

**Validation of a three-dimensional low dose CT
method for assessing migration and loosening in
orthopaedic implants**

by

Cyrus David Brodén

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Philosophy

Department of Surgery and Cancer,

Imperial College London, 2020

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3. Abstract

Aseptic loosening is the most common complication following arthroplasty. Early migration and the development of radiolucent lines are believed to be correlated to aseptic loosening. As of late, computed tomography (CT) is considered an alternative to radiostereometry (RSA) and standard X-rays for assessing these two occurrences. The aim of this thesis is to investigate whether a commercially available CT micromotion analysis (CTMA) software can be used to follow early migration and radiolucent lines in orthopaedic implants.

Cadaveric and clinical studies were performed to estimate the precision, accuracy, and effective dose of CTMA for different orthopaedic implant components using different CT scanners and CT protocols. Precision and effective dose of CTMA were compared to those of radiostereometry. Also, a clinical proof-of-concept study was performed to investigate if CTMA could measure early migration and development of radiolucent lines over time.

The accuracy of CTMA with and without the use of beads was 0.07–0.23 mm and 0.22–0.71°. CTMA with and without the use of beads in the bone had a precision of 0.07–0.31 mm and 0.20–0.54°. CTMA precision did not vary extensively despite the variety of implant types, CT image acquisition equipment, and protocols employed. CTMA achieved a slightly better precision in rotation and a comparable precision in translation to RSA at a slightly higher effective dose. The development of radiolucent lines could be seen in CTMA and followed over time for glenoid components.

In conclusion, CTMA is a tool that could be used to follow early migration and radiolucent lines in orthopaedic implants.

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8. List of Abbreviations

2D	Two-dimensional
3D	Three-dimensional
ALARA	As Low As Reasonably Achievable
CE	Conformite Européenne
CT	Computed tomography
CTDI	Computed tomography dose index
CTMA	CT micromotion analysis
DICOM	Digital Imaging and Communications in Medicine
DLP	Dose length product
FDA	Food and Drug Administration
IMA	Implant Movement Analysis
IRCP	International Commission on Radiological Protection
MAR	Metal artefact reduction
MDR	Medical Device Regulation
MPR	Multiplanar reconstruction
PROMs	Patient Reported Outcomes Measures
RSA	Radiostereometry

1. Introduction

1. 1 Motivation of thesis

Osteoarthritis is a degenerative disease that commonly affects the hip and shoulder joint. Patients with hip and shoulder osteoarthritis requiring arthroplasty treatment has increased during the last decades due to wider indications of treatment and longer life expectancy of patients (1–3). According to the Nordic Arthroplasty Register Association (NARA), the survival rate of cemented hip prosthesis used today is about 96% after ten years (4). In shoulder implants, a metaanalysis of Bohsali estimated the rate of aseptic loosening to 39% five to ten years postoperatively, with 83% of these instances involving the glenoid component (5). With wider indications of arthroplasty the numbers of revisions will increase (1,3). Some of the determinants of failure and loosening of orthopaedic implants include early migration and the development of radiolucent lines. For certain designs of lower extremity implants, early migration after implantation has been correlated to higher revision rates (6,7). As for radiolucent lines, the development and width of radiolucent lines has been correlated to loosening and is commonly used for clinical decisions (8).

Radiostereometry (RSA) has been the gold standard for detecting early migration due to its precision and accuracy (9). However specialized equipment is needed to perform RSA examinations and the image analysis is a complicated process. In addition, the images obtained by RSA are not aimed to capture radiolucent lines because of the low effective dose but also its non-conventional projections (9,10).

With advancements in computed tomography (CT) imaging, clinicians are able to obtain CT images of better resolution at lower effective doses (11). This motivates the use of CT to detect radiolucent lines and apparent minor positional changes of implants. In addition, CT scanners are widely available and does not need specialised laboratories for the image acquisition. In an

experimental setting, Brodén et al. sought to assess whether CT imaging could be used as a method for measuring early migration of acetabular cups. This method presented comparative accuracy and precision to RSA (12). In a clinical setting, Scheerlinck et al. also explored the precision of a CT technique to detect femoral stem migration with a high radiation dose (13). Lately a new commercial development CT micromotion analysis (CTMA), an image registration software sought to assess implant migration using CT scans (14–16).

This thesis seeks to further understand whether CTMA could be used as a tool to measure early migration accurately and precisely, discern the development of radiolucent lines of orthopaedic implants and derive new findings on orthopaedic loosening.

1.2 Aim of this thesis

The main aim of the thesis is to investigate whether CTMA can be used to follow hip and shoulder implants in patients to measure believed surrogate markers for loosening, such as early migration and radiolucent lines. To do so, this thesis will therefore seek to address four objectives:

1. Investigate the accuracy, precision and radiation of the CTMA method in an experimental setting.
2. Compare CTMA to RSA regarding precision and effective dose in a clinical setting.
3. To investigate the precision and effective dose of CTMA in a clinical setting for patients with different types of implants in different hospitals with different CT equipment and CT protocol.
4. To investigate the feasibility of using CTMA in a clinical setting to measure early migration and the development of radiolucent lines of implant components for a cohort of patients followed over 2 years.

1.3 Structure of thesis

In this thesis, Chapter 2-4 will provide a literature review, a deeper explanation of the science behind the CT technology and an explanation of the concept of accuracy and precision.

Chapter 5 will focus on the validation of CTMA to detect early migration in an experimental cadaveric study by calculating its accuracy and precision in shoulder arthroplasty. In the following chapter 6, a clinical study compares CTMA to the gold standard method RSA in terms of precision and effective dose for hip arthroplasty. The generalizability of CT method in a clinical setting will be explored in chapter 7 by evaluating the precision of CTMA of three different shapes of hip implants from three different hospitals with three different CT scanners and CT protocols. This thesis later provides a clinical feasibility study in chapter 8, which determines whether CTMA can detect early migration and progression of radiolucent lines in patients with shoulder arthroplasty over time. The concluding chapter 9 focuses on the findings and methodologies used in this thesis.

2. Literature Review

2.1 History of hip and shoulder arthroplasty

The common expression “necessity is the mother of invention” is true for orthopaedic implants. The invention of both hip and shoulder arthroplasty can be traced to the end of the 19th century. At their inception, these procedures were utilised as treatments for patients with bone damage due to tuberculosis. During the 20th century, improvements in shoulder and hip implants became possible with the growing availability of new materials and incremental innovations in their design. These advancements have made significant strides towards improving quality of life for many orthopaedic patients.

2.1.1 History of hip arthroplasty

Professor Themistocles Gluck invented and implanted the first hip arthroplasty in Germany in 1891 (17,18). He replaced femoral heads destroyed by tuberculosis with prostheses made from ivory (19). Gluck’s experiment led to an extensive period of trial and error using new materials and designs during the first half of the 20th century. Pierre Delbet explored rubber in 1919, and Marius Smith-Petersen explored glass in 1925 (18,19). When the glass femoral arthroplasty shattered under the forces it had to withstand, Smith-Petersen worked with Philip Wiles to develop a stainless-steel arthroplasty. Together, Smith-Petersen and Wiles create the first total hip arthroplasty that was fitted to bone with bolts and screws (19). In 1953, George McKee explored the metal-on-metal arthroplasty using an acetabular component of cobalt chrome (19). A low-friction total hip arthroplasty invented by John Charnley in 1962 became recognized as the first modern hip arthroplasty. It was composed of a metal head, a polyethylene cup, and acrylic cement (19).

Today, various models of hip arthroplasty are available with different bearing surfaces, such as metal-on-metal, ceramic-on-ceramic, metal-on-polyethylene, and ceramic-on-polyethylene (19,20). The metal-on-polyethylene arthroplasty is the most cost-effective solution (19). However, some concerns exist regarding its inflammatory effect in the body. Inflammation can result because of polyethylene wear, this in turn, increases the risk of osteolysis. (21). Implant manufacturers have addressed concerns about wear by irradiating polyethylene with gamma particles to crosslink the polyethylene. In certain implants, the free radicals released during irradiation have also been neutralised with vitamin E (22). Other bearings come with their own risks. For instance, metal-on-metal bearings release metal ions associated with metallosis (19). Previously, clinicians took issue with the brittleness of ceramics because the implants were vulnerable to fracture; however, the creation of new alternative alloys made of zirconium and alumina have settled some of those concerns (19). Lastly, ceramic-on-polyethylene bearings has been suggested to decrease polyethylene wear compared to cobalt chrome bearings on polyethylene (23).

2.1.2 History of shoulder arthroplasty

French surgeon Jules-Emile Péan is acclaimed as the first to perform a shoulder arthroplasty in a patient suffering from tuberculous arthritis (24). In 1892, Péan replaced the joint with a platinum and rubber arthroplasty (Figure 2.1). Still, some evidence—however poorly documented suggests that Péan’s inspiration came from Gluck, the surgeon who performed the first hip arthroplasty (25).

Dr Charles Neer, the father of modern shoulder arthroplasty, treated dislocated proximal humerus fractures with hemiprostheses of vitallium in 1951 (26,27). In 1974, Neer reported the use of the first modern total shoulder replacement with a humeral component and a polyethylene glenoid component (26). Today, shoulder implant components are available in a

variety of materials and designs, such as short stem or stemless humeral stems, metal-backed and polyethylene glenoid components (28).



Figure 2.1 Dr Pean's original shoulder arthroplasty

(Reproduced with permission from Markatos K, Sardiniari S, Brilakis E, Apostolopoulos I, Tsoucalas G, Chronopoulos E. Jules Pean (1830-1898)—A Pioneer Surgeon: His Achievements and His Total Shoulder Arthroplasty. *Surg Innov*. 2019 Dec;26(6):763–5)

2.2 Implant loosening

Today, no universally accepted definition of implant loosening exists. Aseptic loosening is defined inconsistently in the literature by a combination of radiological and clinical findings, such as implant migration or shift, progressive radiolucent lines, clinical symptoms of pain and loss of function, and/or revised implants (8,26,29,30). At times, the literature makes a distinction between radiological loosening and clinical loosening. It is believed that radiological loosening precedes clinical loosening (30). Clinical symptoms, such as pain and loss of function, define clinical failure (30).

Researchers debate the cause of loosening. However, a common explanation is a wear-induced theory. As described earlier, wear debris is believed to create an inflammatory response that stimulates osteoclast activity causing osteolysis around the implant (21). Dumbleton et al. concluded that higher rates of wear are associated with greater osteolysis (31). Other factors of loosening, such as inadequate fixation of the implant postoperatively, might also be important to consider and have been suggested to enhance wear (21,32). For cemented prostheses, insufficient initial fixation is believed to lead to bone resorption and, therefore, initiate the process of loosening. (32,33). The cementing procedure itself can cause a thermal reaction in the bone that leads to bone necrosis (32). For an uncemented arthroplasty, a poor initial fixation is believed to cause motion between interfaces, which prevents bone ingrowth and secondary stability. In turn, the risk of loosening increases (34).

Aseptic loosening has previously been related to two surrogate factors: early migration and the development of radiolucent lines (6-8). Other factors related to loosening include malalignment of implants and infection, but the focus of this thesis remains the early migration and development of radiolucent lines (35,36).

2.3 Predictors of implant loosening

2.3.1 Radiolucent lines

Gaps in the interface between the implant-cement and implant-bone are described as radiolucent lines. This term describes a zone around the implant which is radiolucent. Radiolucent lines have been observed both in cemented and uncemented implants, and their development over time is believed to be associated with an inferior implant survival rate (38). Radiolucent lines are used to assess loosening, but correlation between the development of radiolucent lines and loosening has not yet been clearly established in vivo (37). Development of radiolucent lines is still poorly understood, although its cause could be mechanical in nature.

In an experimental study, Gregory et al. used a micro CT to investigate the implant-cement interface and suggested that the development of radiolucent lines around a keeled glenoid component subjected to cyclic loading might start around the periphery of the glenoid component progressing towards the central keel of the implant (39).

Researchers argue that osteolysis and radiolucency are different based on their appearance (40). It is, however, important to notice that osteolysis is an inflammatory process (21). In contrast, a radiolucent line is a description of a radiolucent zone around the implant. Histological analysis shows that radiolucent consists of fibrous tissue and regions of osteoporosis (41). The fibrous tissue might signal a lack of fixation of the implant.

2.3.1.1 Radiolucent lines in the hip

Radiolucent lines in hip arthroplasty can be described using a seven-zone system of the femur described by Gruen et al. and a three-zone system of the acetabulum described by DeLee and Charnley (Figure 2.2 and Figure 2.3)(40,42–45).

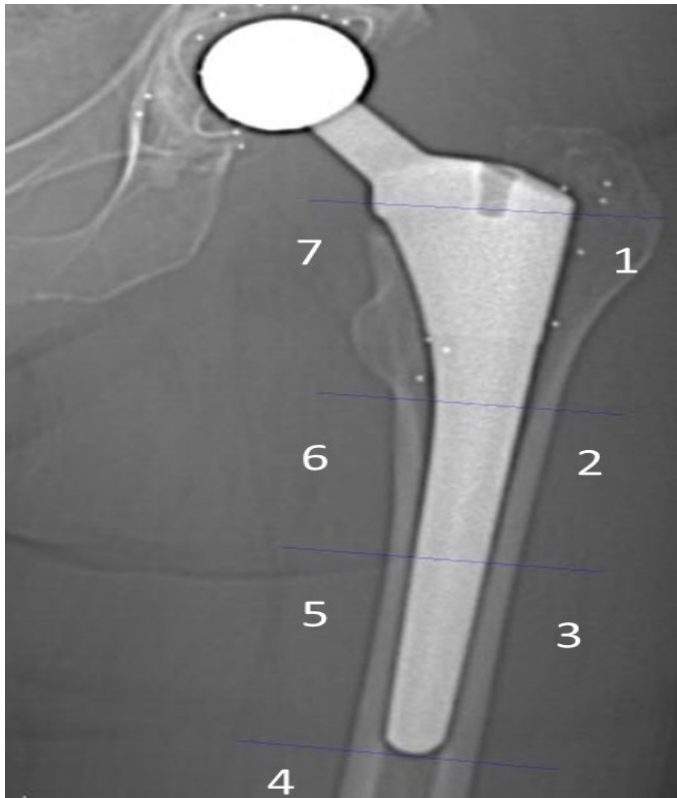


Figure 2.2 Gruen Zones

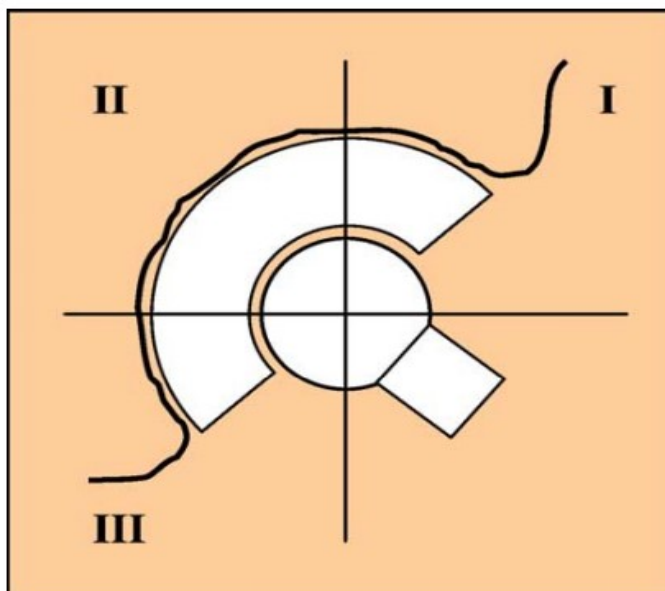


Figure 2.3 DeLee and Charnley zones

(Reproduced with permission from Kneif D, Downing MR, Ashcroft GP, Knight DJ, Ledingham WM, Gibson PH, et al. The correlation between immediate radiolucent lines and early implant migration in cemented acetabular components. J Arthroplasty. 2006 Feb;21(2):215–20.)

2.3.1.2 Radiolucent lines in the shoulder

American Scores

In 2002, Lazarus et al. created the Lazarus grading system for discerning radiolucent lines. Lazarus et al. adapted the Franklin score, which was initially created to discern radiolucent lines in frontal radiographs for use with keeled glenoid components, including glenoid components with multiple pegs (Figure 1.4)(46). Both the Franklin and the Lazarus scoring systems de-emphasise radiolucent development at the peripheral interface of the implant and were created as scoring methods for use on standard radiographs (38,46).

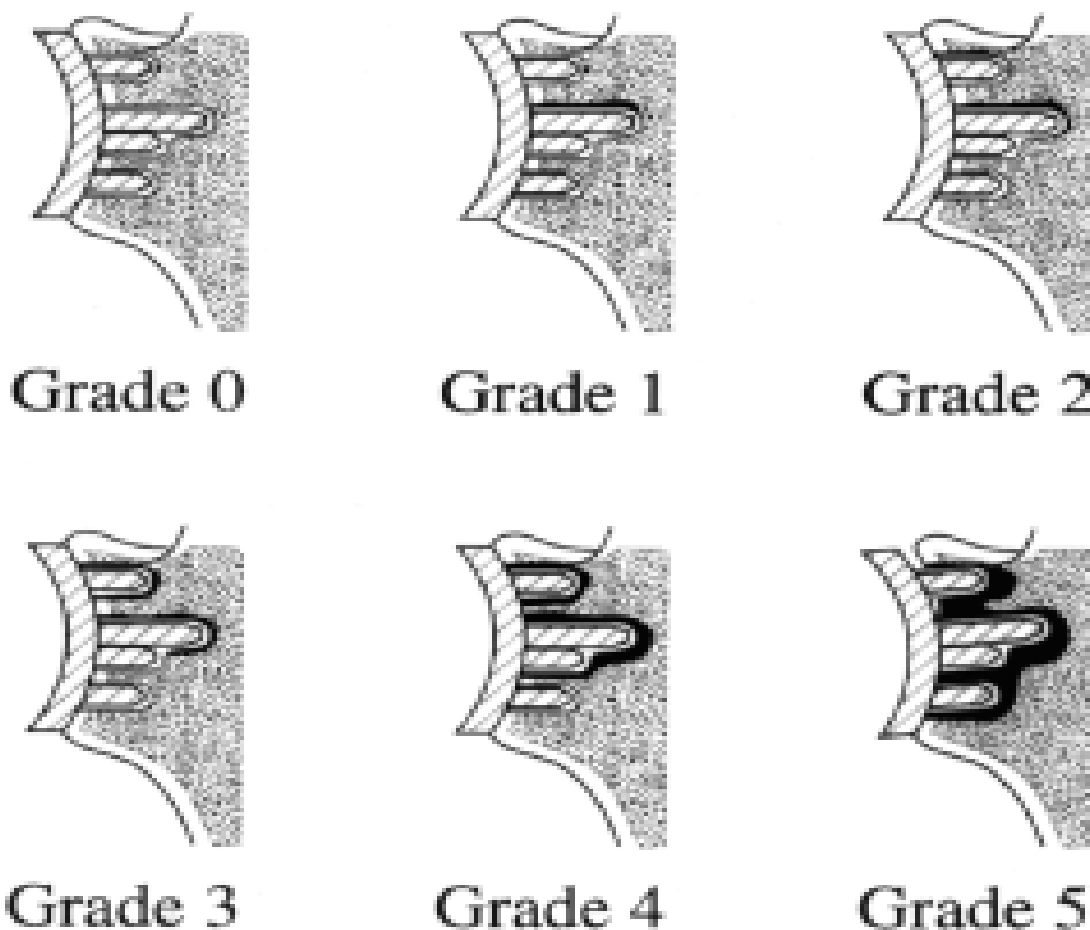


Figure 2.4 Lazarus grading system

Grade based on the width of the radiolucent lines and the involvement of the number of pegs. Grade 5 is considered loose.

(Reproduced with permission from Lazarus MD, Jensen KL, Southworth C, Matsen FA. The radiographic evaluation of keeled and pegged glenoid component insertion. J Bone Joint Surg Am. 2002 Jul;84-A(7):1174–82)

European Scores

The French doctor Molé created the Molé score in 1999 (47). The Molé Score, like the Franklin score, is used to assess radiolucent lines on conventional frontal radiographs of keeled glenoid components. However, the Molé scoring system considers radiolucency development near the periphery of the implant. Since its creation, the Molé score has been adapted and modified to assess glenoid components with pegs and also to be used on axial radiographs (Figure 2.5)(38).

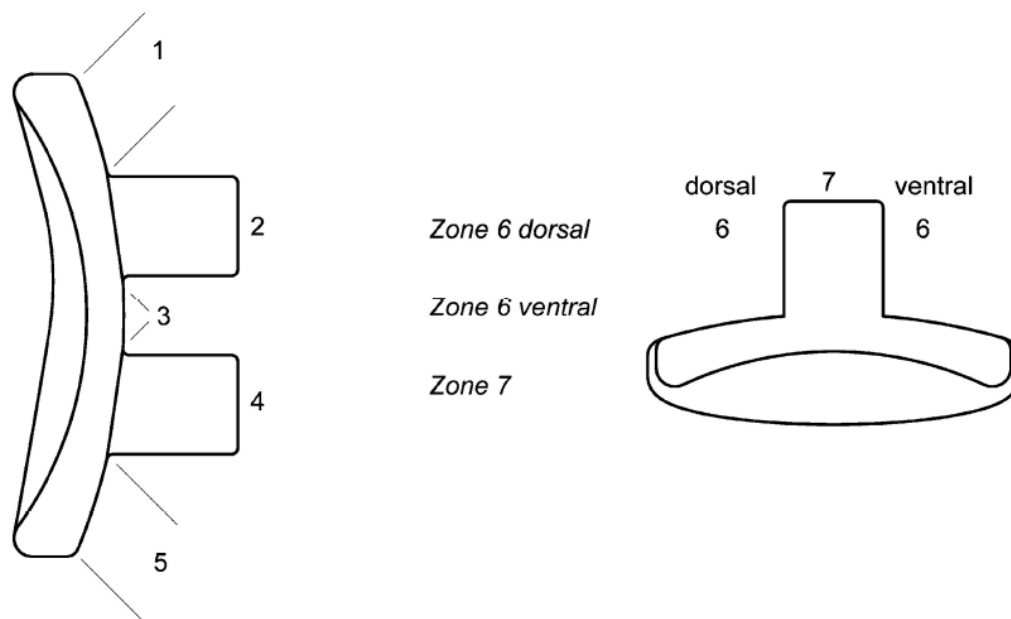


Figure 2.5 Zones used for an adapted Molé score.

For each zone a score from 1 to 3 is given depending on the size of the radiolucent lines.

(Reproduced with permission from Greiner S, Berth A, Kääh M, Irlenbusch U. Glenoid morphology affects the incidence of radiolucent lines around cemented pegged polyethylene glenoid components. Arch Orthop Trauma Surg. 2013 Oct;133(10):1331–9)

2.3.2 Early migration

Previous studies of lower limb arthroplasty, including the hip and knee, have demonstrated that early migration of implants is strongly correlated with the longevity of joint replacement (6,7,48). For hip stems, early migration of 1.2 mm after the first two years indicates a high risk of revision (7). For acetabular cups, a migration over 1 mm within two years is a predictor of implant failure (6). Still, for some types of prostheses, such as the polished tapered hip stem

(Exeter, Stryker), continuous migration is accepted as it is not predictive of loosening (49). When examining the literature, it is important to emphasise that the migration pattern might be different depending on implants and their fixation method. For example, in an uncemented femoral stem, the initial migration occurred within the first six weeks postoperatively. After this period, the implant stabilised (50). It is, therefore, important to differentiate between early migration and continuous migration since uncemented components might have an early migration within the first months postoperatively until long term stability is achieved (50,51).

In shoulder arthroplasty, migration studies of cemented glenoid components show early migration of the glenoid component (8,52,53). However, in shoulder arthroplasty, a threshold measurement of early migration warranting a risk of revision has not yet been established (54). This may be due to the scarcity of radiostereometric studies dedicated to the upper extremities with a short follow-up time.

2.4 Measurement tools

This section reviews a range of radiological methods for assessing early migration and radiolucent lines. The methods presented in this thesis are the conventional radiographs, radiostereometry, and computed tomography (CT).

2.4.1 Conventional radiograph

Conventional radiographs is commonly used to assess implants in orthopaedic care. However, radiographs provide a two-dimensional image of a three-dimensional structure. Therefore, its precision and accuracy in detecting the early migration of an implant at less than 1 mm are not optimal (55). This method is also known to underestimate radiolucent lines (37,56).

2.4.2 Radiostereometry

Developed by Selvik in 1974, radiostereometry (RSA) is today considered the gold standard for monitoring implant migration given its ability to provide superior accuracy and precision compared to standard radiographs (Figure 2.6)(9). The RSA technique, relying on bi-plane radiographs, provides a measurement of the relative position between two rigid bodies (e.g. the prosthesis and the bone) in between two different timepoints (Figure 2.7)(9). To perform standard RSA, it requires the implantation of tantalum markers in the skeleton and prosthetic components and the use of a calibration cage. Tantalum spherical markers are used due its high atomic number which makes the beads easily detectable in radiographs (57). A minimum of three well spread beads are necessary to mark each rigid body. However, to mitigate the risks of marker occlusion and bead movement, five to nine markers are usually inserted (9,57). The distribution and the stability of markers are crucial to guarantee the quality of the registration and are evaluated with two measurements: the condition number and the mean error of rigid body fitting (9). The calibration cage contains markers that are located to identify the position of the roentgen tubes (control markers) but also the coordinate system of the setup (fiducial points)(Figure 2.6)(57). When RSA radiographs have been performed, they are imported into an RSA software to calculate and measure the migration of each segment compared to another segment of interest. The migration is expressed in a fixed coordinate system defined by the calibration cage. The accuracy and precision of RSA depend on several factors, such as the stability and distribution of tantalum markers (57).

Despite its advantages, RSA comes with several limitations. One important difficulty with this technique concerns the detection of radiolucent lines. The RSA's plane radiographs do not provide optimal detection given the low radiation exposure (56,58). Other limitations include the need for expensive and specialized equipment, trained personnel, tantalum-marked prostheses, and obscured markers. The development of model-based RSA has largely

addressed the latter limitation of obscured markers. In this technique, the marking process of the implant can be overcome using virtual surface models of implants based on three-dimensional computer-aided design (CAD), reversed engineering (RE), or elementary geometrical shapes (EGS) (59,60).

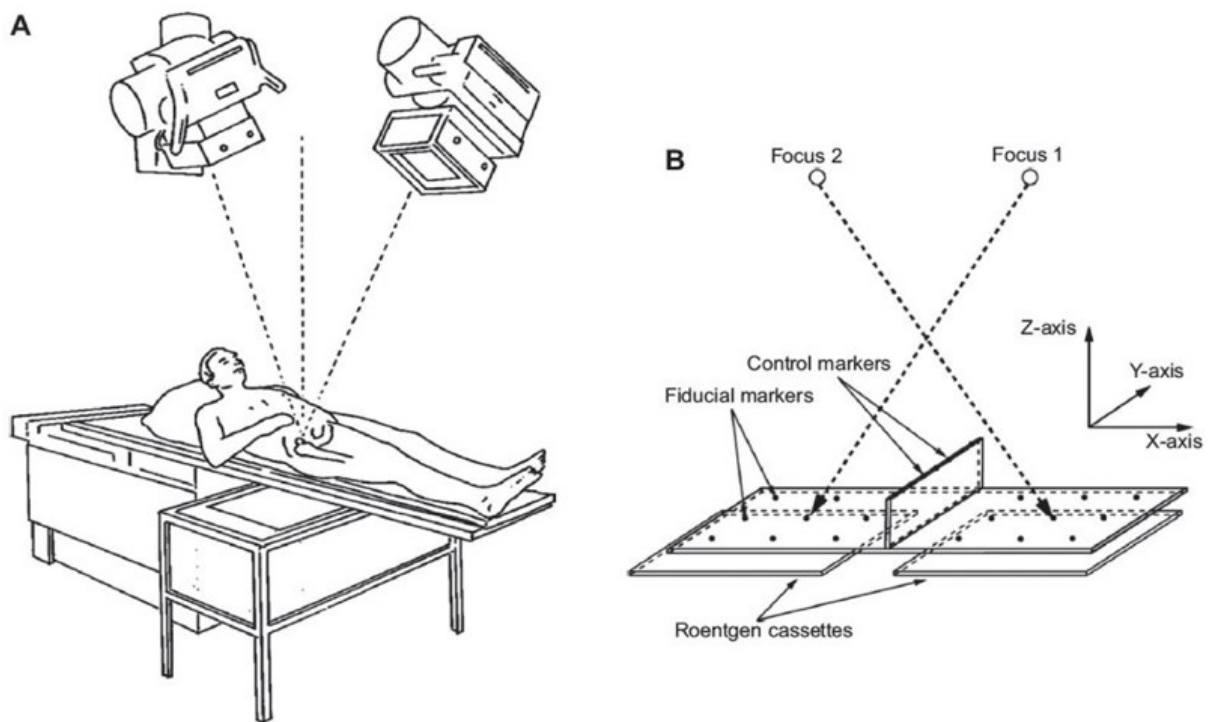


Figure 2.6 RSA setup

(Reproduced with permission from Valstar ER, Gill R, Ryd L, Flivik G, Börlin N, Kärrholm J. Guidelines for standardization of radiostereometry (RSA) of implants. *Acta Orthop*. 2005 Aug;76(4):563–72)

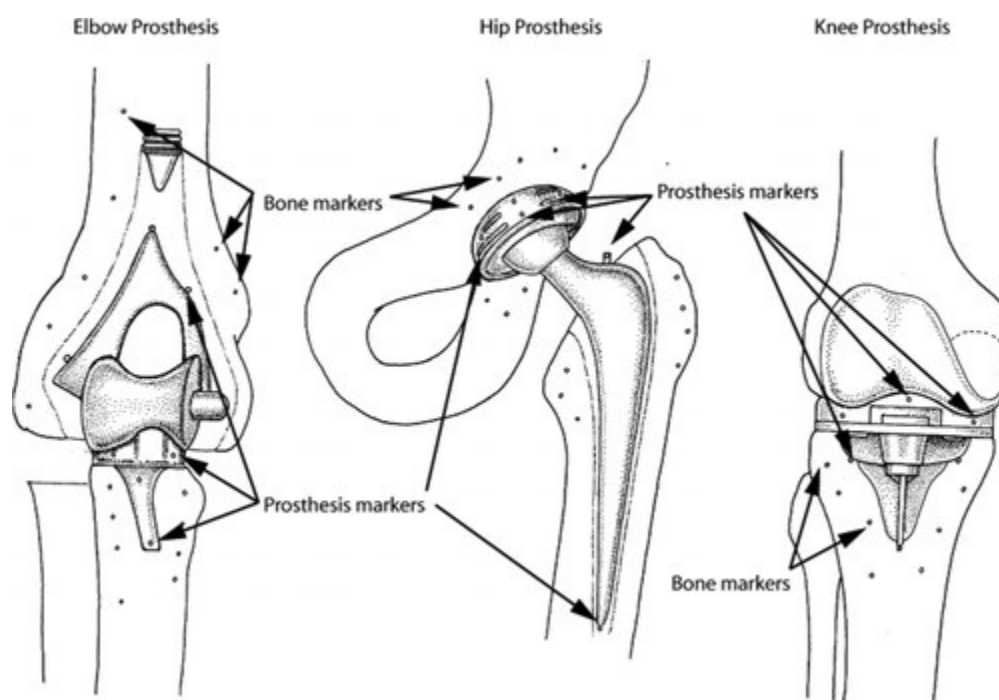


Figure 2.7 Beads inserted in RSA

(Reproduced with permission from Valstar ER, Gill R, Ryd L, Flivik G, Börlein N, Kärrholm J. Guidelines for standardization of radiostereometry (RSA) of implants. *Acta Orthop*. 2005 Aug;76(4):563–72)

2.4.3 Computed tomography

As not every hospital has the stereoradiographic facilities needed to perform RSA, there is an interest in using CT scanners to assess early migration of orthopaedic implants (12). During the last few decades, extensive research has produced a CT image registration method to measure implant migration (11,12,61). The prevention of metal artefacts and reduction of irradiation due to improved CT software and hardware have been important for the development of this technique in a clinical setting (11,62,63). In addition, CT scans may detect radiolucent lines that cannot be observed on standard radiographs or RSA (56,58).

This extensive research has produced a new commercial image registration software called CT-micromotion analysis (CTMA, Sectra, Linköping) (12,61,64–66). The next chapter explains CT scanning and CTMA.

3. Principles of CT and image registration

“As the area of light expands, so does the perimeter of darkness.”
—Albert Einstein

The method used in this thesis relies on CT scanners for data collection and image registration software for data analysis. In this chapter, the principles of the CT technology used throughout the thesis will be explained. To do so, the mechanics of CT scanner imaging will be presented before exploring the image processing tool known as CT micromotion analysis (CTMA).

3.1 The acquisition of CT data

After **X-rays** are **produced**, they **travel** through the patient’s body to reach CT **detectors** (67). **Detectors** convert X-rays to electrical signals, and those signals are made digital with the help of an analogue-to-digital converter (68). The digital signals are used to produce a CT image in a **reconstruction process** with an image reconstruction algorithm (69).

3.1.1 The production of X-rays

In a CT scanner, X-rays are produced in a tube located in the gantry. In the tube, an electrical current heats a cathode filament (Figure 3.1). When the cathode is heated, it releases electrons through the process of thermionic emission (70). These electrons travel in the tube and accelerate towards the anode; the number of electrons travelling is dependent on the electrical current in the tube (71). The acceleration of the electrons towards the anode is determined by the voltage of the tube (70). When the electrons hit the anode, energy is released and converted to heat and photons (70–72). The current and the voltage of the tube is controlled by an x-ray

generator (Figure 3.1) (70). These photons are the basic element of X-rays.

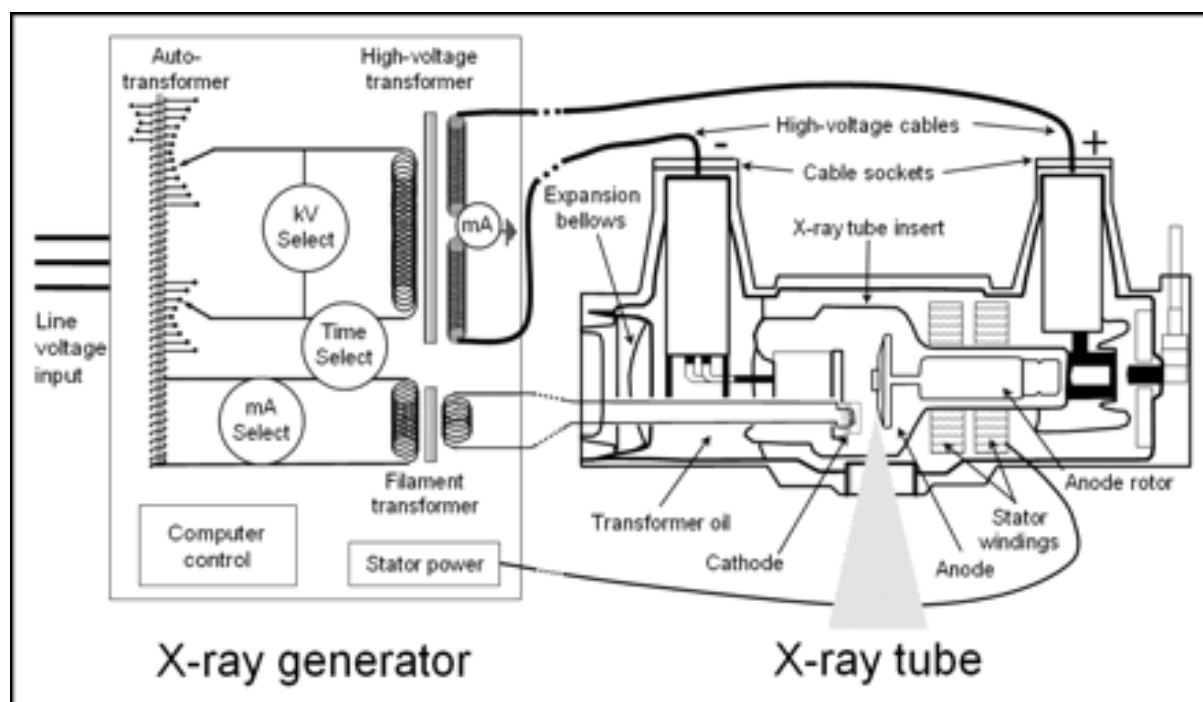


Figure 3.1 The X-ray generator and tube

(Reproduced with permission from Seibert JA. X-ray imaging physics for nuclear medicine technologists. Part 1: Basic principles of x-ray production. J Nucl Med Technol. 2004 Sep;32(3):139–47.)

3.1.2 The travel of X-rays

A beam of X-rays is composed of both low- and high-energy photons. Before the beam travels towards the patient, a filter removes the lower-energy photons to avoid image artefacts (beam-hardening artefacts), which improves the quality of the image (67,73). After the filtering process, the X-ray travels through a collimator, which defines the shape and thickness of the beam (68,73). Thereafter, the beam reaches the patient and traverses the body. As the beam passes through body parts, attenuation of the beam occurs.

3.1.3 The detection of X-rays

The most common detectors used today are solid-state detectors (71,73). They are composed of a scintillator and a photodiode (71,74). When the scintillator is excited by photons, visible light is created. The photodiode of the detector converts light to electrical currents. The

electrical signal that is obtained reflects the attenuation coefficient of the X-ray, and this is converted to a digital signal, which is used for calculations to create the CT image during the image reconstruction process (68).

Different generations of CT scanners vary in the number and structural arrangement of their detectors (68). The hardware and software improve with each generation, enabling higher-quality images at a lower radiation (11). First-generation CT scanners had only one detector, which made data acquisition time-consuming (73). The number of detectors in second-generation scanners was increased to a row of 30, which improved the speed of image acquisition (Figure 3.2)(73).

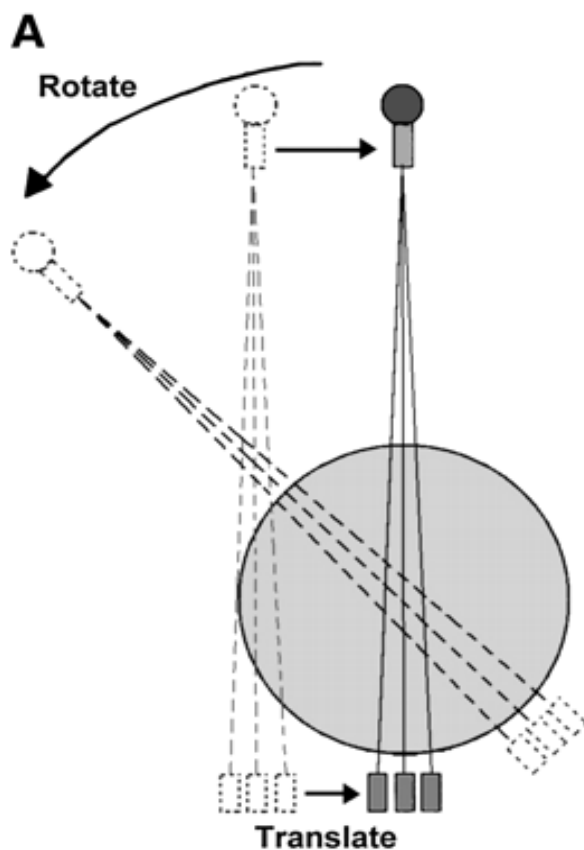


Figure 3.2 Second-generation CT scanner

(Reproduced with permission from Goldman LW. Principles of CT and CT Technology. J Nucl Med Technol. 2007 Sep 1;35(3):115–28.)

Currently, the most commonly used CT scanner is the third generation, which has even more detectors (Figure 3.3)(69). The detectors allow for continuous data collection at 360 degrees of rotation. The fourth-generation CT scanner detectors cover the entire CT gantry (Figure 3.4).

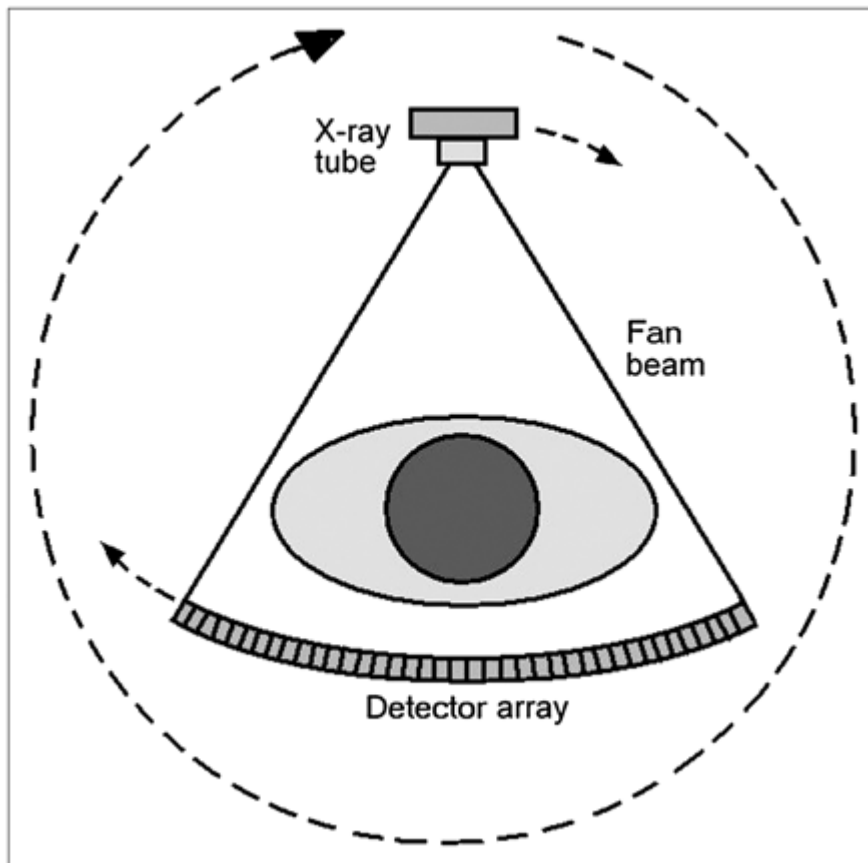


Figure 3.3 Third generation CT scanner

(Reproduced with permission from Goldman LW. Principles of CT and CT Technology. J Nucl Med Technol. 2007 Sep 1;35(3):115–28.)

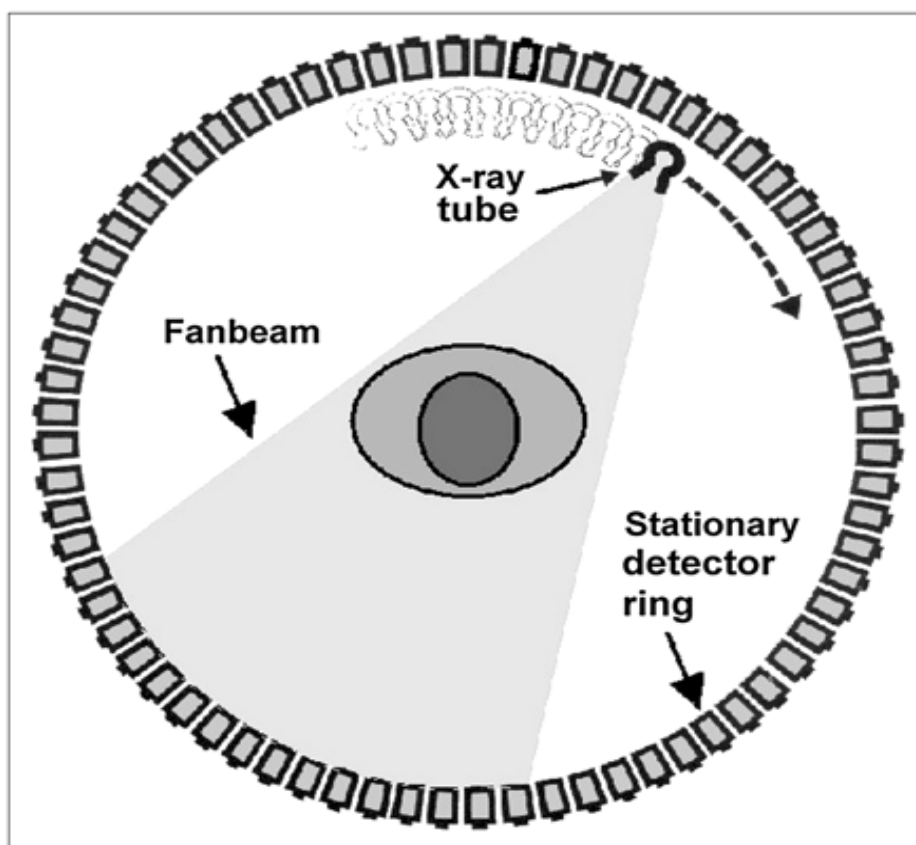


Figure 3.4 Fourth-generation CT scanner

(Reproduced with permission from Goldman LW. Principles of CT and CT Technology. J Nucl Med Technol. 2007 Sep 1;35(3):115–28.)

The invention of the slip ring to acquire helical scans eliminated interscan delays, thereby increasing the speed of data acquisition (69,73). With the helical scan functionalities of new CT machines, the notion of pitch was introduced into the CT protocol. Pitch is the table movement per 360° rotation divided by the slice thickness or X-ray beam width (71,72). Helical scans created challenges, such as overheating of the X-ray tube. This problem was solved with the invention of the multislice CT scanner (MSCT), which uses multiple rows of detectors in z direction and a widened beam (Figure 3.5)(68,71,72). This increased CT volume coverage and speed performance, and decreased the number of rotations and the total use of the X-ray tube (72). The multislice CT scanners are based on the geometry of third-generation scanners.

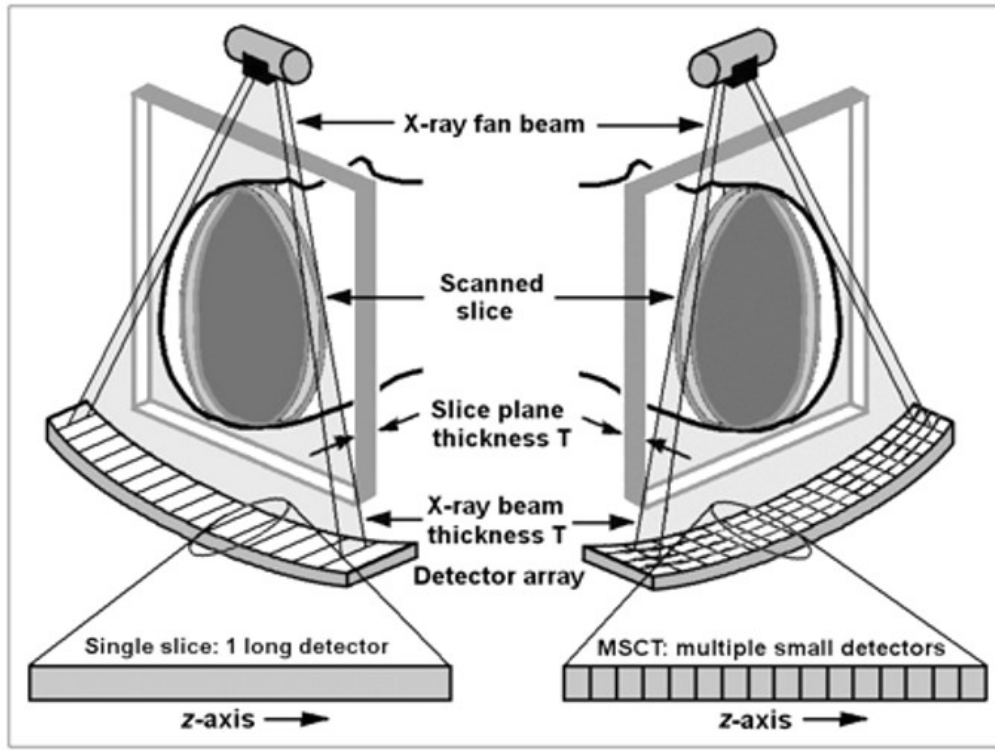


Figure 3.5 CT detectors in multislice CT scanners (MSCT)

(Reproduced with permission from Goldman LW. Principles of CT: Multislice CT. J Nucl Med Technol. 2008 May 15;36(2):57–68)

3.1.4 Reconstruction process

A CT image is a digital image, created with an image reconstruction algorithm using the X-ray attenuation data acquired from the detectors. Attenuation values of the beam are calculated in relation to the Hounsfield units (HU), where water is assigned the value of 0 HU (67). CT images are produced following a grey colour scale where areas of low attenuation (low HU) become black, while bone with higher attenuation (high HU) becomes white (67). Images can be further manipulated by using window settings to increase contrast, which facilitates the visualisation of the CT image (67).

3.2 Image quality

The quality of the CT scans is dependent on factors such as noise, spatial resolution and the presence of artefacts.

3.2.1 Noise

Noise is defined as a random variation of HU in one uniform object; it is an unwanted signal and an undesirable by-product of the image acquisition (68,71).

3.2.2 Spatial resolution

Spatial resolution refers to the CT scanner's ability to reproduce details of an object so that small structures can be differentiated from each other; it reflects how small the objects can be and still appear as separate details (68,75).

3.2.3 Artefacts

3.2.3.1 Beam hardening artefacts

The beam-hardening effect occurs when low-energy photons are absorbed in the body, thereby increasing the mean energy of the beam traversing the body. The detector interprets that the beam, which now has higher energy, was less attenuated by the structure of the body, and therefore dark streaks are created (69,76,77). These artefacts can be avoided by filtering the X-ray beam.

3.2.3.2 Photon starvation artefacts

When the beam must travel through rigid material, more photons are absorbed. The result is a smaller proportion of signal reaching the detector, and more noise (77).

3.2.3.3 Metallic artefacts

Metallic artefacts can be caused by a combination of artefacts that occur due to the interaction of photons with metal inserted in the body. They include beam hardening, photon starvation, and other types of artefacts that are outside the scope of this thesis (76).

3.3 CT protocol

It is important to consider which CT protocol to use for the image acquisition of a CT scan, since it will affect the image quality and the effective radiation of the scan. The aim should be to obtain the highest quality of CT images at the lowest dose possible (71). Some parameters that can be changed for a CT scan are kilovoltage peak, exposure, slice thickness, pitch, rotation time, and increments of the slices (78).

3.4 Image registration

3.4.1 Principles of image registration

Image registration solves the problem of comparison between images by aligning them; it is used extensively for medical image analysis (79). For this thesis, image registration will be used to follow early migration and to visualise the implant-bone interface over time. The software used for the image registration is CT micromotion analysis (CTMA), presented below.

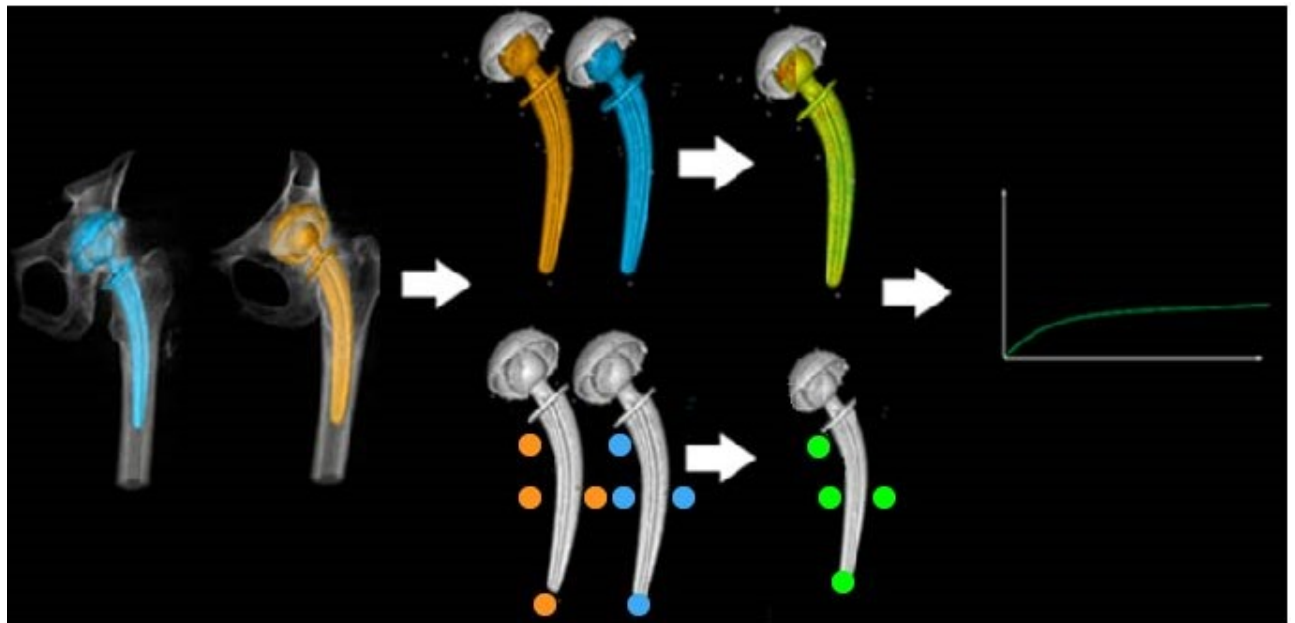
3.4.2 CT micromotion analysis

The CTMA software is a commercial product created by Sectra Orthopaedics (Sectra AB, Linköping). The software has a rigid body image registration function that assesses implant migration relative to bone between two CT images. The underlying principles of CT-based migration measurement have been studied in many scientific publications (80–85). Previous publications have extensively described the CTMA image analysis (14–16). To my knowledge, CTMA is currently the only commercially available tool using image registration to quantify implant migration of orthopaedic implants. Other research groups have explored CT registration methods using research tools not widely available (85,86). These research tools rely on CT data that has been acquired at a high effective dose. In hip arthroplasty, Scheerlink et al reports effective doses between 3.1 to 8.2mSv for each CT scan. In other papers, the effective doses have not been calculated but the CT protocol reveal high voltages and high

current which is correlated to a higher effective dose (86). CT effective doses of this magnitude makes it difficult to ethically justify longitudinal studies to quantify implant migration for several timepoints and might therefore be a limitation to the widespread use of these CT image registration techniques. At last, the precision of the CT method explored by Scheerlink et al. was estimated to not exceed 0.09 mm and 0.14 degrees, however the method of calculation was different than what has been recommended in the RSA guidelines and therefore difficult to compare to RSA (85). Richetti et al. used a CT method that was able to detect shifts of components superior to 5 degrees (86). This CT method was not as precise as gold standard RSA and that might also limit the adoption of this technique.

To assess implant migration in CTMA, two CT data sets are imported into the volume registration tool CTMA for two consecutive image registrations (Figure 3.6). For the first registration, a reference rigid body (the bone) is defined in two separate CT examinations and registered. The reference rigid body can be defined by beads inserted perioperatively in the bone or by the surface anatomy of the bone. For the second registration, the implant is defined by its metallic surface or the tantalum beads inserted inside the component. The two consecutive registrations result in a visual output in the form of registered 2D and 3D volumes and numerical migration values expressed in six degrees of freedom (rotations around and translation along x,y,z) in a CT-based coordinate system (14,15). During the analysis, the consistency of the registered rigid bodies is verified manually with a colour-coded feedback mechanism that illustrates any change in the transformation of either rigid body due to deviation of tantalum beads, bone morphology changes, or implant deformation. The colour green indicates a successful registration (14,15).

CTMA software is a measurement tool, and the migration values are continuous. Before this software is used in a clinical setting, it must be validated. The process of validation will, therefore, be addressed in the next chapter.



1

2

3

4

Figure 3.6 The CTMA process

Two registrations performed to evaluate implant migration relative to bone between two different CT images:

1. First a segmentation of the CT image (thresholding) is performed to expose the metallic structures in the CT image.
- 2-3. The metallic stem and the beads inserted in the bone are registered in two different image registrations. (beads are enlarged for clarity). Visual cues provide feedback alerting the user to any inconsistencies in marker selection or pairing. The green colour indicates successful registration.
4. The migration is quantified in translation and rotation.

4. Method of validation of CT micromotion analysis

Computed tomography micromotion analysis (CTMA) is an image registration tool that measures the migration of an implant relative to the bone between two CT images. All measurement tools have associated errors (87). To acquire reliable results, it is critical that the measurement tool, i.e., software, measures what it is intended to with an acceptable margin of systematic and random error. When a measurement tool has sufficient **accuracy** and **precision**, the method is considered suitable for its use. In radiostereometry (RSA), it is recommended to estimate the accuracy and precision to validate the method, especially when a new RSA system is used (9). The accuracy and precision of the CTMA method reflect not only the errors of the software but also the errors of the CT scanner, since the data used in CTMA originates from CT scanners. Because the outcomes we were interested in were continuous and not dichotomous, sensitivity and specificity were not relevant for the assessment of the tool in this validation process.

4.1 Accuracy

Accuracy is defined as “the closeness of agreement between a measured quantity value and a true value of a measurand” (88). Accuracy is related to systematic measurement error, which is the deviation from a true value (89).

The standard approach to measuring accuracy entails assessing the difference between the measurements of a method and those of the gold standard (9,90). The gold standard is the current best available method. For CTMA measurements, the gold standard is RSA.

Instrumental and observer bias are two common forms of accuracy error. Instrumental bias may be due to the wrong calibration of the instrument. In contrast, observation bias may stem from an error of the operator when performing the analysis, such as orienting the coordinate system in the wrong direction during CTMA, creating biased migration results (89).

According to Ranstam et al., there is an array of methods for calculating accuracy, making comparison between studies difficult due to the lack of consistency (90). In this thesis, we employed a similar method to Sköldenberg et al. and Brodén et al. by calculating the root mean square multiplied by a T-score from a t-distribution (12,91). The T-score is a cut-off point in a t-distribution where the margin of error is at 95% of the confidence interval (Figure 4.1).

4.2 Precision

Also related to variability, and consequently, random errors, precision is defined as the approximate agreement between independent repeated measurements obtained under the same conditions (88,89). Precision influence the power of a study. The more precise the measurement is, the smaller the sample size required to generate the same power for a given effect size in a research study (89).

The precision of RSA is assessed by double examinations (9,88). Two RSA examinations are conducted consecutively with the patient, the X-ray tubes and calibration cage changing position in between the examinations (9). If no movement between the implant and bone occurs between the double examination, the obtained migration values that deviate from 0 reflect the random errors of RSA. We employed the same method to assess precision of the CTMA technique. According to the International Organization for Standardization (ISO standards) of RSA, “precision should be assessed with double measurement and shall be presented as the standard deviation of these calculated migrations. Assuming a normal distribution, the confidence intervals of the error should be expressed as $\pm 1,96 \times SD$, for the 95% confidence interval”(88).

In this thesis, we followed the ISO standard with one slight modification. To avoid underestimating the margin of error of precision in a small sample size, we used a t-distribution instead of a normal distribution. Therefore, the ISO formula for the 95% confidence interval

changed from the formula **1.96 x SD** to **T-score x SD**. A t-distribution is a probability density function that defines the probability for each continuous possible outcome. A t-distribution has wider tails than a normal distribution and is used when the sample size is small (92). When the sample size is small, the margin of error for the 95% confidence interval increases. The sample size defines the degree of freedom of the t-distribution. The larger the sample size becomes, the more the t-distribution begins to resemble a normal distribution (Figure 4.1)(92). The T-score is a cut-off point where the margin of error is at 95% of the confidence interval. For a normal distribution that cut-off point would be the Z-score of 1.96, and for a t-distribution that cut-off point would be greater than 1.96.

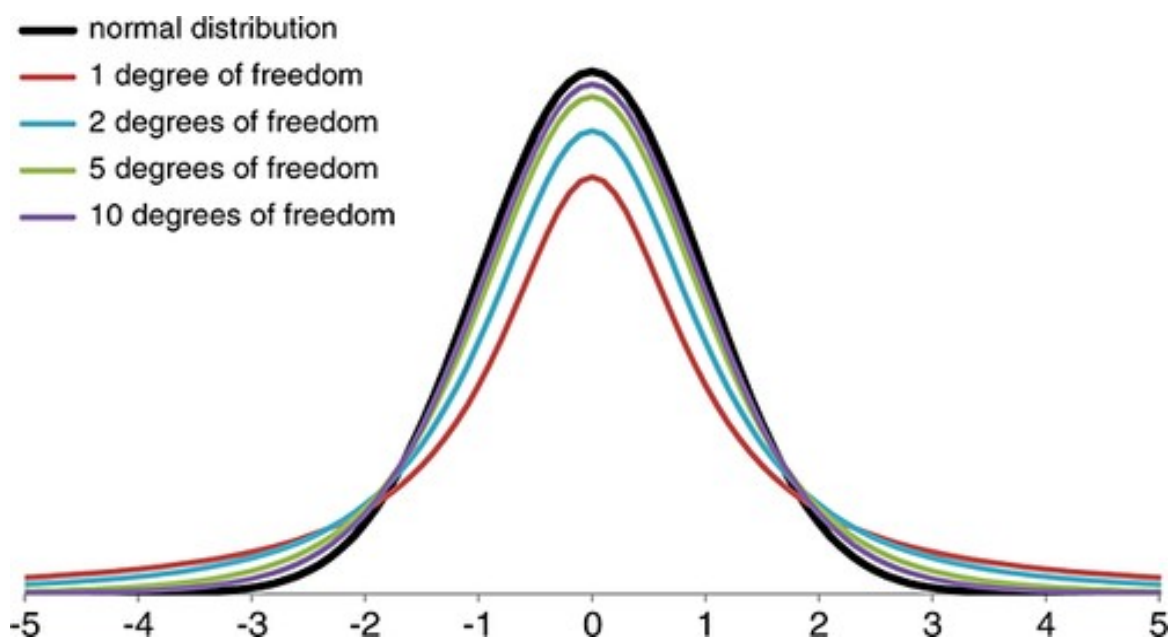


Figure 4.1 Normal and t-distributions for varying degrees of freedom

(Reproduced with permission from Brereton RG. The *t*-distribution and its relationship to the normal distribution: The *t*-distribution and normal distribution. J Chemom. 2015 Sep;29(9):481–3.)

In summary, if migration measured with the CTMA exceeds the calculated precision and accuracy measurement, it is due to real migration and not to systematic and random errors. In the next chapter the accuracy and the precision of CTMA will be estimated in an experimental setting for shoulder arthroplasty.

5. Experimental validation of CTMA in shoulder arthroplasty

This study aims to validate CTMA to measure implant migration in shoulder arthroplasty. A cadaver proximal humerus and a scapula, which had tantalum beads incorporated within them, were prepared to accept a short-stemmed humeral component and a two-pegged glenoid component of a commercial total shoulder arthroplasty (TSA) system. A five degree of freedom micrometer and goniometer equipped rig was used to translate and rotate the implant components relative to the respective bone to predetermined positions. Double CT examinations were performed for each position. CTMA was used to assess these movements to estimate the precision of the method. The accuracy of CTMA was estimated using the rig's micrometers and goniometers as the gold standard. The technique's effective dose was also assessed.

The accuracy of CTMA was in the range of 0.07–0.23 mm in translation and 0.22–0.71° in rotation. The precision was in the range of 0.07–0.15 mm in translation and 0.21–0.54° in rotation. The mean effective dose for the CT scans was calculated to be 0.27 mSv (0.22–0.34 mSv). These results demonstrate that accuracy, precision of CTMA, with and without the insertion of bone markers were comparable to the gold standard method RSA. However, the CT effective dose was slightly higher than RSA.

The majority of the material of this chapter has been published in *Acta Radiologica* and reproduced according to the licensing policy of Sage Journals. Brodén C, Giles JW, Popat R, Fetherston S, Olivecrona H, Sandberg O, et al. Accuracy and precision of a CT method for assessing migration in shoulder arthroplasty: an experimental study. *Acta Radiol Stockh Swed* 1987. 2019 Nov 4;284185119882659

The authors wish to thank Joshua Giles for helping with the design of the rig, Christine Tempelaere (CTE) for the glenoid and humeral preparation and Olof Sköldenberg for assistance with the statistical analysis.

5.1 Introduction

The incidence of total shoulder arthroplasty has been predicted to increase in the next decades (3,93). Therefore, the number of complications such as aseptic loosening will increase (3). Early migration has been correlated with aseptic implant loosening, however this correlation is not clearly established in shoulder arthroplasty (54).

Early migration has historically been measured with radiostereometry (RSA) and mainly used in lower extremity. RSA is considered the gold standard to quantify implant migration because of its excellent accuracy and precision (9). However, RSA is not widely available at all hospitals since there is a need for specialised equipment and trained staff. Another inconvenience with RSA, is that it does not give a detailed visual feedback of the interface, and particularly the progression of radiolucent lines that might contribute to the loosening process.

Improvements in CT have increased resolution and decreased effective dose, motivating the use of widely available CT scanners to quantify implant migration. A CT technique has previously been used in lower limb arthroplasty to assess implant positioning (94). Furthermore, one experimental study has been conducted with a CT technique on acetabular cups comparing its accuracy and precision to RSA (12). However, no such methodological CT study has yet been conducted for shoulder arthroplasty.

The aim of this study was to validate CTMA for use with total shoulder replacement with and without the use of bone markers, and evaluate whether its accuracy, precision, and effective dose were comparable to RSA.

5.2 Material and Methods

5.2.1 Ethics

This work was approved by the National Research Ethic Service (NRES) Committee (reference 13/LO/1839).

5.2.2 The device description

A frozen cadaveric proximal humerus and a scapula were prepared to accept the short-stemmed humeral component and the two-pegged glenoid component, respectively, of a commercially available hybrid total shoulder arthroplasty (TSA) system Affinis Short Stemmed Total Shoulder Prosthesis (Mathys, Bettlach, Switzerland, Affinis Short) (Figure 5.1). The humeral head was resected at the anatomic neck and a cruciate-shaped recess was created in the humeral metaphysis using standard techniques. The width of each arm of the cruciform-shaped recess was then enlarged to facilitate implant translations and rotation during testing. The glenoid was also prepared and reamed using the standard procedure. The two peg holes were then created and subsequently their diameter was enlarged. Next, tantalum beads with 1.0 mm in diameter were inserted into the humeral head and the glenoid bone using a bead injector. In total, nine beads were inserted in the glenoid and 12 in the humerus. The preparation of the glenoid and humeral bone was performed by an orthopaedic consultant specialised in shoulder surgery (CTE).

To accurately assess the ability of CTMA to measure shoulder implant migration, a custom rig was developed with three orthogonal translations and two degrees of rotational freedom (Figures 5.2 and 5.3). The implant mount of the rig is composed of three orthogonally stacked translational stages (Model 9061, Newport, Irvine, CA, USA) with micrometers (Model 148-215, Mitutoyo, Aurora, IL, USA) that produce translations with an accuracy of 0.005 mm and a rotational goniometer (Model GNL 18/M, ThorLabs, Newton, NJ, USA) with an accuracy of 10 arc min (i.e. 0.167°). The first translational stage is affixed to the base while the third

translational stage connects to the goniometer which in turn acts as a mount for a glenoid or humerus implant fixture that were custom-designed. In the case of humeral testing, the fixture holds the ceramic humeral head. The cruciform-shaped short humeral stem can then be attached to the ceramic humeral head (Figure 5.2). For glenoid testing, the fixture incorporates a morse taper to allow the base of the humeral head to be attached. The glenoid component is then fixed to the humeral head component using cyanoacrylate. The humeral head component is included in glenoid testing as the ceramic material of the head could potentially produce CT artefacts and therefore affect accuracy and precision results (Figure.5.3). The bone mount for the humerus or scapula can be interchanged depending on the bone to be tested. This bone mount is connected to the testing rig base by a single axis rotational stage (Model M-481-A, Newport Co., Irvine, CA, USA) with an accuracy of 5 arc min (i.e. 0.083°). The humerus mount is composed of four uprights, each with height adjustable bolts. The humerus can be adjusted to a desired position and orientation and then clamped in place by tightening the four bolts onto the humeral shaft. The scapula mount consists of an upright attached to the base component and a set of clamping jaws which holds the scapula in position (Figure 5.3). Once the implant and bone are fixed in their desired initial position, their relative position can be adjusted to model implant translations and rotations.



Figure 5.1 The shoulder implant used in this experiment
(Affinis Short Stemmed Total Shoulder Prosthesis)

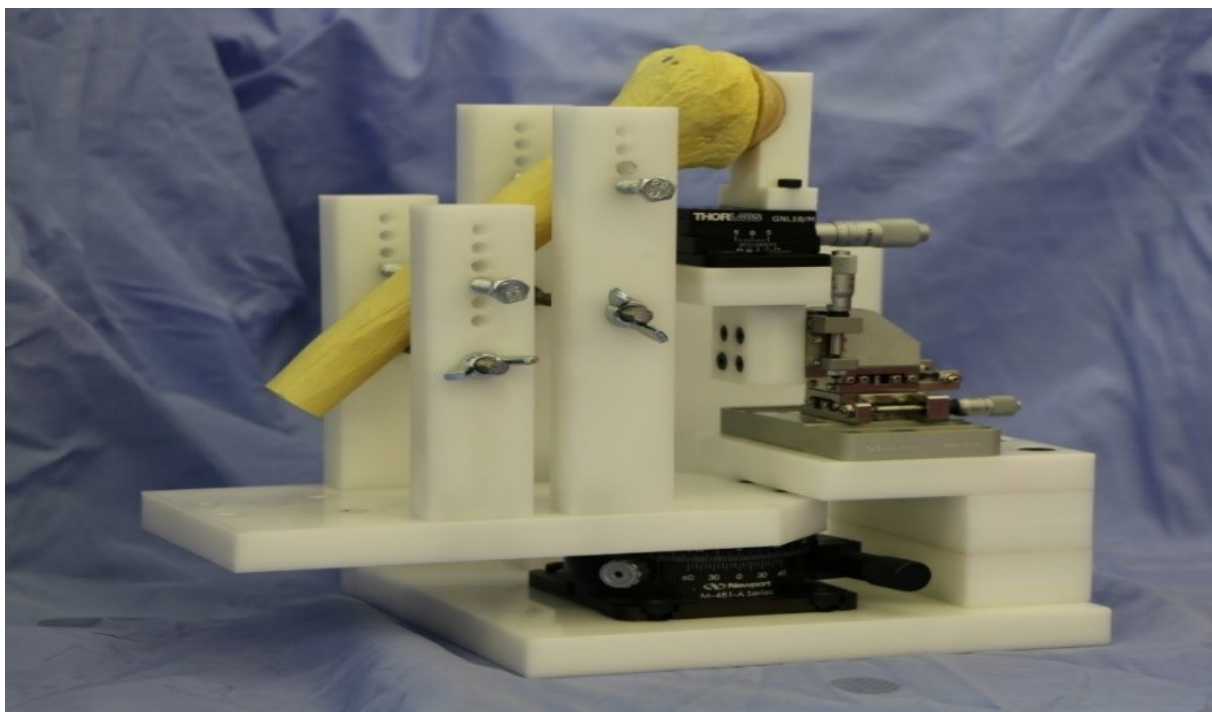


Figure 5.2 Device for humeral testing.
A humeral sawbone model has been used for clarity instead of cadaver bone.

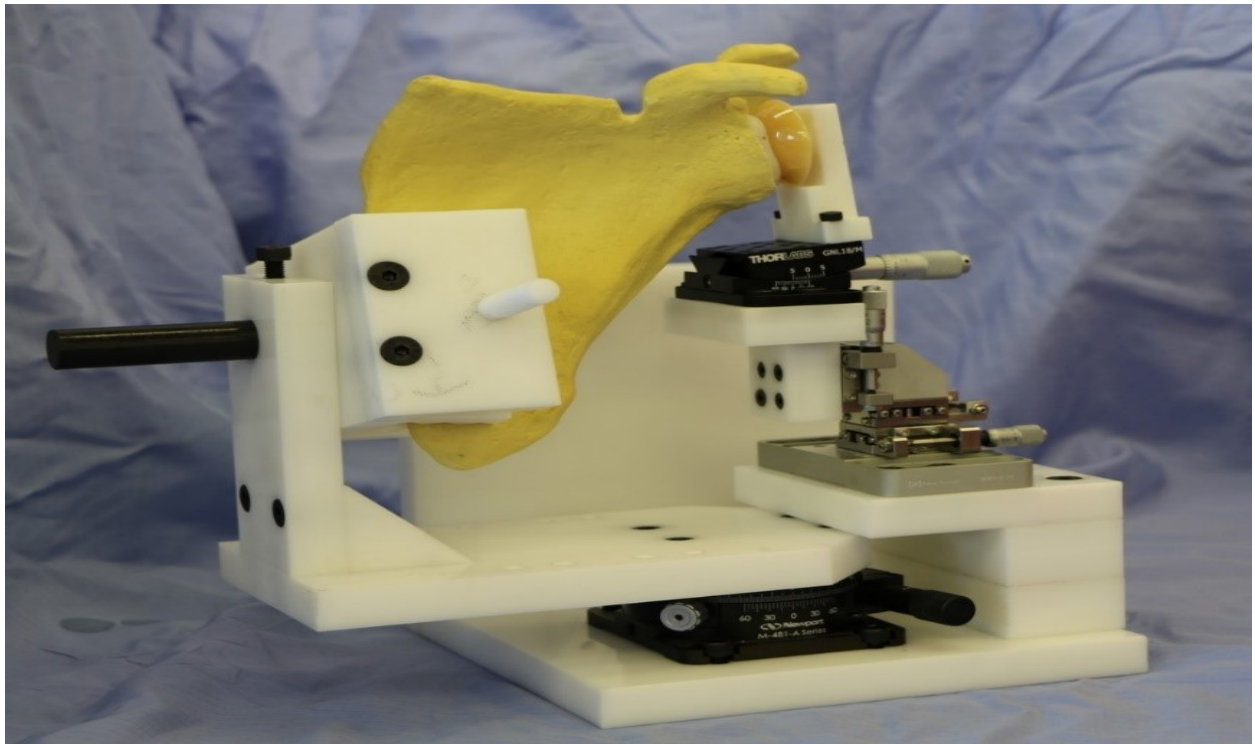


Figure 5.3 Device for glenoid testing.
A humeral sawbone model has been used for clarity instead of cadaver bone.

5.2.3 Study setting

A total of 28 different positions were tested for each component relative to their respective bone: 16 translations and 12 rotations. For each position, a double exam was conducted to estimate the precision of the method. Within a double examination, two scans were conducted without changing the position of the component relative to the bone. However, the entire rig was repositioned between these exams to imitate a double examination in a clinical setting where the patient may shift. Translational and rotational movements were conducted separately. Sixteen translations were performed without returning to the reference position, first along the medial/ lateral axis (x-axis), then the inferior/superior axis (z-axis), and finally the anterior/posterior axis (y-axis). In its final position, the implant had undergone 3 mm of translation along each of the axes for the humeral and 2 mm along each axis for the glenoid component. For the humeral component, scans were taken after translations along each axis of 0, 0.2, 0.5, 1.0, 2.0, and 3.0 mm. For the glenoid component, scans were taken after translations

along each axis of 0.2, 0.5, 1.0, 1.5, and 2.0 mm. The increments differed slightly for the glenoid component since the glenoid bone was smaller and did not permit > 2.0 mm of translation along each axis. The 12 rotations were also performed without returning to the reference position, first around the superior/inferior axis (z-axis) then around the anterior/posterior axis (y-axis). In its final orientation, the implant had undergone 3° of rotation around each of the two axes. The rotation around the y-axis and the z-axis corresponded to inclination and version of the implant, respectively. The design of the rig did not permit rotation around the x-axis. For both components the implant was moved $0, 0.2^\circ, 0.5^\circ, 1.0^\circ, 2.0^\circ$, and 3° around the z-axis and $0, 0.2^\circ, 0.5^\circ, 1.5^\circ, 2.0^\circ$, and 3° around the y-axis.

5.2.4 CT scanner and effective dose

A clinical CT scanner (Ingenuity, Philips, Eindhoven, The Netherlands) was used with shoulder parameters: voltage:120 kVp; pitch:1; rotation time:0.4 s; and automatically modulated tube current. The images were reconstructed into a 768×768 matrix with an x-y pixel size of 0.65 mm and a slice thickness of 1 mm with an increment of 0.5 mm. No metal artefact reduction protocol was used.

The effective dose was computed using the standard method described by the American Association of Physicists (95). The CT dose index volume (CTDI vol), a measurement that quantifies the intensity of CT radiation was multiplied by the scan length of a normal patient shoulder examination to obtain a more realistic value of the dose length product (DLP) (96). The DLP, a measurement that quantifies the total amount of radiation, was thereafter multiplied with a conversion factor of the shoulder, derived from the conversion factor of the neck (0.0052 mSv/mG.cm) and the chest (0.0146 mSv/mG.cm) divided by two (0.0099 mSv/mG.cm), to estimate effective dose (96,97). The effective dose is considered an indicator of possible risk associated with radiation (98).

5.2.5 Image analysis

The CT volumes were analysed with CTMA using two different methods of image registration, one relying on bone markers (beads), and a second technique relying on bone surface anatomy without bone markers.

For CTMA with bone markers, two CT volumes are imported into the graphical user interface and a manual metal thresholding optimization is performed to achieve a clear 3D representation of the implants and/or beads while minimizing metal-related artefacts (Figure 5.4). Two separate registrations are performed: one registration of the bone and a second of the implants. For CTMA of the glenoid component, nine beads in the scapular bone for each CT image were selected for the first image registration of the bone. Thereafter, the beads of the glenoid implants were selected for a second image registration. For CTMA of the humeral component, nine beads in the humerus were selected for the first registration (Figure 5.4). Thereafter, the metallic humeral short stems were selected for the second registration. For all registrations, the software spread 50000 landmarks points over the surface of the beads/implants and these were used by the software in the registration process.

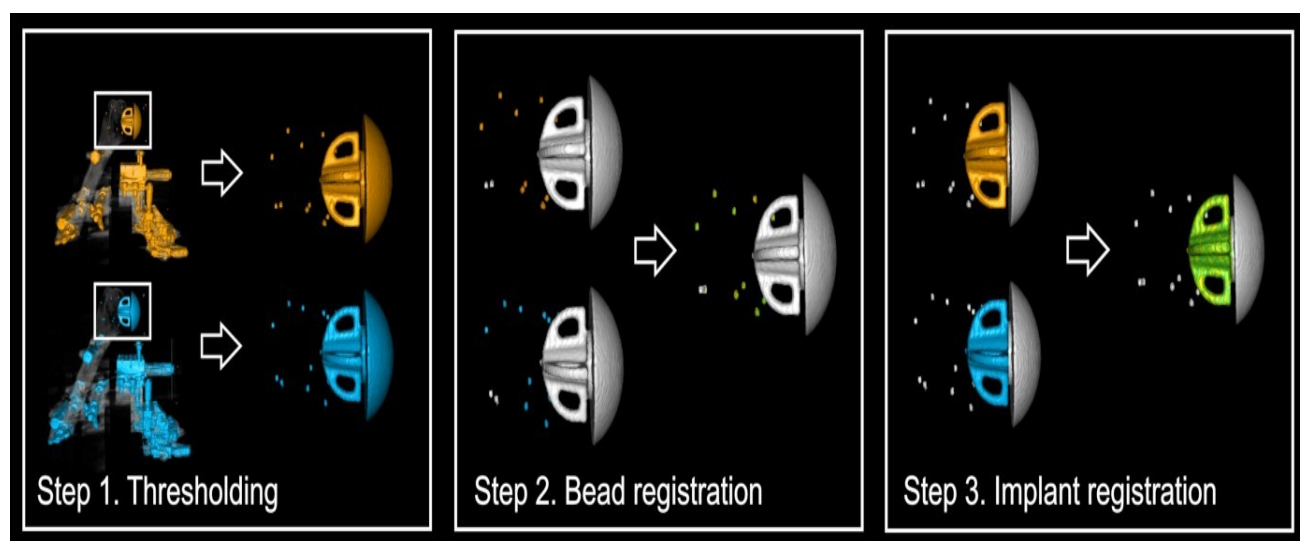


Figure 5.4 The CTMA analysis process with beads for the humeral component

CTMA could also be used without beads in the bone, relying solely on bone surface anatomy for the first bone registration (Figure 5.5). For this analysis, a manual bone thresholding is first performed to achieve a clear 3D representation of the bone. The surface bone anatomy is selected in each CT image and the first registration is then performed. Secondly, a metal thresholding is performed to obtain a clear view of the implants in the two CT volumes. The implants are selected, and a second registration of the implant is then performed. For CTMA of the glenoid component without using beads in the bone, the surface of the scapular bone was selected for the first registration. For the second registration, the beads in the polyethylene glenoid implant were chosen, since the polyethylene of the implant could not be identified on a CT image because of its radio transparency. For CTMA of the humeral component without beads in the bone, the surface of the humeral bones was selected for the first registration (Figure 5.5). For the second registration, the metallic stems were selected and registered.

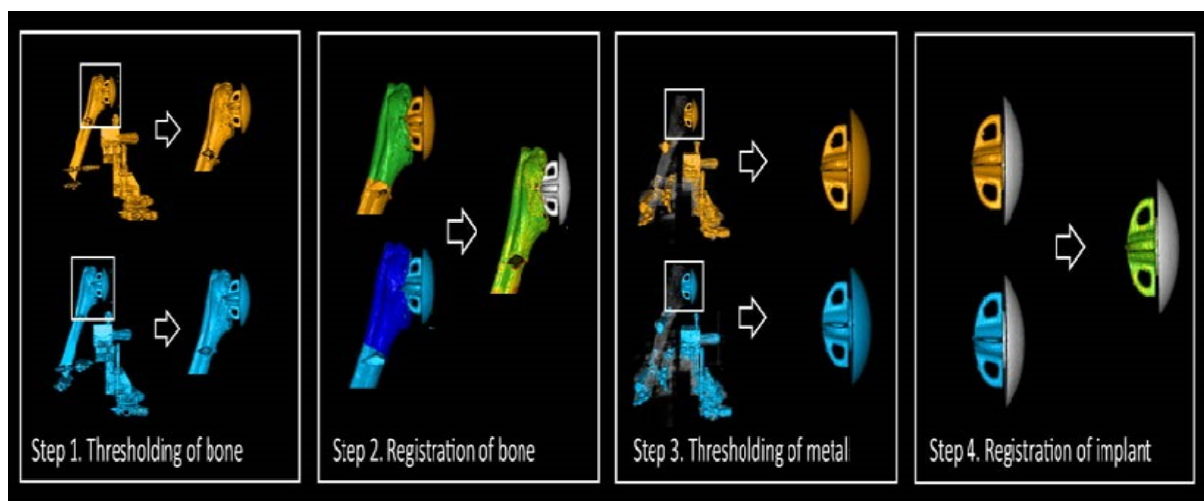


Figure 5.5 The CTMA analysis process without beads for the humeral component.

After these registrations, the CTMA software can calculate the change in relative position between the bone and the implant between the two CT scans. The results are obtained visually and numerically in six degrees of freedom. The migration values in six degrees of freedom is reflecting the movement of the centre of mass of the implant compared to the bone defined by

beads or by the selected bone surface in a CT coordinate system. The CT coordinate system was aligned with the rigs internal coordinate system in this experiment. The CT data was compared to the micrometer values and the techniques precision and accuracy could be established.

5.2.6 Statistics

Statistical tests were conducted in SPSS Statistics. Data from each implant was tested separately for normality using Shapiro-Wilks tests, and histograms. t-distribution table was used since the sample size was small.

Accuracy of a measurement is the “closeness of agreement between a measured quantity value and its true value of a measurand” (88). The difference between the CTMA and micrometer/goniometer measurements between two different positions of the implant was used to estimate accuracy. To calculate accuracy the formula $T \cdot \text{RMS}$ was used where “RMS” represents the root mean square and “T” represents the cut-off point in a t-distribution where the margin of error is at 95% of the confidence interval (12,91).

Precision is defined as the approximate agreement between independent repeated measurements obtained under the same conditions (88,89). The precision of CTMA was assessed by double examinations. Since no movement should occur between the implant and the bone between the two examinations, the migration values that deviates from 0 reflects the random errors of CTMA. The standard deviation of this difference in the pairs of double measurements was calculated and the equation $T \cdot \text{SD}$ was used to calculate the precision (91). The value “T” represents the cut-off point in a t-distribution where the margin of error is at 95% of the confidence interval (12,91).

5.3 Results

For the CTMA analysis using tantalum beads, accuracy was in the range of 0.07–0.23 mm in translation and 0.22–0.71° for rotation (Table 5.1 and 5.2). Precision was in the range of 0.08–0.15 mm in translation and 0.23–0.54° for rotation (Table 5.1 and 5.2). For the CTMA analysis using bone anatomy accuracy was in the range 0.10–0.23 mm in translation and 0.23–0.65° for rotation (Table 5.1 and 5.2). Precision was in the range of 0.07–0.14 mm in translation and 0.21–0.36° for rotation (Table 5.1 and 5.2).

A change in the implant's position of > 0.2 mm between each of the different configurations could be seen in CTMA. Where no movement within the model between the prosthesis and the bone had been induced, the prosthesis showed an overlapping pattern in the software. The visual inspection in the CTMA software showed no significant artefacts from the ceramic head or the humeral stem in titanium.

The potential mean effective radiation dose per CT examination was calculated to be 0.27 mSv (0.22–0.34 mSv). The CTDI_{vol} was estimated to be 3.7 mGy (3–4.5 mGy) and the DLP was estimated to be 27.4 mGy.cm (22.5–33.75 mGy.cm).

Table 5-1 Accuracy and precision of CTMA on the humeral component
For detailed calculations see appendices tables 11.1-11.4

	Accuracy CTMA beads	Accuracy CTMA bone anatomy	Precision CTMA beads	Precision CTMA bone anatomy
X translation, mm	0.11	0.15	0.08	0.10
Y translation, mm	0.07	0.10	0.09	0.07
Z translation, mm	0.09	0.23	0.11	0.14
X rotation, °	0.34	0.45	0.26	0.25
Y rotation, °	0.32	0.35	0.27	0.31
Z rotation, °	0.22	0.23	0.23	0.21

Table 5-2 Accuracy and precision of CTMA on the glenoid component.
For detailed calculations see appendices tables 11.5-11.8

	Accuracy CTMA beads	Accuracy CTMA bone anatomy	Precision CTMA beads	Precision CTMA bone anatomy
X translation, mm	0.23	0.19	0.15	0.10
Y translation, mm	0.17	0.15	0.13	0.08
Z translation, mm	0.20	0.15	0.13	0.12
X rotation, °	0.44	0.34	0.33	0.34
Y rotation, °	0.48	0.27	0.38	0.27
Z rotation, °	0.71	0.65	0.54	0.36

5.4 Discussion

The aim of this cadaveric study was to validate a CT method for implant migration in shoulder arthroplasty with and without the use of bone tantalum markers.

In this study, we found that the precision of the CTMA technique using tantalum beads in the bone, ranged between 0.08-0.15 mm in translation and 0.23-0.54° for rotation. Our results were slightly more precise for the humeral component compared to the glenoid. This could be due to the larger humeral implant size, the non-spherical geometrical shape of the stem and the fact that the registration algorithm used in the software uses landmarks spread over the entire surface of the metal of the humeral implant. In comparison, the glenoid component only had 6 beads that were chosen as landmarks since the polyethylene is not visible in the CT. Therefore, the landmarks are less spread which makes quantification of rotation less precise. For the precision relying solely on bone registration algorithm the results ranged between 0.07-0.14 mm in translation and 0.21-0.36 °in rotation. For the CTMA analysis of the glenoid component, a larger surface area of the scapula was used compared to the registration relying on the tantalum beads in the bone and therefore that could explain the more precise results. RSA shoulder implant studies in the literature report mean glenoid component precision of 0.18 mm and 0.96° in rotation, and for the humeral component a mean precision of 0.61mm and 5.34° in rotation (54). Brinke et al. suggested in a systematic review that the precision is slightly worse on the humeral side than on the glenoid side, especially in rotation. This could be explained due to the use of a symmetric humeral head resurfacing that showed poor rotational precision values (99) We did not use the symmetrical and spherical modular head component in our study since we analysed the movement between the short stem and the humeral bone and this could explain our more precise rotation values. Additionally, our precision of the glenoid component is comparable to the glenoid studies included in Brinke et al.'s systematic review concerning translation; moreover, our results are slightly better with respect to rotation (54).

To our knowledge there are no existing publications in the literature assessing the accuracy of marker-based RSA in shoulder arthroplasty. CTMA accuracy values with markers ranged between 0.07-0.23 mm in translation and between 0.22-0.71° in rotation and without beads CTMA ranged between 0.10-0.23 mm in translation and between 0.23-0.65 °. Sköldenberg et al. reported an accuracy of a marker-free RSA technique of a humeral resurfacing arthroplasty that varied between 0.22 and 0.47 mm and between 0.92° and 1.56° for translation and rotation respectively (91). However, the accuracy in this study was calculated using standard RSA as the gold standard which makes these results difficult to compare to ours.

A migration value obtained in our system that is greater than the accuracy and precision limit would suggest that a true migration of the implant has occurred and could not only be attributed to errors in the system. In hip and knee arthroplasty, different thresholds of implant migration have been established that predict the risk of loosening. It is therefore important that the accuracy and precision of a method is below that threshold, so that a clinically significant implant migration could be meaningfully assessed. However, such a threshold has not yet been established in shoulder arthroplasty.

The probable effective dose in our study was estimated to 0.27 mSv which is a theoretical value of expression since the risk of cancer of a rig is not possible. The more appropriate measurement that could be used in this context is computed tomography index (CTDI). The dose of 0.27 mSv is a higher dose than reported in RSA studies (0.04 mSv) but could potentially be motivated by the added benefit to visualize the implant-bone interface (56,100).

There were some limitations to this study. The accuracy and precision of the CT method were obtained under ideal experimental circumstances with no soft tissue interference. We did not test for combined translation and rotational movement of the implants which would occur in vivo. Additionally, rotations were only conducted around the y-axis and z-axis because of the

construction of the rig that did not permit rotation around the x-axis. Glenoid component loosening is believed to be due to a rocking-horse mechanism. Therefore, we chose to prioritize the rotations around the y and z-axis when constructing the rig to calculate the precision and the accuracy around the axes that were most clinically relevant (30). In this experiment only one type of glenoid and humeral implant was tested and that raises the question of the generalizability of the method to other implants. A further limitation is that the accuracy data obtained in z-translation of the humeral component using beads was not normally distributed. Therefore, the accuracy in z-translation of the humeral component should be carefully interpreted.

In conclusion, this experimental setting CTMA could accurately and precisely detect migration of shoulder implant components with and without the use of beads in the bone, at a low effective dose. Clinical experiments are warranted to determine if the CTMA method could be used in vivo. Therefore, the next chapter explores CTMA in a clinical setting comparing it to the clinical gold standard RSA.

6. CT micromotion analysis compared to radiostereometry for early migration measurements in cemented acetabular cups

The previous chapter validated the CTMA method in an experimental setting. RSA is the current gold standard technique. However, no study has directly compared the two methods in a clinical setting. This study aims to estimate the precision and effective dose of CTMA and compare it to standard RSA in patients with cemented acetabular cups. Ten patients were included and underwent total hip replacement with a cemented cup. CT and RSA double examinations were performed postoperatively. Precision and effective dose data were compared between the two methods. The CT data was analysed with CTMA both with and without the use of bone markers. The RSA images were analysed with standard marker based RSA technique.

The precision of CTMA with bone tantalum markers was in the range of 0.10–0.16 mm in translation and 0.31–0.37 ° in rotation. Without bone markers, the precision of CTMA was in the range of 0.10–0.16 mm in translation and 0.21–0.31 ° in rotation. In comparison, the precision of RSA was in the range of 0.09–0.26 mm and 0.43–1.69 °. The mean CTMA and RSA effective dose was estimated at 0.2 mSv and 0.04 mSv, respectively. CTMA, with and without the use of bone markers, achieves a slightly better precision in rotation and a comparable precision in translation to RSA. CT doses were slightly higher than RSA doses but still at a considerably low effective dose (101).

The majority of the material of this chapter has been submitted to Acta Orthopaedica at the time of submission of this thesis. The authors wish to thank Olof Sköldenberg for performing the RSA analysis and supporting statistical analysis.

6.1 Introduction

Early migration of hip implants is linked to higher revision rates of arthroplasty due to aseptic loosening (6,7). RSA is the current gold-standard method to measure implant migration, given its accuracy and precision (9). Lately there has been greater interest in using CT scans to measure implant migration to address some of the challenges with RSA, such as the need for specialised laboratories and trained personnel to conduct and analyse examinations (11,12). Previous experimental and clinical studies indicate that the accuracy and precision of CT techniques are comparable to those of RSA (12–15). However, to our knowledge there is no clinical study comparing CT and RSA in terms of precision for migration measurements in a clinical setting. CTMA was developed to analyse and measure implant migration between two CT images (14,15). CTMA has features that make it possible to perform the migration analysis of CT data with tantalum beads and, notably, with a technique relying solely on the surface anatomy of bone for the image registration, without the use of beads in the bone (15). The aim of this study is to compare precision and effective dose of the two methods of CTMA to those of standard marker-based RSA in acetabular cups in patients with hip arthroplasty.

6.2 Material and Methods

6.2.1 Study setup

Ten subjects (mean age 66.5 [59–75]; 4 male, 6 female; 10 hips) were selected consecutively from a randomised study at the Orthopaedic Department of Danderyd Hospital comparing proximal migration of two types of cemented cups (Figure 6.1): an argon gas-sterilised polyethylene (PE) group and a Vitamin E-treated PE group (Muller Exceed ABT, Biomet, Warsaw, Indiana, USA). Included in that study were patients aged 40–75 years who had undergone hip arthroplasty. The study excluded patients with inflammatory arthritis, secondary arthritis, or hip dysplasia; and/or ongoing treatment with oestrogen, bisphosphonates, cortisol, or cytostatic drugs six months prior to surgery. The Ethical Committee of the Karolinska Institute approved the use of CT scans in this study (No. 2011/2003-31/1). A posterior approach was used for the surgical procedure. The femoral component of the surgery consisted of an uncemented tapered, proximally porous-coated and hydroxyapatite-coated stem composed of a Ti-6Al-4V titanium alloy (Bi-Metric HA, Biomet) and a 32-mm chromium–cobalt head. Perioperatively, tantalum beads were inserted in the pelvis and liner of the cup. The physiotherapist encouraged all patients to be mobilised at full weight bearing with walking aids.

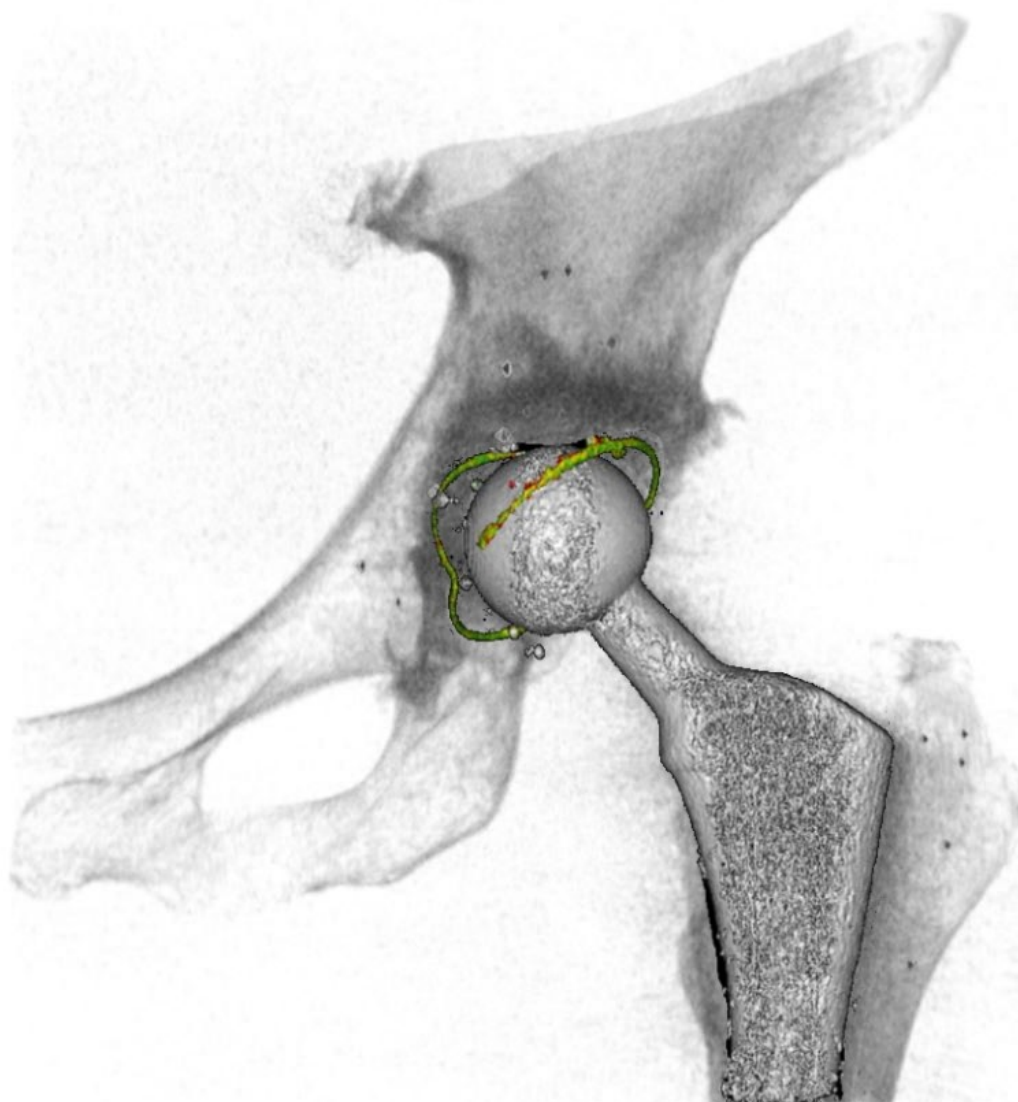


Figure 6.1 A cemented Muller Exceed ABT polyethylene cup in CTMA

6.2.2 Data collection

Follow-up for each patient involved a double examination at one week or three months postoperatively. The postoperative follow-up consisted of the following procedures: (1) positioning the patient in an RSA calibration cage, (2) taking the RSA radiographs, (3) repositioning the X-ray tubes, calibration cage and patient on the table, (4) taking an additional set of RSA radiographs, (5) moving the patient to a CT scanner, (6) taking one CT scan, (7) repositioning the patient in the CT scanner, and (8) taking an additional CT scan.

6.2.3 RSA method

For the RSA technique, a uniplanar calibration cage (Cage 43, RSA Biomedical AB, Umea, Sweden) was used. Digital radiographs (Bucky Diagnost Philips, Eindhoven, the Netherlands) were taken using two X-ray sources angled at 40° to each other. The exposure was set to 120 kV and 8 mAs for each X-ray tube. UmRSA 6.0 computer software (RSA Biomedical, Umea, Sweden) was used for all the RSA migration analysis. An experienced radiographer performed the RSA examinations. An experienced physician with extensive experience in RSA analysed the data. In this study, the condition numbers (the spread of the markers) were below 100, and all mean errors of rigid body fitting (the stability of the markers) were below 0.30 mm.

6.2.4 CT method

A CT scanner (Discovery CT750HD, GE Healthcare, USA) was used to acquire CT scans. The CT protocol was set to 120 kV, 10 mAs, slice thickness 0.625 mm with an increment of 0.31 mm, rotation time 1 s, pitch 0.984. Volumes were reconstructed with an x-y-z resolution of 0.6-0.6-0.6 mm.

The CT scans were analysed with the image registration software CTMA (Sectra, Linköping, Sweden). CTMA was used to analyse migration between two rigid bodies, such as the cup and the bone, in between two CT examinations (Figure 6.2)(15). In a double examination, the position of the implant relative to the bone do not change in between two consecutively performed CT examinations and therefore the CTMA migration measurements reflects the random errors of the method. In this study, the following steps were performed.

1. Two CT volumes were imported into the CTMA software. A threshold segmentation for beads in the bone (2200 Hounsfield units [HU]) or bone thresholding (600 HU) was set. The segmentation allowed us to visualise the beads or bone depending on the CTMA technique that was selected. The same bone threshold was used for all

examinations except in two patients, where the threshold was set to 400 HU and 550 HU due to deviances in the CT reconstruction settings.

2. The beads or the surface anatomy of the pelvis was selected for the image registration of the pelvic bone.
3. The pelvic bone was registered, and a visual overlap of the pelvic beads or the surface of the pelvic bone was achieved.
4. A threshold segmentation of 2200 HU was set to visualise the metallic implant structures such as the thread and beads of the cup. The thread and beads were selected for the image registration of the implant.
5. The implant was registered, and a visual overlap of the beads and thread of the implant was achieved.
6. The software calculated the motion of the implant compared to bone between these two CT volumes in a CT-based coordinate system. The result was a visual output in the form of registered 3D volumes and numerical migration values expressed in six degrees of freedom (translation along and rotation around x,y,z axis in a CT Dicom coordinate system).
7. The CT coordinate system was thereafter modified in a multi-planar reconstruction (MPR) view to obtain a coordinate system comparable to the RSA coordinate system.

The CTMA procedure described in steps 1–7 was performed once using the beads in the bone and once using the surface pelvic anatomy (without beads in the bone) for steps 1–3. This CTMA procedure has previously been illustrated and described in the literature (14,15).

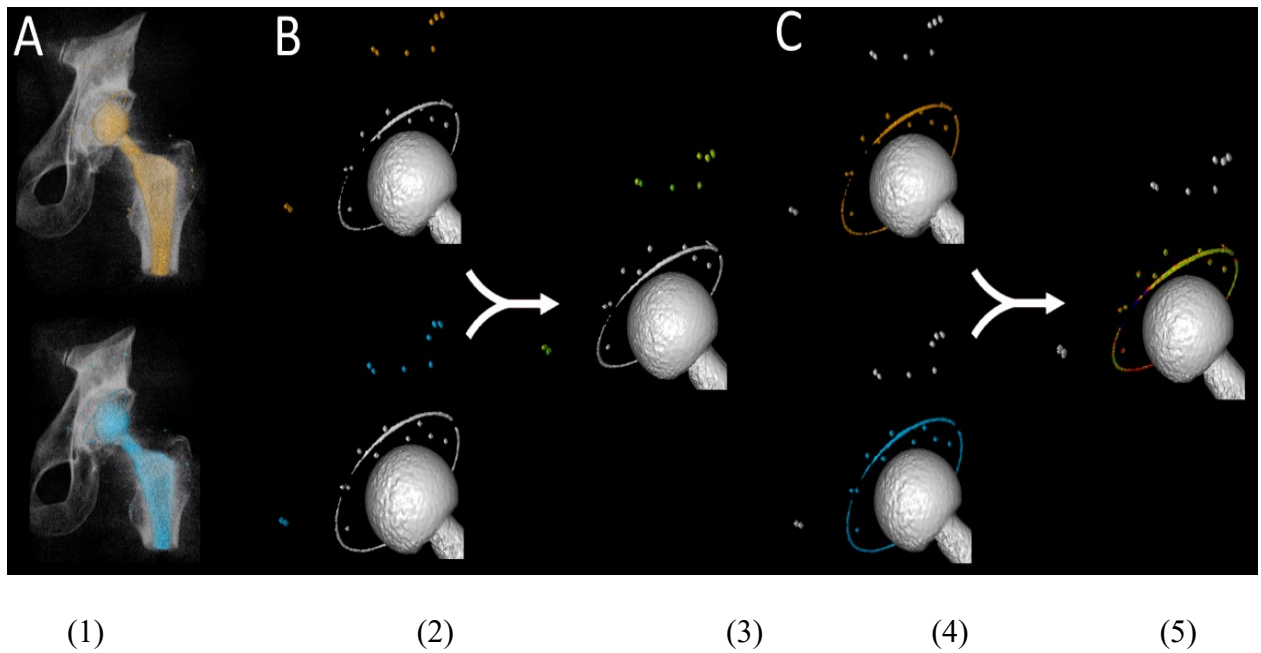


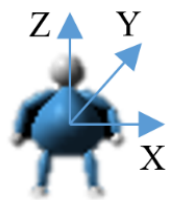
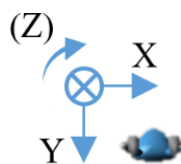
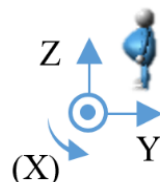
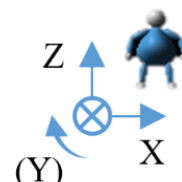
Figure 6.2 The CTMA analysis workflow, using beads inserted in the bone for the pelvic bone image registration.

(1) First a segmentation threshold of 2200 Hounsfield units is set to visualise the metallic structures in the bone and cup, such as beads and threads in two separate CT images (orange and blue colour). (2) The beads in the pelvic bone are selected. (3) When the registration occurs, the green colour indicates a successful registration. (4) The beads and the thread of the cup are selected. (5) Registration occurs, green colour indicates a successful registration.

6.2.5 CT and RSA coordinate systems

The coordinate systems used in RSA and CTMA differ (Figure 6.3). The RSA coordinate system is anatomical, fixed and defined by the RSA calibration cage. The CTMA used the standard Digital Imaging and Communications in Medicine (Dicom) coordinate system that could be modified into that of the RSA coordinate system.

Dicom



RSA

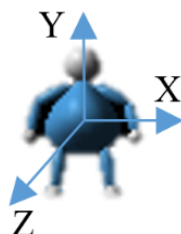
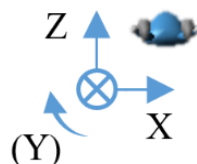
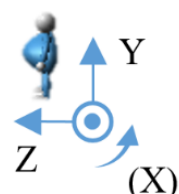
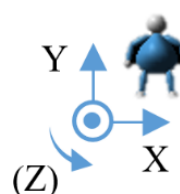


Figure 6.3 The CT DICOM coordinate system of CTMA and the coordinate system of RSA.

The translations are positive in the direction of the arrow; and the rotations are positive in a clockwise direction.

6.2.6 Effective dose

The CT effective dose was estimated using the dose length product (DLP) multiplied by a pelvic conversion factor: 0.0129 mSv/mG.cm from IRCP 103 (97).

The RSA effective dose was estimated with a Monte Carlo simulation using a software PCXMC Dose Calculation available at Danderyd Hospital (STUK, Helsinki, Finland version 2.0.1.4) (84,102).

6.2.7 Precision

Precision is defined as the approximate agreement between independent repeated measurements obtained under the same conditions.(88,89) The precision of CTMA and RSA were assessed by double examinations. Since no movement should occur between the implant and the bone between the two examinations, the migration values that deviates from 0 reflects random errors. According to International Organization for Standardization (ISO) standards of RSA, “Precision should be assessed with double measurement and shall be presented as the standard deviation of these calculated migrations. Assuming a normal distribution, the confidence intervals of the error should be expressed as $\pm 1,96 \times SD$, for the 95% confidence interval (where SD is the standard deviation)”(88).

6.2.8 Statistics

Statistical tests were conducted in SPSS Statistics. Data from each modality (CTMA and RSA) were tested separately for normality using Shapiro-Wilks tests.

For the precision calculation, we used the ISO standard for the 95% confidence interval (CI) **1.96 x SD**, but modified it to the formula **T-score x SD** to take into account the small sample size, a practice prevalent previously in this thesis and other studies using this method (15,91). The T-score was used instead of a Z-score to avoid underestimating the margin of error obtained with this small sample size.

6.3 Results

The upper 95% CI of the precision of CTMA using tantalum beads implanted in the bone for the pelvic bone registration was in the range of 0.10–0.16 mm in translation and 0.31–0.37° in rotation (Tables 6.1 and 6.2). All the implanted beads in the bone and the implant itself were visualised.

The upper 95% CI of the precision of CTMA using bone surface anatomy for the bone registration varied between 0.10 – 0.16 mm in translation and 0.21–0.31 ° in rotation (Tables 6.1 and 6.3). Some artefacts could be observed at the surface of the pelvic bone, but no patients needed to be excluded.

The upper 95% CI of the precision of the gold-standard RSA for this cohort was in the range of 0.09 –0.26 mm in translation and 0.43–1.69 ° in rotation. One patient was excluded from the RSA measurements due to marker occlusion (Tables 6.1 and 6.4).

The CT mean effective dose of the scans used in the CTMA analysis was estimated to be 0.2 mSv (0.18–0.22). The RSA mean effective dose was estimated to be 0.04 mSv (0.036–0.0044).

Table 6-1 Precision comparison between CTMA and gold-standard RSA

	Precision CTMA beads in bone, 95% CI	Precision CTMA bone anatomy, 95% CI	Precision RSA beads 95% CI
X translation, mm	0.14	0.16	0.09
Y translation, mm	0.10	0.14	0.20
Z translation, mm	0.16	0.10	0.26
X rotation, °	0.31	0.25	1.69
Y rotation, °	0.37	0.21	1.56
Z rotation, °	0.33	0.31	0.43

Table 6-2 Precision of CTMA of the cup using beads for the pelvic bone registration,

	Precision 95% CI	Mean	Min	Max	SD
X translation, mm	0.14	0.02	- 0.05	0.17	0.06
Y translation, mm	0.10	0.02	-0.07	0.10	0.04
Z translation, mm	0.16	0.01	-0.12	0.13	0.07
X rotation, °	0.31	0.03	-0.14	0.31	0.14
Y rotation, °	0.37	-0.04	-0.31	0.22	0.16
Z rotation, °	0.33	-0.03	-0.32	0.20	0.15

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 6-3 Precision of CTMA of the cup using surface bone anatomy for the pelvic bone registration

	Precision 95% CI	Mean	Min	Max	SD
X translation, mm	0.16	0.02	-0.03	0.20	0.07
Y translation, mm	0.14	0.01	-0.05	0.09	0.06
Z translation, mm	0.10	0.00	-0.07	0.09	0.04
X rotation, °	0.25	-0.04	-0.28	0.12	0.11
Y rotation, °	0.21	-0.11	-0.23	0.10	0.09
Z rotation, °	0.31	0.00	-0.24	0.19	0.14

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 6-4 Precision of RSA of the cup using beads for the bone registration

	Precision 95% CI	Mean	Min	Max	SD
X translation, mm	0.09	0.01	-0.05	0.08	0.04
X translation, mm	0.20	0.01	-0.10	0.20	0.09
X translation, mm	0.26	-0.06	-0.26	0.07	0.11
X rotation, °	1.69	-0.05	-0.89	1.60	0.75
Y rotation, °	1.56	-0.27	-1.97	0.26	0.69
Z rotation, °	0.43	0.12	-0.16	0.36	0.19

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

6.4 Discussion

The aim of this study was to compare CTMA to the gold-standard RSA in terms of precision and effective dose in a clinical setting.

In this study, the precision of CTMA using beads and surface anatomy was comparable to standard RSA. CT images made additional surfaces available compared to RSA for the image analysis, such as the surface anatomy of the pelvis, metallic thread, and additional markers since marker occlusion did not occur. These results were below the critical threshold of 1 mm of early migrations that is suggested to predict loosening and could therefore be used in a clinical setting (6). The precision of RSA for this cohort was in the range of 0.09–0.26 mm in translation and 0.43–1.69° in rotation. This is in accordance with a review paper by Kärrholm et al. indicating that RSA precision in clinical studies varied between 0.15 and 0.60 mm for translations and between 0.3 and 2° for rotation (103). These values are less precise than those of RSA in an experimental setting, especially in rotation, ranging from 0.04 to 0.09 mm for translations and 0.08 to 0.32° for rotations (12). This difference might be due to the use of sawbones without soft tissues in the experimental study by Brodén et al. (12).

The CT effective dose was estimated using the dose length product (DLP) multiplied by a pelvic conversion (97). This CT dose-estimation method is the most commonly used in clinical routine (97). The mean effective dose of CTMA was 0.2 mSv, while the clinical RSA effective dose was 0.04 mSv. In a study by Blom et al., the effective dose of RSA was estimated to be 0.04 mSv, which is comparable to our findings. The complexity of acquiring RSA images where patient and calibration cage are lined up correctly means that some additional retakes of RSA images could increase the effective dose for RSA. Retakes were not included in our calculation of RSA effective doses. The effective dose for CT is slightly higher than for RSA in our study. However, it is lower than a standard anteroposterior pelvic x-ray (0.7 mSv) (101).

Moreover, the practicalities of CT, in addition to the potential to visualise the bone-implant interface, might justify the slightly higher dose. It is important to consider that this CT dose is suboptimal, since artefacts were observed, and higher doses could theoretically facilitate the analysis of CT scans with CTMA relying solely on the surface anatomy of the bone. The CT dose in this study is markedly at the lower end compared with those used in other CTMA studies with an effective dose ranging between 0.2 and 2.3 mSv (15). However, it is noteworthy that CTMA precision does not appear to have been markedly affected by this lower dosage.

An advantage of CTMA is that a predetermined CT-scan protocol is chosen by a radiographer for the scan, and the positioning of the patient is not as crucial as in RSA, as no calibration cage is involved. For RSA, imaging acquisition must be carefully monitored by a specially trained radiographer. Another advantage of CTMA is that the registration is performed in a 3D visual interface, which prevents the loss of tantalum markers due to marker occlusion. In this study, one RSA examination had to be excluded due to marker occlusions, which did not occur with CTMA.

One limitation of the CTMA software is that the quality of the image registration must be verified manually. This is done with a visual inspection of a colourmap feedback mechanism. Currently in CTMA, there is no equivalent number to the condition numbers and mean error of rigid body fitting to quantify the suitability of the rigid body to give correct measurements; this assessment must rely on the users experience and judgement. A further limitation is that the precision data obtained in x-translation for CTMA without beads and y-rotation for RSA was not normally distributed. Therefore, these precision values should be carefully interpreted.

Another limitation of this study was that CTMA measurements were performed by an experienced CTMA user and therefore raises the question of interobserver variability.

The precision of CTMA for the femoral stem was not investigated in this study. For future investigations, a slightly higher effective dose might be needed to analyse the femur/stem migration. The stem is a metallic component, and the presence of soft tissue around the femur might increase the effective dose needed to obtain CT images of adequate quality without artefacts. More notably, the whole stem was not included in the field of view, which could impact the ability to measure stem precision.

In conclusion, this chapter demonstrates that CTMA, with and without the use of bone markers for image registration, had a comparable precision when compared with standard RSA, and a slightly higher effective dose for cups in hip arthroplasty while still at a considerably low effective dose.

In this clinical study only one type of cup was tested, and the CT images were acquired with only one CT scanner and that raises the question of the generalizability of the method. Therefore, the next chapter explores the precision of CTMA for different types of cups scanned with different types of CT scanners and CT protocols.

7. Generalizability of the CT micromotion analysis technique in acetabular cups

In the previous chapter, CTMA showed a comparable precision in translation and an improved precision in rotation compared to RSA for cemented hip cups. However, the precision of the CTMA technique has not yet been explored for different types of prostheses and different types of CT scanners in a clinical setting. The aim of this chapter is therefore to explore the generalizability of the CTMA technique by evaluating the precision of three different hip cups scanned with three different CT scanners. A total of 24 CT double examinations of 24 hip cups were selected from three ongoing prospective studies: two primary total hip arthroplasty (THA) and one THA revision study. Precision of the CTMA was calculated separately for each study, using both the surface anatomy of the pelvis and tantalum beads inserted in the pelvis.

For the CTMA analysis using the surface anatomy of the pelvis, the precision was in the range of 0.07–0.31 mm in translation and 0.20–0.39° for rotation respectively. For the CTMA analysis using beads the precision was in the range of 0.08–0.20 mm in translation and 0.20–0.43° for rotations. The effective dose per scan ranged between 0.2 and 2.3 mSv. CTMA achieved a clinically relevant and consistent precision between the three different hip cups studied. The use of different hip cup types, different CT scanners or registration method (beads or surface anatomy) had no discernible effect on precision.

The majority of the material in this chapter has been published in *Acta Orthopaedica* and reproduced according to the licensing policy of Taylor & Francis. Brodén C, Sandberg O, Sköldenberg O, Stigbrand H, Hänni M, Giles JW, et al. Low-dose CT-based implant motion analysis is a precise tool for early migration measurements of hip cups: a clinical study of 24 patients. *Acta Orthop*. 2020 Feb 14;1–6. We did not receive any funding for this study.

The author wishes to thank Henrik Olivecrona for helping with the inclusion of patients from other sites, and Olof Sköldenberg for support with the statistical analysis.

7.1 Introduction

It has been discussed in previous chapters that early migration within the first two years after implantation of hip implants is a strong indicator of future loosening (6,103,104). The previous chapters suggest that CTMA can be used to detect implant early migration precisely and accurately and that precision of CTMA is comparable to RSA in a clinical setting. This chapter explores the CTMA tool in a clinical setting, using three different types of hip implant (2 cemented and 1 uncemented) drawn from different centres in Sweden with different CT scanners and different CT protocols. The precision of the CTMA technique is estimated in two different settings: first, omitting bone markers relying solely on the pelvic anatomy for the image registration, and second using bone markers for the image registration.

7.2 Materials and Methods

7.2.1 Subjects and clinical setup

Study subjects were included from 3 ongoing clinical trials at different regions within Sweden: Uppsala University Hospital in Uppsala, Danderyds Hospital in Stockholm, and Gävle Hospital in Gävle. In total, 24 hip implants were included in this study. For every hip, 2 consecutive CT examinations were conducted (i.e. a double CT examination). A different CT scanner, CT protocol and implant was used at each hospital as specified below.

7.2.1.1 Uppsala University Hospital

Study setting

CT examinations from 5 randomly selected patients were included from an ongoing prospective cohort study. The study explores bone mineral density around a hip stem and migration of hip components investigated by RSA. Patients received an uncemented hip arthroplasty with the Collum Femoris Preserving stem (CFP) and the Trabeculae-Oriented Pattern cup (TOP), provided by Waldemar Link Gmbh (Hamburg, Germany)(Figure 7.1). Perioperatively, beads were inserted in the pelvic and femoral bones. RSA was used to analyse component migration, and clinical follow up was performed at 3, 12 and 24 months postoperatively. At the 7 year follow up, a CT double examination was performed. Details of this study can be found in the 2 year follow-up publication (105).

CT examinations

The 2 consecutive CT scan were obtained with a 2x64, dual source CT scanner (Somatom Definition Flash, Siemens, Forchheim, Germany). Between scans the patient was re-positioned on the CT table. Details of CT protocol settings are described in Table 7.1. We did use metal artefact reduction techniques for this CT protocol.

7.2.1.2 Danderyds Hospital

Study setting

CT examinations from 9 consecutively selected patients were included from an ongoing randomised study. The study compared proximal migration of 2 types of cemented cups: an Argon gas-sterilised Polyethylene (PE) group and a Vitamin E treated PE group. (Muller Exceed ABT, Biomet, Warsaw, Indiana, USA) (Figure 7.1). Patients who were included had a diagnosis of primary osteoarthritis planned for total hip arthroplasty. Patients were followed with RSA at 3 months and at 1, 2, 5 year(s) postoperatively. A double CT examination was also performed at 3 months postoperatively. Tantalum beads were inserted in the pelvis and the cup. For more details, the study protocol has previously been published. (106)

CT examinations

2 consecutive CT scans were obtained with a 128-detector CT scanner (Discovery CT750HD, GE Healthcare, Chicago, IL, USA). Between scans the patient was repositioned on the CT table. The CT settings are described in Table 7.1. We did not use any metal artefact reduction techniques for this CT protocol.

7.2.1.3 Gävle Hospital

Study setting

CT examinations from 10 randomly selected patients were included from an ongoing revision THA study on early migration. Included patients had THA revision surgery due to cup loosening and acetabular osteolysis. Exclusion criteria were systemic diseases affecting the skeleton, and/or medication with known effect on bone metabolism. The mean age at surgery was 73 years (49-87). Acetabular reconstruction was performed using an impaction bone graft with a titanium compressing shell and a cemented cup (Lubinus cross-linked UHMW-PE, Waldemar Link, Hamburg, Germany)(Figure 7.1). Tantalum beads were spread in the pelvis. CT scans were performed postoperatively, after 6 weeks, and after 2 years.

CT examinations

2 consecutive CT scans, a double examination, were obtained at 6 weeks postoperatively with a 160 detector Aquilon One CT scanner (Toshiba). In-between the CT examinations the patient was repositioned. Details of CT protocol settings are described in Table 7.1. We did use metal artefact reduction techniques for this CT protocol.



Figure 7.1 The implant types used in the studies

(1) the uncemented TOP cup used in the Uppsala study, (2) a cemented Muller Exceed ABT polyethylene cup from Danderyd, (3) the graft compressing titanium shell and a cemented Lubinus cross linked UHMWP polyethylene cup used in the Gävle study.

Table 7-1 CT settings from three clinical trials

Site CT scanner	Voltage (kVp)	Tube current (mA)	Slice thickness(mm)	Increments (mm)	Pitch	Rotation time (s)
Uppsala ^a	120	23	0.6	0.6	0.9	1
Danderyd ^b	120	10	0.625	0.312	0.984	1
Gävle ^c	120	80–500 ^d	0.5	0.5	0.81	0.5

^aSomatom Definition Flash, Siemens, Forchheim, Germany.

^bDiscovery CT750HD, GE Healthcare, Chicago, IL, USA.

^cAquilon One CT scanner (Toshiba).

^dDynamic tube current.

7.2.2 Precision

The precision of a measurement is defined by the approximate agreement between independent repeated measurements obtained under the same conditions (88,89). In the datasets used in this

study, a double CT examination was performed in which two CT scans were conducted on the same day for each patient. The CT scans were performed under the same conditions consecutively with the patient standing up in between.

7.2.3 Image analysis and evaluation procedure

To assess the precision of the CTMA system, an estimation of the random errors of the method was made. Since no movement had occurred between cup and pelvis in between the two CT examinations, a double examination, the measured migration by the CTMA system reflected the random errors and therefore the precision of the CTMA method.

To assess the measured motion of the cup relative to the pelvis by the software the following steps were performed. (Figure 7.2):

1. The CT volumes were imported into the CTMA system, and an optimization of bone or bead thresholding was performed manually.
2. The reference rigid body (pelvic bone) was defined in 2 separate CT examinations and registered to obtain a visual overlap of the bone of the 2 volumes.
3. A manual thresholding of metal is performed
4. The implant rigid body (the cup) is defined in 2 separate CT examinations and registered to obtain a visual overlap of the implant of the 2 volumes.

The software calculated the motion that has occurred for the implant relative to the pelvic bone between these 2 CT volumes described in the CT-based coordinate system. It resulted in a visual output in the form of registered 3D volumes as well as numerical migration values expressed in six degrees of freedom (rotations around and translation along x,y,z, in a CT DICOM coordinate system).

The CTMA procedure described earlier (step 1-4) was repeated twice. The first series was performed by defining the reference rigid body using the surface anatomy of the pelvis without the use of bone markers (Figure 7.2). The second series was performed using tantalum beads in the pelvic bone to define the reference rigid body. For both series, the implant rigid body was defined either by the metallic surface of the implant or the metallic threads and/or beads in the implant depending on the implant type. During the analysis, the consistency of the registered rigid bodies was verified manually with a colour-coded feedback mechanism that illustrates any change in the transformation of either rigid body due to deviation of tantalum beads, bone morphology changes or implant deformation. The colour green indicated a successful registration.

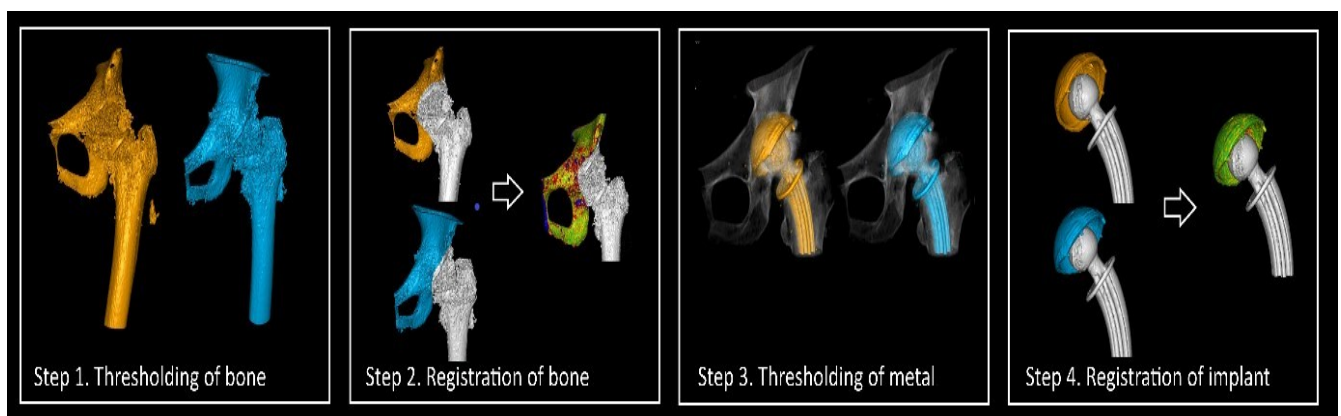


Figure 7.2 Processing schematic for CTMA.

(Step 1) First an optimization of bone thresholding is performed manually. (Step 2) The pelvic bone is defined here by the surface of the pelvic anatomy, a first registration is thereafter performed. (Step 3) A manual thresholding of metal is performed (Step 4) The implant rigid body (the cup) is defined. The user indicates the region of interest for the second registration in the 2 datasets, i.e. the implant. Next the second registration occurs. Green colour indicates a successful registration.

7.2.4 Effective dose

The effective dose of the CT method was estimated for each dataset. The Dose Length Product (DLP) indicates the overall energy delivered along the scan length. DLP is then multiplied by a pelvic conversion factor: 0.0129 mSv/mG.cm, from IRCP 103, that provides the conversion from mGy-cm to mSv, which is the unit of effective dose based on the tissue exposed (95,97).

7.2.5 Statistics

Statistical analysis were performed in SPSS Statistics (SPSS Hong Kong 1804, Westlands Centre, Westlands Road, Quarry Bay, HK). Data from each type of implant was tested separately for normality using the Kolmogorov-Smirnoff test. The precision for each dataset was estimated using the standard deviation of double measurements and the critical value that encompass 95% of Student's t-distribution with $n-1$ degrees of freedom, where n represents the number of patients (91).

7.2.6 Ethics

The Uppsala study was approved by the ethics committee of Uppsala University (Dnr 2007/105/2). The Danderyd study was approved by the ethics committee of Karolinska Institute. (No. 2011/2003-31/1) The Gävle study was approved by the ethics committee of Uppsala University. (Dnr 2015/228).

7.3 Results

For the CTMA technique using the surface of the pelvic anatomy, the precision was in the range of 0.07–0.31 mm in translation and 0.20–0.39° for rotation (Table 7.2). For the CTMA analysis using beads in the bone, the precision was in the range of 0.08–0.20 mm in translation and 0.20–0.43° for rotation (Table 7.3).

For the visual feedback, no movement within the prosthesis and the bone was visualized between any of the sets of 2 CT scans forming a double examination, which agrees with our assumption that no true migration had occurred during patient repositioning in the CT scanner.

The effective dose of CT scans differed between the clinical trials: the mean effective dose was 0.7 mSv for Uppsala; 0.2 mSv for Danderyd's Hospital and 2.3 mSv for Gävle Hospital. Some artefacts could be detected in the CT scans.

Table 7-2 Precision of CTMA of different cups using the pelvic anatomy without beads for registration. For detailed calculations see appendix table 11.9

Hospitals	Translation, mm				Rotation, °		
	N	x	y	z	x	y	z
Uppsala	5	0.07	0.13	0.31	0.37	0.22	0.39
Danderyd	9	0.23	0.11	0.08	0.31	0.28	0.29
Gävle	10	0.12	0.31	0.15	0.28	0.20	0.23

N: Number of patients

Table 7-3 Precision of CTMA of different cups using beads for registration
For detailed calculations see appendix table 11.10

Hospitals	Translation, mm				Rotation, °		
	N	x	y	z	x	y	z
Uppsala	5	0.11	0.09	0.08	0.43	0.23	0.22
Danderyd	9	0.08	0.13	0.13	0.25	0.21	0.29
Gävle	10	0.10	0.20	0.14	0.20	0.22	0.26

N: Number of patients

7.4 Discussion

This chapter has determined the clinical precision of the CTMA method in three ongoing clinical THA studies with variable protocols (e.g. implant type, CT scanner, & CT protocol).

The precision of the CTMA technique using the pelvic surface anatomy was in the range of 0.07–0.31 mm in translation and 0.20–0.39° for rotation. The precision of the technique using beads was in the range of 0.08–0.20 mm in translation and 0.20–0.43° for rotations. Precision values of standard RSA from chapter 6 has been estimated to 0.09–0.26 mm for translation and 0.43–1.69° for rotations in the lower limb, which is less precise in rotation than our findings in this study. CTMA is more precise than the clinically meaningful threshold of 1 mm that has been linked to higher revision risk (6). The precision of CTMA of the three different cups used in this study did not markedly differ, despite there being differences in geometry and implant material. In addition, each type of implant was scanned with a different CT scanner and CT scanning protocol. Scheerlink et al. previously used a CT method to assess early migration in hip prostheses both in a clinical and experimental setting (13). Their precision in vitro did not exceed 0.09 mm and 0.14°. In a clinical setting, Scheerlink et al. presented values such as mean absolute error to estimate precision. Since their methodology to estimate precision was different, the comparison is difficult. However, while this study reports results using low dose CT (which is more challenging but crucial for widespread clinical application) the Scheerlink et al. paper reports exposure of the CT scans of 3.1 to 8.2 mSv, which limits the use of their technique. This is an important difference as the European Commission, in its guidance on exposure in medical and biomedical research, “Radiation protection 99”, gives approximate values of between 0.5 and 10 mSv as the target per person for an entire study of this type (107). In contrast, our method achieved significantly lower radiation doses across different CT scanners and protocols (0.2–2.3 mSv). The quality of the CT images improved with the higher dosage and the segmentation of the image became easier; however, all of the collected data

could be used for the CTMA analysis and the precision did not improve with higher dosage. This effective dose could be compared to our RSA examination in chapter 6 that delivers a dose of 0.04 mSv and a normal anteroposterior pelvic x-ray of 0.7mSv (101). However, in practice RSA examinations involves additional retakes and the effective dose would often be higher than the quoted 0.04 mSv.

This chapter only included acetabular components; thus further studies are needed to evaluate whether the reported precision level is consistent for other implants. For example, the femoral stem has a larger volume, is not spheric, and the material is metallic. These three factors should diminish registration errors if metallic artefacts are minimal. At the same time, the femur is a more elongated and symmetrical bone compared with the pelvis. As a result of these conflicting factors, it is probably not possible to extrapolate from the current results.

An additional limitation in this study is the low sample size. In RSA studies it is recommended to have at least 15 subjects per group (9). Therefore, we used a t-distribution to calculate the precision of CTMA in this small sample size, as previously explained in Chapter 4.

Precision was not compared statistically between the different centres since the aim of this study was to investigate if the precision was below the clinically meaningful threshold of 1 mm predicting implant loosening.

In conclusion, this chapter demonstrates in three ongoing clinical studies that CT-based migration measurement achieves a clinically relevant precision without the need for bone markers. It demonstrates that this technique can be used on different types of cup implants using CT volumes with different CT scanners at different effective doses and still maintain the clinically relevant precision needed to follow early migration of cups in hip arthroplasty

A micromotion analysis system based on low-dose CT scans and free of bone tantalum markers opens the possibility for simpler clinical implant migration follow-up studies over time. Therefore, in the next chapter a feasibility study will be performed using CTMA in a clinical setting to measure early migration and the development of radiolucent lines for a cohort of patients with shoulder arthroplasty followed over 2 years.

8. CT micromotion analysis to assess early implant migration and radiolucent lines in total shoulder arthroplasty

The purpose of this chapter is to investigate the feasibility of the CTMA method to assess early migration and the progression of radiolucent lines over time after shoulder arthroplasty. Seven patients were included in this study and underwent nine primary shoulder arthroplasties. CT scans were conducted preoperatively, immediately postoperatively and after 3,6,12 and 24 months. At each follow-up, postoperative glenoid and humeral component migration, and the development of radiolucent lines were assessed in CTMA. Clinical scores were recorded at all time points except immediately postoperatively.

For the glenoid component, the median translation and the median rotation was in the range of 0.00–0.10 mm and -1.53 – 1.05° at 24 months. The progression of radiolucent lines occurred from the periphery to involve the pegs of the glenoid components for 6 out of 9 cases during the 24-month follow-up after surgery. For the humeral component, the median translation and the median rotation varied between -0.02 and -0.01 mm, and between -0.62 and -0.06° at 24 months. One of the humeral components migrated more than 2mm in distal translation and rotated over 4° in posterior rotation and 2.5° in anteversion. Most of that migration occurred during the first 3 to 6 months. No radiolucent lines could be observed around the humeral components; however, bone resorption could be visualised in eight out of nine cases in relation to the humeral component at 24 months. The Constant Score improved from a mean of 30 (21–51) preoperatively to 68.79 (41–88) at 24 months, while the Oxford Score improved from a mean of 23.67 (13–38) preoperatively to a mean of 43.33 (32–48) after 24 months.

CTMA can be used to identify early migration and the development of radiolucent lines over time. Clinical trials with a larger sample size and longer follow-up are needed to establish the relationship between migration, radiolucent lines and clinical scores.

The author wishes to thank Shirley Fetherston for her support with performing the CT scans and Monica Khanna for her support with the measurements of the pre and immediate postoperative position of the glenoid component.

8.1 Introduction

As mentioned in this thesis, early migration is correlated to loosening in implant arthroplasty (6,7). However, this correlation is not well-defined in shoulder arthroplasty and there is currently no threshold value of early migration correlated to higher revisions rates (54). The main cause of loosening in shoulder arthroplasty is glenoid component aseptic loosening (5). Early migration has previously been measured with RSA (6,7). RSA has excellent accuracy and precision; however, the need for expensive RSA laboratories, trained staff and strict patient positioning during the RSA examinations limits its widespread clinical application (9). In addition, the progression of radiolucent lines, believed to contribute to aseptic loosening, may not be followed on RSA radiographs due to low radiation scans but also due to the angles of X-rays projections not suitable for clinical practice (9). CTMA has previously in this thesis been used to measure early migration in an experimental setting in shoulder arthroplasty and in a clinical setting in hip arthroplasty with good precision and accuracy (14,15). The purpose of this chapter was to evaluate if CTMA could be used in a clinical setting to evaluate early migration and to follow radiolucent lines in shoulder arthroplasty over time.

8.2 Material and Methods

8.2.1 Ethics

The study was approved by the NHS Research Ethics Committees (reference -15/LO/1899).

8.2.2 Study subjects

Nine shoulder arthroplasties in seven patients (two males, five females) with primary osteoarthritis or avascular necrosis of the humeral head with secondary degenerative changes affecting the glenoid, scheduled for a total shoulder arthroplasty procedure were consecutively recruited for this study at the Department of Orthopaedics at St Marys Hospital (Table 8.1). Patients included in the study were between 50 and 80 years of age, had a clinical diagnosis that required an anatomical total shoulder replacement procedure and had good cognitive function. Patients that did not satisfy the inclusion criteria were excluded.

8.2.3 Implant and surgery

All surgical procedures were performed by one of three orthopaedic consultants at the Department of Orthopaedics at St Marys Hospital. A limited deltopectoral approach, with division and repair of the subscapularis was employed. The Affinis Short Stemmed Total Shoulder Prosthesis (Mathys, Bettlach, Switzerland, Affinis Short) was used for all surgical procedures (Figure 8.1). The polyethylene glenoid component of this system, Vitamys, with highly cross-linked polyethylene (HXLPE) and Vitamin E, had been modified by the manufacturer to accommodate eight inserted 0.8 mm steel beads. Palacos cement (Heraeus Medical) was applied with a syringe to the glenoid component before digital pressure was used to insert the implant. The uncemented humeral component consisted of a titanium stem coated with calcium phosphate and an alumina ceramic head. During the surgery, tantalum beads of 1 mm were inserted in the glenoid and the humeral bone. Patients were mobilized according to the standard physiotherapy programme for shoulder arthroplasty of the Upper Limb Section.



Figure 8.1 The Affinis Short Stemmed Total Shoulder Prosthesis

(Image reproduced with permission from Brodén C, Giles JW, Popat R, Fetherston S, Olivecrona H, Sandberg O, Maguire GQ, Noz ME, Sköldenberg O, Emery R. Accuracy and precision of a CT method for assessing migration in shoulder arthroplasty: an experimental study. *Acta Radiol Stockh Swed* 1987. 2019;284185119882659)

8.2.4 CT examinations

All patients were assessed preoperatively with a standard CT scan (CT1) and a standard shoulder X-ray available. These radiological images were available for the orthopaedic consultant's preoperative assessment. For the follow-ups after surgery, CT scans with a limited field of view of the shoulder were performed immediately postoperatively (CT2), at 3 (CT3), 6 (CT4), 12 (CT5) and 24 months (CT6) after surgery (Figure 8.2). CT2 was performed a week after the surgery with the patient lying supine on the CT table. The arm was placed in a neutral position, with attention paid to avoid external rotation of the arm in order not to compromise subscapularis healing after surgery.

The CT scans were conducted with a CT scanner (Ingenuity, Philips, Eindhoven, The Netherlands) with standard shoulder parameters: voltage-120 kVp, pitch-1, rotation time 0.4

seconds, and automatically modulated tube current. The images were reconstructed into a 768×768 matrix with an x-y pixel size of 0.65 mm and a slice thickness of 1 mm with 0.5 mm increments without metal artefact reduction. The images were reconstructed with a bone reconstruction algorithm without the use of metal artefact reduction.

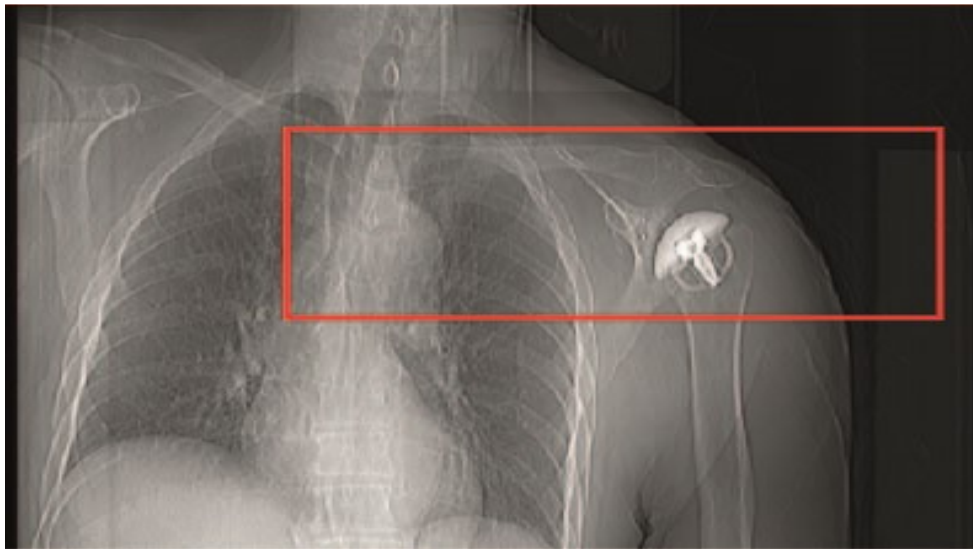


Figure 8.2 The postoperative limited field of view on a scanogram for the CT scan.

8.2.5 CT measurements

Preoperative CT scans were used to measure the version, the inclination of the glenoid and the Walch classification score (108). The immediate postoperative CT scan was used to measure the retroversion and inclination of the glenoid implant after surgery. These measurements were performed in 2D by one radiologist adapting the Multiplanar Reformat (MPR) view of the Carestream PACS system (Carestream, Rochester, US) to a coordinate system described by Gregory et al. creating a scapular plane with the supraspinatus fossa line and the lateral border line of the scapula, comparing it to the glenoid surface or the glenoid component to measure version and inclination of the component (109).

Table 8-1 Patient description and preoperative clinical data

Sex: Male (M) / Female (F)	2M/5F
Mean Age (Range)	65.7 (56–78)
Number of Primary Osteoarthritis /Avascular Necrosis	7 / 2
Walch Score A1/A2/B1/B2	A1: 2 /A2: 4/B1:2/B2:1
Mean Preoperative Retroversion (Range)	5 (0–12)
Mean Preoperative Superior Inclination (Range)	2.9 (-5–14)
Preoperative Constant Score, Mean (Range)	30 (21–51)
Preoperative Oxford Score, Mean (Range)	23.67 (13–38)

8.2.6 Image analysis

The postoperative CT scans were imported in CTMA for the image analysis. The image analysis process has been extensively described in chapters 5–7 of this thesis. The description has also previously been published by Brodén et al. for hip and experimental shoulder implant migration measurements (14,15). The CT scans CT3, CT4, CT5 and CT6 were successively compared to the immediate postoperative scans CT2 to measure the migration of the implant relative to the bone in between these scans. For the image analysis, only the surface anatomy of the bones was used since only two glenoid cases and three humeral cases had stable bead patterns. This was due to an insufficient number and unsatisfying distribution of beads inserted in the glenoid and humeral bone during surgery.

CTMA of glenoid component migration

To assess the measured motion of the glenoid components relative to the scapular bone between two timepoints, the following steps were performed in the CTMA software. (Figure 8.3 for analysis process):

1. The CT volumes were imported into the CTMA system, and an optimization of bone thresholding segmentation was performed manually (threshold value=350–450 Hounsfield Unit).
2. The scapular bone (the reference rigid body) was defined in two separate CT examinations.
3. The scapular bones in two separate CT examinations were registered to obtain a visual overlap of the bone of the two volumes.
4. A manual thresholding segmentation of metal was performed manually (threshold value= 2200 Hounsfield Unit).
5. The beads of each glenoid component (the target rigid body) was defined in two separate CT examinations.
6. The beads of the glenoid components were registered to obtain a visual overlap of the implant of the two volumes.

The software calculated the motion that had occurred for the glenoid component relative to the scapular bone between these two CT volumes described in the CT-based coordinate system. It resulted in a visual output in the form of registered 2D and 3D volumes as well as numerical migration values expressed in six degrees of freedom (translation along and rotations around x,y,z, in a CT DICOM coordinate system). During the analysis, the consistency of the registered rigid bodies was verified manually with a colour-coded feedback mechanism that

illustrates any change in the transformation of either rigid body due to movement of beads or bone morphology changes. The colour green indicated a successful registration.

However, only two glenoid cases and three humeral cases had stable bead patterns due to an insufficient number or unsatisfying distribution of beads. In previous studies by Rahme and Nuttall, several beads were distributed along the glenoid surface but also the acromion to create a rigid body that could be used in RSA analysis (52,53). In our cohort, three to seven beads were inserted in the glenoid bone perioperatively. Since the bead patterns were unstable and could potentially compromise our migration results, the reference rigid body registration was performed with bone registration using the surface anatomy of the scapula or humeral bone.

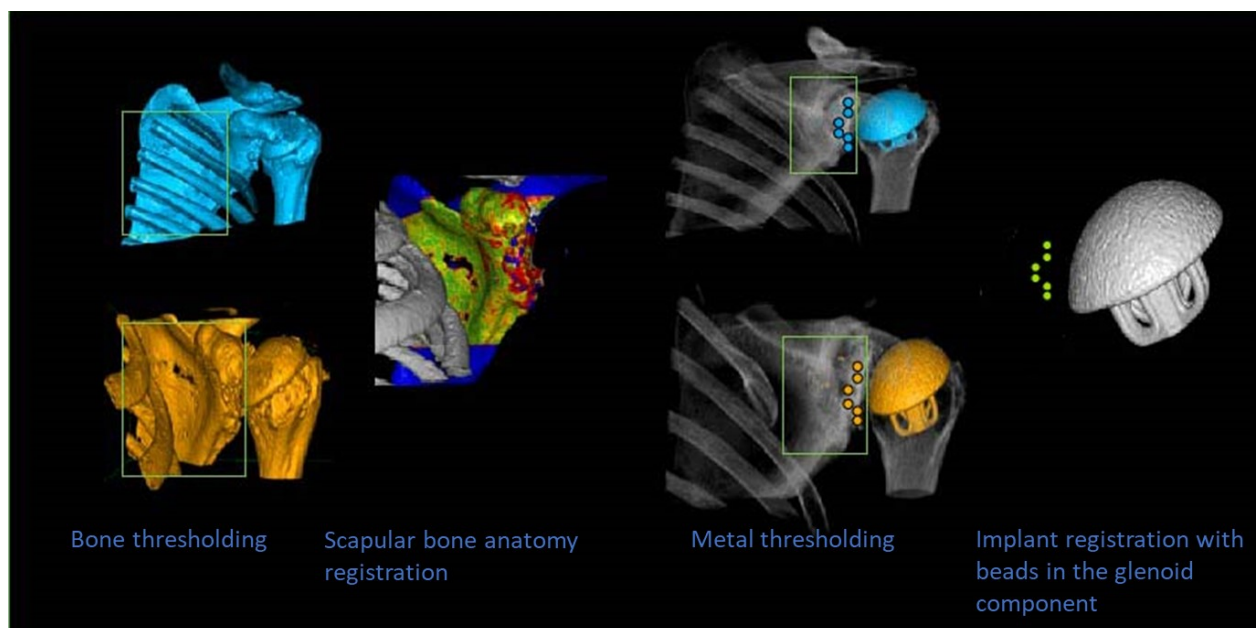


Figure 8.3 CTMA processing schematic for the glenoid component.

Migration of the glenoid component in translation was expressed along the transverse axis (x-axis medial [+] and lateral [-]), the sagittal (y-axis, posterior [+] anterior [-]) and the longitudinal axis (z-axis, distal [+] proximal [-]).

Migrations of the glenoid component in rotation were expressed around the x-axis (forward [+] and backward [-] rotation), around the y-axis (superior inclination [+] / inferior inclination [-]) and around the z-axis (anteversion [+] / retroversion [-]) (Figure 8.4)

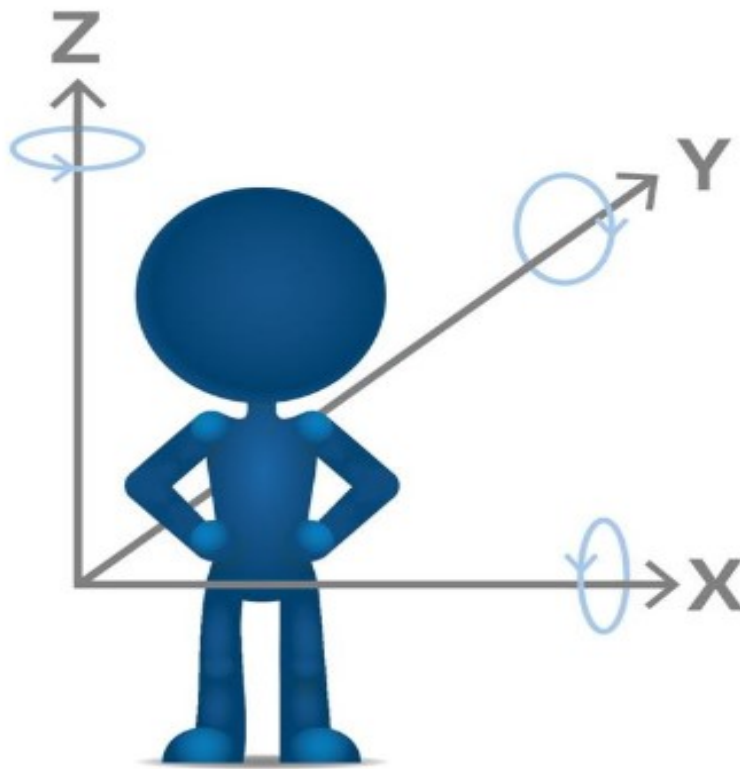


Figure 8.4 The coordinate DICOM system with arrow pointing in the positive direction

(Image reproduced with permission from Sandberg O, Tholén S, Carlsson S, Wretenberg P. The anatomical SP-CL stem demonstrates a non-progressing migration pattern in the first year: a low dose CT-based migration study in 20 patients. Acta Orthop. 2020 Oct 16;1–6.)

CTMA of humeral stem migration

The previous steps 1–6 were repeated for the analysis of the motion of the humeral component using the surface anatomy of the proximal humerus as the reference rigid body and the humeral metallic stem as the target rigid body.

Migration of the humeral component in translation was expressed along the transverse x-axis (medial [+] and lateral [-]), the sagittal (y-axis, posterior [+] anterior [-]) and the longitudinal axis (z-axis, distal [+]) proximal [-]).

Migration of the humeral component in rotation was expressed around the transverse x-axis (forward [+] and backward [-] rotation), around the sagittal y-axis (inferior inclination [+] / superior inclination [-]) and around the longitudinal z-axis (retroversion [+] / anteversion [-])

8.2.7 Postoperative radiolucency measurements

Radiolucent lines were described around the glenoid component, and their width was measured on the axial and frontal view of the postoperative CT scans. The glenoid was divided into four zones and the width of the radiolucent lines were measured (Figure 8.5):

Zone 1: Periphery of the glenoid implant on the superior side

Zone 2: Central part of the glenoid implant involving the superior peg

Zone 3: Central part of the glenoid implant involving the inferior peg

Zone 4: Periphery of the glenoid implant on the inferior side

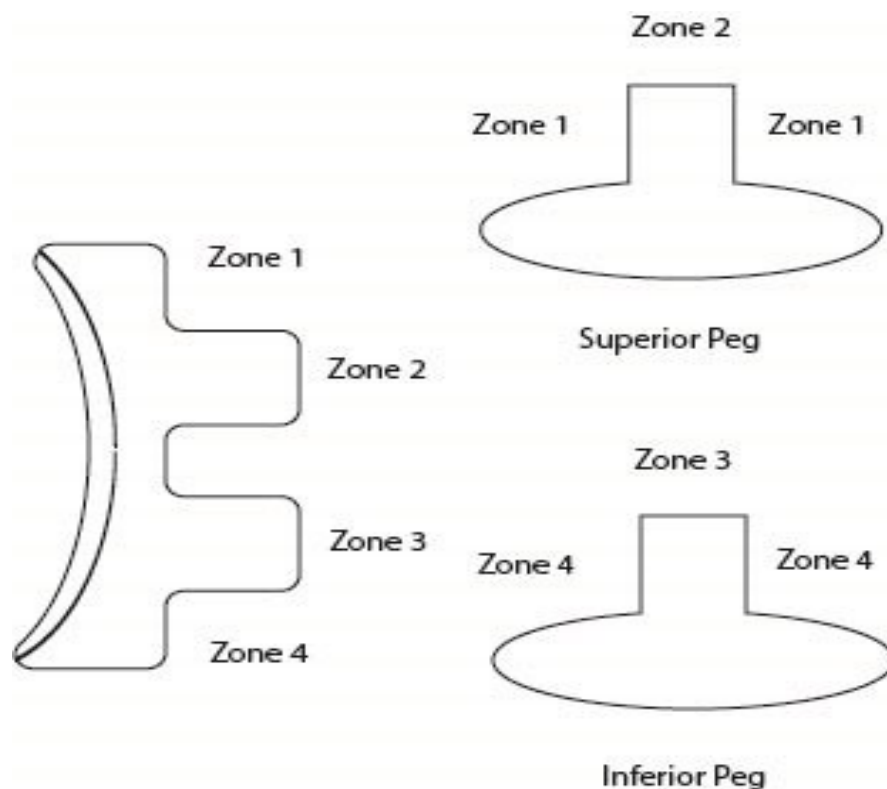


Figure 8.5 Description of radiolucency around several zones of the glenoid component in the frontal and axial view of a CT scan

8.2.8 Postoperative clinical scores

The outcome of the shoulder procedure was evaluated with clinical scores such as the Constant Score and the Oxford Score preoperatively and at 3 (CT3), 6 (CT4), 12 (CT5) and 24 months (CT5) postoperatively. The Constant Score (CSS) assesses the overall value of the functional state of a shoulder on a scale of 100 (110). The CCS is divided into four components: Pain (15 points), Activities of Daily Life (20 points), Range of Motion (40 points) and Power (25 points) (111). The Constant Score is a score adopted by the The Société Européenne pour la Chirurgie de l'Épaule et du Coude (SECEC). Despite the limitations associated with a simple score describing the function of a shoulder, the score is well accepted, practical and not specific for one diagnosis of shoulder disorder (110).

The Oxford Score is a validated and used outcome measurement to assess the patient's subjective feeling of their shoulder (112,113). The Oxford Score (OSS) was created in 1996 and is a 12-item questionnaire with a maximum score of 48 (112,113).

8.2.9 Effective dose

The effective radiation dose was evaluated with the formula conversion factor of the shoulder (k) $\times$ Dose Length Product (DLP) used in previous chapters. For the calculation with $k \times$ DLP, the conversion factor for these calculations was the conversion factor from the IRCP 103 of the neck (0.0052 mSv/mG.cm) and the chest (0.0146 mSv/mG.cm) divided by two (0.0099 mSv/mG.cm), to provide an estimation of the conversion factor of the shoulder (97).

8.2.10 Precision of the method

The precision of the CTMA method was estimated from Chapter 6, a study estimating the precision of CTMA for shoulder arthroplasty (with bone registration) in a cadaveric setting for the glenoid and humeral component of the Affinis Short Stemmed Total Shoulder Prosthesis implant (14). If the glenoid or humeral component in patients shifted more than the precision values, we considered that the component had migrated. The precision for the glenoid component was in the range of 0.08–0.12 mm for translations and 0.27–0.36° for rotations. The precision for the humeral component was in the range of 0.07–0.14 mm for translations and 0.21–0.31° for rotations.

8.2.11 Statistical methods

Descriptive statistics was used for this study. Statistical analysis was performed with Microsoft Excel 2019 software for PC.

8.3 Results

8.3.1 Migration of the glenoid component

One CT exam was excluded from the clinical study for glenoid component migration analysis due to the use of a different CT protocol (CT slice thickness of 2 mm instead of 1 mm). There were no complications after surgery during the two-year follow-up.

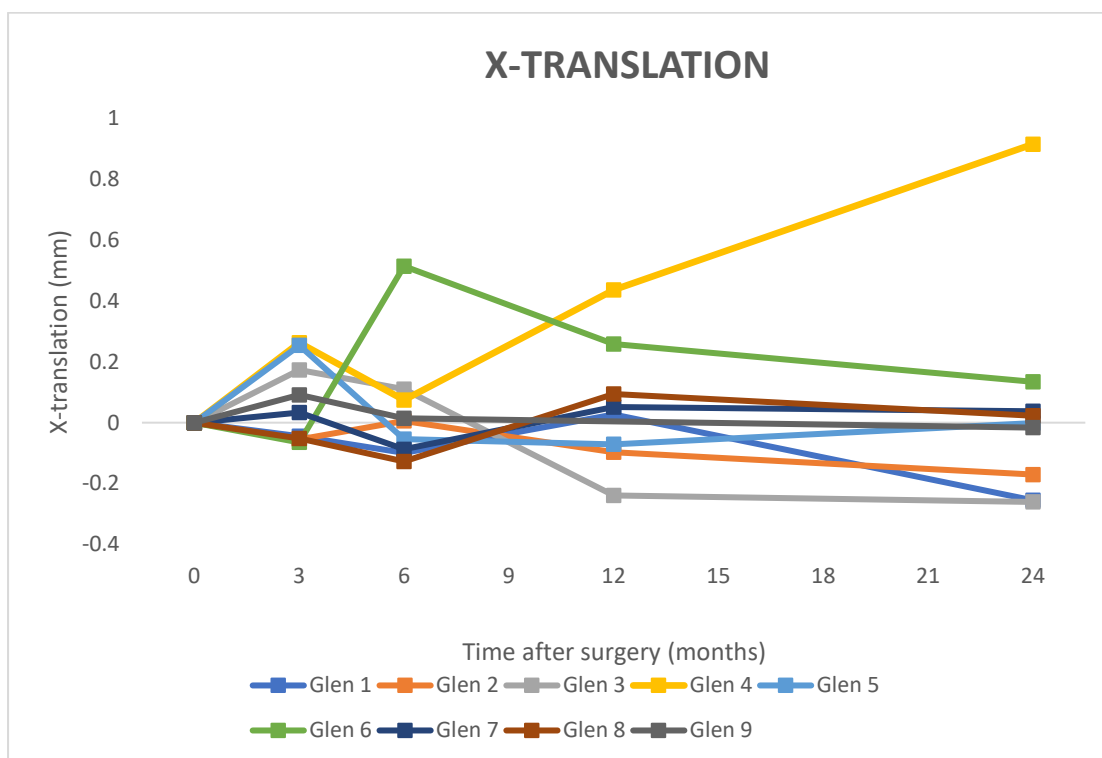
The mean retroversion and the mean superior inclination of the glenoid component immediately directly postoperatively was 2.5° (-5–11) and 0.9° (0–7) respectively.

For the glenoid component migration, the median translation and the median rotation were in the range of 0.00–0.10 mm and -1.53 – 1.05° at 24 months. The median migration of the glenoid component is reported in Table 8.2. The median migration in y- rotation, corresponding to superior/inferior inclination, was 0.11° (-1.45–0.71) at 3 months and 1.05° (-0.62–3.45) at 24 months. Five of nine glenoid implants showed migration over 2° at 24 months, two in posterior rotation (x-rotation) and superior inclination (y-axis), two in only superior inclination (y-axis) and one in anteversion (z-rotation). No specific pattern of glenoid migration could be observed (Figure 8.6).

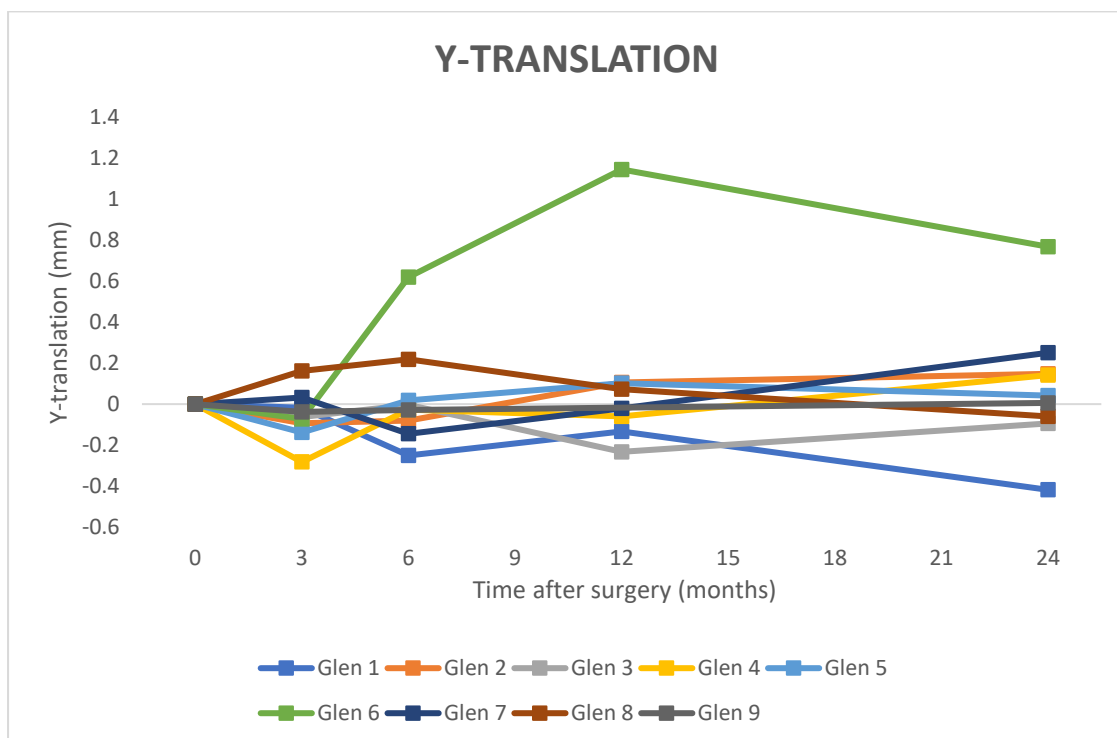
Table 8-2 Median migration (range) of the glenoid implant measured with CTMA using scapular anatomy registration

	Time after surgery (months)			
	3	6	12*	24
Median migration				
X translation (mm)	0.03 (-0.06,0.26)	0.01 (-0.13, 0.51)	0.04 (-0.24, 0.44)	0.00 (-0.26, 0.91)
Y translation (mm)	-0.06 (-0.28, 0.16)	-0.03 (-0.25, 0.62)	0.03 (-0.23, 1.14)	0.04 (-0.42,0.77)
Z translation (mm)	0.04 (-0.16, 0.69)	0.10 (-0.06,0.36)	0.04 (-0.27,0.41)	0.10 (-0.04, 0.34)
X rotation (°)	0.11 (-0.89, 3.99)	-0.68 (-2.19, 0.47)	-0.60 (-2.77, 0.06)	-1.53 (-2.53, 0.01)
Y rotation (°)	0.11 (-1.45,0.71)	0.56 (-0.78, 1.94)	0.77 (-0.83, 2.66)	1.05 (-0.62, 3.45)
Z rotation (°)	0.32 (-0.50, 3.95)	1.01 (-0.20, 1.79)	0.26 (-0.59, 4.52)	0.04 (-0.97, 4.88)

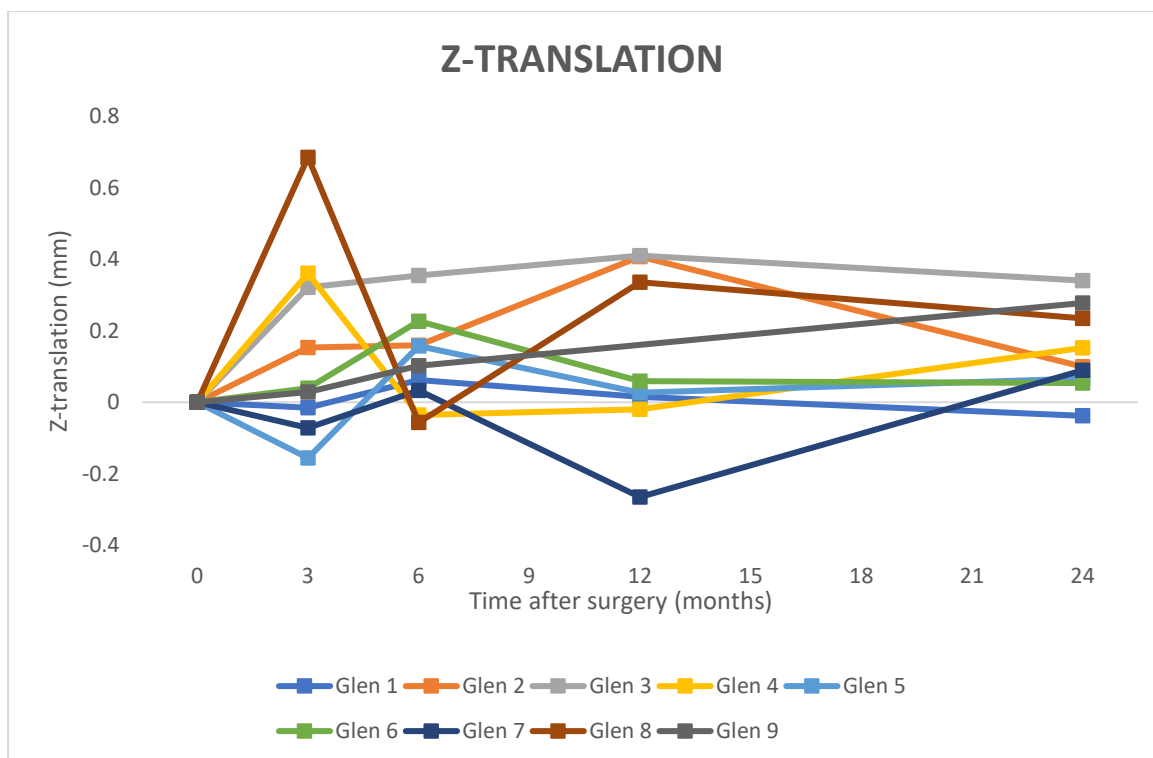
* One examinations at 12 months was excluded



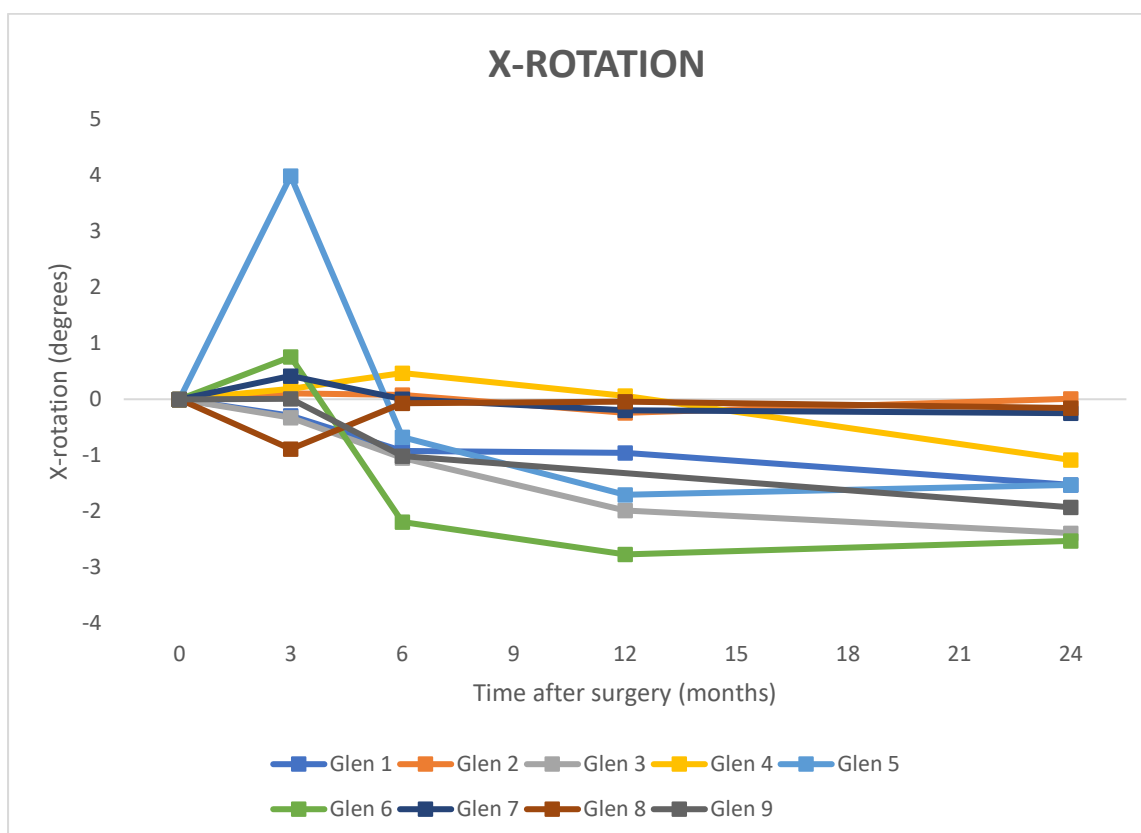
(a)



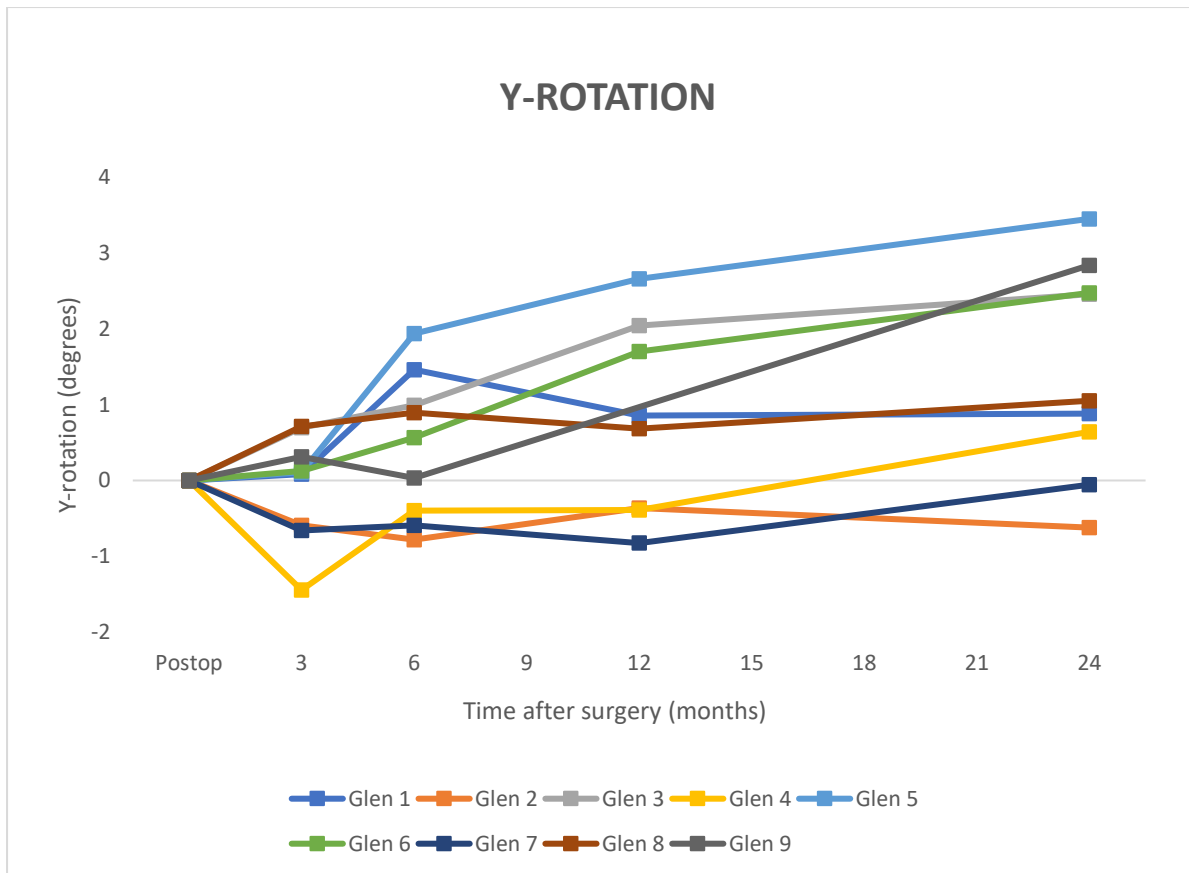
(b)



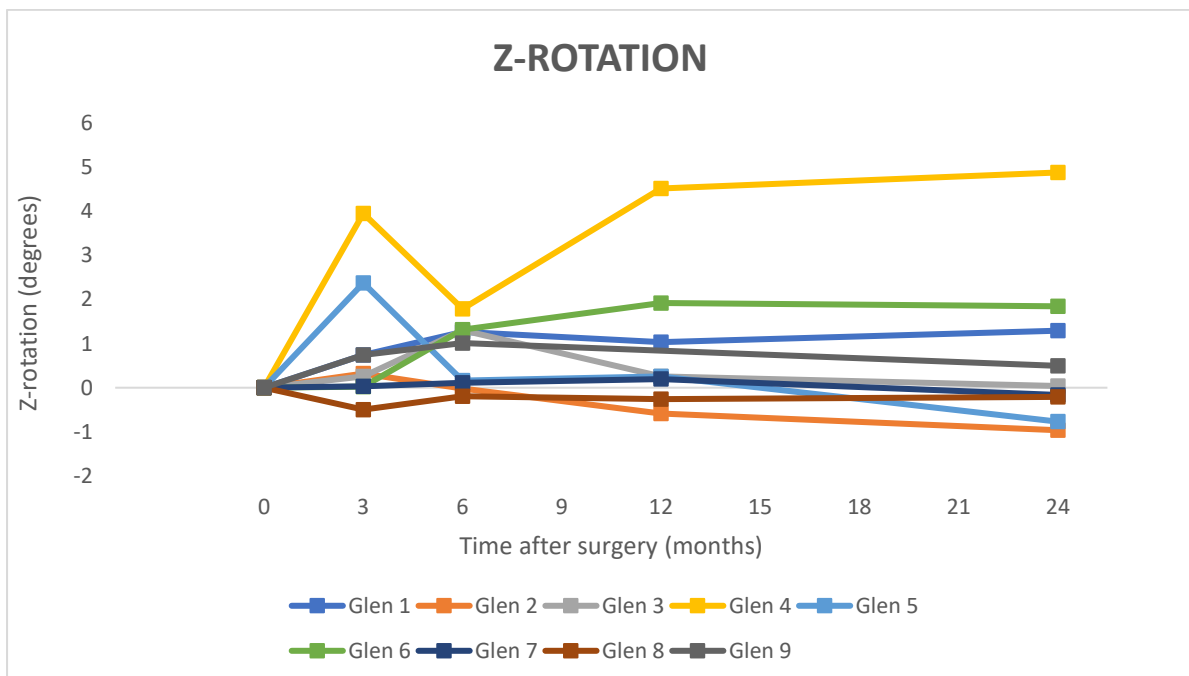
(c)



(d)



(e)



(f)

Figure 8.6 a,b,c,d,e,f Migration in translation and rotation of the glenoid component over 24 months
 Glen: Glenoid component

8.3.2 Radiolucent lines

Radiolucent lines could be observed around all glenoid components. The radiolucent lines developed from the periphery to the centre of the implant for six glenoid components during the follow-up period of 24 months. At 24 months, all nine glenoid components had radiolucent lines that had reached and involved the two pegs of the implant (Table 8.3).

Table 8-3 Development of radiolucent lines around the glenoid component.
Width of lines were measured in range of mm (0; 0-1;1-2; 2-3 mm) For detailed table of radiolucency lines at 3,6 and 12 months see appendix tables 11.11-11.12

Postop					24 months			
	Periphery		Centrally		Periphery		Centrally	
	Zone 1	Zone 4	Zone 2	Zone 3	Zone 1	Zone 4	Zone 2	Zone 3
Glen1	0	0	0	0	0-1	0-1	0-1	0-1
Glen2	0-1	0-1	0	0	1-2	1	0-1	0
Glen3	0	0	0	0	0	0-1	0	0-1
Glen4	0-1	0-1	0	0	1-2	1-2	0-1	0-1
Glen5	0	0-1	0	0-1	1-2	1-2	0-1	0-1
Glen6	0-1	0-1	0	0	1-2	1-2	0-1	0-1
Glen7	0-1	0-1	0	0	1-2	1-2	0-1	0-1
Glen8	0	0	0	0	0	0-1	0-1	0-1
Glen9	0-1	0-1	0	0	2-3	0-1	0-1	0-1



(a)



(b)

Figure 8.7 Development of radiolucent lines around the glenoid component.

a. Glenoid component seen in CTMA directly postoperatively, b. Glenoid component seen in CTMA at 1 year postoperatively with development of radiolucent lines at the cement-bone interface located to the inferior part of the component.

8.3.3 Migration of the humeral component

Three humeral CT exams were excluded from the study for humeral component migration analysis. One humeral CT examination was excluded due to the use of a different CT protocol (CT slice thickness of 2 mm instead of 1 mm). Two other CT examinations were excluded due

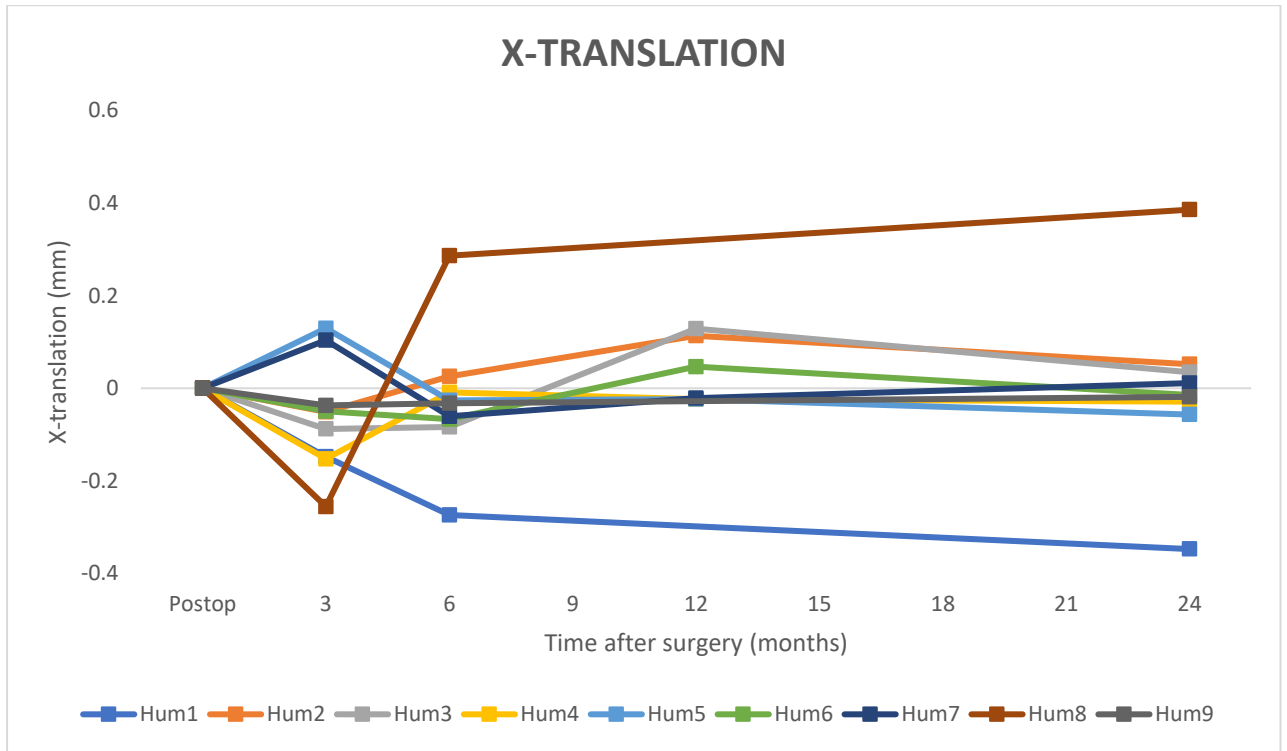
to the very limited field of view of the CT scan humerus with insufficient bony contour of the humerus in data acquisition, which compromised the stability of the humeral bone registration.

For the humeral component migration, the median translation and the median rotation varied between -0.02 and -0.01 mm, and between -0.62 and -0.06 ° at 24 months. The median migration of the humeral component is reported in Table 8.4. The median migration of the humeral component in z-translation, corresponding to distal translation of the stem, was -0.07 (-2.29–0.12) at 3 months and -0.01 (-2.21–0.08) at 24 months. One of the humeral components migrated more than 2mm in distal translation and rotated over 4 ° in posterior rotation and over 2.5° of anteversion. Most of that migration occurred during the first 3 to 6 months (Figure 8.8). The eight other humeral components migrated below 0.5 mm in translation or 1° of rotation.

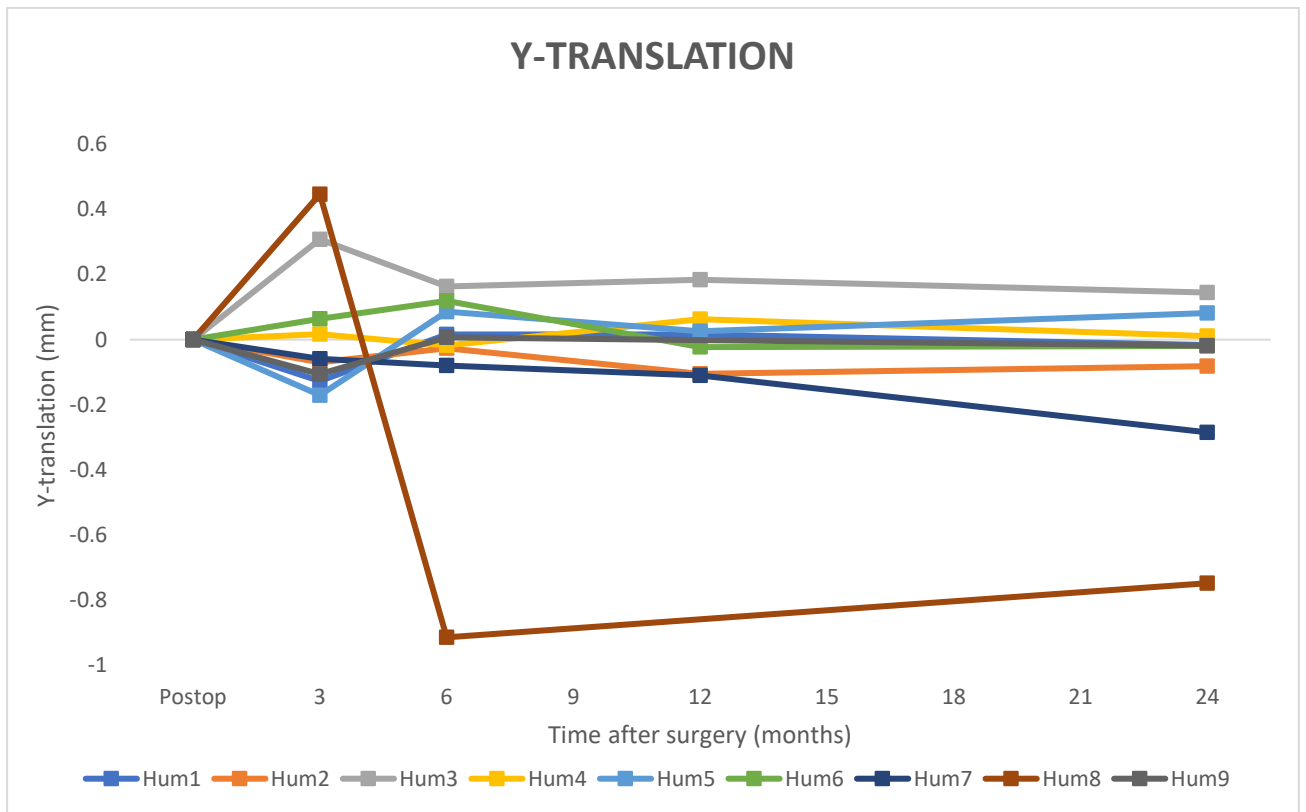
Table 8-4 Median migration of the humeral stem measured with CTMA using humeral anatomy registration (presented with median (range))

Median migration	Time after surgery (months)			
	3	6	12*	24
X translation (mm)	-0.05 (-0.15,0.45)	-0.03 (-0.27, 0.29)	0.01 (-0.02, 0.13)	-0.01 (-0.35, 0.39)
Y translation (mm)	-0.07 (-0.82, 0.31)	0.01 (-0.91,0.16)	0.00 (-0.11, 0.18)	-0.02 (-0.75, 0.14)
Z translation (mm)	-0.07 (-2.29, 0.12)	-0.10 (-2.01, 0.10)	-0.05 (-0.13, 0.05)	-0.01 (-2.21,0.08)
X rotation (°)	0.11 (-3.37,0.37)	0.09 (-3.26, 0.28)	0.10 (-0.33, 0.45)	-0.11 (-4.13, 0.70)
Y rotation (°)	0.16 (-0.12,0.88)	0.18 (-0.22,0.66)	0.37 (-0.01,0.74)	-0.06 (-0.52,0.82)
Z rotation (°)	-0.28 (-3.09,0.48)	-0.21 (-2.76, 0.42)	-0.44 (-1.02, 0.26)	-0.62 (-2.63, 0.90)

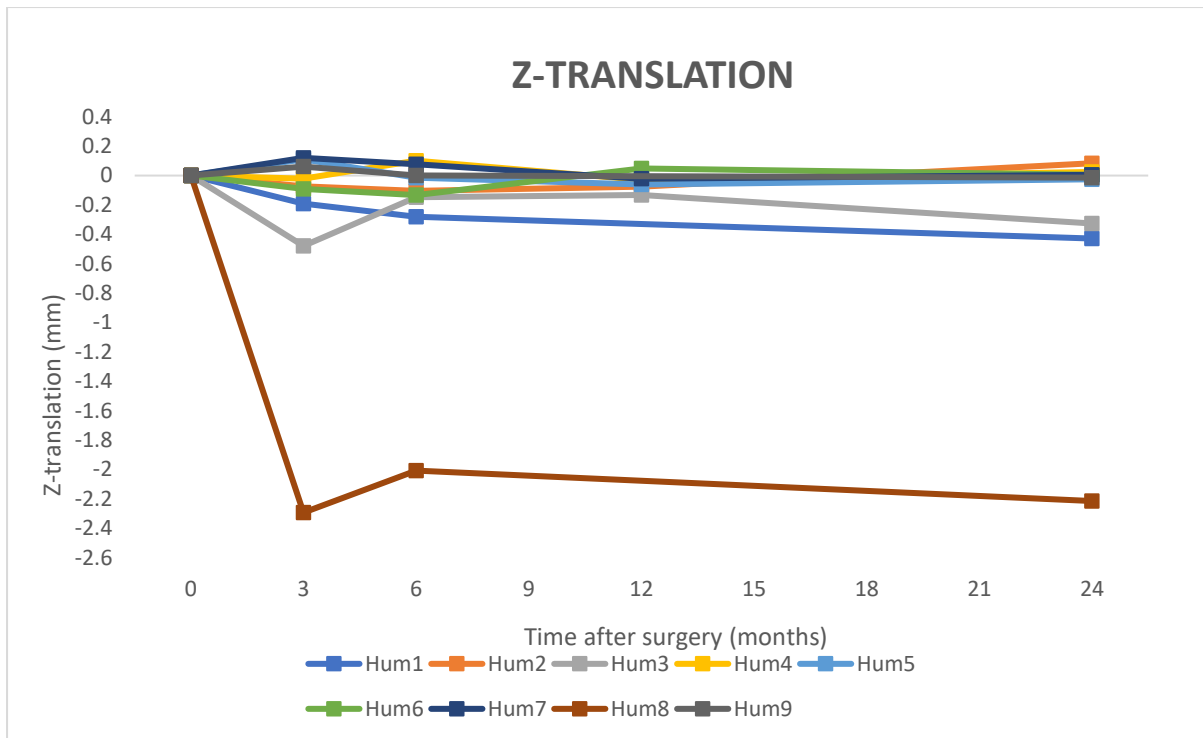
* Three examinations at 12 months were excluded



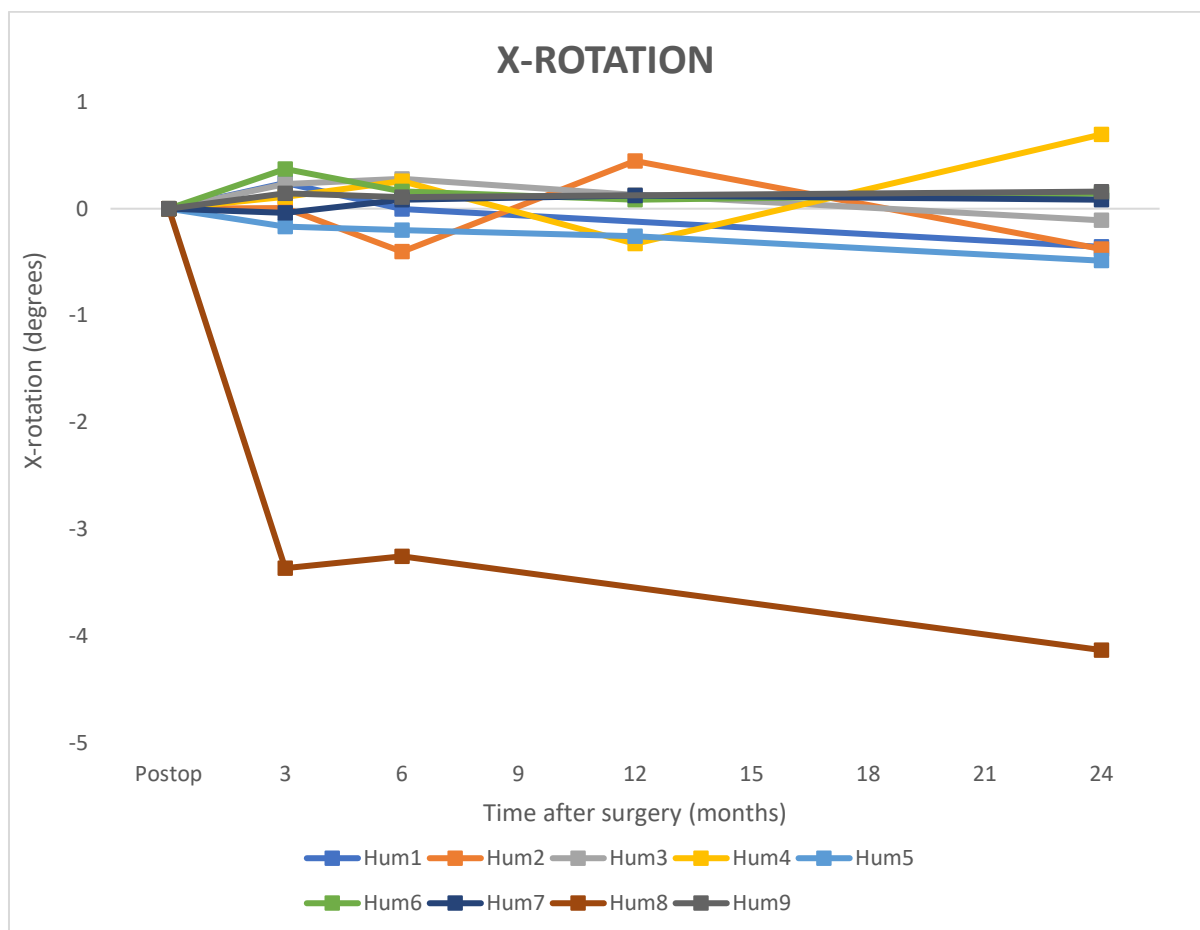
(a)



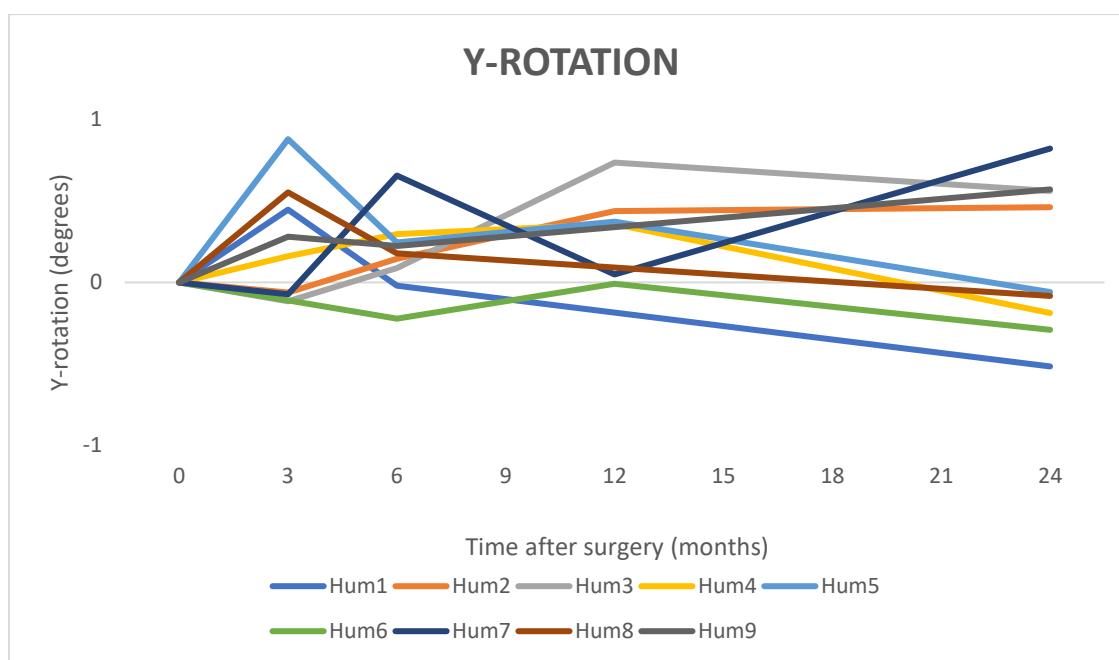
(b)



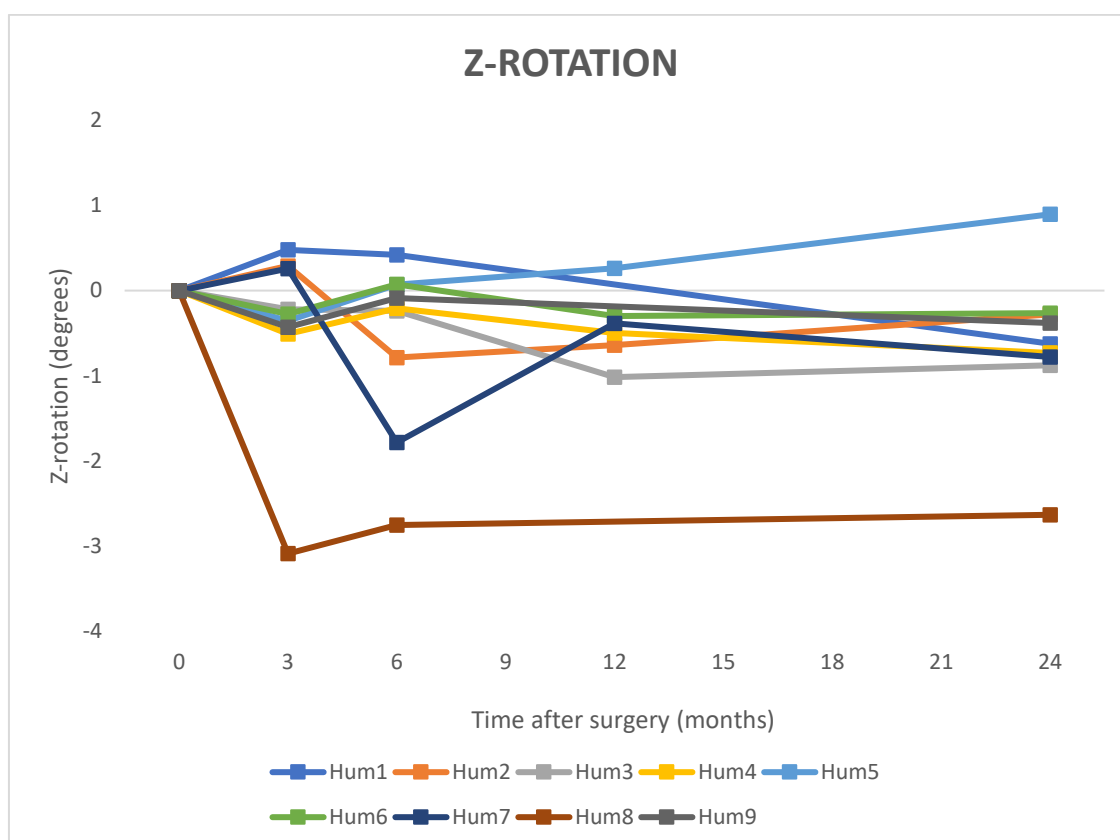
(c)



(d)



(e)

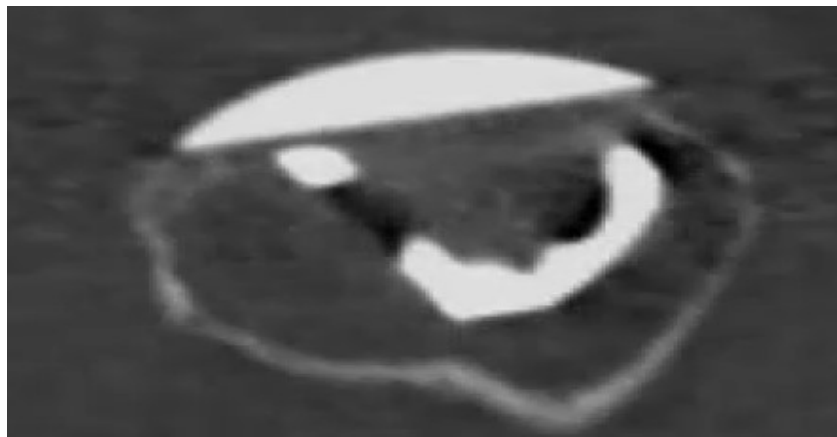


(f)

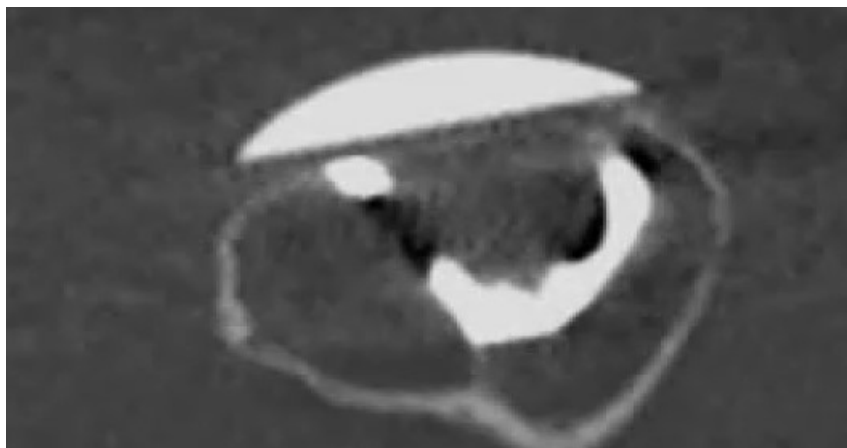
Figure 8.8 a,b,c,d,e,f Migration in translation and rotation of the humeral component over 24 months.
Hum: humeral component

8.3.4 Radiolucent lines and bone resorption

There were no humeral radiolucent lines visualised around the humeral stem. However, progressive calcar resorption of 1–6 mm could be seen in eight out of nine implants during the 24-month follow-up, some starting as early as after 3 months postoperatively.



(a)



(b)

Figure 8.9 Progressive calcar resorption.

a. Humeral component immediately postoperatively, b. Humeral component at 1 year postoperatively with proximal calcar resorption.

8.3.5 Clinical scores

For this cohort, the clinical scores continuously improved over 24 months. The Constant Score improved from a mean of 30 (21–51) preoperatively to a mean of 68.79 (41–88) at 24 months (Figure 8.9). The Oxford Score improved from a mean of 23.67 (13–38) to a mean of 43.33 (32–48) (Figure 8.10).

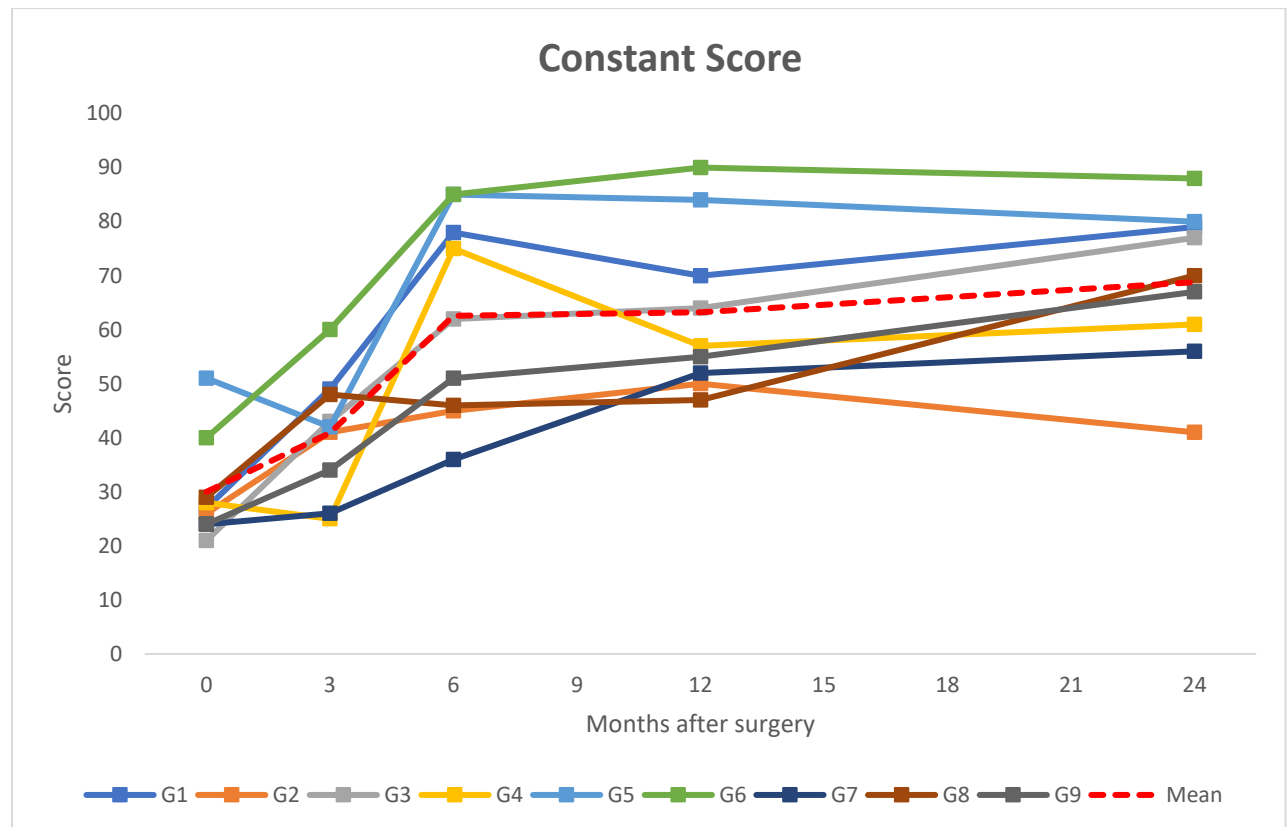


Figure 8.10 Constant scores for each shoulder arthroplasty case

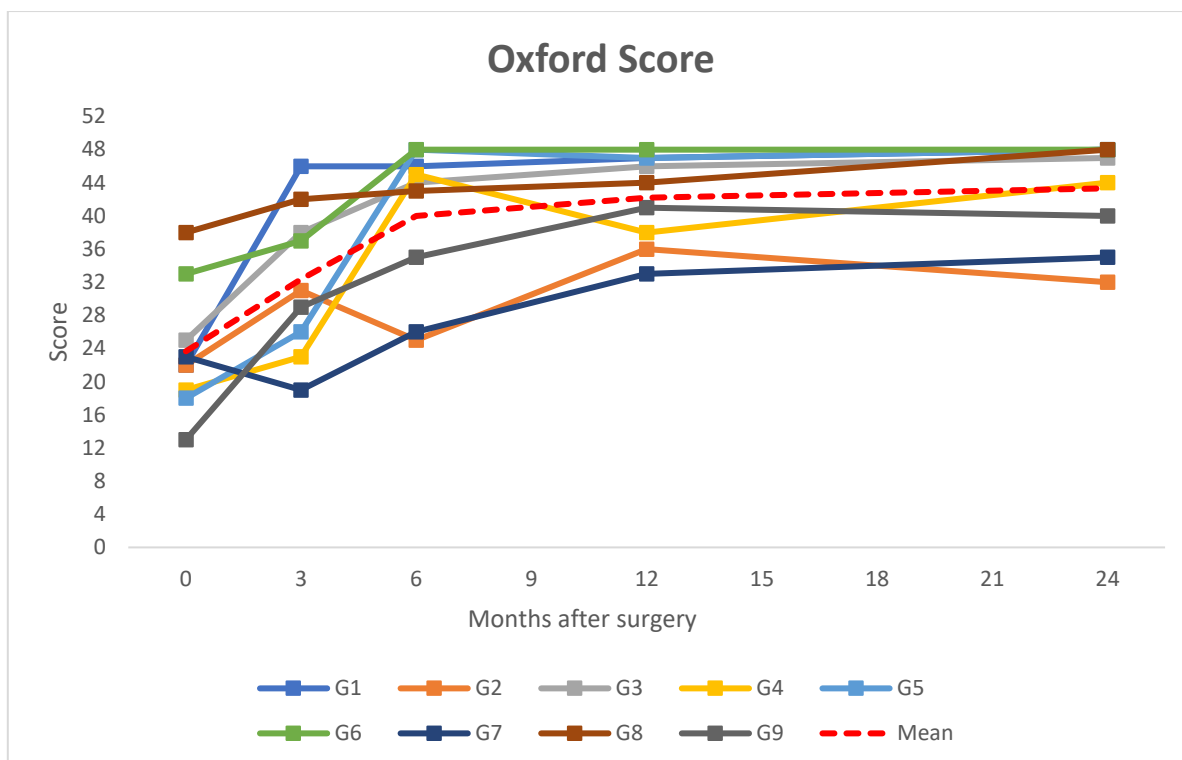


Figure 8.11 Oxford scores for each shoulder arthroplasty case

8.3.6 Effective dose

The mean effective dose of the postoperative CT shoulder scans used for CTMA was calculated to a total of 7.72 mSv (5.4–11.7) or 1.54 mSv per CT scan.

8.4 Discussion

The purpose of this chapter was to investigate if CTMA could be used to measure early migration and the development of radiolucent lines over time in shoulder arthroplasty.

Of the nine glenoid components, five of nine glenoid implants showed migration over 2° at 24 months. In a cohort study of 20 shoulder arthroplasties performed by Richetti et al., 35 percent of their anchor peg glenoid component showed evidence of shift on CT scanning (86). However, in their study, shift was defined as migration superior to 5 ° or more in version or inclination. None of our implants migrated more than 5 °. In our cohort, the glenoid implants migrated without a specific pattern. Rahme et al. performed a radiostereometric study of the migration of a three-pegged cemented glenoid component also without finding any specific pattern of migration (52).

In our cohort, all the glenoid components had a progression of radiolucent lines, therefore no correlation between migration and radiolucent lines could be described. This is in contrast to the findings of Richetti et al., who identified a correlation between migration of the glenoid component and the presence of “osteolysis” around the central peg (86). In a study by Bell et al. on the same implant used in our cohort, only 16% of cases had radiolucency development (114). However, standard X-rays tends to underestimate radiolucent lines compared to CT scans (56).

For the humeral component migration, one humeral component was an outlier with a migration of 2 mm in distal translation and rotation over 4 ° in posterior rotation and over 2.5° in anteversion at 24 months. The migration stabilised between 3-6 months, which is expected since secondary stability should occur at that time with a press fit design. The eight other humeral components migrated below 0.5 mm in translation or 1° of rotation after 24 months, probably due to osseointegration of the uncemented stem.

We did not detect any radiolucent lines around the humeral components; however it is important to notice that artefacts from the titanium stem might have made it more difficult to visualise zones around the stem. These findings are in accordance with those of Bell et al., who did not find any radiolucent lines around the humeral short stem at 1- and 2-year follow-up in standard shoulder X-ray (114).

In our cohort we could see progressive resorption of bone occurring at the calcar region of the humerus in eight out of nine humeral components at 24 months after surgery. This could correspond to stress shielding and it is important to follow this over time since the short stem is theoretically designed to preserve humeral bone stock due to metaphyseal anchorage (115). If significant bone resorption occurs over time in the metaphyseal bone, there might be a risk of humeral component loosening.

There is currently no threshold value of migration in shoulder arthroplasty that is correlated to loosening (54). It is believed that this might be due to the few and short follow-up studies performed on shoulder arthroplasty migration (54). In our study, the magnitude of glenoid component migration was greater than the migration of the uncemented humeral component. In addition, radiolucent lines could be seen in glenoid components but not around the humeral stem. These findings could be due to the different bonding mechanisms between implant components and bone. For the humeral components, bonding occurs between the titanium stem and bone, relying on osseointegration. For the glenoid components, the bonding occurs between implant, cement and bone.

Our findings could be seen in the context of newly published data on the longer-term survival data of the Affinis Short Stemmed Total Shoulder Prosthesis Mathys implant. The survival rates of the Affinis implant was estimated to 95.4 % at nine years which is comparable to the

ten year survival rates of 96% for total shoulder arthroplasty designs registered in the Nordic Arthroplasty register (116,117).

For two of the humeral examinations, the limited field view compromised our visualisation of the humeral anatomy. This decreased the quality of registration since there were limited anatomical landmarks that could be used for the humeral bone registration, which could potentially create unreliable migration results. It is therefore recommended not to limit the field of view to the inferior border of the implant but also include anatomical landmarks of the bone below the implant while being cautious not to expose the patient to unnecessary radiation.

All the patients improved their clinical scores after shoulder surgery and no correlation could be described between migration of the implants and clinical scores. The Constant Score improved from a mean of 30 (21–51) preoperatively to a mean of 68.79 (41–88) at 24 months in our cohort. This is slightly lower than the Constant Score of 76 reported by Bell et al. at one-year follow-up and 86 at two years (114). However, another study comparing stem and stemless implants reported a mean Constant Score of 65 for stemless implants at 32 ± 4 month postoperative follow-up, which is comparable to our results (118). Bell et al. did not have any complications using the Affinis short stem related to the implant itself and this is accordance with our results. (114)

The CT effective dose estimated for postoperative CT scans with the conversion factor $(k) \times$ Dose Length Product (DLP) was estimated to a mean of 7.72 mSv for each implant or a mean of 1.54 mSv per CT scan. This accumulated dose is lower than the effective dose of a routine CT chest without contrast, estimated to 8.2mSv (119).

One of the most considerable limitations of this study was that the precision of CTMA was not estimated in a clinical setting. It has been previously recommended in the RSA guidelines to perform double examinations for each subject in an RSA study to estimate precision (9). The double examinations are important since the precision can vary between different studies depending on the study subject (9). However, for this study, we used precision values from a previous cadaveric study, with the Affinis Short Stemmed Total Shoulder Prosthesis, performed in Chapter 5 and performed by Brodén et al (14). Due to the absence of soft tissues in these cadavers and the experimental setting, the cadaveric CTMA results might be more precise than they would be if double examinations were performed in the clinical setting.

Another limitation is that there is currently no measurement in CTMA equivalent to the condition number or mean error of rigid body fitting in RSA (9). A low condition number in RSA indicates good marker distribution and a lower mean error of the rigid body fitting reflects the stability of markers in RSA. These measurements guarantee a reliable image analysis and reliable migration results (9). In CTMA, marker distribution and stability of markers is currently manually verified in the visual interface and relies on the user's experience and judgement.

A third limitation of this study is that standard radiographs were not performed at the different postoperative CT timepoints to follow the development of radiolucent lines. This would possibly have increased the validity of our findings since development of radiolucent lines has been more extensively studied and priorly measured in standard radiographs (38,46). However, it is also important to note that Yann et al. found that standard radiographs underestimates the detection of radiolucent lines compared to CT (56).

Finally, another limitation is the small sample size that prevents statistical interference. However, the study was designed as a proof of concept study to detect migration and

radiolucent lines over time with CTMA. The aim was to recruit twenty patients as suggested by RSA guidelines (9) but the low volumes in our centre made it difficult to include more patients.

In conclusion, we have investigated the feasibility of this method. This method can detect shifts in migration, development in the interface between bone and implant, such as radiolucent lines, and bone resorption. However, further clinical trials with longer follow-ups with a larger sample size are needed to explore the relationship between migration, radiolucent lines and clinical scores.

In the next chapter a general discussion of the important findings of this thesis will be presented.

9. General discussion

9.1 Research findings

The purpose of this thesis was to investigate whether a commercially available, low-dose CT image registration technique, CT micromotion analysis (CTMA), could be used to explore implant behaviour by detecting early migration and development of radiolucent lines in orthopaedic implants.

Four questions were investigated:

- Is it possible to use CTMA at a low dose in an experimental setting to detect implant migration with acceptable accuracy and precision?
- Is CTMA comparable to the gold standard RSA method in precision and the effective dose for detecting early migration in patients?
- Can CTMA be used with acceptable precision at a low dose for different types of implants using different types of CT scanners and CT protocols?
- Can CTMA be used over two years to detect the development of radiolucent lines and implant migration?

Chapters 2–4 presented a literature review, an in-depth explanation of the science behind the technology used in this thesis and an explanation of the concepts of accuracy and precision.

Chapter 5 described an experimental study with cadavers, measuring the precision and accuracy of the CTMA method in shoulder arthroplasty. We found that CTMA could be used for early implant migration measurement in shoulder arthroplasty in an experimental setting at an acceptable accuracy and precision and at a low effective dose.

In Chapter 6, the precision and effective dose of CTMA was directly compared to the precision of the gold standard RSA method in cemented hip cups in patients. CTMA showed better

rotational precision than RSA, comparable translational precision at a slightly higher effective dose.

In Chapter 7, the generalizability of the CTMA method was investigated. CTMA was used for different types of hip cups with different CT protocols. This revealed that the precision of CTMA was comparable for different hip cups that were scanned with different types of CT scanners and protocols.

In Chapter 8, a proof-of-concept study was conducted that explored the possibility of using CTMA to detect radiolucent lines and migration in patients over time. CTMA was suitable for the detection of early migration and radiolucent lines; however, some limitations of this method were also observed. For example, there was no equivalent number to the RSA condition numbers or the mean error of rigid body fitting to quantify the suitability of the rigid body to give correct measurements. In CTMA, this assessment relies on the user's experience and judgement.

9.1.1 CTMA without insertion of tantalum markers into the bone

The major finding in this thesis was that CTMA without the use of bone markers for registration could be used for early migration measurements and to follow the development of radiolucent lines. This finding has implications on many levels.

For the researcher, this opens up the possibility for further investigations exploring how early migration and the development of radiolucent lines are related to loosening in hip and shoulder arthroplasty without the insertion of tantalum beads in the bone. In our research centre in London, we did not have extensive prior experience of RSA or bead placement; therefore, beads were inserted in an unstable pattern during our clinical proof-of-concept study (see Chapter 8). With an unstable distribution of beads, the migration results are not reliable;

therefore, a bone registration technique without the use of beads prevents loss of data. In addition, CTMA without beads prevents marker occlusion and the risk of prolonging surgeries due to bead insertion. Most research centres with access to CTMA software would be able to perform these studies, since the use of this method depends on data from widely available CT scanners. One concern about CTMA without bone markers is bone remodelling over time that theoretically could compromise the image analysis because CTMA relies on data from the surface anatomy of bone. However, the registration algorithm that compares two CT images uses only the areas of bone anatomy common between the CT scans for the image registration.

For the practising surgeon, CTMA becomes a tool that makes possible postoperative surveillance on the behaviour of implants. CTMA might give visual clues to surgeons on how to improve their surgical techniques, such as cementing, to obtain better outcomes for their patients.

For implant manufacturers, acquiring feedback on implant behaviour could be valuable for improving new arthroplasty designs. This tool could also be used as a quality assessment of prostheses before their release to the market. The need for stricter regulation around the introduction of implants in the market has been debated for years (120). It is known that the implant industry does not undergo the same rigorous clinical trials as pharmaceutical companies releasing new drugs (121). This difference could be due to the diversity of existing medical devices and the difficulty of establishing specific rules for such a heterogenic group of devices. Implant manufacturers in the United States have been using the 510k pathway to get Food and Drug Administration (FDA) approval if their implant has some similarities with an implant already available on the market (122). This saves implant manufacturers time and money by avoiding the need for extensive clinical trials. A similar pathway exists under the Medical Device Directive in Europe, where implant manufacturers often rely on ‘equivalence

data' to get a Conformance Européenne (CE) mark of approval without extensive clinical trials (121). However, the Medical Device Regulations rules (MDR) in Europe, introduced in 2017, with a transition period ending in 2021, are more stringent about the use of equivalence data. These stricter rules potentially make implants safer, but the CE marking is more costly and time-consuming for implant manufacturers (123). CTMA could be a practical tool for tracking implant performance in clinical trials to get CE marking approval.

9.1.2 Development of radiolucent lines

Another important finding was the development of radiolucent lines in all the glenoid components in Chapter 8.

This thesis adopted a descriptive approach to detect radiolucent lines rather than a scoring system previously used in the literature for glenoid components. The original scores of Franklin and Molé assumed that radiolucent lines were measured on a frontal x-ray for keeled glenoid components. However, multiple interpretations of that scoring system have been used for different types of pegged glenoid components and other radiological methods such as CT (37,38,56). The intent of the descriptive approach in this thesis was to detect patterns of radiolucent lines development in different zones around the glenoid component without the use of a scoring system. This approach was inspired by the descriptions of radiolucent lines in the hip at different zones given by Gruen or DeLee and Charnley. The description of the development of radiolucent lines in this thesis was limited to shoulder arthroplasty components. This was the case since our hip implant studies in this thesis involved precision calculations from data acquired at one specific point in time. In contrast the clinical shoulder study in chapter 8 followed patients over 2 years.

Notably, the CT effective dose and protocol might affect one's ability to visualise the development of radiolucent lines. It is known that different CT protocol settings can create

different signal-to-noise ratios (78). In the clinical shoulder study in Chapter 8, the lowest effective dose for one postoperative scan was 0.6mSv, but it is unclear if this CT protocol would underestimate radiolucent lines compared to standard CT protocols with higher effective doses.

9.1.3 Accuracy and precision in CTMA

An additional important finding was that neither accuracy nor precision exceeded 0.31 mm and 0.71° for all the experimental and clinical studies. The precision of CTMA in shoulder and hip arthroplasty with bead registration was 0.08–0.20 mm in translation and 0.20–0.54° in rotation and was consistent when different implants and different CT scanners were used. The precision of CTMA using bone anatomy surface, without beads, in shoulder and hip arthroplasty was 0.07–0.31 mm and 0.20–0.39° and was also consistent when using different implants and different CT scanners.

In Chapter 8, double measurements to calculate precision were not included for the cohort that underwent shoulder arthroplasty. One could speculate that CTMA in the clinical shoulder arthroplasty study might be slightly less precise than it was in the cadaveric shoulder study in Chapter 5. However, as noted in Chapter 7, the CTMA precision of hip cups did not exceed 0.31 mm in translation and 0.43° in rotation. Therefore, it is possible that the clinical precision for shoulder implants could be of this magnitude.

In the literature review in Chapter 2, early migration of implants was explored. Pijls et al. found that a threshold of 1 mm within two years in acetabular cups predicted implant failure (6). For hip stems, Kärrholm et al. found that an early migration of 1.2 mm after the first two years indicated a high risk of revision (7). Richetti et al. used a threshold of 5° in version or inclination as a threshold for meaningful shifts in their glenoid component CT study (86). However, CTMA is more precise than these thresholds and can therefore be used to follow

early migration in shoulder implants and in hip arthroplasty to predict the failure of certain hip implants.

9.1.4 Effective dose

The effective doses of the clinical studies varied between 0.2 mSv and 2.3 mSv per CT scan. This can be compared to the effective dose of a standard pelvic anteroposterior X-ray estimated to 0.7 mSv or a standard pelvic examination CT scan of 3.5 mSv (101,124). The average radiation level for a normal Swedish citizen has been estimated at 2.4 mSv/year (124). It is essential that the effective CT dose is low enough not to compromise patient safety, especially if longitudinal research studies are performed with radiological follow-ups at different points in time. Medical imaging should be performed according to the ALARA principle stating the use of as low as reasonably effective dose possible (78). However, it is important as well not to compromise the CT image quality in the pursuit of the lowest effective dose (78). As described in Chapter 6, the effective dose of 0.2 mSv made the segmentation of the CT image slightly difficult in CTMA due to image artefacts.

9.1.5 Research and clinical impact

As mentioned previously, for researchers, CTMA is a practical tool that could facilitate data acquisition for implant migration studies. CTMA relies on CT scanners that are widely available and does not require special positioning of the patient in the scanner, specialised laboratories, or specially trained staff. In addition, CTMA is not dependent on beads inserted into the bone during surgery. As a result of its simplicity, CTMA might therefore overcome the barrier of entry to perform implant migration studies at different centres around the world and could thus motivate more extensive follow-up studies. For researchers, CTMA could promote understanding of the influence of factors such as radiolucent lines, early migration, and bone remodelling (stress shielding, bone remodelling, osteolysis) on implant loosening. It could also study these factors impact on patient reported outcome measures (PROMS).

Introducing CTMA into clinical practice would require further understanding of factors related to loosening to justify additional patient hospital visits with CT scans to avoid cumulative doses. In current clinical practice at our centre in Sweden, hip arthroplasty is usually followed with a postoperative X-ray and a clinical follow-up visit two to three weeks after surgery without any further radiological exam. It would be advisable to perform a low-dose CT scan to estimate the radiolucent lines and the positioning of the implant immediately after surgery. This would allow the acquisition of baseline data for comparison with potential future CT scans if any hip problems would occur. Hip implants have a good survival rates and if the prostheses have been available on the market with good outcomes in implant registries, switching from a postoperative hip X-ray to a low-dose postoperative CT scan would be the only suggested change. If a patient had any clinical symptoms or a decline in PROMS after a hip procedure, it would be beneficial to perform a new low-dose CT scan and compare this to the postoperative CT scan in order to investigate the cause of the symptoms.

In our centre at St Mary's Hospital in London, a typical follow-up appointment after shoulder arthroplasty includes a direct postoperative shoulder X-ray and a one-year follow-up visit. The latter is a clinical and radiological assessment with a standard shoulder CT scan. It would be valuable to change the postoperative X-ray to a limited-field CT scan to create baseline data for implant positioning and radiolucent lines. In addition, it might be prudent to perform a limited-field CT scan at the one-year follow-up visit. The comparison between these two CT scans might reveal development of radiolucent lines, bone remodelling and early migration that could indicate loosening. If the patient had a satisfactory PROMS and no early migration without extensive development of radiolucent lines the patient should be discharged without any further follow-up appointments. If the patient exhibited a decline in PROMS, pronounced early migration or extensive development of radiolucent lines, additional low-dose CT scans would be reasonable at one-year intervals if no surgical revisions are performed.

When considering changing clinical follow-ups, one must also consider the additional costs that would be associated with the changes suggested and the availability of CT scanners compared to standard X-rays in hospitals.

9.2 Continuity between studies

This thesis included different studies that shared both similarities and differences in their methodologies and findings, both of which will be discussed in this section.

9.2.1 Orthopaedic implants

Several different types of implants were employed in this study. For Chapters 5 and 8, the total shoulder arthroplasty system Affinis short stem was used. For Chapters 6 and 7, three different hip cups were used: a cemented cup (Muller Exceed ABT, Biomet, Warsaw, Indiana, USA); an uncemented trabeculae-oriented pattern (TOP) cup provided by Waldemar Link GmbH (Hamburg, Germany); and a revision cemented cup (a Lubinus cross-linked UHMW-PE, Waldemar Link, Hamburg, Germany). The geometry and materials of these components (hip cups, glenoid components and short humeral stem) varied, but CTMA still displayed satisfactory precision for all of these elements.

9.2.2 CT scanners

Four CT scanners from four different manufacturers were used: Toshiba, GE Healthcare, Siemens and Philips. The number of detectors on the z-axis varied among the CT scanners, but all were helical multi-slice CT scanners. In Chapters 5 and 8, the same clinical 128-detector CT scanner (Ingenuity, Philips, Eindhoven, The Netherlands) was used at St Mary's Hospital in London. In Chapters 6 and 7, three CT scanners were used: the 128-detector CT scanner (Discovery CT750HD, GE Healthcare, Chicago, IL, USA); a 160 detector Aquilon One CT scanner (Toshiba); and a 2x64 dual source CT scanner (Somatom Definition Flash, Siemens, Forchheim, Germany). The dual source CT scanner has two different X-ray sources that increase the speed of data acquisition. Therefore, this scanner is optimal for CT scans requiring fast acquisition, such as cardiac CT images (125). In addition, efficient data acquisition with CT scanners is important for CTMA analysis to prevent movement artefacts in the CT images.

9.2.3 CT protocols

The CT protocols were developed with the help of medical physicists. Acquiring optimal CT images for a CTMA analysis necessitates that the CT protocol be planned, since there is a trade-off between image quality and an effective dose (78). The thickness of slices in the CT protocols varied between 0.5 and 1 mm, with slice increments varying between 0.312 and 0.6 mm. The pitch varied between 0.81 and 1, the voltage was set to 120 kVp, and the tube current varied between 10 and 500 mA. In a longitudinal follow-up, it is advisable to use the same protocol for each CT scan at different time points. This is challenging, since follow-ups can occur over a long time with different radiographers performing the CT scans. In our study, this complication led to certain case exclusions (see Chapter 8).

9.2.4 Effective dose calculations

For all our effective radiation calculations, the DLP was multiplied by a conversion factor corresponding to the patient's irradiated anatomical region that was scanned. This is the most commonly used method in routine clinical practise (78,97). However, one must be aware that there are other methods to calculate effective dose such as CT Impact dosimeter that can model the interaction between the radiation source and tissue, taking into consideration additional parameters of the CT protocol (126). However, these calculations are a more time-consuming and rely on a software that comes with associated costs.

9.2.5 Artefacts and marker occlusions

The advantage of CTMA is that no marker occlusion occurs. As noted in Chapter 6, one of the subjects who underwent RSA was excluded due to this very issue. However, artefacts can occur with CT scanning. Different approaches have been recommended in the literature to decrease metal artefact, such as increasing the tube current or voltage, using metal artefact reduction (MAR) techniques or even changing the position of the patient in the CT scanner (37,63,78).

The protocols used in Chapters 5, 6, and 8 and one protocol from Chapter 7 (Danderyds Hospital) did not include any metal artefact reduction techniques. These CT scans were of polyethylene, ceramic, and titanium components. The interface between the short, uncemented titanium humeral stem and bone in Chapter 8 was difficult to visualise due to artefacts. In Chapter 7, an uncemented trabecular metallic cup and a revision cup with a titanium compressing shell were CT scanned with metal artefact reduction techniques due to the extent of metal in these implants. If metal artefact reduction tools were used, it would be advisable to save both the standard reconstruction image and the modified version of the CT image with the metal artefact reduction technique. This could help in evaluating which CT scans would be most suitable to use for CTMA. In conclusion, it is important to consider the material and the geometry of the implants since metal artefacts in a CT might influence how precisely an implant can be identified and could compromise the visualisation of bone–implant interface in CTMA (127,128).

9.3 Strengths of this work and method

The chronology of this thesis is one strength of this work. An experimental validation was first performed before CTMA was investigated in a clinical setting ending with a clinical proof-of-concept study over time. In the clinical setting, the direct comparison with the gold standard RSA confirmed that CTMA could be an alternative to RSA. Since precision can vary between studies, a direct comparison between CTMA and RSA in the same subjects was important to perform. Another strength of this thesis was that the CTMA technology in these studies used CT data acquired from four different centres, increasing the generalizability of the method.

One advantage of the CTMA technology was the visual interface allowing the observation of early migration and the development of radiolucent lines over time. The visual findings were pronounced, offering more information than was available in the RSA images. The CTMA method's reliance on CT scans is an argument for the widespread adoption of this technology, since CT scanners are widely available in hospitals.

9.4 Limitations of this work

A limitation of this work was the small sample size in our studies, especially in the clinical proof-of-concept study. Another limitation was the short follow-up of two years in the clinical shoulder arthroplasty study in Chapter 8. To find a correlation between the development of radiolucent lines, early migration and loosening, longer follow-up times would be needed. A further limitation of the design of this study was that double measurements were not included of the clinical patients to measure precision. Double measurements were not included in our ethical application, and therefore precision values from our cadaveric study in shoulder arthroplasty were used. This is not optimal and does not support the RSA guidelines that recommend that double measurements be performed for each subject in a clinical study (9). Another challenge with our study in Chapter 8 was the use of different CT protocols for our patient follow-ups. Due to miscommunication with the radiology department, some CT scans were acquired using a different CT protocol and could therefore not be used for the CTMA analysis. Other important limitations of this thesis were that there were no measurements of the inter- or intra-observer reliabilities of CTMA and no study of the hip stem. Both limitations have been addressed in a study by Sandberg et al. for hip stems exhibiting precision measurements of 0.1 to 0.3 mm and 0.1 to 0.4° (16). Sandberg et al. showed that an inexperienced and an experienced user could produce similar results when following the same CTMA process, and a user repeating the same protocol after one month produced similar results (16). It is important to be aware that some of the CTMA image registration steps rely on the observer's judgment. Therefore, experience and education regarding how to use the software is important.

9.5 Future work

This thesis has shown that CTMA can be used to evaluate early migration and the development of radiolucent lines. This tool could be used as an alternative to RSA to evaluate early migration of implants. With CTMA, it could be possible to perform randomised studies to compare the migration and development of radiolucent lines between two different hip or shoulder implants. In hip arthroplasty, since it has been proven that early migration can increase the risk of revision, CTMA could be used as a tool for stepwise introduction of implants, as suggested by Malchau et al. (120).

For shoulder implants, longer cohort studies with larger sample sizes would be needed to study the relationship between early migration, development of radiolucent lines, clinical scores and implant loosening in shoulder arthroplasty. Such studies would determine if a threshold of translation or rotation would be a relevant predictor of glenoid implant failure.

Beyond this, CTMA could be validated for knee implants, although it is important to consider how artefacts around the knee implant components could affect the CTMA analysis. If CTMA is compared to standard RSA in knee implants, it might be challenging to perform RSA examinations for femoral components due to marker occlusion (129).

The image registration technology used in this thesis for CTMA is also used for a software named Implant Movement Analysis (IMA, Sectra AB, Linköping). IMA uses the same image registration algorithm as CTMA to test the stability of an implant at a single point in time (128). Furthermore, IMA could be compared to two RSA examinations performed on the same day in both loaded and unloaded positions (128,130). A predecessor of the IMA software was used by Olivecrona et al. to analyse CT images and visually diagnose hip cup loosening in patients with hip pain after hip implant surgery (65). Two sequential CT scans were used, one in internal rotation and one in external rotation for an image registration of the pelvic bone. Movement

could be detected in the graphical interface at the interface between the cup and the bone as a sign of loosening (65). Thus, this technique could potentially be applied in patients with unexplained pain after shoulder arthroplasty. Two sequential CT scans, one in abduction and one in torsion loading in abduction and external rotation could possibly be used and analysed in IMA to visually detect loosening of the glenoid component. This could improve diagnostic precision and lower the number of diagnostic invasive procedures performed. Such a proof of concept study might be useful to perform with this image registration technique.

9.6 Suggested guidelines for CT micromotion analysis

To conclude this thesis, the following suggested guidelines have been created for future users of CTMA to avoid potential errors and complications when using this technique.

Before the start of the study:

1. Collaborate with a medical physicist to develop a CT protocol with the lowest effective dose possible without compromising image quality. The CT slices should be thinner than 1 mm.
2. Scan the implant (without the patient) in a CT scanner to evaluate the geometry of the implant and artefacts.
 - Evaluate the shape of the implant on the CT image. If the implant is too spherical, the rotations could be difficult to evaluate.
 - Notice the material of the implant and observe artefacts in the CT image that potentially could compromise the quality of the image analysis.
3. If extensive artefacts are observed, change the CT protocol settings, or change the position of the implant in the scanner or experiment with metal artefact reduction techniques.
4. Import two CT images of the implant in the CTMA software to observe whether the shape of the implant or artefacts could possibly compromise the analysis.

Data acquisition:

1. Perform CT scans of patients who underwent arthroplasty with the preselected CT protocol. When using a limited field of view CT, include as many asymmetrical anatomical bone landmarks as possible.

2. Ask the radiology department to save the CT data in original format when there is uncertainty about which image reconstruction would be preferable to use with CTMA.
3. Save data of image reconstruction with and without the use of metal artefact reduction algorithms when metallic implants are scanned, to evaluate the best option for CTMA analysis.
4. Use a similar CT protocol for each CT follow-up.
5. Perform two CT scans (a double examination) at one of the scheduled follow-ups for each patient, to evaluate the precision of the method.

CTMA image analysis:

1. When importing CT images, import reconstructions of the CT images with the maximum number of slices available. Preferably import the bone reconstruction image registration.
2. Use a segmentation threshold that makes the bone or implant visible with a minimum of artefacts in the graphical interface.
3. When applying landmarks to the surface of the bone or implant, be cautious not to apply landmarks by mistake to other anatomical areas where they might compromise image registration.
4. Evaluate the registration carefully with the colour feedback mechanism and by observing the 2D fused CT images. If this is not satisfactory, apply new landmarks and perform the registration again.

10. Bibliography

1. Kurtz S, Ong K, Lau E, Mowat F, Halpern M. Projections of primary and revision hip and knee arthroplasty in the United States from 2005 to 2030. *J Bone Joint Surg Am*. 2007 Apr;89(4):780–5.
2. Nemes S, Gordon M, Rogmark C, Rolfson O. Projections of total hip replacement in Sweden from 2013 to 2030. *Acta Orthop*. 2014 Jun;85(3):238–43.
3. Farley KX, Wilson JM, Daly CA, Gottschalk MB, Wagner ER. The Incidence of Shoulder Arthroplasty: Rise and Future Projections Compared to Hip and Knee Arthroplasty. *JSES Open Access*. 2019 Dec;3(4):244.
4. Junnila M, Laaksonen I, Eskelinen A, Pulkkinen P, Ivar Havelin L, Furnes O, et al. Implant survival of the most common cemented total hip devices from the Nordic Arthroplasty Register Association database. *Acta Orthop*. 2016 Dec;87(6):546–53.
5. Bohsali KI, Wirth MA, Rockwood CA. Complications of total shoulder arthroplasty. *J Bone Joint Surg Am*. 2006 Oct;88(10):2279–92.
6. Pijls BG, Nieuwenhuijse MJ, Fiocco M, Plevier JW, Middelorp S, Nelissen RG, et al. Early proximal migration of cups is associated with late revision in THA: a systematic review and meta-analysis of 26 RSA studies and 49 survival studies. *Acta Orthop*. 2012 Dec;83(6):583–91.
7. Kärrholm J, Borssén B, Löwenhielm G, Snorrason F. Does early micromotion of femoral stem prostheses matter? 4-7-year stereoradiographic follow-up of 84 cemented prostheses. *J Bone Joint Surg Br*. 1994 Nov;76(6):912–7.
8. Rahme H, Mattsson P, Larsson S. Stability of cemented all-polyethylene keeled glenoid components: A RADIOSTEREOMETRIC STUDY WITH A TWO-YEAR FOLLOW-UP. *J Bone Joint Surg Br*. 2004 Aug;86-B(6):856–60.
9. Valstar ER, Gill R, Ryd L, Flivik G, Börlin N, Kärrholm J. Guidelines for standardization of radiostereometry (RSA) of implants. *Acta Orthop*. 2005 Aug;76(4):563–72.
10. Valstar ER. Digital roentgen stereophotogrammetry: development, validation, and clinical application. Leiden; 2001. 176 p. (NUGI).
11. Otten V, Maguire GQ, Noz ME, Zeleznik MP, Nilsson KG, Olivecrona H. Are CT Scans a Satisfactory Substitute for the Follow-Up of RSA Migration Studies of Uncemented Cups? A Comparison of RSA Double Examinations and CT Datasets of 46 Total Hip Arthroplasties. *BioMed Res Int*. 2017;2017:3681458.
12. Brodén C, Olivecrona H, Maguire GQ, Noz ME, Zeleznik MP, Sköldenberg O. Accuracy and Precision of Three-Dimensional Low Dose CT Compared to Standard RSA in Acetabular Cups: An Experimental Study. *BioMed Res Int*. 2016;2016:5909741.
13. Scheerlinck T, Polfliet M, Deklerck R, Van Gompel G, Buls N, Vandemeulebroucke J. Development and validation of an automated and marker-free CT-based spatial analysis

- method (CTSA) for assessment of femoral hip implant migration: In vitro accuracy and precision comparable to that of radiostereometric analysis (RSA). *Acta Orthop*. 2016;87(2):139–45.
14. Brodén C, Giles JW, Popat R, Fetherston S, Olivecrona H, Sandberg O, et al. Accuracy and precision of a CT method for assessing migration in shoulder arthroplasty: an experimental study. *Acta Radiol Stockh Swed* 1987. 2019 Nov 4;284185119882659.
 15. Brodén C, Sandberg O, Sköldenberg O, Stigbrand H, Hänni M, Giles JW, et al. Low-dose CT-based implant motion analysis is a precise tool for early migration measurements of hip cups: a clinical study of 24 patients. *Acta Orthop*. 2020 Feb 14;1–6.
 16. Sandberg O, Tholén S, Carlsson S, Wretenberg P. The anatomical SP-CL stem demonstrates a non-progressing migration pattern in the first year: a low dose CT-based migration study in 20 patients. *Acta Orthop*. 2020 Oct 16;1–6.
 17. Coventry MB. Evolution of hip joint replacement. *Curr Orthop*. 1987 Mar;1(3):290–6.
 18. Gomez PF, Morcuende JA. Early attempts at hip arthroplasty--1700s to 1950s. *Iowa Orthop J*. 2005;25:25–9.
 19. Knight SR, Aujla R, Biswas SP. Total Hip Arthroplasty - over 100 years of operative history. *Orthop Rev*. 2011 Sep 6;3(2):e16.
 20. Cordova LA, Stresing V, Gobin B, Rosset P, Passuti N, Gouin F, et al. Orthopaedic implant failure: aseptic implant loosening—the contribution and future challenges of mouse models in translational research. *Clin Sci*. 2014 Sep 1;127(5):277–93.
 21. Abu-Amer Y, Darwech I, Clohisy JC. Aseptic loosening of total joint replacements: mechanisms underlying osteolysis and potential therapies. *Arthritis Res Ther*. 2007;9 Suppl 1:S6.
 22. Oral E, Christensen SD, Malhi AS, Wannomae KK, Muratoglu OK. Wear resistance and mechanical properties of highly cross-linked, ultrahigh-molecular weight polyethylene doped with vitamin E. *J Arthroplasty*. 2006 Jun;21(4):580–91.
 23. Kim Y-H. Comparison of polyethylene wear associated with cobalt-chromium and zirconia heads after total hip replacement. A prospective, randomized study. *J Bone Joint Surg Am*. 2005 Aug;87(8):1769–76.
 24. De Wilde L, Van Tongel A. The history of shoulder arthroplasty*Note: This chapter is an updated version of Chapter 24, from the first edition of Joint replacement technology, edited by P. A. Revell and published by Woodhead Publishing, 2008.*. In: *Joint Replacement Technology* [Internet]. Elsevier; 2014 [cited 2020 Jun 12]. p. 571–601. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9780857098412500175>
 25. Bankes MJK, Emery RJH. Pioneers of shoulder replacement: Themistocles Gluck and Jules Emile Péan. *J Shoulder Elbow Surg*. 1995 Jul;4(4):259–62.
 26. Schrupf M, Maak T, Hammoud S, Craig EV. The glenoid in total shoulder arthroplasty. *Curr Rev Musculoskelet Med*. 2011 Dec;4(4):191–9.

27. Gregory T, Hansen U, Emery RJ, Augereau B, Amis AA. Developments in shoulder arthroplasty. *Proc Inst Mech Eng [H]*. 2007 Jan;221(1):87–96.
28. Tashjian RZ, Chalmers PN. Future Frontiers in Shoulder Arthroplasty and the Management of Shoulder Osteoarthritis. *Clin Sports Med*. 2018 Oct;37(4):609–30.
29. Papadonikolakis A, Matsen FA. Metal-Backed Glenoid Components Have a Higher Rate of Failure and Fail by Different Modes in Comparison with All-Polyethylene Components: A Systematic Review. *J Bone Jt Surg*. 2014 Jun;96(12):1041–7.
30. Karelse A, Van Tongel A, Verstraeten T, Poncet D, De Wilde LF. Rocking-horse phenomenon of the glenoid component: the importance of inclination. *J Shoulder Elbow Surg*. 2015 Jul;24(7):1142–8.
31. Dumbleton JH, Manley MT, Edidin AA. A literature review of the association between wear rate and osteolysis in total hip arthroplasty. *J Arthroplasty*. 2002 Aug;17(5):649–61.
32. Mjöberg B. Is early migration enough to explain late clinical loosening of hip prostheses? *EFORT Open Rev*. 2020 Feb;5(2):113–7.
33. Mjöberg B. Theories of wear and loosening in hip prostheses: Wear-induced loosening vs loosening-induced wear—a review. *Acta Orthop Scand*. 1994 Jan;65(3):361–71.
34. Maggs J, Wilson M. The Relative Merits of Cemented and Uncemented Prostheses in Total Hip Arthroplasty. *Indian J Orthop*. 2017 Aug;51(4):377–85.
35. Hopkins AR, Hansen UN, Amis AA, Emery R. The effects of glenoid component alignment variations on cement mantle stresses in total shoulder arthroplasty. *J Shoulder Elbow Surg*. 2004 Dec;13(6):668–75.
36. Kunutsor SK, Wylde V, Beswick AD, Whitehouse MR, Blom AW. One- and two-stage surgical revision of infected shoulder prostheses following arthroplasty surgery: A systematic review and meta-analysis. *Sci Rep*. 2019 Dec;9(1):232.
37. Gregory T, Hansen U, Khanna M, Mutchler C, Urien S, Amis AA, et al. A CT scan protocol for the detection of radiographic loosening of the glenoid component after total shoulder arthroplasty. *Acta Orthop*. 2014 Feb;85(1):91–6.
38. Greiner S, Berth A, Kääb M, Irlenbusch U. Glenoid morphology affects the incidence of radiolucent lines around cemented pegged polyethylene glenoid components. *Arch Orthop Trauma Surg*. 2013 Oct;133(10):1331–9.
39. Gregory T, Hansen U, Taillieu F, Baring T, Brassart N, Mutchler C, et al. Glenoid loosening after total shoulder arthroplasty: An in vitro CT-scan study. *J Orthop Res*. 2009 May 26;27(12):1589–95.
40. Zweymüller KA, Schwarzingen UM, Steindl MS. Radiolucent lines and osteolysis along tapered straight cementless titanium hip stems: A comparison of 6-year and 10-year follow-up results in 95 patients. *Acta Orthop*. 2006 Jan;77(6):871–6.

41. Kwong L, Jasty M, Mulroy R, Maloney W, Bragdon C, Harris W. The histology of the radiolucent line. *J Bone Joint Surg Br.* 1992 Jan;74-B(1):67–73.
42. Zhang Y, Putnam AW, Heiner AD, Callaghan JJ, Brown TD. Reliability of detecting prosthesis/cement interface radiolucencies in total hip arthroplasty. *J Orthop Res Off Publ Orthop Res Soc.* 2002 Jul;20(4):683–7.
43. Kneif D, Downing MR, Ashcroft GP, Knight DJ, Ledingham WM, Gibson PH, et al. The correlation between immediate radiolucent lines and early implant migration in cemented acetabular components. *J Arthroplasty.* 2006 Feb;21(2):215–20.
44. Baker P, Rankin K, Naisby S, Agni N, Brewster N, Holland J. Progressive radiolucent lines following the implantation of the cemented Rimfit acetabular component in total hip arthroplasty using the rimcutter technique: cause for concern? *Bone Jt J.* 2016 Mar;98-B(3):313–9.
45. Gruen TA, McNeice GM, Amstutz HC. “Modes of failure” of cemented stem-type femoral components: a radiographic analysis of loosening. *Clin Orthop.* 1979 Jun;(141):17–27.
46. Lazarus MD, Jensen KL, Southworth C, Matsen FA. The radiographic evaluation of keeled and pegged glenoid component insertion. *J Bone Joint Surg Am.* 2002 Jul;84-A(7):1174–82.
47. Molé D, Roche O, Riand N, Lévine C, Walch G. Cemented Glenoid Component: Results in Osteoarthritis and Rheumatoid Arthritis. In: Walch G, Boileau P, editors. *Shoulder Arthroplasty* [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 1999 [cited 2020 Oct 22]. p. 163–71. Available from: http://link.springer.com/10.1007/978-3-642-58365-0_16
48. Pijls BG, Valstar ER, Nouta K-A, Plevier JW, Fiocco M, Middelorp S, et al. Early migration of tibial components is associated with late revision: a systematic review and meta-analysis of 21,000 knee arthroplasties. *Acta Orthop.* 2012 Dec;83(6):614–24.
49. Nieuwenhuijse MJ, Valstar ER, Kaptein BL, Nelissen RGHH. The Exeter femoral stem continues to migrate during its first decade after implantation: 10-12 years of follow-up with radiostereometric analysis (RSA). *Acta Orthop.* 2012 Apr;83(2):129–34.
50. Sesselmann S, Hong Y, Schlemmer F, Hussnaetter I, Mueller LA, Forst R, et al. Radiostereometric migration measurement of an uncemented Cerafit® femoral stem: 26 patients followed for 10 years. *Biomed Tech (Berl).* 2018 Nov 27;63(6):657–63.
51. Wyatt M. Survival outcomes of cemented compared to uncemented stems in primary total hip replacement. *World J Orthop.* 2014;5(5):591.
52. Rahme H, Mattsson P, Wikblad L, Nowak J, Larsson S. Stability of Cemented in-Line Pegged Glenoid Compared with Keeled Glenoid Components in Total Shoulder Arthroplasty: *J Bone Jt Surg-Am Vol.* 2009 Aug;91(8):1965–72.
53. Nuttall D, Birch A, Haines JF, Watts AC, Trail IA. Early migration of a partially cemented fluted glenoid component inserted using a cannulated preparation system. *Bone Jt J.* 2017 May;99-B(5):674–9.

54. Ten Brinke B, Beumer A, Koenraadt KLM, Eygendaal D, Kraan GA, Mathijssen NMC. The accuracy and precision of radiostereometric analysis in upper limb arthroplasty. *Acta Orthop*. 2017 Jun;88(3):320–5.
55. Malchau H, Kärrholm J, Wang YX, Herberts P. Accuracy of migration analysis in hip arthroplasty. Digitized and conventional radiography, compared to radiostereometry in 51 patients. *Acta Orthop Scand*. 1995 Oct;66(5):418–24.
56. Yian EH, Werner CML, Nyffeler RW, Pfirrmann CW, Ramappa A, Sukthankar A, et al. Radiographic and computed tomography analysis of cemented pegged polyethylene glenoid components in total shoulder replacement. *J Bone Joint Surg Am*. 2005 Sep;87(9):1928–36.
57. Shareghi B. Wear and migration in total hip arthroplasty measured with Radiostereometric Analysis. Methodological aspects and clinical studies. Göteborg: Göteborgs universitet; 2018.
58. Valstar E. Digital Roentgen Stereophotogrammetry: development, validation, and clinical application. Doctoral Dissertation. Leiden, Netherlands: Leiden University; 2001.
59. Fraser AN, Tsukanaka M, Fjalestad T, Madsen JE, Röhrli SM. Model-based RSA is suitable for clinical trials on the glenoid component of reverse total shoulder arthroplasty. *J Orthop Res Off Publ Orthop Res Soc*. 2018;36(12):3299–307.
60. Kaptein BL, Valstar ER, Stoel BC, Rozing PM, Reiber JHC. A new type of model-based Roentgen stereophotogrammetric analysis for solving the occluded marker problem. *J Biomech*. 2005 Nov;38(11):2330–4.
61. Olivecrona L, Olivecrona H, Weidenhielm L, Noz ME, Maguire GQ, Zeleznik MP. Model studies on acetabular component migration in total hip arthroplasty using CT and a semiautomated program for volume merging. *Acta Radiol Stockh Swed* 1987. 2003 Jul;44(4):419–29.
62. Lell MM, Meyer E, Schmid M, Raupach R, May MS, Uder M, et al. Frequency split metal artefact reduction in pelvic computed tomography. *Eur Radiol*. 2013 Aug;23(8):2137–45.
63. Wellenberg RHH, Boomsma MF, van Osch JAC, Vlassenbroek A, Milles J, Edens MA, et al. Computed Tomography Imaging of a Hip Prosthesis Using Iterative Model-Based Reconstruction and Orthopaedic Metal Artefact Reduction: A Quantitative Analysis. *J Comput Assist Tomogr*. 2016;40(6):971–8.
64. Olivecrona H, Weidenhielm L, Olivecrona L, Beckman MO, Stark A, Noz ME, et al. A new CT method for measuring cup orientation after total hip arthroplasty: a study of 10 patients. *Acta Orthop Scand*. 2004 Jun;75(3):252–60.
65. Olivecrona H, Olivecrona L, Weidenhielm L, Noz ME, Kardos J, Maguire GQ Jr, et al. A new technique for diagnosis of acetabular cup loosening using computed tomography: preliminary experience in 10 patients. *Acta Orthop*. 2008 Jun;79(3):346–53.

66. Olivecrona L, Crafoord J, Olivecrona H, Noz ME, Maguire GQ, Zeleznik MP, et al. Acetabular component migration in total hip arthroplasty using CT and a semiautomated program for volume merging. *Acta Radiol Stockh Swed* 1987. 2002 Sep;43(5):517–27.
67. Wesolowski JR, Lev MH. CT: History, Technology, and Clinical Aspects. *Semin Ultrasound CT MRI*. 2005 Dec;26(6):376–9.
68. Seeram E. Computed Tomography: Physical Principles and Recent Technical Advances. *J Med Imaging Radiat Sci*. 2010 Jun;41(2):87–109.
69. Goldman LW. Principles of CT and CT Technology. *J Nucl Med Technol*. 2007 Sep 1;35(3):115–28.
70. Seibert JA. X-ray imaging physics for nuclear medicine technologists. Part 1: Basic principles of x-ray production. *J Nucl Med Technol*. 2004 Sep;32(3):139–47.
71. Schofield R, King L, Tayal U, Castellano I, Stirrup J, Pontana F, et al. Image reconstruction: Part 1 – understanding filtered back projection, noise and image acquisition. *J Cardiovasc Comput Tomogr*. 2020 May;14(3):219–25.
72. Goldman LW. Principles of CT: Multislice CT. *J Nucl Med Technol*. 2008 May 15;36(2):57–68.
73. Allisy-Roberts P, Williams J. Computed tomography. In: *Farr's Physics for Medical Imaging* [Internet]. Elsevier; 2008 [cited 2020 Jun 13]. p. 103–19. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9780702028441500119>
74. Shefer E, Altman A, Behling R, Goshen R, Gregorian L, Roterman Y, et al. State of the Art of CT Detectors and Sources: A Literature Review. *Curr Radiol Rep*. 2013 Mar;1(1):76–91.
75. Nieman K, Coenen A, Dijkshoorn M. Computed tomography. In: *Advanced Cardiac Imaging* [Internet]. Elsevier; 2015 [cited 2020 Jun 13]. p. 97–125. Available from: <https://linkinghub.elsevier.com/retrieve/pii/B9781782422822000056>
76. Boas FE, Fleischmann D. CT artifacts: causes and reduction techniques. *Imaging Med*. 2012 Apr;4(2):229–40.
77. Barrett JF, Keat N. Artifacts in CT: Recognition and Avoidance. *RadioGraphics*. 2004 Nov;24(6):1679–91.
78. Eriksson T, Maguire GQ, Noz ME, Zeleznik MP, Olivecrona H, Shalabi A, et al. Are low-dose CT scans a satisfactory substitute for stereoradiographs for migration studies? A preclinical test of low-dose CT scanning protocols and their application in a pilot patient. *Acta Radiol*. 2019 Dec;60(12):1643–52.
79. Zitová B, Flusser J. Image registration methods: a survey. *Image Vis Comput*. 2003 Oct;21(11):977–1000.
80. Otten V, Maguire Jr. GQ, Noz ME, Zeleznik MP, Nilsson KG, Olivecrona H. Are CT Scans a Satisfactory Substitute for the Follow-Up of RSA Migration Studies of

- Uncemented Cups? A Comparison of RSA Double Examinations and CT Datasets of 46 Total Hip Arthroplasties. *BioMed Res Int.* 2017;2017:1–11.
81. Olivecrona H, Maguire GQ, Noz ME, Zeleznik MP, Kesteris U, Weidenhielm L. A CT method for following patients with both prosthetic replacement and implanted tantalum beads: preliminary analysis with a pelvic model and in seven patients. *J Orthop Surg.* 2016 Dec 24;11(1):27.
 82. Olivecrona H, Weidenhielm L, Olivecrona L, Beckman M, Stark A, Noz M, et al. A new CT method for measuring cup orientation after total hip arthroplasty A study of 10 patients. *Acta Orthop Scand.* 2004 Jan 8;75(3):252–60.
 83. Olivecrona L, Olivecrona H, Weidenhielm L, Noz ME, Maguire GQ, Zeleznik MP. Model Studies on Acetabular Component Migration in Total Hip Arthroplasty using Ct and a Semiautomated Program for Volume Merging. *Acta Radiol.* 2003;44(4):419–29.
 84. Brodén C, Olivecrona H, Maguire GQ, Noz ME, Zeleznik MP, Sköldenberg O. Accuracy and Precision of Three-Dimensional Low Dose CT Compared to Standard RSA in Acetabular Cups: An Experimental Study. *BioMed Res Int.* 2016;2016:1–6.
 85. Scheerlinck T, Polfliet M, Deklerck R, Van Gompel G, Buls N, Vandemeulebroucke J. Development and validation of an automated and marker-free CT-based spatial analysis method (CTSA) for assessment of femoral hip implant migration In vitro accuracy and precision comparable to that of radiostereometric analysis (RSA). *Acta Orthop.* 2015;87(2):1–7.
 86. Ricchetti ET, Jun B-J, Cain RA, Youderian A, Rodriguez EJ, Kusin D, et al. Sequential 3-dimensional computed tomography analysis of implant position following total shoulder arthroplasty. *J Shoulder Elbow Surg.* 2018 Jun;27(6):983–92.
 87. Ranstam J. Methodological note: accuracy, precision, and validity. *Acta Radiol Stockh Swed* 1987. 2008 Feb;49(1):105–6.
 88. International Organization for Standardization. ISO 16087:2013. Implants for surgery- Roentgen stereophotogrammetric analysis for the assessment of migration of orthopaedic implants. 2013.
 89. Hulley S. *Designing Clinical Research.* Third. Wolters Kluwer; 2007.
 90. Ranstam J, Ryd L, Onsten I. Accurate accuracy assessment: review of basic principles. *Acta Orthop Scand.* 2000 Feb;71(1):106–8.
 91. Sköldenberg O, Odquist M. Measurement of migration of a humeral head resurfacing prosthesis using radiostereometry without implant marking: an experimental study. *Acta Orthop.* 2011 Apr;82(2):193–7.
 92. Brereton RG. The t -distribution and its relationship to the normal distribution: The t -distribution and normal distribution. *J Chemom.* 2015 Sep;29(9):481–3.
 93. Kim SH, Wise BL, Zhang Y, Szabo RM. Increasing incidence of shoulder arthroplasty in the United States. *J Bone Joint Surg Am.* 2011 Dec 21;93(24):2249–54.

94. Olivecrona H, Weidenhielm L, Olivecrona L, Beckman MO, Stark A, Noz ME, et al. A new CT method for measuring cup orientation after total hip arthroplasty: a study of 10 patients. *Acta Orthop Scand*. 2004 Jun;75(3):252–60.
95. Diagnostic Imaging Council CT Committee. The measurement, reporting, and management of radiation dose in CT. [Internet]. 2008 Jan. Report No.: 96. Available from: https://www.aapm.org/pubs/reports/RPT_96.pdf
96. Zensen S, Guberina N, Opitz M, Köhrmann M, Deuschl C, Forsting M, et al. Radiation exposure of computed tomography imaging for the assessment of acute stroke. *Neuroradiology* [Internet]. 2020 Sep 8 [cited 2020 Nov 22]; Available from: <http://link.springer.com/10.1007/s00234-020-02548-z>
97. Deak PD, Smal Y, Kalender WA. Multisection CT protocols: sex- and age-specific conversion factors used to determine effective dose from dose-length product. *Radiology*. 2010 Oct;257(1):158–66.
98. Harrison JD, Balonov M, Martin CJ, Ortiz Lopez P, Menzel H-G, Simmonds JR, et al. Use of effective dose. *Ann ICRP*. 2016 Jun;45(1_suppl):215–24.
99. Mechlenburg I, Klebe TM, Døssing KV, Amstrup A, Søballe K, Stilling M. Evaluation of periprosthetic bone mineral density and postoperative migration of humeral head resurfacing implants: two-year results of a randomized controlled clinical trial. *J Shoulder Elbow Surg*. 2014 Oct;23(10):1427–36.
100. Blom IF, Koster LA, Brinke BT, Mathijssen NMC. Effective radiation dose in radiostereometric analysis of the hip. *Acta Orthop*. 2020 Jul 3;91(4):1–395.
101. Boettner F, Sculco P, Lipman J, Renner L, Faschingbauer M. A novel method to measure femoral component migration by computed tomography: a cadaver study. *Arch Orthop Trauma Surg*. 2016 Jun;136(6):857–63.
102. Tapiovaara M, Siiskonen T. PCXMC: a Monte Carlo program for calculating patient doses in medical x-ray examinations. 2. ed. Helsinki: STUK; 2008. 49 p. (STUK A).
103. Kärrholm J. Radiostereometric analysis of early implant migration - a valuable tool to ensure proper introduction of new implants. *Acta Orthop*. 2012 Dec;83(6):551–2.
104. Klerken T, Mohaddes M, Nemes S, Kärrholm J. High early migration of the revised acetabular component is a predictor of late cup loosening: 312 cup revisions followed with radiostereometric analysis for 2-20 years. *Hip Int J Clin Exp Res Hip Pathol Ther*. 2015 Oct;25(5):471–6.
105. Lazarinis S, Mattsson P, Milbrink J, Mallmin H, Hailer NP. A prospective cohort study on the short collum femoris-preserving (CFP) stem using RSA and DXA. Primary stability but no prevention of proximal bone loss in 27 patients followed for 2 years. *Acta Orthop*. 2013 Feb;84(1):32–9.
106. Sköldenberg O, Rysinska A, Chammout G, Salemyr M, Muren O, Bodén H, et al. Migration and head penetration of Vitamin-E diffused cemented polyethylene cup compared to standard cemented cup in total hip arthroplasty: study protocol for a randomised, double-blind, controlled trial (E1 HIP). *BMJ Open*. 2016 07;6(7):e010781.

107. Radiation protection 99, Guidance on medical exposures in medical and biomedical research [Internet]. European Commission; 1998. Available from: https://ec.europa.eu/energy/sites/ener/files/documents/099_en.pdf
108. Walch G, Badet R, Boulahia A, Khoury A. Morphologic study of the glenoid in primary glenohumeral osteoarthritis. *J Arthroplasty*. 1999 Sep;14(6):756–60.
109. Gregory TM, Sankey A, Augereau B, Vandenbussche E, Amis A, Emery R, et al. Accuracy of glenoid component placement in total shoulder arthroplasty and its effect on clinical and radiological outcome in a retrospective, longitudinal, monocentric open study. *PloS One*. 2013;8(10):e75791.
110. Constant CR, Gerber C, Emery RJH, Søjbjerg JO, Gohlke F, Boileau P. A review of the Constant score: Modifications and guidelines for its use. *J Shoulder Elbow Surg*. 2008 Mar;17(2):355–61.
111. Roy J-S, MacDermid JC, Goel D, Faber KJ, Athwal GS, Drosdoweck DS. What is a Successful Outcome Following Reverse Total Shoulder Arthroplasty? *Open Orthop J*. 2010 Apr 23;4(1):157–63.
112. Dawson J, Rogers K, Fitzpatrick R, Carr A. The Oxford shoulder score revisited. *Arch Orthop Trauma Surg*. 2009 Jan;129(1):119–23.
113. Dawson J, Fitzpatrick R, Carr A. Questionnaire on the perceptions of patients about shoulder surgery. *J Bone Joint Surg Br*. 1996 Jul;78(4):593–600.
114. Bell S, Coghlan J. Short stem shoulder replacement. *Int J Shoulder Surg*. 2014;8(3):72.
115. Rasmussen JV, Harjula J, Arverud E, Hole R, Jensen SL, Brorson S, et al. The Short-Term Survival of Total Stemless Shoulder Arthroplasty for Osteoarthritis is Comparable to that of Total Stemmed Shoulder Arthroplasty: A Nordic Arthroplasty Register Association Study. *JSES Open Access*. 2019 Dec;3(4):235.
116. Karssiens TJ, Gill JR, Sunil Kumar KH, Sjölin SU. Clinical results and survivorship of the Mathys Affinis Short, Short Stem Total Shoulder Prosthesis. *Bone Jt Open*. 2021 Jan;2(1):58–65.
117. Rasmussen JV, Hole R, Metlie T, Brorson S, Äärimaa V, Demir Y, et al. Anatomical total shoulder arthroplasty used for glenohumeral osteoarthritis has higher survival rates than hemiarthroplasty: a Nordic registry-based study. *Osteoarthritis Cartilage*. 2018 May;26(5):659–65.
118. Berth A, Pap G. Stemless shoulder prosthesis versus conventional anatomic shoulder prosthesis in patients with osteoarthritis: a comparison of the functional outcome after a minimum of two years follow-up. *J Orthop Traumatol Off J Ital Soc Orthop Traumatol*. 2013 Mar;14(1):31–7.
119. Smith-Bindman R. Radiation Dose Associated With Common Computed Tomography Examinations and the Associated Lifetime Attributable Risk of Cancer. *Arch Intern Med*. 2009 Dec 14;169(22):2078.

120. Malchau H, Graves SE, Porter M, Harris WH, Troelsen A. The next critical role of orthopedic registries. *Acta Orthop*. 2015 Jan 2;86(1):3–4.
121. House of Commons, Science and Technology, Committee, House of Commons. Regulation of medical implants in the EU and UK: fifth report of session 2012-13. House of Commons London: The Stationery Office Limited; 2012 Nov. Report No.: Fifth Report of Session 2012–13.
122. Samuel AM, Rath VK, Grauer JN, Ross JS. How do Orthopaedic Devices Change After Their Initial FDA Premarket Approval? *Clin Orthop*. 2016 Apr;474(4):1053–68.
123. Migliore A. On the new regulation of medical devices in Europe. *Expert Rev Med Devices*. 2017 Dec 2;14(12):921–3.
124. Sandgren B, Skorpil M, Nowik P, Olivecrona H, Crafoord J, Weidenhielm L, et al. Assessment of wear and periacetabular osteolysis using dual energy computed tomography on a pig cadaver to identify the lowest acceptable radiation dose. *Bone Jt Res*. 2016 Jul;5(7):307–13.
125. Krauss B, Schmidt B, Flohr TG. Dual Source CT. In: Johnson T, Fink C, Schönberg SO, Reiser MF, editors. *Dual Energy CT in Clinical Practice* [Internet]. Berlin, Heidelberg: Springer Berlin Heidelberg; 2011 [cited 2020 Oct 26]. p. 11–20. Available from: http://link.springer.com/10.1007/174_2010_44
126. Saltybaeva N, Jafari ME, Hupfer M, Kalender WA. Estimates of Effective Dose for CT Scans of the Lower Extremities. *Radiology*. 2014 Oct;273(1):153–9.
127. Radzi S, Cowin G, Robinson M, Pratap J, Volp A, Schuetz MA, et al. Metal artifacts from titanium and steel screws in CT, 1.5T and 3T MR images of the tibial Pilon: a quantitative assessment in 3D. *Quant Imaging Med Surg*. 2014 Jun;4(3):163–72.
128. Röhrli SM. “Great balls on fire:” known algorithm with a new instrument? *Acta Orthop*. 2020 Nov 4;1–3.
129. Uvehammer J, Kärrholm J, Carlsson L. Cemented versus hydroxyapatite fixation of the femoral component of the Freeman-Samuelson total knee replacement: A RADIOSTEREOMETRIC ANALYSIS. *J Bone Joint Surg Br*. 2007 Jan;89–B(1):39–44.
130. Lam Tin Cheung K, Lanting BA, McCalden RW, Yuan X, MacDonald SJ, Naudie DD, et al. Inducible displacement of cemented tibial components ten years after total knee arthroplasty. *Bone Jt J*. 2018 Feb;100–B(2):170–5.

11 Appendices

11.1 Results from experimental shoulder arthroplasty study in chapter 5

Table 11-1: Accuracy of the CTMA on the humeral component with beads

	Accuracy	Mean	Min	Max	SD
X translation, mm	0.11	0.02	-0.07	0.08	0.04
Y translation, mm	0.07	0.01	-0.03	0.05	0.03
Z translation, mm	0.09	-0.02	-0.09	0.02	0.03
X rotation, °	0.34	-0.02	-0.26	0.21	0.15
Y rotation, °	0.32	0.01	-0.20	0.20	0.14
Z rotation, °	0.22	0.04	-0.12	0.13	0.09

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-2 Accuracy of the CTMA on the humeral component without beads

	Accuracy	Mean	Min	Max	SD
X translation, mm	0.15	0.04	-0.03	0.10	0.05
Y translation, mm	0.10	0.02	-0.07	0.06	0.04
Z translation, mm	0.23	- 0.02	-0.19	0.19	0.11
X rotation, °	0.45	-0.04	-0.23	0.26	0.19
Y rotation, °	0.35	-0.03	-0.21	0.13	0.15
Z rotation, °	0.23	-0.05	-0.13	0.11	0.09

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-3 Precision of the CTMA on the humeral component with beads

	Precision	Mean	Min	Max	SD
X translation, mm	0.08	0.00	-0.08	0.09	0.04
Y translation, mm	0.09	0.01	-0.07	0.08	0.04
Z translation, mm	0.11	0.02	-0.08	0.10	0.05
X rotation, °	0.26	0.01	-0.23	0.39	0.13
Y rotation, °	0.27	-0.05	-0.26	0.29	0.13
Z rotation, °	0.23	0.01	-0.17	0.24	0.11

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-4 Precision of the CTMA on the humeral component without beads

	Precision	Mean	Min	Max	SD
X translation, mm	0.10	0.00	-0.08	0.12	0.05
Y translation, mm	0.07	0.00	-0.08	0.08	0.03
Z translation, mm	0.14	0.00	-0.17	0.15	0.07
X rotation, °	0.25	0.03	-0.24	0.25	0.12
Y rotation, °	0.31	0.01	-0.29	0.43	0.15
Z rotation, °	0.21	-0.01	-0.22	0.22	0.10

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-5 Accuracy of the CTMA on the glenoid component with beads

	Accuracy	Mean	Min	Max	SD
X translation, mm	0.23	-0.02	-0.17	0.16	0.1
Y translation, mm	0.17	0.02	-0.06	0.17	0.07
Z translation, mm	0.20	0.02	-0.13	0.16	0.09
X rotation, °	0.44	-0.12	-0.28	0.05	0.14
Y rotation, °	0.48	0.06	-0.11	0.43	0.20
Z rotation, °	0.71	-0.07	-0.47	0.34	0.31

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-6 Accuracy of the CTMA on the glenoid component without beads

	Accuracy	Mean	Min	Max	SD
X translation, mm	0.19	- 0.01	-0.14	0.14	0.09
Y translation, mm	0.15	0.04	-0.03	0.14	0.06
Z translation, mm	0.15	0.01	-0.11	0.11	0.07
X rotation, °	0.34	-0.08	-0.20	0.14	0.12
Y rotation, °	0.27	0.00	-0.07	0.25	0.12
Z rotation, °	0.65	0.13	-0.19	0.4	0.25

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-7 Precision of CTMA on the glenoid component with beads

	Precision	Mean	Min	Max	SD
X translation, mm	0.15	-0.01	-0.14	0.14	0.08
Y translation, mm	0.13	0.00	-0.14	0.15	0.07
Z translation, mm	0.13	0.01	-0.14	0.13	0.07
X rotation, °	0.33	-0.02	-0.33	0.35	0.16
Y rotation, °	0.38	0.01	-0.55	0.34	0.19
Z rotation, °	0.54	0.01	-0.67	0.46	0.26

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-8 Precision of CTMA on the glenoid component without beads

	Precision	Mean	Min	Max	SD
X translation, mm	0.10	0.00	-0.13	0.15	0.05
Y translation, mm	0.08	0.01	-0.07	0.18	0.04
Z translation, mm	0.12	0.00	-0.15	0.14	0.06
X rotation, °	0.34	0.00	-0.38	0.35	0.17
Y rotation, °	0.27	0.02	-0.33	0.28	0.13
Z rotation, °	0.36	0.00	-0.55	0.35	0.18

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

11.2 Results from generalizability hip study in chapter 7

Table 11-9 Precision of CTMA on the hip cup using bone surface anatomy for image registration

	Precision	Mean	Min	Max	SD
<i>Uppsala</i>					
X translation, mm	0.07	0.00	-0.04	0.04	0.03
Y translation, mm	0.13	0.01	-0.04	0.10	0.05
Z translation, mm	0.31	0.04	-0.13	0.20	0.12
X rotation, °	0.37	0.01	-0.23	0.16	0.15
Y rotation, °	0.22	-0.03	-0.15	0.03	0.09
Z rotation, °	0.39	-0.03	-0.17	0.20	0.15
<i>Danderyd</i>					
X translation, mm	0.23	0.01	-0.12	0.24	0.10
Y translation, mm	0.11	-0.03	-0.09	0.07	0.05
Z translation, mm	0.08	-0.03	-0.10	0.00	0.03
X rotation, °	0.31	0.03	-0.15	0.24	0.13
Y rotation, °	0.28	0.01	-0.22	0.22	0.13
Z rotation, °	0.29	-0.03	-0.32	0.10	0.13
<i>Gävle</i>					
X translation, mm	0.12	0.01	-0.09	0.07	0.05
Y translation, mm	0.31	0.00	-0.36	0.16	0.14
Z translation, mm	0.15	0.03	-0.09	0.13	0.07
X rotation, °	0.28	0.03	-0.28	0.18	0.13
Y rotation, °	0.20	0.00	-0.17	0.16	0.09
Z rotation, °	0.23	0.07	-0.05	0.25	0.10

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

Table 11-10 Precision of CTMA on the hip cup using bone markers for image registration

	Precision	Mean	Min	Max	SD
<i>Uppsala</i>					
X translation, mm	0.11	0.01	-0.04	0.07	0.04
Y translation, mm	0.09	-0.01	-0.05	0.03	0.03
Z translation, mm	0.08	0.00	-0.03	0.04	0.03
X rotation, °	0.43	-0.02	-0.27	0.16	0.17
Y rotation, °	0.23	0.02	-0.08	0.14	0.09
Z rotation, °	0.22	-0.04	-0.17	0.03	0.08
<i>Danderyd</i>					
X translation, mm	0.08	0.01	-0.05	0.08	0.04
Y translation, mm	0.13	-0.05	-0.14	0.02	0.06
Z translation, mm	0.13	0.00	-0.11	0.09	0.06
X rotation, °	0.25	0.01	-0.14	0.24	0.11
Y rotation, °	0.21	0.00	-0.13	0.16	0.09
Z rotation, °	0.29	0.07	-0.10	0.30	0.13
<i>Gävle</i>					
X translation, mm	0.10	0.00	-0.04	0.08	0.04
Y translation, mm	0.19	0.01	-0.16	0.14	0.09
Z translation, mm	0.14	-0.01	-0.14	0.10	0.06
X rotation, °	0.20	0.10	-0.01	0.25	0.09
Y rotation, °	0.22	-0.03	-0.27	0.07	0.10
Z rotation, °	0.26	0.07	-0.08	0.27	0.12

Mean = mean registration errors; Min = minimum registration errors; Max = maximum registration errors; SD = standard deviation

11.3 Results from clinical shoulder arthroplasty study in chapter 8

Table 11-11 Radiolucent lines at 3 and 6 months

	3 months				6 months			
	Periphery		Centrally		Periphery		Centrally	
	Zone 1	Zone 4	Zone 2	Zone 3	Zone 1	Zone 4	Zone 2	Zone 3
Glen1	0	0-1	0	0-1	0-1	0-1	0-1	0-1
Glen2	0-1	0-1	0	0	0-1	0-1	0	0
Glen3	0	0-1	0	0-1	0	0-1	0	0-1
Glen4	0-1	0-1	0	0	0-1	0-1	0	0
Glen5	0-1	1- 2	0	0	0-1	0-1	0	0
Glen6	0-1	0-1	0	0-1	1-2	1-2	0-1	0-1
Glen7	1-2	0-1	0	0	1-2	0-1	0	0-1
Glen8	0	0-1	0	0 - 1	0-1	0-1	0-1	0-1
Glen9	1-2	0-1	0	0	1-2	0-1	0	0

Table 11-12 Radiolucent lines at 12 months

	12 months			
	Periphery		Centrally	
	Zone 1	Zone 4	Zone 2	Zone 3
Glen1	0-1	0-1	0-1	0-1
Glen2	1-2	0	0	0
Glen3	0	0-1	0	0-1
Glen4	0-1	0-1	0-1	0-1
Glen5	0-1	1-2	0	0-1
Glen6	1-2	1-2	0-1	0-1
Glen7	1-2	0-1	0-1	0-1
Glen8	0-1	0-1	0	0-1
Glen9	1-2	0-1	0	0

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