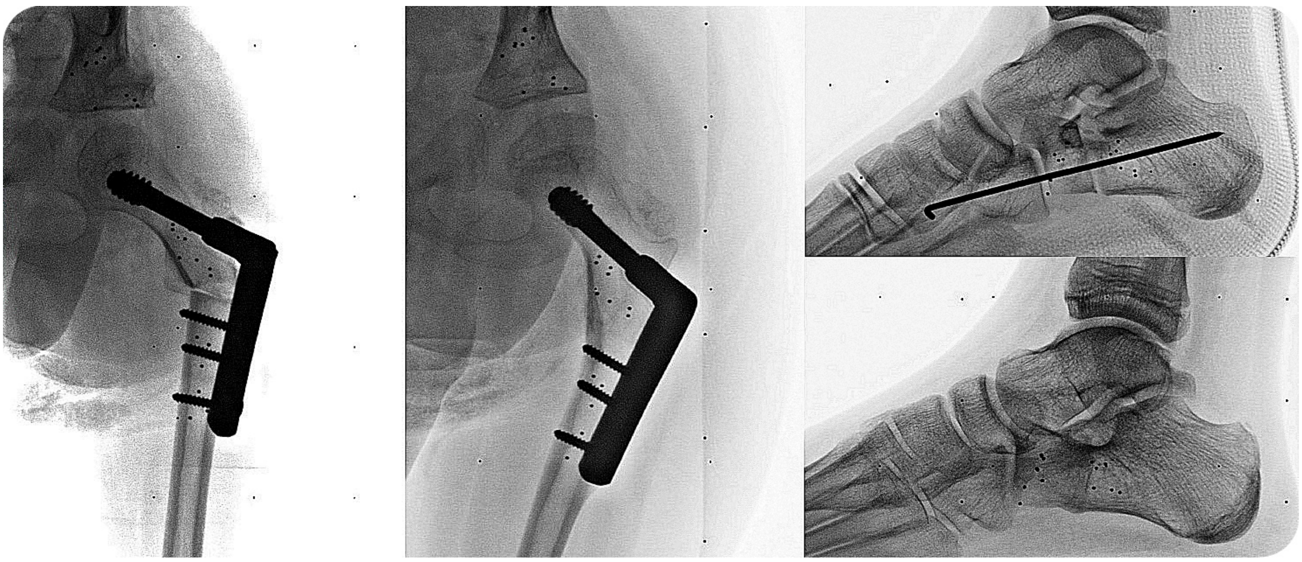
UNIVERSITY OF COPENHAGEN
FACULTY OF HEALTH AND MEDICAL SCIENCES

PhD Thesis

Peter Buxbom, MD

Assessment of Radiostereometric Analysis Stability across Osteotomies in Feet and Hips



Academic advisors: Stig Sonne-Holm, MD, DMSc and Christian Wong, MD, PhD

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Cover Image:
The cover image shows two study patients at their postoperative and 6-month follow-up. The images represent the two primary surgical interventions used in the studies. On the left picture the femoral varisation derotation osteotomy accompanied with the periacetabular osteotomy ad modum Dega. On the right the calcaneal lengthening osteotomy elongated by graft harvested from the patients own iliac crest. During surgery 1.0 mm tantalum markers were inserted on each side of osteotomies, which were later used to perform the radiostereometric analysis. All images have graphically inverted colours.

Institution:
Graduate School of Health and Medical Sciences, University of Copenhagen

Name of department:
Department of Orthopedic Surgery, Hvidovre Hospital

Author:
Peter Buxbom, MD
Department of Orthopedic Surgery,
Hvidovre Hospital, Denmark

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Vurdering af knogleudviklingen efter korrigerende operationer på fødder og hofter hos børn – En radiostereometrisk analyse

Principal supervisor:
Stig Sonne-Holm, MD, DMSc, Associate Professor
Head of Gait Laboratory, Consultant, Chief Surgeon
Department of Pediatric Orthopedic Surgery, Hvidovre Hospital, Denmark

Co-supervisor
Christian Wong, MD, PhD, Chief Surgeon
Department of Pediatric Orthopedic Surgery, Hvidovre Hospital, Denmark

Chairperson:
Benny Dahl, MD, PhD, DMSc, Professor
Department of Orthopedic Surgery
Rigshospitalet, Copenhagen, Denmark

Assessment committee:
Ole Rahbek, MD, PhD, Associate Professor, Chief Surgeon
Department of Pediatric Orthopedic Surgery, Aarhus University Hospital, Denmark

Henrik Lauge-Pedersen, MD, DMSc, Associate Professor, Chief Surgeon
Department of Pediatric Orthopedic Surgery, Lund University Hospital, Sweden

Correspondence:
Peter Buxbom, MD
Department of Orthopedic Surgery, Hvidovre Hospital, Denmark
Email: dr.buxbom@gmail.com

Contents

1 Preface

This PhD thesis is based on clinical work carried out from 2012 to 2015 at the pediatric orthopedic department at Hvidovre Hospital. The Ludvig and Sara Elsass Foundation was the primary funder of this project aiding researchers conducting studies within the field of cerebral palsy. Remaining funding was by the department of orthopedic surgery, Hvidovre Hospital.

Briefly, this thesis was initiated to elucidate the skeletal stability and migration across osteotomies in children undergoing corrective skeletal surgery in the lower extremities at Hvidovre Hospital. A very precise method to assess skeletal migration is by radiostereometric analysis (RSA). This thesis primarily concerns RSA studies assessing stability and migration across periacetabular, femoral and calcaneal osteotomies.

2 Acknowledgements

I would like to express my gratitude to the **Ludvig and Sara Elsass Foundation** as well as the head of department of orthopedic surgery **Peter Gebuhr** for the financial support of this project.

Sincerely thanks to my two supervisors and mentors **Stig Sonne-Holm** and **Christian Wong** for the scientific and academic guidance. Your impressive experience and overview have aided me from the beginning until the very end of the project - making my PhD thesis possible.

Thanks to all colleagues in the pediatric orthopedic department. Especially to **Søren Bødtker** for your dedication and to **Niels Ellitsgaard**, co-author in some articles, for your eternal clinical thoroughness that is always reflected in your commitment to the children.

My greatest gratitude is to my wife **Sarah Buur Bendixen** for the everlasting moral support – even in times of despair.

3 Abbreviations

AI	Acetabular Index
CLD	Crossing Line Distance
CLO	Calcaneal Lengthening Osteotomy
CN	Condition Number
CP	Cerebral Palsy
DO	Dega Osteotomy (Acetabuloplasty)
FG	Femoral Shaft Graft
FHEI	Femoral Head Extrusion Index
GMFCS	Gross Motor Function Classification System
IG	Iliac Crest Graft
ME	Mean Error of Rigid Body Fitting
MTPM	Maximum Total Point Motion
PPV	Pes planovalgus (flatfoot)
RPL	95 % Repeatability Limits (= precision)
RSA	Radiostereometric Analysis
SD	Standard Deviation
VDRO	(Femoral) Varisation Derotation Osteotomy

4 English Summary

Background

There are only published few pediatric orthopedic radiostereometric analysis (RSA) studies within the last decades and none concerning stability and migration across osteotomies. This thesis have evaluated three types of osteotomies with RSA; two regarding the surgical treatment of hip displacement in children with neuromuscular disorders (1) *the periacetabular Dega osteotomy* (DO) and (2) *the femoral varisation derotation osteotomy* (VDRO), and one regarding surgical treatment of children with pes planovalgus (flatfoot) treated with (3) *calcaneal lengthening osteotomy* (CLO). These surgeries have a reported relapse of 16-32 % and 18-36 %, respectively.

Purpose

The purpose of this thesis was to establish whether RSA was a feasible method to evaluate small-scale osteotomies (e.g. CLO), and subsequent to investigate the RSA stability and migration across the three mentioned osteotomy types DOs, VDROs and CLOs.

Methods

Study I assessed the RSA feasibility across a small-scale osteotomy by test-retest observations on a cadaver foot phantom model. The test-retest 95 % repeatability limits (RPLs) were compared with international results. RSA output with mean error of rigid body fitting (ME) above 0.35 mm or condition number above 150 mm^{-1} were excluded.

In study II-IV insertion of 4-6 tantalum markers peroperatively on each side of the DOs, VDROs and CLOs, respectively. RSA follow-ups were for DOs and VDROs planned at 0, 5 weeks, 3, 6, and 12 months and for CLOs the follow-ups were planned at 0, 5, 10 weeks, 6 and 12 months.

To evaluate stability across the osteotomies we defined **RSA stability** as migration below internal RPL in five out of six orientations. Migration was evaluated according to RSA community guidelines.

Results

In study I the feasibility was confirmed achieving acceptable values of RPL, ME and CN, which showed comparability with the RSA results across the CLOs in study IV.

In study II-IV we found RSA stability across the majority osteotomies within the first 5 weeks and across all osteotomies within 3 months.

In study II the mean translations (±SD) at the one-year follow-up of distal periacetabular fragment across RSA stable DOs were 0.55 mm (±0.63) medial, 0.33 mm (±0.33) superior and 0.13 mm (±0.24) posterior. The mean rotations were 1.47° (±2.91) posterior tilt, 0.27° (±1.28) retroversion and 1.76° (±3.10) medial inclination.
In study III the mean translations (±SD) at the one-year follow-up of distal femoral shaft fragment across RSA stable VDROs were 0.51 mm (±1.12) medial, 0.69 mm (±1.61) superior and 0.21 mm (±1.28) posterior. The mean rotations were 0.39° (±2.90) anterior tilt, 0.02° (±3.07) internal rotation and 2.17° (±2.29) varus angulation.
In study IV the mean translations (±SD) at the one-year follow-up of the anterior calcaneal fragment across RSA stable CLOs were 0.23 mm (±0.51) superior and 0.14 mm (±0.40) lateral. The mean rotations were 0.49° (±2.09) supination, 0.78° (±2.03) external rotation and 0.91° (±1.98) dorsiflexion.

Conclusion

Radiostereometric analysis is a feasible method to evaluate RSA stability and migration osteotomies performed on pediatric orthopedic patients - even across small-scale osteotomies. Using the RSA stability definition the majority osteotomies stabilized within the first 5 weeks. All osteotomies were by definition RSA stable within 3 months in accordance to the definition of RSA stability used in this study. The mean migrations at the one-year follow-up significantly differ from zero (the postoperative RSA) across DO for medial, superior and posterior direction and with posterior tilt and medial inclination. For VDROs only significant migration was observed for varus angulation at the one-year follow-up. For CLOs none of the orientations differ significantly from the zero at the one-year follow-up.

5 Dansk Resume

Baggrund

Der er kun publiceret få pædiatriske ortopædiske radiostereometriske analyse (RSA) studier indenfor de seneste årtier, og ingen af disse omhandler RSA stabilitet eller migration omkring osteotomier. Denne afhandling evaluerer tre osteotomityper; to som anvendes i behandlingen af ledskred i hoften hos børn med neuromuskulære lidelser, (1) *den periacetabular Dega osteotomi* (DO) og (2) *den variserende deroterende osteotomi* (VDRO) af lårbensknoglen, som har observeret tilbagefald på 16-32 %, samt én osteomi vedrørende behandlingen af børn der lider af pes planovalgus (platfod) og som er behandlet med en (3) *calcaneus forlængelsesosteotomi* (CLO) med observeret tilbagefald og komplikationsrate på 18-36%.

Formål

Formålet med denne afhandling var at vurdere om RSA var en brugbar metode til at evaluere migration af knoglefragmenterne omkring små osteotomier (såsom CLO) samt efterfølgende at undersøge RSA stabilitet og migration over DOs, VDROs og CLOs.

Metoder

Studie I undersøgte RSAs brugbarhed over mindre en osteotomi ved test-gentest observationer på en fantommodel (en kadaver fod). Efterfølgende blev test-gentest *95% repeatability limits* (RPL) sammenlignet andre internationalt publicerede observationer. RSA data med *mean error of rigid body fitting* (ME) over 0,35 mm eller *condition number* (CN) over 150 mm^{-1} blev ekskluderet.
I studie II-IV blev under operation indsat 4-6 tantalum markører på hver side af henholdsvis DOs, VDROs og CLOs. RSA opfølgninger var ved patienter behandlet med DOs og VDROs planlagt til henholdsvis 0 og 5 uger samt 3, 6 og 12 måneder efter operation. For patienter behandlet med CLOs blev opfølgninger planlagt til henholdsvis 0, 5 og 10 uger samt 6 og 12 måneder efter operation.
For at evaluere stabiliteten over osteotomierne, definerede vi **RSA stabilitet** som migration under den interne RPL i fem ud af seks frihedsgrader. Migration blev beregnet i henhold til de eksisterende internatonale RSA retningslinjer.

Resultater

I studie I blev brugbarheden bekræftet ved opnåelse af acceptable værdier for RPL, ME og CN.

I studie II-IV blev observeret RSA stabilitet over de fleste osteotomier indenfor de første 5 uger, og over alle osteotomier indenfor 3 måneder.
I studie II var de gennemsnitlige migrationer (± SD) ved 1-års opfølgningen af det distale periacetabular fragment 0,55 mm (± 0,63) medialt, 0,33 mm (± 0,33) superiort og 0,13 mm (± 0,24) posteriort. De gennemsnitlige rotationer var 1,47° (± 2,91) posterior tilt, 0,27° (± 1,28) retroversion og 1,76° (± 3,10) medial inklination.
I studie III var de gennemsnitlige migrationer (± SD) ved 1-års opfølgningen af lårbensskaftet distalt for osteotomien 0,51 mm (± 1,12) medialt, 0,69 mm (± 1,61) superiort og 0,21 mm (± 1,28) posteriort. De gennemsnitlige rotationer var 0,39° (± 2,90) anterior tilt, 0,02° (± 3,07) intern rotation og 2,17° (± 2,29) varus vinkling.
I studie IV var de gennemsnitlige migrationer (± SD) ved 1-års opfølgningen af det forreste calcaneus fragment 0,23 mm (± 0,51) superiort og 0,14 mm (± 0,40) lateralt. De gennemsnitlige rotationer var 0,49° (± 2,09) supination, 0,78° (± 2,03) ekstern rotation og 0,91° (± 1,98) dorsifleksion.

Konklusion

RSA-metoden kan anvendes over mindre osteotomier. Under definitionen for RSA stabilitet var flertallet af osteotomierne stabiliseret indenfor de første 5 uger, og over alle osteotomier indenfor 3 måneder. Den gennemsnitlige migration ved 1-års opfølgningen over DOs var signifikant forskellig fra nul i medial, superior og posterior posterior retning samt med posterior tilt og mediale inklination. Over VDROs var kun observeret signifikant migration for varus vinkling, øvrige var ikke signifikant forskellige fra nul. Ingen af retningerne var signifikante forskellige for nul over CLOs ved 1-årsopfølgningen.

6 List of Papers

This thesis is based on four studies. Manuscripts for study I, II and IV are to be submitted or re-submitted. Manuscript for study III is accepted for publication in the international journal of *ACTA Orthopaedica*.

I **Repeatability of Marker Based Radiostereometric Analysis Across Hindfoot Osteotomies.**
Buxbom P, Sonne-Holm S, Wong C.
Manuscript to be submitted.

II **Stability and Migration Across Dega Osteotomies in Children with Neuromuscular disorders by Radiostereometric Analysis - A One Year Follow-up of 18 Hips**
Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.
Manuscript to be submitted.

III **Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Cerebral Palsy by Radiostereometric Analysis - A One Year Follow-up of 25 Hips**
Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.
Manuscript accepted for publication by peer-reviewers at *ACTA Orthopaedica*.

IV **Stability and Migration Across Calcaneal Lengthening in Children - A Radiostereometric Analysis of Twenty Osteotomies**
Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.
Manuscript to be submitted.

7 Introduction

Briefly, this thesis was initiated to evaluate if radiostereometric analysis (RSA) was valid as method to estimate stability across osteotomies and also to assess the postoperative migration across osteotomies performed at Hvidovre Hospital on lower extremities in children. RSA was used to assess continuous migration (translation and rotation) across the osteotomies. This PhD thesis includes four studies; one about the methodology and precision of the RSA method and three about RSA stability and migration across periacetabular, femoral and calcaneal osteotomies, respectively.

7.1 Pes planovalgus (flatfoot) in Children

Pes planovalgus (PPV) or flatfoot is a common deformity in children that is characterized by a minimal or missing medial longitudinal arch[1]. In time the talar head might subluxate medial with the calcaneal bone going in valgus [2,3] (figure 7.1).

Epidemiological studies indicate that most children do not have a medial longitudinal arch at birth, but the arch develops during early childhood. The arch gradually develops and at the age of 5 years it is present in more than 70 % of children [1,4,5]. PPV is present in under 10 % of children at age 7 years [5,6]. The prevalence of PPV is twice as high in boys and correlated to weight. Obese children have triple risk of PPV [1,5,6]. Another group of children with high prevalence of PPV are those suffering from neuromuscular disorders [2,7,8].

The PPV deformity is often divided into flexible and rigid PPV [4]. Rigid PPV has been observed in less than 1% of the affected children. Rigid PPV is in most circumstances painful and the children are in those cases offered surgery [5]. The majority of children with flexible PPV are asymptomatic. Pain during activity has been reported as the main reason for children with PPV to seek an pediatric orthopedic surgeon [4]. Initially the condition is attempted treated with arch support and physiotherapy, but in few children the painful condition persists despite non-surgical intervention and those are offered operation [2,4,8–10].

The choice of surgical procedure is based on intends to restore the medial longitudinal arch and creating the arch stable enough with the least impact on foot joint mobility as possible. The calcaneal lengthening osteotomy (CLO) or calcaneal-cuboideum-cuneiform osteotomy (triple C) are often used [11–13] and with less complications than the arthrodesis' [14–16]. A study by Moraleda et al. (2012) comparing CLO and triple C find slightly better radiographic results after CLO, but similar clinical outcome between the two procedures. However, CLO has a high complication rate and additional surgeries in 18-36 % of these cases to maintain stability have been reported [11,12].

Unfortunately it is unclear and needs clarification, which types of complications and which additional surgeries were needed in these articles.
At Hvidovre Hospital the current postoperative treatment after undergoing CLO is immobilization in a short leg cast and no weight bearing the first 5 weeks, followed be a walking cast for yet another 5 weeks. After 10 weeks full mobilization is allowed according to the level of pain.

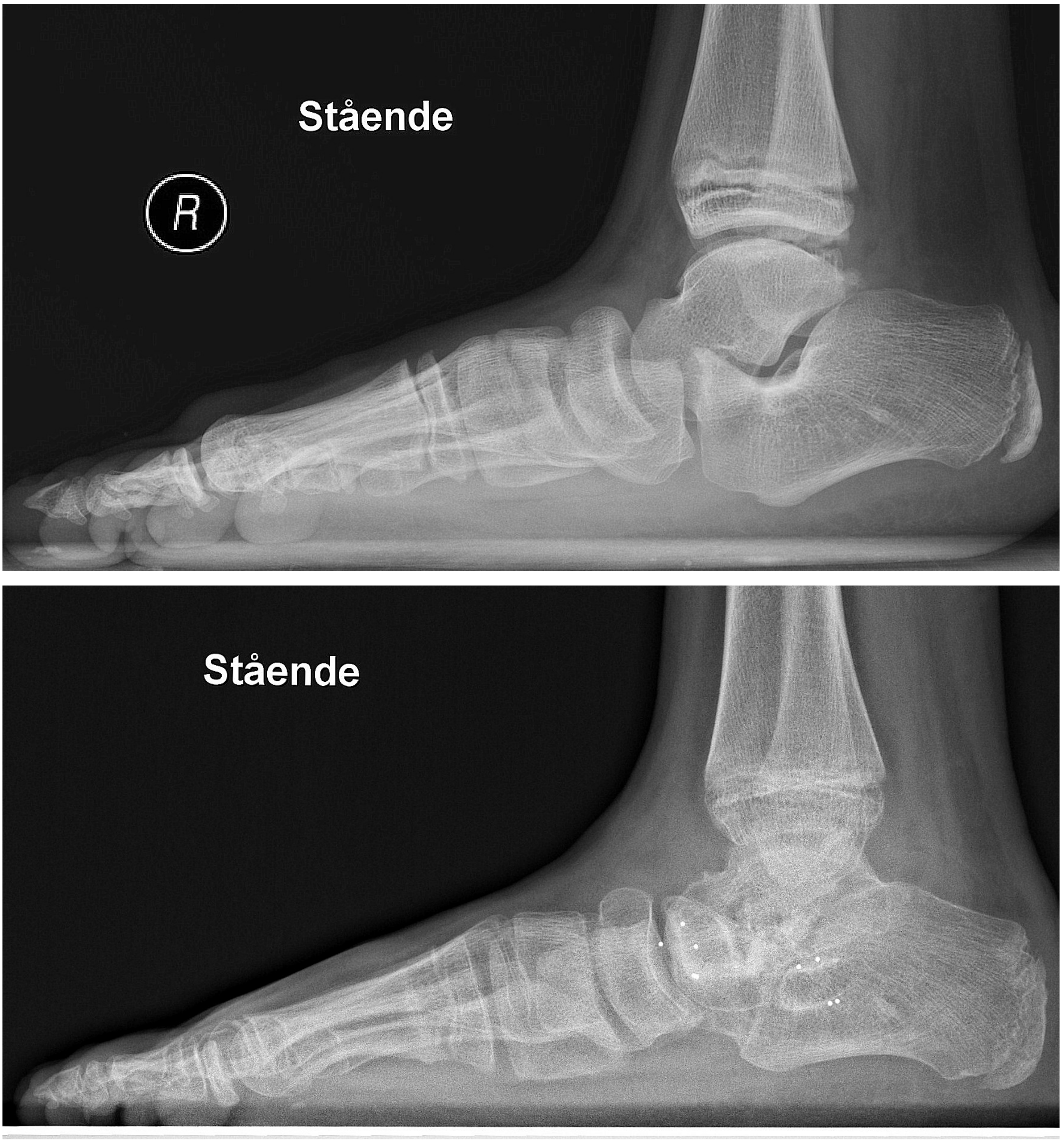

Figure 7.1. Pre- and postoperative standing radiographs of a calcaneal lengthening osteotomy in an 11-year boy. The figure text 'Stående' is Danish for standing.

7.2 Cerebral Palsy

Cerebral palsy (CP) is a multidimensional neurologic disease that begins early in childhood and continues throughout life [17]. For many years, hypoxia during birth was considered the main reason in developing CP. However, now it is a widely accepted assumption that up to 90% of the injuries resulting in CP develop prior to birth [18]. The incidence in Denmark is 2:1.000 in live births and has been stable since the 1990's [19].

CP consists of a very heterogeneous group of children regarding etiology, disability type and severity. The interruption or change in the general development is affected both on a biological and psychosocial level. The motoric retardation is often discovered before the age of 18 months [17,18]. The motor symptoms may also be accompanied by specific or global cognitive problems, communication problems and problems of social interaction, but in contrast to the general perception mental retardation is only observed in around 28 % of the CP patients [20].
CP can be subdivided into spastic, dyskinetic or ataxic [21]. Spastic CP is predominant and represents 75 % of the CP patients. Spastic CP is clinically characterized by increased tonus in some muscle-groups in either one side of the body (unilateral) or both sides (bilateral) [20]. Children with dyskinetic CP have varying muscle-tone and children with ataxic CP have loss of muscular coordination [20]. Whether the disorder gives spasticity, varying or none muscle tone it will in majority of cases lead to improper movements patterns, which can result in declining mobility due to joint contractures and bone deformities [17,22]. The magnitude of the deformity is correlated to the severity of the disorder [22,23].
The severity of CP is often categorized by the Gross Motor Function Classification System (GMFCS) that divides motor function into five levels in relation to daily life activities (figure 7.2).
Various types of treatment aims to prevent progression of these deformities 22. First step is often non-surgical treatment such as orthoses and physiotherapy, application of orthotics and braces. Furthermore medical treatment with intrathecal baclofen and/or injection of various strains of botulinum toxin in high-tension muscles [24]. If non-surgical interventions are insufficient surgical interventions are the next step. The surgical corrective procedures in children with CP can vary from less invasive tenotomies to more invasive skeletal corrective osteotomies [25].

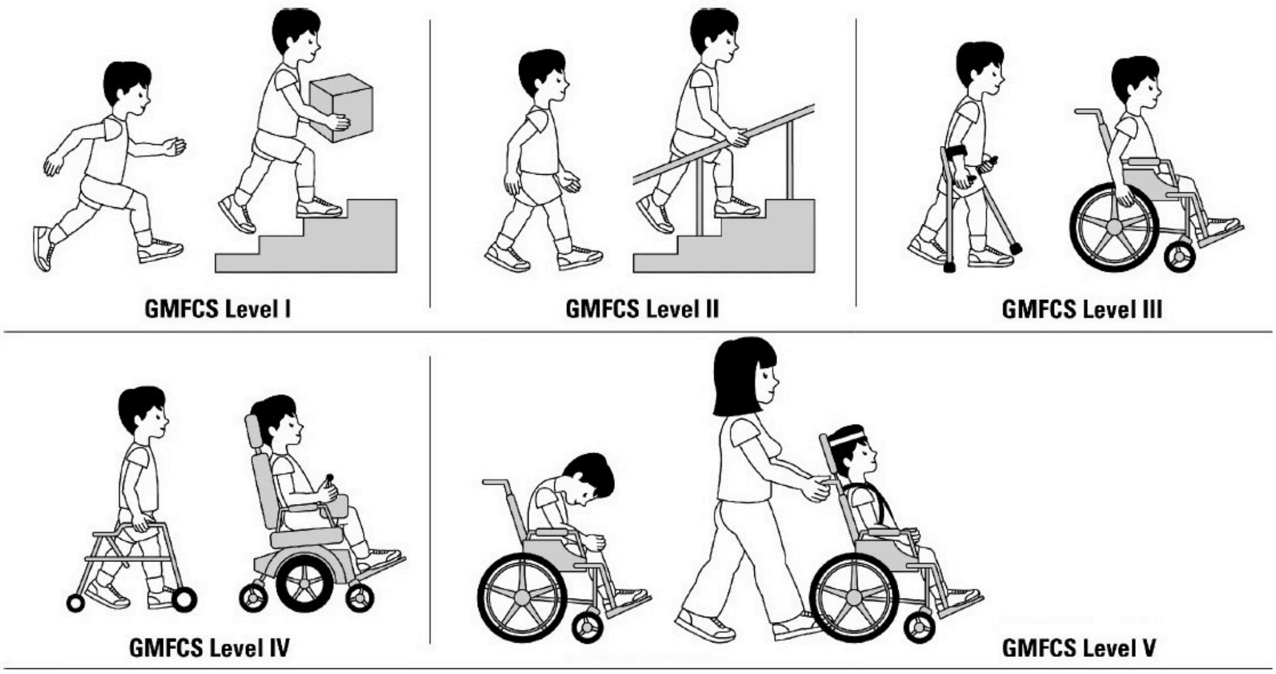

Figure 7.2. Gross Motor Function Classification System (Reprinted with permission from Wolters Kluwer and main author from: Graham HK. Classifying cerebral palsy. J Pediatr Orthop. 2005; 25:128.)

7.3 Hip Dislocation in Children with Cerebral Palsy

Imbalance in the muscles around the hip seems to be the cause of deformities in children with CP. The increased spasticity and shortening of the adductors and iliopsoas muscles is hypothesized to be the primary pathological pathway to hip dislocation in CP [26,27]. Other studies suggest children with CP in general have increased risk of acetabular dysplasia [28,29]. The main deformities are contractures, subluxation and by time total dislocation. The incidence of hip dislocation in children with CP has been observed in 28-35 % [30,31]. There is high correlation between GMFCS and the risk hip dislocation, which ranges from 0-7 % in GMFCS I children to 60-89 % in GMFCS V children in an almost linear pattern [30,32]. The hip stability and position is in focus from early childhood [30] evaluated by and AP radiograph of the pelvis. The instability is assessed by the femoral head extrusion index (FHEI) [33,34] estimating the percentage of the femoral head that is not covered by the acetabular ceiling. If progressive FHEI is observed and between 30-40 % an adductor and psoas tenotomies has relative indication [32,35] and if the FHEI > 50 % then a femoral varus derotation osteotomy (VDRO) and a periacetabular Dega osteotomy (DO) is indicated (figure 7.3) [35–38]. Acetabular index (AI) is a radiological parameter for description of acetabular morphology and degree of potential acetabular dysplasia [26,31,38]. The surgical strategy at the orthopedic department of Hvidovre Hospital is always to do both DO and VDRO in order to reconstruct the hip to minimize the number of these types of surgeries in the lifetime of the children whether or not AI is abnormal and AI had no role deciding time of surgery. The measuring of FHEI and AI are illustrated in figure 7.3.

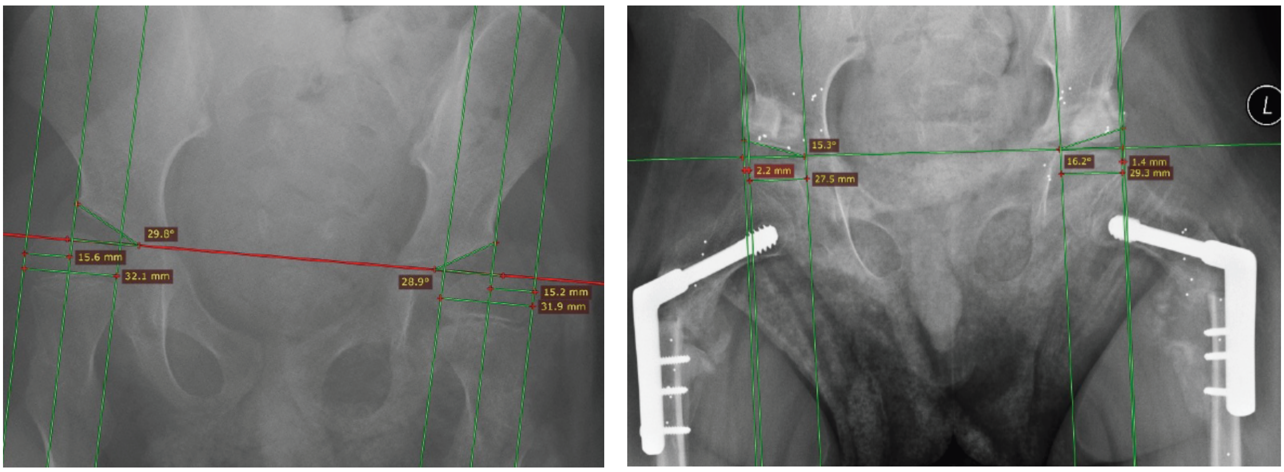

Figure 7.3. Pre- and postoperative measurements of FHEI and ACI in an eight-year old boy with CP whom had performed a femoral VDRO and Dega acetabuloplasty.

Consequences of a subluxated or dislocated hip is poor sitting function, deteriorating gait function and secondary hip arthritis [39,40]. Complications in CP children that underwent VDRO and DO observe the need of reoperations in 16-32 % of surgical treated children and unsatisfactory results have been reported up to 55 % [31,40,41].

At Hvidovre Hospital the current postoperative treatment after undergoing DO and VDRO is immobilization in hip spica cast for 5 weeks and afterwards full mobilization according to the level of pain.

7.4 Radiostereometric Analysis

RSA originates from Lund, Sweden and is earliest described in 1974 by Göran Selvik [42]. RSA has since been used for many purposes and is today a well-recognized method to identify complex 3D migration of skeletal structures with a high methodical repeatability [43–46]. It is often used to assess loosening and wear on joint prosthesis components [47–51]. The RSA technique has also been used to examine fracture and healing of bones in both adults and children, where growth deformities and healing after fractures in children can be detected early [52]. These studies have focused on the knee or ankle to evaluate stalling for tibial-growth deformities [53] and micromotions after external fixator removal [54]. A recent study evaluating micromotions in adults after high tibial osteotomy observed limited micromotions after 6-12 weeks [55]. The feasibility of RSA across CLOs has been verified in a cadaver study [56]. To my knowledge there are no clinical RSA studies focusing on foot or hip of children.

To be able to use the RSA method to assess migration across osteotomies one has to insert tantalum markers on each side of the osteotomy to create clusters of markers visible on the radiographs (see cover image). Furthermore to obtain 3D perception one has to conduct to simultaneous radiographs above a calibration cage (figure 7.4) to be able to extrapolate the exact positions of the markers.

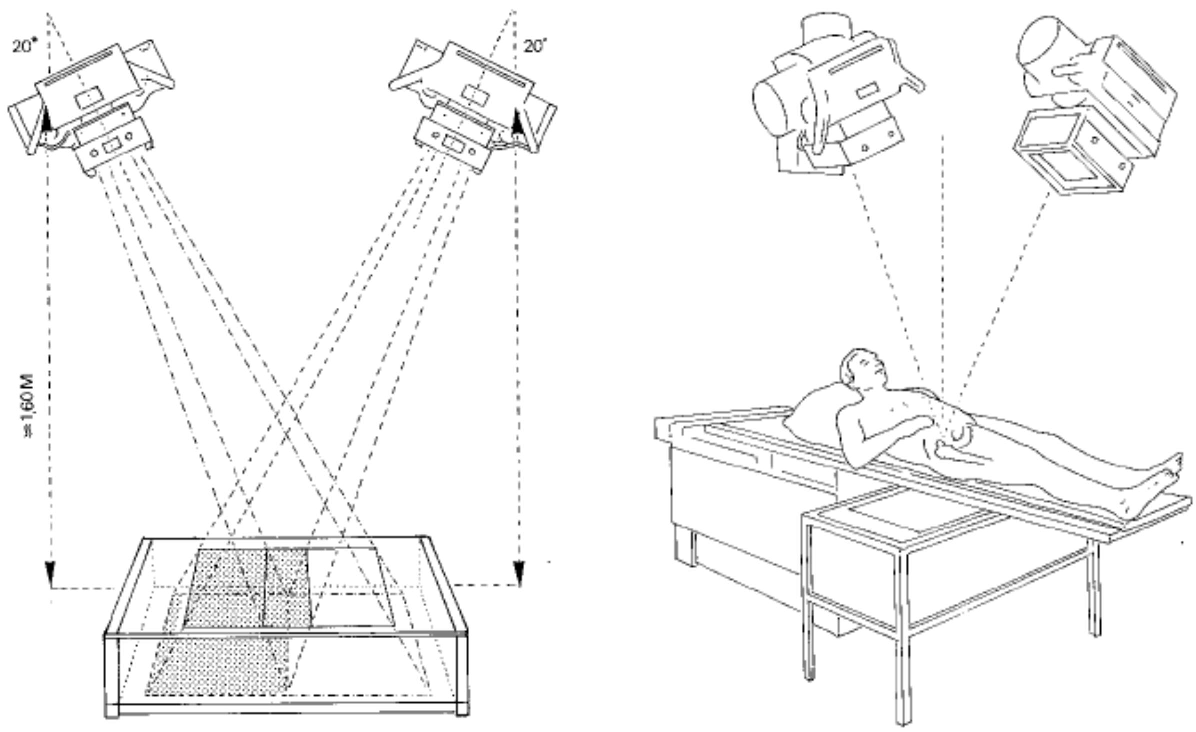

Figure 7.4. Left figure: Angulation of the x-ray tubes and the distance to the calibration cage. Right figure: Positioning of the patient and the region of interest above the calibration cage and in the centre of the x-ray beams (reprinted with permission by the author of the MbRSA manual).

At Hvidovre Hospital we use the MbRSA 3.41 software developed in Leiden University Medical Centre, the Netherlands, to interpret these RSA radiographs and positioning of the markers [47,57]. Figure 7.5 shows an example of how the MbRSA program depicts the clusters of markers turning it into 3D models (the rigid body).

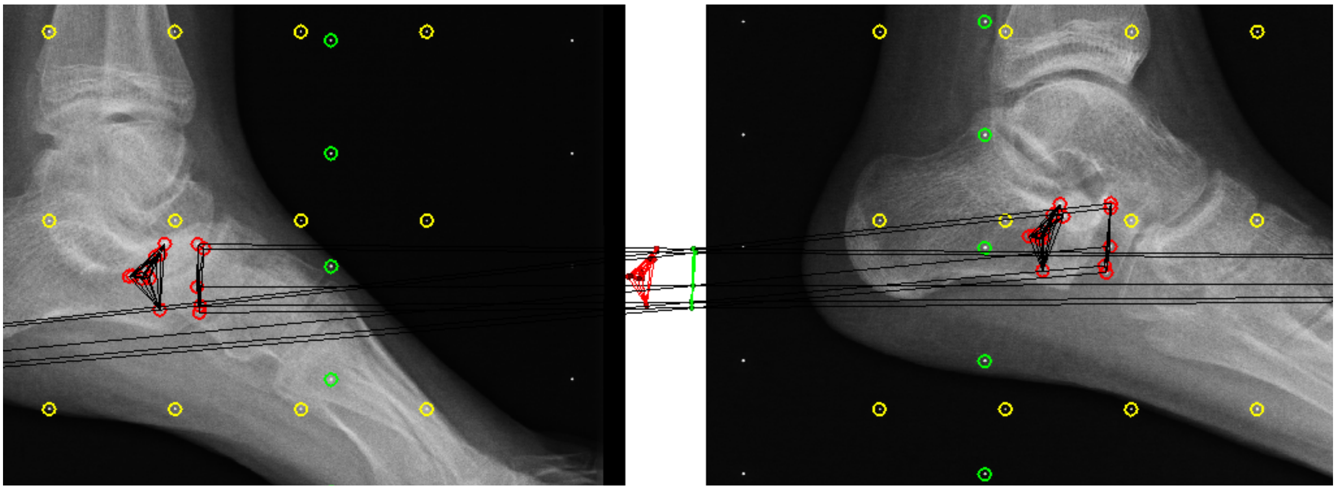

Figure 7.5. MbRSA software depiction of the two marker clusters on each side of a calcaneal lengthening osteotomy.

The MbRSA 3.41 software process data according to the RSA community guidelines [44] with migration in relation to the centre of gravity of the rigid bodies. Each output consist of a information about the selected reference model and the migrating model, translation values of x, y and z, rotation values Rx, Ry and Rz and furthermore maximum total point motion (MTPM), Mean error of rigid body fitting (ME) and condition number (CN), the three latter are explained later.
As the 3D rotations are sequence dependent by the Euler angle Theorem [44] standardized Rx-Ry-Rz sequence is used by the software. The coordinate system is standardly adapted to a right extremity (figure 7.6), thus one need to negate the values of x, Ry and Rz of a left extremity to obtain the correct directions.

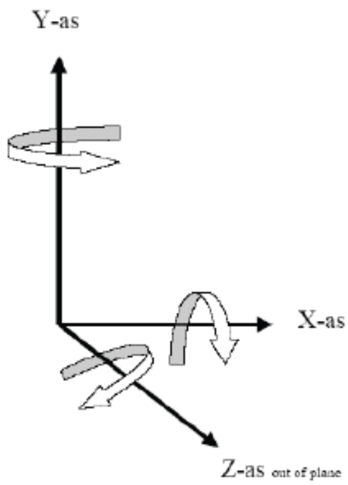

Figure 7.6. The RSA coordinates.

The RSA software determines marker locations by intersection of back-extrapolation according to the coordinates of the calibration cage. Locations are estimated by a computerized least squares method expressed the crossing line distance (CLD) and accepted if CLD < 0.5 mm [58].

Marker stability is assessed by the mean error of rigid body fitting (ME). ME is the mean difference between the relative distances of the residual motion vector d_i of each marker in the rigid body measured and the reference examination [50]. ME is expressed as:

$$\mathrm{ME} = \sqrt{\frac{d_1^2 + d_2^2 \ldots + d_n^2}{n}}$$

By computation of rotation matrices and translation vectors for absolute motion the RSA software minimizes ME using a least-squares method and thereby excludes the actual movement of the rigid body. The standard threshold in the RSA guidelines is acceptance of the results if ME is below 0.35 mm [44]. Under phantom model conditions the precision of RSA has been shown to decrease with increasing ME [50]. In clinical setting ME values of 0.1-0.25 mm are typically obtained [47].
The influence of ME on the precision of the results is measured as the standard deviation (SD) from the true value, which is more often described as the 95 % repeatability limits (RPL) where $\mathrm{RPL} = 1.96 \times \sqrt{2} \times \mathrm{SD}$. The relationship between ME and SD and the relationship between the amount of markers in a rigid body and SD have been tested in a RSA laboratory in Lund in 1986 by Leif Ryd [50] shown in figure 7.7.

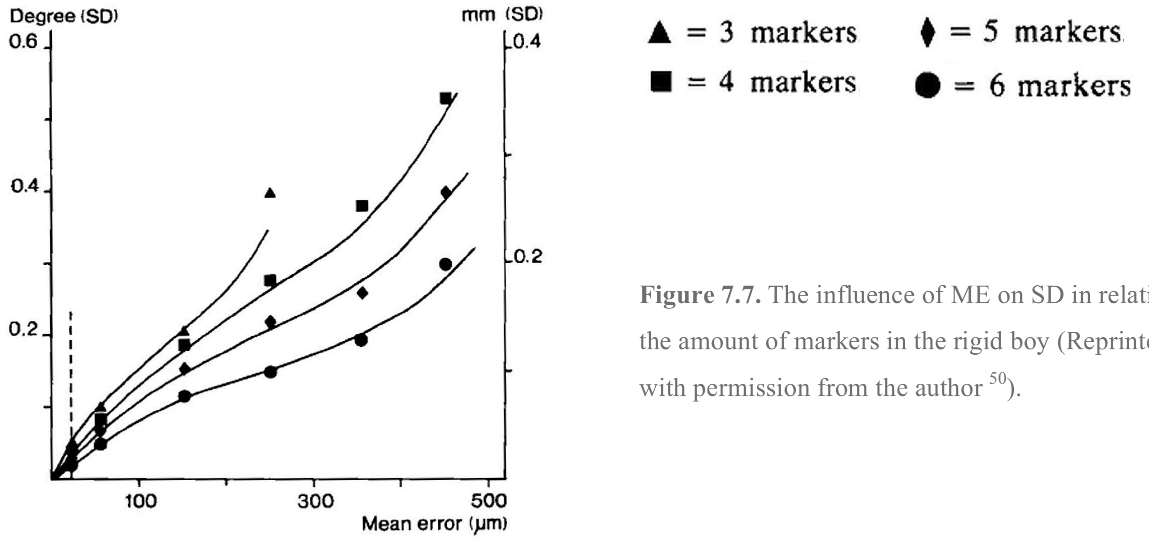

Figure 7.7. The influence of ME on SD in relation to the amount of markers in the rigid boy (Reprinted with permission from the author [50]).

The MbRSA 3.41 software also excludes solitary markers if the intermarker changes are greater than 0.3 mm [58].

The distribution of the markers is assessed by the condition number (CN), which is a value calculated from the distance of the markers to an arbitrary straight line passing through the cluster and is expressed as,

$$\mathrm{CN} = \frac{1}{\sqrt{d_1^2 + d_2^2 \ldots + d_n^2}}$$

where d_i is the shortest possible distance to this arbitrary straight line [50]. A large value of CN is due to small d_i and indicates that the marker cluster approximates a straight line.
As illustrated in the figure 7.8 Söderkvist et al. [59] performed numerical experiments and observed a logarithmic relationship between CN and the rotation error. The RSA guidelines recommend inclusion of RSA data if CN < 120 mm^{-1} in arthroplasties of the adult hip, knee and shoulder [44] or considered higher when studying smaller areas. Other publications studying smaller areas find CN < 150 mm^{-1} acceptable [44,51,54,57,59–61].

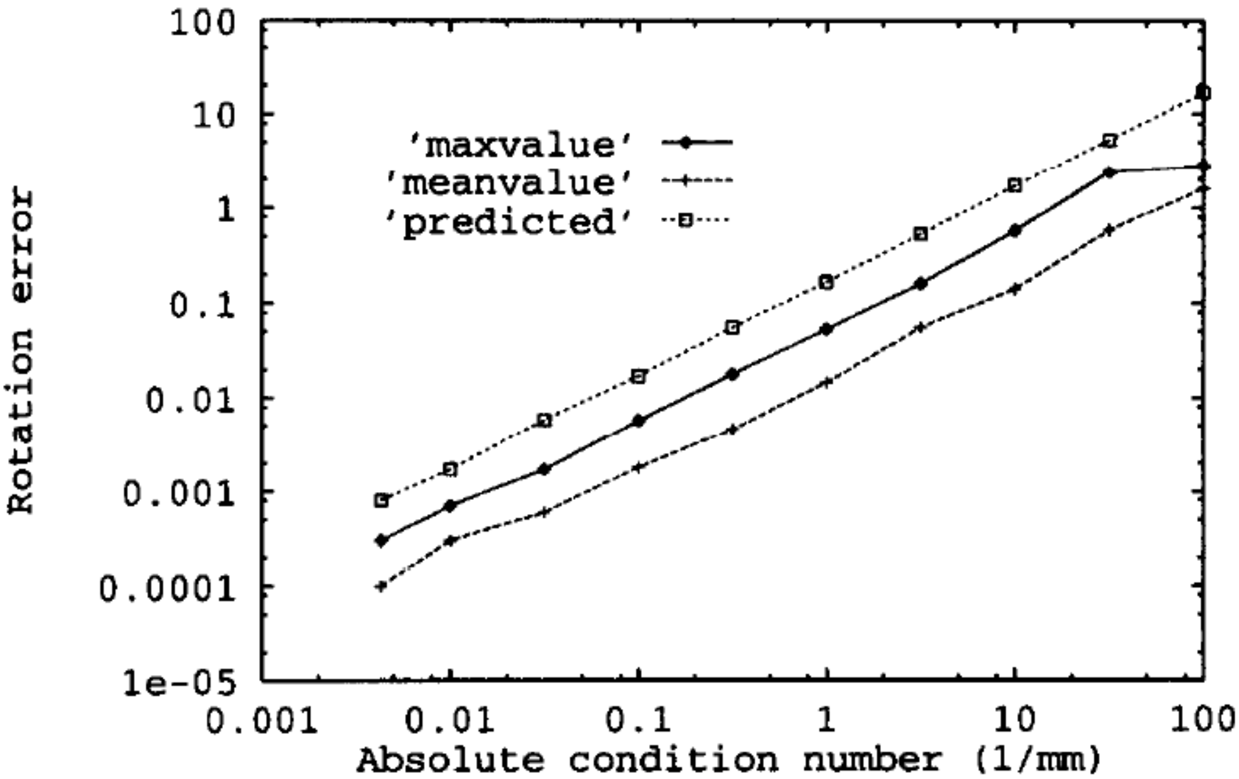

Figure 7.8. Relationship between the condition number and rotation error. (Reprinted with permission from the author [59])

Maximum total point motion (MTPM) values are an attempt to express the total translation and rotation by one value. The MTPM value is the translation of the 3D vector of the one marker within the rigid body that has the largest migration [50]. Hence MTPM values are numerical, and are therefore not always normally distributed [44].

Precision is defined as the repeatability of the method, whereas accuracy represents the closeness of the test result to the real value. The accuracy is more difficult to evaluate because you have to know the exact migration values and compare them to the test results [62,63].
Imprecision is due to two kind of errors; systematic error induced by the methodology and instruments, and random error with unexplainable origin such as Brownian motion [62]. By inclusion of a calibration cage in the RSA setup, one has theoretically been able to reduce the systematic error to a minimum.

Calculation of RPL are defined by Ranstam et al. (2000) [62]. RPL is under the assumption that the true value of migration between the RSA examinations are zero in all 6 degrees of freedom $(\mathrm{df} = \mathrm{x, y, z, Rx, Ry, Rz})$ and the observations follow a normal distribution. With existence of both systematic and random error RPL is calculated as follows. The bias is the mean deviation from the true value and $\mathrm{d_i}$ is the absolute value of motion of each df:

$$\mathrm{bias_{df}} = \frac{\sum_{i=1}^{n} \mathrm{d_i}}{\mathrm{n}}, \qquad \mathrm{d_i} \in \mathbb{R}$$

The standard deviation (SD) of the bias is calculated as

$$\mathrm{SD_{bias_{df}}} = \sqrt{\frac{\sum(\mathrm{d_i} - \mathrm{bias_{df}})^2}{\mathrm{n} - 1}}$$

The 95% repeatability limits (RPL) is then

$$\mathrm{RPL_{df}} = 1.96 \times \sqrt{2} \times \mathrm{SD_{bias_{df}}}\,.$$

Marker based RSA studies testing repeatability observe 0.12-0.20 mm for translation and 0.30-0.36° for rotation [50,64,65].

Only few pediatric orthopedic RSA studies are published within the last decades [66–69] despite the RSA methodology has high precision and radiation doses are lower than in conventional radiographs [50]. These two facts theoretically make the method rewarding in pediatric orthopedic studies, but the setup might be too extensive for some hospitals.

There are other types of RSA than marker based RSA, such as are model based and fluoroscopic RSA. These two were not found feasible and description is omitted.

7.5 Stability of an Osteotomy

One could divide this concept into stability used in a clinical setting and RSA stability:

7.5.1 Stability used in a Clinical Setting

The term 'clinical stability' is used on a daily basis in the orthopaedic practise, but when trying to assess the above definitions; they turn to be dispersedly defined and with only a few of liable measurable parameters to estimate them [70,71]; even when discussing the common concept of fracture stability or healing, opinions are divided. Bhandari et al [71] (2002) showed a clear lack of consensus amongst orthopedic surgeons of which parameters are to be used in the clinical assessment after retrieval of questionnaires from 444 orthopedic surgeons. Almost two-thirds answered that they "often" or "always" use radiological assessment of cortical continuity, callus formation and progressive loss of fracture line on conventional radiograph combined with the ability to weight bear and loss of pain at fracture site on clinical examination when assessing fracture healing. Yet again one-third of the surgeons answer that they "never" or only "sometimes" use these parameters to assess healing. This study also demonstrates that stability was seen as synonymous to healing, which in fact are two closely related, but different concepts. Den Boer et al [72] (1998) chose another approach trying to asses stability in an animal study using computed tomography; the density of the callus was correlated to stiffness and torsional strength. The latter concept of 'stiffness as clinical stability' was quantified in a number of studies to be at least 15 mN/degree in two orthogonal planes across the fracture or osteotomy of [73–75]. However, when using conventional radiographs both radiologists and orthopedic surgeons alike do not agree on assessment of stability [73].

For osteotomies of DO, VDRO and CLO, which are examined in this thesis, only a few of the above described stability parameters are readily available for stability assessment; examining conventional radiographs at follow-ups is difficult because of interference in between grafts and osteosynthesis material. Clinical examination of pain level at weight bearing is often not feasible due to inability to walk at all in the treated patient group with severe CP (GMFCS IV-V) and inability to express pain due to cognitive deficits. Radiological assessment of stability using the callus formation is possible across for example the VDRO, but this has been shown not to correlate to stability [72]. In this perspective RSA as used in this thesis was seen as appropriate in objectifying the stability across osteotomies and in children.

7.5.2 RSA Stability

The RSA method has earlier primarily been used to assess micromotions in arthroplasty for early detection of clinical loosening [44]. In this thesis I wanted to use RSA to assess stability across various osteotomies in children. This entails that the process of gradual healing and minor regional growth in the children during the study period must be considered and included in the assessment of RSA stability. Moreover, minor migration is to be expected in a 'stable' osteotomy due to both methodological systematic and random error. The definition of the repeatability limits (RPL) consists of 95 % of the observations being within the threshold in a normal distribution across two immobile rigid bodies. In the study by Lauge-Pedersen et al. (2006) [66] growth arrest was defined as translation below the internal accuracy. This is adequate when observing only one orientation, but when assessing all six orientations simultaneously as in this thesis, considerations have to be taken into account; statistically one can argue that if the migration between two consecutive observations were within the RPLs in all six orientations, then the osteotomy would be statistically RSA stable, and when considering a 5 % risk of a type I error for each orientation in the normal distribution, the rejection of the null hypothesis (the osteotomy being RSA stable) would be too high using this assumption and well above a p-value of 5 %. Under the assumption of independency between all six orientations the outcome can be considered as binomial distributed, and using a significance level of 5 % in this binomial distribution the risk of a type I error would be 26.5 % (see figure 7.9). Allowing of one of the orientations to be above the RPL using the same binomial distribution would amount to a risk of type I error in 3.3 %.

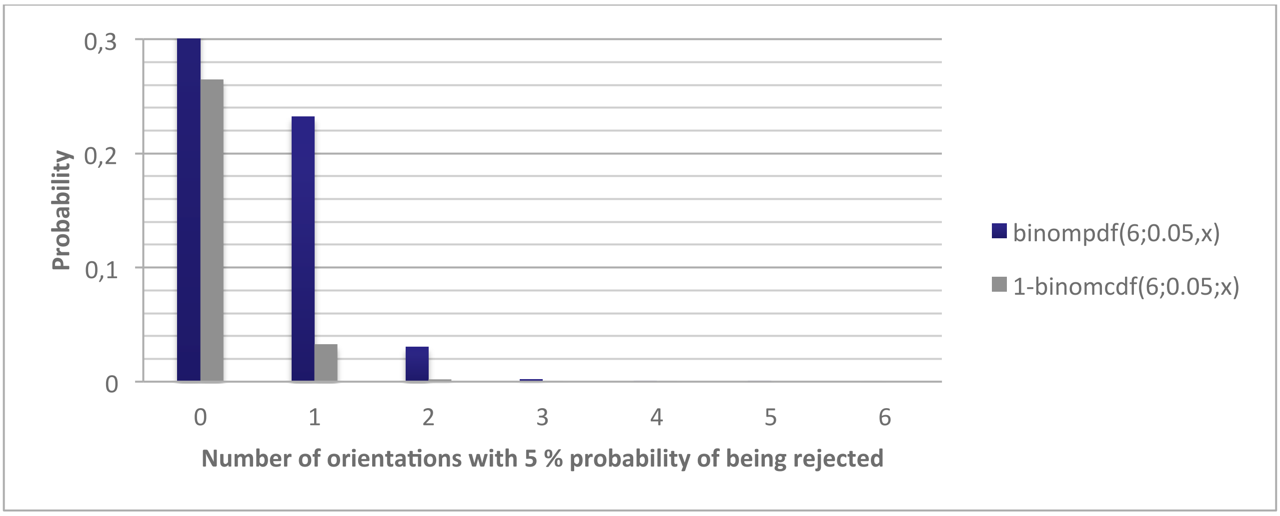

Figure 7.9. Probability of a type I error (1-binomcdf) under assumption of no interdependency between each orientation.

However, there must be some interdependent relationship in between the orientations, but the degree of interdependency as yet is unknown. I acknowledge that this and other important issues as unexplored, but I found the definition of **RSA stability** described below theoretically feasible:

The migrations are below the internal RPLs between two consecutive follow-ups in five of six orientations.

This definition will be used further in this thesis to evaluate the current postoperative regimes following DO, VDRO and CLO. If a postoperative regime is effective, there should be minimal migration across the osteotomy before stability has occurred, thus we wanted to test if all osteotomies are stable at time of cast removal and that **RSA stable** osteotomies at the 1-year follow-up have mean migration that are statistically equal to zero (e.g. the postoperative follow-up).

8 Aims

The primary aim of this thesis was to provide important basic biomechanical understanding in the stability and migration across some lower extremity corrective osteotomies in children.
The first study focuses on the feasibility to use RSA as method across osteotomies. The second to fourth study evaluates RSA stability and migration in periacetabular, femoral and calcaneal osteotomies by RSA, respectively.

8.1 Specific Aims of the Four Studies

I. The primary aim was (a) to assess the marker based RSA feasibility across a small-scale osteotomy in our RSA setup.
Hypothesis: Marker based RSA across a small-scale osteotomy is feasible in our setup.

II. Primary aim was (a) to evaluate RSA stability across periacetabular Dega osteotomies (DO). The secondary aim was (b) to estimate the migration by RSA of the distal fragment of the osteotomy at the one-year follow-up across RSA stable osteotomies.
Hypothesis (a): All DOs are RSA stable after 5 weeks.
Hypothesis (b): The mean migration across RSA stable DOs does not differ significantly from zero mm/degrees at the one-year follow-up.

III. Primary aim was (a) to evaluate RSA stability across femoral varisation derotation osteotomies (VDRO). The secondary aim was (b) to estimate the migration by RSA of the distal fragment of the osteotomy at the one-year follow-up across RSA stable osteotomies.
Hypothesis (a): All VDROs are RSA stable after 5 weeks.
Hypothesis (b): The mean migration across RSA stable VDROs does not differ significantly from zero mm/degrees at the one-year follow-up.

IV. Primary aim was (a) to evaluate RSA stability across calcaneal lengthening osteotomies (CLO). The secondary aim was (b) to estimate the migration by RSA of the distal fragment of the osteotomy at the one-year follow-up across RSA stable osteotomies.
Hypothesis (a): All CLOs are RSA stable after 10 weeks.
Hypothesis (b): The mean migration across RSA stable CLOs does not differ significantly from zero mm/degrees at the one-year follow-up.

9 Material and Methods

In this chapter the methodologies used in study I-IV are described. First is outlined in general the ethical considerations regarding the use of RSA in pediatric orthopedic research. Afterwards a description of study design and methods, study populations and a discussion of the outcome parameters, especially deviation from the RSA community guidelines [44].

9.1 Ethical Considerations

All clinical studies have approval from the Danish Research Ethical Committee: Journal number H-2-2011-124. The studies are conducted according to the Helsinki declaration in human testing. All clinical studies have been submitted and approved by the local ethics committee and the Danish Data Protection Agency.

The RSA markers are comprised of tantalum the 73rd chemical element, which has same characteristics as titanium. It has been implanted in over 5.000 patients within the last 30 years and there have been published over 300 RSA studies [44]. Tantalum has been used in medical devices in over fifty years as needles to sutures and staplers. One patient had a side-effect of chronically urticarial rash, otherwise no side-effects is described in the literature [76].

RSA have earlier been performed on children without any reports or suspicion of complications [53,54,67–69]. The tantalum markers will remain in the skeletal structures for lifetime and osteointegrated in the bone without any prior reports of rejection from the tissues [77]. If any markers by mistake should be placed in the soft tissues there are no history of inflammation or other tissue reactions, the tantalum markers is observed encapsulated in fibrous tissue without any damage to surrounding structures [78]. Tantalum is considered the most biocompatible metal and there haven't been reported any impact of the skeletal growth [79].

In terms of additional radiation by participating in the studies the RSA radiographs generally have lower radiation dose than conventional radiographs, only increasing the annual radiation dose slightly [44]. All double examinations in study I-IV were only conducted if the radiographer interpreted the initial RSA radiograph inadequate. By participating in the trial the children in study II and III are subject to additional radiation of average of 2.0 mSv, which amount to background radiation in Denmark for a few months and increase the lifetime expectancy of cancer with 0.1-0.01

‰. The inclusion in study IV causes additional radiation of less than 0.5 mSv [80,81].

9.2 Study Design, Population, Methods

9.2.1 Study I – Methodological RSA

Study Design, Population and Methods

Study I was designed as a feasibility study, a methodological laboratory experiment, conducted prior inclusion of children to the PhD period to evaluate the precision of the RSA setup at Hvidovre Hospital. A small-scale osteotomy was surgically performed on the human cadaver hindfoot to simulate the osteotomies of the subsequent included studies patients and peroperatively was inserted tantalum markers on each side of the osteotomy. The cadaver foot was thereafter exposed in three series of 10 consecutive RSA radiographs by increasing personnel interference:

1. No alterations between examinations.
2. Altering the RSA setup between each examination.
3. Altering both the RSA setup and the foot position between each examination.

RPL estimates were only included if RSA output had ME < 0.35 mm and CN < 150 mm^{-1} and compared to similar published observations.

9.2.2 Study II – Periacetabular Dega Osteotomies

Study Design, Population and Methods

Study II was designed as a descriptive prospective cohort study with inclusion period from 2012 to 2014. Sample size estimation: $N = 4Z_{\alpha}^2S^2/W^2 = 15$, with $Z_{\alpha} = 1.96$, S=W=*0.5*.

Patients with neuromuscular disorders were offered to participate in the study if they were between the age of two and eighteen years and scheduled for a DO. RSA examinations were conducted postoperatively (in hip spica cast), after 5 weeks (after hip spica cast removal) and 3, 6 and 12 months. The visit window for the RSA recordings was 3 days for the postoperative follow-up, one week at the 5-week follow-up and 2 weeks at the subsequent follow-ups. After the surgical procedure the patients were not allowed/able to weight bear the first 5 weeks. After the first 5 weeks the patients were mobilized without restrictions.

RSA output with CN > 150 mm^{-1} were excluded. If ME > 0.35 mm the data were evaluated individually. This was not to discard any data with initial ME < 0.35 mm and with continuously increasing ME in a manner that could be interpreted as due to growth.

Based on the internal RPLs of double examinations within the study population we defined RSA stability as migration below the RPLs of two consecutive follow-ups in five of six orientations. We elaborated if redefining to migration below the RPLs in all six orientations.

9.2.3 Study III – Femoral Varisation Derotation Osteotomies

Study Design, Population and Methods

Study III was designed as a descriptive prospective cohort study with inclusion period from 2012 to 2014. Sample size estimation: $N = 4Z_\alpha^2 S^2/W^2 = 15$, with $Z_\alpha = 1.96$, $S=W=0.5$. Patients with neuromuscular disorders were offered to participate in the study if they were between the age of two and eighteen years and scheduled for a VDRO. RSA examinations were conducted postoperatively (in hip spica cast), after 5 weeks (after hip spica cast removal) and 3, 6 and 12 months. The visit window for the RSA recordings was 3 days for the postoperative follow-up, one week at the 5-week follow-up and 2 weeks at the subsequent follow-ups. After the surgical procedure the patients were not allowed/able to weight bear the first 5 weeks. After the first 5 weeks the patients were mobilized without restrictions.

Due to high probability of markers in the femoral shaft being covered osteosynthesis material we planned to use the screw tips as additional markers, after testing the internal RPLs with inclusion of these.

RSA output with CN > 150 mm^{-1} were excluded. If ME > 0.35 mm the data were evaluated individually. This was not to discard any data with initial ME < 0.35 mm and with continuously increasing ME in a manner that could be interpreted as due to growth.

Based on the internal RPLs of double examinations within the study population we defined RSA stability as migration below the RPLs of two consecutive follow-ups in five of six orientations. We elaborated if redefining to migration below the RPLs in all six orientations.

9.2.4 Study IV – Calcaneal Lengthening Osteotomies

Study Design, Population and Methods

Study IV was designed as a descriptive prospective cohort study with inclusion period from 2012 to 2014. Sample size estimation: $N = 4Z_\alpha^2 S^2/W^2 = 15$, with $Z_\alpha = 1.96$, $S=W=0.5$. Patients were offered to participate in the study if they were between the age of two and eighteen years and scheduled for a CLO. RSA examinations were conducted postoperatively (in a splint bandage or cast), after 5 (in a walking cast) and 10 weeks (after walking cast removal), 6 and 12 months. The visit window for the RSA recordings was 3 days for the postoperative follow-up, one week at the 5-week follow-up and

2 weeks at the subsequent follow-ups. After the surgical procedure the patients were not allowed/able to weight bear the first 5 weeks. After the first 5 weeks the patients were mobilized without restrictions.

RSA output with CN > 150 mm^{-1} were excluded. If ME > 0.35 mm the data were evaluated individually. This was not to discard any data with initial ME < 0.35 mm and with continuously increasing ME in a manner that could be interpreted as due to growth.

Based on the internal RPLs of double examinations within the study population we defined RSA stability as migration below the RPLs of two consecutive follow-ups in five of six orientations. We elaborated if redefining to migration below the RPLs in all six orientations.

10 Summary of Results

This section briefly outlines the results of the studies. More detailed explanation of the results below can be found in the manuscripts at the back of this thesis.

10.1.1 Study I – Methodological RSA

		x	y	z	Rx	Ry	Rz
1st in vitro	Bias	-0.012	-0.012	-0.077	0.082	-0.011	-0.026
	RPL	0.129	0.069	0.212	0.384	0.256	0.194
2nd in vitro	Bias	-0.019	-0.028	-0.087	0.123	***0.203**	-0.002
	p-value	*0.802*	*0.326*	*0.804*	*0.659*	*0.015*	*0.687*
	RPL	0.073	0.075	0.224	0.422	0.517	0.262
3rd in vitro	Bias	-0.005	***0.015**	***0.063**	***-0.125**	***-0.053**	***0.168**
	p-value	*0.456*	*0.004*	*< 0.001*	*0.012*	*0.030*	*0.035*
	RPL	0.079	0.055	0.181	0.416	0.496	0.454

Table 10.1.
Bias (*or mean* = systematic error),
RPL – 95 % repeatability limits (random error),
* marks p-value < 0.05. Bias was tested by paired t-test and RPL by F-test.

10.1.2 Study II - Periacetabular Dega Osteotomies

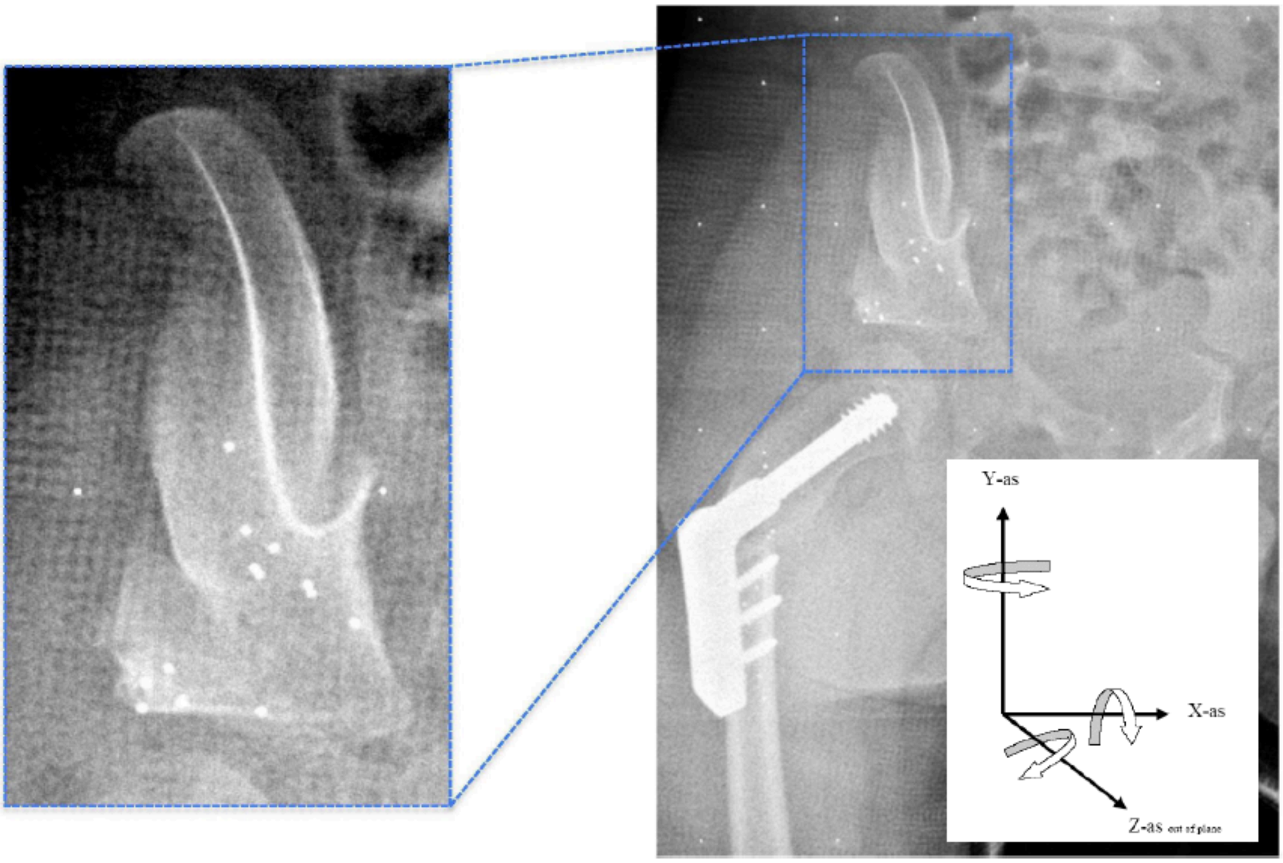

Figure 10.2. Postoperative RSA with magnified region of interest (ROI). The coordinate system illustrates that positive values of a right hip has translation x_+ = medial, y_+ = superior and z_+ = anterior and rotation Rx_+ = anterior tilt, Ry_+ = anteversion and Rz_+ = medial inclination.

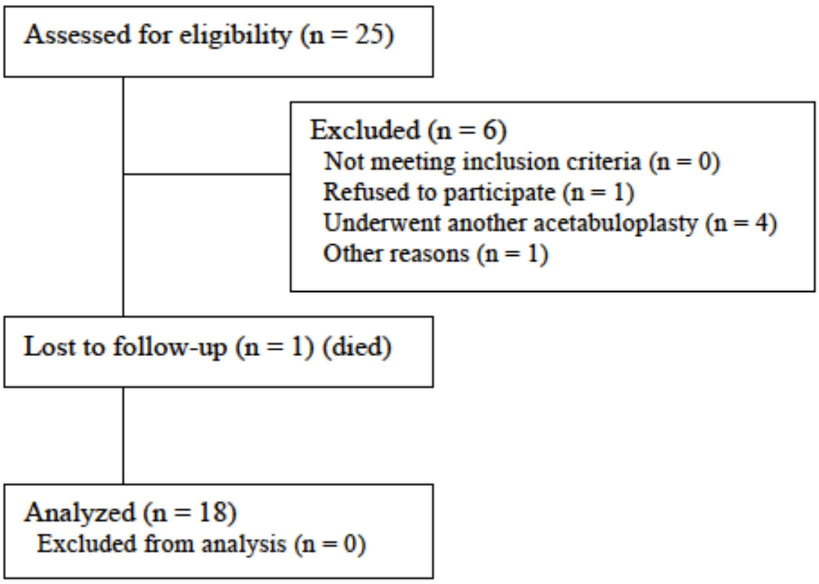

Chart 10.1. Inclusions of patients in study II.

Translation	RPL	Rotation	RPL
x	0.11 mm	Rx	0.41°
y	0.09 mm	Ry	0.74°
z	0.28 mm	Rz	0.38°

Table 10.2. The 95 % repeatability limits (RPL) based on double examinations after the 3-month follow-up and if the DO was assessed radiographic stable (n=16).

Follow-up (n=18)	5 out of 6 directions	6 out of 6 directions
5W	13	8
3M	15	14
6M	18	18
12M	18	18

Table 10.3. RSA stability assessed in relation to RPL at each follow-up. By definition RSA stability was obtained if migration was below the RPL in either five or six of the six orientations.

Direction	Mean	SD	p-value
x	0.55 mm	0.63	***0.002**
y	0.33 mm	0.33	***0.001**
z	-0.13 mm	0.24	***0.035**
Rx	-1.47°	2.91	***0.047**
Ry	-0.27°	1.28	0.383
Rz	1.76°	3.10	***0.028**

Table 10.4. Mean translation and rotation with standard deviation at the one-year follow-up of stable DOs (n=18). P-value is the likelihood of zero being included within the observations, tested by one sample t-test.

10.1.3 Study III - Femoral Varisation Derotation Osteotomies

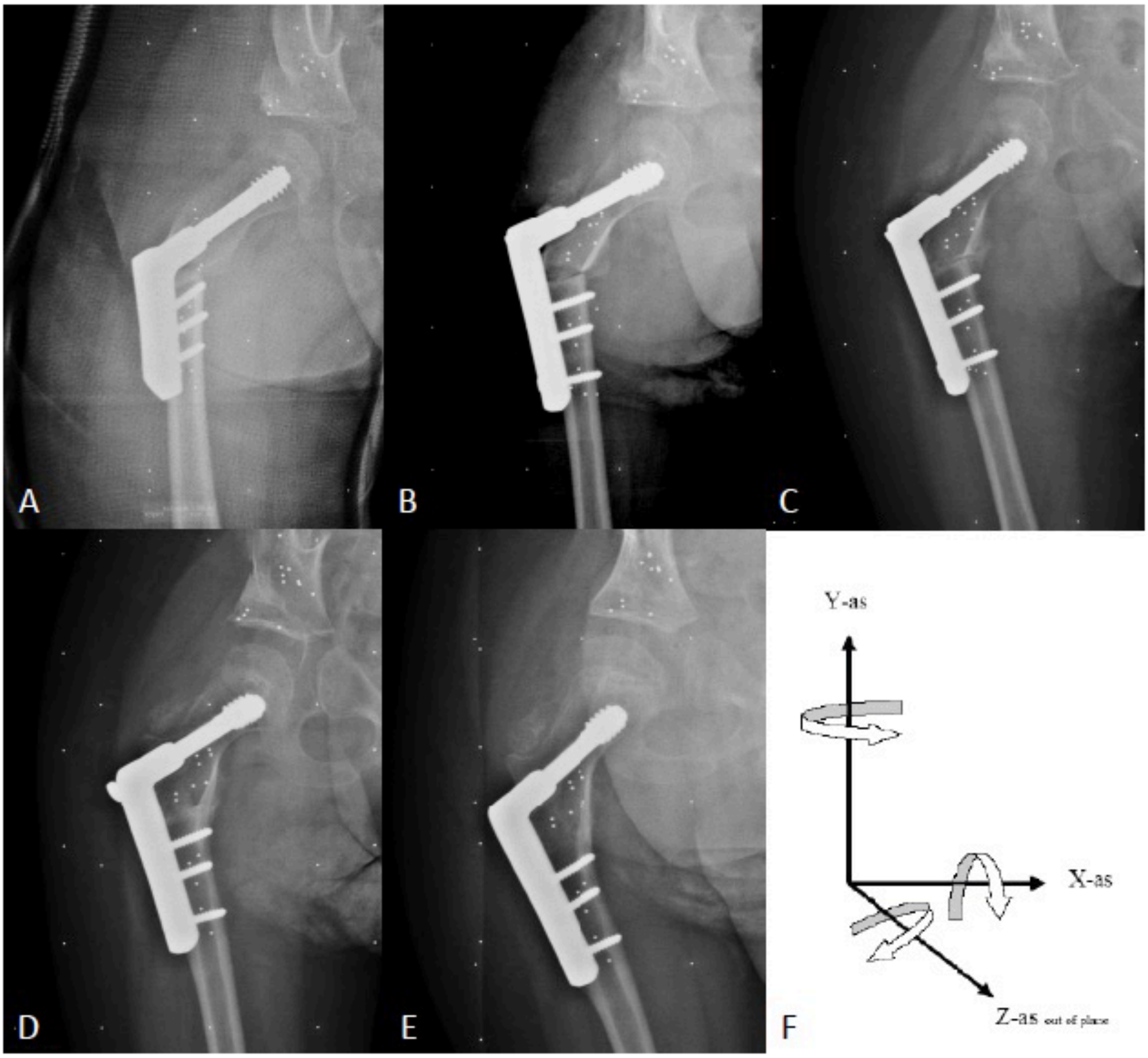

Figure 10.3. A-E: RSA radiographs at postoperative time 0 weeks, 5 weeks, 3 months, 6 months and 12 months, respectively. In figure D and E the VDRO is considered radiographic stable. F: Shows the orientation of the 6 degrees of freedom with positive values of a right distal femur distal. Hence, translations x_+ = medial, y_+ = superior and z_+ = anterior and rotations Rx_+ = anterior tilt, Ry_+ = internal rotation and Rz_+ = varisation.

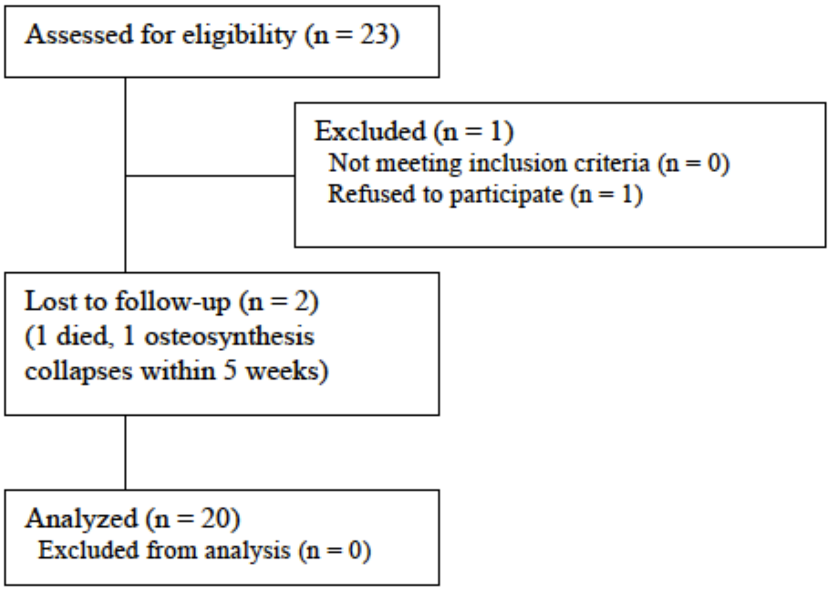

Chart 10.2. Inclusions of patients in study III.

Translation	RPL	Rotation	RPL
x	0.23 mm	Rx	0.81°
y	0.19 mm	Ry	1.24°
z	0.46 mm	Rz	0.58°

Table 10.5. The 95 % repeatability limits (RPL) based on double examinations after the 3-month follow-up and assessment of radiographic stability (n=10). These RPLs are with inclusion of screw tips as additional markers.

Follow-up (n=19)	5 out of 6 directions	6 out of 6 directions
5W	16	15
3M	18	16
6M	19	18
12M	19	18

Table 10.6. RSA stability assessed in relation to RPL at each follow-up. By definition RSA stability was obtained if migration was below the RPL in either five or six of the six orientations.

Direction	Mean	SD	p-value
x	0.51 mm	1.12	0.070
y	0.69 mm	1.61	0.078
z	-0.21 mm	1.28	0.484
Rx	0.39°	2.90	0.565
Ry	0.02°	3.07	0.978
Rz	2.17°	2.29	***0.001**

Table 10.7. Mean translation and rotation with standard deviation at the one-year follow-up of stable VDROs (n=19). P-value is the likelihood of zero being included within the observations, tested by one sample t-test.

10.1.4 Study IV - Calcaneal Lengthening Osteotomies

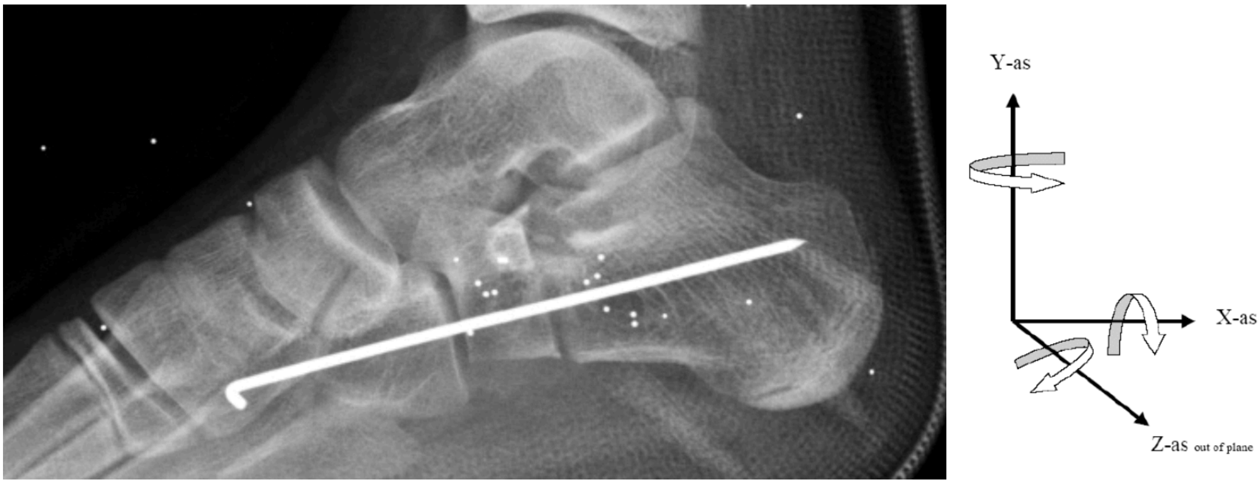

Figure 10.4. The six orientations with positive values of a right feet being; translation x_+ = posterior, y_+ = superior and z_+ = medial and rotation Rx_+ = pronation, Ry_+ = internal rotation and Rz_+ = plantar flexion.

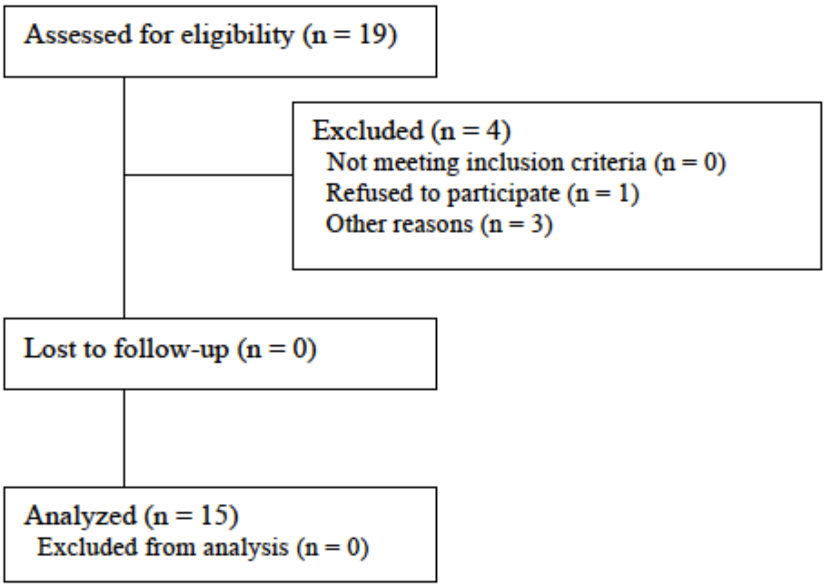

Chart 10.3. Inclusions of patients in study IV. The exclusion of patients by 'other reasons' was the surgeon forgetting to insert the tantalum markers in all three cases.

Translation	RPL	Rotation	RPL
x	0.21 mm	Rx	0.64°
y	0.21 mm	Ry	0.54°
z	0.24 mm	Rz	0.48°

Table 10.8. The 95 % repeatability limits (RPL) based on double examinations after the 10-week follow-up and assessment of radiographic stability (n=16).

Follow-up (n=18)	5 out of 6 directions	6 out of 6 directions
5W	13	8
10W	18	13
6M	18	18
12M	18	18

Table 10.9. RSA stability assessed in relation to RPL at each follow-up. By definition RSA stability was obtained if migration was below the RPL in either five or six of the six orientations.

Direction	Mean	SD	p-value
x	0.00 mm	0.26	0.987
y	0.23 mm	0.51	0.073
z	-0.14 mm	0.40	0.156
Rx	-0.49°	2.09	0.334
Ry	-0.78°	2.03	0.122
Rz	-0.91°	1.98	0.068

Table 10.10. Mean translation and rotation with standard deviation at the one-year follow-up of stable CLOs (n=18). P-value is the likelihood of zero being included within the observations, tested by one sample t-test.

11 Discussion

One of the primary aims was to establish if RSA as method were feasible over a small-scale osteotomy, and if the methodology proved usable to collect data to assess RSA stability and evaluate the migration outcome across osteotomies of DOs, VDROs and CLOs.

11.1.1 The Feasibility of RSA across a Small-Scale Osteotomy

The phantom model of study I illustrated that RSA as method was feasible over a small-scale osteotomy. Al output had CN < 150 mm^{-1} and ME < 0.35 mm, which is important for the RSA results to be valid. Regarding systematic and random error we expected increasing systematic error by introducing increasing methodological interference between each radiograph. This was confirmed by the statistical differences in bias between 2^{nd} and 3^{rd}. The 3^{rd} experiment is most likely to resemble clinical studies and should be performed prior study initiations.

11.1.2 Stability across DO, VDRO and CLO

Regarding the use of RSA as an additional tool to assess stability across an osteotomy with the definition of RSA stability, I find this methodology theoretically plausible and practically usable. As expected we find continuous decreasing migration across the osteotomies as they stabilize. As discussed in chapter 7.5 a big issue is the risk of type I error. As there do not exist any data regarding the interdependency between the orientations, we do not know the p-value setting to obtain the accumulated 95 % likelihood if assessing all six orientations at the same time. Elaborating on the results and if choosing to define RSA stability below RPL in all 6 orientations, would lead to 3 unstable osteotomies in study II and III after the 5-week follow-up, and in study IV the same is the case in 5 patients undergoing CLO with RSA unstable osteotomies at the 10-week follow-up. As we did not observe any major migration or graft collapse across DOs, VDROs or CLOs with current postoperative regime these instabilities would have been found hard to explain and thus interpreted as due to type I error under these assumptions.
Under the argued definition of RSA stability as defined in chapter 7.5, I find RSA stability across most osteotomies within the casting period. Still, 3 DOs and 1 VDRO are RSA unstable at time of mobilization but RSA stabilize within months. As most of the patients treated with DO and VDRO

are GMFCS 4-5 and have limited ambulation, none of the RSA unstable osteotomies collapse during these studies. One should be aware of the risk of complications during the postoperative care when performing surgery on more ambulatory children. In conjunction with the small migration observed at the 1-year follow-up, the definition of RSA stability seem to be valid, but further investigation is needed to exploit the use of it.

11.1.3 Migration across osteotomies in study II, III and IV

In general the observed mean migration is very small across the RSA stable osteotomies at the 1-year follow-up. Regarding the DO migration results show very little motion across the osteotomies at present treatment algorithm, still the mean migration differ statistically from zero in 5 of 6 orientations. This partially might be caused by the three RSA unstable osteotomies that were allowed full mobilisation after 5 weeks. The mean translation is below 1 mm and 2 degrees so it is difficult to interpret the future clinical importance of these earlier statistically significant differences, but hopefully future follow-ups will elucidate the full meaning.

In study III only the orientation Rz was statistically different from zero and observed with mean 2.17° (CI: 1.07-3.27) varus angulation. The significance of this is yet to become clear as it is counter-intuitive to the clinical findings of the usually steepening of the femoral neck in CP children. Further investigation and follow-ups are needed.

In study IV all orientations were statistically equal to zero at the 1-year follow-up re-assuring that the postoperative regime after CLO is valid. Thus we do not find any RSA migration predictors to procedure failure within the one-year follow-up.

Intuitive, all the migrations mimic the directions of healing with a small impaction across the osteotomy in directions of the weight-bearing load. The mean migration of the distal periacetabular fragment of the DOs was at the one-year follow-up statistically significant from zero toward medial, superior and posterior direction with posterior tilt and medial inclination - all directions toward the compression from the hip. Likewise this is observed across the VDRO with statistic significant varus angulation. Both across the DOs and the VDROs the compression is minimal as most of the children are none ambulatory, but still the muscle tension draws toward these directions.

Though none of the directions differed significant from zero, all of the mean migrations of the anterior calcaneal fragment across the CLOs were at the one-year follow-up towards a relapse of the PPV (superior, lateral direction and with supination, external rotation and dorsiflexion).

12 Limitations of the Studies

12.1.1 PROMS, conventional radiographs, RSA stable across VDRO despite material.

12.1.2 Study I – Methodological RSA

Under optimal conditions the cadaver foot should have been from a child, which was not available from the anatomical institute of Copenhagen. The larger skeletal structures in an adult foot of the phantom model might have resulted in better RPLs. Retrospective it would also have been more correct to include a setup where the accuracy calculations were possible, especially if we would have seen collapse over graft or osteotomy with bigger changed in translation or rotation in study II-IV.

12.1.3 Study II-IV DOs, VDROs and CLOs

In general there are some important and uncovered issues of using RSA in children. Around all three osteotomies there might be some kind of remodelling or minor regional growth that impacts the RSA results in a yet unclear manner. A parameter as ME might be evolving over time due to growth transforming the rigid body, which might mimick marker instability. Especially in the DO study we found a positive correlation between time and ME, though not statistical significant ($p = 0.185$). In our studies we did not have difficulties obtaining ME < 0.35 mm, but in pediatric studies with longer follow-up than one year, one might consider the need to increase upper limits of ME exclusion in the end of the study period.

RSA stability could only be assessed at the designated follow-ups. In order to define earlier time of cast removal the study design might have been considered altered with more follow-ups in the beginning of the studies.

This thesis would have benefitted from longitudinal data from patient-related outcome measures (PROMS), which is not part of this thesis.

Continuous standard radiographic measurements might contribute with an attempt to correlate to the RSA data and to emphasize that our population is comparable to other studies. The additional effective radiation dose around the hips would be markedly higher and hard to justify, and would probably not be approved in the local ethical committee.

12.1.4 Study II and III – DOs and VDROs

Not all patient had a neuromuscular disorder. Few patients instead had syndromes such as Angelmans, Rett and Böhring-Opitz syndrome. The two first also have increased risk of hip dislocation, but the development might be different [82,83].

12.1.5 Study III - Femoral Varisation Derotation Osteotomies

The inclusion of screw tips in the femoral shaft as additional markers is a considerable deviation from standard RSA procedure and is only possible under one specific assumption – that the screws do not alter position between follow-ups. The MbRSA software has some precautions itself, that if one screw tip altered position it would be excluded from the rigid body. Furthermore the ME threshold also would have excluded results if marker positioning was poor. We found results acceptable, though with higher RPLs.

In some patients the postoperative pain level caused increased spasticity and four patients were unable to be immobilized in the spica hip cast. Despite this alteration in treatment regime the included patients did not show higher migrations than those with spica hip casting.

12.1.6 Study IV - Calcaneal Lengthening Osteotomies

Three of the fifteen patients in the cohort also suffered from CP with GMFCS 1. These three patients might have a different aetiology in the development of PPV than in otherwise healthy children. It is unclear how this affects the RSA results.

Five patients underwent bilateral surgery. In such situation the evaluation of confounding due to clusters is important [84]. There are more ways of doing so. We chose a graphical approach indicating reasonable basis of inclusion of both sides.

13 Conclusion

On the basis of the present thesis and included studies, the following can be concluded:

- The RSA methodology across small-scale osteotomies is feasible and valid.
- The definition of **RSA stability** as migration below RPL in five out of six orientations is comparable with the clinical outcome.
- Under the definition RSA stability the current postoperative treatment regime after CLO is sufficient. There were found RSA instability after allowing full mobilisation in 3 and 1 patients after DO and VDRO, respectively.
- The mean migrations at the 1-year follow-up of the distal fragment over periacetabular Dega osteotomies were statistically different from zero in 5 out of 6 orientations.
- The mean migrations at the 1-year follow-up of the distal fragment over femoral varisation derotation osteotomies were statistically different from zero in 1 out of 6 orientations.
- The mean migrations at the 1-year follow-up of the anterior fragment over calcaneal lengthening osteotomies did not differ statistically from zero in any of 6 orientations.

14 Perspectives

The estimated migration measurements of these studies provide a foundation to further investigate mechanism of RSA stability and migration across DOs, VDROs and CLOs. Large deviations from the achieved values might be due to early relapse. Longer follow-up of the patient cohorts will supply new hints to which patients that might suffer from relapse during adolescence. Further investigation is needed.

These thesis studies emphasize that the present treatment regime for CLO is sufficient in relation to RSA stability. Future studies might focus on shortening the periods of cast immobilization by conducted more follow-ups in the period of casting. Regarding the 3 RSA unstable DOs and 1 RSA unstable VDRO clinical importance is unclear and longer follow-up is needed.

15 References

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16 Manuscript of Studies I-IV

Repeatability of Marker Based Radiostereometric Analysis Across Hindfoot Osteotomies.

Buxbom P, Sonne-Holm S, Wong C.

Manuscript to be submitted.

I

Stability and Migration Across Dega Osteotomies in Children with Neuromuscular disorders by Radiostereometric Analysis - A One Year Follow-up of 18 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

II

Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Cerebral Palsy by Radiostereometric Analysis - A One Year Follow-up of 25 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript accepted for publication by peer-reviewers at *ACTA Orthopaedica*.

III

Stability and Migration Across Calcaneal Lengthening in Children - A Radiostereometric Analysis of Twenty Osteotomies

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

IV

Repeatability of Marker Based Radiostereometric Analysis Across Hind Foot Osteotomies

Peter Buxbom, Stig Sonne-Holm, Christian Wong

Orthopedic Department, Hvidovre Hospital, Copenhagen, Denmark

Abstract

Background: Radiostereometric analysis (RSA) is considered a valid method to evaluate migration of prostheses, but as only few RSA studies exist within children orthopedic research, preliminary phantom studies are mandatory. **Methods:** After hind foot osteotomy on a cadaver foot, we conducted three experimental setups of test-retest examinations with an increasing amount of systemic error. Afterwards we evaluated bias and repeatabilities (precisions). **Results:** By increasing experimental order we found significant differences in bias in the 3rd setup. In all 3 experiments the repeatabilities differed insignificantly. The 95 % repeatability limits ranged between 0.06-0.22 mm translation and 0.19-0.52° rotation. **Interpretation:** Marker based RSA is feasible across small-scale osteotomies. The 3rd experiment is most likely to resemble clinical studies and should be performed prior study initiations.

Keywords: *Radiostereometric analysis; Accuracy; Precision; Bias; Repeatability; Translation; Migration; Rotation; Phantom, Pilot, Condition Number.*

Introduction

Radiostereometric analysis (RSA) is a well-recognized method to identify complex 3D migration of skeletal structures. The high methodical precisions in studies entail a lower number of included study patients. This benefits both population, by reducing total population radiation dose, and the study duration (1–4). Therefore RSA is an obvious tool within the research of pediatric orthopedics. Only a few pediatric orthopedic RSA studies are published within the last decades (5–9).

The RSA methodology requires calibration and standardization. Performing thourough preparations before commencing a RSA study are required. Considerations of a radiograhic visible cluster of markers without being occluded by osteosynthesis material is important, especially if the surgery involves small skeletal areas. The marker scatter configuration is optimally non-linear and the cluster should exceed 5 markers (2,10). It is customary to protocolize the standardized procedures and validate the method prior to study initiation (1,2,4,10–13). The pre-study validation and precision measurements are beneficially performed on a phantom model (2,4,10,12,14,15).

Precision is defined as the repeatability of the method (16,17). Imprecision is due to two kind of errors; *the systematic error* (or **bias**) which is induced by the methodology of the setup, and *the random error* (or **standard deviation**) with unexplainable origin such as brownian motion and equipment detector uncertainties (16).

Martinkevich et al (9) have recently published a similar phantom study observing repeatabilities 0.11-0.20 mm translation and 0.21-0.90° rotation.

The aim of this study is to assess the precision across a hind foot osteotomy, while introducing increasing amounts of methodological error.

Methods

The precision examinations were conducted by test-retest examinations as recommended by Ranstam et al. (2000) (16).

For phantom model measurements were conducted on a right-sided adult cadaver foot (obtained from Anatomical Institute, Copenhagen University, Denmark), where a calcaneus lengthening was performed; calcaneus was exposed by a modified Ollier incision above sinus tarsi, thereafter a vertical osteotomy on calcaneus one cm behind the articulation with os cuboideum was performed. Six tantalum markers (1 mm diameter, Wennbergs Finmek AB, Gunnilse, Sweden) were inserted prior to insertion of the lengthening graft on each side of the osteotomy. Another 6 tantalum markers were inserted in talus from entry of sinus tarsi, and autograft was inserted into the cavity of sinus tarsi as an extra-articular subtalodesis ad modum Grice. The graft was fixated with 1.2 mm percutaneous Kirsch-ner

wire. Afterwards the lengthening graft in calcaneus was fixed in the osteotomy with one 1.2 mm percutaneous Kirschner wire that also created fixation across the calcaneocuboidal articulation.
After the surgical procedure the cadaver foot was circulated in cast (Scotchcast, 3M) and taken direct to the radiographic department. The radiostereometric examinations were conducted and finished within 3 hours.

Like the methodology of Mäkinen *et al.* (1) we performed three experiments by inducing an increasing amount of systematic error by each experiment:

1st experiment: Ten consecutive radiostereometric radiographs without moving foot or setup.
2nd experiment: Ten consecutive radiostereometric radiographs while moving the setup between each examination, centralizing the beam, but with slight angulation alterations.
3rd experiment: Ten consecutive radiostereometric radiographs while moving the setup and foot between each examination. The foot was then repositioned and rotated slightly within the frame of the detector plate.

The RSA setup included a wheel born carbon fiber enclosed uniplanar calibration cage (LUMC, Leiden, The Netherlands; 85 x 29 x 55 cm) and two radiographic tubes (Arcoma AB, Växjö, Sweden) which were attached to the ceiling and angled at 46° with a height of 160 cm to the digital detector plates (DRX-1C type, Carestream, New York, USA). The radiographs had a spatial resolution size 2560x3072 (grey-scale 8 bit dicom-format).

The cadaver foot was placed with the medial side against the x-ray tubes and with exposure standardized to 60 kV and 5 mA. The radiographs were analysed with MbRSA 3.32 software (LUMC, Leiden, The Netherlands). The translation and rotation were assessed by the RSA software according to the radiostereometric analysis guidelines defined by Valstar et al. (2) with the translations according to the centre of gravity of the rigid bodies. As the 3D rotations are sequence dependent by the Euler angle Theorem (2). Standardized Rx-Ry-Rz sequence is standardly used by the software.

The coordinate system was aligned with the x-axis to the plantar of the foot making positive values of translation x_+ = posterior, y_+ = superior and z_+ = medial and rotation Rx_+ = pronation, Ry_+ = internal rotation and Rz_+ = plantar flexion of a right foot (see figure 1).

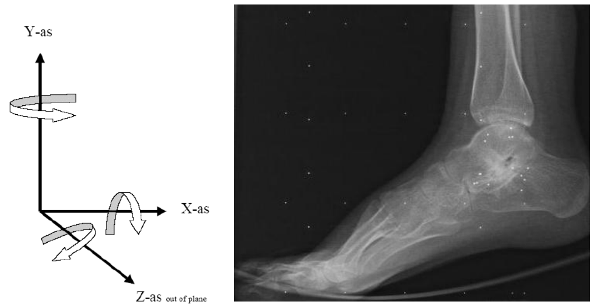

Figure 1 - Orientation of axes for translation and rotation according to a right foot.

The RSA software determines marker locations by intersection of back-extrapolation according to the coordinates of the calibration cage. Locations are estimated by a computerized least squares method expressing the crossing line distance (CLD) and accepted if CLD < 0.5 mm (18).

Marker stability was assessed by the mean error of rigid body fitting (ME). ME is the mean difference between the relative distances of the residual motion vector d_i of each marker in the rigid body, measured according to the reference examination (19). ME is expressed as,

$$ME = \sqrt{\frac{d_1^2 + d_2^2 \ldots + d_n^2}{n}}$$

By computation of rotation matrices and translation vectors for absolute motion, the RSA software minimizes ME using a least-squares method and thereby excludes the actual movement of the rigid body. The standard threshold of ME below 0.35 mm was used (2). The RSA software also excludes solitary markers, if intermarker changes are bigger than 0.3 mm (18).

The distribution of the markers was assessed by the condition number (CN), which is a value calculated from the distance of the markers to an arbitrary straight line passing through the cluster and is expressed as,

$$CN = \frac{1}{\sqrt{d_1^2 + d_2^2 \ldots + d_n^2}}$$

where d_i is the shortest possible distance to this arbitrary straight line (19). A larger value of CN is due to small d_i and indicates that the marker cluster approximates a straight line. As many other studies, we included observations if CN < 150 mm^{-1} (2,12,20–24).

Maximum total point motion (MTPM) values are an attempt to express the total translation and rotation by one value. The MTPM value is the translation of the 3D vector of the one marker within the rigid body that has the largest migration (19). Hence MTPM values are numerical, and are therefore not normally distributed, why results are given with a median and range (2).

Calculations of repeatabilities (or precisions) are according to Ranstam et al. (2000) (16), which are under the assumption that the true value of motion between the RSA examinations is zero in all 6 degrees of freedom ($df = x, y, z, Rx, Ry, Rz$), and the observations follow a normal distribution. Acknowledging the existence of both systematic and random error the repeatability (denominated as bias) is calculated as the average deviation from the true value. Here d_i is the absolute value of motion of each df:

$$bias_{df} = \frac{\sum_{i=1}^{n} d_i}{n},\ d_i \in \mathbb{R}$$

The 95% confidence limit (CL) is then calculated as

$$bias_{df}(95\%CL) = bias_{df} \pm 1.96 \frac{SD_{bias_{df}}}{\sqrt{n}}$$

where SD is the standard deviation and is calculated as

$$SD_{bias_{df}} = \sqrt{\frac{\sum(d_i - bias_{df})^2}{n-1}}$$

The 95% repeatability limit (RPL) is then

$$RPL_{df} = 1.96 \times \sqrt{2} \times SD_{bias_{df}}\,.$$

The bias was tested by a paired t-test and RPL by F-test conducted in RStudio software for R 3.1.1.

Results

Bias (systematic error)

Translation and rotation values are illustrated in table 1.

Between 1st and 2nd experiment statistical significance was observed only for rotation around the y-axis (p_{Ry} = 0.015). The remaining p-values were highly insignificant (p_x = 0.802, p_y = 0.326, p_z = 0.804, p_{Rx} = 0.659, p_{Rz} = 0.687).

In 3rd experiment, where the foot was repositioned between each examination in contrast to the 2nd experiment, statistical significance was observed in all degrees of freedom except translation of the x-axis (p_x = 0.456, p_y = 0.004, p_z < 0.001 , p_{Rx} = 0.012, p_{Ry} = 0.030, p_{Rz} = 0.035)

95 % Repeatability limits

The RPL results were tested by F-test, hence the repeatability (RPL= $1.96 \times \sqrt{2} \times SD$) is numeric and therefor not normally distributed.

All comparisons between RPLs were insignificantly diffenrent. Testing the x-axes in 1st and 2nd experiment we found p_x = 0.088 and all remaining p-values were all above 0.244.

Discussion

When performing orthopedic phantom studies, you often have to choose between synthetic bones or cadavers. In this RSA setup we chose a cadaver foot, so the RSA also included the error produced by the soft tissues. There are some potential disadvantages when working with cadavers samples. Small deformation of segments might occur due to difficulties to maintain constant moisture during the preparations. However, we believe that the K-wire and the cast rigidly fixed the osteotomized segments of the foot, and the RSA examinations were terminated within 3 hours after the surgery making dehydration of the model minimal.

Under optimal conditions the cadaver foot should have been from a child. This was not available, but the use of an adult foot in this study might have resulted in better repeatabilities.

Bias

Regarding *systematic* and *random error* we expected increasing *systematic error* by introducing increasing methodological interference between each radiograph. This was confirmed by the statistical differences in bias between 2nd and 3rd. The 3rd experiment is most likely to resemble clinical studies and should be performed prior study initiations.

Repeatability

As expected, the *random error* (or SD) did not alter significantly by increasing experimental order, as the *random error* theoretically should not change between experiments.

To our knowledge two publication has assessed marker based RSA across small-scale osteotomies (9,25), and we observe similar repeatabilities to these studies.

Studies assessing marker based micromotions across larger anatomical areas observe slight better precisions, e.g. 0.12-0.20 mm translation and 0.30-0.36° rotation (10,19,26).

As in the study by Mäkinen et al. (1995) (1) we observed that the majority of RPLs in the 2D plane (x, y and Rz) had lower values than out-of-plane measurements due to the use of a uniplanar calibration cage.

Conclusion

Marker based RSA is feasible across small-scale osteotomies. In this study we observed 95 % repeatability limits ranging between 0.06-0.22 mm translation and 0.19-0.52° rotation.

In test-retest RSA phantom studies both setup and object should be repositioned between each radiograph to resemble clinical studies.

Table 1 – Experimental Results

1st experiment											
n=10	x	y	z	Rx	Ry	Rz	MTPM	ME	ME Ref	CN	CN Ref
	(mm)	(mm)	(mm)	(°)	(°)	(°)	(mm)	(mm)	(mm)	(mm^{-1})	(mm^{-1})
Bias	-0.012	-0.012	-0.077	0.082	-0.011	-0.026					
SD	0.069	0.035	0.081	0.190	0.139	0.102					
RPL	0.129	0.069	0.212	0.384	0.256	0.194					
Median							0.212	0.054	0.050	43.9	61.1
Min							0.125	0.038	0.029	43.9	61.1
Max							0.269	0.088	0.056	43.9	61.1
2nd experiment											
n=10	x	y	z	Rx	Ry	Rz	MTPM	ME	ME Ref	CN	CN Ref
	(mm)	(mm)	(mm)	(°)	(°)	(°)	(mm)	(mm)	(mm)	(mm^{-1})	(mm^{-1})
Bias	-0.019	-0.028	-0.087	0.123	**0.203***	-0.002					
SD	0.034	0.028	0.079	0.187	0.179	0.142					
RPL	0.073	0.075	0.224	0.422	0.517	0.262					
Median							0.198	0.059	0.041	50.9	61.1
Min							0.118	0.044	0.028	50.9	61.1
Max							0.404	0.083	0.059	50.9	61.1
3rd experiment											
n=10	x	y	z	Rx	Ry	Rz	MTPM	ME	ME Ref	CN	CN Ref
	(mm)	(mm)	(mm)	(°)	(°)	(°)	(mm)	(mm)	(mm)	(mm^{-1})	(mm^{-1})
Bias	-0.005	**0.015***	**0.063***	**-0.125***	**-0.053***	**0.168***					
SD	0.043	0.025	0.072	0.182	0.262	0.169					
RPL	0.079	0.055	0.181	0.416	0.496	0.454					
Median							0.232	0.090	0.053	50.5	61.3
Min							0.168	0.045	0.031	45.1	61.3
Max							0.472	0.180	0.170	50.5	61.3

Results of the three phantom experiments.
Bias or mean (systematic error),
SD – Standard deviation (random error),
RPL – 95 % repeatability limits (represents precision),
MTPM – Maximum Total Point Motion (the longest vector),
ME/ME Ref – Mean error of rigid body fitting for model/reference model (marker stability),
CN/CN Ref – Condition number for model/reference model (marker scatter distribution),
** marks p-value < 0.05. Bias was tested by paired t-test and RPL by F-test.*

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Repeatability of Marker Based Radiostereometric Analysis Across Hindfoot Osteotomies

Buxbom P, Sonne-Holm S, Wong C.

Manuscript to be submitted.

I

Stability and Migration Across Dega Osteotomies in Children with Neuromuscular disorders by Radiostereometric Analysis - A One Year Follow-up of 18 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

II

Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Cerebral Palsy by Radiostereometric Analysis - A One Year Follow-up of 25 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

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III

Stability and Migration Across Calcaneal Lengthening in Children - A Radiostereometric Analysis of Twenty Osteotomies

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

IV

Stability and Migration Across Dega Osteotomies in Children with Neuromuscular Disorders By Radiostereometric Analysis – A One Year Follow-up of 18 Hips

Peter Buxbom, Stig Sonne-Holm, Niels Ellitsgaard, Christian Wong

Orthopedic Department, Hvidovre Hospital, Copenhagen, Denmark

Abstract

Background and Purpose: Studies indicate that 28-35 % of children with cerebral palsy (CP) develop dislocation of the hip that needs surgical intervention. When hip dislocation occurs during childhood the treatment consists of tenotomies, femoral varus derotation osteotomy and acetabuloplasty. The standard acetabuloplasty in early childhood is the Dega osteotomy (DO). Relapse of hip dislocation ha been observed in 16-22 % during adolescence. In this prospective cohort study we performed a radiostereometric analysis (RSA) across DOs in children with neuromuscular disorders. We planned to assess RSA stability and migration across the DOs. **Material and Methods:** Inclusion of children with a neuromuscular disorder that were set up for skeletal corrective surgery of the hip. RSA follow-ups were performed at time 0, 5 weeks, 3, 6 and 12 months after surgery. **Results:** Eighteen DOs were included. RSA data showed stability across the DO in majority cases within the first 5 weeks. Few unstable DOs all had a femoral shaft graft (FG). All DOs with iliac crest graft (IG) were stable. At the one-year follow-up the mean translations (±SD) of distal periacetabular fragment across the DOs were 0.55 mm (±0.63) medial, 0.33 mm (±0.33) superior and 0.13 mm (±0.24) posterior. The mean rotations were 1.47° (±2.91) posterior tilt, 0.27° (±1.28) retroversion and 1.76° (±3.10) medial inclination. **Discussion:** The migration stagnates within the 5-week follow-up indicating stability across the DOs in majority patients. DOs with FG seem to be unstable longer. The mean migration of the distal periacetabular fragment of the DOs was at the one-year follow-up marginal medial, superior and posterior with posterior tilt, retroversion and medial inclination.

Keywords: *Children orthopedics; Hip displacement; Dega Osteotomy; Periacetabular osteotomy; Radiostereometric analysis; RSA.*

1. Introduction

Cerebral palsy (CP) is a multidimensional neurologic disease that begins in pre-birth or early childhood and persist throughout the life (Minciu 2012). The incidence of CP in Denmark is 2 in every 1.000 live births and the incidence has been stable since the 1990's (Ravn et al. 2010). Common symptoms in extremities are spasticity and rigidity, symptoms that lead to decreased motoric function (Minciu 2012). The motor function is often classified by the Gross Motor Function Classification System (GMFCS) used to monitor the severity of the CP (Palisano et al. 1997).

Hip dislocation in children with CP is a common complication and has been observed in 28-35 % with high positive correlation to GMFCS (Samilson et al. 1972; Soo et al. 2006). Hip dislocation causes severe pain and patients have high risk of developing secondary hip arthrosis (Cooperman et al. 1987; Soo et al. 2006).
Treatment is relocation of the hip by adductor and psoas tenotomies, femoral varus derotation osteotomy and acetabuloplasty (Canavese et al. 2010; Dhawale et al. 2013). The degree of hip dislocation is measured on an AP pelvic radiograph by the Femoral Head Extrusion Index (FHEI) measuring the percentage of uncovered femoral head (Reimers 1980). The negative effect of the dislocated hip on acetabulum is measured by the acetabular index (ACI). Treatment is typically indicated if FHEI exceeds 50 % (Canavese et al. 2010). Figure 1 illustrates treatment and measuring of FHEI and ACI.
Despite surgical intervention relapse is observed in 16-25 % and postoperative progressive hip dislocation is believed to be due to the continuous skeletal growth and remodelling (Samilson et al. 1972; Bennet et al. 1982; Dhawale et al. 2013).

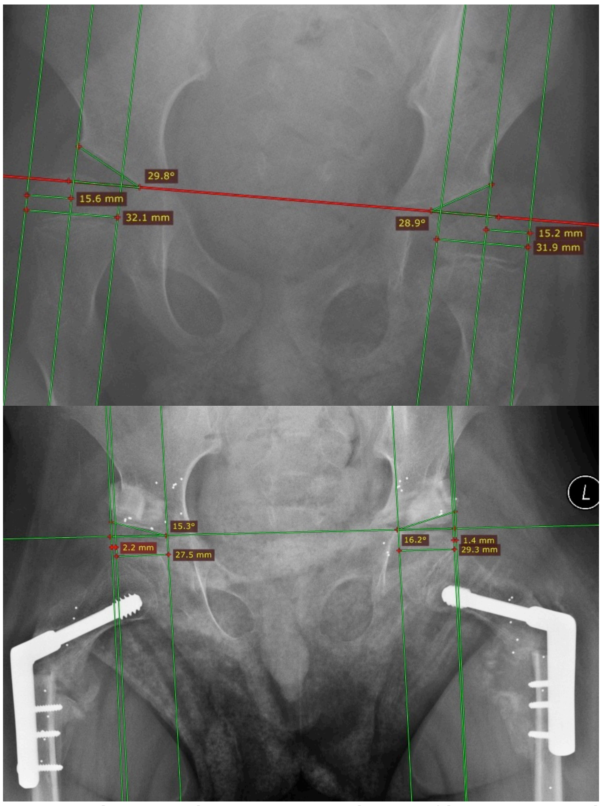

Figure 1. The pre- and postoperative evaluation of hip migration and acetabular dysplasia by FHEI and ACI in an eight-year-old boy with CP.

A recent study show that up to 56 % of children with severe CP who underwent surgical relocation of the hip have longterm unsatisfactory results (Canavese et al. 2010).

Radiostereometric analysis (RSA) is a method with high precision and has the ability to identify complex three-dimensional migration of skeletal structures (Selvik 1978, 1989; Kärrholm et al. 1982; Teeuwisse et al. 1998; Mäkinen et al. 2004; Valstar et al. 2005). Few children orthopedic RSA studies have been published within the last decades, none evaluating the stability across osteotomies (Lauge-Pedersen et al. 2006; Gunderson et al. 2013; Horn et al. 2013; Lauge-Pedersen and Hägglund 2013). A recent RSA study evaluating stability across high tibial osteotomies in adults suggest limited micromotions and stability 6-12 weeks after surgery (Teeter et al. 2015).

The primary aim of this study is to assess the stability across DOs by RSA in children with neuromuscular disorders. Secondary aims are (i) the 1-year follow-up migration of distal periacetabular fragment across RSA stable DOs and (ii) if remodelling or minor regional growth is measurable in the RSA data.

2. Material and Methods

This study was a prospective cohort study with trial period from ultimo 2012 to ultimo 2014. Patients were offered to participate in the study if between the age 2 and 18 years; diagnosed with a neuromuscular disorder and with indication of corrective skeletal hip surgery. The indication for surgery was typically FHEI > 50 %. The only primary exclusion criteria were reoperation.
The follow-up period was one year, and the RSA examinations were performed postoperatively, after 5 weeks, 3, 6 and 12 months. The visit window for the RSA recording was respectively 3 days at postoperative follow-up, one week at the 5-week follow-up and two weeks at subsequent follow-ups.

Surgical procedures:
Tenotomies:
While in general anaesthetics the hip was tested for limitations range of motion (ROM). If limited ROM was assessed due to muscle shortening of the adductor and/or psoas muscles appropriate tenotomies were initially performed.

Femoral Varus Derotation Osteotomy:
A transverse osteotomy was cut approximately 1 cm below the lesser trochanter. K-wires were placed on each side of the osteotomy before cutting the proximal femoral shaft, which were used to control the rotation. Afterwards the varisation and derotation was secured by plate-fixation (Compression Hip Screw, Smith and Nephew, London, England).

Acetabuloplasty:
The pelvic wing was accessed subperiostally by division of the crista apophysis. By osteotome an incomplete interlaminary transiliacal osteotomy above the acetabular ceiling ad modum Dega was performed. Before insertion of either a femoral shaft graft (FG) or iliac crest graft (IG), 4-8 tantalum markers (1 mm diameter, Wennbergs Finmek AB, Gunnilse, Sweden) were inserted on each side of the osteotomy.
While still in general anaesthetics a spica hip cast was placed (Scotchcast, 3M) and the hips were immobilized for 5 weeks. After cast removal the patients were mobilized without restrictions in cooperation with the physiotherapy unit.

The RSA methodology:
By standardized procedure the patient was placed in supine position with the pelvis just above the wheel born carbon fibre enclosed uniplanar calibration cage (LUMC, Leiden, The Netherlands; 85 x 29 x 55 cm) and two ceiled-attached radiographic tubes (Arcoma AB, Växjö, Sweden) were adjusted to the two digital detector plates (DRX-1C type, Carestream, New York, USA) angling 46° with a height of 160 cm from the plates. The exposure was standardized to 65 kV and 12.5 mAs. The RSA outcomes were of spatial resolution size 2560 x 3072 (grey-scale 8 bit dicom-format).

The orthogonal directions and the coordinate system used across the DOs are illustrated in figure 2. With the pelvic wing as reference and the distal periacetabular fragment as model the translations were x_+ = medial, y_+ = superior and z_+ = anterior, and rotations Rx_+ = anterior tilt, anteversion and Rz_+ = medial inclination. Values of the left femoral shaft were negated for x, Ry and Rz to create same directions as for the right femur.

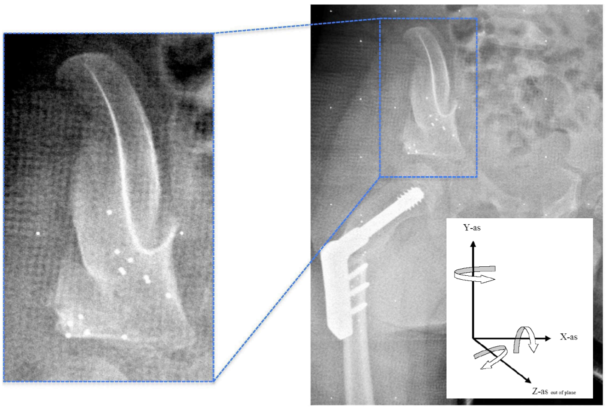

Figure 2. Postoperative RSA with magnified region of interest (ROI). The coordinate system show that positive values of a right hip has translation x_+ = medial, y_+ = superior and z_+ = anterior and rotation Rx_+ = anterior tilt, Ry_+ = anteversion and Rz_+ = medial inclination.

The radiographs were analysed with MbRSA 3.41 software (LUMC, Leiden, The Netherlands).

MbRSA 3.41 software assess translation and rotation by the RSA software according to the radiostereometric analysis community guidelines defined by the Valstar et al. in 2005.

The RSA software determines marker locations by intersection of back-extrapolation according to the coordinates of the calibration cage. Locations are estimated by a computerized least squares method expressing the crossing line distance (CLD) and accepted if CLD < 0.5 mm (Manual 2011).

Marker stability was assessed by the mean error of rigid body fitting (ME). The standard threshold of ME is below 0.35 mm (Valstar et al. 2005), but because of the expectance of remodelling and growth during the study we protocolled to evaluate ME individually and including RSA data if the initial ME observation were 0.35 mm but the subsequent observations were continuously increasing in a manner that could be interpreted as remodelling or growth. ME is expressed as,

$$ME = \sqrt{\frac{d_1^2 + d_2^2 \ldots + d_n^2}{n}}$$

By computation of rotation matrices and translation vectors for absolute motion, the RSA software minimizes ME using a least-squares method and thereby excludes the actual movement of the rigid body.

The marker distribution was assessed by the condition number (CN). The RSA ISO standards state that CN should be below 120 mm^{-1} when studying adult hip, knee or shoulder arthroplasties, but may be higher when studying other smaller structures. Like other studies we included observations if CN < 150 mm^{-1} (Söderkvist and Wedin 1993; Onsten et al. 2001; Börlin et al. 2002; Bragdon et al. 2004; Valstar et al. 2005; Gunderson et al. 2010; Fong et al. 2011).
CN was calculated from the distance of the markers to an computed straight line passing through the cluster and is expressed as,

$$CN = \frac{1}{\sqrt{d_1^2 + d_2^2 \dots + d_n^2}}$$

where d_i is the shortest possible distance to this arbitrary straight line (Ryd 1986)

Maximum total point motion (MTPM) values attempts to express the total translation and rotation by one value (unit in mm) (Ryd 1986). Hence MTPM values are absolute, and therefore potentially not normal distributed. Results are therefore given with a median and range (Valstar et al. 2005). In terms of using MTPM to assess on going bone remodelling or growth, we tested the whether residuals were normal distributed and in that case performed linear regression on data.

Calculations of repeatabilities (RPL) are according to Ranstam et al. (2000) (Ranstam et al. 2000), which are under the assumption that the true value of motion between the RSA examinations is zero in all 6 degrees of freedom ($df = x, y, z, Rx, Ry, Rz$), and the observations follow a normal distribution. To internally validate RSA setup, all double examinations recorded after the 6-month follow-up were used to assess setup RPL (precision). RPL is calculated as the 95 % deviation from the true value (Ranstam et al. 2000).

$$RPL_{df} = 1.96 \times \sqrt{2} \times SD_{df} \, .$$

where SD is the standard deviation for each df and calculated as

$$SD_{df} = \sqrt{\frac{\sum_{i=1}^{n}(d_i - \sum(d_i/n))^2}{n-1}} \quad d_i \in \mathbb{R}$$

and d_i is the absolute value of motion of each df.

Based on internal RPLs obtained by RSA double examinations during the study period, we defined a RSA stable DO as observations of two consecutive follow-ups with migration below the internal RPL in five out of the six orientations.

To evaluate if the RSA data showed any indication of remodelling and/or minor regional growth we planned to do with mixed effect model regression analysis on migration, ME and MTPM using the statistical software R. Before performing the analysis we tested whether the residual were normal distributed. Statistical significant positive inclinations of ME and MTPM would be interpreted as remodelling and/or minor regional growth.

The RSA setup at Hvidovre Hospital was prior study initiation validated on a phantom model. RPLs were estimated for translation 0.055-0.224 mm and rotation of 0.194-0.517°.

Ethical Considerations:
The Danish Research Ethical Committee approved the study: Journal number H-2-2011-124. Patients were included after signed informed consent.

3. Results

Primary inclusion consisted of 23 acetabuloplasties. One patient sadly died two days after surgery due to respiratory distress. Four other patients were excluded from this study having undergone either Salter or Chiari osteotomies. Thus study material includes 18 DOs (9 left and right) in 15 patients with a one-year RSA follow-up. There were no dropouts during the study period. Three patients underwent bilateral surgery and all had their second operation within one month of the first surgery. One patient missed the three month follow-up otherwise all recordings were completed (completion rate 0.989).
All of the included patients also had performed femoral varus derotation osteotomies with insertion of tantalum markers. These results will be published as a separate study.

Demography:
The cohort consisted of 7 boys and 8 girls with median age were 5.9 years (range: 3.4-11.6) and 7.5 years (range: 3.0-13.7) respectively. Ten patients suffered from spastic tetraplegic, three had hypotonic tetraplegic and two spastic diplegic. The primary neuromuscular diagnose was cerebral palsy (n=13) and the remaining were Bohring-Opitz syndrome (n=1) and Retts Syndrome (n=1).
All had severe disabilities (GMFCS ≥ 3) from their neuromuscular disorder classified as GMFCS 3 (n=2), 4 (n=4) and 5 (n=9).
Twelve of the 15 patients had some degree of mental retardation and 9 of these suffered from epilepsy. The main comorbidity was obstipation of which 11 of the patients received daily medication. The patients were also medicated for sleeping disorders and/or respiratory problems. The median number of daily medical products was 3 (range: 0-6).

Pre-, Per- and Postoperative Observations:
At time of surgery the median height was 103 cm (range: 90-150), median weight 17 kg (range: 13-40) and thereby median BMI 16 kg/m² (range: 15-20). ASA classification was assessed prior sedation by experienced anaesthesiologists and graduated ASA 1 (n=1), ASA 2 (n=7) and ASA 3 (n=7).
The median duration of surgery was 247 minutes, which included approximately one hour of casting (range: 169-431). Assessment of perioperative blood loss was estimated to median 250 mL, but ranging from 50 mL to 1700 mL.
Four senior children orthopedic surgeons were responsible for all surgeries, and no perioperative complications were assessed.
Eight of the DOs were grafted with bone cortical bone removed from the femoral shaft during the femoral varus derotation osteotomy and the remaining seven DOs had an autologous iliac crest graft.
The median casting period was 4.86 weeks (range: 4.29-6.86)
During the one year follow-up two patient suffered from postoperative complications with superficial skin infections

treated successfully with per oral antibiotics. Otherwise no complications were observed in relation to the DOs.

Radiographic Evaluation:
Results of the radiographic evaluation is summarized in table 1.

	FHEI		ACI	
	Median	**Range**	**Median**	**Range**
PreOP	55 %	(42-78)	28°	(21-39)
PostOP	-5 %	(-23-26)	17°	(11-33)
Difference	57 %	(24-92)	13°	(0-20)

Table 1. Median and range of femoral head extrusion index (FHEI) and acetabular index (ACI) evaluated on AP pelvic radiographs preoperative, postoperative and the difference between these two measurements (n=18).

Results of the Radiostereometric Analysis:
Three of the 90 RSA follow-ups were excluded from the data; One follow-up was due to CN > 150 mm^{-1}; two follow-ups because of marker instability (ME > 0.35 mm). One value above 0.35 mm was accepted at 12-month follow-up in a 3-year-old girl showing continuously increasing ME (0.24, 0.27, 0.30 and 0.39 mm) and thus interpreted as due to remodelling and/or minor regional growth (figure 9).The median number of markers of each rigid body was five and ranged from 3 to 10. The median CN was 77 mm^{-1} (range: 26-148). The median ME was 0.20 mm (range: 0.05-0.39).

Internal Repeatabilities:
RPLs on double examinations at follow-up at 6 or 12 months (n=16) are summarized in table 2. The MTPM median of these data was 0.23 mm (range: 0.12-0.69).

Translation	RPL	Rotation	RPL
x	0.11 mm	Rx	0.41°
y	0.09 mm	Ry	0.74°
z	0.28 mm	Rz	0.38°

Table 2. The 95 % repeatability limits (RPL) based on double examinations at 16 follow-ups of 16 patients after assessment of radiographic stability (n=16).

Stability across the Dega Osteotomies:
The testing of RSA stability in relation to the RPLs across DO is summarized in table 3.

Follow-up (n=18)	6 of 6 directions	5 of 6 directions
5W	8	13
3M	14	15
6M	18	18
12M	18	18

Table 3. RSA stability assessed in relation to RPL at each follow-up. By definition RSA stability was obtained if migration was below the RPL in either five or six of the six orientations.

Translation and Rotation:
Table 4 summarizes the mean migration of the RSA stable DOs at the one-year follow-up. Figure 3 to 8 show illustrates the progression of translation and rotation of the distal peri-acetabular fragment across the DO.

Direction	Mean	SD
x	0.55 mm	0.63
y	0.33 mm	0.33
z	-0.13 mm	0.24
Rx	-1.47°	2.91
Ry	-0.27°	1.28
Rz	1.76°	3.10

Table 4. Mean migration and standard deviation at the one-year follow-up of stable DOs (n=18).

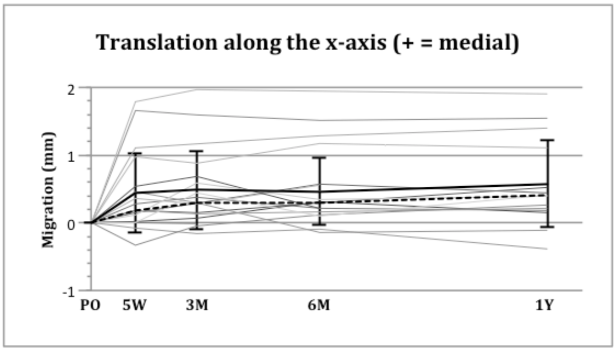

Figure 3. Medial-lateral translation. Linear regression of the RSA stable DOs estimated medial progression by 0.14 mm per year. Dashed line (median); solid black line (mean); error bars (SD).

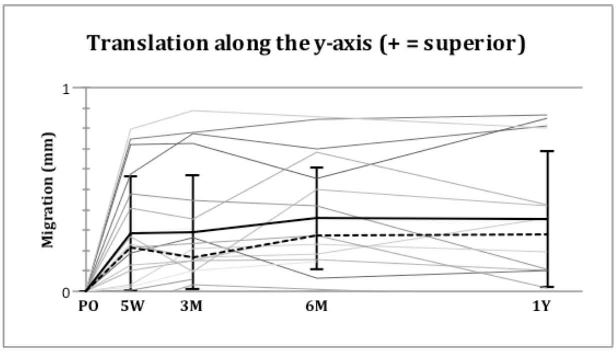

Figure 4. Superior-inferior translation.. Linear regression of the RSA stable DOs estimated superior progression by 0.05 mm per year. Dashed line (median); solid black line (mean); error bars (SD).

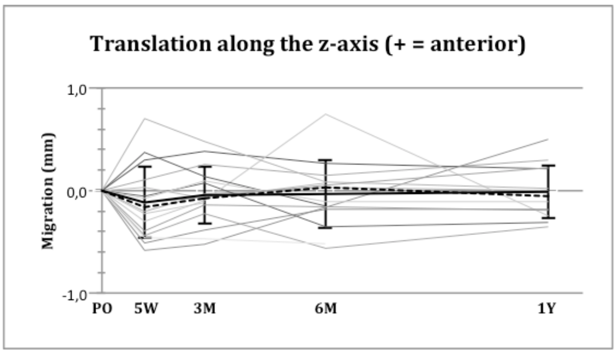

Figure 5. Anterior-posterior translation. Linear regression of the RSA stable DOs estimated anterior progression by 0.09 mm per year. Dashed line (median); solid black line (mean); error bars (SD).

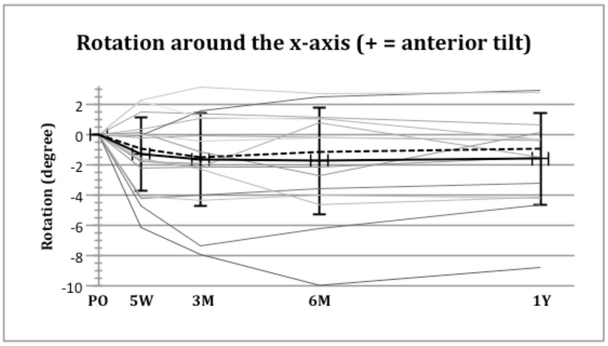

Figure 6. Anterior-posterior tilt. Linear regression of the RSA stable DOs estimated progression by 0.07° anterior tilt per year. Dashed line (median); solid black line (mean); error bars (SD).

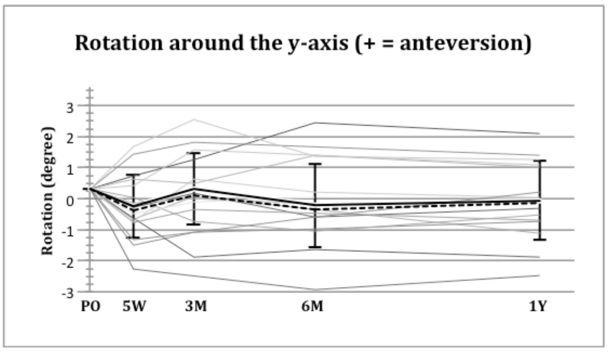

Figure 7. Anteversion-retroversion. Linear regression of the RSA stable DOs estimated progression by 0.38° retroversion per year. Dashed line (median); solid black line (mean); error bars (SD).

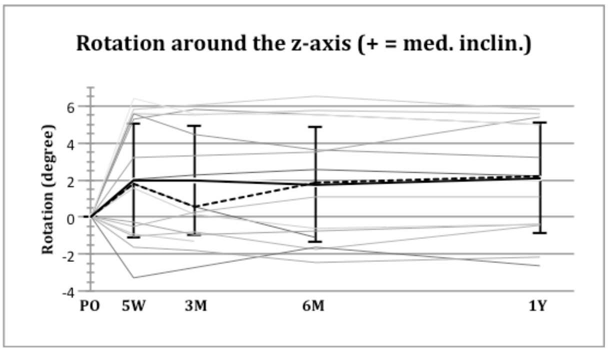

Figure 8. Medial-lateral inclination. Linear regression of the RSA stable DOs estimated progression by 0.22° medial inclination per year. Dashed line (median); solid black line (mean); error bars (SD).

Remodelling and/or Minor Regional Growth:
In relation to ME (figure 9) a linear regression analysis estimates a positive inclination with coefficient 0.026 mm per year (CL: -0.013-0.065, p = 0.18).

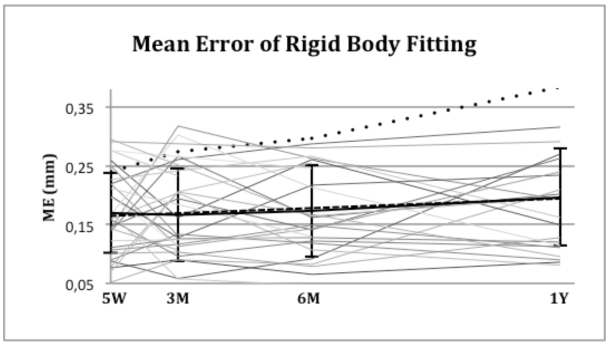

Figure 9. Mean error of rigid body fitting over time. Mean ME (solid) and median ME (dashed). The dotted black line illustrates a patient with RSA data inclusion despite ME > 0.35 mm at the one-year follow-up.

Similar to ME the MTPM performing linear regression analysis on data of stable DOs we find a statistical insignificant positive inclination with coefficient 0.05 mm per year (CL: -0.24-0.34, p = 0.76).

Maximum Total Point Motion:
Figure 10 illustrates initial total migration within the first 5 weeks. The total migration continuously stagnates the subsequent follow-ups. The figure also emphasize increased instability across DOs with FG.

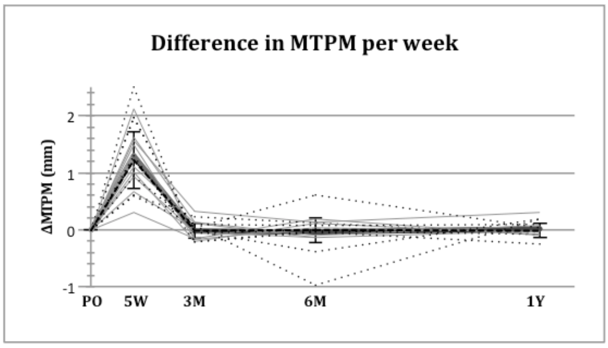

Figure 10. Difference in maximum total point motion (ΔMTPM) in two consecutive follow-up. The median MTPM (dashed) and error bars (SD) illustrate total migration within the first 5 weeks. The total migration continuously stagnates the subsequent follow-ups. Dotted and solid grey lines represents femoral shaft graft and iliac crest graft, respectively.

4. Discussion

In this study RSA examinations were performed throughout 1 year after Dega acetabuloplasties in a cohort of children with neuromuscular disorders. The cohort had similar demography and FHEI as other studies (Sankar et al.; Canavese et al. 2010; Davids et al. 2013); thus the study population seem representable and comparable to similar studies.
RSA in children acetabuloplasties seems feasible. Only three of the 90 RSA follow-ups were excluded from the data; One follow-up was due to CN > 150 mm^{-1}; two follow-ups because of marker instability (ME > 0.35 mm). One follow-up with ME > 0.35 mm was accepted at 12-month follow-up in a 3-year-old girl showing continuously increasing ME.
RPLs were similar or marginal higher to earlier performed phantom model studies.

The primary aim of this study is to assess the stability across DOs by RSA in children with neuromuscular disorders. We defined a RSA stable DO as observations of two consecutive follow-ups with migration below the internal RPL in five out of six orientations. The majority of DOs were RSA stabilized within the first 5 weeks.

A secondary aim (i) was the 1-year follow-up migration of distal periacetabular fragment across RSA stable DOs. We estimated a marginal translation in medial, superior and posterior direction. The distal periacetabular fragment tend to rotate toward posterior tilt, retroversion and medial inclination.

The maximum superior translation in all RSA data was 0.88 mm, thus we found no signs of graft collapse in either FG og IG.

Another secondary aim (ii) was whether remodelling or minor regional growth were measurable across stable DOs evaluated by ME and MTPM. We find the argument plausible as dispersion of markers within the two clusters would increase ME. Also remodelling or growth between the two clusters would create migration and thereby increased MTPM. Both measurements were observed with positive inclination, but statistical insignificant. Despite these conditions further studies with longer follow-up are needed to any minor regional growth. The ME inclination of 0.03 mm per follow-up year might suggests the need to increase the upper limit of ME exclusions in children RSA stduies by this factor. Stagnation of this factor is expected when nearing skeletal maturity.

The GMFCS classification was used to all included patients. Originally the GMFCS is only validated to children with CP. Despite the non-existing validation of GMFCS to Bohring-Opitz syndrome and Retts syndrome we find the equivalent reasonable as children both conditions have neuromuscular disorders and increased risk of hip dislocation (Tay et al. 2010).

In this study we did not observe any reoperations for redislocation within the one year follow-up, thus it is too soon predict indicators for relapse. Progressional superior translation and/or lateral inclination seem rational predictors of relapse, but this study could not establish the evidence. Further studies with longer follow-up are needed.

Acknowledgement

We are grateful to our statistician Thomas Kallemose for the help and scientific discussions regarding methodological issues of this study.

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Repeatability of Marker Based Radiostereometric Analysis Across Hindfoot Osteotomies

Buxbom P, Sonne-Holm S, Wong C.

Manuscript to be submitted.

I

Stability and Migration Across Dega Osteotomies in Children with Neuromuscular disorders by Radiostereometric Analysis - A One Year Follow-up of 18 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

II

Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Cerebral Palsy by Radiostereometric Analysis - A One Year Follow-up of 25 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript accepted for publication by peer-reviewers at *ACTA Orthopaedica*.

III

Stability and Migration Across Calcaneal Lengthening in Children - A Radiostereometric Analysis of Twenty Osteotomies

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

IV

Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Neuromuscular Disorders and Syndromes - One Year RSA Results

Peter Buxbom, Stig Sonne-Holm, Niels Ellitsgaard, Christian Wong

Department of Orthopedics, Hvidovre University hospital, Copenhagen, Denmark
Correpondance: dr.buxbom@gmail.com

Abstract

Background and Purpose: Studies indicate that 28-35 % of children with cerebral palsy (CP) develop dislocation of the hip that needs surgical intervention. When hip dislocation occurs during childhood surgical treatment consists of tenotomies, femoral varus derotation osteotomy (VDRO) and acetabuloplasty. Relapse is observed in 16-22 % during adolescence. In this prospective cohort study we performed a descriptive evaluation of translation and rotation across VDROs in children with neuromuscular disorders and syndromes by radiostereometric analysis (RSA). We planned to assess RSA stability and migration across the VDROs. **Material and Methods:** Inclusion of children with a neuromuscular disorder that were set up for skeletal corrective surgery of the hip. RSA follow-ups were performed at time 0, 5 weeks, 3, 6 and 12 months after surgery. **Results:** Twenty-seven femoral VDROs were included; two patients were excluded during the study period. RSA data showed stability across the VDRO in majority cases within the first 5 weeks. At the one-year follow-up the mean translations (±SD) of femoral shaft distal of the VDRO were 0.51 mm (±1.12) medial, 0.69 mm (±1.61) superior and 0.21 mm (±1.28) posterior. The mean rotations were 0.39° (±2.90) anterior tilt, 0.02° (±3.07) internal rotation and 2.17° (±2.29) varus angulation. **Interpretation:** The migration stagnates within the first 5 weeks indicating stability across the VDRO in majority patients. The mean migration of the femoral shaft distal of the VDRO was at the one-year follow-up marginal medial, superior and posterior with anterior tilt, internal rotation and slight larger values of varus angulation.

Keywords: *Children orthopedics; Hip dislocation; Femoral varus derotation osteotomy; Radiostereometric analysis.*

1. Introduction

Cerebral palsy (CP) is a multidimensional neurologic disease that begins in pre-birth or early childhood and persist throughout life (Minciu 2012). The incidence of CP in Denmark is 2 in every 1.000 live births and the incidence has been stable since the 1990's (Ravn et al. 2010). Common symptoms in extremities are spasticity and rigidity. This is symptoms that lead to decreased mobility (Minciu 2012). The motor function is often classified by the Gross Motor Function Classification System (GMFCS), which classifies the severity of the CP (Palisano et al. 1997).

Hip dislocation in children with CP is a common complication and has been observed in 28-35 % with high positive correlation to GMFCS (Samilson et al. 1972; Soo et al. 2006). Hip dislocation causes severe pain in the longterm since there is high risk of developing secondary hip arthrosis (Cooperman et al. 1987; Soo et al. 2006). The degree of hip dislocation is measured on an AP pelvic radiograph by the Femoral Head Extrusion Index (FHEI), where the percentage of uncovered femoral head is measured (Heyman and Herndon 1950; Reimers 1980).
Treatment is surgical 'relocation' of the hip by combined procedures of adductor and psoas tenotomies, femoral varus derotation osteotomy (VDRO) and acetabuloplasty (Canavese et al. 2010; Dhawale et al. 2013) (figure 1). Despite surgical intervention relapse is observed in 16-25 % and postoperative progressive hip dislocation is believed to be due to the continuous effect of CP, skeletal growth and remodelling. In rare cases the relapse is caused by malunion, non-union or pseudoarthrosis (Samilson et al. 1972; Bennet et al. 1982; Dhawale et al. 2013). A recent study show that up to 56 % of children with severe CP who underwent surgical relocation of the hip have longterm unsatisfactory results (Canavese et al. 2010).

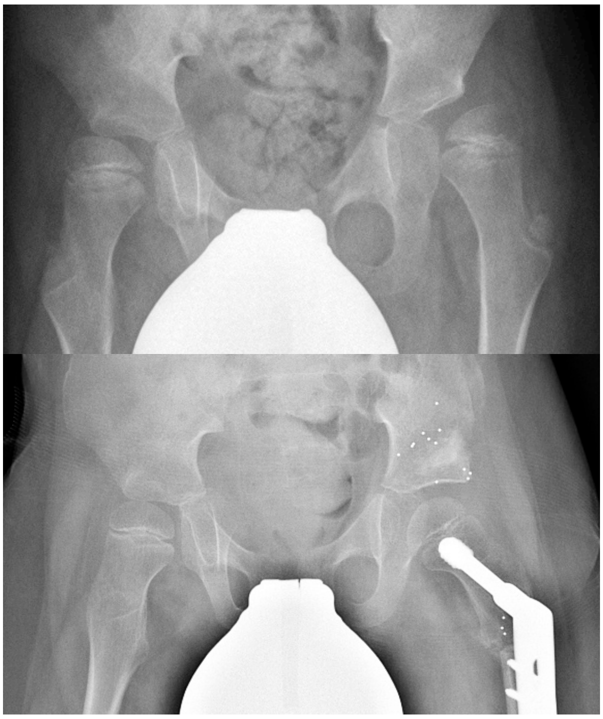

Figure 1. The figure shows the preoperative and six-month postoperative AP pelvic radiographs of a seven-year-old boy with severe left hip lateralization and acetabular dysplasia.

Radiostereometric analysis (RSA) is a method with high precision and has the ability to identify complex three-dimensional migration of skeletal structures (Selvik 1978, 1989; Kärrholm et al. 1982; Teeuwisse et al. 1998; Mäkinen et al. 2004; Valstar et al. 2005). Only a few orthopedic RSA studies in children have been published within the last decades. None of these have evaluated the stability across osteotomies (Lauge-Pedersen et al. 2006; Gunderson et al. 2013; Horn et al. 2013; Lauge-Pedersen and Hägglund 2013). A recent RSA study has evaluated stability across high tibial osteotomies in adults, and showed limited micromotions and stability 6-12 weeks after surgery (Teeter et al. 2015).

The primary aim of this study is to assess if initial stability across VDROs performed on children with neuromuscular disorders and syndromes are RSA detectable 5 weeks post-operatively. The secondary aim is to estimate the one-year follow-up migration of the femoral shaft distal of the VDRO in stable osteotomies by our definition of RSA stability of an osteotomy; this estimation might be used to early detection of relapse in future studies.

2. Material and Methods

This study was a prospective cohort study with trial period from ultimo 2012 to ultimo 2014. Patients had a neuromuscular disorder or syndrome and between the age 2 and 18 years, where corrective skeletal hip surgery were indicated and planned. The indication for surgery was typically FHEI > 50 %. The only primary exclusion criteria were a revision surgery.
The follow-up period was one year, and the RSA examinations were performed postoperatively, after 5 weeks, 3, 6 and 12 months. The visit window for the RSA recording was respectively 3 days at postoperative follow-up, one week at the 5-week follow-up and two weeks at subsequent follow-ups. A maximum of 3 attempts were used to obtain acceptable RSA radiographs to minimize the exposure of radiation.
This study was approved by the local Danish Research Ethical Committee (Journal number H-2-2011-124), and patients were included according to guidelines.

Surgical procedures:
In general anaesthetics (GA) hips were tested for limitations in range of motion (ROM), and appropriate tenotomies were performed, typically in iliopsoas and the adductor muscles. Afterwards the varus derotation osteotomy was initiated by a lateral skin incision and a k-wire guide was centralized in the femoral neck. Prior placing the femoral neck screw 4-8 tantalum markers (1 mm diameter, Wennbergs Finmek AB, Gunnilse, Sweden) were inserted primarily on the medial side of the screw. Subsequently we performed a transverse osteotomy approximately 1 cm below the lesser trochanter. K-wires were placed on each side of the osteotomy before cutting the proximal femoral shaft, which were used to control the rotation. Four to eight tantalum markers were placed through the osteotomy down the diaphysis of the femur in alternately anterior and posterior directions and placing the markers as far distal as possible. Afterwards the varisation and derotation was secured by plate-fixation (Compression Hip Screw, Smith and Nephew, London, England). An important procedure to obtain optimal RSA radiographs was to estimate the best rotation of hip according to the patella position with most visible markers under fluoroscopy. All patients had subsequently performed an acetabuloplasty a modum Dega, Salter or Chiari. Still in GA the hips were immobilized in a spica cast (Scotchcast, 3M) for 5 weeks. After 5 weeks the cast was removed and patients were mobilized without restrictions in cooperation with the physiotherapy unit.

The RSA methodology:
The patients were placed in supine position with the pelvis just above the wheel born carbon fibre enclosed uniplanar calibration cage (LUMC, Leiden, The Netherlands; 85 x 29 x 55 cm) in a standardized manner rotating the hip according to patella when RSA were recorded. Two ceiled-attached radiographic tubes (Arcoma AB, Växjö, Sweden) were adjusted to the two digital detector plates (DRX-1C type, Carestream, New York, USA) angling 46° with a height of 160 cm from the plates. The exposure was standardized to 65 kV and 12.5 mAs. The RSA outcomes were of spatial resolution size 2560 x 3072 (grey-scale 8 bit dicom-format).

The orthogonal directions and the coordinate system used across the VDRO are illustrated in figure 2. The femoral neck was used as reference position and migration was measured with the femoral shaft distal of the VDRO as the model. The migration would be described as follows; translations transverse(x_+) = medial, longitudinal(y_+) = superior and sagittal(z_+) = anterior, and rotations Rx_+ = anterior tilt, Ry_+ = internal rotation and Rz_+ = varisation. Values of the left femoral shaft were negated for x, Ry and Rz to create same directions as for the right femur.

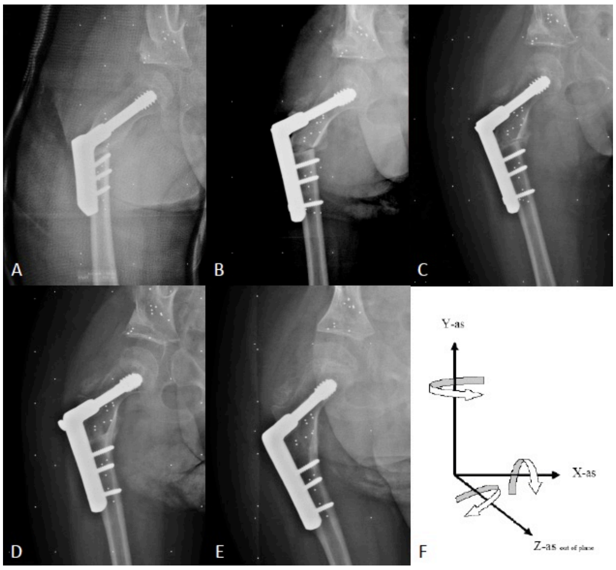

Figure 2. RSA radiographs at postoperative time 0 weeks (A), 5 weeks (B), 3 months (C), 6 months (D) and 12 months (E). In figure D and E the VDRO is considered radiographic stable. F: Shows the orientation of the 6 degrees of freedom with positive values of a right distal femur distal. Hence, translations x_+ = medial, y_+ = superior and z_+ = anterior and rotations Rx_+ = anterior tilt, Ry_+ = internal rotation and Rz_+ = varisation.

The radiographs were analysed with MbRSA 3.41 software (LUMC, Leiden, The Netherlands). MbRSA software assesses translation and rotation by the RSA software according to the radiostereometric analysis community guidelines defined by Valstar et al. in 2005 (Valstar et al. 2005). We also included the screw tips in the femoral shaft as additional markers if too many of the tantalum markers were covered by osteosynthesis material. The 95 % repeatability limits (RPL) of the screw tips and markers were estimated by double examinations at 6-month or one-year follow-up if radiographs indicated healing across the osteotomy (internal RPL). RPL was calculated as the 95 % deviation from the true value (Ranstam et al. 2000).

$$RPL_{df} = 1.96 \times \sqrt{2} \times SD_{df} \, .$$

Based on the internal RPL we defined a RSA stable VDRO as observations of two consecutive follow-ups with migration below the internal RPL of each of the six orientations. In addition we elaborate on the definition if altering it to stable if the migration is below the RPL in only five out of six orientations. The RSA setup at Hvidovre Hospital was prior study initiation validated on a phantom model. RPL of translations were 0.06-0.22 mm and rotations 0.19-0.52°. MTPM median was 0.16 mm (range: 0.07-0.59).

Marker stability was assessed by the mean error of rigid body fitting (ME), and if the standard threshold of ME was below 0.35 mm (Valstar et al. 2005). However, we expected remodelling and growth of the children in the study period, hence evaluation of ME individually was protocolled; RSA data were included if initial ME observation were below 0.35 mm but the subsequent observations were allowed to continuously increase in a manner that could be interpreted as bone remodelling or growth.

The marker distribution was assessed by the condition number (CN). The RSA ISO standards state that CN should be below 120 mm^{-1} when studying adult hip, knee or shoulder arthroplasties, but may be higher when studying other smaller structures. Like other studies we included observations if CN < 150 mm^{-1} (Söderkvist and Wedin 1993; Onsten et al. 2001; Börlin et al. 2002; Bragdon et al. 2004; Valstar et al. 2005; Gunderson et al. 2010; Fong et al. 2011).

Maximum total point motion (MTPM) values is an attempt to express the total translation and rotation by one single value (unit in mm) (Ryd 1986). The MTPM values are therefore absolute and potentially not normal distributed, hence results are therefore given with a median and range (Valstar et al. 2005). MTPM was used as a surrogate measure for on going bone remodelling or growth. We planned to test the data by linear regression analysis if the case the residuals proved normal distributed.

3. Results

Primary inclusion consisted of 22 patients, where 27 femoral VDROs were performed. RSA data from two patients were excluded from the study. One patient died two days after surgery due to respiratory distress and one patient suffered from collapse of the osteosynthesis material discovered at the 5-week RSA follow-up. Thus 25 femoral VDROs in 20 patients (14 and 11 left and right side, respectively) with one year RSA follow-up period. There were no dropouts during the study period. All of the included patients also had performed acetabuloplasties with insertion of tantalum markers (Buxbom et al. 2016). Five patients underwent bilateral surgery; one in one session and three had their second operation within one month of the first surgery and one TS waited six month for the second surgery. Two patients missed their three-month follow-up otherwise all RSA recordings were obtained (completion rate 0.985).

Demography:

The cohort consisted of 10 boys and 10 girls with a median age of 9.4 years (range: 3.4-16.8) and 8.9 years (range: 3.0-13.7) respectively. Ten patients suffered from spastic tetraplegic, seven had spastic diplegic, two had hypotonic tetraplegic and one was dyskinetic. The primary neuromuscular diagnose was cerebral palsy (n=17) and the remaining were Bohring-Opitz syndrome (n=1), Retts Syndrome (n=1) and Angelman syndrome (n=1).

All patients had severe disabilities (without ambulation or using assistive devices). They were classified by the GFMCS score for cerebral palsy (Graham 2005). However this was applicable for all, even though they had a variety of diagnoses. Patients were distributed GMFCS 3 (n=4), 4 (n=5) and 5 (n=11). Fourteen of the 20 patients had some degree of mental retardation and ten of these suffered from epilepsy. The main comorbidity was obstipation of which ten of the patients received daily medication. The patients were also medicated for sleeping disorders and/or respiratory problems. The median number of daily medical products was 2 (range: 0-6).

Pre-, Per- and Postoperative Observations:

The median height was 126 cm (range: 90-166), median weight 25 kg (range: 13-70) and hence median BMI 17 kg/m^2 (range: 15-27) at time of surgery. ASA classification was assessed prior sedation to two ASA-1, ten ASA-2 and eight ASA-3 by experienced anaesthesiologists.

The derotation and varisation were estimated by the surgeon during surgery, hence median 30° of external rotation (range 0-45) and 30° varisation (range 20-40). Ten of the 26 hips also had shortening femur osteotomy ranging from 1.5 to 2.0 cm. The median duration of surgery was 247 minutes (range: 97-431), which also included approximately one hour of casting. Assessment of perioperative blood loss was estimated to median 290 mL and ranging from 50 mL to 1700 mL. Four senior children orthopedic surgeons were responsible for all surgeries, and all surgeries were without perioperative complications. The median casting period were 4.9 weeks (range: 0.00-6.86) and four GMFCS 5 patients were postoperatively treated without cast and not permitted mobilization for 5 weeks *(this was also the case in the excluded patient with osteosynthesis failure).* In seven of the 25 surgeries postoperative complications occurred during the one year follow-up. Two patients suffered from superficial skin infections treated successfully with per oral antibiotics. Two patients experienced femoral shaft fractures on the ipsilateral side (one patient after 10 weeks and the other after 12 weeks; both during physiotherapy). Both patients continued in the study as the fractures were far distal from the markers. Two patients had asymptomatic heterotopic ossification (Brooker Classification 2 (Brooker et al. 1973)).

The median casting period were 4.9 weeks (range: 0.00-6.86) and four GMFCS 5 patients were postoperatively treated without cast and not permitted mobilization for 5 weeks (this was also the case in the excluded patient with osteosynthesis failure).

Evaluation of Conventional AP Pelvic Radiographs:

The median pre- and postoperative FHEI values were 54 % (range: 42-78) and 11 % (range: -23-35), respectively. The median reduction of extrusion was ΔFHEI 44 % (range: 12-92). For the median pre- and postoperative neck-shaft angle (NSA, (Hoaglund and Low 1980)) values were 164° (range: 145-178) and 120° (range: 105-145), respectively. The median angle reduction (ΔNSA) 45° (range: 29-60).

	FHEI		NSA	
	Median	**Range**	**Median**	**Range**
PreOP	54 %	(42-78)	164°	(145-178)
PostOP	11 %	(-23-35)	120°	(105-146)
Diff.	44 %	(12-92)	45°	(29-60)

Table 1. Median and range of femoral head extrusion index (FHEI) and neck shaft angle (NSA) evaluated on AP pelvic radiographs preoperative, postoperative and the difference between these two measurements (n=18).

Results of the Radiostereometric Analysis:

Despite using a standardized setup, the hip spica cast restricted mobility of the operated leg and thus region of interest, and as predicted many of the tantalum markers were covered or partly covered by the osteosynthesis material in the femoral shaft distally of the VDRO in the postoperative RSA. RSA data were initially only valid in 8 of the 25 femoral VDROs. If using a different follow-up RSA as reference model, where patients were without hip spica cast, 19 RSA datasets were valid indicating a difficulties with the postoperative RSA. The excluded and invalid data were in 5 patients due to loose markers (ME > 0.35 mm) and one with insufficient markers distribution (CN > 150 mm^{-1}).

As protocolled we then included the tip of the screws in the femoral shaft as additional markers and this increased the number of valid dataset to 19 hips from 17 patients equal to 95 follow-ups (19 x 5). Ten follow-ups were subsequent excluded; two because of CN > 150 mm^{-1}, three because of loose markers (ME > 0.35 mm) and five follow-ups because of coverage by osteosynthesis material. The median number of markers was five (range: 3-9). The median CN was 46 mm^{-1} (range: 19-150) and ME was 0.19 mm (range: 0.04-0.47). Three of the patients were accepted despite ME > 0.35 mm, all of these patients had initial ME below 0.35 mm as protocolled but subsequent follow-ups had continuously increasing ME interpreted as minor regional growth.

Internal Repeatabilities and Independency:

RPL of double examinations from follow-up 6- or 12-months (n=10) with inclusion of screw tips are summarized in table 2. The MTPM median of these data was 0.34 mm (range: 0.27-0.80). Independency between data from bilateral surgeries was tested graphically and interpreted without suspicion of confounding by cluster (Seaman et al. 2014), thus both sides from patients were included.

Translation	RPL	Rotation	RPL
x	0.23 mm	Rx	0.81°
y	0.19 mm	Ry	1.24°
z	0.46 mm	Rz	0.58°

Table 2. The 95 % repeatability limits (RPL) based on double examinations at 10 follow-ups of 10 patients after radiographic stable VDRO when including screw tips in the femoral shaft as additional markers.

RSA Stability across the VDRO:

The testing of RSA stability across VDRO is summarized in table 3. Moreover, the table also show results of what happens if the RSA stability definition is altered to migration below RPL in only five of the six orientations.

Follow-up (n=19)	6 of 6 directions	5 of 6 directions
5W	15	16
3M	16	18
6M	18	19
12M	18	19

Table 3. Assessment of RSA stability across VDRO in relation to RPLs either if the migration of two consecutive were below RPL in all six directions and if < RPL in five of six directions.

Translation and Rotation:

Table 4 summarizes the mean migration of the RSA stable VDROs at the one-year follow-up. Figure 3 to 8 show the progression of translation and rotation of the femoral shaft distal of the VDRO. In four of the figures there are some outliers, which are commented in the figure text.

Direction	Mean	SD
x	0.51 mm	1.12
y	0.69 mm	1.61
z	-0.21 mm	1.28
Rx	0.39°	2.90
Ry	0.02°	3.07
Rz	2.17°	2.29

Table 4. Mean migration and standard deviation at the one-year follow-up of stable VDROs (n=18).

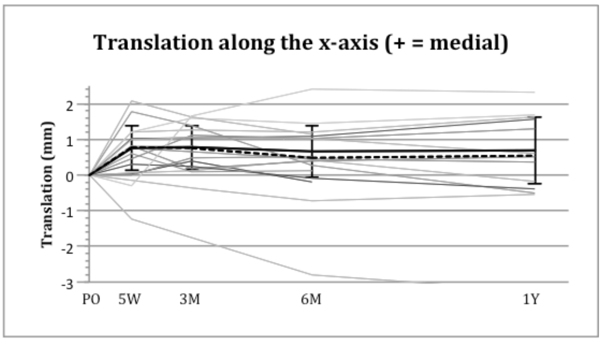

Figure 3. Medial-lateral translation. The bottom outlier (patient #15) was by our RSA definition unstable the whole trial period with extremely long surgery time because of the need to reposition the osteosynthesis material. Linear regression of the RSA stable VDROs estimated medial progression by 0.09 mm per year. The dashed line (median), the solid line (mean) and the error bars (SD) are exclusive the outlier.

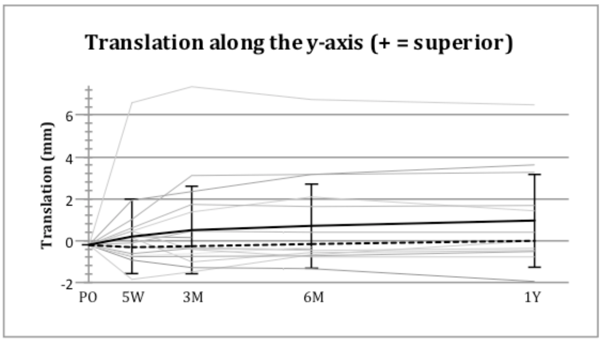

Figure 4. Superior-inferior translation. The top outlier (patient #3) showed large migrations within the first 5 weeks. This VDRO was RSA stable within the first three months. Linear regression of the RSA stable VDROs estimated superior progression by 0.41 mm per year. The dashed line (median), the solid line (mean) and the error bars (SD) are inclusive the outlier.

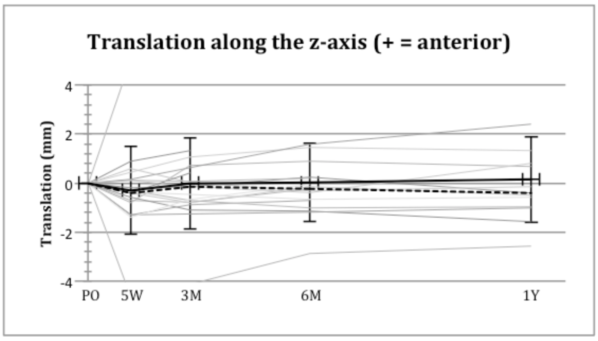

Figure 5. Anterior-posterior translation. The top outlier (patient #3) showed large migrations within the first 5 weeks. This VDRO was RSA stable within the first three months. The bottom outlier (patient #6) showed large migrations within the first 5 weeks. This VDRO was not RSA stable before the six-month follow-up. Linear regression of the RSA stable VDROs estimated anterior progression by 0.10 mm per year. The dashed line (median), the solid line (mean) and the error bars (SD) are exclusive outliers.

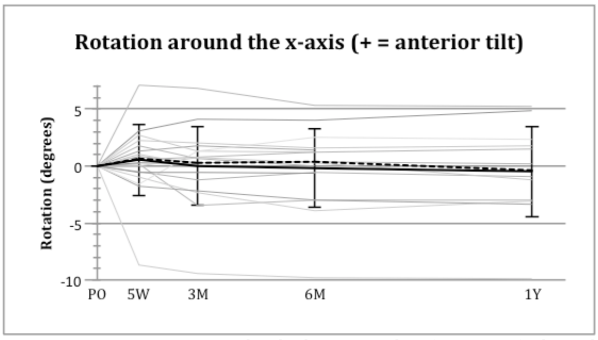

Figure 6. Anterior-posterior tilt. The bottom outlier (patient #3) showed large migrations within the first 5 weeks. This VDRO was RSA stable within the first three months. The top outlier (patient #6) showed large migrations within the first 5 weeks. This VDRO was not RSA stable before the six-month follow-up. Linear regression of the RSA stable VDROs estimated progression by 0.82° posterior tilt per year. The dashed line (median), the solid line (mean) and the error bars (SD) are exclusive outliers.

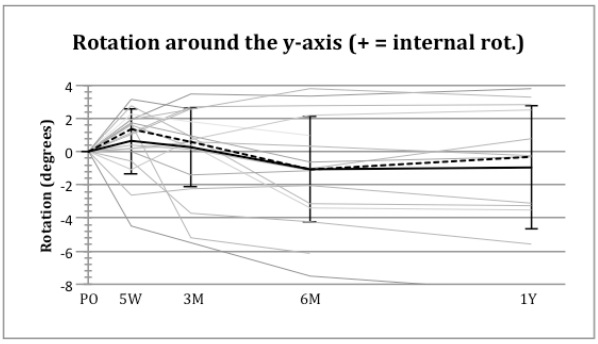

Figure 7. Internal-external rotation. The bottom outlier (patient #15) was by our RSA definition unstable the whole trial period with extremely long surgery time because of the need to reposition the osteosynthesis material. Linear regression of the RSA stable VDROs estimated progression by 0.92° external rotation per year. In contrast to the other migration figures the mean seem to bend toward internal rotation after the 6-month follow-up. The dashed line (median), the solid line (mean) and the error bars (SD) are exclusive the outlier.

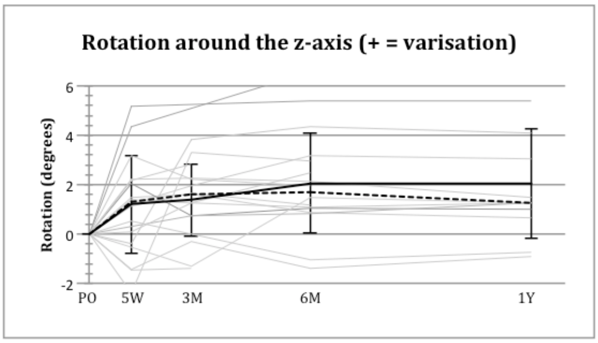

Figure 8. Varus-valgus. There are no singled out outliers. Linear regression of the RSA stable VDROs estimated progression by 0.71° varus angulation per year. Dashed line (median); solid line (mean); error bars (SD).

Maximum Total Point Motion:
Figure 9 shows the difference in MTPM between to follow-ups (ΔMTPM). There are significant greater migrations at the 5-week follow-up. Decreasing ΔMTPM values are observed the remaining trial period.

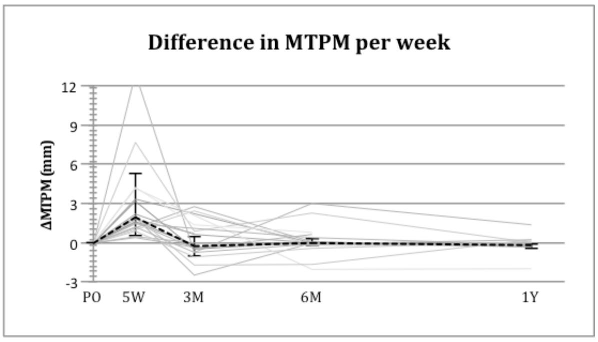

Figure 9. ΔMTPM per week across each VDRO. The dashed line is the median MTPM value and error bars depict the 1st and 3rd quartiles.

4. Discussion

In this study radiostereometric analysis were performed 0, 5 weeks, 3, 6 and 12 months after 27 femoral VDRO in a cohort of children with neuromuscular disorders and syndromes. The cohort had similar demography and FHEI as in other studies (Sankar et al.; Canavese et al. 2010; Davids et al. 2013); thus the study population seem representable and comparable to other studies regarding children with neuromuscular disorders and hip dislocation - but discrepancy between the perioperative evaluated varisation and the pre- and postoperative NSA measurements is found similar in another study (Geretschläger et al. 2005).
There are practical and technical obstacles in achieving adequate RSA recordings - especially for the postoperative recording due to the fixed hip angle in the spica hip cast. For this reason it was necessary to include screw tips in femoral shaft as marker, thus heightening the ME values as expected. Three of the 19 RSA results were accepted despite ME > 0.35 mm. This was due to, that they had an initial ME value below 0.35 with continuously small increasing values above 0.35. We could justify this since it was interpreted as due to either remodelling or minor regional growth. The assumption of including the screw tips as markers seem plausible, since the MbRSA software would detect loose markers or instable screw tips by increasing ME. Comparing the RPL to the phantom model results the RPL approximately doubled when including the screw tips as additional markers. We found the RPL of the put-of-plane directions (z an Ry) to be mostly

affected by addition of screw tips as markers when using uniplanar calibration cage as seen in other studies (Bragdon et al. 2004; Stilling et al. 2012).
The primary aim of this study was to assess the stability across VDROs by RSA in children with neuromuscular disorders and syndromes. We defined an osteotomy as RSA stable if measurements in two consecutive follow-ups had migration below the internal RPL of each six orientations. We tried to examine if our definition was adequate by changing it to two consecutive follow-ups with migration below the RPL in only five out of six orientations. However, we found only marginal difference in RSA stability between these two definitions. When using the first definition one of the patients would never achieve an RSA stable osteotomy through out the full study period. This is contradictory to the clinical history, since shortly after ending the study the patient had removed the osteosynthesis material and continued physiotherapy and still today has no signs of relapse or collapse across the VDRO. This indicate that the second definition of RSA stability to be more clinical appropriate. When considering the statistical aspects you would achieve a risk of type I errors in 5 % of each orientation. Evaluating all six orientations together under the assumption of being binomial distributed would render a likelihood as high as 26 % risk of type I error. There is interdependency between migration of the orientations minimizing this risk, but it would still be larger than 5 %. A definition of RSA stability of migration above RPL in whole two orientations will theoretically induce higher risk of type II error. Hence the second definition of RSA stability is the better choice. The second definition of RSA stability seems the best choice in this perspective; we would then conclude and to our knowledge for the first time show that VDROs are stable within five weeks postoperatively by RSA in 95 % of the included VDROs.
The secondary aim was to estimate the mean migration of the femoral shaft distal of the VDRO in stable osteotomies at the one-year follow-up. The VDRO demonstrated only marginal migration despite a relative high varus angulation at only year of follow-up. The VDROs initially migrated with progressive external rotation through out the first six months, but stagnated and with subsequent slight median internal rotation from the six-month follow-up to the one-year follow-up (figure 7).
It proved rather difficult to obtain visible markers in the femoral shaft in both RSA radiographs when the patients still were cast immobilized. We managed to obtain sufficient markers by inclusion of the screw tips in the femoral shaft. Despite this technical difficulty the RSA results seem valid since the internal RPL are only slightly higher than those of phantom models, and the ME and CN are still within thresholds. The GMFCS classification was used to all included patients. Originally the GMFCS classification is only validated for children with CP, but we found it applicable and feasible for the group of patients, since they demonstrates traits of clinical manifestations of neuromuscular disorders and increased risk of hip dislocation (Beckung et al. 2004; Tay et al. 2010). Despite these shortcomings of the study the results are still important as it relates to a better biomechanical understanding of stability, migration and healing across VDROs. In future studies regarding the definition of RSA stability our second definition could be testes for applicability on different types of osteotomies and moreover used in period of casting to evaluate if the cast duration could be shortened. The high precision of the RSA method would also be an appropriate tool for assessment of risk factors of long-term relapse.

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Repeatability of Marker Based Radiostereometric Analysis Across Hindfoot Osteotomies

Buxbom P, Sonne-Holm S, Wong C.

Manuscript to be submitted.

I

Stability and Migration Across Dega Osteotomies in Children with Neuromuscular disorders by Radiostereometric Analysis - A One Year Follow-up of 18 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

II

Stability and Migration Across Femoral Varus Derotation Osteotomies in Children with Cerebral Palsy by Radiostereometric Analysis - A One Year Follow-up of 25 Hips

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

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III

Stability and Migration Across Calcaneal Lengthening in Children - A Radiostereometric Analysis of Twenty Osteotomies

Buxbom P, Sonne-Holm S, Ellitsgaard N, Wong C.

Manuscript to be submitted.

IV

Stability and Migration Across Calcaneal Lengthening Osteotomies in Children - A Radiostereometric Analysis of Twenty Osteotomies

Peter Buxbom, Stig Sonne-Holm, Niels Ellitsgaard, Christian Wong

Orthopedic Department, Hvidovre Hospital, Copenhagen, Denmark

Abstract

Background and Purpose: Pes planovalgus (PPV) or flatfoot is a common defomity in children. The calcaneal lengthening osteotomy (CLO) seems to be the procedure of choice. We planned to assess RSA stability and migration across the CLOs in a prospective cohort study. **Material and Methods:** Inclusion of children planned CLO. RSA follow-ups were performed at time 0, 5, 10 weeks, 6 and 12 months after surgery. **Results:** Twenty CLOs were included. RSA data showed stability across the CLO in majority cases within the first 5 weeks. The remaining RSA stabilized within the subsequent 5 weeks. At the one-year follow-up the mean translations (±SD) of the anterior calcaneal fragment across the CLOs were 0.23 mm (±0.51) superior and 0.14 mm (±0.40) lateral. The mean rotations were 0.49° (±2.09) supination, 0.78° (±2.03) external rotation and 0.91° (±1.98) dorsifelxion. **Discussion:** Migration stagnates within the 10-week follow-up indicating stability across the CLOs in all patients. DOs with FG seem to be unstable longer. The mean migration of anterior calcaneal fragment across the CLOs was at the one-year follow-up marginal superior and lateral direction with rotation of supination, external rotation and dorsiflexion.

Keywords: *Children orthopedics; Pes planovalgus; Flatfoot; Calcaneal lengthening osteotomy; Radiostereometric analysis.*

1. Introduction

Pes planovalgus (PPV) or flatfoot is a common defomity in children. Epidemiological studies indicate that most children do not have a medial longitudinal arch at birth, but the arch develops in an age of aproximately 5 years (Staheli et al. 1987). There has been observed increased incidence of PPV in boys, children with obesity and neuromuscular disorders (Staheli et al. 1987; Evans and Rome 2011; Kadhim and Miller 2014). The deformity has often been divided into flexible and rigid PPV, with in under 1 % of PPV being rigid (Pfeiffer et al. 2006). In majority cases the PPV is asymptomatic, but pain during activity has been reported as the main reason for children with PPV to seek an pediatric orthopedic surgeron (Bouchard and Mosca 2014). The indications for surgery is typically in rigid PPV or intractable pain and physical disability despite nonsurgical treatment (e.g. arch support, physiotherapy) (Evans and Rome 2011; Bouchard and Mosca 2014).

Choice of surgical intervention is often based on restoring the medial longitudinal arch with the least impact on foot joint mobility. Calcaneal lengthening osteotomy (CLO) or calcaneal-cuboideum-cuneiform osteotomy (triple C) is often performed (Moraleda et al. 2012) and with less complications than arthrodesis' (Saltzman et al. 1999). A study by Moraleda et al. (2012) comparing CLO and triple C find equal clinical outcome between the two procedures, but slightly better radiographic results in favor of CLO. Still complications have been reported high, and with need of additional surgeries in 18-36 % to maintain stability in adults (Bolt et al. 2007; Moraleda et al. 2012).

Radiostereometric analysis (RSA) is a method with high precision and has the ability to identify complex three-dimensional migration of skeletal structures (Selvik 1978, 1989; Kärrholm et al. 1982; Teeuwisse et al. 1998; Mäkinen et al. 2004; Valstar et al. 2005). The feasiblity of RSA across CLOs has been verified in a cadaver study (Martinkevich et al. 2015). A recent RSA study evaluating stability across high tibial osteotomies in adults suggest stability 6-12 weeks after surgery (Teeter et al. 2015). Of our knowlegde there are no RSA studies available evaluating stability across osteotomies in children and in general there few children orthopedic RSA studies published (Lauge-Pedersen et al. 2006; Gunderson et al. 2013; Horn et al. 2013; Lauge-Pedersen and Hägglund 2013).

Figure 1 – Postoperative and six-month follow-up RSA radiographs of an eleven-year-old boy whom underwent calcaneal lengthening on the right foot.

The primary aim of this study is to assess the stability across CLOs by RSA. The secondary aim is estimate the 1-year follow-up migration across the CLO in RSA stable osteotomies.

2. Methods

This study was a prospective cohort study with trial period from ultimo 2012 to ultimo 2014. Patients prepared for CLO

and between the age 2 and 18 years were offered to participate in the study.
The follow-up period was one year, and the RSA examinations were performed postoperatively, after 5 and 10 weeks, 6 and 12 months. The visit window for the RSA recording was respectively 3 days at postoperative follow-up, one week at the 5-week and 10-week follow-up and two weeks at subsequent follow-ups.

Calcaneal Lengthening Procedure:
Autograft was initially harvested from the iliac crest. On the lateral side of the foot the procedure begins with a modified Ollier skin incision. Nervus peroneus superficialis and nervus suralis are respected. The extensor digitorum brevis muscle is loosened from its origin and soft tissue in sinus tarsi is resected. An osteotomy was made in calcaneus approximately 1 cm behind the articulation with the cuboid bone. Before insertion of autograft 4-6 tantalum markers (1 mm diameter, Wennbergs Finmek AB, Gunnilse, Sweden) were inserted on each side of the osteotomy. The autograft and calcaneocuboidal articulation were fixed with one or two percutaneous K-wires.
While still in general anaesthetics a circular cast (Scotchcast, 3M) was applied below knee level and the patient were not allowed any weight bearing the first 5 weeks. After 5 weeks the cast and k-wires were removed followed by a walking cast the subsequent 5 weeks.

The RSA methodology:
By standardized procedure the patient was placed in supine position with the medial side of the foot pointing towards the ceiling, just above the wheel born carbon fibre enclosed uniplanar calibration cage (LUMC, Leiden, The Netherlands; 85 x 29 x 55 cm) and two ceiled-attached radiographic tubes (Arcoma AB, Växjö, Sweden) were adjusted to the two digital detector plates (DRX-1C type, Carestream, New York, USA) angling 46° with a height of 160 cm from the plates. The exposure was standardized to 60 kV and 5 mAs. The RSA outcomes were of spatial resolution size 2560 x 3072 (greyscale 8 bit dicom-format).

The orthogonal directions and the coordinate system used across the CLOs are illustrated in figure 2. The posterior calcaneal fragment was used as reference position and migration was measured with the anterior calcaneal fragment as the model. Hence, translations x_+ = posterior, y_+ = superior and z_+ = medial, and rotations Rx_+ = pronation, Ry_+ = internal rotation and Rz_+ = plantar flexion. Values of left feet were negated in x, Ry and Rz to create same directions as for right feet.

Figure 2 – The 6 orientations with positive values of a right feet being; for translation x_+ = posterior, y_+ = superior and z_+ = medial; for rotation Rx_+ = pronation, Ry_+ = internal rotation and Rz_+ = plantar flexion.

The radiographs were analysed with MbRSA 3.41 software (LUMC, Leiden, The Netherlands).

MbRSA 3.41 software assesses translation and rotation by the RSA software according to the radiostereometric analysis community guidelines defined by the Valstar et al. in 2005.

Marker stability was assessed by the mean error of rigid body fitting (ME). The standard threshold of ME is below 0.35 mm (Valstar et al. 2005), but because of the expectance of remodelling and growth during the study we protocolled to evaluate ME individually and might include RSA data if the initial ME observation were 0.35 mm and the subsequent observations had continuously increasing ME in a manner that could be interpreted as remodelling or growth. ME is expressed as,

$$ME = \sqrt{\frac{d_1^2 + d_2^2 \ldots + d_n^2}{n}}$$

By computation of rotation matrices and translation vectors for absolute motion, the RSA software minimizes ME using a least-squares method and thereby excludes the actual movement of the rigid body.

Marker distribution was assessed by the condition number (CN). The RSA ISO standards state that CN should be below 120 mm^{-1} when studying adult hip, knee or shoulder arthroplasties, but may be higher when studying other smaller structures. Like other studies we included observations if CN < 150 mm^{-1} (Söderkvist and Wedin 1993; Onsten et al. 2001; Börlin et al. 2002; Bragdon et al. 2004; Valstar et al. 2005; Gunderson et al. 2010; Fong et al. 2011).
The MbRSA software calculates CN from the distance of the markers to an computed straight line passing through the cluster and is expressed as,

$$CN = \frac{1}{\sqrt{d_1^2 + d_2^2 \ldots + d_n^2}}$$

where d_i is the shortest possible distance to this arbitrary straight line (Ryd 1986)

Maximum total point motion (MTPM) values attempts to express the total translation and rotation by one value (unit in mm) (Ryd 1986). Hence MTPM values are absolute, and therefore potentially not normal distributed. Results are therefore given with a median and range (Valstar et al. 2005).

The precision of our RSA setup was assessed by calculation of internal repeatabilities (RPLs) in accordance to Ranstam et al. (2000) for all 6 degrees of freedom (df). The setup evaluation was based on double examinations after follow-ups where the CLO was assessed radiographic stable and earliest at the 6-month follow-up. RPL is calculated as the 95 % deviation from the true value (Ranstam et al. 2000).

$$RPL_{df} = 1.96 \times \sqrt{2} \times SD_{df}\ .$$

where SD is the standard deviation for each df and calculated as

$$SD_{df} = \sqrt{\frac{\sum_{i=1}^{n}(d_i - \sum(d_i/n))^2}{n-1}} \quad d_i \in \mathbb{R}$$

and d_i is the absolute value of motion of each df.

Based on the internal RPLs obtained from double examinations during the study period, we defined a RSA stable CLO as observations of two consecutive follow-ups with migration below the internal RPL in five out of six orientations. We elaborate on observations if redefining the RSA stability to migrations below RPL in 6 out of 6 orientations.

The RSA setup at Hvidovre Hospital was prior study initiation validated on a phantom model. RPL of translations were 0.06-0.22 mm and rotations 0.19-0.52°. MTPM median was 0.16 mm (range: 0.07-0.59).

Ethics:
The Danish Research Ethical Committee approved the study: Journal number H-2-2011-124.
To minimize the exposure of radiation a maximum of 3 attempts were used to obtain acceptable RSA radiographs.

3. Results

Inclusion consisted of 20 CLOs in 15 patients. There were no dropouts during the study period. Five patients underwent bilateral surgery; four patients had operated both feet at same procedure; one patient had the second operation one year later.
One patient missed the 3-month follow-up otherwise all RSA examinations were obtained (completion rate 0.99).

Demography:
The cohort consisted of 9 boys and 6 girls with median age were 11.3 years (range: 7.0-15.5) and 11.4 years (range: 9.5-16.2) respectively. Three patients suffered from mild cerebral palsy with spastic diplegia, otherwise the patients did not suffer from any conditions.

Pre-, Per- and Postoperative Observations:
At time of surgery the median height was 147 cm (range: 117-184), median weight 35 kg (range: 23-75) and hence median BMI 17 kg/m^2 (range: 13-23). ASA classification was assessed prior sedation by experienced anaesthesiologists and graduated ASA 1 (n=9) and ASA 2 (n=6).
The median duration of surgery per foot was 113 minutes (range: 57-179), which also included approximately 15 minutes to half an hour of casting. The estimated perioperative blood loss ranged between a few mL to 250 mL.
Four senior children orthopedic surgeons were responsible for all surgeries, and no perioperative complications were reported. Within the one-year follow-up the only postoperative complication was that one patients suffered from a superficial skin infection treated successfully with per oral antibiotics.

The median time of casting without weight bearing was 4.9 weeks (range: 4.3-5.3) and subsequent median time in a walking cast 5.0 weeks (range: 4.0-6.0).

Results of the Radiostereometric Analysis:
One patient was excluded having CN > 150 mm^{-1} of markers in anterior calcaneal fragment. Four follow-ups in one patient were excluded because marker instability (ME > 0.35 mm). Of the remaining 18 included CLOs the median CN was 84 mm^{-1} (range: 37-149). The median ME was 0.13 mm (range: 0.02-0.34), thus data did not indicate the need to include individual follow-ups with ME > 0.35 mm at the end of the study period.

Internal Repeatabilities:
RPLs on double examinations at follow-up at 6 or 12 months and (n=16) are summarized in table 2. The MTPM median of these data was 0.16 mm (range: 0.07-0.59).

Translation	RPL	Rotation	RPL
x	0.21 mm	Rx	0.64°
y	0.21 mm	Ry	0.54°
z	0.24 mm	Rz	0.48°

Table 2. The 95 % repeatability limits (RPL) based on double examinations at 16 follow-ups of 16 patients after the 6-month follow-up and assessment of radiographic stability (n=16).

Stability across the Calcaneal Lengthening Osteotomies:
The testing of RSA stability in relation to the RPLs across CLOs is summarized in table 3.

Follow-up (n=18)	5 of 6 directions	6 of 6 directions
5W	13	8
10W	18	13
6M	18	18
12M	18	18

Table 3. Assessment of RSA stability across CLOs in relation to RPLs either if the migration of two consecutive were below RPL in five directions and or six of six directions.

Translation and Rotation:
Table 4 summarizes the mean migration of the RSA stable DOs at the one-year follow-up. Figure 3 to 8 show illustrates the progression of translation and rotation of the anterior calcaneal fragment across the CLO.

Direction	Mean	SD
x	0.00 mm	0.26
y	0.23 mm	0.51
z	-0.14 mm	0.40
Rx	-0.49°	2.09
Ry	-0.78°	2.03
Rz	-0.91°	1.98

Table 4. Mean migration and standard deviation at the one-year follow-up of stable CLOs (n=18).

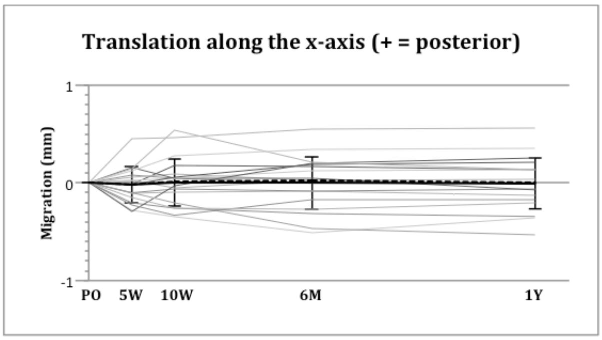

Figure 3. Posterior-anterior translation. Dashed line (median); solid black line (mean); error bars (SD).

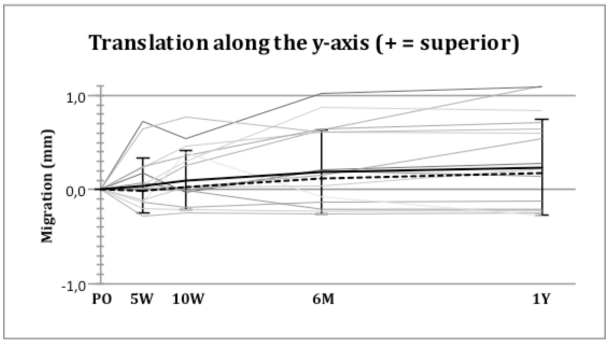

Figure 4. Superior-inferior translation. Dashed line (median); solid black line (mean); error bars (SD).

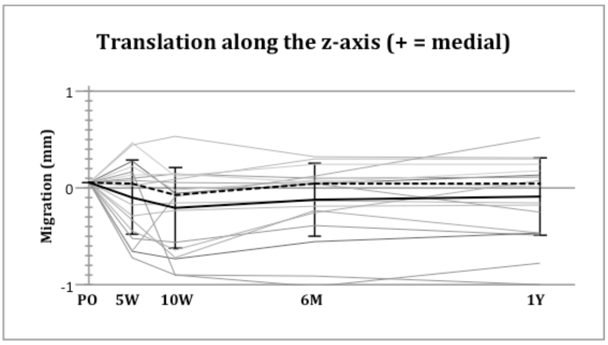

Figure 5. Medial-Lateral translation. Dashed line (median); solid black line (mean); error bars (SD).

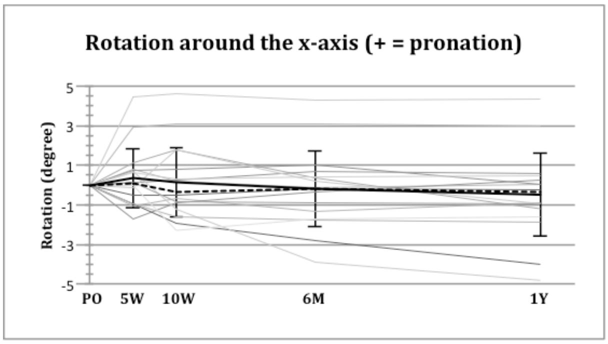

Figure 6. Pronation-supination. Dashed line (median); solid black line (mean); error bars (SD).

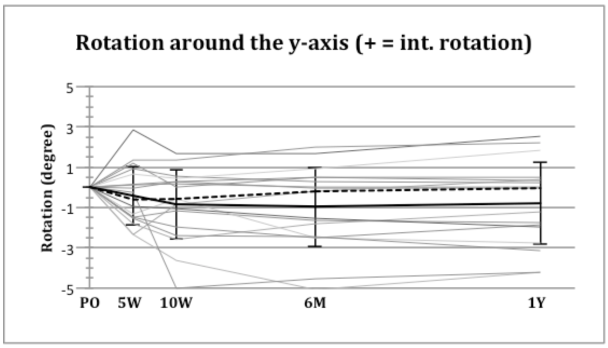

Figure 7. Internal-external rotation. Dashed line (median); solid black line (mean); error bars (SD).

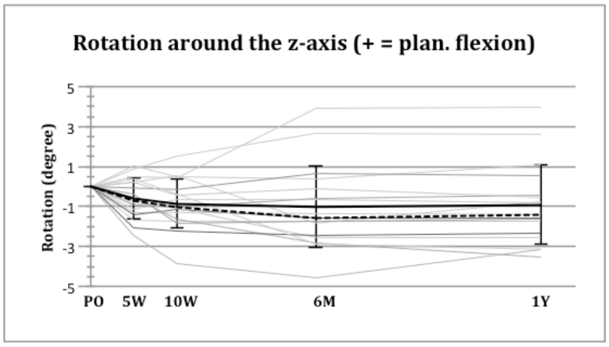

Figure 8. Plantar flexion-dorsiflexion. Dashed line (median); solid black line (mean); error bars (SD).

Maximum Total Point Motion:
Figure 9 illustrates initial total migration within the first 5 weeks. The total migration continuously stagnates at the subsequent follow-ups.

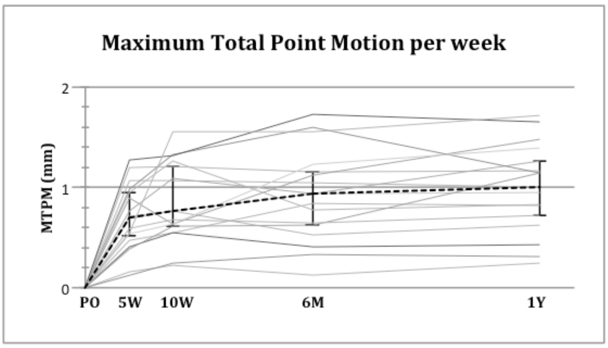

Figure 9. Maximum total point motion (MTPM). The median MTPM (dashed) and error bars (1st and 3rd quartile) illustrate initial total migration within the first 5 weeks. The total migration continuously stagnates the subsequent follow-ups.

4. Discussion

In this study RSA follow-ups were performed consecutively one year after a CLO in a cohort of children. Despite small anatomical size of the studies area it rendered feasible to produce valid RSA outcome.

The primary aim of this study was to assess the stability across CLOs by RSA in children. We defined a RSA stable CLO as observations of two consecutive follow-ups with migration below the internal RPL in five of six orientations. In addition we wanted to elaborate if redefining this threshold to migration below RPLs in all six of six orientations. With the primary definition we found RSA stability in 13 of 18 CLOs at 5-weeks follow-up and 18 of 18 CLOs at 10-weeks follow-up. These findings are similar to the clinical outcome and radiographic interpretation of stable across the CLOs in this study. Thus this definition seems most appropriate. Our finding are similar to another study assessing micromotions across high tibia osteotomies finding limited micromotions after 6 to 12 weeks (Teeter et al. 2015). Under the redefinition of RSA stability 5 of 18 CLOs are not considered RSA stable at the 10-weeks follow-up, and one should consider casting the children longer. This would be inconsistent with the clinical outcome of this cohort with no complications (e.g. non-union or collapse across the CLO). The migration above RPL in one of six orientations is interpreted as be due to statistical variation with a degree of micromotions. Using the primary definition will minimize the risk of type I errors.

The secondary aim was to estimate the mean migration of the anterior calcaneal fragment across the CLO in stable osteotomies at the one-year follow-up. Migration was marginal with a marginal displacement of the anterior calcaneal fragment in superior and lateral direction with rotation of supination, external rotation and dorsiflexion.

Acknowledgement

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17 Postscript

‘What we call the beginning is often the end. And to make an end is to make a beginning. The end is where we start from’

Thomas Stearns Eliot (1943)