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Periacetabular Osteotomy in patients with Hip Dysplasia investigated with Imaging Modalities

Doctoral Dissertation

Inger Mechlenburg, PT, MSc, PhD

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Evaluation committee

Jan Erik Madsen, Professor, MD, PhD
Department of Clinical Medicine
University of Oslo, Norway

Mikael Boesen, Associate professor, MD, PhD
Head of Musculoskeletal Research Unit at Department of Radiology
Bispebjerg and Frederiksberg Hospital, Denmark

Bjarne Møller Madsen, Professor, MD, DMSc (Chairman)
Department of Orthopaedic Surgery
Aarhus University Hospital, Denmark

Correspondence

Inger Mechlenburg, PT, MSc, PhD
Orthopaedic Research Unit
Aarhus University Hospital
Tage Hansens-gade 2, Building 10A
8000 Aarhus C
Tel +45 5115 6585, Fax +45 8949 7429
E-mail: inger.mechlenburg@au.dk
Web: www.OrthoResearch.dk

Inger Mechlenburg, Associate professor
Centre of Research in Rehabilitation (CORIR)
Department of Clinical Medicine
Aarhus University
Palle Juul-Jensens Boulevard 82, 8200 Aarhus
Tel +45 5115 6585, Fax +45 8949 7429
E-mail: inger.mechlenburg@au.dk
Web: http://www.en.auh.dk/research/

The research presented in this doctoral dissertation was performed at the Orthopaedic Research Unit at Aarhus University Hospital.

Previous work from the Orthopaedic Research Unit at Aarhus University Hospital

PhD projects	Completed
1. Martin Lind	1996
2. Ole Rahbek	2002
3. Michel Ulrich-Vinther	2002
4. Søren Kold	2003
5. Thomas Bo Jensen	2003
6. Brian Elmengaard	2004
7. Marianne Nygaard	2005
8. Mogens Berg Laursen	2005
9. Alma B. Pedersen	2006
10. Berit Zippor	2007
11. Mette Ørskov Sjøland	2007
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17. Jørgen Baas	2008
18. Stig Jakobsen	2008
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21. Anders Troelsen	2009
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36. Nina Dyrberg Lorenzen	2012
37. Mette Sørensen	2012
38. Jeppe Barckman	2013
39. Rikke Vestergaard	2013
40. Charlotte Hartig-Andreasen	2013
41. Samir Munir	2013
42. Sys Hasslund	2014
43. Anette Liljensøe	2014
44. Lone Ramer Mikkelsen	2014
45. Birgit Skoffer	2015
46. Jeppe Lange	2015
47. Karen Toftdahl Bjørnholdt	2015
48. Mikkel Tøttrup	2015

DMSc theses:	Completed
1. Martin Lind	1998
2. Søren Overgaard	2000
3. Steffen Jacobsen	2006
4. Michael Ulrich-Vinther	2007
5. Anders Troelsen	2012

Indhold

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Inger Mechlenburg, April 2015

List of papers

This doctoral dissertation is based on the following articles, which will be referred to in the text by their Roman numerals (I–VIII).

I Mechlenburg I, Nyengaard JR, Gelineck J, Soballe K. Cartilage thickness in the hip joint measured by MRI and stereology – a methodological study. Osteoarthritis Cartilage. 2007 Apr;15(4):366-71.*

II Mechlenburg I, Kold S, Søballe K. No change detected by DEXA in Bone Mineral Density after Periacetabular Osteotomy. Acta Orthop Belg. 2009 Dec;75(6):761-6.

III Mechlenburg I, de Raedt S, Nyengaard JR, Gelineck J, Søballe K. Cyst volume in the acetabulum and femoral head decrease after periacetabular osteotomy. Hip Int. 2012 May-Jun;22(3):313-8.

IV Mechlenburg I, Nyengaard JR, Gelineck J, Søballe S, Troelsen A. Cartilage thickness in the hip joint measured by MRI and stereology before and after periacetabular osteotomy. Clin Orthop Relat Res. 2010 Jul;468(7):1884-90. ¤

V Mechlenburg I, Nyengaard JR, Gelineck J, Søballe K. Cartilage Thickness and Cyst Volume Unchanged 10 year after Periacetabular Osteotomy Among Patients Without Hip Symptoms. Clin Orthop Relat Res. 2015 Mar 31. [Epub ahead of print]

VI Mechlenburg I, Hermansen F, Thillemann T, Søballe K. Blood Perfusion and Bone Formation before and after minimally invasive periacetabular osteotomy analysed by PET combined with CT. Int Orthop. 2013 May;37(5):789-94.

VII Birch S, Liljensoe A, Hartig-Andreasen C, Soballe K, Mechlenburg I. No correlations between radiological angles and self-assessed quality of life in patients with hip dysplasia at 2-13 years of follow-up after periacetabular osteotomy. Acta Radiol. 2015 Feb;56(2):196-203

VIII Mechlenburg I, Daugaard H, Søballe K. Radiation exposure to the orthopaedic surgeon during periacetabular osteotomy. Int Orthop. 2009 Dec;33(6):1747-51.

* Included in my PhD dissertation (2007)
¤ Included in Doctoral dissertation of Anders Troelsen (2012)

Preface

My interest and first studies in the joint preserving technique as a treatment of hip dysplasia started out with thinking that it was unequivocally good to preserve the biological hip instead of replacing it with a total hip arthroplasty. Later on, I discovered that in several countries close to Denmark, the periacetabular osteotomy was only used sporadically or not used at all. The explanation was either that they did not have the patients with radiographic verified hip dysplasia or that they did not believe in the value of applying the periacetabular osteotomy to patients with symptoms of hip dysplasia. I became more skeptical to the universal value of preserving the biological hip joint since it had not been shown to be superior to hip arthroplasty or to conservative treatment in a randomized controlled trial. It would be difficult to perform a randomized controlled trial in Denmark because the periacetabular osteotomy has already been implemented and shown to be an effective procedure for surgical correction of the dysplastic hip. Therefore, professor Søballe and I decided to design our subsequent studies to investigate the biological changes after periacetabular osteotomy in prospective cohort studies with medium to long-term follow-up.

Recently, a phenomenological analysis of the experiences of young women adjusting to life with hip dysplasia and deciding on treatment choices has been published [49]. This study showed that the diagnosis of hip dysplasia challenged the way young women viewed themselves. And once the women began to understand the long-term implications of having hip dysplasia they all began a search to save their biological joint, delaying the need for an artificial joint for as long as possible. This study confirms the value of preserving rather than replacing from a patient-perspective. And after having performed my clinical studies with medium to long-term follow-up, I feel more assured that the joint preserving treatment improves the natural history of the dysplastic hip in some of the patients. However, as long as no randomized controlled trials have been performed, we do not know if periacetabular osteotomy is more efficacious in reducing hip pain and improve hip function than e.g. sham surgery or than hip resistance training.

Abbreviations

AI Acetabular Index Angle

AP Antero Posterior x-ray imaging plane

BMD Bone Mineral Density

BMI Body Mass Index

DXA Dual-energy X-ray Absorptiometry

dGEMRIC gadolinium-enhanced MRI of cartilage

CE Center Edge angle

CI Confidence Interval

CV Coefficient of Variation

CT Computed Tomography

HAGOS the Copenhagen Hip And Groin Outcome Score

HOOS Hip disability and Osteoarthritis Outcome Score

MRI Magnetic Resonance Imaging

mSv millisievert

PET Positron Emission Tomography

OA Osteoarthritis

OR Odds Ratio

PAO Periacetabular osteotomy

SF-36 Short Form 36

THA Total Hip Arthroplasty

TLD Thermo Luminescent Dosimeters

QoL Quality of Life

2D Two-dimensional

3D Three Dimensional

Summary of papers

The minimal invasive periacetabular osteotomy (PAO) is a joint-preserving procedure that effectively corrects hip dysplasia, provides pain relief, improved radiographic results and a low rate of complications. The aim of this doctoral dissertation was to examine biological changes in bone, cartilage and blood perfusion after PAO in patients with hip dysplasia. Furthermore, to investigate the relationship between the acetabular angles and health-related quality of life (QoL) after PAO. And finally, to study the level of radiation to the surgeon during PAO.

Chapters 3 to 7 investigate the first research question "Which biological changes take place in bone and cartilage 2-10 years after PAO?". In Chapter 3, a precise and efficient method for estimating the thickness of the articular cartilage in the hip joint is developed using stereologic methods and Magnetic Resonance Imaging (MRI). The method is applied on 26 patients scheduled for PAO. In chapter 4, a cohort of patients with hip dysplasia are followed with Dual-energy X-ray absorptiometry (DXA) prior to and 1 and 2½ years after PAO to investigate changes in acetabular bone mineral density after PAO. Moreover, to examine whether bone mineral density correlates with postoperative migration of the osteotomised acetabular fragment measured with radiostereometric analysis. Chapter 5 explores the same cohort of patients with MRI and examines how many patients had acetabular or femoral head cysts and investigates whether the volume of the subchondral bone cysts change after PAO. In chapter 6, it is examined whether changes in the thickness of the cartilage in the hip occur after PAO. Further, it is explored how many patients had an acetabular labral tear and whether labral tears are associated with thinning of the cartilage after PAO. Chapter 7 investigates the long-term changes in cartilage thickness and volume of subchondral bone cysts measured with MRI and stereology 10 years after PAO.

The second research question "What is the level of changes in blood perfusion and bone formation in the acetabular fragment after PAO?" is evaluated in chapter 8. Blood perfusion and bone formation is quantified before and after PAO by positron emission tomography (PET) combined with computed tomography (CT).

Chapter 9 evaluate the third research question "Is there a relationship between the radiological parameters and health-related QoL after PAO" The Short Form-36 and Beighton questionnaires are collected to investigate the health-related QoL for patients with hip dysplasia operated with PAO and to investigate whether QoL is associated with the acetabular angles or hypermobility.

In chapter 10, the fourth research question is investigated "Does the level of radiation during PAO impose a health risk to the surgeon?" The radiation exposure to the orthopaedic surgeon and to the surgeon's fingers, thyroid gland, and forehead during intraoperative fluoroscopy in PAO is measured with thermo luminescent dosimeters (TLD).

Finally, the results of the above described studies and future studies are discussed in chapter 11 and 12.

Resumé af artiklerne

Ledbevarende hofteoperation er et effektivt indgreb til at reducere smerter ved at korrigere hofteskålens placering hos patienter med hoftedysplasi, og dette indgreb er forbundet med få komplikationer. Formålet med denne disputats er at undersøge biologiske ændringer efter en ledbevarende hofteoperation i henholdsvis knoglevæv, ledbrusk og i blodgennemstrømningen i det afmejslede knoglefragment. Formålet er dernæst at undersøge forholdet mellem de acetabulære vinkler og helbredsrelateret livskvalitet efter ledbevarende hofteoperation. Og til sidst at undersøge, hvor stor en bestråling kirurgen er udsat for under den ledbevarende hofteoperation. Under hensyn til disse formål formuleres fire forskningsspørgsmål.

Kapitel 3 til 7 behandler det første forskningsspørgsmål "Hvilke biologiske ændringer sker i knoglevævet og i ledbrusken 2-10 år efter den ledbevarende hofteoperation?". I kapitel 3 beskrives en præcis og effektiv metode til at måle tykkelsen af ledbrusken i hofteleddet ved hjælp af stereologiske metoder og MR-skanning. I kapitel 4 bliver en kohorte af patienter med hoftedysplasi fulgt med DXA-skanninger før samt 1 og 2½ år efter operationen for at undersøge ændringer i knoglemineral tætheden i hofteskålen. Desuden undersøges det, om der er sammenhæng mellem knoglemineraltætheden og postoperative mikro-bevægelser af det afmejslede knoglefragment målt med stereorøntgen. I kapitel 5 undersøges den samme kohorte patienter med MR-skanninger med henblik på at opgøre, hvor mange af patienterne, der har knoglecyster samt at undersøge, om volumen af disse cyster ændrer sig efter ledbevarende hofteoperation. I kapitel 6 bliver det undersøgt, om der sker ændringer i tykkelsen af ledbrusken efter operationen, ligeledes med MR-skanning. Endvidere bliver det målt, hvor mange patienter, der har en skade på ledlæben, samt om der er sammenhæng mellem en sådan skade og tykkelsen af ledbrusken efter ledbevarende hofteoperation. Kapitel 7 forholder sig til langtidsændringerne i tykkelsen af ledbrusken og volumen af knoglecyster 10 år efter operationen.

Det andet forskningsspørgsmål " I hvilket omfang ændres blodgennemstrømningen i det afmejslede knoglefragment efter ledbevarende hofteoperation hos patienter med hoftedysplasi?" behandles i kapitel 8. Blodgennemstrømningen og knogle-nydannelsen bliver kvantificeret før og efter ledbevarende hofteoperation ved hjælp af PET/CT-skanninger.

I kapitel 9 evalueres det tredje forskningsspørgsmål "Er der sammenhæng mellem de radiologiske parametre og helbredsrelateret livskvalitet efter ledbevarende hofteoperation?" Spørgeskemaerne SF-36 og Beighton bliver anvendt til at undersøge den helbredsrelaterede livskvalitet og hypermobilitet hos patienter med hoftedysplasi opereret med ledbevarende hofteoperation og i tillæg til dette at undersøge om der er sammenhæng mellem helbredsrelateret livskvalitet og hypermobilitet eller de acetabulære vinkler.

I kapitel 10 bliver det fjerde forskningsspørgsmål behandlet " Indebærer bestrålingen, som kirurgen er udsat for under den ledbevarende hofteoperation en sundhedsrisiko?" Den radioaktive bestråling af kirurgen, dennes fingre, skjoldbruskkirtlen og pande under brug af røntgengennemlysning ved ledbevarende hofteoperation bliver målt med termoluminescente dosimetre.

Til slut bliver resultaterne af de førnævnte studier diskuteret og fremtidige studier beskrevet i kapitel 11 og 12.

Aim and outline of dissertation

The aim of this doctoral dissertation was to examine biological changes in bone, cartilage and blood perfusion after Periacetabular Osteotomy (PAO) in patients with hip dysplasia. Furthermore, to investigate the relationship between the acetabular angles and health-related quality of life (QoL) after PAO. And finally, to study the level of radiation to the surgeon during PAO.

To achieve this aim, four research questions were examined:

1. Which biological changes take place in bone and cartilage 2-10 years after PAO? (chapter 3-7).

2. What is the level of changes in blood perfusion and bone formation in the acetabular fragment after PAO? (chapter 8).

3. Is there a relationship between the radiological parameters and health-related QoL after PAO? (chapter 9)

4. Does the level of radiation during PAO impose a health risk to the surgeon? (chapter 10).

Chapter 1 General introduction

Hip dysplasia

The prevalence of hip dysplasia in adults in Denmark is in one study estimated to be 3.4% [79] and in another study 4.3% in males and 3.6% in females [53]. Hip dysplasia is bilateral in 30-40% of the cases [79]. Not everyone will experience clinical symptoms and require treatment. In most instances, hip dysplasia is not diagnosed until adulthood due to no or few clinical symptoms in adolescence or due to limited knowledge about the disease among general practitioners. The prevalence of hip dysplasia varies throughout the literature, depending on the cut-off values applied when measuring the CE-angle. Some researchers define a hip dysplastic as a CE-angle $\leq$ 25˚ [45;165;198] whereas others use CE-angle $\leq$ 20˚ [35;79]. Wiberg [198] states that CE angles below 20˚ may be considered definitely pathologic and indicating a defective development of the acetabular roof, and values over 25˚ definitely normal. Values between 20˚ and 25˚ are uncertain. Furthermore, ethnic differences in prevalence exist, such as high prevalence in Japan and in Sami-dominant area in North Norway [70;84;203] and low prevalence in Africa [95]. Excessive joint laxity in children with hip dysplasia has been described in one study from 1970 [201]. Excessive joint laxity also known as hypermobility results in an increased Beighton score. However, no association was found between Beighton hypermobility score or health-related quality of life and hip dysplasia in 2081 19-years-old Norwegians [43]. The etiology to hip dysplasia is multifactorial [21;173] and a meta-analysis have identified 5 commonly known risk factors to be associated with hip dysplasia in newborns: breech presentation, female, left hip affected, first born and family history of hip dysplasia [139].

Morphological changes

The dysplastic hip joint has a complex morphology characterised by a wide shallow acetabular cavity with an excessively oblique articulating roof. The acetabular cover of the femoral head is globally deficient [7;189] and the acetabular rim is hypertrophied possibly due to excessive pull from the often hypertrophic labrum. The acetabulum may be anteverted [6;87;88;123] or retroverted [88;103;159]. But the presence of acetabular retroversion (identified by the cross over sign or the ischial spine sign) is probably an independent abnormality of hip dysplasia [127].

The femoral head are in many cases aspheric or deformed [28]; the joint can be congruent in the load-bearing regions [63] or incongruent [108], but the weight-bearing area between the acetabular roof and head is reduced. The articular cartilage is significantly thicker than normal [132]. Hip dysplasia is associated with increased anteversion of the femoral neck [7;76] and with coxa valga (neck-shaft angle>135˚) that results in a reduced abductor lever arm [22;28]. The head-neck offset may be insufficient [27]. However the deformities vary from individual to individual and retroversion of the femoral neck has also been reported in hip dysplasia [22].

Acetabular angles

Hip dysplasia is defined by a centre-edge (CE) angle of Wiberg of less than 25˚ measured on an anteroposterior pelvic radiograph [198] with the patient in supine or standing position. The CE angle (Figure 1) is obtained by drawing a vertical line through the femoral head perpendicular to the horizontal line extending through the centre of both femoral heads. A line is then drawn from the centre of the femoral head to the most superolateral point of the acetabulum [39]. Measured on CT images, normal value for the CE angle is 41˚ (SD 7˚) giving a normal range (+ 2SD) of 27 - 55˚ [174]. The CE angle may be affected by the position of the patient during x-ray [46;186] and may be slightly lower in standing than in the supine position. The CE angles reported in this dissertation are primarily measured on supine radiographs. But in 2008 we changed our protocol for radiographs for assessing patients with potential hip deformities and thus the CE angles measured after that are based on weight bearing AP radiographs.

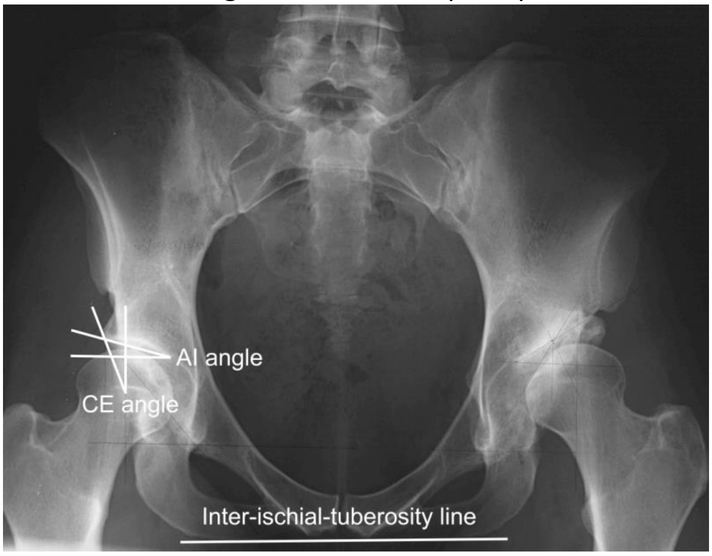

Figure 1. The Center-Edge (CE) angle [198] and the Acetabular Index (AI) angle Tönnis [182] measured on an anterior-posterior radiograph of patient with bilateral hip dysplasia. The right hip has a CE angle of 20˚ and an AI angle of 15˚. The left hip is severely dysplastic with a CE angle of -17˚ and AI angle of 8˚ and a large os acetabuli is seen. Also the left acetabulum is retroverted identified by the ischial spine sign.

The acetabular index (AI) angle by Tönnis [182] is formed by a line parallel to the inter-teardropline and a line from the lateral point to the medial point of the weight-bearing portion of the acetabulum (Figure 1). We chose, however, to replace the inter-teardropline with an inter-ischial tuberosity line because the position of the teardrop changes after PAO. According to Tönnis, normal values for Tönnis angle are below 10˚ [182], but other report normal values of 10 $\pm$ 2˚ [109]. Tallroth et al. also found the upper normal value to be 12˚ measured on CT images [174]. As hip dysplasia is often bilateral, the angles should be measures for both hip joints on the radiograph.

Osteoarthritis as a result of hip dysplasia

Patients with hip dysplasia are prone to develop osteoarthritis (OA) of the hip at a young age [31;203]. In the hip joint biomechanical factors seem to be important in development of OA, such as; joint incongruence due to developmental or congenital malformations [93], excessive high loads [91;110;111] due to reduced contact area between the acetabulum and the femoral head [117] and caused by a reduced abductor lever arm that increases the load per contact-area in the hip joint [83;189].

A degenerated or damaged labrum may initiate cartilage degeneration in dysplastic hips [75;90;113]. Labral lesions and acetabular rim fractures are results of the overload of the acetabular rim [90], and arthroscopic studies show that the labrum often is affected in dysplastic hips [113;114], supposedly because of the high strain placed on it due to reduced bony support. Also, cartilage degeneration and subchondral cysts generally arise in the anterolateral part of the acetabulum [133;205].

The above emphasise increased contact stress in the joint as a possible explanation for OA in hip dysplasia and it may indicate a simple understanding of OA. On the contrary, OA is complex whole joint disease with inflammatory mediators released by cartilage, bone and synovium. Subchondral bone may play a substantial role in the process, as a mechanical hamper, as well as a source of inflammatory mediators implicated in the OA pain process and in the degradation of the deep layer of cartilage [14].

Untreated severe dysplasia will invariably lead to OA [198], but the rate and the extent of secondary OA development in mild to moderate hip dysplasia is unknown [75]. OA in dysplastic hips is associated with increasing age, the severity of dysplasia measured by the CE angle and labral tears [82]. Aronson [9] argued that up to 50% of the patients with hip dysplasia would suffer from OA by the end of the fifth decade.

The initial clinical symptoms of OA are often vague, but usually is noncharacteristic pain in the groin present radiating to the anterior femur and the knee when loading the joint - especially at the end of range positions. The walking distance is reduced and some experience locking, snapping, weakness or instability of the hip joint [191]. When OA progresses most patients develop a loading triad: pain when a movement is initiated, followed by temporary alleviation, succeeded by worsening. The pain is often localized in the groin with pain radiating down the femur and the greater trochanter and possibly down to the knee. The overall hip function of the patients operated on at our institution is measured with either the Harris Hip Score [60], the Hip dysfunction and Osteoarthritis Outcome Score (HOOS) [129] or the Copenhagen Hip and Groin Outcome Score (HAGOS) [180].

The radiological symptoms of OA are narrowing of the joint space, increased sclerosis of the head and acetabulum, cysts in the head or acetabulum, osteophytes and later loss of sphericity of the femoral head. In these studies Tönnis' classification [182] is used to determine the grade of OA. A more quantitative method to estimate OA on x-rays is measuring the minimal joint space width [78]. Early OA before radiographic appearance can be detected with delayed gadolinium-enhanced MRI of cartilage (dGEMRIC), especially the dGEMRIC index in the anterior weight-bearing region of the hip is a useful predictor [86]. CT can be applied preoperative if there is uncertainty about the degree of OA anteriorly or posteriorly in the dysplastic hip joint. But it is challenging to assess early OA based on joint space width on CT images because no normal values exist for joint space width in the hip measured with CT which makes it difficult to assess whether the joint space with is reduced or if it is within normal biological variation. Complicating the matter further, the joint space width is not uniform in the hip joint; being lower in the posterior than in the anterior part.

PAO – the trans-sartorial approach

The Bernese PAO is one of the most frequently and successfully used techniques today [101] and it has become the gold standard for acetabular reorientation [181]. Professor Kjeld Søballe has further developed the Bernese technique to a minimally invasive surgical approach called the trans-sartorial approach [184]. All PAO procedures in patients included in this dissertation were performed with trans-sartorial PAO technique by professor Søballe.

Spinal anaesthesia is used with injection of a local anaesthetic into the subarachnoid space. The patient is positioned on a radiolucent table to allow use of fluoroscopy during surgery. The incision is made from the anterior superior iliac spine descending 7 cm along the sartorius muscle. The lateral femoral cutaneous nerve is located and isolated, and the inguinal ligament is cut at the attachment to the anterior superior iliac spine. In the direction of the fibers, the sartorius muscle is split and the deep fascia of the muscle is cut. The iliopsoas muscle and the medial part of the sartorius muscle are retracted medially to allow room for performing of the osteotomies. First the pubic bone is cut and then under fluoroscopic control the ischial osteotomies and the posterior iliac osteotomy are performed (Figure 2). For the latter, an oblique view is used to ensure that the cut is extra-articular and to avoid penetration of the posterior column of the acetabulum [166].

Figure 2. The use of fluoroscopy during PAO to control the osteotomies and avoid intra-articular cuts.

After the iliac bone is osteotomised, the acetabular fragment is reoriented; first adduction and then extension to optimise lateral and anterior coverage of the femoral head. The correction is performed by measuring the AI angle and the CE angle with a specially made measuring device peroperative, using the fluoroscope. The aim is an AI angle between 0-10˚ and a CE angle of 35˚ if possible (Figure 3).

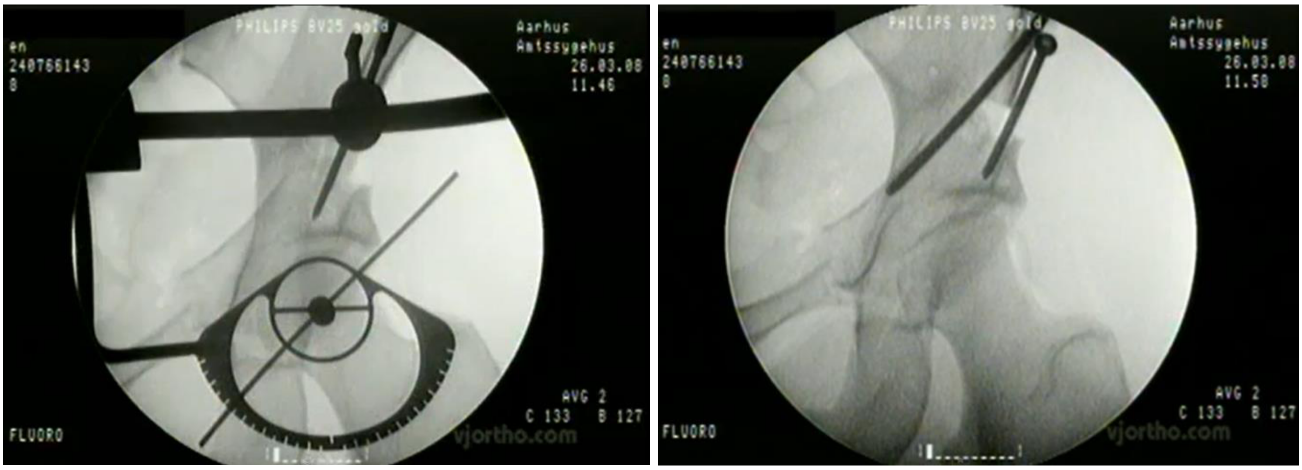

Figure 3. Measurement of the CE angle to assess the lateral coverage with a specially made device and fluoroscopy. The aim is a CE angle of 35˚. Control of position of the two cortical screws with use of fluoroscopy. Also the version of the acetabulum is evaluated and in this case the anterior rim is covering the femoral head well.

Care is taken not to overcorrect the position of the acetabulum which may result in impingement [126]. Intraoperative fluoroscopy is applied to evaluate the lateral and anterior coverage of the femoral head, the version of the acetabulum and the fixation of the two cortical screws inserted in the iliac crest into the medial aspect of the acetabulum (Figure 3). Before closing the operation field, local anaesthesia is infiltrated in the affected muscles. The mean duration of the operation is an hour and 10 minutes, average blood loss is 200 (150-350) ml, and the percentage receiving allogenic blood transfusions is 3.4% [185].

While in hospital (2-4 days) the patients are seen daily by a physiotherapist for active hip range of motion exercises. The patients are mobilised 6 hours postoperatively, and on the first day patients are allowed 30 kg of weight-bearing and given instructions in maintaining the weight-bearing limit with the use of crutches. During the hospital stay patients are instructed in a standardised rehabilitation program. The program is progressed by the physiotherapist after 6 weeks and the patients start walking with full weight-bearing after 6-8 weeks. In addition, the patients receives physiotherapy-supervised training twice a week starting 6 weeks after surgery until pre-set functional goals are achieved. The focus in the rehabilitation program is strength and stability training and normalization of walking. Control x-ray examinations are performed after 8 weeks. If the patients experience problems after 8 weeks, they are informed to contact the orthopaedic department.

After PAO, the goal is to decelerate the osteoarthritic process and patients ought to maintain appropriate body weight and live physically active lives with aerobic exercise or muscle strengthening exercise as recommended by the Osteoarthritis Research Society International (OARSI) and the European League Against Rheumatism (EULAR) as optimal treatment guidelines for the management of early hip OA [208-210]. As to pharmacological pain treatment of early hip OA paracetamol is first choice and NSAID, at the lowest effective dose, should be added or substituted in patients who respond inadequately to paracetamol. In patients with increased gastrointestinal risk, non-selective NSAIDs plus a gastroprotective agent, or a selective COX-2 inhibitor should be used.

The main advantage of the PAO (Bernese or trans-sartorial) compared to other pelvic osteotomies is that the posterior column is kept intact, conserving the stability of the pelvic ring. The implications are; that the patients can partial weight-bear on the first postoperative day and that the shape of the pelvis is minimally changed [188] hence majority of female patients will be able to deliver a child vaginally [191;192]. With trans-sartorial PAO surgical approach the tensor faciae latae muscle and the abductor muscles are kept intact and the sartorius muscle is split in fibre direction. Detached or cut abductor muscles can result in weakness in abduction strength of the hip and this is avoided with the trans-sartorius approach. Moreover, the osteotomised fragment is stable fixated with the use of only 2 screws [115]. Finally, PAO is more cost-effective than total hip arthroplasty (THA) in Tönnis grade-1 and grade-2 OA when the patient is young and when functionality in sports is important [162].

Labral tears

Patients with developmental dysplasia of the hip may present with acetabular rim overloading, labral hypertrophy, and tear. As shown by Parvizi et al. [141] isolated arthroscopic treatment of labral tear is likely to fail in most patients. Thus, hip arthroscopic treatment of the labrum is not a viable option in patients with evidence of abnormal hip morphologies and labral tear. Instead, three approaches exist to relieve symptoms in these patients namely; opening into the hip joint "arthrotomy" and attempt to repair the labrum as part of a PAO, perform PAO with concomitant arthroscopy or perform PAO followed by arthroscopic treatment at some point postoperatively if the patient still experiences pain and if a labral tear is confirmed by MRI with contrast. The rationale for the latter approach as applied at Aarhus University Hospital is that PAO normalises the distribution of force in the joint and relieves the strain on the rim and the labrum and hence alleviates the symptoms. The presence of labral tears in hip dysplasia has been observed in 78 - 94% of hips [47;102;116] and there is documented no difference in outcome when performing arthrotomy as part of a PAO or performing PAO with arthroscopic treatment after surgery if hip symptoms persist [61;107;170;185]. Whatever approach is used, there is biomechanical evidence that the labrum in dysplastic hips should be preserved during surgery [63].

Complications associated with PAO

PAO is a challenging surgical procedure, and the complication rate is initially high [50;163;187] but drops markedly with experience [38]. Nonetheless, beyond the learning curve the procedure is associated with a 5.9% risk of major complications [206]. With a steep learning curve [23], it is clear that the potential complications are numerous. The complications are not equally severe and can be divided into major, moderate and minor:

- Major: Intraarticular osteotomy, major nerve injury, deep vein thrombosis, arterial thrombosis, infection in joint, major haemorrhage, reflex sympathetic dystrophy, osteonecrosis of the acetabular fragment, osteonecrosis of the femoral head, subluxation of the hip [29;38;179].

- Moderate: loss of fixation, pubic or iliac non-union, excessive lateral or anterior correction leading to impingement, heterotopic ossification, haematoma, [26;38;124;189].

- Minor: transient lateral femoral cutaneous nerve dysaesthesias, superficial stitch abscess, removal of symptomatic screws [179].

An underlying diagnosis other than developmental dysplasia increases the prevalence of minor complications, while a major complication is more likely with longer surgery time, greater blood loss, and proximal femoral osteotomy [179].

Physical function after PAO

PAO offers good pain relief in symptomatic hip dysplasia [105;147;193] and results in an outcome comparable with that of total hip replacement [65]. Instead of compromising a subsequent hip replacement, PAO may improve results after hip replacement in dysplastic hips [13;142;191]. What does PAO offer in terms of physical function. Most studies have used surgeon or patient-reported outcome measures to evaluate function [12;51;52;120;170]. Few studies have measured function objectively. That is however very different from subjectively assessed function and often there is no significant correlation between subjective and objective function. Possible explanations for that paradox are that different factors independent of one's physical function affect how the individual rates function. Probably, pain, personality, ability to cope, satisfaction with the surgery and the treatment during hospitalization affect the way the individual perceives his or her physical function.

In two earlier studies from our institution we have investigated both objective and subjective function. In a cross-sectional study [73] kinematic data for walking and running were recorded in patients with hip dysplasia scheduled for PAO and in an age and gender-matched control group. An 8-camera motion-capture system and a force plate were applied and we found that the peak hip

extension angle during walking was significantly lower in the patients than in the controls. Also, the peak net joint moment of hip flexion during walking was lower in the patients than in the control group. In a similar gait analysis study, based on patients scheduled for the Bernese PAO, gait dynamics was measured and compared to a control group of healthy women. The patient group showed increased dorsiflexion of the ankle and knee flexion in the second half of the stance phase. The hip flexor joint moment in the patient group was reduced in the second half of the stance phase [145]. Both studies found lower hip flexion moment in patients compared to the control group which indicates weak iliopsoas muscles.
In a prospective study we evaluated walking and running in the same cohort of patients with hip dysplasia 6 and 12 months after PAO to investigate if movement was normalized [74]. We found that the peak joint moment of hip flexion increased 6 and 12 months after PAO compared with baseline during walking. In running, the improvement did not reach statistical significance after 12 months. In addition, the peak hip extension angle during walking increased 12 months after PAO but did not reach statistical significance. No significantly differences existed between the patients and healthy controls after 12 months for the hip extension angle and hip flexion moment which were our primary outcome measures. This means that based on these data and these primary outcomes, PAO does normalize gait and running for the outcome measures we investigated. Pedersen et al. also performed a follow-up study on their cohort 18 months after PAO [144]. They found that patients walked with increased extension angle of the knee joint during the entire stance phase compared to the preoperative movement pattern. The hip flexor moment was unchanged and lower than that of healthy control persons which is in contrast to our study. However, the study included only 9 patients and may be underpowered to detect an increased hip flexor moment.

Chapter 2 Methods and materials

In the following a general introduction to the overall principles for stereology, MRI, PET/CT and DEXA image production will be given. In addition, an overview of the included patients in the different studies will be outlined.

Stereology

Since stereological methods are used in four of the studies in this dissertation (I, III, IV, V), a general account of the main principles will be given.

Stereology is the three-dimensional (3D) interpretation of two-dimensional (2D) cross sections of biological structures. The methods are practical techniques for estimating quantitative information about 3D structures based on measurements from section planes or projections [57;136]. The biological structures we are interested in visualizing are 3D but with imaging modalities, we obtain 2D images. The amount of the cartilage that can be seen on each MR image is a small part of the entire articular cartilage in the hip joint and in each image, we only have access to 2D information. Stereology consists of methods to obtain 3D information from 2D images. Two-dimensional images generate a profile of the structures and with stereological methods, we can sample parts of the structure in such a way that conclusions from the samples can be drawn for the entire structure. It is time consuming to sample every image visualizing the structure of interest and thus we use systematic uniformly random sampling. Random sampling means that every image has an equal probability of being selected for the sample. Systematic uniformly random sampling is more efficient that random sampling and means that we take e.g. 4-5 images out of total 14 images. The systematic component is that we sample for instance every 3rd image and the random component is that we look up a number between 1-3. These images constitutes an unbiased sample of images covering the hip joint.

With stereological methods length, surface and volume of a structure can be measured. If we are interested in estimating length or surface area we have to deal with isotropy of the images or obtain the estimates from a spherical structure. Isotropy means that all directions of the image will have the same probability of being selected. The hip joint has a spherical shape (identical properties in all directions) and therefore isotropic and the assumptions for using stereological principles are met.

For estimates like volume, surface area and length, it is important that we convert them to total values. For this purpose we use the Cavalieris principle [136]. In study I we used a typical stereological method to estimate the thickness of cartilage in the hip joint (method 1 and 2). We sampled images applying systematic uniformly random sampling. We had a random start of image and test lines were used to estimate the thickness of the cartilage in each image. After that, these area estimates were summed and the mean cartilage thickness was calculated. In study III and V we used another stereological method to estimate the volume of bone cysts. All MR images through the hip were selected and test points were used to estimate the area of the cysts in each image. After that, these area estimates for each cyst were combined and multiplied with the distance between the images. This way we obtained estimates of the total volume of bone cysts irrespectively of their shape.

When using stereological methods to estimate length, surface area or volume, it is important that the image thickness is much thinner that the diameter of the structure one would like to measure. Otherwise, a large bias is introduced in the estimates, especially for volume [48].

MR Imaging (MRI)

MR imaging is used in study I, III, IV, V and a summary of image production is given. Atoms consist of a nucleus and a shell which is made up by electrons. In the nucleus there are protons which are positively charged. The protons are constantly spinning around an axis, in other words they are said to possess a spin. When the protons in a person are exposed to an external magnetic field in a MR scanner, the protons are aligned either parallel or anti-parallel to the direction of the magnetic field. This results in a magnetic field in the person, longitudinal to the external field. Moreover, protons in a strong magnetic field move around in a certain way called precession. The precession frequency is higher, the stronger the magnetic field is. When a person is positioned in the MR scanner, radiofrequency pulses are sent into the body to affect the alignment of the protons. Two things happen; some protons are lifted to a higher level of energy (decreasing the longitudinal magnetization) and the protons starts to precess in phase (creating a transversal magnetization). After the radiofrequency pulse is switched off, the protons go back to their lower level of energy and the longitudinal magnetization goes back to it's original value described by the longitudinal relaxation time (T_1). The transversal magnetization disappears when the radiofrequency pulse is switched off and this process is described as the transversal relaxation time (T_2). Different tissues have different relaxation times; water has long T_1 and T_2 and fat has short T_1 and T_2 [1].

Radiofrequency coils are used to send in the radiofrequency pulse to excite the protons and to receive the resulting signal. Different pulse sequences (series of radiofrequency pulses) can be used and the choice of pulse sequence will determine what kind of signal you get out of a tissue [1]. The sequence used in study I, III, IV and V was a fat-suppressed 3D fast low-angle shot sequence with a 50˚ flip angle. The time between two pulse sequences (TR) was 60 ms and the time between the radiofrequency pulse and the echo (TE) was 11 ms. This sequence provides images which presents cartilage with a hyperintense signal (white appearance) and subchondral bone with hypointense signal (black appearance). The sequence has been used to grade cartilage abnormalities in patients with hip osteoarthritis [130] and has been shown to be accurate for the detection of cartilage abnormalities in the knee joint [140;155].

The advantages with MR imaging are that the technique does not use ionizing radiation, which means that it is possible, and ethically sound to perform serial scans in patients over time, which we did with our cohort of patients in study I, III, IV and V. The appearance of a specific tissue e.g. cartilage can be enhanced by designing the acquisition protocol to assure excellent tissue contrast between different types of tissues [1]. Moreover, with MR imaging it is possible to acquire images in every plane in the body without reposition the patient [1]. MR imaging has high sensitivity and specificity to identify soft tissue pathology like hip labral tears or degeneration [24].

There are no known side effects from MR scanning but MR imaging is contraindicated in patients with pacemakers, defibrillators or other implanted electronic devices due to the metal being affected by the external magnetic field. Metal from e.g. hip or knee prostheses also disturbs the images acquisition and causes metal-related artifacts To reduce such artifacts the prosthesis should be positioned parallel to the direction of the main magnetic field, a small field of view, high-resolution image matrix and thin sections should be used [97]. With respect to hardware composition, a titanium alloy may help reduce metal-related artifacts. MR scanning is well tolerated by most patients although some patients do not like to be placed in the relatively narrow MR scanner. Also, certain types of MR contrast agents injected intravenously in high doses can be harmful for patients with severe kidney disease and should not be used in those patients. This should not be confused with the gadolinium contrast agent (diluted to a concentration of 2 mmol/l) injected directly in the hip joint as used in study IV for MR arthrography [146] or with the dGEMRIC technique which has been shown to improve delineation of hip joint cartilage compared to non-enhanced MRI [20]. We used MR arthrography to visualize labrum lesions since these are difficult to visualize and only two modalities can be used; either MR arthrography or ultrasonography performed by an experienced radiologist specialized in musculoskeletal ultrasonography.

Reproducibility

The reproducibility of MRI-based estimation of cartilage volume of the knee has been reported to be high with coefficient of variation (CV) between 3.2-5.4% [59]. This paper did not use the exact same scan protocol as we did in study I, III, IV and V. Thus, it is relevant to investigate the reproducibility of our scan protocol, with double scanning of the patients included in our studies in the scanner used in our study. We double MRI scanned 13 patients with hip dysplasia with a few minutes between scan and re-scan and with complete repositioning of the patients, the set-up of traction applied to the affected leg and the MRI system. Then one observer went through the two sets of images and measured the thickness of the cartilage with the three different stereological methods. Based on those measurements the CV and the coefficient of error of the mean (CE) could be estimated [57]. The CV ranged between 5-11%. For the method that was deemed optimal and used in study IV and V, the CV was 3-5%. For the method used in study III, the reproducibility of the stereological measurements based on double MR imaging was investigated on 13 sets of images and reported as limits of agreement. Both the CV and the limits of agreement describe the absolute reproducibility of a method opposed to the relative reproducibility. The limits of agreement for the stereological measurements of cyst volume based on MRI was -1.45 - 2.01 and the CV was 18% meaning the method was only moderately reproducible.

Positron Emission Tomography – Computed Tomography (PET/CT)

A combined PET/CT scanner has an x-ray tube and x-ray detectors located opposite each other in a ring to collect CT data and furthermore multiple rings of detectors that record the radioactive emission from the radiotracers used in PET scanning. The combined PET/CT scans provide 3D images that visualize the anatomic location of abnormal metabolic activity or functional processes in the body. The combined scans have synergistic advantages over PET or CT alone and minimizes their individual limitations [4]. CT produces shadow images resulting from the attenuation of x-rays by the body and the images provide very detailed images of the anatomy of the scanned area. Often low dose CT is used at PET/CT examinations, which is also the case in study VI. Before the PET/CT scanning a radiotracer is either injected into the body or inhaled as a gas. Gamma detectors with coincidence-circuits identify the emission from the radiotracer and an imaging device produces the PET images showing the distribution of the radiotracer. The CT scan takes a couple of minutes whereas the PET scan can take up to 90 minutes. The patients are informed to avoid movements during the scanning.

In study VI we used [O-15]-water to measure blood perfusion and [F-18]-fluoride to produce quantitative images interpreted as new bone formation in the acetabular fragment. The patients had an arterial line placed in the radial artery for blood sampling and continuous arterial blood activity was measured after injection of [O-15]-water. The mechanism of action of [O-15]-water is based on the distribution and clearance of water from the tissues [66]. Due to the small size of the water molecule, the distribution of [O-15]-water in the acetabular fragment reflects the tissue perfusion at the capillary level. Since water [O-15]-water is not chemically trapped in tissue, it will be cleared gradually from the tissue by blood flow and the larger the blood flow is, the faster the clearance occurs [66]. [O-15]-water has a half-life of 2 minutes and thus decays rapidly. Because of the rapid decay of [O-15]-water, the images are limited by noise when showing the distribution of water in acetabular fragment [66].

After injection of [F-18]-fluoride we collected 40 blood samples of arterial blood for the establishment of the time-activity curves used for kinetic modeling of the distribution of the [F-18]-fluoride which is a bone-specific tracer whose uptake depends on osteoblastic activity [54]. [F-18]-fluoride ions accumulates in the skeleton, especially in the axial skeleton (e.g. vertebrae and pelvis). [F-18]-fluoride diffuses through capillaries into bone extracellular fluid space, where it binds chemically at the surface of bone crystals, especially at sites of newly mineralizing bone [54]. Thus, increased [F-18]-fluoride will show up as areas of increased osteogenic activity on the PET images. [F-18]-fluoride has a half-life of 110 minutes and will essentially be cleared from the body within 24 hours after the injection. The patients are informed to drink plenty of water after the PET/CT scan to clear the body from radiotracers.

PET/CT examinations provide images and information on functional processes in the body that can not be obtained by any other imaging modality. The combined PET/CT is an advantage because it allows performing both examinations at the same time without having to reposition the patient and because the accuracy of the images is higher than what can be obtained from separate PET and CT examinations.

The disadvantages of the modality is that the radiation dose to the patient is relatively high, e.g. 4.9 mSv from each PET/CT examination used in study VI. Furthermore, the total examination time is long (3-4 hours) and because the PET scan is so lengthy, the patients might have difficulties in lying still which results in motion artifacts.

Reproducibility

One study has performed a double PET/CT scans to investigate the reproducibility of [O-15]-water to measure blood perfusion in tumors using the same method as used in study VI. They found measurements of blood perfusion in lung tumors were reproducible with an excellent intraclass correlation coefficient of 0.98 (95% CI 0.92–0.99) [194]. However, the intraclass correlation coefficient is a relative measure of reproducibility and it is highly influenced by the range of the measured values [10] and hence one should be careful to translate the results to another group of patients. There has been no studies performing double scans measuring blood perfusion in bone. Hence, the reproducibility of the method applied in bone is unknown but it is probably lower than in tumor tissue because blood perfusion and radiotracer clearance is slower in bone. Neither are any studies published on the reproducibility of measuring new bone formation with PET/CT and [F-18]-fluoride but a study has compared five different quantitative methods for the measurement of bone plasma clearance at the hip and lumbar spine using [F-18]-fluoride PET/CT [151]. All five methods strongly correlated but there were systematic differences between the results of the methods and the authors concluded that one should be cautious if comparing studies that use different methods of quantification of bone plasma clearance.

Dual-energy X-ray Absorptiometry (DXA)

The measurement principle of DXA is based on the differential absorption of x-rays of two different energy levels to distinguish tissues of different radiographic density [199]. Beams of low x-ray radiation is emitted below the scanner bed and passes through the body of the patient. Some of the x-rays that passes through the body will be absorbed by tissue. An x-ray detector inside the scanning arm measures the amount of x-ray that passes through the body and this data is used to produce an image of the scanned area. Digital imaging is used to identify the skeletal regions of interest followed by estimates of x-ray attenuation in these regions. With the use of an algorithm the attenuation at high and low energy x-ray radiation is compared and bone mineral density (BMD) in g/cm^2 can be estimated. At low energy (30-50 keV), bone attenuation is greater than soft tissue attenuation, whereas at high energy (> 70 keV), bone attenuation is similar to soft tissue attenuation [199].

The DXA derived BMD is not a true volumetric measure since it is based on the 2D x-ray projected area of a 3D structure. The third dimension, depth, is not directly measured because it is in the same direction as the x-rays. This contributes to an in-built error in the DXA derived estimations of BMD [199]. This error in the DXA measurements will be constant over time within the individual patient and hence it does not give rise to bias in the repeated DXA measurements in the cohort of patients followed for 2½ years in study II.

The time used for a DXA examination is short and the radiation is very low i.e. one DXA scan of the hip contributes with an effective dose of 0.0025 mSv to the patient [68]. Factors that affect the DXA performance are inconsistent patient positioning, patient movements during scanning, artifacts due to orthopedic hardware or clothing, positioning of the regions of interest and different observers selecting regions of interest and performing the analyses. Normally the regions of interest are generated automatically using edge-detection software but in study II, the observer manually drew the regions of interest to fit to each patient's acetabular anatomy because the regions had to be fitted between the screws inserted at PAO and this procedure may have affected the reproducibility of the measurements. DXA is not as precise as CT when it comes to examining very small regions of interest as we did in study II which may explain why we detected changes in bone density after PAO in an earlier CT based study [118] and not in study II. Furthermore, DXA does not enable the observer to differentiate between cortical and trabecular bone. And finally, the DXA-derived estimation of BMD tends to overestimate the BMD of tall and heavy individuals [55;207].

Reproducibility

DXA-derived measurements of bone mineral content has a high accuracy. The gold standard for measuring bone mineral content is laboratory assessment of ashed bones, and DXA measurements of bone mineral content are within 7–9% of ashed bone measurements [16]. In study II we investigated the reproducibility of DXA-derived regions of interest. We performed double DXA examinations with 5 patients with complete repositioning of the patients and the DXA equipment and calculated the limits of agreement, which represent the differences between double scanning for 95% of a population. The limits of agreement for our measurements of the region of interest were -021-0.16 g/cm^2 for the smallest region of interest and -0.17-0.01 g/cm^2 for the largest region of interest. The reproducibility of our method was only moderate also when compared to other studies reporting CV of 5% for DXA of the hip [106]. The CV varies with each observer, each region of interest and probably with each patient population and should be investigated in each individual study. Nevertheless, it is foreseeable that using standard DXA software for the femoral trochanteric region and larger regions of interest will result in a higher reproducibility than in an experimental set up with very small regions of interest close to metal screws.

Overview of the included patients

The patients included in the studies were all diagnosed with hip dysplasia and either scheduled for PAO or had already been operated with PAO at Aarhus University Hospital. The vast majority of patient have been operated by professor Kjeld Søballe and a small number of the patients have been operated by other surgeons who were learning the operational technique. To be scheduled for PAO and to be included in the studies the patient had to fulfil the following inclusion criteria: radiologically diagnosed hip dysplasia with a CE-angle < 25° [198], pain and reduced function, OA degree ≤ 1 according to the criteria of Tönnis [37], minimum 110° flexion in the hip and good rotation and closed growth zones in the pelvis. For all studies except study VII following exclusion criteria were used: Diseases that predispose to hip dysplasia (e.g. Down's syndrome, Charcot-Marie-Tooth disease, Ehlers-Danlos syndrome, cerebral paresis, meningomyelocele), Legg-Calvé-Perthes disease, need for a femoral intertrochanteric osteotomy, previous surgery of the hip, non-spherical femoral head, subluxated femoral head (interrupted Shenton's line ≥ 5 mm), pregnancy or potential pregnancy, metal implants such as pacemaker (study I, III, IV, V). Study VII included patients from a clinical database with all PAO operated patients at Aarhus University Hospital and only patients with diseases predisposing to hip dysplasia, diseased or immigrated patients and patients whose address could not be retrieved were excluded from the study. Ethical approval was obtained from the Central Denmark Region Committee on Biomedical Research Ethics for all studies except study VII and VIII.

In the Table below is an overview of the included patients in the different studies:

Study	N	Gender Female/male	Age in years median (range)	Time of inclusion	Of note
I	26	22/4	39 (19-53)	2003-2004	Cohort included to be followed over time with serial scans
II	28	25/3	41 (19-53)	Same cohort as study I. Two patients were excluded from study I due to metallic implants. Those two patients were included in study II	
III	26	22/4	39 (19-53)	Same cohort as study I	Same values for CE, AI angle and pain presented in tables in study III and IV since cohort is the same
IV	26	22/4	39 (19-53)	Same cohort as study I	Same figure illustrating the stereological method presented in study I and study IV since same methodology was used
V	26	22/4	39 (19-53)	Same cohort as study I	
VI	12	9/3	33 (23-55)	2005-2007	
VII	388	311/77	40.5 (18-72)	2012	Mean age instead of median age presented
VIII	23 PAOs	-	-	2005	

Chapter 3

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Cartilage thickness in the hip joint measured by MRI and stereology – a methodological study

I. Mechlenburg M.Sc.†*, J. R. Nyengaard M.D., D.M.Sc.‡, J. Gelineck M.D.§ and K. Soballe M.D., D.M.Sc.†

† *Department of Orthopaedics, University Hospital of Aarhus, Denmark*

‡ *Stereologic and Electron Microscopy Research Laboratory and Mind Center, University of Aarhus, Denmark*

§ *Department of Radiology, University Hospital of Aarhus, Denmark*

Abstract

Objective: The purpose of this study was to develop a precise and efficient method for estimating the thickness of the articular cartilage in the hip joint and hence three different stereologic methods were tested based on Magnetic Resonance Imaging.

Design: Twenty two females and four males with hip dysplasia underwent MRI. The thickness of the femoral and acetabular cartilage was estimated.

Results: The results for all three methods showed that the observed total variance on cartilage thickness is small. The mean thickness of the acetabular cartilage measured by the three different methods ranged between 1.15 mm and 1.46 mm. The mean thickness for the femoral cartilage measured by the three different methods ranged between 1.18 mm and 1.78 mm. The measurements took 15–20 min per hip to carry out.

Conclusion: Methods 1 and 3 are as precise but we favour method 3 because the measurements are done on images obtained through the center of the femoral head which means that the cartilage surface is intersected perpendicular and partial volume effect avoided. We suggest that this method can be advantageous for assessing the progression of osteoarthritis in dysplastic hips after periacetabular osteotomy.

Key words: Magnetic resonance imaging, Hip dysplasia, Stereology, Cartilage.

Introduction

Magnetic resonance imaging (MRI) is non-invasive and non-ionizing, thus advantageous for assessing the progression of osteoarthritis in dysplastic hips. Articular cartilage has minimal reparative potential and degeneration of the cartilage surface leads to osteoarthritis. The point at which accumulated microdamage becomes irreversible is not known[1].

Periacetabular osteotomy has been introduced to improve acetabular coverage of the femoral head and reduce the risk of secondary osteoarthritis in patients with symptomatic hip dysplasia[2,3]. When periacetabular osteotomy is performed the results of surgery are largely dependent on the degree of preoperative osteoarthritic involvement[4]. As periacetabular osteotomy is performed on dysplastic hips to prevent osteoarthritic progression, changes in the thickness of the articular cartilage is a central variable to follow over time. When periacetabular osteotomy is performed and contact pressure on cartilage is reduced, additional joint degeneration is assumed to be slowed or prevented unless irreparable damage to the cartilage has happened at the time periacetabular osteotomy is performed. Studies have described different methods based on MRI to visualize and quantify articular cartilage thickness[5–7]. In order to develop an unbiased and precise method to quantify cartilage thickness, stereologic methods are useful. Stereologic methods are used to obtain quantitative information about three-dimensional structures based on observations from section planes or projections.

The purpose of this study was to develop a precise and efficient method for estimating the thickness of the articular cartilage in the hip joint and hence three different stereologic methods based on MRI were investigated. Such a stereologic method can be used to evaluate the effect of periacetabular osteotomy and give a better indication for surgery.

Material and method

The study was accepted by the local ethical committee. After signed consent, 22 females and four males presenting 26 dysplastic hips were studied. Median age was 39 (19–53) years and all patients had spherical femoral heads. The patients were scheduled for periacetabular osteotomy and had the following radiologic and clinical characteristics: center-edge angle of Wiberg was 24° or less[8], osteoarthritis degree 0 or 1 according to the classification of Tönnis[9], closed growth zones in the pelvis, symptomatic/painful hip and

*Address correspondence and reprint requests to: Inger Mechlenburg, Praestevaenget 5, 5871 Frorup, Denmark. Tel: 45-65371093; Fax: 45-89497429; E-mail: inger.mechlenburg@ki.au.dk

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minimum 110° flexion in the hip joint. Excluded from the study were patients with metal implants, cases where the dysplasia might have been caused by neurological illnesses, Legg–Calvé–Perthes disease or sequelae after earlier hip surgery. Also, patients where an intertrochanteric femoral osteotomy was necessary were excluded from the study.

MAGNETIC RESONANCE IMAGING

The examinations were performed on a 1.5 Tesla MRI scanner (Siemens, Erlangen, Germany) using a body array surface coil. A fat suppressed three-dimensional FLASH sequence was used. The imaging matrix was 256 × 256, field of view 220 × 220 mm with a section thickness of 1.5 mm, TR/TE 60.0/11.0, with a flip-angle of 50° and time of acquisition was 9.38 min. To show the acetabular and femoral cartilages separately, an ankle traction device was used during MRI. This device pulled the leg distally with a load of 10 kg.

DOUBLE EXAMINATIONS

The first 13 patients were examined twice within a few minutes, with complete repositioning of the patient and set-up in order to obtain an estimate of precision of the method used.

STEREOLOGIC METHODS

Three different stereologic methods to measure the thickness of cartilage were tested and evaluated for precision and efficiency. The assumption of using these principles is either to use isotropic images or to deal with a spherical surface. Based on X-rays of all included patients, we assumed that the femoral heads were spherical. We opened the MR images and measured the cartilage thickness in a software (Grain 32, Dimac and KT Algorithms) designed for stereological purposes. The measurements were performed manually by one person without knowledge of clinical data or results of other examinations. The interface between femoral and acetabular cartilage was identified as a result of the traction device used during MRI. The interface between cartilage and bone was uncomplicated to discriminate in most images.

Method 1: On the sagittal images of the hip joint every third image per series was sampled which added up to four to five images. In the software a grid of approximately 15 vertical test lines was selected and located on the images and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was manually measured (Fig. 1). Approximately 60–80 measured distances were summed and the mean distance/thickness of the acetabular and femoral cartilage, respectively, was calculated[10].

Method 2: On the sagittal images of the hip joint every third image per series was sampled which added up to four to five images. A grid of approximately 15 vertical test lines was selected and located on the images and where the test lines intercepted the cartilage, the distance following the direction of the test line through the cartilage was manually measured (Fig. 2). Approximately 60–80 measured distances were summed[11] and the mean distance/thickness of the acetabular and femoral cartilage, respectively, was calculated.

Method 3: Four reconstructed images through the center of the femoral head were used (Fig. 3). This consisted of a sagittal, a coronal and two images placed 45° between coronal and sagittal. On each of the four images a grid of 15–20 radial test lines was selected and located on the images and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was manually measured [Fig. 4(a–d)]. Approximately 60–80 measured distances were summed and the mean distance/thickness of the acetabular and femoral cartilage, respectively, was calculated.

The precision of the estimates depends on the methods used and the objects investigated[12]. In addition to calculate the observed total variation (CV = SD/mean) of the cartilage thickness, it can also be determined if the variation stems primarily from the stereologic procedure or from the biological variation of cartilage thickness. This can be done by

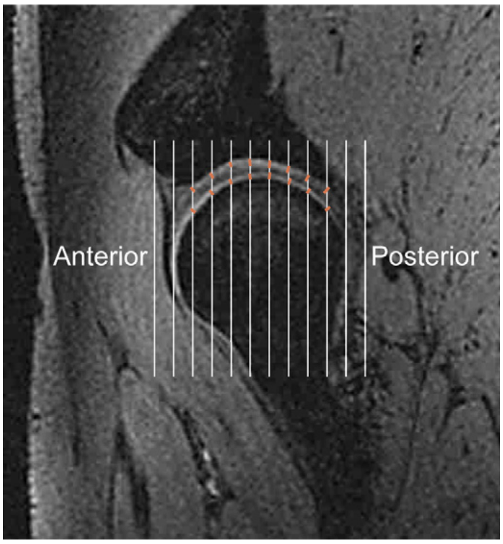

Fig. 1. A grid of vertical test lines was placed on the images and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was measured.

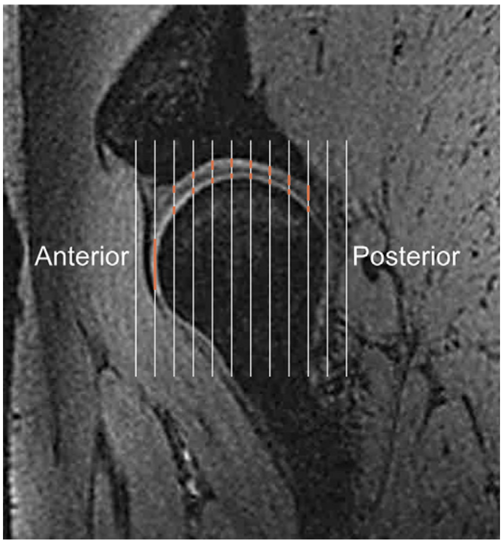

Fig. 2. A grid of vertical test lines was placed on the images and where the test lines intercepted the cartilage, the distance following the direction of the test line through the cartilage was measured.

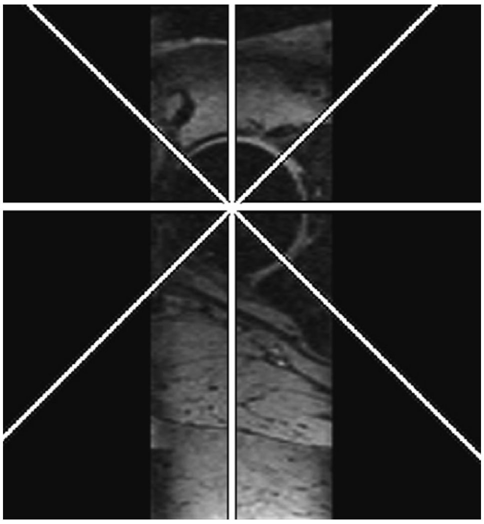

Fig. 3. Axial slice of the femoral head showing how the Four reconstructed MR images through the center of the femoral head are positioned.

calculating the error variance (CE = SEM/mean) which is an estimate of the variation of the stereologic procedure and knowing that we also can identify the influence of the stereologic procedure on the total variation. We estimated the precision of the methods by performing double measurements on images of 13 patients who had the MRI procedure repeated within few minutes with complete repositioning of the patient and set-up. After double measurements the coefficient of variance (CV) and the coefficient of error of the stereologic procedure (CE) were estimated for the thickness of the acetabular and femoral cartilage[12,13].

Results

The mean thickness for the acetabular and femoral cartilage estimated with the three described methods is shown in Table I. The observed total variation was highest for method 2 which makes the least precise method of the three. Methods 1 and 3 do equally well in relation to total variation and error variance. The two methods are quite similar but the estimations in method 1 are based on sagittal images whereas the measurements in method 3 are performed on center images. All three methods took 15–20 min per hip to carry out.

The effect on error variance of method 3 if sampling fewer measurements is shown in Fig. 5.

Discussion

All the three methods (1–3) tested in this study were swift and reproducible, but produced different mean cartilage thickness estimates. The stereologic sampling procedure deployed in method 2 yielded a CV^2 twice as high as methods 1 and 3 in the same patients.

Precision was equally good in methods 1 and 3; but we favour the former because it deploys images obtained through the centre of the femoral head allowing perpendicular cartilage surface intersection. We thereby avoid the potential bias (partial volume effect) that may otherwise arise from oblique intersection of the cartilage of the femoral head because of its spherical form and the parallel nature of the imaging planes.

The results for all three methods showed that the observed total variance (coefficient of variation, CV) on cartilage thickness is small. CV includes the biological variation, CV(bio), and error variance of the method (coefficient of error of the mean, CE). The following relationship exists: $CV^2 = CV^2(\mathrm{bio}) + CE^2$. Normally, a study is designed such that $CE^2/CV^2 \sim 0.2–0.5$, because the CE will then only have a limited influence on the total variation (CV)[12]. In this study, $CE^2/CV^2 = 0.08$ for method 1, $CE^2/CV^2 = 0.06$ for method 2 and $CE^2/CV^2 = 0.08$ for method 3. This means that the methodological error variance has basically no influence on CV.

We also studied the effect on CE at a lower number of measurements to test the effect of reducing the overall time consumed by these methods.

Using one half of the measurements for cartilage thickness estimation produced a CE of 0.03. With 1/4 of the measurements, the CE was 0.05, with 1/8 0.08 and with 1/16 0.11.

Based on CE, sampling of 1/8 of the measurements (no. approx. 10) will produce an acceptable error variance of the method and time consumption will drop to about 5 min per hip. However, given the heterogeneity of cartilage loss in osteoarthritis caused by hip dysplasia it is likely that the dependency of measurement precision on sampling increases with the severity of disease. It is also possible that the relative performance of the three methods varies with the severity, heterogeneity and distribution of cartilage loss. In the first place we have tested these methods for precision. The next move is to refine method 3 in order to make it possible to measure cartilage thickness in four quadrants. This will enable us to identify the distribution of cartilage loss.

Joint space narrowing in the weight-bearing area is a well-known radiological finding in hip osteoarthritis indicative of articular cartilage wear in the weight-bearing area[14]. However, the threshold of clinical relevance[15] of such narrowing is difficult to establish because it is often classified qualitatively[16]. A subjective qualitative assessment of joint space narrowing is not sufficient for drawing conclusions about cartilage thickness as joint space narrowing does not appear before osteoarthritis has progressed as shown by Nishii *et al.*[17] who detected a high prevalence of cartilage abnormalities in 70 dysplastic hips without joint space narrowing. For that reason estimating the cartilage thickness by the presented stereologic methods based on MRI may be used as a means of early diagnosis of osteoarthritis before the radiographic change is evident. MRI and traction can be applied to patients with hip dysplasia in order to evaluate the cartilage thickness before deciding to perform a periacetabular osteotomy. If the articular cartilage is shown obviously thin and irregular on MRI, periacetabular osteotomy may be avoided[18].

In addition, MRI and traction can evaluate cartilage abnormalities of the acetabulum and femoral head separately. Nishii *et al.*[19] conducted MRI evaluations in patients with hip dysplasia and found that abnormalities of the acetabular cartilage seemed to occur earlier than those of the femoral cartilage in general. Hasegawa *et al.*[16] reported on the basis of MRI that acetabular sclerosis preceded femoral head sclerosis in dysplastic hips and another study disclosed a significant tendency for more frequent occurrences of cysts in the acetabulum than in the femoral head[20]. This might be due to the limited area where the main load transfer occurs in the acetabular cartilage as compared with the femoral cartilage during gait and stairs climbing in the

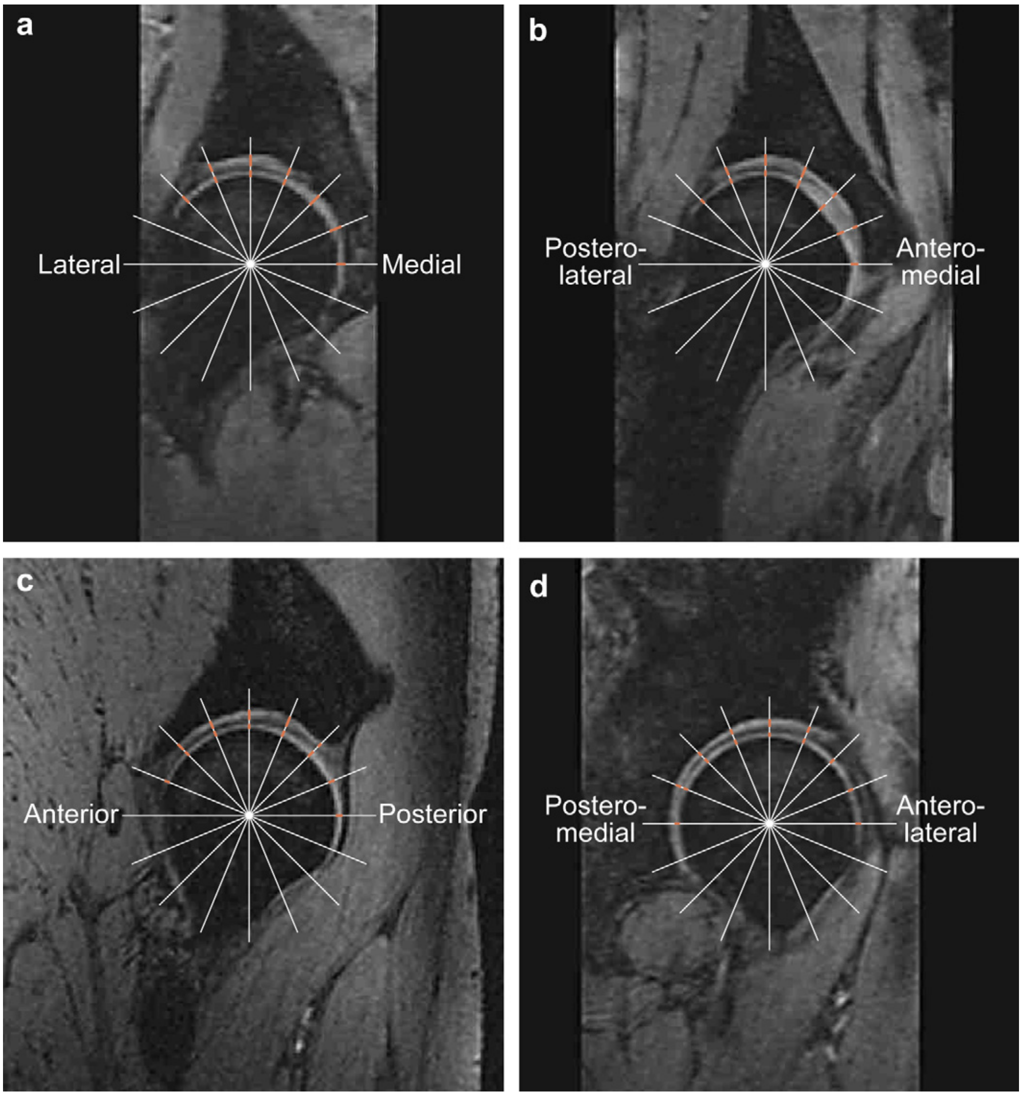

Fig. 4. (a–d) On each of the four images a grid of radial test lines was placed and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was measured.

patient with hip dysplasia[19]. Biomechanical analysis of the dysplastic hip joint has shown that the compressive stress is extremely high at the anterosuperior portion of the weight-bearing area[21,22]. Several clinical studies on dysplastic hips support these results by showing that articular cartilage degeneration appears mainly in the anterosuperior part of the weight-bearing area of the femoral head and acetabulum[17,23,14].

Nakanishi *et al.* measured cartilage thickness of the femoral head with MRI and traction on 10 normal volunteers[24]. They found the cartilage to be thickest in the central portion around the ligamentum teres (mean 2.8 mm). The medial and the lateral portions were almost of the same thickness (medial 1.3 mm, lateral 1.1 mm). Nishii *et al.* made computational analysis of MRI and found average cartilage thickness to be significantly greater in dysplastic hips than in normal hips (1.77 mm vs 1.34 mm)[25]. In another study the cartilage thickness of the femoral head on six cadavers was measured using different MRI pulse sequences and in that study the measured mean thickness of the cartilage

Table I
Thickness of acetabular and femoral cartilage, standard deviation (SD), coefficient of variation (CV) and coefficient of error of the mean (CE)

Acetabular cartilage					Femoral cartilage				
Method	Thickness (mm)	SD (mm)	CV	CE	Method	Thickness (mm)	SD (mm)	CV	CE
1	1.15	0.05	0.05	0.01	1	1.22	0.06	0.05	0.01
2	1.46	0.17	0.11	0.03	2	1.78	0.20	0.11	0.03
3	1.26	0.04	0.03	0.01	3	1.18	0.06	0.05	0.02

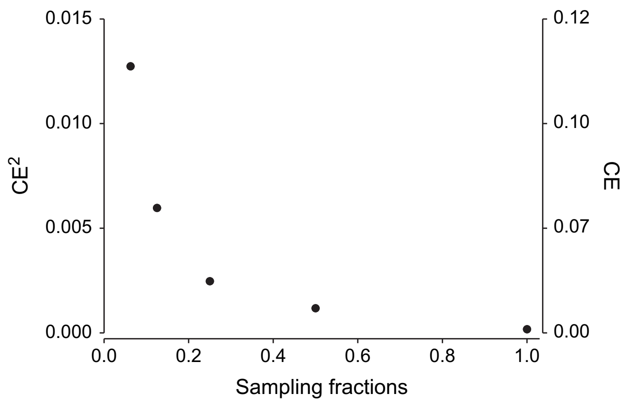

Fig. 5. The effect on error variance of method 3 when sampling fewer measurements.

ranged between 1.36 mm and 1.70 mm.[26] These measurements of cartilage thickness are not directly comparable to our results but they seem to be somehow greater than what we found in this study. The cause of this discrepancy is not based on chemical-shift as we used fat-suppression which eliminates this phenomenon.

Also, we have investigated if metallic artefacts from the screws inserted in the pelvis at periacetabular osteotomy pose a potential problem for these methods used. There are only minor artefacts from the titanium screws and these do not interfere with the measurements of cartilage thickness.

In conclusion, methods 1 and 3 were as precise but we favour method 3 sampling four reconstructed images through the center of the femoral head and using radial test lines because using this method we avoid partial volume effect. We suggest that the method can be advantageous for assessing the progression of osteoarthritis in dysplastic hips after periacetabular osteotomy.

Acknowledgments

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Chapter 4

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ORIGINAL STUDY

No change detected by DEXA in bone mineral density after periacetabular osteotomy

Inger MECHLENBURG, Søren KOLD, Kjeld SØBALLE

From the University Hospital of Aarhus, Denmark

The purpose of this study was to assess acetabular bone mineral density after periacetabular osteotomy and to examine whether bone mineral density correlates with postoperative migration of the osteotomised acetabular fragment. Twenty-five female and three male patients scheduled for periacetabular osteotomy were consecutively included. The patients were scanned by dual energy X-ray absorptiometry (DEXA) at 1 week, 1 year, and 2½ years after surgery. Radiostereometric analyses (RSA) were done at 1, 4, 8, and 24 weeks after surgery. Two and a half years after periacetabular osteotomy, no significant changes in bone mineral density or any biological effect on bone remodelling due a changed loading pattern in the acetabulum could be detected. There was no significant correlation between bone mineral density and migration of the acetabulum.

Dual energy X-ray absorptiometry is not an appropriate method to demonstrate the changes in bone mineral density after periacetabular osteotomy or to predict postoperative acetabular migration.

Keywords : periacetabular osteotomy ; bone mineral density ; DEXA.

INTRODUCTION

Periacetabular osteotomy (PAO) is a well-established joint preserving procedure (*7*) that offers good pain relief in symptomatic hip dysplasia (*16,24*). PAO increases acetabular coverage (*14*) and medialises the femoral head (*4*) (fig 1). As a result, the distribution of load in the hip joint is altered after surgery.

We conducted a study employing dual energy X-ray absorptiometry (DEXA) to estimate bone mineral density (BMD) in the acetabulum after surgery. In the same group of patients, radiostereometric analysis data (RSA) (*13*) were obtained to determine whether correlation exists between BMD and the postoperative migration of the acetabular fragment.

Our hypothesis was that bone density would decrease in the lateral part and increase in the medial part of the acetabulum after PAO and we hoped to find a biological confirmation of the effect of the PAO on the load redistribution within the hip joint. Increased bone density may be a remodelling

■ Inger Mechlenburg, MSc, PhD, Postdoc Fellow.
■ Søren Kold, MD, PhD, Consultant Orthopaedic Surgeon.
■ Kjeld Søballe, MD, DMSc, Professor.
Department of Orthopaedics, University Hospital of Aarhus, Denmark.
Correspondence : Inger Mechlenburg, c/o secretary Tina Stenumgaard, Department of Orthopaedics, University Hospital of Aarhus, Tage-Hansens Gade 2, 8000 Aarhus C, Denmark.
E-mail : INGER.MECHLENBURG@KI.AU.DK

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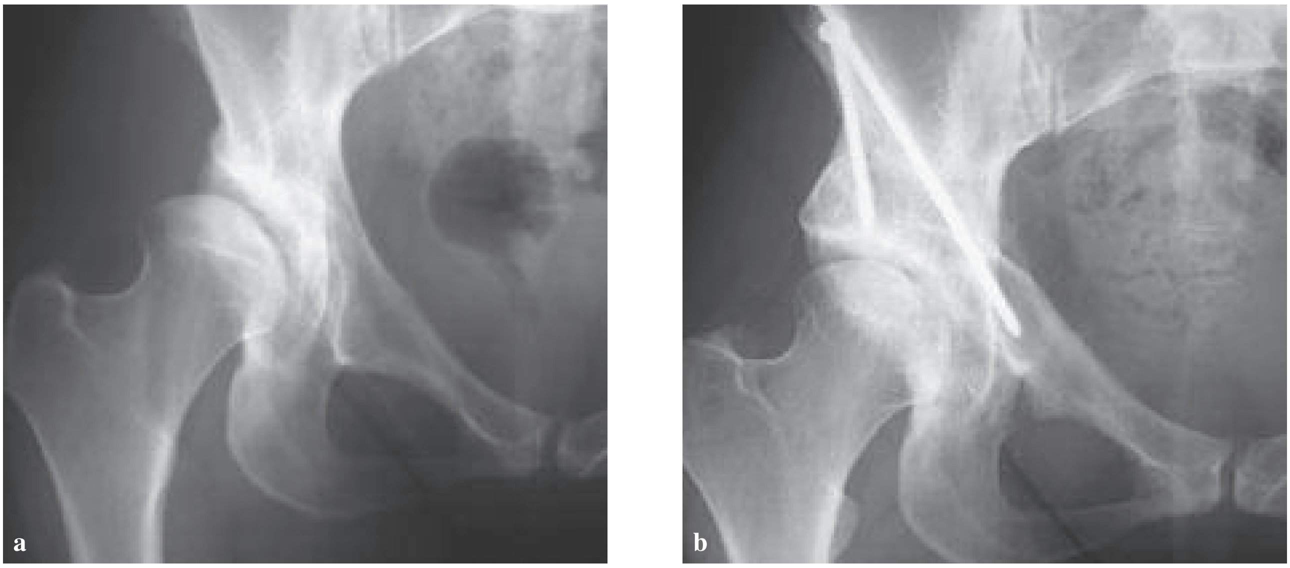

Fig. 1(a-b). — Radiograph before and 6 months after periacetabular osteotomy. Preoperatively (1a), insufficient coverage of the femoral head and acetabular roof obliquity. Postoperatively (1b), the femoral head is covered by the acetabulum and the acetabular roof is horizontal.

response caused by changed load distribution in the hip joint or a higher level of physical activity (*15*), but it could also indicate progression of the osteoarthritis (*1,19*).

We also hypothesised that the degree of migration of the acetabular fragment was correlated to acetabular bone density. Low acetabular bone density might result in poor primary fixation of the cortical screws, and consequently to migration of the osteotomised acetabular fragment from the re-oriented position after surgery. If a correlation was found, dual energy X-ray absorptiometry (DEXA) could be helpful preoperatively to determine the risk of migration. If a threshold value was found, it could be an argument to avoid PAO in those patients at risk or to consider alternative fixations in these cases.

MATERIAL AND METHODS

The study was designed as a case series and accepted by the local ethics committee. After signed consent, 28 patients, 25 females and 3 males, scheduled for PAO were consecutively included. A minimally invasive transsartorial approach was used (*21*). The median age of the patients was 41 (19-53) years.

The patients were DEXA scanned three times : 7 days (5-12 days), 1 year, and 2½ years after PAO. A hologic QDR 2000 dual-energy X-ray densitometer, USA (200 Volts AC, 50 Hz, 8.5 Amps) was used. The patients were positioned supine in a standardised manner with the legs secured in neutral rotation by a frame (fig 2).

BMD was calculated on the DEXA images in two-well defined regions of interest (ROI). The ROI's were drawn starting at the acetabular joint line and extended 1.4 cm proximally (fig 3). ROI one (R1) was located laterally to the lateral screw, and ROI two (R2) between the lateral and the medial screw. These regions were not exactly the same from patient to patient because the position and size of the ROI depended on the individual's acetabular anatomy and the position of the screws. However, for each patient the same ROI's were used at all follow-up scans. All BMD analyses were completed by one technician 2 days after the whole series of DEXA images had been taken to ensure identical positioning of the ROI.

We examined whether we would obtain the same BMD value at a second measurement under identical conditions. Thus, to estimate the precision of the applied method, double scanning with complete repositioning of the patient and set-up was performed on five patients one year postoperatively. ROI location and BMD measurement were done by the same person who had performed all other measurements.

Fig. 2. — Patient positioned supine on scanner bed with legs secured in neutral rotation by a frame.

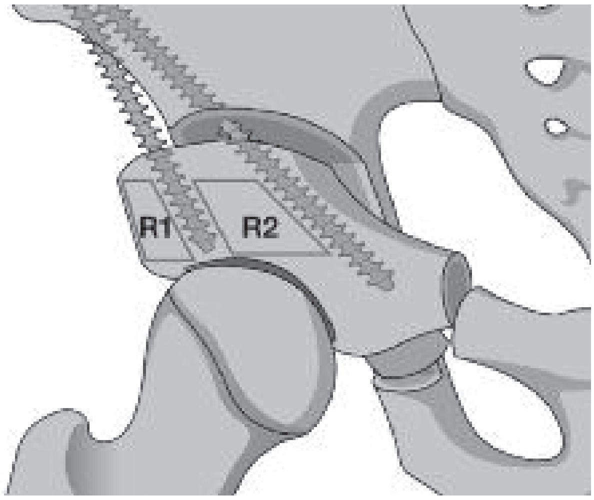

Fig. 3. — Position of the regions of interest : R1 and R2. The size of R1 is approximately 2 cm^2 and for R2 4 cm^2. The same technician placed all ROIs on all DEXA images to ensure similarity in positioning of the ROIs.

During PAO, five tantalum markers (1 mm) were inserted into the acetabular fragment and five markers (0.8mm) were inserted into the iliac bone above the fragment to enable radiostereometric analysis. With the patient supine on the scanner bed and a calibration box (Carbon Box Aarhus, MEDIS, Netherlands) placed beneath the patient, a 3D coordinate system of the tantalum markers was created. The patient was exposed to two simultaneously firing X-ray tubes (150 microSv, 96 kV and 13 mAs) positioned at a 40° angle to each other. One week after surgery, the first stereo radiograph was taken, and the initial position of the acetabular fragment was determined in relation to fixed points on the iliac bone. Follow-up radiostereometric examinations were performed at 4, 8, and 24 weeks postoperatively. The software (RSA-CMS, MEDIS, the Netherlands) allows a precise calculation of the migration of the acetabular fragment between examinations (*22,23*), expressed as translation and rotation of the centre of gravity of the markers inserted into the acetabular fragment.

Postoperative BMD data were tested for correlation with data for acetabular migration with Pearson's coefficient of correlation. Two-tailed tests were used and the p-values were considered significant if $p < 0.05$. The effect size for the paired t-test was calculated (*25*) to demonstrate the magnitude of the difference between BMD at baseline and 2½ years postoperatively, independent of sample size. Precision of the DEXA method used was calculated as 95% limits of agreement (*2*).

RESULTS

Three patients were lost to final follow-up and two DEXA images could not be analysed, leaving us with data concerning 23 patients of the 28 included. We found that BMD was unchanged 2½ years postoperatively compared with BMD immediately after and 1 year after surgery for the lateral ROI as well as for the medial ROI (table I).

There was no significant correlation between baseline BMD in the lateral ROI and postoperative migration of the acetabulum or between baseline BMD in medial ROI and postoperative migration of the acetabulum (table II).

The limits of agreement (LOA) between repeated BMD results obtained by double scanning were calculated. Given the first BMD measurement for the lateral ROI, we could expect with 95% confidence that the difference to the second measurement would be between - 0.21 – 0.16 g/cm^2 (fig 4). For the medial ROI, the LOA was - 0.17 – 0.01 g/cm^2 (fig 5).

Table I. — Bone mineral density (BMD) measured 1 week postoperatively (baseline), and 1 and 2½ years after surgery in a lateral and a medial region of interest (ROI)

	Lateral ROI			Medial ROI		
n = 23	Baseline	1 year	2½ years	Baseline	1 year	2½ years
Mean BMD g/cm^2	1.41	1.33	1.26	1.78	1.84	1.74
95% CI for mean	1.20 – 1.62	1.15 – 1.51	1.07 – 1.45	1.60 – 1.96	1.63 – 2.05	1.52 – 1.97
SD	0.52	0.43	0.46	0.43	0.52	0.55

Table II. — Correlations between bone mineral density (BMD) at baseline in lateral and medial regions of interest (ROI) and migration of the acetabular fragment in translation and rotation 6 months after surgery (n = 23)

		Lateral ROI (R1)	Medial ROI (R2)	Medial translation	Proximal translation	Posterior translation	Anterior tilt	Internal rotation	Adduction
Lateral ROI (R1)	Pearson Correlation	1	.140	.243	.192	.347	-.256	.248	.272
	Sig. (2-tailed)		.524	.222	.338	.076	.197	.212	.170
Medial ROI (R2)	Pearson Correlation		1	-.143	-.130	-.201	.303	-.298	.041
	Sig. (2-tailed)			.516	.554	.357	.159	.168	.854
Medial translation	Pearson Correlation			1	.792	.286	.025	.041	.006
	Sig. (2-tailed)				.000	.113	.893	.823	.975
Proximal translation	Pearson Correlation				1	.040	.138	-.076	-.119
	Sig. (2-tailed)					.828	.450	.678	.517
Posterior translation	Pearson Correlation					1	-.158	.133	.155
	Sig. (2-tailed)						.387	.469	.398
Anterior tilt	Pearson Correlation						1	-.993	-.998
	Sig. (2-tailed)							.000	.000
Internal rotation	Pearson Correlation							1	.993
	Sig. (2-tailed)								.000
Adduction	Pearson Correlation								1
	Sig. (2-tailed)								

DISCUSSION

Several factors may explain why acetabular bone density did not change over time as a result of PAO. First of all, the resolution of DEXA images is poor, making it difficult to clearly identify the acetabular joint line and to position the ROI at exactly the same place on all images. Secondly, our ROIs were small (2-4 cm^2) and thus more sensitive to small changes in positioning in the same patient. The operator had to construct the ROI to suit the individual anatomy of the patients, and she attempted to choose the same ROI on later images obtained from the same patient. Thirdly, our method, based on double scanning, was not sufficiently precise. Other studies show that DEXA of the hip joint is a precise method for determining BMD when positioning and rotation are strictly controlled (*5,6,10,18*). But in this study, the LOA for the lateral ROI was - 0.21 – 0.16 g/cm^2, meaning that if we have a first BMD measurement of 1 g/cm^2, the next measurement on the same patient could show everything from 0.79 g/cm^2 to 1.16 g/cm^2. This is not precise enough to identify the small changes in BMD expected to occur in our study. After having analysed our data statistically, we knew the variation of the data, and we were able to calculate the number of patients that should have been included in the study to detect

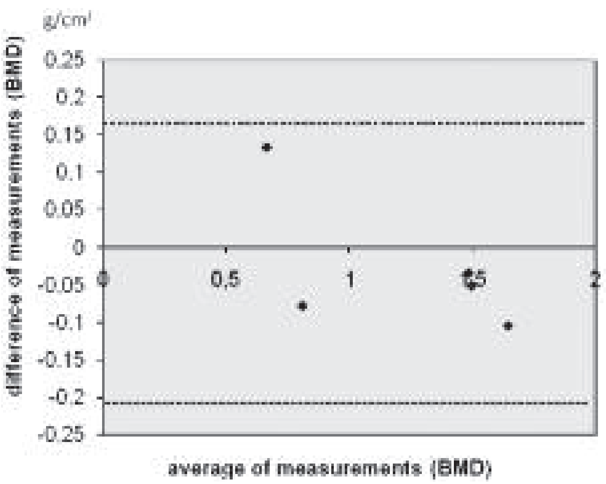

Fig. 4. — Bland-Altman plot of the difference against the average BMD measurement, based on five repeated measurements. The dotted lines represent the 95% limits of agreement for the lateral ROI.

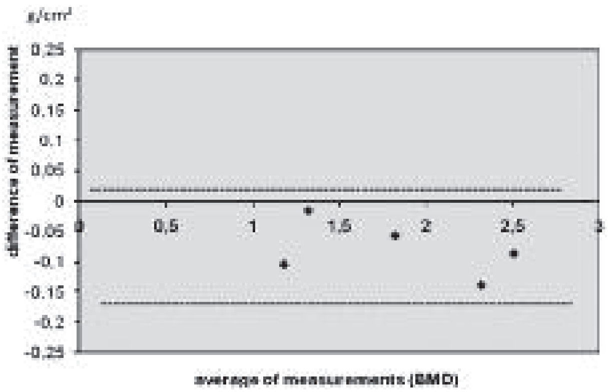

Fig. 5. — Bland-Altman plot of the difference against the average BMD measurement, based on five repeated measurements. The dotted lines represent the 95% limits of agreement for the medial ROI.

a difference in BMD with this method. We found that with a power of 0.80 and alpha = 0.05, the sample size should have been 88 patients.

Contact pressures in dysplastic hips are higher than in normal hips (*8,12,17*), and stress distribution is concentrated in a smaller weight-bearing area (*11*). PAO results in reduced contact stress (*9,20*) and a changed load distribution (*3*). Postoperatively, load on the lateral part of the acetabulum is decreased and load on the medial part is increased. It is plausible that this change in load distribution will affect bone density of the acetabulum over time, although the biological effect of PAO in terms of bone remodelling due to changes in loading pattern could not be clearly objectivised in this study because no changes in BMD were found after PAO. Neither did we find evidence for our initial hypothesis about a correlation between BMD and migration of the acetabulum. However, there was hardly any postoperative migration of the acetabular fragment (*13*) and hence no correlation with BMD. The degree of acetabular migration correlated significantly in a few directions of translation and rotation.

In conclusion, there was no correlation between BMD in the acetabulum and the amount of migration of the osteotomised fragment after PAO, and we did not find changed acetabular BMD over time. DEXA, as applied in this study, is not an appropriate method to demonstrate the changes in BMD in the hip due to changed loading or a suitable method to predict postoperative acetabular migration.

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Chapter 5

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ORIGINAL ARTICLE

Cyst volume in the acetabulum and femoral head decreases after periacetabular osteotomy

Inger Mechlenburg [1], Jens R. Nyengaard [2], John Gelineck [3], Sepp De Raedt [1], Kjeld Søballe [1]

[1] Department of Orthopaedics, University Hospital of Aarhus, Aarhus - Denmark
[2] Stereology and Electron Microscopy Research Laboratory and Mind Center, University of Aarhus, Aarhus - Denmark
[3] Department of Radiology, University Hospital of Aarhus, Aarhus - Denmark

ABSTRACT: *In a series of 26 consecutive patients scheduled for periacetabular osteotomy (PAO), we examined how many had acetabular or femoral head cysts, investigated whether the volume of the cysts changed after PAO, calculated the precision of the method applied and scored their hip symptoms. Magnetic resonance imaging (MRI) was performed before PAO and at 1 and 2½ years post-operatively. The number of cysts was noted and the total cyst volume in each patient was estimated with a design-based stereological method and the precision of the method was calculated.The patients filled out The Hip disability and Osteoarthritis Outcome Score (HOOS) four years after PAO.*

Preoperatively, 12 patients had acetabular or femoral head cysts (22 cysts), 1 year postoperative, 15 patients had cysts (23 cysts) and 2½ years postoperative, 15 patients had cysts (18 cysts). Mean total acetabular cyst volume per patient decreased significantly from 1 year (1.96 cm3, SD 3.97) to 2½ years (0.96 cm3, SD 1.70) after PAO (p= 0.04). The Limits Of Agreement for measurement of cyst volume was ± 1.73 cm^3.

The mean subscore for Pain was 75, Symptoms 75, ADL 83, Sport/recreation 63 and Quality Of Life 62.

The number of patients having cysts did not change notably after PAO. But the mean total cyst volume/patient decreased significantly between 1 and 2½ years after PAO. The PAO patients rated their hip comparable to the scores for patients six months after total hip replacement.

KEY WORDS: *Periacetabular ostotomy, Bone cysts, Stereology*

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INTRODUCTION

Patients with hip dysplasia are prone to developing osteoarthritis of the hip at a young age (1-3). The reasons for this are not fully understood, but an explanation may be that the reduced contact area between the acetabulum and the femoral head as well as a reduced abductor lever arm increase the load per contact-area in the hip joint (4-6). The increased load leads to strain on the articular cartilage and subchondral bone and this is believed to result in hip osteoarthritis and joint degeneration. As osteoarthritis progress, bone cysts may appear in the acetabulum or the femoral head (7) with cysts more commonly found in the acetabulum than in the femoral head, and most frequently in the anterior part of the hip (8) (Fig. 1).

The periacetabular osteotomy (PAO) is used to treat developmental dysplasia of the hip with favourable intermediate to long-term results (9-12). The procedure involves separating the acetabulum from the pelvis, reorienting the acetabulum to increase coverage of the femoral head, and fixating the reoriented fragment to the pelvis. Computer modeling of PAO for hip dysplasia suggests that the effect of the correction of the acetabulum is to change the joint loading to be closer to that of the normal hip (13, 14).

Complete or partial healing of cysts 5 to 6 years after PAO has been observed in 17 of 21 hips with cysts before surgery (15). Whether this is due to screws inserted in the bone cyst inducing a healing process or due to change of joint loading is not known. No other existing literature have confirmed or excluded healing of bone cysts after PAO. This prospective

Fig. 1 - *Sagittal MR image of hip joint showing an acetabular cyst located anterolaterally.*

study of a series of patients scheduled for PAO aims to: 1) examine how many patients had acetabular or femoral head cysts before and at 1 and 2½ years after PAO; 2) investigate whether the volume of the bone cysts change after PAO; 3) calculate the precision of the method applied; and 4) evaluate the patient-assessed hip problems after PAO.

PATIENTS AND METHODS

The study was approved by The Biomedical Research Ethics Committee (Journal Number: 20030021) and registered with Clinical Trials.gov (NCT00119977) and all patients gave signed consent for participation in the study.

Patients

We prospectively followed 26 (22 females and four males) dysplastic hips scheduled for PAO. Median age at the time of PAO was 39 years (range, 19-53 years). All participants had spherical femoral heads. The participants had the following radiographic and clinical characteristics: center-edge angle of Wiberg was 24° or less (16), osteoarthritis degree 0 or 1 according to the classification of Tönnis (17), closed growth zones in the pelvis, a painful hip and a minimum of 110° flexion in the hip. We excluded patients with metal implants, neurologic illnesses, Legg-Calvé-Perthes disease, or sequelae from previous hip surgery. We also excluded patients for whom an intertrochanteric femoral osteotomy was planned.

Surgical protocol

All patients had PAO using the trans-sartorial approach (18).The pubic bone was osteotomised and under fluoroscopic control the ischial osteotomies and the posterior iliac osteotomy were performed. The subchondral bone cysts were not treated at PAO.

While in hospital (4-5 days) the patients were seen daily by a physiotherapist for active hip range of motion exercises. The patients were mobilised six hours post-operatively, and on the first day patients were allowed a maximum of 30 kg of weight-bearing and given instructions in maintaining the weight-bearing limit with the use of crutches. Four weeks after discharge, rehabilitation was continued by two physiotherapists specialised in orthopaedics. The patients came to the hospital for physiotherapy twice a week and each exercise session was one hour with a 30-minute aerobic and strength program followed by a 30-minute program of mobility and gait training in the hydrotherapy pool. From the eighth post-operative week, the patients were allowed to fully weight-bear. Physiotherapy ended approximately 2-3 months after PAO, when the physiotherapists assessed that the patient had achieved the pre-determined functional goals of walking at speed without crutches and the ability to run. After discharge from hospital, the patients were seen for reviewed by the physiotherapist and by the surgeon. X-ray examinations were performed at eight weeks, six months and ten years.

Radiographic examiniations

Two angles were measured on pre- and post-operative AP radiographs: center-edge (CE) angle and acetabular index (AI) angle (17) by one observer (IM). The CE angle assesses the superior coverage of the acetabulum and a normal CE angle is above 25°. The AI angle evaluates the orientation of the acetabular roof and normal AI angles are below 10°. The radiographic data demonstrated good correction of the acetabular fragment in this study (Tab. I).

All 26 patients had a MRI scan pre-operatively, 25 returned for MRI at one year and 21 at 2½ years post-operatively. The examinations were performed on a 1.5-T scanner (Siemens Magnetom Symphony, Erlangen, Germany) using a body array surface coil to achieve the optimum balance between the largest possible field of view and the highest possible spatial resolution. A fat-suppressed 3-D fast low-angle shot (FLASH) sequence was obtained because we also wanted to visualise the articular cartilage with a high signal and high contrast (19). The imaging matrix was 256 x 256, field of view 220 x 220 mm with a section thickness of 1.5 mm. TR/TE was 60.0/11.0 ms, flip angle was 50°, and the time of acquisition was 9.38 min. Double MRI of the first 13 included participants were performed pre-operatively with complete repositioning of the participants and setup to obtain an estimate of precision of the method used and to calculate the limits of agreement (20).

A phantom was MRI imaged with the same scan protocol as used for the patients and an MRI physicist did a thorough test to verify the spatial resolution and the geometry. The images of the phantom were measured to assess whether the measured distances agreed with the known geometric dimensions of the phantom. The validity of the measurements of cartilage thickness was confirmed as the spatial resolution of the MR images was ideal and there were no geometrical distortions.

We also investigated whether metallic artifacts from the screws inserted in the pelvis at PAO posed a potential problem for the methods used. There were only minor artifacts from the titanium screws, and these were in the iliac bone and did not interfere with the measurements of cyst volume.

To measure the volume of the cysts in the acetabulum and femoral head, we used a design-based stereological method: Cavalieris principle. Stereologic methods are used to obtain quantitative information about 3-D structures based on observations from section planes or projections (21). Stereology can be used to minimise the workload using sampling and still provide reliable quantitative information about the whole structure of interest. This method is based on sagittal images through the hip joint. The series of sagittal images covering the hip joint (6-8 images) was assessed for bone cysts and analysed with a design-based stereological method: Cavalieris principle in a stereological software (Visiopharm, Hoersholm, Denmark). When a cyst was present on an image, the tester (IM) would point to the centre of it. The software randomly placed two lines through the centre. Where these lines intercepted the outer boundary of the cyst was confirmed by the tester and four points of the cyst were randomly sampled (Fig. 2). Based on these 4 points, the software estimated the area of the cyst. This was repeated on the following images where the cyst or another cyst was present. Finally, the total cyst area in each series of images was multiplied with the slice thickness and the volume of the cysts in each patient was estimated. The same person (IM) measured cyst volume on all images. The contrast of the MRI images was not adjusted before or during measuring because this may change the appearance and possibly the size of the cysts, thus affecting the measurements.

TABLE I - SUMMARY OF RADIOGRAPHIC ANGLES AND PAIN MEASURED BEFORE AND 8 WEEKS AFTER PERIACETABULAR OSTEOTOMY IN 26 HIPS

	Pre-operative Mean (range)	8 week post-operation Mean (range)
CE angle (°)[a]	13 (-27 to 24)	31 (20 to 40)
AI angle (°)[b]	17 (39 to 7)	2 (-4 to 10)
Pain VAS[c]	7 (4 to 9)	1 (0 to 4)

[a] Centre edge angle.
[b] Acetabular Index angle.
[c] Visual Analog Scale.

Clinical outcome

Four years after PAO, the patients were asked to fill out The Hip disability and Osteoarthritis Outcome Score (HOOS). HOOS is a questionnaire to assess the patients' opinion about their hip and associated problems (22). HOOS consists of 5 subscales; Pain, other Symptoms, Function in daily living (ADL), Function in sport and recreation (Sport/Rec) and hip related Quality of life (QOL). The last week is taken into consideration when answering the questions. Standardised answer options are given (5 Likert boxes) and each question gets a score from 0 to 4. A normalised score (100 indicating no symptoms and 0 indicating extreme symptoms) is calculated for each subscale.

Statistics

Data for cyst volume pre- and post-operatively was tested by Paired t-test. For analysis of the clinical precision of the stereological measurements, we calculated the random variation within the method and the 95% repeatability limit calculated as SD × √2 × 1.96. Bias ± the 95% repeatability limit is identical to the 95% limits of agreement (LOA) as described by Bland and Altman (20). The systematic variation (bias) between the double examinations was estimated as the mean difference between the two measurements. The difference between the two measurements followed a normal distribution (Shapiro-Wilk test) and we tested these by a paired t-test. Statistical analyses were performed with SPSS 11.0 (Chicago, IL) software package.

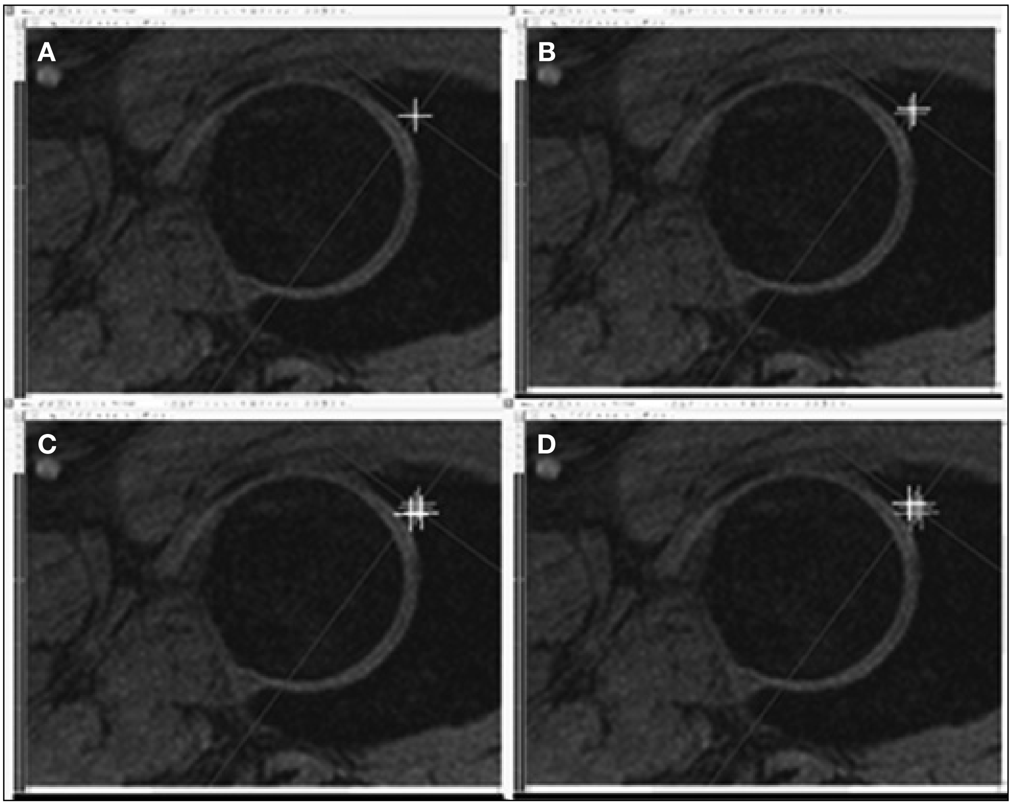

Fig. 2 (A-D) - *Cyst size measurement, showing the two lines placed through the centre of the cyst and the random selection of four points on the cyst boundary.*

RESULTS

11 of 26 patients had acetabular cysts preoperatively (21 cysts, mean total cyst volume/patient 3.44 cm3, SD 6.712) and one patient had a cyst in the femoral head (volume 8.05 cm3). One year after PAO, 13 of 26 patients had acetabular cysts (19 cysts, mean total cyst volume/patient 1.96 cm3, SD 3.97) and two patients had femoral head cysts (4 cysts, mean total cyst volume/patient 3.98 cm3, SD 4.10). At 2½ years after PAO 13 of 26 patients had acetabular cysts (16 cysts, mean total cyst volume/patient 0.96 cm3, SD 1.70) and two patients had femoral head cysts (four cysts, mean total cyst volume/patient 0.80 cm3, SD 0.72).

The mean total acetabular cyst volume/patient decreased significantly from one to 2½ years after PAO (p=0.04). All acetabular cysts were located antero-laterally in the acetabulum except for one that was postero-lateral. The femoral head cysts were positioned antero-laterally and antero-medially (Tab. II).

Precision of the stereologic method has been estimated based on double MRI scanning and double measurement of cyst volume. We calculated the random and the systematic variation within the method. The Limits of agreement and 95% confidence interval for the systematic variation was

TABLE II - STEREOLOGICAL MRI RESULTS FOR CYST MEASUREMENT

	Pre-operative n=26	1 year post-operative n=25	2½ years post-operative n=21
Acetabular mean cyst volume/ patient cm^3 (SD), number of patients with cysts []	3.44 (6.71) [11]	1.96 (3.97) [13]	0.96 (1.70)* [13]
Femoral head mean cysts volume/ patient cm^3 (SD), number of patients with cysts []	8.05 [1]	3.98 (4.10) [2]	0.80 (0.72) [2]
Number of acetabular cysts (anterolateral/ posterolateral) location	21 20/1	19 18/1	16 15/1
Number of femoral head cysts (anterolateral/ anteromedial) location	1 1/0	4 3/1	4 3/1

* statistically significant different (p=0.04) compared to previous time period tested with paired t-test.

estimated (Tab. III). LOA for measurement of cyst volume was ± 1.73 cm^3 indicating a moderately precise method and there was no significantly systematic variation between the first and second measurement as seen on the 95% CI. 4 years after PAO the patients' opinion about their hip and associated problems was assessed by HOOS. 22 of 26 patients returned the HOOS and the mean subscore for Pain was 75 SD (17), Symptoms 75 (19), ADL 83 (16), Sport/ recreation 63 (26) and Quality Of Life 62 (17). The HOOS subscores were similar between the patients with bone cysts and those with no cysts assessed 2½ years after PAO.

DISCUSSION

We have reported a design-based stereological method to MRI to measure the 3-D size of bone cyst in patients with hip dysplasia.

11 of 26 patients had acetabular cysts preoperatively (21 cysts) and one patient had a cyst in the femoral head. One year after PAO, 13 patients had acetabular cysts (19 cysts) and two patients had femoral head cysts (4 cysts). At 2½ years after surgery 13 patients had acetabular cysts (16 cysts) and two patients had femoral head cysts (4 cysts). Thus, there are two more patients with bone cysts 2½ years after PAO compared to pre-operative evaluation, but there are fewer cysts and the cyst volume per patient has been to shown to be 3½ times lower.

We found the all acetabular cysts except one to be located anterolaterally in the acetabulum and that is in accordance with other studies (15, 23) showing that cysts generally occur in high stress areas of the joint, where degeneration and defects of articular cartilage are commonly found.

The size of bone cysts has been measured 2-D on radiographs (24) but this is problematic because only one area can be measured and the cyst is not quantified in the z-direction. In this study we have estimated the 3-D size of bone cysts.

TABLE III - PRECISION OF REPEATED STEREOLOGIC MEASUREMENTS OF CYST VOLUME OBTAINED BY DOUBLE MRI FOR 13 PATIENTS

Analysis method	Mean (range)	$SD_{dif-intra}$ [a]	Bias ± LOA	95% CI [b]
Cyst volume (cm^3)	4.85 (0.34 – 13.55)	0.88	0.28 (± 1.73)	-0.16; 0.73

[a] $SD_{dif-intra}$ is the random variation within a method comparing double examinations.
[b] 95% confidence interval for the bias.

The natural history of osteoarthritic bone cysts after PAO has only once before been examined, a retrospective study showed complete or partial healing of cysts as observed in 17 of 21 hips after PAO (15). This study's results are in line with the former and add further evidence for bone cysts' to potentially heal after PAO.

Empirical knowledge suggests that acetabular bone cysts arise due to cartilage breakdown followed by a fissure into the subchondral bone. That allows joint fluid to communicate with the bone leading to breakdown of bone tissue. Another explanation is that high contact pressure leads to hardening of the subcondral bone and subsequent breakdown of bone tissue below the pressure point. We hypothesise that reducing the joint loading and alleviating stress on the labrum with PAO, unloads the cartilage below and allows a healing process of the cysts to take place and hence may prevent its subsequent progression.

A recent study reported good intra- and inter-reader agreement on detecting bone cyst on 1.5T MR images as also employed in this study (25). The precision of our measurements of cyst volume expressed as the LOA was ± 1.73 cm^3. The precision of the method could be improved by sampling more points than only four of each image where a cyst is present and if the precision of this stereological method had been higher, we probably would have been able to detect a statistically significant lower volume of acetabular cysts one year post-operatively compared to pre-operative base line values.

Four years after PAO, the patients' rated their hip and associated problems on the HOOS to be between 62-83, lowest for hip related Quality of life and for Function in sport and recreation and highest for Function in daily living. Unfortunately, we are unable to evaluate the changes in hip function over time as HOOS scores were not collected pre-operatively. The HOOS subscores were similar between the patients with bone cysts and those with no cysts assessed 2½ years after PAO. The scores were comparable to that of patients six months after total hip replacement (22).

In conclusion, the number of patients having cysts did not change notably after PAO but the mean total cyst volume/ patient decreased significantly between one and 2½ years after PAO. We believe that the cysts remodeled as a result of decreased local stresses in the subchondral bone after reorientation of the acetabular fragment at PAO. Eight weeks after PAO, all hips had CE angles above 20° and low VAS scores and four years after PAO the scores for activities of daily living were high, reflecting a long term high functional capacity in these patients.

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Address for correspondence:
Inger Mechlenburg, PhD
Department of Orthopaedics
Aarhus University Hospital
Tage-Hansens Gade 2
8000 Aarhus C, Denmark
inger.mechlenburg@ki.au.dk

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Chapter 6

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CLINICAL RESEARCH

Cartilage Thickness in the Hip Measured by MRI and Stereology Before and After Periacetabular Osteotomy

Inger Mechlenburg MSc, PhD, Jens R. Nyengaard MD, DMSc, John Gelineck MD, Kjeld Soballe MD, DMSc, Anders Troelsen MD, PhD

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Abstract

Background Untreated hip dysplasia can result in a degenerative process joint and secondary osteoarthritis at an early age. While most periacetabular osteotomies (PAOs) are performed to relieve symptoms, the osteotomy is presumed to slow or prevent degeneration unless irreparable damage to the cartilage has already occurred.

Questions/purposes We therefore determined (1) whether changes in the thickness of the cartilage in the hip occur after PAO, and (2) how many patients had an acetabular labral tear and whether labral tears are associated with thinning of the cartilage after PAO.

Patients and Methods We prospectively followed 22 women and four men with hip dysplasia with MRI before PAO and again 1 year and 2½ years postoperatively to determine if cartilage thinning (reflecting osteoarthritis) occurred. The thickness of the femoral and acetabular cartilage was estimated with a stereologic method. Three and one-half years postoperatively, 18 of 26 patients underwent MR arthrography to investigate if they had a torn acetabular labrum.

Results The acetabular cartilage thickness differed between 1 and 2½ years postoperatively (preoperative 1.40 mm, 1 year postoperatively 1.47 mm, and 2½ years postoperatively 1.35 mm), but was similar at all times for the femoral cartilage (preoperative 1.38 mm, 1 year postoperatively 1.43 mm, and 2½ years postoperatively 1.38 mm.) Seventeen of 18 patients had a torn labrum. The tears were located mainly superior on the acetabular rim.

Conclusion Cartilage thickness 2½ years after surgery compared with preoperatively was unchanged indicating the osteoarthritis had not progressed during short-term followup after PAO.

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.
This work was performed at the University Hospital of Aarhus, Aarhus, Denmark.

I. Mechlenburg (✉), K. Soballe, A. Troelsen
Department of Orthopaedics, University Hospital of Aarhus, Tage-Hansens Gade 2, 8000 Aarhus C, Denmark
e-mail: inger.mechlenburg@ki.au.dk

J. R. Nyengaard
Stereologic and Electron Microscopy Research Laboratory and Mind Center, University of Aarhus, Aarhus, Denmark

J. Gelineck
Department of Radiology, University Hospital of Aarhus, Aarhus, Denmark

Introduction

Patients with hip dysplasia are prone to having osteoarthritis of the hip develop at a young age [5, 47]. The reasons for this are not fully understood, but it is generally believed the reduced contact area between acetabulum and the femoral head and a reduced abductor lever arm increase the contact pressures [1, 11, 24]. Such increased contact pressure reportedly results in degeneration (thinning) of cartilage and eventually osteoarthritis [5, 18, 26, 42].

The condition of the acetabular labrum is also important given reports suggesting a degenerated or damaged labrum initiates cartilage degeneration in dysplastic hips [12, 13, 19]. Arthroscopic studies suggest the labrum is affected in 55% to 96% of symptomatic hips [19, 20]. Labral tears presumably result from overload of the acetabular rim [13] and the high strain placed on the labrum from reduced bony support [23, 27].

PAO provides effective correction of hip dysplasia [23] relieves joint pain [17, 35] improves function [44], and one report suggests surgery may alter the natural history of hip dysplasia and improve hip longevity [45]. The preoperative integrity of cartilage is reportedly an important determinant of survival when performing PAO [14, 25, 34, 38], but it is important that the cartilage does not degenerate or further degenerate after PAO. We assume that improving the position of the existing contact surface at PAO will lead to decreased pressures and thereby avoid cartilage degeneration/thinning after PAO.

We therefore asked whether: (1) changes in the thickness of the cartilage in the hip occur after PAO, and (2) how many patients with PAO had acetabular labral tears and whether labral tears were associated with thinning of the cartilage after PAO.

Patients and Materials

We prospectively followed 22 women and four men presenting with 26 dysplastic hips who were scheduled for PAO. Their median age at the time of PAO was 39 years (range, 19–53 years). All patients had spherical femoral heads. The patients had a center-edge angle of Wiberg [46] of 24° or less, osteoarthritis degree 0 or 1 according to the classification of Tönnis [39], closed growth zones in the pelvis, a painful hip, and minimum 110° flexion in the hip. At the time of surgery we did not know if the patients had a labral tear before PAO and even if we suspected a tear, it would not have influenced our choice of treatment. We excluded patients with metal implants, neurologic illnesses, Legg-Calvé-Perthes disease, or sequelae from previous hip surgery. We also excluded patients for whom an intertrochanteric femoral osteotomy was planned. All 26 patients had MRI preoperatively, 25 returned for MRI 1 year postoperatively, and 21 returned 2½ years postoperatively. Eighteen of 26 patients agreed to undergo MR arthrography (MRA) 3½ years after PAO to determine whether they had an acetabular labral tear. The study was approved by our local ethical committee and all patients gave signed consent for participation in the study.

The examinations were performed on a 1.5-T scanner (Siemens Magnetom Symphony, Erlangen, Germany) using a body array surface coil to achieve the optimum balance between the largest possible field of view and the highest possible spatial resolution. Continuous ankle traction with a load of 10 kg was used during MRI to separate the acetabular and femoral cartilages. The traction was applied 5 minutes before the images were obtained. This regimen reportedly separates the surfaces sufficiently to make them distinct [28, 30]. A fat-suppressed 3-D fast low-angle shot (FLASH) sequence was obtained. The FLASH sequence allows thin slices and a 3-D data set to observe the articular cartilage with a high signal and high contrast. The imaging matrix was 256 × 256 and field of view was 220 × 220 mm with a section thickness of 1.5 mm. TR/TE was 60.0/11.0 ms, the flip angle was 50°, and the time of acquisition was 9.38 minutes. Double MRI of the first 13 included patients was performed preoperatively with complete repositioning of the patients and setup to obtain an estimate of precision of the method used calculated as limits of agreement [2]. We computed the levels of agreement (LOA) between repeated stereologic measurements of cartilage thickness obtained by double MRI. Given the first stereologic measurement for acetabular cartilage, we could expect with 95% confidence that the difference to the second measurement would be between −0.17 and 0.13 mm. For the femoral cartilage, the LOA was −0.18 to 0.1 mm.

Field inhomogeneity and gradient nonlinearity of an MR scanner will distort the images. To validate the resolution and spatial linearity of the system, phantom measurements were performed. A phantom (MRI Deluxe Phantom, Data Spectrum Corporation, Hillsborough, NC, USA) with a diameter of 21.6 cm containing inserts for measurement of resolution and linearity was used. The phantom was placed in the magnet's isocenter and images were acquired using the sequence used for clinical imaging (T1 W 3-D Flash, slice thickness 1.5 mm, pixel resolution 0.43 × 0.43 mm). The spatial linearity and resolution were measured manually using Syngo on a Siemens MR workstation. To validate the linearity the distances between the parallel plates in the insert were measured and compared with the true dimensions as specified by the vendor. For validating the resolution the size of the rods in the resolution insert were measured and compared with the true dimensions. The measurements of both parameters were in good agreement with the dimensions specified by the phantom vendor.

We also investigated whether metallic artifacts from the screws inserted in the pelvis during the PAO posed a potential problem for the methods used. There were only minor artifacts from the titanium screws, and these were in the iliac bone and did not interfere with the measurements of cartilage thickness.

All patients had PAO using the transsartorial approach [40]. The incision was made from the anterior-superior iliac spine descending 6 cm distally. The fascia over the sartorius muscle was incised and the lateral femoral cutaneous nerve was exposed and was noticeable in the operation field throughout surgery. With this approach, the tensor fasciae latae muscle and the abductor muscles are kept intact and the sartorius muscle is split in the direction of the fiber. The pubic bone was osteotomized and under fluoroscopic control, and the ischial osteotomies and posterior iliac osteotomy were performed. The capsule was not opened for inspection of labral tears; we presumed the PAO would normalize the distribution of force in the joint and relieve the strain on the rim and the labrum and therefore alleviate any symptoms of a possible tear of the labrum. If a patient continuously experiences pain after PAO, we obtain an MRA to observe the labrum and if a tear is found, we offer the patient arthroscopy.

While in the hospital (4–5 days), the patients were seen daily by a physiotherapist for active hip ROM exercises. The patients were mobilized 6 hours postoperatively, and on the first day, patients were allowed 30 kg of weightbearing and given instructions in maintaining the weightbearing limit with the use of crutches. From the eighth postoperative week, the patients were allowed full weightbearing.

Four weeks after discharge, rehabilitation was initiated by one of two physiotherapists specialized in orthopaedics. The patients came to the hospital for physiotherapy twice a week and each exercise session was 1 hour with a 30-minute aerobic and strength program followed by a 30-minute program of mobility and gait training in the hydrotherapy pool. Physiotherapy was ended 2 to 3 months after PAO when the physiotherapists assessed that the patient had achieved predetermined functional goals, eg, walking at speed without crutches and the ability to run.

After discharge from the hospital, the patients were seen by the physiotherapist at 8 weeks and by the surgeon at 8 and 24 weeks, 1, 2½, 5, and 10 years. AP hip radiographs were taken at each visit. Patients were asked to assess the degree of pain on a visual analog scale before surgery and 8 weeks after PAO, and a reduction in pain was observed 8 weeks after PAO (Table 1).

To assess acetabular correction, the center-edge and acetabular index angles [39] were measured by one observer (IM) on AP radiographs of the pelvis preoperatively and postoperatively. The radiographic data showed correction of these indices (Table 1).

To measure the thickness of the acetabular and femoral cartilage, we used our earlier developed stereologic method that is reliable and time-efficient (requiring approximately 20 minutes per hip) [21, 22]. Stereologic methods are used to obtain quantitative information regarding 3-D structures based on observations from section planes or projections [33]. Stereology can be used to minimize the workload using sampling and still provide reliable quantitative information about the whole structure of interest. This method is based on four images through the center of the femoral head: a true coronal, a true sagittal, an oblique coronal 45° forward angled, and an oblique coronal 45° backward angled. On each of the four images, a grid of 15 to 20 radial test lines was selected and located randomly on the images and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was measured manually in software (Grain 32, Dimac, and KT Algorithms, Aarhus, Denmark) designed for stereologic purposes (Fig. 1). The approximately 60 to 80 measured distances were summed and the mean thickness of the

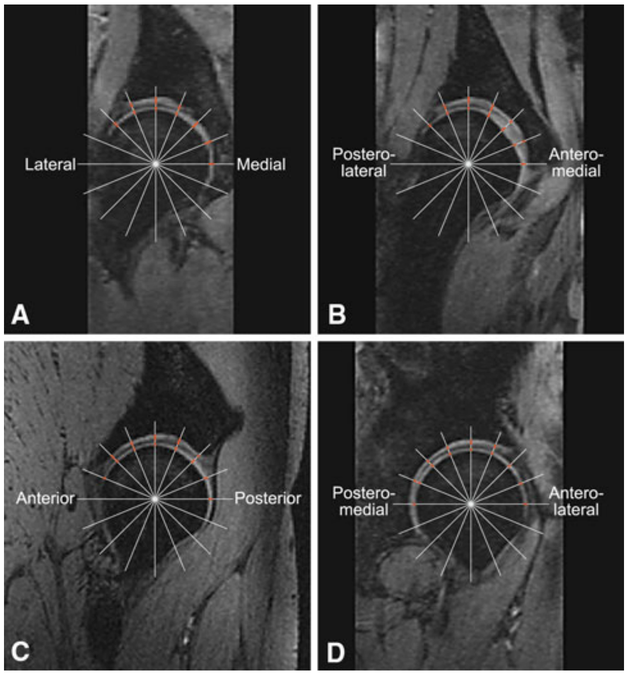

Fig. 1A–B On each of four reconstructed MR images, (**A**) lateral-medial, (**B**) posterolateral-anteromedial, (**C**) anteroposterior, and (**D**) posteromedial-anterolateral, a grid of 15 to 20 radial test lines was superimposed, and where the test lines intercepted the cartilage, the orthogonal distance through the cartilage was measured manually. The approximately 60 to 80 measured distances were summed, and the mean thickness of the acetabular and femoral cartilage was calculated.

Table 1. Evaluation of radiographic angles and pain before and 8 weeks after PAO in 26 hips

Parameter	Preoperative	Postoperative	Difference
Center-edge angle (degrees; range)	13 (−27 to 24)	31 (20 to 40)	18
Acetabular index angle (degrees; range)	17 (39 to 7)	2 (−4 to 10)	−15
Visual analog scale	7 (4 to 9)	1 (0 to 4)	−6

acetabular and femoral cartilage, respectively, was calculated. Systematic uniformly random sampling ensured the location of the test lines intercepting the cartilage was sampled with the same probability. Therefore, we did not need to use anatomic landmarks to compare preoperative and postoperative cartilage thickness. One observer (IM) measured cartilage thickness on all images. The contrast of the MR images was not adjusted before or during measuring because this may change the appearance of the cartilage boundaries and thus affect the thickness measurements. The cartilage measures were not affected by partial volume because we used center MR images (through the center of the femoral head). It was not difficult to differentiate the labrum from the cartilage on the images. As noted previously, 18 of the 26 patients agreed to undergo MRA 3½ years after PAO to investigate if they had an acetabular labral tear. Applying standardized aseptic technique and guided by fluoroscopy, 8 mL of diluted gadolinium contrast media (Gd-DTPA 2 mmol/L; Magnevist, Schering, Berlin, Germany) was injected into the hip through an anterior approach. Before injection, the intraarticular position of the needle point was verified by injecting a few drops of iodinated contrast media. There were no adverse affects. MRA was performed using the same 1.5-T scanner as used for MRI in this study. Initially, three scout sequences in the axial, sagittal, and coronal planes were obtained. This was followed by T1-weighted sequences with fat suppression: true coronal, oblique axial (parallel to the femoral neck), oblique coronal 45° forward angled, and oblique coronal 45° backward angled (TR/TE 376/20, slice thickness 4 mm, field of view 220 × 220, matrix 256 × 256). Finally, a coronal STIR sequence through the entire pelvis was performed (TR/TE 410/27, TI 170, field of view 400 × 400, matrix 256 × 256). MRA and intraarticular contrast injections were performed by a senior radiologist (JG) specialized in musculoskeletal MRI. All images were assessed by masked rereadings separated by 4 weeks and it was noted where the labral tears were located on the acetabular rim (Fig. 2). The criteria for labral tears seen with MRA were (1) displacement or (2) absence of the labrum; (3) contrast media through the base of the labrum causing detachment with or without displacement; and intrasubstance (4) linear; (5) cystic; or (6) irregular presence of contrast media. Intermediate signal intensity and irregular margins were interpreted as degenerative changes [41].

Data for cartilage thickness were normally distributed and we used a repeated measures ANOVA to determine differences in cartilage thickness between preoperative and 1 and 2½ years postoperatively. Statistical analyses were performed with SPSS 11.0 (Chicago, IL) software package.

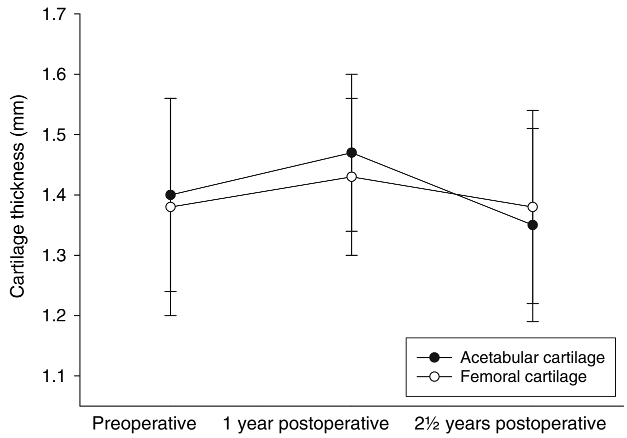

Fig. 2 The mean acetabular and femoral cartilage thickness and SD in 26 dysplastic hips estimated with MRI and stereology before and after periacetabular osteotomy are shown.

Results

The acetabular cartilage was thicker (p = 0.04) 1 year after surgery compared with 2½ years postoperatively. Preoperatively, the mean thickness of the acetabular cartilage was 1.40 mm (SD 0.16), 1 year postoperatively 1.47 mm (SD 0.13), and 2½ years postoperatively 1.35 (SD 0.16). The femoral cartilage was unchanged 2½ years postoperatively compared with preoperatively (Fig. 2). The mean thickness for the femoral cartilage before surgery was 1.38 mm (SD 0.18), 1 year postoperatively 1.43 mm (SD 0.13), and 2½ years postoperatively 1.38 mm (SD 0.16).

Seventeen of 18 patients had labral tears at 3½ years, and in the one patient without a tear, degenerative changes of the labrum were identified. At the rereadings of the images, the radiologist reproduced the results regarding presence of labral tears in all cases. The tears were located mainly superior on the acetabular rim and in some cases, the tears extended anterosuperiorly and posterosuperiorly. All tears were identified by contrast media through the base of the labrum (Fig. 3) causing detachment with or without displacement in some cases in combination with linear intrasubstance. Because only one of the patients examined with MRA did not have a labral tear, we did not test for an association between labral tears and cartilage thickness.

Discussion

Untreated hip dysplasia can result in a degenerative process in the joint and eventually secondary osteoarthritis at an early age. We assume that the reduction of excessive joint pressure achieved at PAO promotes the processes involved in cartilage repair and thus prevents cartilage degeneration/

Fig. 3 An axial MRA view shows an anterosuperior labral tear in which intraarticular contrast medium outlines a detachment of the labrum.

thinning after PAO. We therefore asked whether: (1) changes in the thickness of the cartilage in the hip occur after PAO, and (2) how many patients with PAO had acetabular labral tears and whether labral tears were associated with thinning of the cartilage after PAO.

We acknowledge limitations to our study. First, in some patients it was difficult to identify the interface between femoral and acetabular cartilage, although traction was used during MRI to separate the acetabular and femoral cartilage. The traction approach has been used by several authors [16, 28, 30, 31], and is not always well received by patients. We applied 10 kg of traction and found it separated the femoral and acetabular cartilage sufficiently in the patients with little muscle tissue around the hip, whereas the same load had a smaller separating effect on heavier patients with well-developed muscles. We did not apply heavier traction because it possibly would have been uncomfortable for the patients. This may have resulted in an underestimation of the mean cartilage thickness because the areas not fully separated were in the center of the joint where cartilage is thicker compared with the periphery. Second, we had no functional outcome measures although such measures would have been appropriate to collect prospectively. Had we done so, we could have documented the physical function of the included patients before and after surgery and determined whether cartilage thickness is associated with functional outcome. If there is only a weak association between cartilage thickness (or thinning) and function, cartilage thickness may not be a good surrogate for symptoms or progression of osteoarthritis. Third, the use of randomization in stereology and averaging of thickness eliminates the possibility of measuring the same places in the cartilage layer before and after surgery (PAO). Instead, we measured approximately 60 to 80 distances in randomized regions of the acetabular and in the femoral cartilage in each hip, and these measures were averaged so the mean thickness of the acetabular and femoral cartilage could be obtained. Systematic uniform random sampling ensured that all regions of the cartilage were sampled with the same probability before and after the PAO. However, if local areas of cartilage were thinning with time we could not detect such changes and if they were small regions, the mean thickness would be not be substantially less given the large number of points.

We found the mean thickness of the femoral and the acetabular cartilage was unchanged 2½ years compared with preoperatively and we interpret this as suggesting there were no major degenerative changes short-term after PAO. We also found the acetabular cartilage was 0.12 mm thicker 1 year after surgery compared with 2½ years after surgery. This may be explained as an effect of inflammation [8, 9] and concomitant swelling in response to surgery [3]. Another explanation may be cartilage thickness dynamically adapts to increased exercise by hypertrophy [5]. During the first year after PAO, the patients are likely to be more active than before surgery as a result of reduced pain, increased function, and participation in the postoperative rehabilitation program. The first 8 postoperative weeks, the patients are allowed to weightbear with only 30 kg but after that, they put full weight on the surgically treated leg and there are no restrictions for participation in physical activity. Our data suggest cartilage thickness 2½ years after PAO is similar to that before surgery, therefore, we do not know if the increased thickness 1 year after PAO is an indication of regeneration or degeneration of cartilage or if it is a random result. Geometric distortions of the MR images are ruled out as an explanation because our MR physicist has validated the resolution and spatial linearity of the system, and the same protocol was used at all scannings. Others have shown [36] cartilage thickness can be analyzed with high accuracy by an MRI fat-suppressed FLASH sequence with high resolution like we used. The person performing the measurements practiced the method before performing the actual and recorded measures to become experienced in making similar judgments in all images and therefore, the finding of thicker acetabular cartilage is not likely to be a systematic error of measurements. Yet, the increased cartilage thickness is small and within the LOA for our method so we consider it a random result.

All but one patient examined with MRA had a labral tear and we observed degenerative changes of the labrum in the patient who did not have a tear. We did not examine the patients for labral tears preoperatively, therefore, we cannot document that the tears were present before surgery.

However, others have found labral tears were present in 64% to 78% of patients with symptomatic hip dysplasia [7, 15]. On the rereadings of MRA, the detection of labral tears was reproduced completely by the radiologist. Others also have reported MRA is a reliable radiographic tool for diagnosing acetabular labral tears [4, 6]. Labral tears may be associated with cartilage disorders in hip dysplasia [10, 29, 32], and we presume there is an association between labral tears and cartilage thinning. Because 17 of 18 patients had labral tears, we could not test for an association between labral tears and cartilage thickness.

The preoperatively and postoperatively measured angles of our patients correspond well with those reported by others [18, 35, 37, 43]. We observed a large reduction in pain 8 weeks after surgery compared with before, also reported by others [17, 35, 44], and PAO performed for the treatment of hip dysplasia evidently reduces the pain.

We did not find gross thinning of the cartilage 2½ years after PAO with the applied stereologic method, although most patients had labral tears. We speculate this is because PAO normalizes the distribution of force in the joint and relieves the strain on the cartilage and the labrum.

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Chapter 7

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Clinical Orthopaedics and Related Research®
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BASIC RESEARCH

Cartilage Thickness and Cyst Volume Are Unchanged 10 Years After Periacetabular Osteotomy in Patients Without Hip Symptoms

Inger Mechlenburg PhD, Jens Randel Nyengaard DMSc, John Gelineck MD, Kjeld Soballe DMSc

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Abstract

Background Periacetabular osteotomy (PAO) may affect cartilage thickness and cyst volume in patients with hip dysplasia. However, as no studies randomizing patients to either PAO or conservative treatment have been performed, to our knowledge, it is unknown if PAO directly affects the development or progression of osteoarthritis in patients with hip dysplasia.

Questions/purposes We investigated (1) changes of cartilage thickness in the hip after PAO; (2) how many patients had subchondral bone cysts in the acetabulum or femoral head; (3) changes in cyst volume; and (4) patients' hip function and pain after PAO.

Patients and Methods In this prospective study, 26 patients (22 women and four men) with hip dysplasia were enrolled with the goal of having MRI of the hip before undergoing PAO and again at 1, 2½, and 10 years after PAO. Of the 26 patients, 17 (65%) underwent complete followup 10 years after PAO, whereas nine could not be included. Of those nine, three had undergone THA, three had substantial hip symptoms, and three were lost to followup. Thickness of acetabular and femoral cartilage and volume of subchondral bone cysts were estimated in the remaining 17 patients. Ten years postoperatively, the patients' Hip disability and Osteoarthritis Outcome Scores (HOOS) were collected.

Results Preoperatively, the mean thickness of the acetabular cartilage was 1.38 ± 0.14 mm compared with 1.43 ± 0.07 mm 10 years postoperatively ($p = 0.73$). The mean thickness of the femoral cartilage preoperatively was 1.37 ± 0.20 mm compared with 1.30 ± 0.07 mm 10 years postoperatively ($p = 0.24$). Seven patients had an increase in cyst volume, six had a decrease, and four had no cysts to start with and remained without cysts. Preoperatively, the median total cyst volume per patient was 6.0 cm^3 (range, 1.6–188.3 cm^3) compared with 2.9 cm^3 (range, 0.7–8.2 cm^3) ($p = 0.18$) at 10 years followup. At 10 years, the mean subscores for the HOOS were: pain, 79 ± 16;

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Each author certifies that his or her institution approved the human protocol for this investigation, that all investigations were conducted in conformity with ethical principles of research, and that informed consent for participation in the study was obtained.

I. Mechlenburg (✉), K. Soballe
Department of Orthopaedic Surgery, Aarhus University Hospital, Tage Hansens Gade 2, 8000 Aarhus C, Denmark
e-mail: Inger.mechlenburg@au.dk; inger.mechlenburg@ki.au.dk

I. Mechlenburg
Department of Clinical Medicine, Aarhus University, Aarhus, Denmark

J. Gelineck
Department of Radiology, Aarhus University Hospital, Aarhus, Denmark

J. R. Nyengaard
Stereology and Electron Microscopy Laboratory and CSGB, Aarhus University, Aarhus, Denmark

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symptoms, 73 ± 17; activities of daily living, 85 ± 14; sport/recreation, 68 ± 22; and quality of life, 61 ± 19.
Conclusions Ten years after PAO, approximately 25% of the patients who have the procedure will have substantial hip pain and/or undergo hip arthroplasty. Of the patients who do not have substantial hip pain or an arthroplasty, cartilage thickness appears to be preserved. Future studies are needed to help us decide which patients are most likely to succeed with PAO at long-term followup.
Level of evidence Level II, therapeutic study.

Introduction

Transsartorial periacetabular osteotomy (PAO) [24] is performed in young patients with hip dysplasia to relieve hip pain and increase hip-related physical function [5, 6]. Use of PAO may help postpone or prevent hip osteoarthritis (OA), but to our knowledge, no studies randomizing patients to either PAO or conservative treatment have been done, therefore we do not know whether PAO directly affects the development or progression of OA in patients with hip dysplasia.

Joint space narrowing is a strong radiographic indicator of degenerative changes associated with hip OA [8, 9], but the progression of hip OA also can be monitored by changes in cartilage thickness and size of subchondral bone cysts [14, 16]. Subchondral bone cysts can be caused by pressure on the cartilage and the subchondral bone, which causes the joint fluid to leak into the bone. The swelling and inflammation associated with OA can put extra pressure on the cartilage. With PAO, the biologic hip is preserved and subchondral bone becomes capable of regeneration [14, 17], but it is unclear whether the cartilage is able to regenerate.

We asked if cartilage thickness and cyst volume changed during the 10 years after PAO and how patients described their hip pain and function 10 years after that procedure. Specifically, we investigated (1) if changes in hip cartilage thickness occurred after PAO, (2) how many patients had acetabular or femoral head cysts before undergoing PAO, (3) changes in cyst volume in the years after PAO, and (4) patient-assessed hip function and pain after PAO.

Methods

We performed a prospective cohort study with a 10-year followup. Our study included 26 patients (22 women and four men) with hip dysplasia scheduled for PAO between April 2003 and June 2004 at our institution. Eighty-six patients with hip dysplasia were assessed for eligibility in the study. Nine patients declined to participate and 51 were excluded. Of those excluded, 11 had a THA and three had an intertrochanteric femoral osteotomy simultaneous with the PAO (Fig. 1).

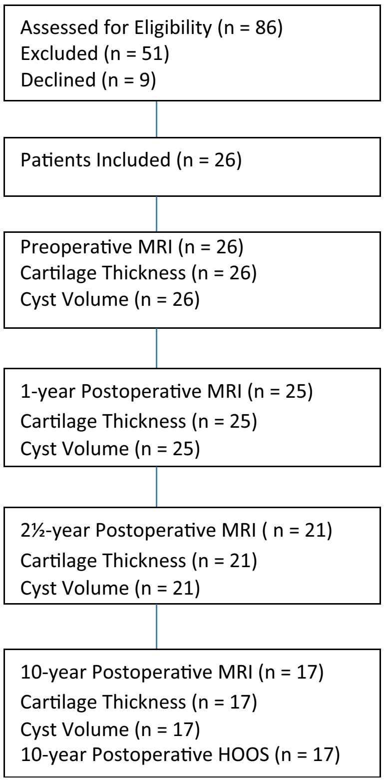

Fig. 1 Twenty-six patients with hip dysplasia scheduled for PAO were included in the study. Patients were seen at our institution between April 2003 and June 2004. HOOS = Hip disability and Osteoarthritis Outcome Scores.

The median age of the study patients at the time of PAO was 39 years (range, 19–53 years). Study inclusion criteria were: center-edge angle of Wiberg [26] 24° or less; OA degree, 0 or 1, according to the classification of Tönnis [25]; spherical femoral heads; closed growth zones in the pelvis; painful hip; and minimum 110° flexion in the hip. Exclusion criteria were: metal implants, neurologic illnesses, Legg-Calvé-Perthes disease, or previous corrective pediatric hip surgery. Written informed consent was obtained from patients and ethical approval was received from the Central Denmark Region Committee on Biomedical Research Ethics (Journal No 20030021). The study was registered at Clinical Trials.gov (NCT00119977).

All PAOs were performed by one surgeon (KS) using the transsartorial approach [24]. When performing the correction of the acetabulum, a specially made measuring device was used to measure the center-edge angle, using fluoroscopic guidance. This was done to avoid overcorrection of the acetabulum which can result in impingement [19].

The 26 study patients underwent MRI preoperatively; 25 patients were available for followup 1 year postoperatively which included another MRI series. Twenty-one patients were available for the 2½-year followup, and 17 (65%) underwent MRI at the 10-year postoperative followup. Of the nine who did not return for followups, three had undergone THA, three had substantial hip symptoms, and three were lost to followup. We compared baseline clinical and demographic data between the 17 who returned at 10 years with the nine who were lost to followup, and found that the 17 patients obtained a lower postoperative acetabular index angle ($p = 0.04$) (Table 1).

Imaging examinations were performed on a 1.5 Tesla Scanner (MAGNETOM® Symphony 1.5T eco; Siemens Corporation, Erlangen, Germany), using a body array surface coil. A fat-suppressed three-dimensional fast low-angle shot sequence was obtained. The imaging matrix was 256 × 256, and the field of view was 220 × 220 mm, with a section thickness of 1.5 mm. The repetition/echo time (TR/TE) was 60.0/11.0 ms, flip angle was 50°, and acquisition time was 9.38 minutes.

Continuous ankle traction was applied to the patient's leg during MRI to separate the acetabular and femoral cartilages. One person (IM) measured the thickness of the acetabular and femoral cartilage using a stereologic method we developed and which has been shown to be precise and efficient [15]. Based on repeated stereologic measurements of cartilage thickness obtained by preoperatively double MRI on 13 patients in this study, the limits of agreement are between −0.17 and 0.13 mm for acetabular cartilage and between −0.18 to 0.1 mm for femoral cartilage [15]. The stereologic method is based on four images through the center of the femoral head and was described in a previous study [16].

We used a design-based stereologic method (Cavalieri's principle) to measure the volume of cysts in the acetabulum and femoral head on sagittal images through the hip. The method was described previously [14]. All measurements were performed by one person (IM). Measurements of bone cysts, based on the same method, provided a limit of agreement between −1.45 and 2.01 cm.

Ten years after surgery, the Hip dysfunction and Osteoarthritis Outcome Score (HOOS 2.0) questionnaire [20] was used to measure patient-reported outcome in the subscales symptoms, pain, activities of daily living, function in sport and recreation, and hip-related quality of life. HOOS ranges from 0 to 100, with 100 equal to the best possible score. The HOOS scores were collected for all 17 patients when they came for MRI.

We present the results of the 17 patients who completed the 10-year-followup, and when pre- and postoperative comparisons were performed, only data from these 17 patients are compared. Data for cartilage thickness and cyst volume were tested for normality using the Shapiro-Wilk test and Q-Q plots. Normal distribution was assumed for cartilage thickness and differences between preoperative and 10-year postoperative data were tested by paired t test. Differences between preoperative cartilage thickness and radiographic angles in patients lost by the 10-year followup and the remainder of the patient group were tested using an unpaired t test. Data regarding cyst volume were not from a normal distribution and differences between preoperative and 10-year postoperative data were tested using Wilcoxon signed rank test. Stata® software, version 13.0 (StataCorp LP, College Station, TX, USA) was used for statistical computations.

Results

For the 17 patients who had MRI before surgery and 10 years later, the acetabular cartilage was unchanged 10 years after surgery compared with the preoperative acetabular cartilage thickness ($p = 0.73$). Preoperatively, the mean thickness of the acetabular cartilage was 1.38 ± 0.14 mm; and 10 years postoperatively, it was 1.43 ± 0.07 mm (Fig. 2). The patients' femoral cartilage was unchanged 10 years postoperatively compared with

Table 1. Baseline data for the 26 patients in the cohort

Patients	Age (years) Median (range)	Sex, females/ males	Preoperative center-edge angle Mean (SD)	Postoperative center-edge angle Mean (SD)	Preoperative acetabular index angle Mean (SD)	Postoperative acetabular index angle Mean (SD)	Preoperative acetabular cartilage thickness Mean (SD)	Preoperative femoral cartilage thickness Mean (SD)
Completed followup (n = 17)	43 (19–53)	16/1	15° (8°)	33° (6°)	16° (7°)	0.5° (4°)	1.4 mm (0.1 mm)	1.3 mm (0.2 mm)
Lost to followup (n = 9)	40 (25–52)	6/3	9° (15°)	29° (7°)	21° (10°)	4° (5°)	1.5 mm (0.2 mm)	1.4 mm (0.2 mm)

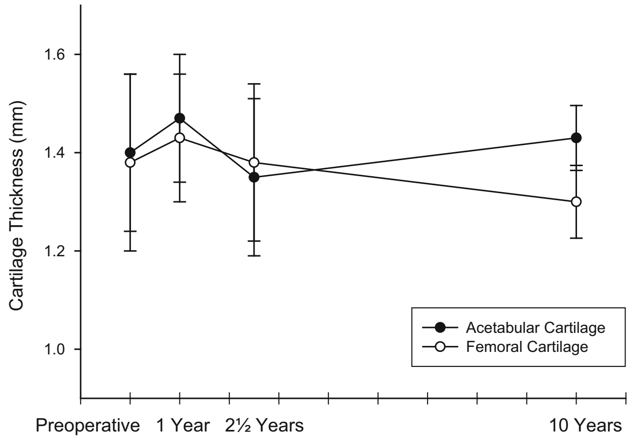

Fig. 2 Mean (± SD) acetabular and femoral cartilage thicknesses of dysplastic hips estimated with MRI and stereology before and after periacetabular osteotomy are shown.

preoperatively ($p = 0.24$). The mean thickness for the femoral cartilage preoperatively was 1.37 ± 0.20 mm and at 10 years postoperatively, it was 1.30 ± 0.07 mm.

Among the 17 patients who had MRI before surgery and 10 years later, seven had an increase in cyst volume, six had a decrease, and four had no cysts to start with and remained without cysts (Table 2). All acetabular cysts were located anterolaterally in the acetabulum except one that was located posterolaterally. Femoral head cysts were positioned anterolaterally and anteromedially.

The volume of bone cysts was unchanged 10 years after PAO compared with volume before surgery ($p = 0.18$). The median total cyst volume per patient preoperatively was 6.0 cm^3 (range, 1.6–188.3 cm^3) and 10 years postoperatively, it was 2.9 cm^3 (range, 0.7–8.2 cm^3). Preoperatively, three patients had cyst volumes greater than 80 cm^3. Ten years later, outcomes for the same three patients were: one had undergone a THA, one had radiologically verified OA, and one was lost to followup.

For the 17 patients who completed the 10-year MRI, self-assessed mean subscores for the HOOS were: pain, 79 ± 16; symptoms, 73 ± 17; activities of daily living, 85 ± 14; sport/recreation, 68 ± 22; and quality of life, 61 ± 19 (Table 2).

Discussion

Symptomatic patients with hip dysplasia undergo PAO to relieve pain, increase function, and hopefully, to delay or prevent the development of OA and the need for subsequent THA. It also is possible that the procedure may allow cartilage and bone repair [7], although the former has not been observed to our knowledge. We followed a cohort of patients for 10 years and investigated: (1) if changes in the thickness of hip cartilage take place after PAO; (2) how many of the studied patients had acetabular or femoral head cysts; (3) whether the volume of cysts changed after PAO; and (4) patient-reported hip function and pain after PAO.

We acknowledge limitations to our study. First, we had 10-year followup on only 17 of 26 study patients. There was no difference in preoperative cartilage thickness in patients who completed 10-year MRI and those who did not, but the 17 patients had a lower postoperative acetabular index angle after PAO (a less steep acetabulum) and tended to have less severe hip dysplasia with higher preoperative center-edge angle and lower preoperative acetabular index angle. From the electronic health records we collected information regarding the outcome of the nine patients not returning for the 10-year followup; three patients had THAs, three had hip symptoms, and three were lost to followup The three patients who underwent THAs most likely had thinner cartilage, lower HOOS scores, and possibly larger cyst volume at the time of revision compared with the preoperative measurements. One of the three patients with hip symptoms had verified hip OA and did not want a THA, one had labral degeneration treated with hip arthroscopy, and one had an injection of steroid and local anesthetic. Second, a limitation to our approach of measuring and presenting a mean cartilage thickness is that tissue loss in hip dysplasia is initiated in the anterolateral region [7] and the mean thickness may not show localized loss of cartilage. However, it has been shown with three-dimensional delayed gadolinium-enhanced MRI that there are biochemical changes globally in dysplastic hips [4]. Although tissue degeneration may initiate locally, OA is a biologically mediated event that affects the entire joint. Finally, our sample size was small and therefore had low statistical power to detect changes.

Ten years after PAO, six patients (23%) had substantial hip pain and/or had undergone THA and another three patients (12%) were lost to followup. Among the 17 patients (65%) who completed the 10-year MRI, cartilage thickness appeared to be preserved. Measurements of cartilage thickness represent radiographic joints space width or joint space narrowing [3, 12], which is considered the reference standard for assessment of progression of hip OA. Jacobsen et al. [10] reported that joint space width less than 2 mm is associated with patient-reported pain in or around the hip, which is in line with the acceptable pain scores of the 17 patients who did not experience thinning of the cartilage during the 10-year period after PAO.

Among the 17 patients who had MRI before surgery and 10 years later, seven had an increase in cyst volume, six had a decrease, and four had no cysts to start with and remained without cysts. It is likely that cyst volume has increased in the six patients with hip pain or THA and the

Table 2. Total cyst volume per patient (on MRI) and HOOS at followup

Patients		Total cyst volume per patient (cm^3)				HOOS at 10 years					Outcomes[#] for 9 patients not attending 10-year followup
Age at PAO	Sex	Preoperative	1 year postoperative	2½ years postoperative	10 years postoperative	Pain	Symptoms	ADL	Sport/ recreation	Quality of life	
41	F	1.6	1.5	1.7	None	85	65	82	50	63	
39	F	2.9	1.9	2.1	None	58	70	82	69	63	
47	F	3.4	2.9	2.5	*	∼	∼	∼	∼	∼	Hip arthroscopy 7 years after PAO
30	F	18.2	2.1	13.2	None	98	90	100	100	81	
47	M	None	8.5	7.0	*	∼	∼	∼	∼	∼	Lost to followup
52	F	188.3	146.2	62.4	*	∼	∼	∼	∼	∼	Hip OA but does not want THA
47	F	29.2	24.8	7.9	4.9	69	80	86	50	63	
45	F	1.9	0.6	2.6	*	∼	∼	∼	∼	∼	Lost to followup
25	F	6.7	9.2	*	*	∼	∼	∼	∼	∼	THA 8 years after PAO
53	F	4.0	9.6	5.7	2.9	68	45	54	31	38	
27	M	None	0.6	0.4	*	∼	∼	∼	∼	∼	THA 9 years after PAO
36	M	117.2	40.8	5.4	*	∼	∼	∼	∼	∼	Lost to followup
43	F	5.4	6.6	4.2	None	90	75	97	75	63	
27	F	None	10.9	2.9	None	73	55	82	75	81	
37	F	80.6	68.8	13.1	*	∼	∼	∼	∼	∼	THA 4 years after PAO
44	F	None	None	*	3.5	70	60	78	44	63	
52	F	None	None	None	2.7	80	90	94	56	88	
47	F	None	None	None	0.7	98	95	90	63	75	
32	F	None	None	None	8.3	80	75	91	88	38	
44	F	None	None	*	2.3	100	80	100	100	81	
30	F	None	None	None	7.4	53	60	79	44	31	
48	M	None	None	None	1.9	93	85	88	88	63	
19	F	None	None	None	None	88	95	100	88	56	
29	F	None	None	None	None	50	35	53	44	19	
40	F	None	None	*	*	∼	∼	∼	∼	∼	Hip injection of steroid/ local anesthetic
52	F	None	*	*	None	98	80	96	94	81	

PAO = periacetabular osteotomy; HOOS = Hip disability and Osteoarthritis Outcome Score; ADL = activities of daily living; OA = osteoarthritis; *did not attend MRI; ∼ did not complete HOOS at 10-year followup; [#]from the electronic health record.

three lost to followup. In a worst-case scenario we have a preponderance of worsening with time. As for the 17 patients completing 10-year MRI, volume of subchondral bone cysts was unchanged 10 years after PAO. However, the number of patients with an acetabular or femoral head cyst before PAO was low and we encourage caution with any interpretations. Since six patients had a decrease in cyst volume, a regenerative process can take place in the bony tissue after PAO where the biomechanical loading on the hip changes [2, 11]. In our study, this was supported by all bone cysts except two being located anterolaterally in the hip, where degeneration in the dysplastic hip often is found [7] and where peak contact stress is localized [21, 27]. Nakamura et al. [18] also found partial or complete cyst remodeling in 17 of 21 hips 5 years after patients underwent PAO. However, to our knowledge, cyst remodeling after PAO has not been reported in the literature, other than by Nakamura et al.

For the 17 patients without failed PAO, the patient-reported HOOS scores indicate acceptable hip function and pain up to 10 years after the procedure. The presence of bone cysts did not directly influence patient-reported hip function and pain. Patients with cysts did not score lower than those with no cysts on the HOOS assessments. Two patients had generally low HOOS scores but neither had bone cysts. Different patient-reported outcome scores are used to describe the mid- to long-term clinical outcomes after PAO and therefore are not directly comparable to the

HOOS scores applied in our study, but our scores are in a similar range of acceptable scores for pain, function, and quality of life as reported by others [1, 13, 22, 23].

Ten years after PAO, approximately 25% of the patients having a PAO will have substantial hip pain and/or undergo an arthroplasty. Of the patients who do not, cartilage thickness appears to be preserved. Future studies will need to help us decide which patients are most likely to succeed with a PAO at long-term followup.

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Chapter 8

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ORIGINAL PAPER

Blood perfusion and bone formation before and after minimally invasive periacetabular osteotomy analysed by Positron Emission Tomography combined with Computed Tomography

Inger Mechlenburg · Flemming Hermansen · Theis Thillemann · Kjeld Søballe

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Abstract
Purpose Sufficient blood perfusion is essential for successful bone healing after periacetabular osteotomy (PAO). The purpose of this study was to quantify blood perfusion and bone formation before and after PAO analysed by positron emission tomography (PET) combined with computed tomography (CT).
Methods Twelve dysplastic patients (nine women) were included consecutively in the study and all were operated upon by the senior author (KS). Median age was 33 (23–55) years. Initially, two patients were PET scanned in a pilot study to test our models for calculation of the physiological parameters. The following ten patients had their hip joints PET/CT scanned immediately before PAO and three to four weeks after. Oxygen-15-water was used to quantify blood perfusion and Flourine-18-fluoride was used to produce quantitative images interpreted as new bone formation in the acetabular fragment.
Results The blood perfusion of the operated acetabulum before surgery was 0.07±0.02 ml/min/ml, and after surgery 0.19±0.03 ml/min/ml (p=0.0003). Blood perfusion of the non-operated acetabulum was 0.07±0.02 ml/min/ml before PAO and 0.07±0.02 ml/min/ml after surgery (p=0.47). The fluoride-clearance per volume bone of the operated acetabulum was 0.02±0.01 ml/min/ml preoperatively, and 0.06±0.01 ml/min/ml postoperatively (p=0.0005). Fluoride-clearance of the non-operated acetabulum was 0.01±0.01 ml/min/ml before PAO and 0.02±0.01 ml/min/ml after PAO (p=0.49).
Conclusion Blood perfusion and new bone formation increased significantly in the acetabular fragment. Thus, the results of this study do not support the concern about surgically damaged vascularity after PAO.

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I. Mechlenburg · T. Thillemann · K. Søballe
Orthopaedic Research Unit, Aarhus University Hospital, Aarhus, Denmark

F. Hermansen
PET-Center, Aarhus University Hospital, Aarhus, Denmark

I. Mechlenburg (✉)
Department of Orthopaedics, Aarhus University Hospital, Tage-Hansens Gade 2, 8000 Aarhus, Denmark
e-mail: Inger.Mechlenburg@KI.AU.DK

Introduction

In periacetabular osteotomy (PAO) used for the treatment of hip dysplasia, the osteotomised acetabular fragment is reoriented and fixed with two screws to achieve better acetabular coverage. Bone healing is believed to be complete eight weeks after surgery and, from that time, the patients are allowed to fully weight-bear on the operated hip. Sufficient blood perfusion is held to be essential to successful bone healing after PAO, and from the time when Ganz et al. published their technique for performing the PAO [3], it has been a concern that PAO could potentially cause avascular necrosis of the acetabular fragment. Osteonecrosis of the acetabular fragment has been reported after PAO [2, 7, 11] and if hip osteoarthritis after PAO rapidly progresses, necrosis of the acetabular fragment should be suspected.

Beck et al. [1] performed an anatomical study of PAO through a modified Smith-Peterson approach and demonstrated that the acetabular fragment remains vascularised by the supra-acetabular and acetabular branches of the superior gluteal artery, the obturator artery and the inferior gluteal artery.

Blood perfusion in vivo during PAO has been studied by laser Doppler flowmetry in ten patients [5]. After complete separation of the acetabular fragment, nine out of ten patients had pulsatile signals, but the blood flow significantly decreased by 77 %. On termination of the surgical procedure, five out of eight patients showed a clear pulsatile signal in the supraacetabular area. In another study, 20 patients were examined with MRI [6], and three patients showed evidence of reduced vascularity six weeks after PAO has never been examined. The six-month scan showed some persistent vascular changes for one patient but the scan at one year showed complete resolution.

The effect on blood perfusion to the acetabular fragment and new bone formation after minimally invasive PAO has never been examined. The minimally invasive technique has been used for more than 400 cases at our institution and we have not encountered avascular necrosis of the acetabular fragment. Thus, we postulate that the minimally invasive PAO does not critically affect blood perfusion after surgery. The purpose of this study was to quantify blood perfusion and bone formation before and after PAO analysed by positron emission tomography (PET) combined with computed tomography (CT).

Patients and methods

The study was approved by The Biomedical Research Ethics Committee (Journal number: 20050005; Issue date: March 30th 2005) and registered with Clinical Trials.gov (NCT00119444), and all patients gave signed consent for participation in the study.

Twelve dysplastic patients (nine women) scheduled for PAO were included consecutively in the study. Median age was 33 (23–55) years. The participants had the following radiographic and clinical characteristics: centre-edge angle of Wiberg [18] was 24° or less, osteoarthritis degree 0 or 1 according to the classification of Tönnis [12], closed growth zones in the pelvis, a painful hip, and minimum 110° flexion in the hip. We excluded patients with neurological illnesses, Legg-Calvé-Perthes disease, or sequelae from previous hip surgery. We also excluded patients for whom an intertrochanteric femoral osteotomy was planned.

All patients had PAO using the trans-sartorial approach [13]. The incision was made from the anterior superior iliac spine descending six centimetres distally. The fascia over the sartorius muscle was incised and the lateral femoral cutaneous nerve was exposed and was visible in the operation field throughout surgery. With this approach the tensor faciae latae muscle and the abductor muscles are kept intact and the sartorius muscle is split in the fibre direction. The pubic bone was osteotomised and under fluoroscopic control the ischial osteotomies and the posterior iliac osteotomy were performed. Spinal anaesthesia was administered to all patients undergoing the procedure and local infiltration analgesia was administered before the wound was closed. A solution of 50 mL ropivacaine (2 mg/mL), 1 mL ketorolac (30 mg/mL), and 0.5 mL epinephrine (1 mg/mL) was prepared and loaded into a 100 mL syringe and infiltrated in deep tissues (iliopsoas muscle, tensor fascia latae muscle) and subcutaneous tissues. To reduce blood loss, 10 mg/kg of tranexamic acid was given at the beginning of surgery and repeated three hours postoperatively. For thromboprophylaxis, an injection of 2.5 mg fondaparinux was administered subcutaneously for two days, beginning on the day after surgery.

All patients followed the same program for PAO that included preoperative multidisciplinary information and well-defined optimised multimodal pain treatment for one week including 1 g paracetamol six-hourly starting in the post anaesthesia care unit. In cases of insufficient analgesia, when pain exceeded 30 mm on a visual analog scale up to maximum 100 mm, the patient was given supplemental oxycodone (5–10 mg orally). While in hospital (two to three days) the patients were seen daily by a physiotherapist for active hip range of motion exercises. The patients were ambulatory six hours after surgery and allowed 30 kg of weight-bearing and given instructions in maintaining the weight-bearing limit using crutches. Six to eight weeks after discharge, patients attended the outpatient clinic and radiographs were examined. If there was good callus formation and no radiographic changes in position of the acetabulum compared to postoperative recordings, progressive weight bearing was allowed up to full weight bearing. To assess the acetabular correction, the centre-edge angle and the acetabular index angle [12] were measured by one person (IM) on pre- and postoperative AP pelvic radiographs.

Initially, two patients were PET scanned with a PET scanner without CT in a pilot study to test our models for calculation of the physiological parameters. The following ten patients had their hip joints PET/CT scanned before PAO and three to four weeks after surgery. The first five patients were scanned on a Siemens Biograph 40 (USA) PET/CT scanner, and the following five on a Siemens Biograph 40 Truepoint (USA) PET/CT scanner. The PET/CT scanner combines PET and CT technology in the same gantry.

PET/CT acquisition protocol

The PET scanner was cross calibrated with the well-counter and the continuous arterial blood activity counter.

The patients had an arterial line placed in the radial artery for arterial blood sampling. A venflon was placed in an antecubital vein for tracer injection. The patients were positioned supine on the table with the legs in neutral rotation. The legs were supported by pillows and velcro tape in order to reduce movement. A scout acquisition was performed followed by a low-dose CT-scan, a dynamic water scan, and a dynamic fluoride scan.

[O-15]-water scans

A dynamic scan was performed for 6.5 minutes after bolus injection of [O-15]-water. Simultaneous arterial blood activity was measured every 0.5 second.

[F-18]-fluoride

A dynamic scan was performed for 90 minutes after bolus injection of [F-18]-fluoride. Forty arterial blood samples were collected, with the timing: 12×5 s, 4×10s, 4×20s, 4×30s, 5×60s, 6×300 s, 5×600 s, totalling 90 minutes The blood activity was measured in a well-counter.

Image processing

Low-dose 512×512 pixels CT images were constructed. The 128×128 pixels PET images were constructed and corrected for random events, detector sensitivity, dead-time, attenuation, and scatter.

Image analysis

The CT images were transferred to a Syngo Multimodality Workplace (VE36A SL10P25, Siemens). In the software (MI application, molecular imaging), transverse images were chosen and the number of images showing the relevant part of the lower acetabulum were noted. The multiframe polygon function was chosen and the regions of interest (ROI) were manually drawn on the approximately five axial CT images (4-mm slice thickness) covering the relevant part of the acetabulum. At first, the ROIs were drawn on the postoperative CT images in order to define the area below the osteotomy line (Fig. 1). The ROIs were drawn on the first CT image and then copied to the following images below and adjusted to fit the bony edges of the acetabulum. After that, the ROI defined on the postoperative CT images for both operated and non-operated acetabulum were copied to the preoperative CT images.

The regions of interest were then projected onto the dynamic [O-15]-water and the [f-18]-fluoride scans and mean time-activity curves were generated.

Compartment analysis

Perfusion was determined from the [O-15]-water scans. A one-compartment model was used. The time-activity

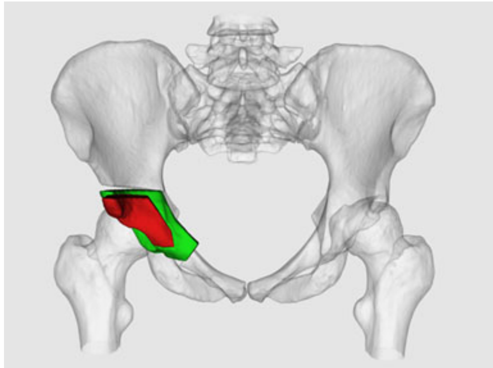

Fig. 1 Three-dimensional reconstruction based on CT images of hip illustrating region of interest (*red area*) defined for the right acetabular fragment (*green*) after surgical correction at periacetabular osteotomy

curves were fitted for K_1, k_2, and the delay, where K_1 is the perfusion [ml blood/min/ml bone]. The fluoride-clearance per volume bone (K_i) [ml blood/min/ml bone] was determined by applying Patlak graphical analysis to the time-activity curves of the fluoride scans, fitting the data from 45 to 90 minutes.

Statistics

Distribution of the data for blood perfusion and bone formation were assessed with scatter-plots and histograms, and normally distributed data were presented as mean ± one standard deviation (SD). In the normally distributed data the paired *t*-test was used to evaluate differences pre- and post-operative. Intercooled Stata software version 11.0 (StataCorp, College Station, TX) was used for statistical computations

Results

Acceptable correction of the acetabulum at PAO was demonstrated by the radiographic data (Table 1). Patlak analysis showed that the Patlak curves were reasonably flat from 45 to 90 minutes. They curved for times less than 45 minutes. Also non-linear regression with fitting for K_1, k_2 and k_3 was not stable if only the first 45 minutes were used. It turned out, that 90 minutes were required in order to calculate the fluoride uptake (K_i). Some patients had pain and could not stay in the scanner for the entire 90 minutes of the fluoride scan, which, therefore, could not be analysed. The water scans were as expected very noisy. Some of the water time-activity curves were too noisy to be analysed with the compartment model. Therefore data of sufficiently high quality was available for five out of ten patients for the water scans and for six out of ten patients for the fluoride scans (Table 2).

Table 1 Demographic data and results of clinical and radiographic examinations of the ten patients operated on by the periacetabular osteotomy

Case no.	Gender	Age at surgery (years)	Osteoarthritis degree at surgery	AI-angle preop./postop.	CE-angle preop./postop.
1-dx	F	23	0	14/0	20/30
2-dx	M	43	0	18/5	14/30
3-sin	F	33	0	16/13	20/32
4-dx	F	55	0	17/5	20/34
5-dx	F	29	1	27/12	0/26
6-sin	M	31	0	17/8	20/35
7-dx	F	24	0	10/−4	19/35
8-sin	M	36	0	19/−3	15/30
9-dx	F	44	0	11/−3	22/35
10-sin	F	34	1	28/1	0/27

F female, *M* male, *dx* dexter, *sin* sinister

The mean blood perfusion on the operated acetabulum before surgery was 0.07±0.02 ml/min/ml, and after surgery 0.19±0.03 ml/min/ml (p=0.0003). Blood perfusion on the non-operated acetabulum was 0.07±0.02 ml/min/ml before PAO and 0.07±0.02 ml/min/ml after surgery (p=0.47). The mean fluoride-clearance per volume bone on the operated acetabulum was 0.02±0.01 ml/min/ml preoperatively, and 0.06±0.01 ml/min/ml postoperatively (p=0.0005). Fluoride-clearance on the non-operated acetabulum was 0.01± 0.01 ml/min/ml before PAO and 0.02±0.01 ml/min/ml after PAO (p=0.49). All analysed fluoride-scans had the duration of 90 minutes, fitted from 45 to 90 minutes. Shorter analysis periods were tried, but the results varied up to a factor of two.

Discussion

The blood flow to the acetabular fragment has been of some concern in PAO used for the treatment of hip dysplasia. This study shows that blood perfusion increased significantly in the acetabular fragment, demonstrating that blood perfusion to the acetabular fragment is not compromised three to four weeks after minimally invasive PAO. New bone formation in the acetabular fragment on the operated side increased significantly, also indicating sufficient blood perfusion. Thus it seems that the biological response to PAO is that bone blood flow increases and the mineralisation next to the osteotomy site accelerates. During minimally invasive PAO care is taken to position the osteotomy lines as far from the joint as possible in order to leave a large bony fragment with potential for sufficient blood supply, and these results convince us that this procedure is appropriate.

This is the first paper applying PET/CT to quantify blood perfusion and bone formation before and after PAO in vivo. We were inspired by a study [10] quantifying blood perfusion and new bone in the allograft around revisions of total hip arthroplasty. The group has performed several PET

Table 2 Blood perfusion and fluoride-clearance measured by PET/CT on the operated acetabulum and the non-operated acetabulum before and after periacetabular osteotomy for ten patients with hip dysplasia

Case no.	Preop. blood perfusion operated side ml/min/ml	Postop. blood perfusion operated side ml/min/ml	Preop. blood perfusion contralateral side ml/min/ml	Postop. blood perfusion contralateral side ml/min/ml	Preop. fluoride-clearance operated side ml/min/ml	Postop. fluoride-clearance operated side ml/min/ml	Preop. fluoride-clearance contralateral side ml/min/ml	Postop. fluoride-clearance contralateral side ml/min/ml
1-dx	0.05	Missing	0.05	Missing	0.002	0.06	0.002	0.02
2-dx	0.05	Missing	0.05	Missing	0.03	0.06	0.02	0.03
3-sin	0.06	0.20	0.06	0.06	0.03	0.07	0.02	0.02
4-dx	0.06	0.15	0.06	0.06	0.02	0.05	0.02	0.01
5-dx	0.10	Missing	0.09	Missing	0.01	0.04	0.01	0.01
6-sin	0.08	Missing	0.07	Missing	0.02	Missing	0.01	Missing
7-dx	0.07	0.20	0.07	0.07	Missing	Missing	Missing	Missing
8-sin	0.06	0.18	0.07	0.06	0.02	0.06	0.02	0.01
9-dx	Missing	0.20	Missing	0.14	0.02	Missing	0.02	Missing
10-sin	0.10	0.23	0.10	0.10	Missing	Missing	Missing	Missing

dx dexter, *sin* sinister

studies [14, 15, 17] on orthopaedic patients and report the method to be sensitive to visualise osteonecrosis that cannot be seen on plain radiographs [16]. That study did not report technical problems as we had in this study, namely, failed PET scannings due to patient movement during scanning or technical problems affecting the data sampling. Because of the long acquisition time of the PET scan, it was difficult for the patients to lie unmoving for 90 minutes. Furthermore, these patients have hip pain both before surgery and three to four weeks after, and thus they were informed prior to the PET/CT scanning that they could have oral analgesia if they thought it would be a problem to lie motionless. Most patients asked for oral analgesia before the PET scannings.

From these two PET/CT scannings, the dose of radiation to each patient was equivalent to three times the normal background radiation; thus, we could not justify asking more patients than the included ten patients to undergo PET/CT scanning, although we would have liked to have had data on more patients.

PET/CT image artefacts are due primarily to metallic implants, respiratory motion, use of contrast media and image truncation [9]. The presence of metallic implants is seen as areas of high density, which cause artefacts on the CT images [4]. The two titanium screws that fix the acetabular fragment after the periacetabular osteotomies caused only minor artefacts that did not interfere with the ROIs on the CT images. To minimise the presence of artefacts due to metallic implants, the physician asked the patient to remove all metallic objects prior to scanning.

The PAO is a technically demanding procedure and can be prone to creation of secondary mechanical abnormalities of the hip joint if the acetabular correction is excessive or insufficient and these two conditions can lead to further labral and cartilage degeneration. The patients in this study were operated upon via minimally invasive PAO and satisfactory correction of the acetabular morphology was obtained after PAO. The mean duration of the minimally invasive PAO is 70 (50–85) minutes [8] and average intraoperative blood loss is 250 (200–350) mL [13]. It is likely that blood flow may be more seriously affected with longer surgery time and greater blood loss.

In conclusion, blood perfusion of the acetabular fragment is not critically compromised after minimally invasive PAO and the formation of new bone in the fragment increases within the first postoperative month. Thus, the results of this study do not support the concern about surgically damaged vascularity after PAO. We found PET/CT to be a useful method for evaluation of blood perfusion and bone formation but problems with patient motion should be considered before initiating a similar study.

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Contribution of authors All co-authors took part in the planning of this study and in the writing of this article. Flemming Hermansen and Theis Thillemann were responsible for PET scanning of the patients. Kjeld Søballe diagnosed and operated upon all patients. As the first author Inger Mechlenburg was responsible for coordination of the different elements in this study and responsible for the inclusion of the patients and overall responsible for the decisions made in this study. All authors declare that they have no financial or personal relationships with other people or organisations that could inappropriately influence their work.

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Chapter 9

Original Article

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No correlations between radiological angles and self-assessed quality of life in patients with hip dysplasia at 2–13 years of follow-up after periacetabular osteotomy

Sara Birch[1], Anette Liljensøe[2], Charlotte Hartig-Andreasen[2], Kjeld Søballe[2] and Inger Mechlenburg[2]

Abstract

Background: Only few studies have described patients' health-related quality of life (QoL) after periacetabular osteotomy (PAO). Thus, there is a lack of data on the self-assessed outcome of patients operated with PAO, and none of the existing studies correlate the results from Medical Outcomes Short Form-36 questionnaire (SF-36) with the radiological parameters.

Purpose: To investigate the health-related QoL for patients with hip dysplasia operated with PAO and to investigate whether QoL is associated with the acetabular angles or hypermobility.

Material and Methods: Out of 388 patients, 228 patients (mean age, 40.5 years; mean follow-up, 7.1 years) returned the SF-36 and Beighton questionnaires. The patient's QoL was compared to reference data from a Danish population. Center-edge (CE) and acetabular index (AI) angles were measured before and after PAO and the association with the patients' QoL was tested with logistic regression.

Results: For both men and women the postoperative SF-36 score was significantly lower than for the reference data for a Danish population, especially for those dimensions concerning physical health. No association was found between the patients' CE or AI angles before or after PAO and their subsequent QoL. Significant associations were found between both Physical Component Score (PCS) and physical function (PF) and follow-up time after the operation. The adjusted OR for a PCS $\geq$ 50 was 0.87 (95% CI 0.76–0.99) and for a PF $\geq$ 85 0.81 (95% CI 0.71–0.91). No association between hyper mobility and PCS, PF, or bodily pain (BP) was found.

Conclusion: The physical components of QoL in patients undergoing PAO are significantly lower than the Danish population used as reference. Furthermore, the results suggest that physical function after PAO decreases with longer follow-up time. Neither the acetabular angles nor hypermobility is associated with the physical components of QoL.

Keywords

Periacetabular osteotomy, health-related quality of life, acetabular angles, hypermobility

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Introduction

Developmental hip dysplasia is one of the most common hip disorders among children and adults and the prevalence for the adult population is estimated to be around 4%, with a higher prevalence among women compared to men (1,2).

The periacetabular osteotomy (PAO) aims to increase coverage of the femoral head by a reorientation of the acetabulum (3). This change of hip

[1]Department of Physiotherapy and Occupational Therapy, Herning Regional Hospital, Denmark
[2]Department of Orthopedic Surgery, Aarhus University Hospital, Denmark

Corresponding author:
Sara Birch, Department of Physiotherapy and Occupational Therapy, Herning Regional Hospital, Gl. Landevej 61, DK-7400 Herning, Denmark.
Email: Sara.Birch@vest.rm.dk

biomechanics is believed to delay or prevent the development of osteoarthritis (4,5).

The center-edge (CE) angle according to Wiberg (6) and the acetabular index (AI) angle according to Tönnis (7) are used as tools to diagnose hip dysplasia (1,8). Several studies show that PAO results in a significant improvement of the radiographic parameters and a short-term improvement of physical function (PF) (8–10). However, only few studies have correlated radiographic parameters with the clinical outcome after surgery (11–13).

Siebenrock et al. reported that a postoperative AI angle outside the interval of 0–10° negatively influenced the outcome after PAO at 10 years of follow-up (13), although they were not able to verify this correlation at 20 years of follow-up (5). Two retrospective case studies found that a postoperative CE angle outside the range of 30–40° predicted conversion to total hip arthroplasty (THA) (14,15). In contrast, other studies found no association between acetabular correction and patient satisfaction or PF despite a significant change in the radiographic parameters (5,11).

Several previous studies describing the outcome after PAO have used the surgeon-assessed Merle d'Aubigné and Postel score or the Harris Hip score (13,16). Only few studies have described the patients' quality of life (QoL) after the operation using the Medical Outcomes Short Form-36 questionnaire (SF-36) (10,15,17). Thus, there is a lack of data on the self-assessed outcome of patients operated with PAO, and none of the existing studies have compared the results from SF-36 with the radiological parameters.

The purpose of this study was: (i) to describe the health-related QoL for patients with hip dysplasia operated with PAO compared to reference data for a Danish population; (ii) to estimate a possible correlation between the radiographic parameters and the patients' health-related QoL; and (iii) to examine if the health-related QoL differs between hypermobile and non-hypermobile patients.

Material and Methods

The patients were identified from a clinical database at the Department of Orthopedics at Aarhus University Hospital in Denmark. All patients operated with PAO at this department from January 1999 to December 2010 ($n = 529$) were assessed for eligibility in the study. Initially, 141 patients were excluded, 80 patients because of subsequent THA operation, 40 patients were excluded from the study because of Legg-Calve-Perthes (LCPD) and other syndromes causing hip dysplasia, two patients due to death, two patients emigrated, 10 patients were from countries outside Denmark, and for seven patients it was impossible to retrieve their addresses. During April 2012, SF-36 and Beighton score were sent to 388 patients and 228 of these returned the questionnaire (59%).

Patients with bilateral PAO involvement ($n = 66$) only entered into the study once and data were measured at the first operated hip. If both hip joints were operated at the same time, the right hip was chosen ($n = 3$). Preoperative data consisted of body mass index (BMI) calculated from body weight and height at the time of the operation, diagnosis, and date of operation and were retrieved from medical records. BMI was measured in a standardized manner before surgery by a nurse. BMI was missing for 35 patients.

The patients' self-reported assessments of health were evaluated by SF-36. This is a general health assessment tool validated for measuring the global functional outcome (18). It consists of 36 items in eight dimensions which are summarized in the two summary measures of physical and mental health. For each dimension, item scores were coded, summed, and transformed to a scale from 0 (worst health) to 100 (best health). Data from the questionnaire were dichotomized in high and low QoL. Cut-off points to define high *versus* low QoL were calculated *a priori* using the first quartile of SF-36 data from a Danish reference population. Data from the questionnaire were entered into Quality Metric Health Outcomes Scoring Software 4.5 and compared with reference data from a Danish population collected in 1994. The reference data were derived from a Danish study based on a representative group of 6000 persons aged over 15 years (19). To control for confounding, we controlled for the following parameters: age at follow-up, gender, follow-up time, BMI at the time of the operation, working status, and level of education.

Beighton score is a test to diagnose general joint hypermobility and consists of five different tests. Four of these tests are performed bilaterally. Each positive Beighton test counted as 1 point, giving a maximum of 9 points. Since there is no universally accepted cut-off level for the diagnosis of general joint hypermobility, we defined a Beighton score of five or more positive tests out of nine to be the criterion for hypermobility (20,21). Along with the questionnaires the patients were asked to specify their education after high school classified into one of five categories (none, student, short [1–2 years], medium [3–4 years], long [$\geq$ 5 years]) and their working status classified into one of three categories (employed, unemployed, and student/retired).

On preoperative and postoperative antero-posterior (AP) digital radiographs of the pelvis, the CE and AI angles were measured by two readers blinded for the data on the patients' QoL. The radiological angles were based on either lying or weight-bearing images. The weight-bearing images were first choice, but if these were not available lying pictures were used. Both the lying and the weight-bearing images were based on standardized protocols. The CE angle was obtained by drawing a vertical line through the femoral head perpendicular to the horizontal inter-ischial-tuberosity-line (22). A line was then drawn from the center of the femoral head to the most supero-lateral point of the acetabulum (Fig. 1). The AI angle was formed by a line parallel to the inter-ischial-tuberosity-line and a line from the lateral point to the medial point of the weight-bearing portion of the acetabulum (Fig. 1).

Radiographs of poor quality were excluded if two of the authors agreed that measurements of angles were not possible.

Intra-observer and inter-observer variability was assessed on the first 26 measurements of the acetabular angles (Table 1) and computed according to the Bland-Altman approach (23). Intra- and inter-observer assessments showed similar agreement to those reported in the literature (24,25).

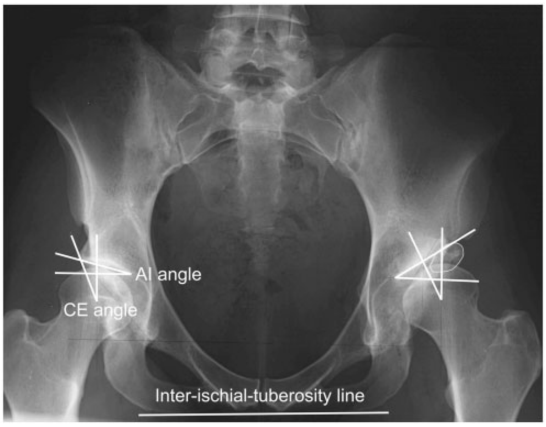

Fig. 1. The CE and AI angles measured on an AP radiograph of a patient with bilateral hip dysplasia. The right hip has a CE angle of 20° and an AI angle of 15°. The left hip is severely dysplastic with a CE angle of –17° and an AI angle of 33° and a large os acetabuli is seen (encircled).

Table 1. Inter-observer and intra-observer variability of CE and AI angles.

	Measurements (*n*)	Mean difference	Standard deviation	95% limits of agreement
Interobserver				
CE angle	26	1.50°	±3.3°	–5.0°–8.0°
AI angle	26	–0.08°	±2.7°	–5.5°–5.3°
Intraobserver				
CE angle	26	–0.08°	±1.5°	–3.1°–2.9°
AI angle	26	0.27°	±1.0°	–1.8°–2.4°

Statistical analysis

Data are presented as means with standard deviation (SD) when normally distributed and as medians with interquartile ranges (IQR) when not normally distributed. The categorical data are presented as prevalence. In the normally distributed data the Students t-test was used to evaluate differences from pre- to postoperative. Before the t-test the assumptions of the model were tested. Distribution of the data was assessed by qq-plots, histograms, and scatterplots. When testing differences between the study group and the reference data, binomial test was used. A logistic regression analysis was performed to estimate a possible association between the different exposures and QoL. The odds ratios were adjusted for age, sex, follow-up, BMI, working status, and level of education. The assumptions for the logistic regression were met: all the observations in the sample (*n*) were independent; had the same probability of event; the response variable (SF-36) was dichotomized; and the sample sizes (*n*) were determined in advance. Stata software version 11.0 (StataCorp, College Station, TX, USA) was used for statistical computations.

Results

The demographic characteristics of the study group are presented in Table 2. Analysis showed no differences between the group of patients that participated in the study and those that were invited but did not participate.

For both men and women the SF-36 score for the study group was significantly lower than for the reference data from a Danish population, especially for those parameters concerning the physical health (Table 3). The median score for women was significantly lower for the subscales PF, bodily pain (BP), general health (GH), and vitality (VT) ($P < 0.001$) with a difference between the two groups from 10 to 22 points. The median Physical Component Score (PCS) was 49.2 (IQR, 38.8–55.0) and significantly less than in the reference data of Danish women (54.6 [IQR 50.3–57.0], $P < 0.001$). The difference between the male patients and the reference data of Danish men aged above 18 years was significant for PF ($P < 0.001$) and BP ($P < 0.001$).

Preoperative radiographic material was excluded for seven patients and postoperative radiographs were excluded for two patients. The mean CE and AI angles changed significantly from pre- to postoperative. The CE angle increased mean 18° ($P < 0.001$) and the AI angle decreased mean 14° ($P < 0.001$) and was after PAO within the normal range for these acetabular angles (Table 2). There was no association between any of the radiological data and the health-related QoL (Table 4).

Table 2. Demographic and radiographic data for the study population of 388 patients with hip dysplasia operated with PAO. Data are shown for the group of responders and non-responders and presented as mean (range) or numbers (%).

Parameter	Responders ($n = 228$)	Non-responders ($n = 160$)	P value
Demographic data			
Women	189 (83)	122 (76)	0.1
Men	39 (17)	38 (24)	0.1
Age (years)	40.5 (18–72)	39.5 (18–66)	0.4
Age at time of operation (years)	33.4 (13–61)	32.4 (13–58)	0.3
BMI (kg/m^2)	23.9 (16.9–33.2)	–	–
Bilateral involvement	66 (29)	36 (23)	0.2
Follow-up (years)	7.1 (1.9–13.6)	7.1 (1.9–13.5)	0.9
Congenital hip dislocation	24 (10.5)	–	–
Hypermobile	35 (16.3)	–	–
Level of education		–	–
None	16 (7.4)		
Student	27 (12.5)	–	–
Short (1–2 years)	65 (30.1)	–	–
Medium (3–4 years)	83 (38.4)	–	–
Long (≥5 years)	25 (11.6)	–	–
Working status			
Employed	155 (69.2)	–	–
Unemployed	53 (23.7)	–	–
Student/retired	16 (7.1)	–	–
Radiographic data			
CE angle preoperative	14 (–29–50)	13 (–12–30)	0.8
CE angle postoperative	31 (0–49)	32 (15–50)	0.4
AI angle preoperative	18 (–2–43)	18 (3–45)	0.9
AI angle postoperative	4 (–20–28)	4 (–14–20)	0.3

BMI is missing for 35 patients.

Preoperative data is missing for seven responders and 11 non-responders. Postoperative data is missing for two responders.

The mean follow-up on the patients was 7.1 years (range, 1.9–13.6 years). The association between PCS and PF and the number of years after the PAO operation (follow-up) was statistically significant after adjusting for potential confounders, i.e. gender, age, BMI, working status, and level of education. A 1-year difference in follow-up time between two patients with the same gender, age, BMI, level of education, and working status increases the risk of having a low PCS with 13% and low PF with 19% for the person with the longest follow-up time. The adjusted OR for PCS was 0.87 (95% CI 0.76–0.99) and for PF 0.81 (95% CI 0.71–0.91) (Table 5).

The prevalence of patients with hypermobility in the study group was estimated to be 16.3%. There were no significant differences in PCS, PF, and BP for hypermobile patients compared to non-hypermobile patients after adjustment for gender, age, follow-up, BMI, working status, and level of education.

Discussion

The aim of this study was to describe the self-assessed QoL in patients with hip dysplasia after PAO; to estimate a possible association between the CE and AI angles and the self-assessed QoL; and finally to examine if the health-related QoL differs between hypermobile and non-hypermobile patients.

As expected the SF-36 score was lower for the PAO group compared to the reference data from the Danish population. For women in particular, the differences were considerable. The medians score differences in the four physical subscales (PF, RP, BP, and GH) were between 10 and 22 points. The scores of the women differed in general more from the reference data than for the men, suggesting that men achieve a QoL closer to the reference data after a PAO. The Minimal Clinical Important Difference (MIREDIF) in SF-36 was in the sample size calculation *a priori* set at

Table 3. QoL assessed with SF-36 for women and men in the study group and in a database of reference data.

Women	Study group ($n=190$)	Danish population ($n=2141$)	P value
PF	80 (55–94.9)	95 (85–100)	<0.001
RP	87.5 (50–100)	100 (75–100)	–
BP	62 (41–84)	84 (62–100)	<0.001
GH perceptions	72 (50–87)	82 (67–92)	<0.001
VT	62.5 (43.8–75)	75 (55–85)	<0.001
SF	100 (75–100)	100 (87.5–100)	–
RE	100 (75–100)	100 (66.7–100)	–
MH	83.3 (70–90)	84 (72–92)	0.94
PCS	49.2 (38.8–55.0)	54.6 (50.3–57.0)*	<0.001
MCS	55.7 (50.1–59.6)	55.7 (49.8–58.5)*	1.00
Men	**Study group ($n=39$)**	**Danish population ($n=1943$)**	**P value**
PF	90 (75–100)	95 (90–100)	<0.001
RP	94 (75–100)	100 (75–100)	–
BP	74 (51–100)	84 (72–100)	<0.001
GH perceptions	77 (52–92)	82 (67–92)	0.20
VT	75 (50–87.5)	75 (60–85)	0.20
SF	100 (87.5–100)	100 (100–100)	–
RE	100 (100–100)	100 (100–100)	–
MH	85 (75–95)	88 (76–92)	0.52
PCS	52.2 (44.7–56.4)	55.0 (51.8–57.1)*	0.20
MCS	57.4 (54.4–60.8)	56.7 (52.4–58.9)*	0.20

Data are reported as median (IQR). The differences between the two groups are calculated with test for binomial distribution. The reference data are from a Danish population of men and women aged above 18 years, respectively.
*Reference data for a Danish population from 35–45 years.
BP, bodily pain; GH, general health; MCS, Mental Component Score; MH, mental health; PCS, Physical Component Score; PF, physical function; RE, role emotional; RP, role physical; SF, social function; VT, vitality.

Table 4. Crude and adjusted odds ratios (ORs) for high QoL with different radiological angles.

	OR (95% CI)	P value	Adjusted OR* (95% CI)	P value
CE angle <30° or >40°				
Physical Component Score	0.78 (0.45–1.33)	0.36	0.62 (0.32–1.19)	0.15
Physical function	1.07 (0.63–1.81)	0.80	1.15 (0.59–2.23)	0.68
Bodily pain	0.73 (0.43–1.25)	0.23	0.68 (0.35–1.33)	0.26
AI angle >10°				
Physical Component Score	1.01 (0.97–1.05)	0.62	0.67 (0.27–1.66)	0.39
Physical function	1.01 (0.97–1.05)	0.32	0.85 (0.33–2.16)	0.73
Bodily pain	1.01 (0.97–1.04)	0.60	0.89 (0.35–2.27)	0.81

The table shows the OR for high QoL (PCS ≥50, PF ≥85, BP ≥62) for a CE angle <30° or >40° compared to one 30–40° and for an AI angle >10° compared to one <10°. OR is calculated with logistic regression analysis.
*The crude OR adjusted for sex, age, follow-up, BMI, working status, and level of education.

10 points, since a difference of 10 points between reference data and patients with a chronic disease is considered clinically important (19). Hence, we consider the results from this study both significant and clinically relevant. However, the Mental Component Scores (MCS) were comparable, suggesting that physical health has no negative influence on the mental QoL for PAO patients at a medium-term follow-up.

Table 5. Association between follow-up and QoL.

	OR (95% CI) follow-up	*P* value	Adjusted OR* (95% CI) follow-up	*P* value
Physical Component Score	0.92 (0.85–1.0)	0.06	0.87 (0.76–0.99)	0.04
Mental Component Score	0.98 (0.89–1.08)	0.65	0.94 (0.82–1.07)	0.32
Physical function	0.87 (0.79–0.94)	0.001	0.81 (0.71–0.91)	<0.001
Bodily pain	0.96 (0.89–1.05)	0.37	0.94 (0.83–1.06)	0.29

The table shows the odds ratio (OR) for high QoL (PCS $\geq$50, MCS $\geq$50, PF $\geq$85, BP $\geq$62) per year since the operation. OR is calculated with logistic regression analysis.
*The crude OR adjusted for sex, age, BMI, working status, and level of education.

Only few studies have described the QoL among patients undergoing PAO with the generic questionnaire SF-36 (10,15,17). Van Bergayk and Garbuz reported a mean PCS of 49.2 and a mean MCS of 54.7 for 22 patients with a follow-up of 2.0–3.5 years after PAO (10). Our results are comparable to these scores. At mean follow-up of 7.1 years we found a mean PCS and MCS of 46.9 and 53.7, respectively. However, this study shows that the PCS decrease over time after PAO and the follow-up in our study is substantial longer than in the study of van Bergayk and Garbuz (10). Troelsen et al. reported a median PCS of 48.31 and a MCS at 57.95 for 87 PAO patients with a mean follow-up of 6.8 years after the PAO (15). Those scores are comparable with the combined median scores for men and women in this study (49.66 and 56.34, respectively).

The PAO operation aims to relieve pain, improve the PF, and extend the lifetime of the patients' own hip and to improve the patients' PF. The SF-36 PCS has shown to increase from preoperatively 33.9 to 49.2 2.0–3.5 years postoperatively (10) however, this study suggests that the physical improvements achieved by the PAO will not last. The association between follow-up and the PF and follow-up and the PCS was statistically significant. After adjustment the odds of having a PCS $\geq$ 50 become 13% lower for every year after the operation and the odds of having a PF $\geq$85 becomes 19% lower. Based on the results we cannot conclude that PF decreases for the individual but for the group as a whole PF decreases with longer follow-up.

It was not possible to find other studies investigating self-assessed QoL over time after a PAO surgery, but Steppacher et al. reported a drop in PF measured with Merle d'Aubigne and Postel score from 16.7 at 10-year follow-up to 15.8 at 20-year follow-up (5). The same pattern is found for patients after a THA surgery due to osteoarthritis (26,27). Söderman et al. found that the SF-36 PF scores both 3 and 10 years after THA were lower than the general populations and that the scores decreased from 2 to 10 years of follow-up (27) A possible reason for the drop in PF and the PCS in this study may be progression of osteoarthritis after the operation and a weak but significant correlation between the postoperative grade of OA and the SF-36 score has been established (17).

In contrast to our hypothesis the results in the present study showed no association between the radiological parameters and the physical aspect of SF-36. A possible explanation might be that the study group consisted only of patients with preserved hips at a mean follow-up at 7.1 year and those with conversion to THA were excluded. If these patients had been asked to fill out the SF-36 before their THA operation we might have been able to find an association.

Excessive joint laxity in children with hip dysplasia has been described in one study (28). Hypermobility results in an increased Beighton score. However, Engesaeter et al. found no association between Beighton hypermobility score or EQ-5D and hip dysplasia in 2081 19-year-old Norwegians (29). General joint hypermobility is claimed to be present in 5–15% of the general population. It occurs more frequently in children compared to adults and girls are slightly more affected than boys (30). The prevalence of hypermobility in the present study was estimated to 16%. There is no universally accepted cut-off level for the diagnosis of general joint hypermobility but in Denmark the most used cut-off point is $\geq$4. To ensure that the Beighton score was not overestimated by the patients, we defined the cut-off level to be $\geq$5 instead of $\geq$4. As for Engesaeter et al., no association between hypermobile patients and self-assessed QoL was found and the prevalence of general joint hypermobility was only slightly higher than in the general population.

There are some limitations in this study. First, only 228 patients out of the 388 eligible patients returned the SF-36 questionnaire. This means that the self-assessed QoL for 41% of the cohort is unknown. However, we did not find any statistical significantly difference in demographic or radiographic data between patients returning the questionnaires and those who did not return it. Hence we consider the data obtained representative. Second, the SF-36 was not sent to the patients before the PAO. Thus, it was not possible to evaluate if the SF-36 score of the participants had changed over time but merely to compare the SF-36 score for the group of patients with reference data from a Danish population. Due to the size of the study group, we presume that these data give a valid estimation of the individuals' QoL during the years after the operation. Third, the indications for PAO have changed during the study period. From 2003 hips with moderate osteoarthritis (Tönnis grade 2) were no longer offered PAO.

In conclusion, this study shows that the physical components of the QoL in patients undergoing PAO due to hip dysplasia are significantly lower than the Danish population used for reference. Furthermore, the improvements in PF after PAO seem to be temporary and decrease over time. We found no association between the radiological angles and QoL. Finally, the QoL among hypermobile patients with symptomatic hip dysplasia treated with PAO is not different from the QoL for non-hypermobile patients.

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Chapter 10

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ORIGINAL PAPER

Radiation exposure to the orthopaedic surgeon during periacetabular osteotomy

Inger Mechlenburg · Henrik Daugaard · Kjeld Søballe

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Abstract The objective of this study was to directly measure the radiation exposure to the orthopaedic surgeon and to measure dose points to the surgeon's fingers, thyroid gland, and forehead during intraoperative fluoroscopy in periacetabular osteotomy (PAO). In a series of 23 consecutive periacetabular osteotomy procedures, exposure monitoring was carried out using thermo luminescent dosimeters. The effective dose received by the operating surgeon was 0.008 mSv per operation which adds up to a yearly dose of 0.64 mSv from PAO. The median point equivalent dose (mSv) exposure under PAO was 0.009 for the forehead and thyroid gland, 0.045 for the right index finger, and 0.039 for the left index finger. The effective estimated yearly dose received by the operating surgeon was very low. Wearing a lead collar reduces radiation exposure to the thyroid gland while the lead gloves did not protect the surgeon's fingers.

Résumé L'objectif de cette étude est de mesurer l'exposition aux rayons X au niveau des mains et de la thyroïde des chirurgiens orthopédistes après utilisation de l'amplificateur de brillance au cours d'une ostéotomie périacétabulaire. Matériel et méthode: une série de 23 ostéotomies pericétabulaires a été réalisée en utilisant l'ampli. Résultat: la dose effective reçue par le chirurgien était de 0,008 mSv par intervention et doit s'additionner avec la dose de 0,64 mSv du fait de l'ostéotomie péri acétabulaire. La dose moyenne d'exposition était de 0,009 pour le tronc et la glande thyroïde, de 0,045 pour l'index droit et de 0,039 pour l'index gauche. En conclusion: les doses reçues par le chirurgien sont très basses. Le port d'un collier de protection permet de diminuer les radiations au niveau de la thyroïde et l'utilisation de gants de plomb ne permet pas de protéger les mains des chirurgiens.

I. Mechlenburg (✉) · H. Daugaard · K. Søballe
Department of Orthopaedics, University Hospital of Aarhus,
Tage-Hansens Gade 2,
8000 Aarhus C, Denmark
e-mail: INGER.MECHLENBURG@KI.AU.DK
URL: www.orthoresearch.dk

Introduction

Orthopaedic surgeons are exposed to ionising radiation during intraoperative fluoroscopy in procedures such as periacetabular osteotomy (PAO), but spine and trauma surgeons also perform a number of procedures requiring X-ray examination. PAO is a procedure performed by only a few surgeons, and at our institution one surgeon performs approximately 80 such operations per year. Thus, the same surgeon is assumed to have a higher radiation exposure than his colleagues. During fluoroscopy, the surgeon is exposed to either primary or scatter radiation due to the necessary proximity to the fluoroscope. The assistant surgeon, nurses, and anaesthetists are better protected against radiation from the fluoroscope because they can distance themselves from the fluoroscope when it radiates, thus the exposure is reduced to nearly immeasurable values; but also due to staff rotations, such that the assistant surgeons and nurses do not assist all of the PAO procedures, their exposures are limited [2, 14, 17, 18].

In the orthopaedic theatre much is done to reduce the radiation and protect the staff by employing short screening time and intermittent radiation. In addition, the staff is required to use personal shielding to protect against X-ray exposure. However, it must be remembered that the shielding is only relative and most shields do not filter out the entire X-ray beam [19].

In many situations, the effective whole body radiation dose is only a fraction of the dose to a single organ or tissue

[7, 10, 12]. In these cases, the individual organs become the critical factors in the assessment of radiation hazards. For this reason, we wanted to undertake a study measuring the radiation exposure to the orthopaedic surgeon using intra-operative fluoroscopy at PAO. Only the orthopaedic surgeon was monitored as he and his hands are positioned close to the X-ray source. Thus, the purpose of this study was to directly measure the radiation exposure to the orthopaedic surgeon and to measure dose points to the surgeon's fingers, thyroid gland, and forehead (reflecting the dose to the lens of the eye) during intraoperative fluoroscopy in a series of consecutive PAO.

Materials and methods

A prospective study of radiation exposure to the orthopaedic hip surgeon was carried out at Aarhus University Hospital. Twenty-three consecutive PAO procedures performed by one surgeon were monitored using thermo luminescent dosimeters (TLD; TLD Poland, Krakow, Poland). TLD are small discs made of lithium fluoride with a diameter of 4.5 mm and a thickness of 1 mm. When irradiated, the energy of irradiation is absorbed. This energy appears in the form of light, the intensity of which is proportional to the energy initially absorbed on irradiation. The light intensity can be measured and, when calibrated, is equivalent to the radiation dose received. The accuracy of the TLD technique is ±2.5% as found in the Department of Medical Physics at Aarhus University Hospital which was involved in the study [11].

The TLDs were secured to the operating surgeon's forehead (reflecting lens dose), to the thyroid gland under and above the lead collar, to the right and left second finger under the gloves, and to the third finger above the lead gloves. Furthermore, a personal TLD was carried at the waist under the lead apron (Fig. 1).

Fig. 1 Positions of the thermo luminescent dosimeters (TLDs) exposed to radiation during fluoroscopy. The TLDs were secured to the operating surgeon's forehead, the thyroid gland under and above the lead collar, on the second finger under the gloves, and on the third finger above the lead gloves in a standardised manner. Furthermore, a personal TLD was carried at the waist under the lead apron. Background radiation was monitored with a background TLD. The exact same lead apron and collar were used during all operations

During each procedure the surgeon used the same lead apron and collar (Burlington Medical Supplies Inc., Newport News, VA) with a lead equivalence value of 0.35 mm. Lead gloves were sterile gloves for single use with a fixed filter equivalent value of 2.5 mm (Protech Proguard RR, model RR-1, Emerson & Co, Genoa, Italy). To monitor background radiation, a personal TLD was attached to the surgeon's jacket hanging outside the orthopaedic theatre during the PAO procedure. At monthly intervals the TLDs were sent to the Department of Medical Physics at Aarhus University Hospital where the TLD values were estimated on a Toledo 654 Tld reader (D.A. Pitman Ltd, Weybridge, England).

PAO

PAO is a joint preserving surgical treatment of hip dysplasia performed to prevent osteoarthritis. The senior author (KS) performs a newly developed minimal incision trans-sartorial approach [25]. At PAO, the osteotomised acetabular fragment is redirected three-dimensionally in an adducted, extended, and rotated position. Two cortical screws inserted in the iliac crest fix the acetabular fragment. The surgeon's use of fluoroscopy ensures correct placement of the ischial and posterior cut and also assists in evaluating the acetabular correction and finally placement and fixation of the screws. When evaluating the cuts with fluoroscopy, the surgeon needs to maintain the osteotome in place with his left hand.

Fluoroscopic device

For all PAO procedures, the departments standard X-ray equipment was used (mobile C-arm, Philips BV 25 Gold, Philips Medical Systems, Netherlands) and inspected at regular statutory checks. In intermittent fluoroscopy mode

Fig. 2 a Vertical fluoroscopy with the X-ray source under the patient and the image intensifier above the patient. The surgeon keeps the osteotome in place during fluoroscopy and therefore has to be close to the X-ray source and the radiated patient. **b** False profile—60° oblique projection with the X-ray source under the patient and the image intensifier above the patient

(low definition), automatic dose rate control was applied, controlled by a surgeon-operated foot switch. A standard fluoroscopy format was employed; shutters and a collimator were not used. Two standardised set-ups of the device were used: (1) vertical fluoroscopy with the X-ray source under the patient and the image intensifier above the patient, and (2) a false profile—60° oblique projection with the X-ray source under the patient and the image intensifier above the patient (Fig. 2a,b). The distance between the X-ray source and the patient was modified to the particular situation as it was occasionally needed to distance the fluoroscope from the patient to get a better view. Consequently, the distance between fluoroscope and patient was not standardised but the distance was recorded.

On each TLD was a number used as a reference for positioning the TLD during the operation and for recording the TLD value at the Department of Medical Physics. Correct positioning of the TLDs was checked by a nurse and the orthopaedic surgeon before and after the operation to ensure that no TLDs were registered faulty.

To test the protective performance of the gloves, attenuation control of ten lead gloves was performed using a phantom (Gammex Solid Water, Middelton, WI, USA). To imitate the geometry of the clinical practice, the phantom had a height of 20 cm, with both length and width 25 cm. The phantom was positioned on the image intensifier and a lead glove, with a TLD above and inside, was placed on the phantom. The distance from the X-ray tube to the phantom was 66 cm and three single pulses (100 kV, 3 mA) of one second for each glove were applied. The doses to TLDs above and inside the glove were measured. With this set-up, the TLDs received radiation direct from the X-ray beam and scattered radiation from the phantom, which makes it similar to clinical practice.

Wilcoxon signed rank test was used to test for differences between exposure values with and without lead shielding and for the phantom measurements.

Results

The mean operation time was 70 minutes (range 50–85) and mean exposure time was 37 seconds per operation. In vertical projection, the mean distance between the X-ray tube and the patient was 27 cm (20–30), the mean voltage was 91 kV, and the mean mA was 2.9. In false profile, the mean distance between the X-ray tube and the patient was 27 cm, the mean voltage was 71 kV, and the mean current was 2.6 mA.

The effective dose received by the operating surgeon was 0.008 mSv (0–0.08) per operation, which adds up to an annual dose of 0.64 mSv from PAO. The equivalent dose exposures per operation are shown in Table 1.

The exposure to the thyroid gland was significantly reduced by the collar ($p<0.001$) while the exposure to the

Table 1 The median point equivalent dose (mSv) exposure measured with TLD under PAO

	Forehead	Thyroid gland	Thyroid collar	Right finger	Right glove	Left finger	Left glove
Median	0.009	0.009	0.023	0.045	0.032	0.039	0.031
Minimum	0.000	0.000	0.000	0.007	0.010	0.013	0.011
Maximum	0.057	0.059	0.087	0.142	0.231	0.141	0.167
25th percentile	0.005	0.005	0.012	0.028	0.019	0.022	0.021
75th percentile	0.023	0.012	0.043	0.094	0.045	0.085	0.053

TLD thermo luminescent dosimeter, *PAO* periacetabular osteotomy

The TLDs were secured to the operating surgeon's forehead, to the thyroid gland under a lead collar, on the thyroid lead collar, to the right and left second finger under lead gloves, and to the third finger on the glove surgeon's fingers was not reduced by wearing lead gloves. However, the attenuation control showed that the dose to the TLD inside the lead-lined gloves was significantly reduced ($p=0.011$) compared to the dose above the gloves.

Discussion

Our aim was to measure the occupational exposure to the orthopaedic surgeon during intraoperative fluoroscopy in PAO. A surgeon performing 80 procedures a year receives an effective dose of 0.64 mSv/year. This exposure level is relatively low and corresponds to results from other studies on occupational exposure in orthopaedic surgery [7, 10, 12, 13, 20, 22]. The low dose in this study is explained by personal shielding, short exposure time, and use of intermittent fluoroscopy. Wearing a lead collar under PAO significantly reduces radiation exposure to the thyroid gland. But using lead gloves does not reduce the dose received by the surgeon's fingers, and the surgeon's fingers receive the most exposure per operation. The lead-lined gloves turned out to be poorly absorptive in this study, although the attenuation control showed that the dose to the TLDs was significantly reduced inside the gloves. These contradictory results are difficult to explain. The manufacturer of the gloves claims the attenuation properties of the gloves in primary X-ray beams of 100 kV to be 26%, but the manufacturer also states that the gloves are not intended for use in or adjacent to the primary X-ray beam. The intent of the gloves is to reduce the amount of scattered radiation exposure to the hands from the primary X-ray beam during fluoroscopy, but according to our measurements the gloves do not provide effective protection of the surgeon's fingers during PAO.

This study confirms the findings of other studies [3, 9] such that, in orthopaedics, the limiting dose is that to the fingers and hands. This differs from previously studied groups, such as radiologists and cardiologists [15, 26], in whom the limiting factor is the dose to the lens of the eye. The extremity dose is of particular relevance in orthopaedic practice because of the proximity of the hands to the beam during radiation. The recommended annual dose limit for the extremities is 500 mSv [1, 5, 6], and even if we selected the highest measured dose to the hands (0.231 mSv) and multiplied by 80 (18.48 mSv) the dose did not exceed this value. The dose data provided in this study may be used as the basis for setting diagnostic reference levels for fluoroscopy use in PAO procedures.

Modern orthopaedic practice involves increased exposure of the surgeon to ionising radiation [8, 21, 23], and there is uncertainty in predicting the effects of low-dose radiation; hence, it is wise to act on the basis that there is no safe dose of radiation. The personal shielding used in this study did not filter out the entire X-ray beam as the median value of the TLDs under the thyroid collar and gloves was not zero. A threshold below which stochastic damage from radiation does not occur has never been demonstrated, and many now believe that a threshold does not exist. What seems clear is that the greater the exposure to radiation the more likelihood there is of incurring serious side effects such as cancer [1, 4, 16], cataracts [23], and birth defects [1, 4, 24].

In conclusion, the effective estimated yearly dose received by the operating surgeon was very low, and this low dose is explained by the short operation and exposure time. Wearing a lead collar reduced radiation exposure to the thyroid gland while the lead gloves did not protect the surgeon's fingers. Our current precautions appear to be adequate, but safe fluoroscopy practice with PAO in the future is dependent on repetition of studies similar to this one as techniques and workloads change.

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Chapter 11

General discussion

The aim of this doctoral dissertation was to examine biological changes in bone, cartilage and blood perfusion after PAO in patients with hip dysplasia. Furthermore, to investigate the relationship between the acetabular angles and health-related QoL after PAO. And finally, to study the level of radiation to the surgeon during PAO. The dissertation has addressed four research questions, explored in the individual chapters:

1. Which biological changes take place in bone and cartilage 2-10 years after PAO? (chapters 3-7)

2. What is the level of changes in blood perfusion and bone formation in the acetabular fragment after PAO? (chapter 8)

3. Is there a relationship between the radiological parameters and health-related QoL after PAO? (chapter 9)

4. Does the level of radiation during PAO impose a health risk to the surgeon? (chapter 10)

The four research questions will be discussed individually in this general discussion. Limitations of the studies will be discussed and finally, a general conclusion is given.

Which biological changes take place in bone and cartilage 2-10 years after PAO?

Development of a method to measure cartilage thickness

In study I we developed and tested 3 stereologic sampling methods to estimate cartilage thickness from MR images because we were interested in a method that could be used to study the progression of OA over time in patients operated with PAO. We were inspired by work of Nishii et al. who described continuous traction on the leg during MRI to separate the joint surfaces in the hip [130;132]. When applying traction to the hip joint, joint fluid floats in between the articular surfaces and enables one to measure the cartilage thickness on the femoral head and on the acetabulum separately. Partial volume effect is a factor to consider when imaging the spherical femoral head because slices or parts of the curved cartilage can be averaged together in a single slice and thereby lead to overestimation of the cartilage thickness. Partial volume effect can be decreased by using thin MR slices, small field of view, and high imaging matrix sizes, which our radiologist aimed at with slice thickness of 1.5 mm, field of view of 220 x 220 mm and size of imaging matrix of 256 x 256. In MRI, the resolution is defined by the size of the imaging voxels. Voxels are 3D cubes and the size of the voxel depends on the matrix size, the field of view and the slice thickness [1]. The depth of the voxel is the slice thickness and hence our chosen sequence in study I, III, IV and V resulted in voxels of 1.5mm x 0.43 x 0.43mm. Cheng et al. have addressed the effect of using MR sequences with anisotropic voxels when measuring cartilage thickness in the hip joint [25]. They MR imaged a cadaver hip joint and measured the acetabular and femoral cartilage thickness along the radial direction from the center of the femoral head in increments of 10˚. Then they sectioned the hip joint, measured the true thickness of the acetabular and femoral cartilage in the coronal plane, and simulated the thickness in increments of 10˚ in a mathematical model. They found that when scanning with anisotropic sequences and measured the acetabular and femoral cartilage thickness along the radial direction from the center of the femoral head, then the bigger the angle of the reconstructed slices compared to the scan plane, the higher the overestimation of cartilage thickness [25]. This is particularly relevant for our method 3 (study I) in which we sampled a sagittal, a coronal and 2 images angled 45˚ between coronal and sagittal. The 3 slices except for the sagittal slice will suffer from being angled 45˚-90˚compared to the scan plan. This indicates that our measures on cartilage thickness derived from method 3 may be overestimated. We favored method 3 because this method theoretically avoids the partial volume effect. However, based on the work from Cheng et al. the slices should have been even thinner and the voxels less anisotropic to avoid partial volume effect. However, since the MR scanner and the specific MR sequence was kept constant between baseline and the 3 follow-ups, the same potential overestimation of cartilage will exist in all measures and therefore not result in bias in the results of study IV and V. As stated in the introduction that when using stereological methods to estimate length, partial volume effect is avoided by using slices much thinner that the diameter of the structure to be measured. We used slices of 1.5 mm and with a mean thickness of the acetabular cartilage of 1.26 mm and femoral cartilage of 1.18 mm, the measurements will suffer from some degree of partial volume effect. The advantages with the presented MR-based stereological method is that it is a fast and reproducible method. It requires some experience to perform reliably but no specialist skills are required. We had planned to further develop method 3 to measure cartilage thickness in 4 quadrants to enable us to detect regional cartilage thinning. We never accomplished to develop the method further due to the time frame of first authors post.doc. position.

Since screws made of titanium were used to fixate the acetabular fragment during PAO, only minor artifacts were seen on the postoperative MR images and those artifacts did not interfere with the articular surfaces where cartilage thickness was measured (Figure 4 and 5).

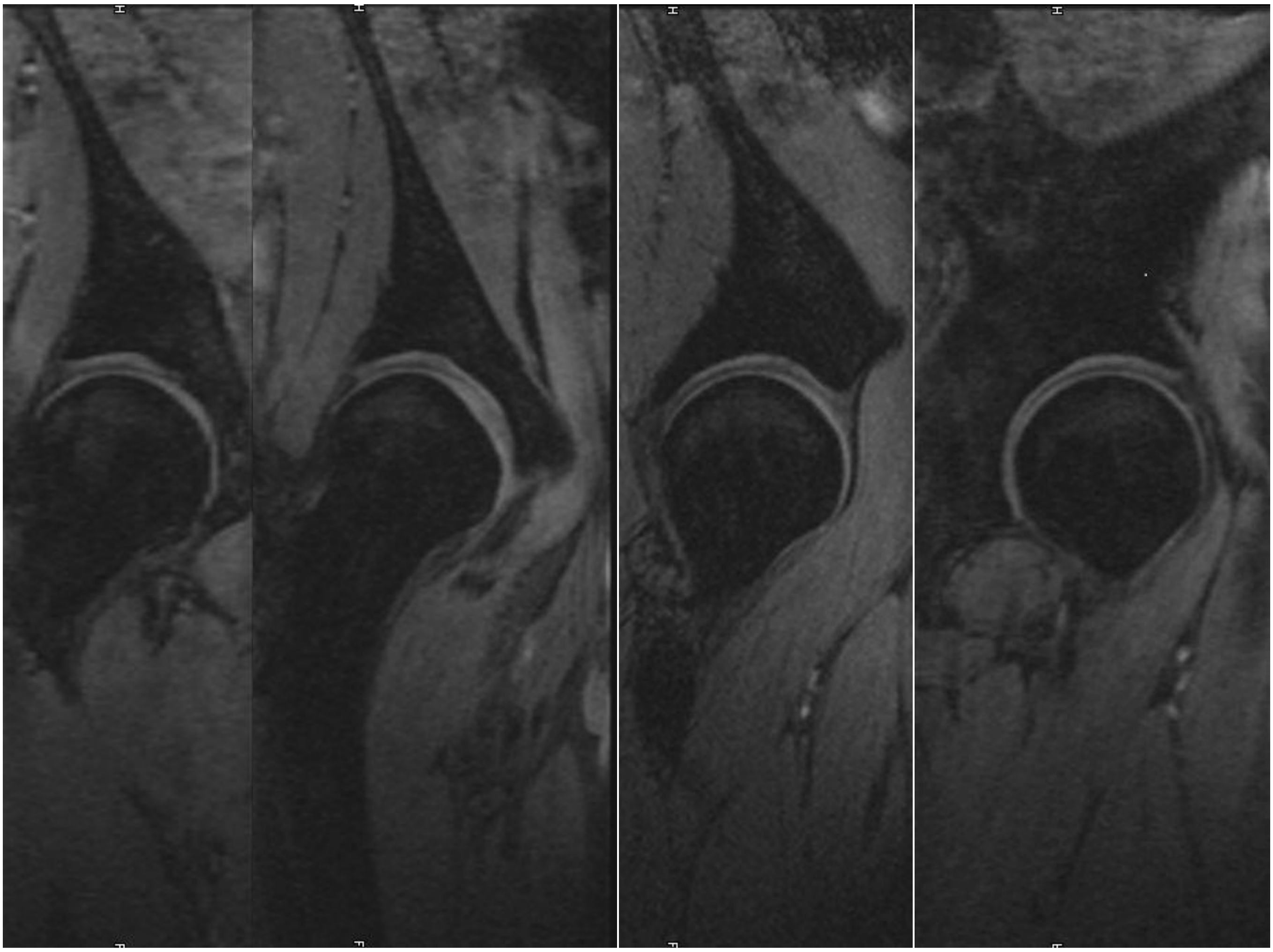

Figure 4. Four reconstructed MR images through the center of the femoral head of a patient preoperative. The four presented images consist of a coronal, an image obliquely angled 45˚, a sagittal and an image obliquely angled 45˚between coronal and sagittal.

At PAO the acetabulum is reoriented to obtain better coverage of the femoral head but the reorientation does not affect the ability to perform the stereological measurements because they do not require the recognition of anatomical landmarks on the acetabulum. The 4 images used in method 3 are reconstructed through the center of the femoral head and the center is unchanged after PAO.

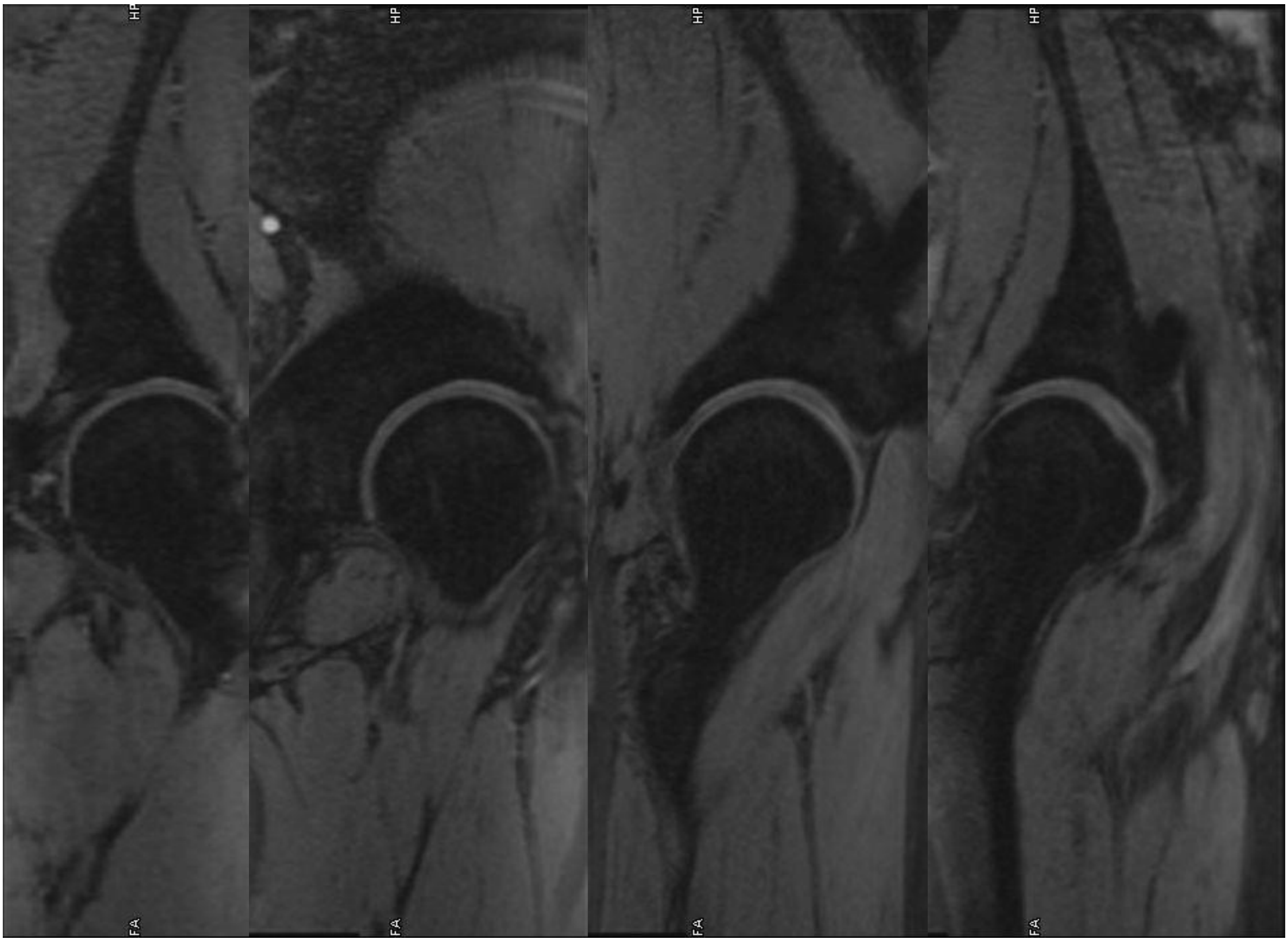

Figure 5. Four reconstructed MR images through the center of the femoral head of the same patient as shown in Figure 4 one year postoperative. The four presented images consist of a coronal, an image obliquely angled 45˚, a sagittal and an image obliquely angled 45˚between coronal and sagittal.

After having MR imaged the patients preoperatively, we decided to evaluate the validity of the measurements and we scanned a plastic cube with the MR sequence used in the study to test the validity of the measured distances. We found measurement errors with up to 6% longer distances than the actual geometric dimensions of the cube. At that point, we consulted the hospital MRI physicist who scanned a genuine phantom with the same sequences on the same MR scanner to verify the resolution and the geometry, which he found to be perfect. Then we used the software for the stereological measurements and measures the distances on the images from the genuine phantom and found the distances to fit precisely. Probably the plastic cube was not suitable for MR imaging for verification of the geometry.

MRI is probably the most important imaging modality to evaluate degenerative changes to the cartilage and MRI is applied especially in the knee joint [34]. It can be used for monitoring the morphological changes in the cartilage after surgery, training or pharmaceutical interventions.

When we initiated the MRI examinations on the patients with hip dysplasia only few 3D sequences to visualize cartilage existed whereas now several different 3D sequences (spin-echo and gradient-recalled echo) are used to assess the structure of cartilage quantitatively [33;36]. We used a fat-suppressed 3D Fast Low Angle Shot (FLASH) sequence with slice thickness of 1.5 mm, field of view of 220 x 220 mm and size of imaging matrix of 256 x 256. FLASH is a T_1 weighted gradient-recalled echo sequence. This sequence allows thin slices, a 3D data set and visualizes the articular cartilage with a high signal and high contrast and reduced metal artifacts on the tissue around the metal screws.

We decided to quantify cartilage thickness in the hip joint with stereological methods because these methods can minimize the work load by using sampling and still provide reliable quantitative information. Others choose to quantify hip cartilage thickness [2] or cartilage volume [20] with the use of the dGEMRIC technique and automatic or semiautomatic segmentation of the cartilage. Several researchers use parametric MRI techniques that provides information about degeneration of the cartilage and can be used as a biomarker of cartilage degeneration. Parametric MRI mapping has been used in patients with hip dysplasia to show site-specific changes in the images of the acetabular and femoral cartilage [131].

Bone mineral density in the acetabular fragment and postoperative migration

In study II no changes in BMD in the acetabular fragment could be detected 1 and 2½ years after PAO. As concluded in the paper DXA is not a suitable method to investigate possible changes in bone density in a small acetabular fragment after PAO because DXA does not possess the required precision to detect changes in a very small region. As stated in the paper, the study turned out to be greatly underpowered to detect a difference in BMD with the SD from the actual study. In an earlier paper [119], we have demonstrated increased bone density in the same region in the antero- and postero-medial quadrant of the acetabulum 2 years after PAO. In the antero-lateral and the postero-lateral quadrant, bone density was unchanged. In that study we used CT and 3D design-based sampling principles to investigate changes in acetabular bone density after PAO and with that method the changes were very convincing based on only 6 consecutive patients. When the mechanical situation changes, due to a medialized hip joint center [148;171;177] and improved acetabular coverage [8;172;212], the distribution of load and force is moved medially [83;202], and subchondral bone is stimulated to remodel to adapt to these changes. A remodeling processes leads to increased bone density medially and decreased density laterally. The clinical implications of the bone remodeling in the acetabulum is that bone has the potential to adapt to changed loading situations as after PAO and hence preserve the hip joint after PAO. In study II we did not find bone remodeling after PAO but since we have found the changes in an earlier work, we believe that acetabular bony tissue has potential to remodel on the cortical and the trabecular level after PAO due a changed loading pattern in the acetabulum. Moreover, the potential for microstructural remodeling is pronounced when the patients are healthy [200] and physically active [42]. Along with this line, a CT-based study has investigated whether there was gross remodeling of the acetabulum or the femoral head in response to the change in loading following a PAO, which was not the case [154]. Okano et al. found BMD of the lumbar spine, distal radius, and calcaneus to be significantly higher in patients with dysplasia than in healthy control persons which suggest an underlying genetic or hormonal mechanism in hip dysplasia [137].

In study II we also examined whether BMD correlates with postoperative migration of the osteotomised acetabular fragment which we had investigated in an earlier study [115]. Radiostereometric examinations were performed at 1 week, 4 weeks, 8 weeks and 6 months after PAO. Six months postoperatively, the acetabular fragment had migrated mean 0.7 (0.8) mm medially, and mean 0.7 (0.5) mm proximally. Mean rotation in adduction was 0.5 degrees (1.3). In other directions, mean migration was below 0.5 mm/ degrees. There were no statistically significant differences in migration at 8 weeks and 24 weeks postoperatively in either translation and rotation, indicating that the acetabular fragment was stable at 8 weeks postoperative. When correlating these translations and rotations to BMD we found no significant correlation and hence the migration of the acetabular fragment observed after PAO cannot be not explained by low BMD in patients. The greatest amount of migration of the fragment occurred within the first 4 postoperative weeks and can probably be explained by small movements when the fragment "settle in" after the patients starts weight bearing. The migration in our cohort was very small and do not give cause for concern but reoperations due to acetabular migration after PAO have been reported in the literature [206].

Subchondral bone cysts in the acetabulum or femoral head

Subchondral bone cyst formation in the hip increases as OA worsens. Lee et al. [98] have developed a MR-based hip OA evaluation system and correlated the MRI findings to clinical parameters measured on the HOOS questionnaire. Subchondral cyst and bone marrow edema (seen in bone under areas where cartilage is damaged) showed the highest correlation with HOOS and hip range of motion. The same research group [92] evaluated the relationship between MRI findings in hip OA with self-reported pain and physical function measured with HOOS. They found that subchondral cysts were related to greater self-reported hip pain and disability. Although we in study III found a statistically significant reduction in total cyst volume per patient between 1 and 2½ year follow-up this did not affect function and pain assessed by the HOOS at 4 years follow-up. Also in study V the presence of bone cysts did not seem to affect the HOOS score which indicates that our studies were underpowered to show a relationship between volume of bone cysts and function and pain.

While subchondral bone cysts in hips have been described in several studies, their etiology remains unclear. Inui et al. [71] studied bone cysts from 150 dysplastic hips in 97 patients by CT. Of the 150 hips, 94 acetabulum and 55 femoral heads were found to contain cysts. The rate of cyst presentation in the hip increased as the joint space width became narrower. Moreover, bone cysts in dysplastic osteoarthritic hips were found to communicate with the joint space in all cases.

This suggests that the formation and enlargement of the cysts in dysplastic hips may be influenced by the joint fluid. It is believed that subchondral bone cysts can be caused by pressure on the cartilage and the subchondral bone, which causes the joint fluid to leak into the bone through channels in the cartilage.

We were interested in measuring subchondral bone cysts quantitatively and thus we measured how many patients had cysts and estimated the total volume of cyst per patient. In study III we found that the number of patients having subchondral bone cysts in the acetabulum or femoral head increased by 2 patients 2½ years after PAO. More interesting, the mean total cyst volume per patient decreased both clinically and statistically significant between 1 and 2½ years after PAO. We interpret the decreased volume of cysts as an evident regenerative process in the bone tissue after changed loading and especially after unloading the acetabular edge. This is supported by the position of the bone cysts with all but 1 acetabular cyst and 1 femoral head cyst being located anterolateral in the hip joint where the peak contact stress is localized in dysplastic hips [131;211]. Strains experienced by bone stimulate remodeling processes, which can increase or decrease bone density and evidently also change the microarchitecture of the bone. Nakamura et al. also has found partial or complete cyst remodeling in 17 of 21 hips 5 years after PAO [125]. Whether this is due to the screw inserted in the bone cyst and thereby inducing a healing process or due to change of joint loading is not known. Apart from the study of Nakamura and study III, cyst remodeling after PAO has not previously been reported in the literature.

Short-term changes in cartilage thickness

In study IV we wanted to clarify how the articular cartilage in the hip joint is affected by PAO in patients with hip dysplasia. Hence, we performed a prospective study of 26 patients who underwent MRI with traction before and 1 and 2½ years after PAO and called in the patients again for 10-year follow-up (Study V). The lack of exposure of the patients to ionizing radiation makes MRI an appealing method for imaging a group of patients several times. The traction worked well for patients with low body weight and less muscle mass but had a smaller separating effect on patients with higher muscle mass. We decided not to change the weight applied to the traction device because we did not want to risk measurement variation due to different traction procedure. A recommendation for future studies applying traction and MRI would be to add traction weight according to patient weight.

Mean cartilage thickness was unchanged 2½ years after PAO compared with preoperatively and we interpret this, as there were no measurable degenerative changes short-term after PAO. The acetabular cartilage was 0.12 mm thicker 1 year after surgery compared with 2½ years after surgery but since our data show that cartilage thickness 2½ years after PAO is similar to that before surgery, the increased thickness at year is probably due to swelling of the cartilage [32]. A limitation to our approach of measuring and presenting a mean thickness is that tissue loss in hip dysplasia is initiated in the anterosuperior region and the mean thickness may not show a localized loss of cartilage. However, it has been shown by 3D dGEMRIC technique that the dGEMRIC index shows a global decrease in the distribution of cartilage damage in dysplastic hips [64]. So, although tissue degeneration may initiate locally, OA is a biologically mediated event that affects the entire joint.

Seventeen of 18 patients in study IV had a torn labrum as shown by MRI with contrast. The tears were located mainly superior on the acetabular rim. A recent review included 8 studies and 775 patients operated with PAO to evaluate the prevalence of intra-articular pathology identified with either arthroscopy or with open arthrotomy [156]. The conclusion was that the prevalence of labral injuries and pathologic conditions of cartilage, at the time of PAO is substantial. Moreover, that labral tears and chondral injury are better recognized with concomitant arthroscopy when compared with arthrotomy at the time of PAO. The review did not investigate whether the treatment of labral or chondral injuries can improve patient outcome and reduce reoperations.

Henak et al. [63] used finite element modeling to evaluate chondro-labral mechanics in the dysplastic hip to provide insight into mechanics that precede OA. They found that the labrum in dysplastic hips supports 2.8-4.0 times more of the load transferred across the joint than in normal hips. Moreover, they found that dysplastic hips do not have significantly different congruency in the primary load-bearing regions compared to normal hips, but are less congruent in some unloaded regions. And interesting, that dysplastic hips are not subjected to elevated cartilage contact stresses which is in contrast to several studies that have found markedly elevated peak stress in dysplastic hips [83;110;112;149] and a relationship between contact area and contact pressure [213]. Nevertheless, the results emphasize the key role of the labrum in dysplastic hips and underline that the labrum should be preserved during surgery.

Long-term changes in cartilage thickness and volume of subchondral cysts

In study V, we found that 10 years after PAO about 25% of the patients had developed substantial hip pain and/or undergone THA. In the 17 patients who had MRI both before surgery and 10 years later, acetabular cartilage was unchanged 10 years after surgery compared with preoperative acetabular cartilage thickness. Preoperatively, mean thickness of patient acetabular cartilage was 1.38 ± 0.14 mm; and 10 years postoperatively, 1.43 ± 0.07 mm. Also, femoral cartilage was unchanged 10 years postoperatively compared with preoperatively. Mean thickness for patient femoral cartilage preoperatively was 1.37 ± 0.20 mm; and at 10 years postoperatively, 1.30 ± 0.07 mm.

The volume of bone cysts was unchanged 10 years after PAO compared with volume before surgery. Median total cyst volume per patient preoperatively was 6.0 (range, 1.6−188.3) cm^3 and 10 years postoperatively, 2.9 (0.7−8.2) cm^3. One could point out that it is not the sheer size of the cyst that matters but the degree of progression. We did not correct for body size, and a 90 kg male would presumably be less affected by a 10 cm^3 cyst than a 50 kg female. Preoperatively, 3 patients had cyst volumes greater than 80 cm^3. Ten years later, outcomes for the same 3 patient hips were: 1 had been converted to THA, 1 had radiologically verified OA, and 1 was lost to follow-up.

According to the GRADE guidelines [58] there are 3 different levels of outcome measures: Patient relevant outcomes such as mortality or disability which should be given highest priority because such outcomes measures are critical for patients and decision makers. The next level consist of outcomes important but not critical for patients and decision makers e.g. pain or health-related QoL. Finally, there is a level of outcomes not important for either patients or decision makers e.g. surrogate outcomes such as biomarkers. Both cartilage thickness and volume of subchondral bone cysts are biomarkers that measure the degree of OA and both outcomes can be placed on the lowest level of outcome measures in the GRADE guidelines. We used biomarkers to investigate which biological changes take place in bone and cartilage 2-10 years after PAO and we argue that these biomarkers are measures and hallmarks for the progression of OA. There is an increased likelihood for hip failure defined as THA or severe hip pain if the cartilage thickness decreases and the volume of cyst increases. Nevertheless, these biomarkers are substitutes for a meaningful outcome for patients and decision makers who would probably have a preference for outcomes like hip failure or pain. This does not mean that we should not use biomarkers as outcome but it underlines that we should be aware that biomarkers are surrogate outcomes and that these outcomes do not provide meaningful information to the patients. Therefore, we have complemented the collection of biomarkers in study V with data on patient-reported outcomes like pain, function and QoL, which are measures from the second level of the GRADE guidelines.

The 17 patients who completed 10 year MRI had acceptable hip function and pain out to 10 years after PAO. The self-assessed mean subscores for HOOS were pain, 79±16; symptoms, 73±17; activities of daily living, 85±14; sport/recreation, 68±22; and quality of life, 61±19. Based on the standard deviation of these scores, there is great variation in how well the patients do at 10 years follow-up and this is for the best of the lot because it excludes those who failed to report, or who went on to a THA or hip arthroscopy. Other studies have presented similar mid- to long-term scores for pain, function and QoL [3;107;148;170].

In the absence of placebo controlled randomised trials on PAO prospective long-term follow-up studies are very important. Only a small number of studies have analysed the medium- to long-term clinical and radiographic results obtained with PAO for the treatment of hip dysplasia [3;67;148]. Few studies have reported the survival rate of the biological hip after PAO with conversion to total hip replacement or progression of OA as end point. Burke at al. reported a survival rate of 94% at 58 months following PAO [23], Matheney et al. had a survival rate of 84% at 10 years after PAO [107]. Hartig-Andreasen et al. showed a hip survival rate of 74.8% at 12.4 years [61], and Steppacher et al. reported a survival rate of 60.5% at 20 years [170]. The survival rate in this cohort was 84.6% with failure defined as THA or manifest OA.

Sambandam el al. performed a systematic meta-regression analysis of 23 eligible studies on 1,113 patients to investigate risk factors for conversion to THA after PAO. Multivariate analysis showed that the odds of having a THA increases with grade 2/grade 3 OA (3.36 times), joint penetration (3.12 times), low preoperative Merle de'Aubigne score (1.59 times), late proximal femoral osteotomies (1.59 times), presence of preoperative subluxation (1.22 times), previous hip operations (1.14 times), and concomitant proximal femoral osteotomies (1.09 times) [160]. We found that the 9 patients who were lost to 10 year follow-up were characterized by a higher postoperative AI angle after PAO and tended to be more dysplastic with higher preoperative CE angle and lower preoperative AI angle. But our cohort is far too small to guide us in the assessment on which patients are most likely to succeed with PAO at long-term follow-up.

What is the level of changes in blood perfusion and bone formation in the acetabular fragment after PAO?

The duration of PAO can be long and blood flow to the acetabular fragment may be seriously decreased during surgery. Sufficient blood perfusion is vital to avoid osteonecrosis of the acetabular fragment and to the bone healing in the pelvis and after PAO. PAO may potentially cause avascular necrosis of the acetabular fragment, which has been reported [44;72;179]. Hurson et al. applied MRI to evaluate signs of ischemia of the acetabular fragment at 6 weeks, and 6 and 12 months after PAO. Three patients showed evidence of reduced vascularity at 6 weeks. In 2 of these, there were focal changes suggestive of subclinical ischemia. The 6-month MRI showed some persistent vascular changes and the 1-year MRI showed complete resolution [69].

In study VI, we performed a PET/CT study to estimate blood perfusion and new bone formation immediately before PAO and 3-4 weeks after PAO. It was a difficult method to apply because it requires the patients to lie on the scanning table without movement for nearly 2 hours. This was impossible for some of the patients because they had postoperative pain, although given analgesics. Hence, data of sufficiently high quality at both pre- and postoperative PET/CT scans were only available for 6 out of 10 patients. Even with those relatively few data, the results were very convincing with significant increased blood perfusion and new bone formation in the acetabular fragment.

Hempfing et al. measured acetabular perfusion by laser Doppler flowmetry in 10 patients. After complete separation of the acetabular fragment, 9 out of 10 patients had pulsatile signals, but the blood flow significantly decreased by 77%. Corrective positioning of the fragment induced no further drop of the blood flow signal but a loss of pulsatility in 6 patients. After a recovery period of about 30 min following preliminary fixation of the fragment, reestablishment of the pulsatile signal and an increase of the blood flow signal was seen. All osteotomies healed within 8 weeks without showing signs of necrosis during a minimum follow-up of 1 year [62].

Kiyama et al. measured intraoperative blood of the lateral femoral cutaneous nerve during PAO and detected decreased blood flow of the nerve by more than 50%. They concluded that the decreased blood flow rather than direct mechanical trauma to the nerve cause persistent symptoms after surgery. Excessive traction by retractors is thought to be the main cause of blood flow reduction [89].

Complex surgeries may require blood transfusions but blood transfusions can result in severe adverse transfusion reactions [104]. A recent study with 108 patients undergoing PAO showed that the rate of allogenic blood transfusion was 20% and that 94% of the patients received transfusions including autologous blood, intraoperative cell saver, and postoperative allogenic blood transfusion [150]. Atwal et al. has shown that preoperative autologous donation is a safe and cost effective method of managing blood loss after PAO [11]. Based on data from the first 120 patients operated with the trans-sartorial approach, the percentage receiving allogenic blood transfusions was 4% [185]. Pre-donation of autologous blood is not used at our department but in patients who bleed a lot during surgery (approximately 1 out of 10), the cell salvage procedure is used involving recovering blood lost during PAO and re-infusing it into the patient. Whether patients undergoing PAO will require some form of blood transfusion depends on preoperative level of hemoglobin [150] but predominantly on the loss of blood under surgery and hence efforts should be made to reduce the time to perform a PAO [96]. Also there are different blood donation policies around the world [143] and cultural differences between hospitals and countries in blood transfusion policies because the decision is not always based on low level of hemoglobin but as much on a subjective assessment of whether the patient looks pale and tired.

Is there a relationship between the radiological parameters and health-related quality of life after PAO?

Study VII differed from the other clinical studies in this dissertation in respect to patient selection. In study I-VI the patients were a selected group of patients with hip dysplasia and no previous corrective pediatric hip surgery or no concomitant femoral osteotomy. Study VII is based on patients in our clinical database of all PAO patients operated at the Department of Orthopedics at Aarhus University Hospital since 1999. Initially, patients with OA grade 0, 1 or 2 were candidates for a PAO but from 2003 hips with Tönnis OA grade 2 were no longer offered PAO. Altogether, the patient group in study VII consists of a more mixed patient group compared to the other studies in this dissertation which may affect the results with greater variation in the scores. Patients with previous corrective pediatric hip surgery can obtain good results from PAO [169] but the short-term improvements are smaller and more variable than those seen in patients who have not undergone prior corrective hip surgery.

In study VII we aimed to investigate the self-assessed QoL in patients with hip dysplasia 2-13 years after PAO. We used the SF-36 questionnaire that consists of 36 items in 8 dimensions which are summarized in the two summary measures of physical component score and mental component score. We found that the SF-36 score was lower for the PAO group compared to the reference data from the Danish population [17]. For women the median scores were lower in the 4 physical subscales: physical function, bodily pain, general health and vitality with a difference between the 2 groups from 10 to 22 points. We consider the difference clinically relevant because a difference of 10 points on the SF-36 score between reference data and patients with a chronic disease is considered clinically important [17-19]. The difference between the male patients and the reference data was significant for physical function and bodily pain. Thus, patients operated with PAO score lower than a Danish age- and gender-matched population on the physical component scores on the SF-36. The mental component scores of the SF-36 for the PAO operated patients were comparable with reference data, suggesting that physical health has no negative influence on the mental QoL for PAO patients at a medium-term follow-up. Van Bergayk and Garbuz reported a mean physical component score of 49.2 and a mean mental component score of 54.7 for 22 patients with a follow-up of 2.0–3.5 years after PAO [193]. Our results are comparable to these scores. At mean follow-up of 7.1 years, we found a mean physical component score of 46.9 and a mean mental component score of 53.7.

In the study of Van Bergayk and Garbuz [193] the SF-36 physical component score increased from preoperatively 33.9 to 49.2 postoperatively, however, our study suggests that the physical improvements achieved by the PAO will not last. The association between follow-up and the physical function and follow-up and the physical component score was significant. A logistic regression analysis was performed to estimate a possible association between the different exposures and QoL. The odds ratios were adjusted for age, gender, follow-up, BMI, working status and level of education and it showed that a 1 year difference in follow-up time between 2 patients with the same age, gender, BMI, level of education and working status increases the risk of having a low physical component score with 13% and low physical function with 19% for the person with the longest follow-up time. We have not found other studies investigating self-assessed QoL over time after a PAO surgery, but Steppacher et al. [170] reported a drop in physical function measured with Merle d'Aubigne and Postel score from 16.7 at 10-year follow-up to 15.8 at 20-year follow-up. The same pattern is found for patients after a THA surgery due to OA [128;167]. Soderman et al. found that the SF-36 PF scores both 3 and 10 years after THA were lower than in the general population and that the scores decreased from 2 to 10 years of follow-up. When physical function decrease after PAO, it may be due to continuing hip symptoms, soft-tissue symptoms or progression of OA. Biedermann et al. have shown that there is a weak but significant correlation between the postoperative grade of OA and the SF-36 score [15].

We also investigated whether there is an association between patients' CE or AI angles before or after PAO and their subsequent self-assessed QoL. We were surprised to find no association between the radiological parameters and the physical aspect of SF-36. After all, we consider the PAO procedure to be successful if optimal correction is achieved based on the postoperative CE and AI angles. A possible explanation might be that the study group consisted only of patients with preserved hips at a mean follow-up at 7.1 year and those with conversion to THA were excluded. If these patients had been asked to fill out the SF-36 before their THA operation, we might have been able to find an association. Another explanation may be that the radiological parameters are associated to degree of OA as shown by Jessel et al. [82] in patients with hip dysplasia but not associated to self-assessed limitations in physical function as assessed by the SF-36.

The rationale for studying hypermobility among patients with symptomatic hip dysplasia was to investigate whether the prevalence of hypermobility in this patient group is higher than the prevalence in the general population. If the prevalence of hypermobility among patients with hip dysplasia had turned out to be higher, then it would indicate an association between general loose ligaments in an individual and the development of a dysplastic hip joint possibly due to reduced support from the ligaments in maintaining the femoral head firmly in the acetabulum. As stated by Anda in his thesis from 1991 "the growth and the hemispherical morphology of acetabulum are dependent on the presence of a normally growing and correctly placed spherical femoral head that works as a convex matrice. If for some reason the normal development is disturbed pre- or postnatally, pathologic relations may develop between the femoral head and the acetabulum" [5]. We asked the patients to fill out the Beighton score to investigate the prevalence of hypermobility in the study group and to examine if the health-related QoL differs between hypermobile and non-hypermobile PAO patients. The prevalence of hypermobile patients in the study group was estimated to be 16.3%. There were no significant differences in the physical component score, physical function or bodily pain for hypermobile patients compared to non-hyper mobile patients after adjusting for age, gender, follow-up, BMI, working status and level of education.

Hypermobility is the term used to describe the ability to move joints beyond the normal range of movement. The prevalence of general joint hypermobility is estimated to be present in 5-15% of the general population. It occurs more frequently in children compared to adults and girls are slightly more affected than boys [158]. The prevalence of hypermobility in the present study was estimated to 16% and hence not higher than in the general population. This may seem to contrast the clinical findings of a great range of motion in the hip joint in the majority of patients with hip dysplasia. The reason may be that patients with hip dysplasia have a high range of hip motion due to lack of acetabular coverage and not due to generalized hypermobility.

There is no universally accepted cut-off level for the diagnosis of general joint hypermobility but in the most commonly used cut-off point is $\geq$ 4 [157]. To ensure that the Beighton score was not overestimated by the patients, we defined the cut-off level to be $\geq$ 5 instead of $\geq$ 4. We found no association between hypermobility and self-assessed QoL, which is in line with the results of Engesaeter et al. [43] who studied a much larger group than we did (2081 persons).

Does the level of radiation during PAO impose a health risk to the surgeon?

Fluoroscopic imaging is used during PAO to help the surgeon perform the osteotomies without cutting intra-articular, to measure the CE angle with a specially made measuring device and to evaluate acetabular coverage anteriorly, and finally to control of position of the 2 cortical screws used to fixate the acetabular fragment. Lehmann et al. have shown that intraoperative fluoroscopic assessment of PAO correction correlates with that from the postoperative radiographic assessment. Measurement of lateral CE angle shows the highest correlation with the fewest outliers. Acetabular inclination and anterior CE angle also correlated but extrusion index and medial offset distance should be used with more caution [99].

The use of intraoperative fluoroscopy exposes the surgeon and support staff to ionizing radiation and the risk of overexposure is real, particularly when considering its insidious effect over time [56]. Since the PAO has a steep learning curve, it is often performed by only few surgeons at a specialised hospital. At the Orthopaedic Department at Aarhus University Hospital only 2 surgeons performs all PAO procedures which on one hand secures a specialist surgery performance but on the other hand exposes the same surgeons to a higher level of surgery-related radiation. Thus, in study VIII we set out to directly measure the radiation exposure to the orthopaedic surgeon and to measure dose points to the surgeon's fingers, thyroid gland, and forehead during intraoperative fluoroscopy in PAO. In a series of 23 consecutive PAO procedures, exposure monitoring was carried out using thermo luminescent dosimeters (TLD).

A plastic casing holds a sheet of thermos luminescent material used as a dosimeter, and some metal foil to filter the radiation to be recorded. After the designated monitoring period, the TLD is collected and read by a TLD-reader which heats up the TLD, detects the resulting light emission, and calculates the radiation exposure to the person wearing that particular TLD. Finger TLD is one form of extremity dosimetry. It measures the radiation exposure of person's hands by a special ring or strip containing a small TLD in contrast with the whole body TLD.

We found that the effective dose received by the surgeon was 0.008 mSv per operation, which adds up to a yearly dose of 0.64 mSv from PAO. The median point equivalent dose (mSv) exposure under PAO was 0.009 for the forehead and thyroid gland, 0.045 for the right index finger, and 0.039 for the left index finger. The effective estimated yearly dose received by the operating surgeon was very low and we do not consider it a health risk because it is well below the recommended yearly limits of radiation of 50 mSv to the torso and 500 mSv to the hands [164]. The average yearly exposure of the public to ionizing radiation is 3.6 mSv, of which 3 mSv is from background radiation and 0.6 mSv from diagnostic radiographs. Whole body and hand radiation exposure to the hand surgeon wearing a lead apron during routine intraoperative use of the fluoroscope has been investigated. The total measured radiation exposures for the whole body exposure dosimeters were 0.16 mSv, 0.07 mSv for eye, and less than 0.011 mSv and they also concluded that the measured whole body and hand radiation exposure received by the hand surgeon represents a minimal risk of radiation [190].

One can question the generalizability of the results of this study since the study subject is one person who is very experienced in performing the osteotomies, assessing the CE angle and control the position of the 2 screws which results in limited use of intraoperative fluoroscopy. Our initial objective was to measure the radiation exposure to the specialist surgeon who performs a great number of procedures and therefore presumably is exposed to a high level of surgery-related radiation. The effective radiation dose received by the operating surgeon was very low and the results can be generalized to surgeons of a comparable level of specialization. Consequently, younger surgeon at the beginning of the learning curve for PAO should expect to receive a somewhat higher effective radiation dose from intraoperative fluoroscopy used during PAO.

In an experimental study, computer assisted surgery was used to place pedicle screws and compare radiation exposure with fluoroscopic pedicle screw placement. Fluoroscopy time was reduced and placement accuracy increased while adding no additional time to the procedure [195]. Also, PAO can be performed with computer assisted surgery where the surgeon can visualize and gain important intra-operative 3D feedback during the procedure [8;100;121]. Theoretically, the use of computer assisted surgery will reduce the radiation exposure received by the surgeon because the navigation system will provide the surgeon with intra-operative tracking of the acetabular fragment and display the acetabular angles in real-time. However, computer assisted surgery requires a preoperative CT image of the patients and thus increases the radiation exposure received by the patient.

Initiating factors for OA in hip dysplasia and OA classifications

As stated in the introduction OA is a whole joint disease probably initiated and driven by biomechanical stress [175] and inflammation [168] leading to degradation of cartilage [176], bone marrow lesions (also denoted bone marrow edema) [161;176] and synovitis (inflammation of the synovial membrane) [152]. However, in hip dysplasia the mechanical component (reduced acetabular coverage that leads to increased joint contact stress) is apparent as an initiating factor leading to OA because these patients are characterized by their young age and their female gender and because other known predisposing factors for OA such as trauma and obesity are not evident in the patient history.

Different classifications can be used to assess the grade of OA in the hip joint. Based on pelvic radiographs the classification of Tönnis [183] and of Kellgren and Lawrence [85] can be used. Both classifications are visual assessments based on the presence of osteophytes, cysts, subchondral sclerosis, and narrowing of the joint space. These 2 classification are very similar in their grading; in Tönnis one grades from 0-3 and with Kellgren and Lawrence the grading is from 0-4. A more quantitative method to grade hip OA is to measure the minimal joint space width in the upper weight-bearing part of the joint [77]. There are also MRI-based grading classifications for hip OA; the Hip OA MRI Scoring System (HOAMS), which is a comprehensive whole organ assessment of nearly all findings, and the Hip Inflammation MRI Scoring System (HIMRISS), which selectively scores only active lesions (bone marrow lesion, synovitis/effusion) [81]. In the studies in this dissertation, the Tönnis classification was used because it is the standard classification used at the Department of Orthopaedic Surgery at Aarhus University Hospital. Likewise, it is standard to obtain radiographs with the patients standing and weight bearing because the position of the patients have been shown to affect the values of the acetabular angles [186]. Terjesen et al. evaluated the reliability of the Kellgren and Lawrence and the method where the minimal joint space width in the upper weight-bearing part of the joint is measured in patients with hip dysplasia [178]. They found that measuring joint space is the most reproducible classification in patients with hip dysplasia.

Study limitations

Several limitations should be kept in mind when interpreting the results of this dissertation. First, we did not include a control group of healthy individuals in any of the studies. Thus, we do not know if measurements of cartilage thickness in the hip joint in healthy individuals changes within 2½ or 10 years. It would have been optimal to compare the cartilage thickness in the patients undergoing PAO with an age and gender matched control group who had been MR imaged on the same MRI scanner with the same scan parameters because it would allow us to differentiate potential changes induced by PAO from the biological variance in cartilage thickness.

Second, we included a cohort of patients with hip dysplasia and performed multiple examinations (MRI, DXA and RSA) and followed the cohort over time. This means that the results obtained on cartilage thickness, volume of cysts, BMD and fragment migration are not based on independent samples from the patient population. To be included into the cohort, the patients had to fulfill the inclusion criteria and not fulfill any of the exclusion criteria. By that, the cohort is already a selected group of patients, which limits the generalizability of the results. When we then perform multiple examinations in the same selected cohort, these results are not independent which should be kept in mind when generalizing the results to patients with hip dysplasia undergoing PAO.

Third, the main outcome when planning the studies was estimation of cartilage thickness and thus the sample size was estimated based on guesses (we had no knowledge on SD for the measurements) on those measurements. Because of the small sample size, we did not have sufficient power in the DXA study increasing the risk of type II error in that study.

Fourth, selection bias may have occurred in the studies with multiple radiological examinations, since the patients should be able to transport themselves to the examinations. Those patients not able to do that have declined to enter the studies.

Conclusion

Concerning biological changes, we could not verify the changes in bone density after PAO, we have demonstrated in an earlier study. However, DXA is not sufficiently sensitive to demonstrate the changes in BMD in the acetabulum after PAO.

The number of patients having subchondral bone cysts did not change notably after PAO. But the mean total cyst volume per patient decreased significantly between 1 and 2½ years and was unchanged 10 years after PAO. We interpret the decreased volume of cysts as a regenerative process in the bone tissue after PAO. This is a novel finding because partial healing of bone cysts after PAO has not been shown with measures of cyst volume before.

Cartilage thickness 2½ years after surgery compared with preoperatively was unchanged indicating the OA had not progressed during short-term follow-up after PAO. Also, 10 years after surgery, cartilage thickness was unchanged compared with preoperative. However, the 10-year measurement was limited by only 17 patients out of the initially 26 having MRI both before surgery and 10 years later. Also, our MRI-based cartilage findings are novel results. The 10-year follow-up showed that about 25% of the patients having PAO developed substantial hip pain and/or underwent THA. But in the patients who do not have substantial hip pain or a THA, cartilage thickness appears to be preserved.

PET/CT before and after PAO showed that blood perfusion and new bone formation increased significantly in the acetabular fragment after PAO. Thus, the trans-sartorial approach do not cause for concern about surgically damaged vascularity after PAO. This study is the first to investigate the blood perfusion in the acetabular fragment after PAO in living patients.

No relationship could be identified between the radiographic parameters and health-related QoL after PAO. The physical components of QoL in patients undergoing PAO are significantly lower than in the Danish general population. Moreover, physical function after PAO decreases with longer follow-up time.

In relation to radiation from intraoperative fluoroscopic imaging, the surgeon can perform PAO surgeries without having to worry about excessive radiation because the effective estimated annual dose received by the operating surgeon is very low. Wearing a lead collar reduces radiation exposure to the thyroid gland while the lead gloves do not protect the surgeon’s fingers.

Chapter 12

Future studies

Hip dysplasia is a significant risk factor for the development of OA [77;122], but not everyone with radiologically verified hip dysplasia develops OA. Given that patients with hip dysplasia and hip pain are preferably operated on before OA progresses, we will never know whether these patients would have developed OA. In a longitudinal study comparing 136 controls with 81 persons with mild or moderate hip dysplasia followed for a decade, Jacobsen et al. [80] did not document a tendency for radiological degeneration. From a scientific point of view, a randomised controlled trial should be performed to investigate the efficacy of PAO in patients with hip dysplasia. In line with the principles laid down in Health Care Technology Assessment, the efficacy of new technologies should be assessed before implementing the technology. However, such studies lack for a majority of operations, also for clinically successful operations like THA or total knee arthroplasty. The reason that surgical procedures can be implemented into practice without any formal evaluation of safety and efficacy is because, unlike drug products, a verification is not mandatory by regulation authorities. However, patients, surgeons and decision makers have a common interest in investigating the efficacy of PAO. As described by Wartolowska et al. [197] it is reasonable to assume that surgery is associated with a placebo effect. Firstly, because invasive procedures have a stronger placebo effect than non-invasive ones and, secondly, because a confident diagnosis and a decisive approach to treatment, typical for surgery, usually results in a strong placebo effect. A recent survey [196] among British shoulder surgeons showed that surgeons generally agreed that a placebo component to surgical intervention might exist. Furthermore, that the surgeons supported placebo use in clinical trials and considered it ethical. With the increased use of PAO worldwide and expanded indications for PAO, such as acetabular retroversion and femoroacetabular impingement, it is problematic that the efficacy of PAO has not been investigated in a randomised controlled trial. Thus, we aim to perform a randomised controlled trial where the patients are randomised to either PAO or to resistance training of the hip muscles. The outcome measures in a such a study will be patient-reported outcomes, functional tests and test of dynamic muscle strength.

With the described studies, outcome after PAO has been investigated primarily on changes in the tissue of the patients. We would also like to measure outcome in terms of physical activity to investigate how active the patients are and whether they participate in high impact activities. Currently, we are running a clinical study where objectively measured physical function and physical activity in 45 patients undergoing PAO is being investigated. Studies based on questionnaires and pedometers have shown that patients with hip dysplasia become more physically active after PAO [134;135]. This study will demonstrate whether increased physical function after PAO results in increased physical activity and what type of activity the patients engage in.

Another study we will undertake aims to examine musculo-tendinous pathology with ultrasonography and muscle test (strength and pain) in 100 patients with hip dysplasia prior to and 1 year after PAO. We have experienced that PAO in some patients does not decrease their hip pain sufficiently and some of these patients report to have the same kind of pain as before PAO. We suspect that musculo-tendinous pathology may play a key role in that. Sustained hip pain and immobilisation have a negative impact on the iliopsoas muscle, psoas and the hip adductors in terms of atrophy and decreased hip muscle strength [40;153]. Pathological changes of the iliopsoas muscle has been found in 18-50% of patients with hip dysplasia [30;41] and in this study we will investigate the muscles acting close to the hip joint and investigate the possible pathological changes and whether the resulting symptoms disappear after PAO.

Finally, we plan to undertake a study to develop a method based on CT and statistical shape modelling with which we can quantitatively assess preoperative hip congruency in dysplastic hips. There is consensus that hip congruency must be evaluated prior to PAO and that the outcome of surgery is dependent on good congruency. But the existing congruency classifications are not reliable and there is no clear agreement regarding what comprises a congruent joint [27;94] as shown in a study where six observers rated hip congruency using two classifications [138;204] and found intra observer reliability kappa values of 0.43 and 0.37, respectively.

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