and the biologic variation in the basic outcome measures of children with CP was not evaluated. Opposite, other methodological concerns were present regarding independent seating that would make it difficult to ascertain a true biologic variation. The risk of measurement errors was low since objective data output from the original Tekscan software was used.

In *study IV* the chosen basic measurements were found to have good to excellent intra-variability, which is prerequisite for using these measures for further calculations. However, the children in the first grade showed low intra-variability for the more complex measures, which could be caused by a larger biologic variation in younger children. This should be recognized when evaluating seating performance in children younger than 8 years.

The chosen basic outcomes have been used in other studies. Gutierrez et al [81] uses a single 3 seconds recording by the Tekscan Clinseat sensor to describe seating in adults with spinal cord injury (SCI). Output included maximum pressure, contact area, active area of the highest 75% of the maximum pressure and distance from each side's peak pressure location to the CoF. A formula for calculating asymmetry indices was proposed. Nielsen et al [65] investigates seat load characteristics in children with scoliosis using the Tekscan Clinseat sensor for assessing asymmetry indices. Miller et al [78] used the FSA to evaluate sacral pressures in healthy persons seated upright and reclined. Fradet et al [8] used both the FSA and Pliance-X to characterise interface pressure and quantify the quality of the seated posture in children with CP compared to non-disabled children and found that the sensor resolution in both mats were too low for assessment of tuber.

Some studies report inconsistencies between the use of average pressure or peak pressure in the evaluation of interface pressure [80]. Sprigle et al [105] and Pipkin et al [79] reports peak pressures to be too volatile and lacking stability and concludes that it is not a reliable measure. Furthermore, Gutierrez et al [81] found that the SD for the peak pressure ranged between 6% and 20% and the SD for the mean pressure ranged between 1.2% and 5.5% illustrating the larger deviation in peak pressures. Present study finds excellent intra-variability of both peak pressure and mean pressure, though change in LR pelvic tilt with back change was only seen by peak pressure tilt. This illustrates the volatile nature of peak pressures and it is recommended that LR pelvic tilt is primarily assessed by average pressure.

Some limitations to the basic measures are present. Firstly, peak pressure for each side is in present study assumed to be tuber pressure. This assumption could be imprecise. It is assumed that the tuber creates the highest interface pressure in each side of the seating area; but that is not necessarily the case in for example very pathological seating patterns. In addition, the peak pressure is chosen to comprise of a 2x2 sensor area but the area of the tuber is most likely larger. Aissaoui et al [71] documents that the tuber pressure is rectangular reflecting the curvilinear nature of the ischial bone, hence a rectangular peak pressure area would have been

more appropriate for evaluating tuber pressure. Secondly, the distance from tuber to CoF is in itself not flawed; but the location of each point has some limitations. Tuber position might vary as mentioned. In addition the CoF is based on maintaining postural balance, which the children with CP in *study V* are unable to do. The standardised method for supporting the children minimises the inconsistencies of the CoF location. Thirdly, sacral pressure is defined as the average of the 2 sensors with peak pressure adjacent to each side of the midline. This basic parameter is limited by its computed nature. As with the tuber pressure it is assumed that the highest pressures next to the midline are caused by the sacrum or coccyges. This measure could have been biased by deformations of the sacrum or coccyges or by pressure redistribution seen in for example diaper use in patients with CP in *study V*. The measurement of sacral pressure in present study benefits from the high resolution of the CONFORMat as opposed to the study by Miller et al [78], where sacral area is defined as almost the entire seating area due to the low resolution of the FSA mat.

*Study IV* uses the basic outcome measures to evolve further measures. Five appropriate measures of seating performance are proposed, three of them assessing seated pelvic tilt. However, some limitations and methodological concerns may be raised for each of the five measures.

The AP pelvic tilt is defined as the presence of sacral pressure because the sacrum is the only clearly definable point in the coronal plane. This is in contrast to the two other pelvic tilt measurements, which are based on an index between two sagittal plane or frontal plane opposing measurements. This limits the comparability of the measures. In *study IV*, it is assumed that an anterior pelvic tilt occurs when the back position is changed from normal to up-right. This will result in a decrease of sacral pressure, which was substantiated by the findings in *study IV* establishing content validity of the AP pelvic tilt parameter. AP pelvic tilt has previously only been assessed in gait analysis or supine radiographics, which both differ from the seating position.

LR pelvic tilt is defined as the average pressure asymmetry index, which will detect a pelvic tilt caused by anatomical, physiological and biomechanical factors. The force asymmetry index is similar to the pressure asymmetry index and is introduced by Gutierrez et al [81], who concludes that it describes a potential risk for skeletal problems and muscular problems in balance maintenance. Balance is a function controlled by a range of factors; hence the LR pelvic tilt outcome should not be used directly to describe problems in balance maintenance. Present study suggests that if a pathological seated LR pelvic tilt is found, further testing should be made for diagnosing the cause.

Pelvic rotation is defined as the asymmetry index of the two side's distances from tuber of CoF. This parameter is based on the biomechanical assumption, that the location of the two tubera can define pelvic rotation. The mechanical centre of pelvic rotation is located near the spine, with the pelvic ring being a more or less rigid structure to be rotated. Therefore, the distance from the sacrum to each side's tuber is not changed by the rotation of the pelvis as seen in figure 10. Postural equilibrium can only be maintained if the CoF is located within the base of support and is in the seated position located in the midline and anterior to the perineum as stated by Nielsen et al [65]. Because its location is not determined by the rotation of the pelvis, the distance from tuber to CoF will decrease on one side and increase on the other side when the pelvis is rotated [65]. A potential limitation

to this measure is that the exact localization of both the tuber and the CoF might be imprecise. Opposite to present definition, Gutierrez et al [81] defined the distance asymmetry as the risk of acquiring pressure sores since it gives qualitative information about the likelihood that all upper body force is centred on one point. The different definition can be explained by different basic assumptions on the biomechanical aspects of seating. Gutierrez et al assumes that it is the location of the CoF that lateralizes resulting in an increase of the distance to one tuber and decrease of distance to the other tuber. This assumption requires loss of postural stability. Present study attempts to keep the postural stability stable by having the children in *study IV* sit as still as possible and by the standardised method for manual support of the children in *study V*. Present study assumes that when CoF remains near the midline, and the distances to each tuber differ, it is caused by a pelvic rotation.

Both LR pelvic tilt and pelvic rotation might be limited by the fact that the content validity of the measures was not assessed as standardized as it was for AP pelvic tilt. However, pilot testing was done by having children rotate or lateralize their torso while assessing seating performance, which indicates content validity.

Soft tissue quantity is defined as area asymmetry index and compares the area of each side of the seating area similar to previous studies [81]. However, by comparing each side, the parameter only detects unilateral pathology. A bilateral pathology may most likely result in symmetrical pathological loading areas, which will not be detected by this outcome. This outcome is speculative and studies are needed to assess if this measure can detect a change in soft tissue quantity.

Pressure ulcer risk is defined by the area with the highest 25% of peak pressure. According to Nielsen et al [65] the soft tissue covering the two tubera and the sacrum have higher pressure ulcer risk, due to a sustained compression being put on a small area. Taule et al [108] calls for methods of identifying prominent skeletal structures or muscle atrophy. This outcome can identify the area with the 25% highest pressure and may direct pressure ulcer strategies in the seating impaired and prevent ulcers. A limitation is the use of peak pressure, which has been shown to be too volatile, lacking stability and to be less reliable [79;105]. This imprecision might be reduced by using a longer timeframe for the seating recording.

### **Seating performance in children with CP**

*Study V* finds that hip reconstruction improves seated pelvic tilt in children with CP and that the seated pelvic tilt is not correlated to the supine radiographic pelvic tilt. Different theories exist as to how unilateral or bilateral subluxation and scoliosis, leads to pelvic tilt making different management strategies relevant. Black et al [15] studied 80 CP patients with 86 pathological hips and found that 70 patients had unilateral subluxation or dislocation on the high side of a LR pelvic tilt. Suprapelvic obliquity was defined secondary to structural scoliosis and infrapelvic obliquity as caused by imbalances or contractures below the pelvis and usually preceding suprapelvic obliquity. Opposite to this, Porter et al [67] found that 103 had hip pathology on the high side and 104 on the low side. Frischhut et al [66] used radiographic measurements to separate supra- and infra pelvic muscle imbalances causing pelvic tilt. 14 patients with CP underwent hip reconstruction, but no conclusion could be drawn as to the effect on pelvic tilt. Patel et al [109] measures pelvic obliquity on sitting antero-posterior full spine radiographs and finds that pelvic obliquity tends to diminish in supine compared to sitting radiographs [109].

Present study measures pelvic tilt from an infra pelvic view by only addressing uni- or bilateral hip dislocation. Studies have implied that hip dislocation and scoliosis are intertwined, hence the lacking evaluation of a possible scoliosis is a limitation. However, it was not found ethical to perform extensive radiographic evaluation in all included children only for assessment of possible spinal curves [82]. Furthermore present study concerns seated interface pressure assessments for evaluation of functional seated pelvic tilt in contrast to other studies that uses radiological measurements for assessment of pelvic tilt.

The functional and dynamic pelvic movement during sitting is a complex movement influenced by interacting factors and most likely differs from the static supine assessment of pelvic position obtained from radiographics. Frischhut et al [66] found no changes in pelvic tilt after hip reconstruction by radiographic measurements, which could be due to the static and supine nature of the assessment. However, interface pressure measurements of the dynamic seating position over time might detect the anatomical, physiological and biomechanical aspects of seating and changes in pelvic tilt. This is in accordance with the fact that no correlation between radiographic pelvic tilt and interface pressure pelvic tilt was found in *study V*. The decrease in seated LR pelvic tilt was primarily seen in children with bilateral subluxation only undergoing unilateral surgery, though an increase in radiological MP asymmetry was seen. Patel et al [109] reports pelvic obliquity to be different when comparing seated and supine assessments. Consequently, supine radiographic pelvic tilt and seated interface pressure pelvic tilt must be considered discrepant assessment methods that are not directly comparable.

Due to the complexity of seated pelvic movement, the improvement in LR pelvic tilt seen in *study V* may not only be caused by the anatomical unilateral relocation of the hip joint. Biomechanical and physiological factors such as the unilateral release of the adductors, change in muscle tone, spasticity, pain, prolonged rehabilitation, tetraplegic CP or other unknown factors might play a role in the observed change of LR pelvic tilt. Postoperative pain in one hip and the presence or absence of chronic pain in the contralateral hip might cause increased spasticity or pain-induced spasms [16]. Rodby-Bousquet et al [82] did not, however, find pain and postural asymmetry to be correlated. Scoliosis of the spine could also be an anatomic cause of LR pelvic tilt. The study is limited by not quantifying these factors and they might therefore be confounders to the effect.

*Study V* found an insignificant increase of anterior pelvic tilt, which cannot be explained by the release of the iliopsoas and rectus femoris tendons, since this theoretically would cause a posterior pelvic tilt. On the other hand, the tendon releases were unilateral, which could affect the complex nature of pelvic tilt in an unknown direction. Theoretically, the unilateral release could increase the pelvic rotation assuming bilateral spasticity. This is in accordance with the bilateral group having the lowest improvement in pelvic rotation.

If the many confounding factors affecting the complex nature of pelvic tilt were to be individually addressed the study population should have been very large. This study only included 18 children with CP with a heterogenic symptomatology, which limits the study and might be a cause of a type 2 error. On the other hand the study did find a significant change in pelvic tilt.

The fact that the children did not sit independently is a limitation to the study. However, assessment of seating performance in children with CP, GMFCS IV

and V, was only feasible with this standardised algorithm for manual support, which is acknowledged as not being an optimal condition, but nevertheless the standardization partly corrects the measurement errors. Since children with CP displays great heterogeneity of disabilities and severity, research on these children is often an art of the possible. The included children did not have the cognitive ability to understand the seating instructions as the children in *study IV* did, which poses a potential imprecision, though this has been limited by using a standardised method for supporting the children. If this approach had not been used the study could not have been performed and the question whether hip reconstruction improves functional seating performance, could not have been sought answered. The unsupported feet were chosen to assess only interface pressure between the seat and the examination bed. If a foot rest had been applied another source of pressure redistribution would need assessment, though children with CP would always be seated in a wheel-chair using a foot-rest influencing the seated interface pressure.

*Study IV* found a larger biologic variation in the basic outcomes in children younger than 8 years, which poses a limitation to the methodology in *study V*. This study included children with a median age of 7 years, indicating that more than half of children might have had too large age-related biologic variations of their seating performance. However, the fact that they did not have independent seating and needed manual support may have decreased the age-related biologic variation, but still poses support-related variations.

*Study V* did not find any correlation between seated interface pressure pelvic tilt and supine radiographical pelvic tilt. It could be discussed if this is caused by imprecisions of the radiographical measurements. The intra-rater coefficients of variance for the MP and AI measurements were very good, but inter-rater measurements were not performed, which could disguise a systematic error in the measurements. In combination with the low number of included children, this could have biased the correlation. Present study has set the definition for the uni- or bilateral group as an MP of 30% as proposed in several other studies. Chan et al [10] reports that MP is within acceptable limits if it is below 30% and Hägglund et al [87] recommends that hips with a MP of 33-40% should be considered at risk and with a MP above 40% should receive surgical intervention. However, it is unknown how far the hip needs to dislocate in order to affect the seating interface pressure and if other radiographical measurements such as for example Hip Shaft Angle (HSA) or Center Edge (CE) is more appropriate for this purpose [110]. Another limitation to the radiographical assessment is that no evaluation of whether formation of a pseudoacetabulum affected seating performance [110].

The 5 measures of seating performance were evaluated for normal children and for children with CP before surgery. When comparing the 5 measures of these two groups of children significant differences in all of the 3 pelvic tilt outcomes and the soft tissue quantity outcome were found. In all three pelvic tilt dimensions children with CP have higher values than normal children. This indicates that the pelvis before surgery in seated children with CP is more postero-lateral tilted and rotated than normal children. This difference may partly be explained by the fact that the children with CP had hip pathology. On the other hand, similar differences were seen when comparing the normal children with the postoperative values. As discussed, anatomical, physiological and biomechanical factors influence pelvic movement during dynamic sitting in children with CP. This comparison has some

limitations by the two groups not being completely comparable. The ages of the children with CP ranged between 4-10 years and between 7-14 years for the normal children. Furthermore, the methodology for making the assessments of seating performance differed between the two groups, since the normal children had independent seating and the children with CP needed manual support.

## Generalisability

The evaluation of pain assessment tools in *study I* has good external validity due to the evidence-based approach and may aid others in the choice of a relevant pain assessment tool for a specific use. The translation resulted in a Danish version of the r-FLACC pain score for assessment of pain in children with cognitive impairments and is primarily only applicable for the Danish population. The reporting of the process of translation, though, is generalizable to all language translations.

*Study II* only included children with CP not able to self-report pain in a postoperative setting. The psychometric properties of the r-FLACC score are primarily generalizable to this setting and pain assessment in a procedural or everyday setting should only be done with caution. When testing the r-FLACC in a postoperative setting, the entire range of the scale was applied and validated. A hypothesis is that procedural pain would require accuracy in the “severe pain-scores” of the scale and everyday pain would require accuracy in the “mild pain-scores” of the r-FLACC, which increases the applicability of present version of the r-FLACC to these situations. Breau et al [18] conclude that the NCCPC in a daily day setting can differentiate between pain and distress, especially with long-term pain, which has not been established with the r-FLACC.

*Study III* found epidural analgesia to be superior to LIA for early pain assessment in children with CP undergoing unilateral hip reconstruction. This finding is generalizable to both bilateral surgery and other lower extremity surgery in children with CP. Since this study only included children who postoperatively were casted in a hip-spica, the results are primarily applicable to other surgery also including postoperative casting, since the effect of casting on postoperative pain has not been established.

In accordance with Aissaoui et al [71] the generalizability of the proposed outcome measures of seating performance in *study IV* are increased due to the reporting of an asymmetry index instead of an absolute peak pressure or pressure value. Often a high inter-individual variability exists in maximal pressure data which decreases the comparability of interface pressures. The intra-variability of the 5 proposed parameters of seating performance is only assessed in normal children, hence are not directly applicable to adult. On the other hand the 5 proposed measures of seating performance is based on general anatomical, biomechanical and physiological theories. In addition it may be assumed that healthy adults have less biologic variation in their seating parameters. Hence, the measures may be applied to adults though with caution.

In *study V*, the 3 parameters of seating performance concerning pelvic tilt are applied to children with CP indicating external validity of the parameters to patient groups with pathological seating. The results, though, are primarily generalizable to children with CP undergoing unilateral hip reconstruction. Further studies are needed to assess the effect of bilateral hip reconstruction.



# 9. Conclusion

## **Pain**

After evaluation of pain assessment tools for children with CP and cognitive impairments the r-FLACC pain score is found superior due to its psychometric properties, clinical feasibility, use of core pain behaviours and flexibility regarding individualization. The standardised translation method used for the r-FLACC resulted in a high quality Danish pain assessment tool that may become a gold standard of pain assessments in children with CP.

The psychometric properties of the Danish version of the r-FLACC pain score were established using a standardized method proposed by the COSMIN group. Hence, the Danish version of the r-FLACC pain score is both valid and reliable for pain assessment in children with CP in a postoperative setting.

Epidural analgesia may be considered superior for early postoperative pain management in children with CP undergoing unilateral hip reconstruction and postoperatively casted in a hip-spica. Due to the substantial decrease in postoperative pain and opioid consumption, epidural analgesia may be considered as first choice in children with CP.

## **Seating performance**

The basic measures of seating performance have been identified and their intra-variability assessed to be good to excellent in normal children. These measures have been the basis for defining 5 appropriate measures of seating performance including 3 measures for pelvic tilt. This may be used in the analyses of seating performances in a clinical situation and aid in detecting changes in seating over time or after an intervention.

Unilateral hip reconstruction improves seating performance in children with CP. No correlation between seated interface pressure pelvic tilt and radiographically assessed pelvic tilt was found indicating that radiographic and interface pressure pelvic tilt are discrepant assessment methods that are not directly comparable. The orthopedic surgeon should base the decision of surgery on many factors including functional seating performance and pelvic tilt. In children with bilateral subluxation of the hips an improvement in functional seated pelvic tilt can be obtained by a unilateral procedure on the most symptomatic hip. However, each child with CP is different and surgical indication should be based on all aspects and symptoms of the individual child.

# 10. Perspectives and future research

## **Pain**

The r-FLACC pain score has the potential for becoming the gold standard of pain measurements in children with cognitive impairments e.g. CP in Denmark. The implementation process of the r-FLACC from research based to daily use is ongoing. Future research may translate the r-FLACC into other languages making international studies on pain in children with CP possible. Translation into the other Nordic languages may be a first step for research collaboration relating to pain in CP.

The translated Danish version is validated for use in a postoperative setting; but awaits a validation process for use with procedural pain, pain during daily day activities or chronic pain. Furthermore back translations from other-language translations of the r-FLACC may be compared with present study and finalising the harmonisation step and increasing the validity of comparisons of pain assessments in future international pain studies in children with CP.

Epidural analgesia in children with an intrathecal baclofen pump or scoliosis of the spine is commonly considered safe, but prospective studies are needed for accurate risk assessment. In addition, the effect of epidural analgesia on spasticity and spasms among children with CP need further research in order to accurately determine the effect on postoperative pain. The effect of casting on the level of muscle spasms and consequently postoperative pain is also an interesting topic for future research.

## **Seating performance**

The proposed measures of seating performance have the potential to be used in the setting of both clinical and research-related assessment. This study has tested the content validity of the AP pelvic tilt; but further studies are needed to test the content validity of the LR pelvic tilt and the pelvic rotation.

Dynamic and functional seated pelvic tilt has not previously been objectively assessed in children with CP undergoing hip reconstruction. This study has attempted so, though acknowledging the limitations, which may be addressed in future studies. Functional seating performance and seated pelvic tilt need to be evaluated in a larger study population, where both uni- and bilateral hip reconstructions is included. Furthermore the confounding factors of pelvic tilt need to be objectively assessed in relation to seating performance. Future studies need to evaluate the relation between functional dynamic seated pelvic tilt and radiographic anatomical pelvic tilt by i.e functional radiology or seated EOS imaging. Present study has resulted in several questions related to how the pelvis is positioned in seated children with CP. Additional research into the subject is needed in order to get a more complete picture of seating performance in children with CP.

# 11. References

- 1 Pedersen LK, Rahbek O, Nikolajsen L, Møller-Madsen B: Assessment of pain in children with cerebral palsy focused on translation and clinical feasibility of the revised FLACC score. *Scand J Pain* 2015;9:49-54.
- 2 Pedersen LK, Rahbek O, Nikolajsen L, Møller-Madsen B: The revised FLACC score: Reliability and validation for pain assessment in children with cerebral palsy. *Scand J Pain* 2015;9:57-61.
- 3 Pedersen LK, Nikolajsen L, Rahbek O, Duch BU, Møller-Madsen B: Epidural analgesia is superior to local infiltration analgesia in children with cerebral palsy undergoing unilateral hip reconstruction. *Acta Orthop* 2016;87.
- 4 Horstmann HM, Bleck EE: *Orthopaedic Management in Cerebral Palsy*. ed Second edition, Mac Keith Press, Blackwell Publishing, 2007.
- 5 Koman AL, Smith BP, Shilt JS: Cerebral palsy. *Lancet* 2004;363:1619-1631.
- 6 Rosenbaum P, Dan B, Leviton A, Paneth N, Jacobson B, Goldstein M, Bax M: Proposed definition and classification of cerebral palsy, April 2005. *Dev Med Child Neurol* 2005;47:571-576.
- 7 Elkamil A, Andersen G, Hagglund G, Lamvik T, Skranes J, Vik T: Prevalence of hip dislocation among children with cerebral palsy in regions with and without a surveillance programme: a cross sectional study in Sweden and Norway. *BMC Musculoskeletal Disord* 2011;12:284.
- 8 Fradet L, Tiernan J, Mcgrath M, Murray E, Braatz F, Wolf SI: The use of pressure mapping for seating posture characterisation in children with cerebral palsy. *Disabil Rehabil Assist Technol* 2011;6:47-56.
- 9 Sewel MD, Eastwood DM, Wimalasundera N: Managing common symptoms of cerebral palsy in children. *BMJ* 2014;349.
- 10 Chan G, Miller F: *Assessment and Treatment of Children with Cerebral Palsy*. *Orthop Clin North Am* 2014;45:313-325.
- 11 Nolan J, Chalkiadis G.A, Low J, Olesch C.A, Brown T.C.K: Anaesthesia and pain management in cerebral palsy. *Anaesthesia* 2000;55:32-41.
- 12 Pin TW, McCartney L., Lewis J, Waugh MC: Use of intrathecal baclofen therapy in ambulant children and adolescents with spasticity and dystonia of cerebral origin: a systematic review. *Dev Med Child Neurol* 2011;53:885-895.
- 13 Hagglund G, Andersson S, D ppe H, Pedersen HL, Nordmark E, Westbom L: Prevention of severe contractures might replace multilevel surgery in cerebral palsy: results of a population-based health care programme and new techniques to reduce spasticity. *J Pediatr Orthop B* 2005;14:269-273.
- 14 Novacheck TF, Gage JR: Orthopedic management of spasticity in cerebral palsy. *Childs Nerv Syst* 2007;23:1015-1031.
- 15 Black BE, Griffin PP: The Cerebral Palsied Hip. *Clin Orthop Rel Res* 1997;338:42-51.

- 16 Hagglund G, Aliksson-Schmidt A, Lauge-Pedersen H, Rodby-Bousquet E, Wagner P, Westbom L: Prevention of dislocation of the hip in children with cerebral palsy: 20-year results of a population-based prevention programme. *BJJ* 2014;96-B:1546-1552.
- 17 McGrath PJ, Rosmus C, Camfield C, Campbell MA, Hennigar A: Behaviours Caregivers use to Determine Pain in Non-Verbal, Cognitively Impaired Children. *Dev Med Child Neurol* 1998;40:340-343.
- 18 Breau LM, McGrath PJ, Camfield C, Rosmus C, Finley GA: Preliminary validation of an observational pain checklist for persons with cognitive impairments and inability to communicate verbally. *Dev Med Child Neurol* 2000;42:609-616.
- 19 Breau LM, Finley GA, McGrath PJ, Camfield CS: Validation of the Non-communicating Children's Pain Checklist-Postoperative Version. *Anesthesiol* 2002;96:528-535.
- 20 Crosta QR, Ward TM, Walker AJ, Peters LM: A review of pain measures for hospitalized children with cognitive impairment. *J Spec Pediatr Nurs* 2014;19:109-118.
- 21 Malviya S, Voepel-Lewis T, Burke C, Merkel S, Tait A: The revised FLACC observational pain tool: improved reliability and validity for pain assessment in children with cognitive impairment. *Paediatr Anaesth* 2006;16:258-265.
- 22 Breau LM, Camfield CS, McGrath PJ, Finley GA: Risk factors for pain in children with severe cognitive impairments. *Dev Med Child Neurol* 2004;46:364-371.
- 23 Penner M, Xie WY, Binopal N, Switzer L, Fehlings D: Characteristics of Pain in Children and Youth With Cerebral Palsy. *Pediatrics* 2013;132:407-413.
- 24 Parkinson KN, Dickinson HO, Arnaud C, Lyons A, Colver A, on behalf of the SPARCLE group: Pain in young people aged 13 to 17 years with cerebral palsy: cross-sectional, multicentre European study. *Arch Dis Child* 2013;98:434-440.
- 25 Ramstad K, Jahnsen R, Skjeldal OH, Diseth TH: Characteristics of recurrent musculoskeletal pain in children with cerebral palsy aged 8 to 18 years. *Dev Med Child Neurol* 2011;53:1013-1018.
- 26 Hadden KL, Baeyer CL: Global and Specific Behavioral Measures of Pain in Children with Cerebral Palsy. *Clin J Pain* 2005;21:140-146.
- 27 Malviya S, Voepel-Lewis T, Tait AR., Merkel S, Lauer A, unro H, arley F: Pain management in children with and without cognitive impairment following spine fusion surgery. *Pediatr Anesth* 2001;11:453-458.
- 28 Høiness PR, Capjon H, Lofterød B: Pain and rehabilitation problems after single-event multilevel surgery including bony foot surgery in cerebral palsy. *Acta Orthop* 2014;85:646-651.
- 29 Ramelet AS, Rees NW, McDonald SUE, Bulsara MK, Huijjer AHUDA: Clinical validation of the Multidimensional Assessment of Pain Scale. *Pediatr Anesth* 2007;17:1156-1165.
- 30 Voepel-Lewis T, Malviya S, Tait AR, Merkel S, Foster R, Krane EJ: A Comparison of the Clinical Utility of Pain Assessment Tools for Children with Cognitive Impairment. *Pediatr Anesthesiol* 2008;106:72-78.
- 31 Chen-Lim ML, Zarnowsky C, Green R, Shaffer S, Holtzer B, Ely E: Optimizing the Assessment of Pain in Children Who Are Cognitively Impaired Through the Quality Improvement Process. *J Pediatr Nurs* 2012;27:750-759.

- 32 Johansson M, Carlberg EB, Jylli L: Validity and reliability of a Swedish version of the Non-Communicating Children's Pain Checklist - Postoperative Version. *Acta Paediatr* 2010;99:929-933.
- 33 Massaro M, Pastore S, Ventura A, Barbi E: Pain in cognitively impaired children: a focus for general pediatricians. *Eur J Pediatr* 2013;172:9-14.
- 34 Massaro M, Ronfani L, Ferrara G, Badina L, Giorgi R, D'Osualdo F, Taddio A, Barbi E: A comparison of three scales for measuring pain in children with cognitive impairment. *Acta Paediatr* 2014;103:495-500.
- 35 Voepel-Lewis T, Merkel S, Tait AR, Trzcinka A, Malviya S: The Reliability and Validity of the Face, Legs, Activity, Cry, Consolability Observational Tool as a Measure of Pain in Children with Cognitive Impairment. *Anesth Analg* 2002;95:1224-1229.
- 36 Schade JG., Joyce BA, Gerkenmeyer J, Keck JF: Comparison of three preverbal scales for postoperative pain assessment in a diverse pediatric sample. *J Pain Symptom Manage* 1996;12:348-359.
- 37 Stevens B: Development and testing of a pediatric pain management sheet. *Pediatr Nurs* 1990;16:543-548.
- 38 Hunt A, Goldman A, Seers K, Crichton, Moffat V, Oulton K: Clinical validation of the Paediatric Pain Profile. *Dev Med Child Neurol* 2004;46:9-18.
- 39 Solodiuk JC, Scott-Sunderland J, Meyers M, Myette B, Shusterman C, Karian VE, Harris SK, Curley MAQ: Validation of the Individualized Numeric Rating Scale (INRS): A pain assessment tool for nonverbal children with intellectual disability. *Pain* 2010;150:231-236.
- 40 Collignon P, Giusiano B: Validation of a pain evaluation scale for patients with severe cerebral palsy. *Eur J Pain* 2001;5:433-442.
- 41 Crellin D, Sullivan TP, Babl FE, O'Sullivan R, Hutchinson A: Analysis of the validation of existing behavioral pain and distress scales for use in the procedural setting. *Pediatr Anesth* 2007;17:720-733.
- 42 de Jong A, Baartmans M, Bremer M, van Komen R, Middelkoop E, Tuinebreijer W, van Loey N: Reliability, validity and clinical utility of three types of pain behavioural observation scales for young children with burns aged 0-5 years. *Pain* 2010;150:561-567.
- 43 Kelly A, Powell CV, Williams A: Parent visual analogue scale ratings of children's pain do not reliably reflect pain reported by child. *Pediatr Emerg Care* 2002;18:159-162.
- 44 Kerr DR, Kohan L: Local infiltration analgesia: a technique for the control of acute postoperative pain following knee and hip surgery: a case study of 325 patients. *Acta Orthop* 2008;79:174-183.
- 45 Andersen KV, Pfeiffer-Jensen M, Haraldsted V, Søballe K: Reduced hospital stay and narcotic consumption, and improved mobilization with local and intraarticular infiltration after hip arthroplasty: A randomized clinical trial of an intraarticular technique versus epidural infusion in 80 patients. *Acta Orthop* 2007;78:180-186.
- 46 Andersen KV, Bak M, Christensen BV, Harazuk J, Pedersen NA, Søballe K: A randomized, controlled trial comparing local infiltration analgesia with epidural infusion for total knee arthroplasty. *Acta Orthop* 2010;81:606-610.
- 47 Essving P, Axelsson K, Kjellberg J, Wallgren Ö, Gupta A, Lundin A: Reduced morphine consumption and pain intensity with local infiltration analgesia (LIA) following total knee arthroplasty. *Acta Orthop* 2010;81:354-360.

- 48 Leelanukrom R, Suraseranivongse S, Boonrukwanich V, Wechwini S: Effect of wound infiltration with bupivacaine on postoperative analgesia in neonates and infants undergoing major abdominal surgery: a pilot randomized controlled trial. *J Anesth* 2012;26:541-544.
- 49 Brenn BR, Brislin RP, Rose JB: Epidural analgesia in children with cerebral palsy. *Can J Anesth* 1998;45:1156-1161.
- 50 Ali Sakr Esa W, Toma I, Tetzlaff JE, Barsoum S: Epidural analgesia in labor for a woman with an intrathecal baclofen pump. *Int J Obstetr Anesth* 2009;18:64-66.
- 51 Ganapathy S: Wound/intra-articular infiltration or peripheral nerve blocks for orthopedic joint surgery efficacy and safety issues. *Cur opin Anaesthesiol* 2012;25:615-620.
- 52 Muthusamy K, Recktenwall SM, Friesen RM, Zuk J, Gralla J, Miller NH, Galinkin JL, Chang FM: Effectiveness of an anesthetic continuous-infusion device in children with cerebral palsy undergoing orthopaedic surgery. *J Pediatr Orthop* 2010;30:840-845.
- 53 Rawal N: Epidural Technique for Postoperative Pain: Gold Standard No More? *Reg Anesth Pain Med* 2012;37:310-317.
- 54 Lubicky JP, Bernotas S, Herman JE: Complications related to postoperative casting after surgical treatment of subluxed/dislocated hips in patients with cerebral palsy. *Orthop* 2003;26:407-411.
- 55 Long LS, Ved S, Koh JL: Intraoperative opioid dosing in children with and without cerebral palsy. *Pediatr Anesth* 2009;19:513-520.
- 56 Moore RP, Wester T, Sunder R, Schrock C, Park TS: Peri-operative pain management in children with cerebral palsy: comparative efficacy of epidural vs systemic analgesia protocols. *Pediatr Anesth* 2013;23:720-725.
- 57 Nemeth BA, Montero RJ, Halanski MA, Noonan KJ: Epidural Baclofen for the Management of Postoperative Pain in Children With Cerebral Palsy. *J Pediatr Orthop* 2015;35:571-575.
- 58 Two R, Verjee-Lorenz A, Clayson D, Dalal M, Grotzinger K, Younossi ZM: A Methodology for Successfully Producing Global Translations of Patient Reported Outcome Measures for Use in Multiple Countries. *Value Health* 2010;13:128-131.
- 59 Wild D, Grove A, Martin M, Eremenco S, McElroy S, Verjee-Lorenz A, Erikson P: Principles of Good Practice for the Translation and Cultural Adaptation Process for Patient-Reported Outcomes (PRO) Measures: Report of the ISPOR Task Force for Translation and Cultural Adaptation. *Value Health* 2005;8:94-104.
- 60 Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, Bouter LM, Vet HC: The COSMIN checklist for assessing the methodological quality of studies on measurement properties of health status measurement instruments: an international Delphi study. *Qual Life Res* 2010;19:539-549.
- 61 Mokkink LB, Terwee CB, Patrick DL, Alonso J, Stratford PW, Knol DL, Bouter LM, de Vet HCW: The COSMIN study reached international consensus on taxonomy, terminology, and definitions of measurement properties for health-related patient-reported outcomes. *J Clin Epidemiol* 2010;63:737-745.
- 62 Mokkink LB, Terwee CB, Knol DL, Stratford PW, Alonso J, Patrick DL, Bouter LM, de Vet HCW: The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: A clarification of its content. *BMC Med Res Methodol* 2010;10:22.

- 63 Scholtes VA, Terwee CB, Poolman RW: What makes a measurement instrument valid and reliable? *Injury* 2011;42:236-240.
- 64 Terwee CB, Bot SDM, Boer MR, Windt DAWM, Knol DL, Dekker J, Bouter LM, Vet HCW: Quality criteria were proposed for measurement properties of health status questionnaires. *J Clin Epidemiol* 2007;60:34.
- 65 Nielsen C, Gutierrez-Farewik EM, Hirschfeld H, Saraste H: Seat load characteristics in children with neuromuscular and syndrome-related scoliosis: effects of pathology and treatment. *J Pediatr Orthop B* 2008;17:139-144.
- 66 Frischhut B, Krismer M, Stockl B, Landauer F, Auckenthaler Th: Pelvic tilt in neuromuscular disorders. *J Pediatr Orthop B* 2000;9:221-228.
- 67 Porter D, Michael S, Kirkwood C: Patterns of postural deformity in non-ambulant people with cerebral palsy: what is the relationship between the direction of scoliosis, direction of pelvic obliquity, direction of windswept hip deformity and side of hip dislocation? *Clin Rehabil* 2008;21:1087-1096.
- 68 Lampe R, Mitternacht J: Correction versus bedding: Wheelchair pressure distribution measurements in children with cerebral palsy. *J Child Orthop* 2010;4:291-300.
- 69 Bojsen-Møller F: *Bevægeapparates anatomi*. ed 11, 1999.
- 70 Strobl WM: Seating. *J Child Orthop* 2013;7:395-399.
- 71 Aissaoui R, Kauffmann C, Dansereau J, de Guise JA: Analysis of pressure distribution at the body-seat interface in able-bodied and paraplegic subjects using a deformable active contour algorithm. *Med Eng Phys* 2001;23:359-367.
- 72 Yu CH, Chou TY, Chen CH, Chen P, Wang FC: Development of a modularized seating system to actively manage interface pressure. *Sensors* 2014;14:235-14252.
- 73 Dey ZR, Nair NR, Shapcott N: Evaluation of the Force Sensing Application pressure mapping system. *J Med Eng Tech* 2013;37:213-219.
- 74 Bouten CV, Oomens CW, Baaijens FP, Bader DL: The etiology of pressure ulcers: Skin deep or muscle bound? *Arch Phys Med Rehabil* 2003;84:616-619.
- 75 Wolf SI, Mikut R, Kranzl A, Dreher T: Which functional impairments are the main contributors to pelvic anterior tilt during gait in individuals with cerebral palsy? *Gait Posture* 2014;39:359-364.
- 76 Drummond: Relationship of Spine Deformity and Pelvic Obliquity on Sitting Pressure Distributions and Decubitus Ulceration. *JPO* 1985;5:396-402.
- 77 Field D, Livingstone R: Clinical tools that measure sitting posture, seated postural control or functional abilities in children with motor impairments: a systematic review. *Clin Rehabil* 2013;27:994-1004.
- 78 Miller SK, Aberegg L, Blasiolo K, Parker M, Fulton J: A prospective assessment of sacral pressures in healthy volunteers seated upright and reclined with legs elevated in a recliner. *Ostomy Wound Manage* 2014;60:52-59.
- 79 Pipkin L, Sprigle S: Effect of model design, cushion construction, and interface pressure mats on interface pressure and immersion. *J Rehabil Res Dev* 2008;45:875-882.
- 80 Stinson MD, Crawford SA, Porter-Armstrong AP: Interface pressure measurements: Visual interpretation of pressure maps with MS clients. *Disabil Rehabil* 2008;30:618-624.

- 81 Gutierrez EM, Alm M, Hultling C, Saraste H: Measuring seating pressure, area, and asymmetry in persons with spinal cord injury. *Eur Spine J* 2004;13:374-379.
- 82 Rodby-Bousquet E, Czuba T, Häggglund G, Westbom L: Postural asymmetries in young adults with cerebral palsy. *Dev Med Child Neurol* 2013;55:1009-1015.
- 83 Linder-Ganz E, Engelberg S, Scheinowitz M, Gefen A: Pressure-time cell death threshold for albino rat skeletal muscles as related to pressure sore biomechanics. *J Biomech* 2006;39:2725-2732.
- 84 Brogren E, Hadders-Algra M, Forsberg H: Postural Control in Sitting Children with Cerebral Palsy. *Neurosci Biobehav Rev* 1998;22:591-596.
- 85 Pemberton PA: Pericapsular Osteotomy of the Ilium for Treatment of Congenital Subluxation and Dislocation of the Hip. *JBJS* 1965;47:65-86.
- 86 Salter RB: Role of Innominate Osteotomy in the Treatment of Congenital Dislocation and Subluxation of the Hip in the Older Child. *JBJS* 1966;48:1413-1439.
- 87 Häggglund G, Lauge-Pedersen H, Persson M: Radiographic threshold values for hip screening in cerebral palsy. *J Child Orthop* 2007;1:43-47.
- 88 Faraj S, Atherton WG, Stott NS: Inter- and intra-measurer error in the measurement of Reimers' hip migration percentage. *JBJS* 2004;86-B:434-437.
- 89 Dijk M, Koot HM, Abu Saad HH: Observational Visual Analog Scale in Pediatric Pain Assessment: Useful Tool or Good Riddance? *Clin J Pain* 2002;18:310-316.
- 90 Knapp TR: The overemphasis on power analysis. *Nurs Res* 1996;6:379-381.
- 91 Lenth RV: Some practical guidelines for effective sample size determination. *Am Statistician* 2001;55:187-193.
- 92 Hoening JM, Heisey DM: The abuse of power: The pervasive fallacy of power calculations for data analysis. *Am Statistician* 2001;55:1-6.
- 93 Martinkevich P, Møller-Madsen B, Gottliebsen M, Kjeldgaard Pedersen L, Rahbek O: Validation of the translated Oxford ankle foot questionnaire in 82 Danish children aged between five and 16 years. *BJJ* 2015;97-B:420-426.
- 94 McGraw KO, Wong SP: Forming Inferences About Some Intraclass Correlation Coefficients. *Psychological Methods* 1996;1:30-46.
- 95 Shrout PE, Fleiss JL: Intraclass correlations: Uses in assessing rater reliability. *Psychological bulletin* 1979;86:420-428.
- 96 Tjernstrøm F, Bjørklund M, Malmstrøm EM: Romberg ratio in quiet stance posturography - Test to retest reliability. *Gait Posture* 2014;42:27-31.
- 97 Müller R, Büttner P: A critical discussion of intraclass correlation coefficients. *Stat Med* 1994;13:2465-2476.
- 98 Hunt KA, Franck LS: Special needs require special attention: A pilot project implementing the paediatric pain profile for children with profound neurological impairment in an in-patient setting following surgery. *J Child Health Care* 2011;15:210-220.
- 99 da Silva FC, Thuler LCS: Cross-cultural adaptation and translation of two pain assessment tools in children and adolescents. *J Pediatr (Rio J)* 2008;84:344-9.



- 100 de Vet HCW, Terwee CB, Knol DL, Bouter LM: When to use agreement versus reliability measures. *J Clin Epidemiol* 2006;59:1033.
- 101 Dahl JB, Rasmussen LS: Comparison of two active analgesic interventions: A suggestion for an approximated placebo control. *Acta Anaesthesiol Scand* 2012;56:669-671.
- 102 Lunn TH, Husted H, Solgaard S, Kristensen BB, Otte KS, Kjersgaard AG, Gaarn-Larsen L, Kehlet H: Intraoperative Local Infiltration Analgesia for Early Analgesia After Total Hip Arthroplasty: A Randomized, Double-Blind, Placebo-Controlled Trial. *Reg Anesth Pain Med* 2011;36:424-429.
- 103 Rawal N: Local Infiltration Analgesia and Other Multicomponent Techniques to Improve Postoperative Outcome-Are We Comparing Oranges and Apples? *Reg Anesth Pain Med* 2011;36:417-420.
- 104 Kehlet H., Andersen LØ: Local infiltration analgesia in joint replacement: the evidence and recommendations for clinical practice. *Acta Anaesthesiol Scand* 2011;55:778-784.
- 105 Sprigle S, Dunlop W, Press L: Reliability of Bench Tests of Interface Pressure. *Ass Tech* 2003;15:49-57.
- 106 Stinson MD, Porter-Armstrong AP, Eakin PA: Pressure mapping systems: reliability of pressure map interpretation. *Clin Rehabil* 2003;17:504-511.
- 107 Morais Filho MC, de Godoy W, Santos CA: Effects of Intramuscular Psoas Lengthening on Pelvic and Hip Motion in Patients With Spastic Diparetic Cerebral Palsy. *J Pediatr Orthop* 2006;26:260-264.
- 108 Taule T, Bergfjord K, Holsvik EE, Lunde T, Stokke BH, Storlid H, Sorheim MV, Rekand T: Factors influencing optimal seating pressure after spinal cord injury. *Spinal Cord* 2013;51:273-277.
- 109 Patel J, Shapiro F: Simultaneous progression patterns of scoliosis, pelvic obliquity, and hip subluxation/dislocation in non-ambulatory neuromuscular patients: an approach to deformity documentation. *J Child Orthop* 2015;9:356.
- 110 Morrell DS, Pearson JM, Sauser DD: Progressive Bone and Joint Abnormalities of the Spine and Lower Extremities in Cerebral Palsy. *RadioGraphics* 2002;22:257-268.

# 12. Appendices

## Tables

	Total	1. grade	3. grade	5.grade	7.grade
<b>NB</b>					
Total area/cm <sup>2</sup> (SD)	885.5 (186.0)	663.0 (75.7)	807.8 (75.6)	907.2 (120.4)	1096.2 (113.5)
Right area/ cm <sup>2</sup> (SD)	439.0 (91.9)	329.2 (38.9)	401.3 (37.4)	449.4 (59.8)	543.0 (55.7)
Left area/ cm <sup>2</sup> (SD)	446.5 (94.9)	333.8 (37.7)	406.5 (40.1)	457.8 (62.0)	553.2 (59.6)
Total pressure/mmHg(SD)	47.1 (6.4)	43.4 (4.8)	44.7 (5.6)	48.3 (4.9)	50.8 (7.5)
Right pressure/mmHg(SD)	23.5 (3.4)	21.6 (2.6)	22.6 (3.3)	24.0 (2.7)	25.0 (3.9)
Left pressure/mmHg(SD)	23.7 (3.6)	21.8 (2.9)	22.1 (2.7)	24.2 (3.1)	25.8 (4.1)
Right tuber pressure/mmHg(SD)	103.6 (40.8)	77.6 (26.6)	92.7 (28.9)	114.9 (44.3)	120.3 (43.8)
Left tuber pressure/mmHg(SD)	106.6 (49.2)	78.0 (25.3)	84.4 (20.9)	123.5 (58.4)	128.2 (52.7)
Right distance	7.8 (1.6)	6.5 (1.0)	7.2 (1.6)	8.2 (1.5)	8.8 (1.2)
Left distance	7.6 (1.7)	6.0 (1.1)	7.2 (1.4)	8.0 (1.7)	8.7 (1.3)
<b>UB</b>					
Total area/ cm <sup>2</sup> (SD)	870.3 (181.6)	648.9 (65.9)	787.0 (71.3)	894.6 (112.8)	1081.8 (96.8)
Right area/ cm <sup>2</sup> (SD)	431.9 (90.6)	322.6 (35.6)	390.7 (36.3)	442.3 (55.4)	537.9 (49.4)
Left area/ cm <sup>2</sup> (SD)	438.5 (91.8)	326.3 (32.6)	396.4 (36.9)	452.3 (59.0)	543.9 (48.9)
Total pressure/mmHg(SD)	52.1 (6.9)	47.1 (4.2)	49.9 (5.4)	53.6 (5.6)	56.1 (8.0)
Right pressure/mmHg(SD)	25.9 (3.7)	23.3 (1.8)	25.0 (2.6)	26.6 (3.5)	27.9 (4.6)
Left pressure/mmHg(SD)	26.2 (3.7)	23.8 (3.2)	24.8 (3.3)	27.1 (3.1)	28.1 (3.8)
Right tuber pressure/mmHg(SD)	114.1 (58.2)	69.8 (21.4)	93.6 (38.4)	133.4 (57.7)	143.9 (66.5)
Left tuber pressure/mmHg(SD)	117.3 (54.1)	76.4 (40.9)	86.7 (26.4)	142.4 (49.9)	146.4 (53.0)
Right distance	8.4 (1.6)	7.1 (1.4)	8.3 (1.6)	8.7 (1.5)	9.2 (1.2)
Left distance	8.3 (1.5)	7.1 (1.4)	7.9 (1.1)	8.2 (1.3)	9.7 (1.0)

**Table 1** Basic parameters of seating performance. Mean area, pressure, peak pressure and distance parameters for normal relaxed back position (top panel) and up-right back position (bottom panel). Values are mean (SD).

	ICC-total	ICC-1.grade	ICC-3.grade	ICC-5.grade	ICC-7.grade
Right area - normal/up-right	<b>0.99 / 0.99</b>	<b>0.97 / 0.90</b>	<b>0.97 / 0.95</b>	<b>0.99 / 0.98</b>	<b>0.98 / 0.98</b>
Left area - normal/up-right	<b>0.99 / 0.99</b>	<b>0.97 / 0.93</b>	<b>0.96 / 0.93</b>	<b>0.99 / 0.99</b>	<b>0.98 / 0.99</b>
Right pressure - normal/up-right	<b>0.92 / 0.92</b>	<b>0.78 / 0.66</b>	<b>0.95 / 0.87</b>	<b>0.91 / 0.88</b>	<b>0.93 / 0.97</b>
Left pressure - normal/up-right	<b>0.93 / 0.92</b>	<b>0.88 / 0.85</b>	<b>0.89 / 0.91</b>	<b>0.92 / 0.93</b>	<b>0.95 / 0.91</b>
Right peak pressure - normal/up-right	<b>0.95 / 0.94</b>	<b>0.84 / 0.74</b>	<b>0.97 / 0.92</b>	<b>0.95 / 0.91</b>	<b>0.95 / 0.94</b>
Left peak pressure - normal/up-right	<b>0.91 / 0.87</b>	<b>0.86 / 0.93</b>	<b>0.85 / 0.87</b>	<b>0.91 / 0.90</b>	<b>0.89 / 0.71</b>
Right seat area - normal/up-right	<b>0.85 / 0.96</b>	0.31 / 0.90	<b>0.87 / 0.87</b>	<b>0.97 / 0.91</b>	<b>0.95 / 0.92</b>
Left seat area - normal/up-right	<b>0.83 / 0.97</b>	0.25 / 0.90	<b>0.83 / 0.86</b>	<b>0.96 / 0.96</b>	<b>0.92 / 0.93</b>
Right seat pressure - normal/up-right	<b>0.92 / 0.92</b>	<b>0.83 / 0.84</b>	<b>0.96 / 0.87</b>	<b>0.95 / 0.90</b>	<b>0.92 / 0.93</b>
Left seat pressure - normal/up-right	<b>0.92 / 0.93</b>	<b>0.75 / 0.90</b>	<b>0.91 / 0.91</b>	<b>0.96 / 0.93</b>	<b>0.92 / 0.87</b>
25% max pressure areal- normal/ up-right	<b>0.71 / 0.70</b>	0.39 / 0.58	<b>0.64 / 0.38</b>	<b>0.65 / 0.52</b>	<b>0.87 / 0.86</b>
Right distance - normal/up-right	<b>0.70 / 0.67</b>	0.52 / 0.31	<b>0.68 / 0.81</b>	<b>0.69 / 0.65</b>	0.48 / 0.75
Left distance - normal/up-right	<b>0.75 / 0.77</b>	0.38 / 0.61	<b>0.60 / 0.58</b>	<b>0.78 / 0.79</b>	<b>0.72 / 0.67</b>

**Table 2** One-way analysis of variance Intra-Class Correlations for the measures of seating performance with normal relaxed back position and up-right back position. Bold: ICC > 0.60 (good and excellent reliability).

	Total	1. grade	3. grade	5. grade	7. grade
<b>NB</b>					
Pelvic LR tilt (index)	0.04	0.05	0.04	0.04	0.05
Pelvic AP tilt (mmHg/kg)	1.6	2.0	1.6	1.7	1.3
Pelvic rotation (index)	0.08	0.09	0.07	0.09	0.07
Soft tissue quantity (index)	0.02	0.01	0.02	0.02	0.02
Pressure ulcer risk (cm <sup>2</sup> )	26.3	25.1	26.1	23.9	29.8
<b>UB</b>					
Pelvic LR tilt (index)	0.04	0.06	0.04	0.05	0.03
Pelvic AP tilt (mmHg/kg)	1.3	1.6	1.3	1.4	0.9
Pelvic rotation (index)	0.07	0.09	0.08	0.07	0.05
Soft tissue quantity (index)	0.02	0.02	0.02	0.02	0.01
Pressure ulcer risk (cm <sup>2</sup> )	22.5	29.8	23.3	14.0	25.2

**Table 3** Mean parameters for pelvic obliquity, soft tissue quantity and pressure ulcer risk nor normal children seated in a normal back position (NB, top panel) and up-right back position (UB, bottom panel).

	Preop	Postop	Diff <sub>mean</sub>	95% CI*	P-value**
MPr <sub>op</sub> (mmHg)	28.4	27.3	1.1	-5.2-7.3	0.73
MPr <sub>non-op</sub> (mmHg)	25.9	24.6	1.3	-4.0-6.7	0.60
PP <sub>op</sub> (mmHg)	104.9	92.6	12.3	-14.8-39.5	0.35
PP <sub>non-op</sub> (mmHg)	81.4	87.5	-6.1	-31.8-19.5	0.62
SP <sub>total</sub> (mmHg)	77.1	72.9	4.2	-21.2-29.5	0.73
SP <sub>pr kg</sub> (mmHg/kg)	4.2	3.7	0.5	-1.0-1.9	0.49
Dist <sub>op</sub> (cm)	3.9	3.8	0.1	-0.6-0.8	0.74
Dist <sub>non-op</sub> (cm)	4.6	4.8	-0.2	-1.0-0.6	0.63
AI <sub>op</sub> (°)	30.0	15.2	14.8	10.9-18.7	<b>0.00</b>
AI <sub>non-op</sub> (°)	22.9	22.6	0.2	-2.0-2.5	0.82
AI index	0.21	0.29	-0.08	-0.24-0.09	0.35

\*95% CI for Diff<sub>mean</sub>

\*\* Students t-test testing preoperative=postoperative.

**Table 4** Basic measurements of seating performance in children with CP preoperatively (Preop) and postoperatively (Postop). MPr: mean pressure; PP: peak pressure; SP: sacral pressure; Dist: distance from CoP to peak pressure; AI: acetabular index.

	Normal	CP (Preop)	Diff <sub>mean</sub>	95% CI*	P-value**
n	65	18			
LR pelvic tilt, mean*** (index)	0.06	0.09	0.04	0.00-0.06	<b>0.03</b>
AP pelvic tilt (mmHg/kg)	1.6	3.7	2.1	1.5-2.7	<b>0.00</b>
Pelvic rotation (index)	0.08	0.20	0.12	0.07-0.17	<b>0.00</b>
Soft tissue quantity (index)	0.03	0.06	0.03	0.01-0.04	<b>0.00</b>
Pressure ulcer risk (cm <sup>2</sup> )	26.3	26.4	0.2	-7.0-7.3	0.97

\*95% CI for Diff<sub>mean</sub>

\*\* Students t-test testing normal children=CP.

\*\*\* Mean pressure asymmetry index.

*Table 5 Parameters of pelvic obliquity for normal children compared to children with CP preoperatively.*

# Figures

<b>r-FLACC score for pain assessment in children with cerebral palsy.</b>	
<b>Face:</b>	
0 point:	No particular expression or smile
1 point:	Occasional grimace/frown; withdrawn or disinterested; <i>appears sad or worried</i>
2 point:	Consistent grimace or frown; frequent/constant quivering chin, clenched jaw; <i>distressed-looking face; expression of fright or panic</i>
<i>Individualized behavior:</i>	
<b>Legs:</b>	
0 point:	Normal position or relaxed; <i>usual tone &amp; motion to limbs</i>
1 point:	Uneasy, restless, tense; <i>occasional tremors</i>
2 point:	Kicking, or legs drawn up; <i>marked increase in spasticity, constant tremors or jerking</i>
<i>Individualized behavior:</i>	
<b>Activity:</b>	
0 point:	Lying quietly, normal position, moves easily; <i>Regular, rhythmic respirations</i>
1 point:	Squirming, shifting back and forth, <i>tense or guarded movements; mildly agitated (e.g. head back and forth, aggression); shallow, splinting respirations, intermittent sighs.</i>
2 point:	Arched, rigid or jerking; <i>severe agitation; head banging; shivering (not rigors); breath holding, gasping or sharp intake of breaths, severe splinting</i>
<i>Individualized behavior:</i>	
<b>Cry:</b>	
0 point:	No cry/verbalization
1 point:	Moans or whimpers; occasional complaint; <i>occasional verbal outburst or grunt</i>
2 point:	Crying steadily, screams or sobs, frequent complaints; <i>repeated outbursts, constant grunting</i>
<i>Individualized behavior:</i>	
<b>Consolability:</b>	
0 point:	Content and relaxed
1 point:	Reassured by occasional touching, hugging or being talked to. Distractible.
2 point:	Difficult to console or comfort; <i>pushing away caregiver, resisting care or comfort measures</i>
<i>Individualized behavior:</i>	

**Figure 1** The r-FLACC score for pain assessment in children with cerebral palsy. Revisions from the original FLACC score to this r-FLACC score are noted in italics [1].

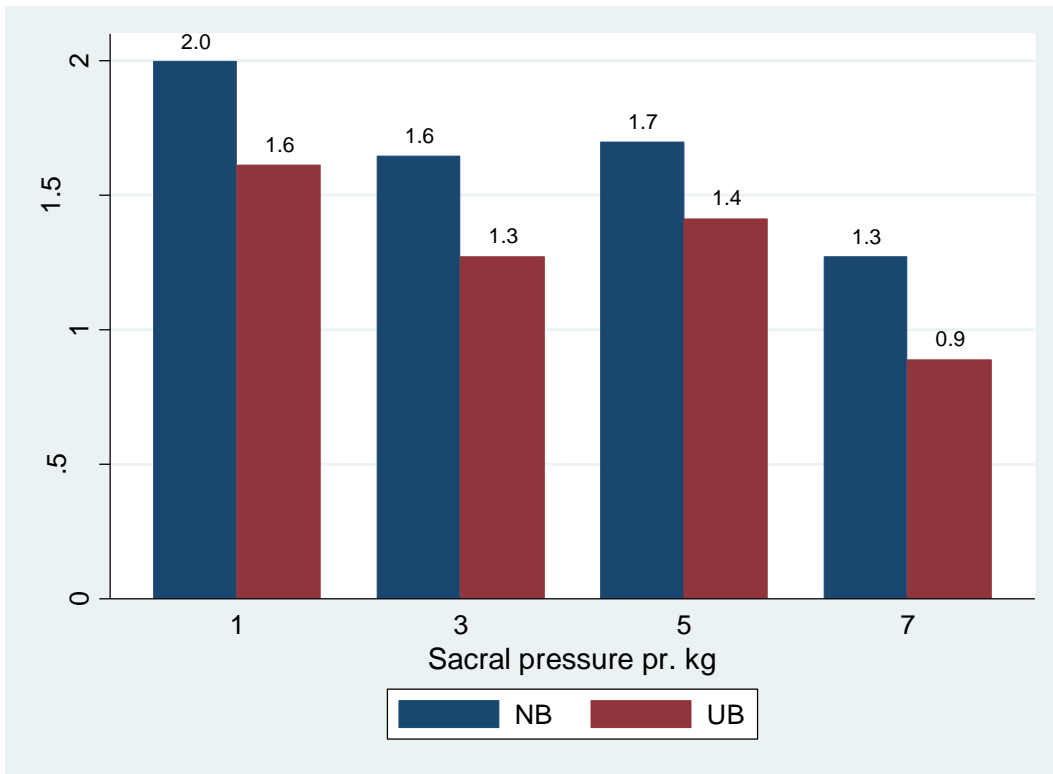


Figure 2 AP pelvic tilt in normal children stratified into grade.



## Papers I-V

- I. Assessment of pain in children with cerebral palsy focused on translation and clinical feasibility of the revised FLACC score. **Scandinavian Journal of Pain 9 (2015) 49-54.**
- II. The revised FLACC score: reliability and validation for pain assessment in children with cerebral palsy. **Scandinavian Journal of Pain 9 (2015) 57-61.**
- III. Epidural analgesia is superior to local infiltration analgesia for early postoperative pain management in children with cerebral palsy undergoing unilateral hip reconstruction. **Acta Orthopaedica 2016; 87 (2): 176-182.**
- IV. Definition and intra-variability of outcome measures of seating performance in 65 healthy children. **Submitted to Gait & Posture.**
- V. Hip reconstruction improves functional seating performance in children with cerebral palsy. **Submitted to Journal of Pediatric Orthopaedics.**



