Imaging of hip trauma

Occult, suspect and concomitant fractures

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Cover illustration: MRI of the pelvis and hips (coronal T1 sequence) of a 60-year old man with nephrosclerosis. The image demonstrates occult bilateral femoral neck fractures. (*Authors' image*)

“When you come to a fork in the road, take it”

Yogi Berra

American baseball player (1925-2015)

To my family

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ABSTRACT

Background: Between one and nine percent of all hip fractures are occult or suspect and further examinations with computed tomography (CT) and/or magnetic resonance imaging (MRI) are vital for further handling. Statistically robust conclusions have not been previously reported. **Aims**: To evaluate the extent to which the observer agreement (*reliability*) differs between different modalities and different observers; if high reliability for CT in the study cases reflects the actual fracture status (*accuracy*): if occult and suspect fractures are different entities and if experience influences the diagnostics; if exclusively pelvic fractures after low-energy trauma to the hip frequently occur and to what extent ~~concomitant~~ hip and pelvic fractures co-exist. **Methods and Material:** Patients with normal or suspect radiographs and with subsequent examination with CT and/or MRI were reviewed and scored by four observers with varying radiological experience. Statistical analyses were performed with linear weighted kappa (κ) statistics and chi-square tests. **Results:** Observer agreements for all interpreters were high for CT and MRI but the accuracy for CT was inferior to MRI – in the study cases. There was a higher rate of fractures among suspect than among occult cases, both at review of radiography and at MRI. At MRI there were frequent concomitant hip and pelvic fractures as well as exclusively pelvic fractures. **Conclusions:** Occult and suspect fractures are different entities. Experience improves the diagnostic performance for both radiography and CT but is of less importance for fracture diagnosis with MRI. The reliability of CT for an experienced reviewer is high but does not necessarily correlate with high accuracy in the study population. Exclusively pelvic fractures at MRI are common after hip trauma. Hip and pelvic fractures are not mutually exclusive.

Keywords: Hip fractures, Occult, Pelvic, Radiography, Computed tomography, Magnetic resonance imaging, Observer variation

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SAMMANFATTNING PÅ SVENSKA

Bakgrund: Ungefär 2 % av alla höftfraktur är ockulta eller suspekta och kan inte adekvat diagnosticeras med konventionell radiografi varför vidare utredning med datortomografi (DT) och/eller magnetkameraundersökning (MR) är avgörande för fortsatt handläggning. Studier stora nog för statistiskt hållbara slutsatser har inte gjorts för radiografi, DT eller MR för ockulta eller suspekta höftfrakturer. ***Syfte***: Syftet med avhandlingen var att utvärdera i vilken utsträckning den diagnostiska överensstämmelsen (*reliability*) skiljer sig mellan olika bedömare och modaliteter; om hög *reliability* för CT i utvalda fall korrelerar med verkligt frakturstatus (*accuracy*); om radiografiskt ”ockulta” respektive ”suspekta” frakturer är olika entiteter och om radiologisk erfarenhet är betydelsefull för diagnostiken; om isolerade bäckenfrakturer efter låg-energi trauma mot höften är vanligt förekommande och i vilken utsträckning höft- och bäckenfrakturer samexisterar. ***Metoder***: Materialet avser retrospektiv bildbehandling. Konsekutiva patienter över 50 år med klinisk misstänkt höftfraktur med normal eller suspekt (fraktur) radiografi och efterföljande undersökning med DT och/eller MR samlades in under 9 år. Bilderna har eftergranskats av fyra radiologer med varierande radiologisk erfarenhet. Fallen diagnosticerades som negativ, suspekt eller definitiv fraktur och kategoriserades som cervikal eller trokantär fraktur. Materialet bearbetades statistiskt med linjärt viktad kappa (κ) respektive chi-två-fördelning. ***Resultat***: Den diagnostiska överensstämmelsen mellan eftergranskarna var hög för DT och MR men den diagnostiska ”korrektheten” (*accuracy*) var lägre för DT i flera fall. En högre andel suspekta än ockulta frakturer kunde verifieras vid såväl eftergranskning av radiografi som på MR. På MR noterades att samtidigt förekommande höft och bäckenfrakturer var vanligt samt att en fjärdedel av höfttraumapatienterna hade enbart bäckenfrakturer. **Konklusioner**: Radiologisk erfarenhet skärper diagnostiken för radiografi och CT men är av underordnad betydelse för diagnostik av ockulta och suspekta frakturer med MR. Ockulta och suspekta frakturer är olika entiteter. CT har hög *reliability* för erfarna bedömare men i enstaka fall återspeglar detta nödvändigtvis inte den diagnostiska ”korrektheten”. Isolerade bäckenfrakturer är vanligt vid höfttrauma. Höft- och bäckenfrakturer kan förekomma samtidigt.

LIST OF PAPERS

This thesis is based on the following studies, referred to in the text by their Roman numerals.

I. Collin D, Dunker D, Göthlin J.H, Geijer M. **Observer variation for radiography, computed tomography, and magnetic resonance imaging of occult hip fractures.** Acta Radiol. 2011 Oct 1;52(8):871-4.

II. Collin D, Göthlin J.H, Nilsson M, Hellström M, Geijer M. **Added value of interpreter experience in occult and suspect hip fractures: a retrospective analysis of 254 patients.** Emerg Radiol. 2016 Feb 25. [Epub ahead of print].

III. Collin D, Geijer M, Göthlin J.H. **Computed tomography compared to magnetic resonance imaging in occult or suspect hip fractures. A retrospective study in 44 patients.** Eur Radiol. 2016 Jan 8. [Epub ahead of print].

IV. Collin D, Geijer M, Göthlin J.H. **Prevalence of exclusively and concomitant pelvic fractures at magnetic resonance imaging of suspect and occult hip fractures.** Emerg Radiol. 2016 Feb;23(1):17-21.

CONTENT

ABBREVIATIONS

AO	Arbeitsgemeinshaft für Osteosynthesefragen
AP	Antero-Posterior
CT	Computed Tomography
DHS	Dynamic Hip Screw
HIS	Hospital Information System
HTA	Health Technology Assessment
MRI	Magnetic Resonance Imaging
OTA	Orthopaedic Trauma Association
PACS	Picture Archiving and Communication System
RIS	Radiology Information System
STIR	Short Tau Inversion Recovery
TE	Echo Time
TR	Relaxation Time

DEFINITIONS

All definitions below are adapted for the purpose of the current thesis, applicable to occult and suspect hip fractures after low-energy trauma.

Accuracy	The extent of which image interpretations represent the truth according to an acceptable reference standard
Agreement	The likelihood that one observer will indicate the same response as another observer
Bone bruise	Injuries of cancellous bone consistent with oedema, haemorrhage and/or trabecular disruptions best visualised with MRI as ill delineated areas of low signal intensity on T1-weighted images and high signal intensity areas on T2-weighted or STIR images
Clinical utility	Evaluation of diagnostic accuracy with regard to appropriate management based on the best available evidence about the criteria for the intervention
Fracture (at MRI)	Ill or well defined abnormal bone marrow low signal on T1-weighted sequences flanked by high signal areas of various intensity on STIR or fat-saturated T2-weighted sequences

Gold standard	An imaging modality with the highest accuracy for detection of hip fracture, against which other imaging modalities are compared
Incidence	The rate at which a specified event occur during a specified period in a specified population
Low-energy trauma	Injuries caused by the equivalent to falls from standing height or less
Occult fracture	A fracture where the clinical findings are suggestive of a fracture but without radiographic evidence at index admission
Prevalence	The proportion of particular findings in the population being studied
Reliability	Measures the level of diagnostic agreement by different observers (*inter-observer* reliability) or by the same observer (*intra-observer* reliability) on the same images under identical conditions
Suspect fracture	Clinical suspicion of fracture with inconclusive radiographic changes in cancellous or cortical bone suggestive of fracture but not enough for final diagnoses

INTRODUCTION

Anatomy in relation to fracture

Hip and pelvis

The proximal femur forms the hip joint with the pelvis. It consists of head, neck and two bony processes called the greater and lesser trochanters within the trochanteric region. The bony pelvis is a ring-shaped structure bordered posteriorly by the sacrum and coccyx; laterally by the ilium; and anteriorly by the ischium and pubis; the latter three bones are fused as the innominate bone. The innominate bone is joined posteriorly over the sacroiliac joint to the sacrum, a triangular bone comprising five vertebral segments, and anteriorly by the strong ligaments of the pubic symphysis (Figure 1). Isolated pelvic fractures may occur after low-energy trauma to the hip, but as rigid bone rings tend to break at two sites, careful evaluation for a second fracture or for disruption of the pubic symphysis or sacroiliac joints must be made. Also, fractures of the pubic rami often involve both the superior and inferior rami, may be unilateral or bilateral and are frequently accompanied by sacral fractures. Non-displaced fractures of the pelvic bones may be hard to diagnose at routine radiography due to obscuring bowel gas and limited quality of standard radiographic anteroposterior (AP) projections. Also, the fracture extent is frequently underestimated. Thus, additional imaging with CT and/or MRI may be performed in difficult cases for full diagnostic evaluation.

Anatomical landmarks of the pelvis and hip

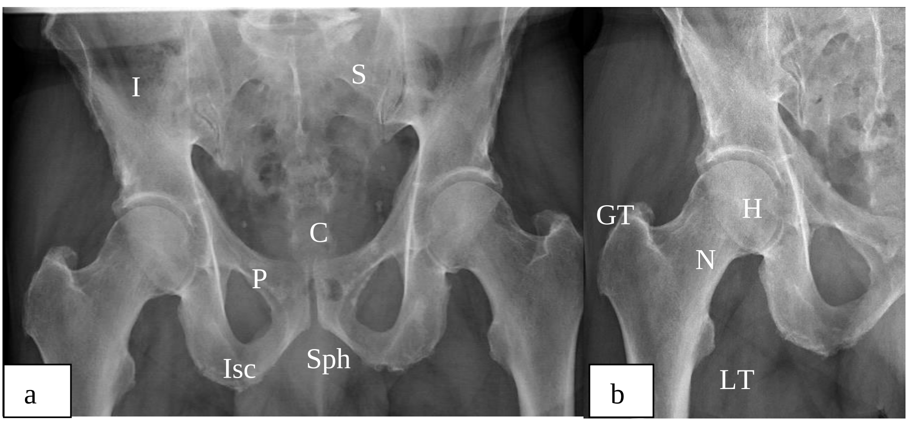


Figure 1. AP radiographs of pelvis and hip: a) I=Ilium, Isc=Ischium, P=Pubic bone, S=Sacrum, C=Coccyx, Sph=Symphysis. b) H=Femoral head, N=Femoral neck, GT=Greater trochanter, LT=Lesser trochanter.

Blood supply

There are many anatomical variations of the blood supply to the proximal femur. In standard anatomy textbooks, the femoral head and neck is supplied by three main sources: the *medial femoral circumflex artery* (MFCA), the *lateral femoral circumflex artery* (LFCA) and the *obturator artery* (OA). The MFCA is the largest contributor of blood supply to the femoral head. Together with the LFCA it forms an extracapsular ring at the base of the femoral neck and supports the femoral head through intracapsular terminal branches that runs parallel to the femoral neck. The obturator artery supplies the femoral head through the ligamentum teres and plays an important role in children and adolescents with remaining cartilage in their epiphyseal line which prevents blood from flowing through it. However, in adulthood the obturator artery becomes atretic and constitutes only a minor component of the blood supply to the femoral head [3]. Thus, the adult femoral head is almost entirely dependent upon arteries that pass through the femoral neck region. In event of a femoral neck fracture, these ascending intracapsular arteries may rupture with interruption of blood supply to the femoral head. Thus a devastating result of femoral neck fractures may be avascular necrosis of the femoral head [4]. In addition, even if debated in the literature, the ruptured vessels may cause intracapsular hematoma with an increased intracapsular pressure and possibly a tamponade effect which can further reduce blood flow to the femoral head [5-7]. The extracapsular region of the proximal femur constitutes bone with good blood supply from branches from the deep femoral artery, nutrient vessels and multiple periosteal vessels why the rates of avascular necrosis are lower with intertrochanteric fractures than with cervical fractures [8].

Trabecular bone

There are five definable trabecular groups in the proximal femur [9]: Principal compressive (PCT), principal tensile (PTT), secondary compressive (SCT); secondary tensile (STT) and greater trochanteric trabeculae (GTT). PCT is vertically oriented and extends from the femoral head into the femoral neck; PTT is oriented in an arcuate manner, extend from below the fovea to the lateral margin of the greater trochanter; SCT extends from the lesser trochanter towards the greater trochanter; STT start below the PTT and end superiorly, just after midline, along the upper end of femur; GTT is curvilinear in the greater trochanter. Trabecular bone mass decreases with age in a typical sequential pattern [10]. Non-weight bearing trabeculae (GTT, STT and PTT) are lost earliest (Figure 2a).

The properties of internal-weight bearing are linked to the orientation of the trabecular groups and loss of trabecular integrity plays an important role in the occurrence of predominantly trochanteric hip fracture [11]. As trabecular integrity decreases with age trabecular load-bearing properties will gradually change. This may partly explain why the same trauma mechanism, i.e., falls on the greater trochanter, leads to different types of fractures, including incomplete fractures (intact medial cortex).

Cortical bone

While trabecular bone certainly is of importance in determining resistance to fracture in the trochanteric region, cortical bone has been shown to play a major part in the femoral neck [11, 12]. The cortical bone is generally encasing trabecular bone and can sustain greater load than trabecular bone and deforms little before failure [11]. The cortical thickness of the proximal femur varies between 1-5 mm in middle-aged and elderly people and is thickest along the inferomedial portion of femoral neck and the intertrochanteric region [13, 14]. In age related bone loss, the resorption from the endocortical inner surface exceeds new bone formation from the outer, periosteal, side [15]. As the cortices are thinning out with age, the risk of hip fracture increases. The periosteum is a fibrous tissue and plays a major part in bone growth and repair and encloses almost every extra-cartilaginous cortical bone in the body. Thus, the femoral neck within the hip joint that is not protected by periosteal bone formation is predominantly vulnerable [15, 16].

Calcar femorale

The *calcar femorale* is a vital structure of the proximal femur and redistributes load bearing strain by decreasing the force in the posterior and medial femur and increasing the force in the anterior and lateral aspects [17]. The properties of the calcar femorale resemble cortical bone but it is less dense, less stiff and has a slightly less mineral content [18]. The calcar femorale is commonly involved in hip fracture and it has been proposed that if the calcar femorale is broken the fracture can be considered unstable [19]. On the other hand, a fracture starting in lateral cortex may go through the posterior cortex without affecting the reinforced medial cortex and may thus be termed stable. In the literature the calcar femorale is often confused with the medial cortex (Figure 2b-c) but is in fact a dense vertically oriented structure that reinforces the medial cortex to the mid-level of the lesser trochanter and from there runs posteriorly to the neutral axis of femur in a medial to lateral direction [20].

Anatomy of trabecular bone and the calcar femorale

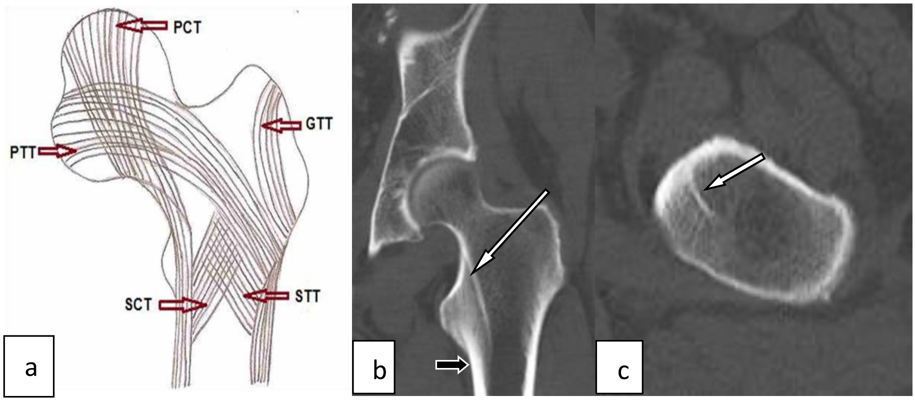


Figure 2a-c). Trabecular groups and the calcar femorale are depicted: a) PCT=principal compressive, PTT=principal tensile, SCT=secondary compressive, STT=secondary tensile and GTT=greater trochanteric trabeculae. b) Coronal and c) transversal CT images. The calcar femorale is seen as a white strand (white arrows), running distally from the medial femoral neck in a posterior and lateral manner. It should not be confused with the medial cortex (black arrow).

Hip joint capsule

In case of a hip fracture the joint capsule may be disrupted. The capsule is a strong and dense structure that envelopes the femoral head and neck and originates from the labrum and the bony acetabular rim. The capsule inserts anteriorly to the intertrochanteric line and posteriorly to the base of the neck close to the intertrochanteric crest and the lesser trochanter. The capsule is thinning out distally with its thinnest part posteriorly. The capsule has two sets of fibers; longitudinal and circular; and is reinforced by three strong ligaments (the iliofemoral, ishiofemoral, and pubofemoral ligaments) [21]. Fractures within the line of insertion of the joint capsule are by definition intracapsular while fractures that does not directly involve the joint capsule are extracapsular [22].

Fracture classification

There is no existing clinical decision rule that allow clinicians to exclude a non-displaced hip fracture without imaging [23]. Radiographically occult or suspect hip fractures are non-displaced and may be incomplete. Thus all fractures in the thesis belonged either to Garden type 1 or type 2 for cervical fractures [1] or to type 1 of the Tronzo classification system [24] for incomplete trochanteric fractures or to type 1 in the Evans classification system [25] for non-displaced trochanteric fractures. The different classification systems are used in clinical trials to group fracture patterns together in order to draw general conclusions about which treatment regime suits better with which fracture subtype. Typically, hip fractures are grouped into stable and unstable categories since the degree of stability is important in terms of how the fracture heals with an optimally surgically placed device. Fracture healing is best accomplished for stable (non-displaced) fractures while complications are more likely to occur among unstable, more or less comminute fractures. Occult and suspect fractures are non-displaced and can be regarded as stable.

Cervical fractures

Among the different classification systems for cervical hip fractures (AO, AO subgroup, Pauwels, Garden), the most widely used is the Garden classification system (Figure 3a) which also have shown the best reliability [1, 26, 27]. Garden stage I and II fractures are considered non-displaced and inherently stable fractures that can be treated with internal fixation. Garden stage III-IV constitute displaced fractures, usually treated with either hemi- or total arthroplasty [28]. Radiographically occult or suspect hip fractures are non-displaced and may be incomplete.

Trochanteric fractures

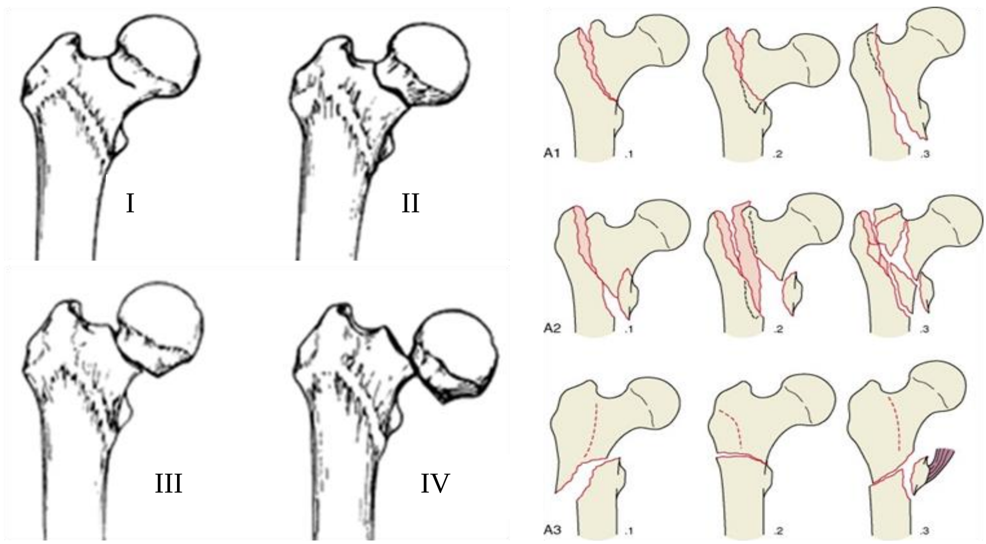
There are several classification systems for trochanteric fractures [24, 29, 30]. The most frequently used are AO/OTA classification [2] and the Evans classification modified by Jensen [30]. For the AO/OTA system, trochanteric fractures are labelled as type 31-A. These fractures are in turn divided into the groups A1, A2 and A3, and each group is further subdivided into three subgroups (Figure 3b). Group A1 fractures are two-part fractures defined as inherently stable meaning that secondary displacement after surgical treatment is uncommon. Group A2 represent fractures with multiple fragments and are generally regarded as unstable, even if some authors consider A2.1 as stable

[31]. Fractures belonging to the A3 group are unstable and commonly described as reverse oblique and simple transverse [32].

Fractures belonging to Evans/Jensen type I are non-displaced, either at initial radiography or after reduction, and are considered stable. Type II (Evans type III and IV) fractures are difficult to reduce in only the coronal or the sagittal plane, while Type III (Evans type V) comprises very unstable fractures, problematic to reduce in both planes. Type I and II of the Tronzo classification system are non-comminute fractures, without and with dislocation, respectively. Type III and IV fractures are more or less comminute and deviated and type V presents with reverse obliquity. Tronzo type I and II fractures are considered stable of which type I entails *incomplete* trochanteric fractures. Types III, IV and V are defined as unstable [24].

Cervical fractures *Trochanteric fractures*

Garden I-IV *AO/OTA 31.A*



a b

Figure 3a-b. a) Garden classification of femoral neck fractures [1]. b) AO/OTA classification of the trochanteric region[2]. (a. Copyleft under Creative Commons Attribution; b. Redrawn from Müller, M.E, et al).

Basicervical fractures

Intracapsular fractures include the femoral head and neck and extracapsular fractures the trochanteric- and subtrochanteric region. A unique type of hip fracture, commonly termed basicervical, is described in the literature [33, 34]. Basicervical fractures occur at the base of the femoral neck and involve both the intra- and extracapsular region. The fractures correspond to an intermediate type between cervical and trochanteric fractures, not classified as a separate entity in commonly used classification systems [2, 24, 25, 29] but equivalent to 31- B2.1 according to the AO/OTA classification system (Figure 4). These fractures have potentially greater instability than stable intertrochanteric fractures [35] but are generally treated in a similar manner as trochanteric fractures and were for the purpose of this thesis classified as extracapsular.

Basicervical fracture

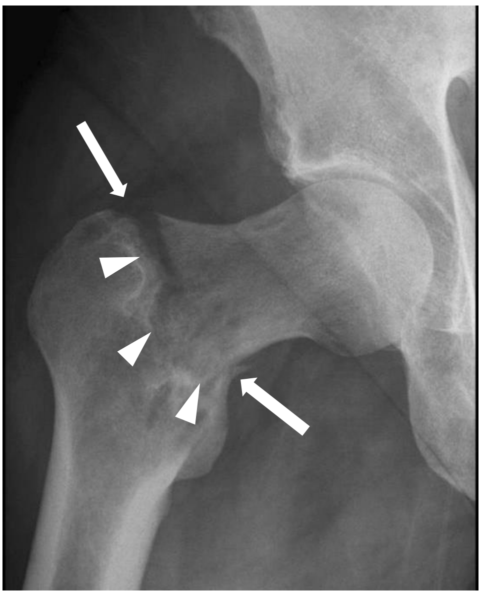


Figure 4. AO/OTA classification of basicervical fracture 31-B2. The fracture (white arrows is depicted just proximal to and alongside the intertrochanteric line (arrowheads)

Incomplete fractures

Femoral neck fractures suffer from high rates of subsequent displacement and the possibility of developing avascular necrosis. Occasionally, femoral neck fractures are incomplete with maintained integrity of the posteromedial cortex, thus belonging to Garden I fractures in the Garden classification system. These fractures are potentially more stable than non-displaced complete fractures (Garden II). Even if surgical treatment of non-displaced femoral neck fractures is uncontroversial and the contemporary treatment of choice [36, 37] it is interesting to note that perusal of the literature reveals two reports on 38 and 56 patients suggesting that conservative treatment is a valid option for these fractures [38, 39]. Of the various classification systems only the Tronzo classification system [24] encompasses *incomplete* trochanteric fractures. An incomplete trochanteric fracture emanates from the greater trochanter towards the lesser trochanter without breaching of the medial cortex and is frequently seen among radiographically occult or suspect fractures at MRI. In incomplete trochanteric fractures the lesser trochanter is not displaced, there is no comminution and the cortices of the proximal and distal fragments are aligned. Two recent reports advocate that incomplete trochanteric fractures can only with certainty be diagnosed with MRI and may be considered for conservative treatment [40, 41]. In this context, on the basis of treatment regimes, incomplete fractures may be regarded as a separate entity.

Epidemiology

Health Technology Assessment (HTA) means determination of the value of medical technology. Its purpose is to bridge clinical and outcomes research with policy making to answer the key questions of buyers, providers and users of health care services: do these methods work? For whom and at what cost? How do they compare with alternative methods? HTA should explore and analyze technical properties, safety, efficacy-effectiveness, economic impact, social, legal and possibly political consequences. The clinical utility of radiology is its capacity to make a decision possible to adopt or to reject a therapeutic action with best possible consequences for patients, staff and the clinical context [42].

There are no clinical decision rules that allow clinicians to exclude hip fractures without imaging. Most hip fractures can be diagnosed by conventional radiography. Frequently, AP pelvis and hip radiographs plus a cross table lateral radiograph are performed. Good quality radiography has a sensitivity of 90-98% and only a minor proportion of fractures will be missed

[23]. The occult, or “hidden” hip fracture is a fracture where the clinical findings are suggestive of a fracture but this is not confirmed by radiography [23]. A radiographically suspect fracture may show subtle radiographic signs that are not sufficient for definite diagnosis. In radiology, several diagnostic methods are taken for granted without thorough evaluation. One example is occult hip fractures where computed tomography and magnetic resonance imaging as second-line investigation have not been evaluated with reasonable statistical robustness. The advantages of prompt and accurate diagnoses are in the literature presented as ethical, humanitarian, social, economic, decrease in co-morbidity and mortality, faster treatment and rehabilitation planning. In short, delayed diagnoses are associated with higher costs, prolonged suffering and poorer health outcome [43-45].

The established second-line imaging investigations for detection of occult or suspect hip fractures are radionuclide scanning (scintigraphy), CT and MRI. Radionuclide scanning is expensive and requires intravenous radioactive isotopes, thus usually not favored due to its delay in results. False-positive scans are common as any process that leads to increased bone turnover will demonstrate increased radionuclide uptake. Also, the poor spatial resolution of scintigraphy makes diagnosis of the entire fracture extent difficult. Ultrasonography have not gained acceptance while MRI is widely accepted and regarded as gold standard for fracture diagnosis. On the other hand, CT is readily available in both hospitals and emergency departments, is fast to perform with few contraindications and is frequently used as second line examination in routine practice for these reasons. Even if CT has been reported to have somewhat lower accuracy in fracture diagnosis compared to MRI, the data directly comparing the performance of CT with MRI for radiographically occult or suspect hip fractures in the elderly is sparse [46-49]. If CT can be shown to have comparable accuracy to MRI, there will be extensive implications because of its fastness and widespread availability. The lack of larger materials of CT and MRI and questionable statistical robustness prompted the current thesis.

Hip fractures are a major and increasing health problem worldwide with the highest incidence among citizens of advanced age. Elderly people are the fastest growing age group in the world [50]. Compromised bone strength, such as osteoporosis, is closely related to older age why the incidence of “older-age low-trauma fracture” is likely to increase. Hip fracture is one of the most devastating result of osteoporosis; it requires the patient to be admitted to hospital and causes serious morbidity, excess mortality and high socio-economic costs [44]. Even if age-adjusted incidence rates for hip fracture remain stable [51], the number of hip fractures worldwide is estimated to rise from 1.7 million in 1990 to 6.3 million in 2050 [52]. In Sweden, the annual incidence of hip fractures is about 18 000 out of a population of 9.5 million, among the highest reported incidence in the world and is expected to double from year 2002 to 2050 [53].

The diagnosis of hip fracture can usually be made by plain radiography [23]. Observational studies suggest that treatment within 24 hours is beneficial in terms of shorter hospital stay, better functional outcome and lower rates of complications and mortality [44, 54, 55]. However, other studies have been published, showing no significant difference between timing of surgery and adjusted mortality rates. A delay in surgery may offer an opening to optimise conditions of co-morbidity and consequently reduce the risk for perioperative complications [56, 57]. Even if timing of surgery may not unequivocally affect mortality and morbidity, clinical guidelines recommend surgical treatment within 24-48 hours [58-60]. The recommendations are based on that elderly patients "are at risk of complications, and on compassionate grounds merit early intervention" [61]. Besides patients requiring orthopaedic attention and intervention, the medical, rehabilitative, social and psychological consequences strongly influence the health care economics [62-65].

Costs

The estimated costs for treatment and rehabilitation of hip fractures in Sweden are estimated to 2.3k million SEK. The costs are identified as those for the orthopaedic department, geriatric care, other acute care and rehabilitation facilities, such as nursing homes or municipal home-help [66]. On an individual level the estimated average cost over a 1-year period has been found to increase with advancing age and has been calculated to between 140,000 – 400,000 SEK, where the higher interval represent patients aged 100 years [67]. Hip fractures account for more than half fracture-related direct medical costs and the average length of hospital stay for hip fracture is higher than, for example, heart attacks and chronic obstructive pulmonary disease [68].

Incidence of occult and suspect hip fractures

The vast majority of all patients with hip fractures can readily be diagnosed with radiography but in a few cases the fracture is invisible or inconclusive at radiography why second-line examinations with CT and/or MRI are vital for further handling. These fractures are termed "occult" or "suspect". When supplementary radiological examination is necessary it is most commonly performed with MRI [69-71] and less commonly with CT [72-74]. Several guidelines support MRI as the imaging of choice for suspected hip fracture not evident on initial radiographs [23, 75, 76]. The prevalence of radiographically occult and suspect fractures are not yet established in the literature but is estimated to be between one and nine percent [23, 70, 77, 78].

At our clinic, approximately every third patient with clinical suspicion of hip fracture is confirmed with radiography and about 1000 patients annually are surgically treated [79-82]. Of these, about 50 patients annually have inconclusive radiographs with evidence of fracture at second-line imaging with CT and/or MRI. In very rare cases the CT examination is also inconclusive, prompting further examination with MRI. However, the incidence of these rare occult fractures after CT cannot successfully be calculated. One reason is that the scarcity of these fractures provides poor statistical basis. Another reason is that CT in most cases is sufficient for confirmation or exclusion of fracture, wherefore a “gold standard” MRI is lacking for the majority of the cases. The incidence of occult fractures after CT is, however, very low.

Imaging History

Radiography

Late at night on November 8, 1895, Wilhelm Conrad Röntgen (1845-1923), a German physicist discovered the X-ray. In mathematics, the letter x denotes the unknown. Röntgen referred to the radiation as “X” to indicate a yet mysterious type of rays [83]. In fact, X-rays are electromagnetic radiation with short wavelengths within the range of 0.01-10 nanometres (1×10^{-9} m), which corresponds to a frequency in the range 30 petahertz to 30 exahertz (3×10^{16} to 3×10^{19} Hz) and energies typically around 100 eV to 100 keV [84]. For medical applications, X-rays are usually produced in vacuum tubes by accelerating electrons and letting them bombard a metal target, commonly made of tungsten (W) with 74 protons in the nucleus. If the energy of the colliding electrons is high enough some of them (approximately 5%) will approach the nucleus of the target metal atoms, decelerate and change direction due to the positive charge of the protons and lose kinetic energy in form of a photon. These emitted photons constitute the X-rays [84]. By letting the X-rays travel through a patient towards an X-ray detector on the other side, a radiograph can be produced, representing the various amount of absorbed radiation (attenuation) from tissues of different densities inside the body. The predominant phenomenon that produces good contrast for different tissues on the radiographs is the photoelectric effect. The phenomenon occurs when an x-ray photon uses up all of its energy by interacting with one of orbiting electrons of the atom, usually from the closest shell to the nucleus (K-shell). In the interaction, the electron is ejected from the atom and the x-ray photon is completely absorbed in the process. The process can only take place if the electron binding energy is equal to, or less than, the x-ray photon energy. Also, with increasing atomic number, the photoelectric effect is more likely to occur [85]. Thus, x-ray photons that pass throw bone (high atomic number) are absorbed to a higher extent which results in a low exposure to the correlating part of the film. Rontgen took the very first X-ray of his wife Anna Bertha´s hand two weeks after his discovery (Figure 5).

Insights on the medical implications for skeletal trauma spread quickly in 1896 after a publication "Über eine neue Art von Strahlen" [86]. After coverage in international papers, such as *The New York Sun* and a publication in the *British Medical Journal* his discovery soon became replicated in Europe and America. In 1901, Röntgen was awarded the first Nobel Prize in Physics "in recognition of the extraordinary services he has rendered by the discovery of the remarkable rays subsequently named after him".

Figure 5. "Hand mit Ringen". Print of Wilhelm Rontgen's famous X-ray, of his wife Bertha's hand, taken on 22 December 1895.

In the course of the history of the X-rays, the images are still produced by a certain amount of radiation being absorbed by the different densities of different tissues. However, the radiographic equipment has developed from analogue systems, through computed radiography (CR) to direct and indirect digital systems (DR) with faster automatically processed imaging of increasing quality [87]. Today, radiography is realised in a variety of fields, from medicine and industry to numerous areas of inspection, e.g., as metallurgical material identification and diverse security systems. The medical applications of radiography have expanded from viewing skeletal structures and lung lesions, such as tuberculosis, to abdominal studies with barium X-ray absorbers (contrast agents) in purpose to coat the inside wall of the gastrointestinal tract for various characteristics, such as contour and patency. As a consequence, the annual number of radiography examinations in Sweden has increased from 1.7 million in 1960 to 4 million in 2005, of which the percentage of hip and pelvis examinations can be estimated to 10% [88].

Computed Tomography

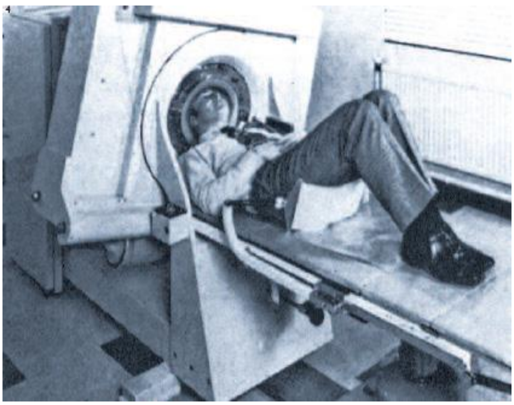


Figure 6. The first clinical prototype EMI brain scanner installed at Atkinson Morley´s Hospital, in London, England 1971.

In 1979, the South African born physicist Allan Cormack (1924-1998) and the British engineer Godfrey Hounsfield (1919-2004) shared the Nobel Prize in physiology or Medicine, “for the development of computer assisted tomography”. The idea of computed tomography (CT) is based on letting both the x-ray source and the digital detector rotate around the patient’s body to produce a sectional image. As two dimensional imaging of conventional X-ray was limited in distinguishing between soft tissue of differing densities, Cormack hypothesised that more information about these tissues could be obtained if the conventional X-ray techniques allowed imaging from multiple directions. To accomplish this assumption he devised an algorithm with the use of a computer to calculate the data. The algorithm constitutes the mathematical foundation for tomographic reconstruction and in the early 60s he showed that different attenuation from different tissues could be calculated by letting the X-rays pass from many different angles. In the late 60s, Hounsfield, unaware of Cormack´s significant work, built a prototype device intended to measure the exact variations in attenuation across a phantom using a single gamma ray source with a single detector [89]. By measuring the difference in attenuation and by rotating the device in small steps about the phantom he showed that the internal composition of the phantom could be reconstructed, solely by using external measurements. In 1971, CT was introduced in clinical praxis by imaging the brain of patient with a brain tumour. The same year, the entity of brain scans generated by CT was presented at the *32nd Congress of the British Institute of Radiology*. Shortly thereafter, the presentation was published as an abstract in the *British Journal of Radiology* [90]. In 1973, the first CT in Sweden was installed at the Karolinska Hospital, at the Department of Neuroradiology. It was the third CT to be delivered outside the UK [91]. The following years CT scanners were distributed in Asia, Europe and the U.S. However, as for radiography, the early CT scans were radiation intensive and produced images with low resolution. They also required several hours to yield the scans and to process the data. From the mid-1970s, developments in CT technology and high performance computing techniques have evolved rapidly. In 1975 the scan time had been reduced from several minutes for an 80 x 80 matrix to 20 seconds for a 320 x 320 matrix and one year later to 5 seconds for a matrix size of 512 x 512. In the late 1980s, scan times were down to 3 seconds and matrix sizes up to 1024 x 1024. In the early 1990s multi-slicing with 4-slice scanners and 0.5 second scan times were used in clinical praxis [92]. Development of multi-slice scanners has continued through the 21st century. Today, scanners capable of scanning 256 slices per gantry rotation are state of the art. They can cover 40 mm in less than 0.4 seconds and produce images of the whole body with high spatial resolution in about 30 seconds. Three-dimensional (3D) reconstruction algorithms with routine applications for volume scanning for cardiovascular studies, oncology and trauma are implemented. The usage of CT has dramatically increased since it was introduced. In the U.S, the number of CT scans has increased from three million in 1980, to 20 million in 1995, to over 60 million in 2005 [93]. In Sweden, the annual number of CT examinations have more than doubled from 340.000 in 1995 to 650.000 in 2005 of which 3.500 examinations where of the pelvis and hips [88]. Thus, the high imaging quality for a wide range of illnesses and the rapid acquisition time has made

CT the work horse for a wide range of conditions. However, the role of CT in diagnosing radiographically occult and suspect hip fractures is not entirely evaluated. Even if CT has the ability to detect most such fractures, the main advantage compared to MRI lies within the capability in assessing mineralised cortical bone [94] rather than marrow changes adjacent to the fracture line [95]. Several previous studies have been published on the value of CT as a good second-line investigation but the studies comprise relatively small materials, lacks an imaging gold standard for all cases or show inferior diagnostic accuracy compared to MRI [46-49, 72, 73, 96]. Thus, the performance of CT in hip fracture diagnostics is not fully evaluated.

Radiation concerns

Due to its very short wavelength, X-rays can penetrate materials that light cannot. However, the high energy levels of these short waves can break chemical bonds in living tissue resulting in altered cell structure and predispose for cancer. Through the decades of exponentially increased use of X-ray techniques, evidence of radiation carcinogenesis soon followed. In order to reduce radiation doses to patients and staff, various safety procedures, such as collimated x-ray beams, the use of lead shielding, and rapid exposures with high frequency generators was developed. Thus, parallel to the development of imaging performance, manufacturers focus on how to reduce the radiation dose, limiting the possibility of radiation induced cancers, without compromising the image quality. Educational efforts are made in instructing staff in how to adjust peak voltage (kVp) and tube current-time product (mAs). New software technologies have been developed such as the implementation of digital radiography and the use of automatic exposure control (AEC), allowing automatic dose adjustments for CT based on the patients attenuation, which can vary longitudinally (z-axis) and angularly for the patient’s body composition and body organ examined. Studies have showed that digital radiography and AEC can reduce patient dose by 50% with preserved imaging quality [97-99]. Thus, despite invariant low patient compliance in emergency room settings and intensive unit care, imaging with acceptable radiation doses can easily be achieved.

Magnetic Resonance Imaging

Unlike radiography and CT, which use x-rays, differences between tissues can be pictured in high detail due to the magnetic properties of atomic nuclei. The technique is based on that magnetic fields and radio waves cause atoms to emit radio signals. By introducing gradients in the magnetic field, Paul Lauterbur (1929 – 2007), an American chemist, introduced the use of magnetic gradient fields to determine the spatial origin of the radio waves emitted from the nuclei of the object of study. His findings were published in 1973 [100]. As for early radiography and CT, the MRI technique was at first slow. In order to speed up the process, the English physicist Peter Mansfield (born 1933) in 1977 developed the mathematical foundation for obtaining more rapid and precise imaging through very fast gradient variations, known as echo planar imaging (EPI). Lauterbur and Mansfield shared the Nobel Prize in Physiology or Medicine in 2003 for their achievements in developing magnetic resonance imaging. During the last decades, the number of MRI scanners as well as scans performed increases continuously worldwide from 10 scanners in 1980 to an estimate of 35.000 installed scanners in 2012 [88]. In Sweden, approximately 270.000 MRI examinations were performed in 2005 of which 63.000 were of the extremities, (explicit numbers of hip and pelvis examinations were not reported).

The sensitivity (100%) and specificity (93 - 100%) of MRI in detecting occult hip fractures is well established and MRI has been recognised as the reference standard investigation for diagnosing these cases [94]. Since MRI is highly sensitive in discriminating between hydrogen protons densities it has the ability to delineate various tissues, such as cortical and trabecular bone. In case of a fracture, oedema and haemorrhage, with high water content, will accumulate within the injured area in trabecular bone and can be recognised as fracture or bone bruise. In addition, an advantage of MRI is the capability to reveal possible alternative diagnoses including soft tissue injuries [101].

Radionuclide bone scan

Before the era of MRI, radionuclide bone scans (RNS) were considered the modality of choice for occult hip fractures [102]. The fundamentals of bone scanning have changed little since it was invented in the late 1950s, but as for all other imaging modalities, the technology has turned it lighter, smaller and faster as computers have become more powerful. The technique is based upon intravenous injections of a radioactive tracer, usually an isomer of technetium-99, symbolised as ^{99m}Tc. This isomer is linked to methylene diphosphonate (MDP) with a high affinity to the metabolic activity of bones. The 99mTC MDP tracer emits photons about the same wavelength as conventional X-rays (140kEv) and can be detected by the salt crystals in the gamma camera, digitized and converted to images.

However, even if the sensitivity and specificity of bone scintigraphy is only slightly lower than for MRI considerable limitations have been reported in the literature [103-106]. False positive scans are common due to increased bone turnover in other pathologies than fractures (e.g., arthritis, soft-tissue injury and tumour) and the full fracture extent may be hard or impossible to assess, due to inferior spatial resolution. Thus, usage of bone scanning may result in inadequate treatment. Additionally, in common clinical praxis patients are not scanned until 72 h after injury in order to avoid false negative scans. This is due to age related changes in the global radionuclide uptake, such as impaired renal function with delayed tissue clearance and impaired perfusion to the region of interest [105, 107]. Even if some authors suggest that modern three-phase radionuclide scan procedures within 24 h are equally accurate, hence avoiding unnecessary waiting until 72 h, further studies is required to support this assertion [105, 108].

Ultrasonography

Like MRI, ultrasound is not ionising radiation. Probes, called transducers, emit sound waves in the megahertz (MHz) range and detects the ultrasound echoes reflected as images. Some of the waves are reflected back from superficial tissue boundaries (between fluid and soft tissue, soft tissue and bone) while others travel further and are reflected by deeper boundaries. The distance the reflected waves have travelled to the specified organ is calculated by using the speed of sound in tissue (1540m/s) [109] and the delay of each echo. The active elements in the transducers are made of piezoelectric ceramic crystals, which have the capability to convert electrical signals to mechanical vibrations and vice versa. The intensities of the reflected waves and the distance they have travelled are displayed on a monitor. Solid materials reflects most of the waves and will appear as “whitish” on the screen while fluids readily transmits sound and will appear within a “black” spectrum [110]. The usage of ultrasound of the hip may detect alterations of bone surfaces and account for adjacent effusions or haemorrhage and capsular thickening. However, since the sound wavels are reflected at the bone/fluid boundary, the fracture extent of non-displaced fractures may be hard or impossible to assess. Only one small study using ultrasound on 10 patients with evidence of hip fracture at MRI has been reported, with 100% sensitivity and 65% specificity [111]. Thus, even if ultrasound has no known harms and may be available around the clock it is not validated as a useful diagnostic tool in detection of occult hip fractures.

Treatment of hip fractures

Historical background

The event of hip fracture could be a devastating injury, frequently accompanied by death. The oldest description of a femoral neck fracture may be from the 14th century, of the historical German Emperor Charles IV (1316-1378), who died from pneumonia. A thorough examination of his almost complete skeletal remnants revealed a fracture of his left femoral neck, presumably the indirect cause of his demise [112].

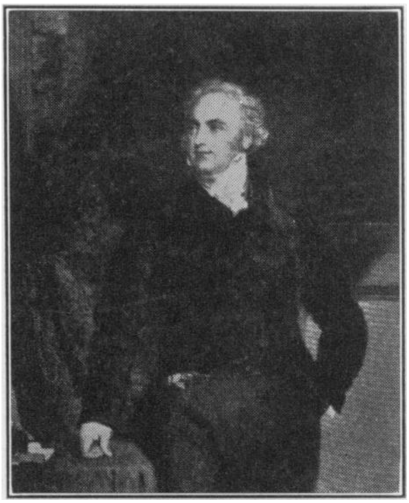


Figure 7. Portrait of Sir Astley Cooper (1768 – 1841) by Sir Thomas Lawrence in the possession of the Royal College of Surgeons of England

Internal fixation

In 1822, Sir Astley Cooper, an English surgeon and anatomist, pioneered classifications of hip fractures into intra- and extracapsular (Figure 7). He also assumed that non-union of femoral neck fractures should be attributed to diminished blood supply to the femoral head; "*...the bones are consequently drawn asunder by the muscles, and that there is a want of nourishment of the head of the bone...*" and "*In all the examinations which I have made of transverse fractures of the cervix femoris, entirely within the capsular ligament, I have never met with one in which an ossific union had taken place.*") [113]. In 1845, Robert Smith contributed by reporting that impacted intracapsular fractures were more likely to heal [114]. Shortly after, surgeons developed strategies for aligning the fragments as a basis of healing. In 1902, reduction and traction under anesthesia and immobilisation with whole-body cast from the rib cage to the toes for eight to twelve weeks were reported by Royal Whitman [115]. In 1911, Fred Cotton performed *artificial impaction* of the fragments by using a large wooden hammer on the greater trochanter [116]. However, the conservative treatment regimes were associated with high mortality and complication rates, such as secondary displacement or non-union, as well as pulmonary infections, pressure ulcers and thromboembolism due to prolonged bed rest. Also, fracture healing was frequently accompanied with varus deformity and shortening of the leg, due to non-balanced contracting forces from the muscles about the hip. In 1931, Smith-Peterson first published the report on a surgical technique with a three flanged nail for open reduction and internal fixation under roentgenologic control [117]. This rotational stable nail increased the rate of union and reduced complications associated with conservative treatment regimes due to prolonged bed rest, commonly with immobilsation in plaster for months. The Smith-Peterson method was further refined by Sven Johansson (Gothenburg, Sweden, were this thesis was written), who in the early 1930s cannulated the nail with the purpose to insert the nail over a thin guiding wire using roentgenologic control. Thus, Johansson's technique implemented the idea of closed reduction with internal fixation technique. His development became valid for a wider range of fragile patients as the surgical procedure was minimaly invasive [118]. In 1937, Thornton made a breakthrough in the treatment of trochanteric fractures by developing a plate to be added at the lateral end of the Smith-Petersen nail [119]. After this so called "nail-plate" other similar devices soon followed (Jewett 1941, McLauglin 1947) [120, 121]. However, these fixed angle devices did not allow impaction, which often caused the nail to perforate the femoral head or to predispose for non-union due to distraction between the fragments. Also, the unbalanced mechanical forces on the osteosynthesis from loadbearing at rehabilitation could cause the device to bend, break or disengage at the nail-plate junction. To counter this problem, Pugh (1955) developed a self-adjusting (telescoping) nail-plate system with a fixed angle of 135 degrees that allowed impaction [122]. A biomechanical study by Brodetti (1941) showed that a *bolt screw* was superior to a *nail* for experimental fractures [123]. In 1956, Charnley devised a compression screw-plate with "spring-loading". The idea was to force the femoral head and neck together and then to maintain constant compression between the opposed fragments with the compression spring, allowing to accomodate for bone resorption. [124]. Even if Charnley´s screw-plate had a tendency to cut out of the femoral head [125] it constitutes, together with the Pugh nail-plate [126] the foundation for modern designed devices for internal fixation, such as Richards Medical Compression Hip Screw.

Arthroplasty

Total hip replacement surgery constitutes one of as the most successful operations in all of orthopedic medicine [127]. In 1822, White, a Brithish surgeon, performed the first successful resection of the femoral head for tuberculosis in Europe [128]. Major hip surgery rapidly followed. In 1826, Barton performed a femoral osteotomy on a sailor with an ankylosed hip. The procedure took seven minutes which was an acceptable speed in the era of pre-anesthesia surgery [129]. The aim was to create pseudarthrosis by manipulating the osteotomy gap every few weeks. However, new methods were sought which required reconstruction of the hip joint itself. In 1891, the surgeon Glück developed a short term successful hip implant of ivory which he used in five resected tuberculous joints [130]. Even if these implants later failed due to chronic infection, the concept of biocompatibility was developed. In 1923, Smith-Petersen by chance discovered that an excised piece of glass, removed from a patient's back was "lined by a glistening synovial sac, containing a few drops of clear yellow fluid." From his observations he designed a glass mould: "*...A mould of some inert material, interposed between the newly shaped surfaces of the head of the femur and the acetabulum, would guide nature's repair...*" [131]. As some moulds broke, Smith-Petersen investigated other materials from 1923 to 1937 until his dentist, Cooke, suggested Vitallium (a cobalt chrome alloy, at that time recently implemented in contemporary dentistry). Vitallium could be easily shaped and showed to have enough strength and in 1938, Smith-Petersen developed an arthroplasty cup constructed from this material [131]. Together with the British surgeon Wiles, Smith-Petersen later developed the first total hip arthroplasty of stainless steel (Figure 8), implanted by Wiles in 1938 [132].

In this same period, Thompson developed a curved prothesis which was further refined by the British surgeon McKee who first experimented with various uncemented designs. However, after the introduction of bone cement (polymethylmediacrylate) McKee's cement fixed total hip arthroplasty was the first widely used cemented prosthesis. Unfortunately, after implant failures and revisions it was discovered that this prothesis shredded metal particles [133]. In the early 1960s, Charnley made history by anchoring the femoral head prosthesis to the shaft of femur by acrylic cement and by using a small prosthetic head articulating against polymer in order to reduce plastic erosion [134]. Charnley's arthroplasties have shown good functional results in mid and long term follow up [135]. His implant design is equal, in principle, to the designs currently used. It comprises a polyethylene acetabular component, a metal femoral stem and acrylic bone cement.

Figure 8. Philip Wiles' metal on metal total hip arthroplasty from 1938

Current treatment options

Stable femoral neck fractures

Conservative treatment

There are few studies comparing conservative versus surgical treatment of stable non-displaced intracapsular fractures [136, 137]. Even so, conservative treatment has been historically described. The patient can be treated with analgesia and limited bed rest, followed by gentle mobilisation, but subsequent displacement is frequent. Raaymakers and Marti have reported displacement rates of 14% to 31% upon resuming weight bearing after one week [138-140]. Also, the authors concluded that secondary displacement predominantly occurred in patients over 70 years of age. Simon et al [141] noted a displacement rate of 28% after early resumption of weight-bearing and Verheyen et al [142] reported a displacement rate of 46% after conservative treatment with partial weight-bearing. Thus, the relatively high rates of failure have made surgical treatment preferable.

Internal fixation

The aim of surgical treatment is to accomplish fracture healing, facilitate early, relatively painless mobilisation, and to prevent complications associated with prolonged bed rest. Morbidity and mortality after hip fracture is multifactorial depending on type of fracture, patients' age, co-morbidity and pre-operative level of functioning. Also, the timing of surgery plays an important role with several studies advocating treatment within 48 hours [44, 143-146]. It has been shown that internal fixation of non-displaced femoral neck fractures can reduce the risk of displacement to less than 5% [147], even if higher incidences have been reported [148]. The procedure is usually fast and atraumatic and well tolerated by most fragile patients. Also, internal fixation has shown a lower incidence of peri-operative complications and a lower 1-year mortality rate compared to hemiarthroplasty [149]. Thus, internal fixation has been widely spread as the method of choice.

Arthroplasty

Arthroplasty can be used for non-displaced intracapsular fracture, but the procedure is associated with higher morbidity and mortality compared to internal fixation [149]. However, in patients with history of symptomatic hip osteoarthritis or other diseases affecting the hip joint, total hip arthroplasty (THA) is usually indicated.

Unstable femoral neck fractures

Conservative treatment

Before surgical treatment with various implants was introduced, displaced femoral neck fractures were managed conservatively with traction and bed rest. However, the risk of secondary displacement seemed inevitable, and the accompanying fatal complications were close to certain [113]. Thus conservative treatment of these fractures is usually limited for non-ambulatory patients with high surgical and anesthesia risks [136, 150].

Internal fixation

After extramedullary implants came into being in the 1930s [119], the predominant treatment for non-displaced as well as displaced intracapsular fractures has been various procedures with internal fixation. However, several contemporary randomised studies have shown failure rates of 35 to 50 percent for internal fixation of displaced intracapsular fractures [149, 151-154]. Also, slightly better outcomes in terms of pain score and functional status have been reported for arthroplasty compared to internal fixation [155-158]. Together, during the last two decades, this have resulted in a dramatic increase of arthroplasty procedures for displaced intracapsular fractures [159].

Arthroplasty

Even if displaced femoral neck fractures predominantly are treated with arthoplasty, the type of implants best suited for treatment are still debated. The two types of arthroplasty implants available are: total hip arthroplasty (THA) and hemiarthroplasty. In the procedure of THA, the entire hip is replaced, i.e., both the femoral head and the acetabulum. Thus, the THA implant consists of two separate prosthetic parts articulating against each other. In hemiarthroplasty procedures, only the femoral head is replaced, thus leaving the other part of the joint intact.

There are two main types of hemiarthroplasties: *unipolar* and *bipolar* designs. The *unipolar* consists of a metallic stem that is placed within the intramedullary femoral canal and an artificial femoral head that articulates directly with the native acetabular cartilage.

Regardless of which hemiarthroplasty that is used, erosion of the acetabular cartilage is likely to occur during the course of time. Thus, to decrease the erosion of the acetabular cartilage, *bipolar* designs have been developed. These types integrate an additional internal articulation through a smaller metallic head that fits inside a second larger one. As the bipolar design allows additional articulation within the implant, the erosion of the acetabular cartilage may be less than with unipolar designs. However, the literature on possible advantages for either design is sparse apart from a single study by Cornell et al [160], that showed a better functional outcome for the bipolar design. Also, an advantage of the bipolar design is that it can be converted to a THA later, if necessary.

Trochanteric fractures

Conservative treatment

Prior to the era of orthopedic surgery, trochanteric fractures were managed with bed rest, walking support, whole body cast and traction. The literature from the 1800s reveals that these fractures healed [113], but with various amount of deformity, leading to impared functionality. However, acceptable healing rates were challenged by unacceptable high rates of morbidity and mortality due to prolonged immobilisation. In 1957, Clawson reported mortality rates of 40% for conservative treatment [161]. As a result, most trochanteric fractures are now surgically treated. Yet, an exception to the surgical approach are incomplete trochanteric fractures which in small studies have been reported to tolerate conservative treatment with equally good outcomes as after surgery [40, 41, 96].

Internal fixation

After the sliding hip screw (SHS) was introduced in the 1950s, and hithertho modified, stable and *questionable* unstable trochanteric fractures (AO/OTA 31.A1-A2), in which medial support can be restored after reduction, are conventionally treated with extramedullary internal fixation, such as the dynamic hip screw (DHS) or the compression hip screw (CHS). The lag screw in these devices easily glides within the lateral plate and provides controlled collapse of the fragments as well as load sharing between the fragments and the implant [162].

However, for *clearly* unstable fractures (AO/OTA 31.A3) internal fixation with extramedullary devices is regularly accompanied by adverse events of metal failure, non-union, secondary displacement and cut-out [163]. In order to cope with relatively high failure rates after extramedullary internal fixation of unstable fractures, intramedullary devices, such as the Gamma nail and the intramedullary hip screw (IHS) have been developed. During the past decades several studies have been conducted in order to compare the performance of extra- and intramedullary fixation [164-168]. The studies reveal conflicting results, partly due to multifactorial base-line properties, such as bone quality and the patients' pre-operative functional level, various degrees of fragmentation and inhomogenous interpretations of fracture classification systems. Also, individual surgical skill as well as the large number of various implants obscure the treatment results. However, in a recent study on 2716 patients from the Norwegian Hip Fracture Register (NHFR) on reverse oblique trochanteric (n=390) and subtrochanteric fractures (n=2326), extramedullary fixation was compared with intramedullary nailing. The study concluded that both groups had significantly more reoperations for patients treated with SHS [168]. Also. intramedullary nailing for these fractures has been shown to be more cost-effective compared to SHS fixation [169]. Even if there is no clearly superior treatment of questionable unstable fractures, the literature supports that clearly unstable fractures (AO/OTA 31.A3) should be treated with intramedullary nails [168-172].

Arthoplasty

Arthroplasty can be used for trochanteric fractures but perusal of the literature reveals little evidence on important differences between replacement arthroplasty compared to different strategies of internal fixation [170, 173]. However, arthroplasty for intertrochanteric fractures may be justified in highly comminuted cases [174, 175]. Also, patients with pathologic fractures, severe osteoporosis or with a prior history of symptomatic osteoarthritis may benefit of primary arthroplasty [176-178].

Statistical methods for determining observer agreement

In radiology research evaluation of diagnostic performance for categorical variables is usually based on interpretations by two or more observers. The level of agreement between observers for a specific condition is important as it reflect the reliability of a method in determining a specific condition. A high level of agreement may reflect high reliability of a particular method for a specific condition. There are various statistics that can be used for the purpose of determining the level of agreement. A partial list of the most common measures includes; *percentage agreement* which is straightforward but does not correct for agreement occurring by chance; *Cohen's kappa* (1960), which is limited to *two* observers and has the ability to correct for chance agreement [179]; *Fleiss' kappa* (1971), which describes a way to extend Cohen's kappa by allowing *multiple* observers classify all or some of the subjects, even if *ordered* categorical data does not apply [180]. However, as Cohen's and Fleiss' kappa tends to decrease with an increasing number of categories, the various variations of the *intraclass correlation* (ICC) that is less sensitive to these changes have been argued to be a better alternative [181]. Contrarily, most ICC tends to increase as the number of categories increases and is probably best suited for continuous data [182]. It is clear that statistical methods range from simple to complex and can be used to show or summarize various aspects of medical research. However, statistics does not allow us to draw definite conclusions about any hypothesis we might have and should only be used as a tool to compare methodologies or treatments. Thus, statistical methods are solely a way to describe the data and should be interpreted with caution.

Percentage agreement

The result of proportion of agreement can be expressed as *percentages of agreement* and explained as the number of agreements in observations divided by the total number of observations.

Table 1. Radiography of extracapsular fractures

		Musculoskeletal radiologist		
		Fracture	Negative	Total
	Fracture	7	4	11
Resident	Negative	12	352	364
	Total	19	356	375

In Table 1, 375 patients were assessed for occult intertrochanteric fractures by two observers with varying experience in radiology. The overall proportion of agreement (p_o) is calculated as follows (Equation 1):

$$p_o = \frac{7+352}{375} = 0.96 \qquad [1]$$

The value of 0.96 tells us that the observers agree in 96% of their assessments. As the number of *negative* readings is large relative readings positive for fracture, agreement on *negative* readings will dictate the value of overall agreement (p_o) and may give a false impression of performance. This can be illustrated by calculating separate proportions of agreement for positive (p_{pos}) and negative (p_{neg}) readings after which any lack of correspondence becomes apparent. The number of agreement on positive readings for fracture in Table 1 can be expressed as the readings that both observers agree on divided by all positive readings (Equation 2).

$$p_{pos} = \frac{7+7}{(7+4)+(7+12)} = 0.47 \qquad [2]$$

Agreement on negative diagnoses can be calculated as (Equation 3):

$$p_{neg} = \frac{352+352}{(12+352)+(4+352)} = 0.98 \qquad [3]$$

The results from equation 1, 2 and, 3 should be interpreted as the two observers agreed 96% of the time overall, on inconclusive cases 98% of the time, but on occult fractures only 47% of the time. A valid criticism against percentage of agreement is that it does not correct for agreements that would be expected by chance, consequently the level of the overall proportion of agreement may be overestimated. Also, the weakness of p_{pos} and p_{neg} is that confidence intervals cannot be calculated. For these reasons, percentages of agreement should not be used as a solitary measure of inter-observer agreement [179, 183].

Cohen's kappa

Cohen's kappa (κ) has the ability to *correct* for the level of chance agreement and is the most commonly used statistic that measures the proportion of agreement between *two* observers who report two or more categories [183, 184]. The level of agreement that is expected to occur by chance (p_e) can be calculated from Table 1 as (Equation 4):

$$p_e = \frac{11}{375} \cdot \frac{19}{375} + \frac{364}{375} \cdot \frac{356}{375} = 0.92 \qquad [4]$$

The value of κ can be calculated by subtracting the chance agreement (p_e) from the overall agreement (p_o), and dividing the remainder by the number of cases on which agreement is not expected to occur by chance (Equation 5).

$$\kappa = \frac{p_o - p_e}{1 - p_e} \qquad [5]$$

Table 2 shows the strength of agreement beyond chance for various ranges of κ that were suggested by Landis and Koch [185]. The intervals for level of agreement are completely arbitrary.

Table 2. Guidelines for strength of Agreement

κ Value	Strength of agreement beyond chance
< 0	Poor agreement
0–0.2	Slight agreement
0.21–0.40	Fair agreement
0.41–0.60	Moderate agreement
0.61–0.80	Substantial agreement
0.81–1.00	Almost perfect agreement

In kappa statistics, all disagreement is expressed in terms of total disagreement. If there is no agreement between the observers, kappa will equal a value of (-1.0). When agreement is at chance level, the value will be zero (0). In case of complete agreement, kappa will equal the value of one (1.0). For practical purposes only the range from zero (0) to (+1) is of interest. Interpretations of intermediate values are subjective but researchers generally seek Kappa values greater than 0.80 for acceptable implementation of the results in clinical praxis [183].

Interpretation of kappa

For the data in Table 1, the κ value is calculated as (Equation 6):

$$\kappa = \frac{p_o - p_e}{1 - p_e} = \frac{0.96 - 0.92}{1 - 0.92} = 0.5 \qquad [6]$$

How can the discrepancy between κ and the overall agreement (p_o) be explained? If the prevalence of one of the categories is high, chance agreement for that category will also be high and kappa will adopt chance-adjusted *low* values. The values calculated from Table 1 show that there is good overall agreement ($p_o = 0.96$) but only moderate chance corrected agreement ($\kappa = 0.5$). The discrepancy between the unadjusted level of agreement (p_o) and κ in Table 1 is caused by an imbalance of the marginal distribution of totals due to the vast number of negative cases. The characteristics of the marginal totals is caused by "prevalence" – defined as "*the true proportion of cases of various types in a population*" and bias - defined as "*the bias of one observer relative to another*" [186]. Thus, low values of κ may not necessarily reflect low rates of overall agreement. This paradox was described by Feinstein et al [184] who suggested that, for clarification of rare findings, one should include the three indices; κ, positive agreement, and agreement on negative findings. In addition, a confidence interval (CI) should always be presented in conjunction with the kappa value to reflect sampling error [184, 187]. The standard error (SE) and the 95% CI for κ in Table 1 can be calculated as follows (Equation 7 and 8):

$$SE = \sqrt{\frac{p_o \cdot (1-p_o)}{n \cdot (1-p_e)^2}} \qquad SE = \sqrt{\frac{0.96 \cdot (1-0.96)}{375 \cdot (1-0.92)^2}} = 0.13 \qquad [7]$$

$$CI_{95\%} = \kappa \pm 1.96 \cdot SE(\kappa) \qquad CI_{95\%} = 0.5 \pm 1.96 \cdot 0.13 \qquad [8]$$

Weighted kappa

If the number of categories increases, kappa tends to decrease since each additional category may predispose for disagreement. If, however, the categories are ordered (e.g., *negative*, *suspect*, *definite*) a weighted kappa coefficient can be used to account for the different levels of disagreement between the categories. Usually, the weights are linear or quadratic. Linear weights are used when the difference between the first and second category has the same importance as the difference between the second and third category, etc. Quadratic weights are preferable if the difference between the first and second category is less important than the difference between the second and third category, etc. For example, if one observer scores *negative* for fracture and the other a *definite* fracture, the level of disagreement can be considered greater than for differences between scoring a *suspect* fracture and a *definite* fracture. Thus, if the categories are ordered and if more than two categories are included, weighted Kappa should be used since weighted kappa in these cases can reflect the actual agreement better than does the unweighted.

Fleiss' kappa

Like all kappa statistic, Fleiss' kappa [188] are based on Equation [5], and as for Cohen's kappa it is sensitive to bias (i.e., biased observer) and prevalence (e.g., a large number of negative cases relative positive cases). Thus, both Cohen's and Fleiss' kappa lack criterions for the correctness of the scorings and infers that all observers are deemed equally competent to score their findings [179, 188]. However, an important feature of Fleiss' kappa is that it has the capability to measure agreements between *multiple* observers while correcting for chance agreement. For this reason, Fleiss' kappa is often used in the medical sciences. However, Fleiss' kappa does not apply for ordered categorical ratings [183, 188] and was deemed less suitable for agreement analyses on the scoring of negative, suspect and definite fractures in this thesis.

Intraclass correlation

Intraclass correlation (ICC) can be used for categorical data for two or multiple observers to calculate observer agreement [183, 189]. However, for different study designs, different ICC equations are used but all ICC variants share the same underlying assumption that ratings from observers for a set of subjects are composed of a true score component and measurement error component. The equation for this can be written as:

$$X_{ij}=\mu+r_i+rc_{ij}+e_{ij} \qquad [9]$$

where, X_{ij} is the score provided to subject i by observer j, μ is the grand mean of the true score for variable X, r_i is the deviation of the true score from the mean for subject i, and e_{ij} is the dimension of random noise. The ratio of the sums of various variance component estimates between (0) and (1). An estimate of one (1) indicates perfect agreement whereas an estimate of zero (0) is equivalent with random agreement. The equation [9] can be clarified as:

$$\text{ICC} = \frac{\textbf{Variance (patients)}}{\textbf{Variance (patients)+Variance (observer)+Variance (error)}} \qquad [10]$$

Thus, equation [10] tell us that ICC is highly dependent on the variance of the assessed population where higher values may be obtained for a more heterogeneous population than for a more homogeneous one despite similar levels of agreement. Thus, the ICC values cannot be stated to translate a *true* level of agreement, and there is no evident cut-off value (e.g., 0.75 proposed by Burdock et al) to specify a level of agreement that can be inferred in clinical praxis [188, 190]. In 1979, Shrout and Fleiss [191] described three classes of ICC for reliability and termed them Case 1 – 3; each case applicable to different observer agreement study designs. Case 1 can be defined as: observers for each subject are selected at random from a larger population of observers. This infers that the observers who rate one subject are not necessarily the same as those who rate another. Case 2 can be defined as: the same set of observers rate each subject, which corresponds to a fully-crossed table (*Observer x Subject*) test. It should be emphasised that the observers in Case 2 are considered a random effect since they constitute a random sample from a larger population of observers. Case 3 can be defined as: each subject is rated by each of the same observers, who are the only observers of interest. This last case does not permit generalisations to other observers and is infrequently implemented in radiological research. Shrout and Fleiss also showed that in each case, one can use ICC in two ways: (1) to estimate the reliability of a single rating, or, (2) to estimate the reliability of a mean of several ratings. Thus, the authors described a total of six different versions of the ICC. The most appropriate ICC for agreement analyses in this thesis would apply to Case 2. However, as ICC is best suited for calculations of continuous data and less suitable for calculating ordered categorical data (e.g. negative, suspect, definite) it was deemed inappropriate to use ICC as a statistic tool in this thesis.

AIMS

The overall aim of this thesis was to evaluate the reliability and accuracy of imaging of occult and suspect hip fracture

To achieve this, the specific aims are defined in papers I-IV. The aims were to

I. in a large material, assess observer agreement for radiography, CT and MRI and to evaluate to what extent observer experience or patients' age influence diagnostics

II. discriminate between occult and suspect fractures at radiography compared to MRI and clinical outcome and to evaluate the importance of experience

III. evaluate observer reliability and accuracy of CT

IV. assess the co-existence of pelvic and hip fractures.

METHODS AND MATERIAL

Patients and data collection

All radiologic examinations in the thesis were retrospectively reviewed. Data collection was performed between 1st of January 2006 and 31st of March 2015. The examinations were retrieved from the hospital picture and archiving systems (PACS) and the requisitions from the radiology information systems (RIS). Patients referred for radiography with clinical suspicion of hip fracture after a fall with negative or equivocal fracture diagnosis were identified. Included were consecutive patients with normal or equivocal radiography with remaining clinical suspicion of hip fracture and second line examination with CT and/or MRI, usually within 24 hours (range 0 – 18 days). In a few cases a negative or inconclusive CT examination prior to MRI delayed the final diagnoses. Excluded were patients with systemic bone disease, metastases, skeletal hip abnormalities and inferior imaging quality.

In **paper I**, the patients were collected from two trauma centres. Cut-off age was 60 years or older. In **paper II-IV**, all cases were from a single trauma centre. Patients 50 years or older were included. The clinical course in all cases was determined from the hospital information system (HIS). The four cohorts (**paper I-IV**) were overlapping (Table 3).

*Table 3. Study period and number of overlapping patients (paper **I – IV**)*

Period	2006-01-01 2008-12-31	2006-01-01 2013-12-31	2006-01-01 2014-12-31	2006-01-01 2015-03-31
Paper	**I**	**II**	**III**	**IV**
I	N/A	89	27	89
II		N/A	42	254
III			N/A	44

N/A = Not applicable

The patients in **paper I** were collected from 1st of January 2006 to 31st of December 2008; 103 examinations (40 CT and 63 MRI) were from Skåne University Hospital, Lund and the remaining 272 patients (192 CT and 107 MRI) from Sahlgrenska University Hospital, Mölndal, of which 27 underwent both CT and MRI. Male/female ratio 0.47. Mean age 81 years (range 60 –107). In **paper II**, patient collection from 1st of January 2006 to 31st of December 2013. Male/female ratio 0.49. Mean age 81 years (range 50-107). In **paper III**, patient collection from 1st of January 2006 to 31st of

December 2014. Male/female ratio 0.47. Mean age 84 years (range 58 – 103). In **paper IV**, patient collection from 1st of January 2006 to 31st of March 2015. Male/female ratio 0.56. Mean age 81 years (range 50 - 107).

Imaging

Digital radiography was performed with standard imaging protocols, with an AP pelvis radiograph, plus an AP and a cross table lateral hip radiograph. All CT studies (paper **I** and **III**) in Mölndal were performed with a 16 row helical scanner (Somatom Sensation, Siemens, Erlangen, Germany) with a medium sharp reconstruction kernel (B60s) at 120 kVp and 70mA. The CT examinations in Lund were performed on a 40-detector row helical scanner (Philips Brilliance 40, Eindhoven, The Netherlands) with different reconstruction algorithms, both medium sharp and sharp. The scan protocols consisted of multi-planar reconstructions in at least three orthogonal planes with 1–3 mm slice thickness and 50% overlap.

The MRI studies in Mölndal were performed on a 1.5 T Siemens Sensation scanner (Siemens, Erlangen, Germany). The scan protocol 2006 to 2009 consisted of a 5 mm slice thickness coronal turbo spin-echo (SE) T1-weighted sequence (TR=470, TE=12) and a coronal fat-suppressed FSE T2-weighted sequence (TR=5060, TR=104). From 2010 the protocol changed to a 3.5 mm slice coronal turbo spin-echo (SE) T1-weighted sequence (TR=518, TE=14) and a 4 mm slice coronal short-tau inversion recovery (STIR) sequence (TR=4760, TE=67. The interslice gap was 1 mm. The MRI examinations in Lund were performed on a 1.5 T Philips Intera scanner (Philips, Eindhoven, The Netherlands). The scan protocol consisted of a 4 mm slice thickness coronal turbo spin-echo (SE) T1-weighted sequence ((TR=400, TE=16) and a STIR sequence (TR=2500, TE=60) and an interslice gap of 1 mm.

Image review

All imaging studies in paper **I** was reviewed by three observers with varying radiological experience; a resident, a general radiologist and a musculoskeletal radiologist. All imaging studies in paper **II** were reviewed by two musculoskeletal radiologists in consensus. All imaging in paper **III** was reviewed by two musculoskeletal radiologists. All imaging in paper **IV** was reviewed by one musculoskeletal radiologist and all hip fractures, with or without concomitant pelvic fractures, were verified by a second musculoskeletal radiologist. In all papers (**I - IV**) the observers worked independently of each other and only patient age and gender was presented. The use of PACS tools such as zoom, pan, window and level settings was allowed. A fracture was scored for trauma related breaks of cortical and trabecular bone (with or without subtle signs of "bone bruise" at CT) or in the presence of abnormal trauma related marrow signal changes at MRI. The radiological results were classified as no fracture, suspect fracture, or definite fracture. Diagnostic reliabilities were calculated for intra- and extracapsular fractures on the whole material and were treated as separate entities. This infers that a suspect or definite diagnosis of extracapsular fractures was regarded as negative when agreement for intracapsular fractures was calculated. Accordingly, when avulsions of the greater trochanter were excluded, scoring of suspect or definite avulsion fracture of the greater trochanter alone was regarded as negative for trochanteric fracture.

Statistical analysis

In **paper I – III** observer analyses with bi-rater linear weighted Cohen's kappa (κ) were performed to evaluate observer agreement. The diagnosis suspicion of fracture was given less statistical weight than definite or no fractures in case of observer disagreement. Kappa (κ)-values < 0 were translated as indicating no agreement, 0.01–0.20 slight agreement, 0.21–0.40 fair agreement, 0.41–0.60 moderate agreement, 0.61–0.80 substantial agreement, and 0.80–0.99 almost perfect agreement [185].
In paper **II** chi-square tests were performed to analyse differences in numbers of occult, suspect and definite hip fractures and in paper **IV** a chi-square test was performed for differences in prevalence of concomitant pelvic fractures with femoral neck or trochanteric fractures.

Compliance with ethical standards

The studies in this thesis were approved by the Regional Board of Ethics

RESULTS

In **Paper I**, the diagnostic reliability for radiography, CT and MRI was calculated. The material comprised 375 patients. After index radiography, 232 patients were examined with CT and 170 with MRI. Of these, 27 patients underwent both CT and MRI. At radiography, the observer agreement for intracapsular fractures was substantial for the specialists ($\kappa = 0.66$). The resident scored twice as many equivocal fractures as the other two observers. The agreements between the resident and the general radiologist as well as between the resident and the musculoskeletal radiologist was only moderate ($\kappa = 0.56$ and 0.54, respectively).

At radiography observer agreement for extracapsular fractures was substantial for all three observers ($\kappa = 0.69–0.72$). When fractures of the greater trochanter were excluded the agreement was only moderate, with kappa (κ) values ranging from 0.43 to 0.50 (Table 4).

Table 4. Radiography of extracapsular fractures when avulsion fractures of the greater trochanter were excluded

		Musculoskeletal radiologist			
		Fracture	Suspect	Negative	Sum
Resident	Fracture	7	2	2	11
	Suspect	8	11	35	54
	Negative	4	14	292	310
	Sum	19	27	329	375

Linear weighted kappa (95% CI): 0.43 (0.31 – 0.55) SE 0.06
There were moderate observer agreement (k = 0.43) for extracapsular fractures (avulsion fractures of the greater trochanter were excluded) on radiography between the specialist in musculoskeletal radiology and the resident for 375 patients aged over 60 years.

Age and gender did not influence the kappa values for any modality. At radiography, corresponding statistics for intra-observer analyses performed for the specialist in general radiology was moderate for intracapsular fractures ($\kappa = 0.60$) and substantial for extracapsular fractures ($\kappa = 0.73$). At CT, the interobserver agreement was almost perfect for both intracapsular fractures ($\kappa = 0.85$-0.87) and extracapsular fractures ($\kappa = 0.91$-0.97) and the intraobserver agreement for both intra- and extracapsular fractures was equally high ($\kappa = 0.94$ and 0.95). At MRI, the observer agreement was almost perfect with kappa (κ) values for intracapsular fractures ranging from 0.95 to 0.97 and for extracapsular fractures from 0.93-0.97. The kappa values remained almost perfect (κ = 0.91 – 0.94) when avulsion fractures of the greater trochanter were excluded. Corresponding statistics for intraobserver agreement was 0.99 and 1.0, respectively.

In **Paper II**, the clinical utility of experienced review of radiography and MRI in occult and suspect hip fractures was assessed. The material comprised 254 patients. All primary reporting was made by general specialists in radiology. At radiography, there were approximately twice as many primarily reported *suspect* diagnoses (86/254=34%) compared to review (37/254=15%) and approximately twice as many *false negative* cases (62/168=37%) compared to after review (36/173=21%). Of the 168 primarily reported negative cases, 20 definite fractures were found after review and of the primarily reported 86 suspect cases, 24 definite fractures were scored at review. As all 44 reviewed definite fractures were verified with MRI, the experienced review reduced the number of cases that were likely to require further imaging by 17% (44/254). In total, MRI changed the primary radiographic reports in 148 cases (58%) compared to 63 after review (25%). Significantly more fractures were found after MRI among radiographically suspect diagnoses than among negative cases for both primary reporting and at review (P<0.0001).

The diagnostic discrepancies for radiography between primary reporting and review were underscored by the low linear weighted kappa value (κ = 0.31) while observer agreement for MRI was almost perfect (κ = 0.99). There were no suspect fracture diagnoses at MRI. All patients with normal MRI as well as patients that received conservative treatment had an uneventful clinical course.

Paper III compared the diagnostic performance of CT and MRI in primarily reported negative cases or suspect fractures. The material comprised 44 patients. All primary reporting was made by general specialists in radiology. At primary CT reporting there were 18 suspect fractures and 26 negative cases. At CT review there were no suspect fractures. Six of the 20 primary reported negative CT diagnoses were scored as either cervical or trochanteric fractures at review. Thus, there was disagreement on CT diagnosis between primary reporting and review in 24 cases.

There were no diagnostic discrepancies between primary reporting and review of MRI. Totally 20 fractured and 24 normal cases were found. MRI changed the primary reported CT diagnoses in 27 cases (61%) and the reviewed CT diagnoses in 14 (32%) and 15 (34%) cases, respectively (the reviewers disagreed only on one case). At primary reporting there were nine false negative cases (5 cervical; 4 trochanteric) and all 18 suspect cases were changed (7 negative; 8 cervical; 3 trochanteric). Both reviewers scored nine false negative cases (6 cervical; 3 trochanteric). One reviewer had three false positive cases (2 cervical; 1 trochanteric), the other had four (3 cervical; 1 trochanteric). Both reviewers changed two fracture diagnoses; one from cervical to trochateric and one from trochanteric to cervical.

Paper IV analyses the frequencies of exclusively pelvic fractures as well as concomitant pelvic fractures at MRI of radiographically occult and suspect hip fractures. The material comprised 316 patients. In 132 patients there were hip fractures only (42%). In 73 patients there were no signs of fracture (23%). Eighty-two patients had exclusively pelvic fractures (26%) of which 69 patients had two or more pelvic fractures (84%) and 50 patients had fractures of two or more pelvic bones (61%). Sixty-seven patients had ipsilateral fractures only (82%) and fifteen patients (18%) had at least one pelvic fracture on the contralateral side of the hip trauma (Table 5).

Table 5. Distribution of exclusively pelvic fractures in 316 patients with trauma to the hip examined with MRI after negative or equivocal radiography

	No. of patients	Bilateral	Ipsilateral	Contralateral
Single pelvic fracture				
Sacrum	4		3	1
Ramus	5		5	
Acetabulum	3		3	
Iliac wing	1		1	
Multiple pelvic fractures				
Sacrum	4	4		
Rami	15		13	2
Sacrum + Rami	35	6	29	
Sacrum + Acetabulum	2	1	1	
Sacrum + Acetabulum + Rami	4	1	3	
Rami + Acetabulum	9		9	
Total	82	12	67	3

In 29 patients there were concomitant hip and pelvic fractures (9%) of which 10 pelvic fractures (35%) were on the contralateral side. It is interesting to note that only two (10%) of the concomitant pubic rami fractures were detected at review of radiography (Figure 9). The frequency for concomitant pelvic fractures was higher for trochanteric fractures but the difference was not statistically significant (P = 0.12).

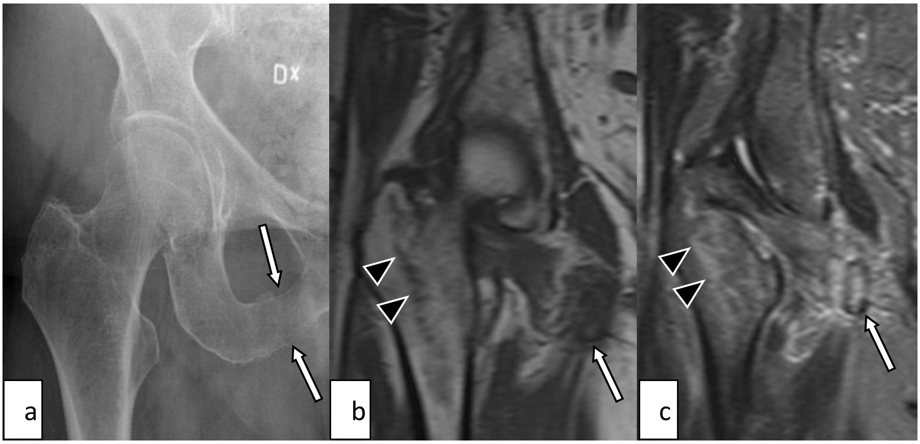


Figure 9. Female aged 85 years with clinical suspicion of hip fracture after a fall. Initial radiography (a) shows a fracture of the inferior obturator ring (arrows). MRI the following day, coronal T1 (b) and STIR image (c) shows a trochanteric fracture (arrowheads) and a concomitant obturator ring fracture (arrow).

DISCUSSION

GENERAL DISCUSSION

Introduction

Correct radiographic and CT diagnosis is dependent, not only on good examination technique, but to a high degree on observer experience. However, an occult fracture cannot be diagnosed even by experienced observers with awareness of normal anatomic features and a thorough and systematic interpretation of the radiographs and with adequate standard for the acquisition technique.

In some cases, equivocal findings of fracture will be present. Typically, the findings comprise subtle loss of integrity with inconclusive angulations of the osseous structures, borderline impaction or sclerotic lines that are not enough for definite diagnosis but are not entirely normal. The inexperienced radiologists may overlook these subtle signs of fracture; either downgrading the images from suspect to normal or from definite to suspect fracture.

Reliability versus accuracy

In order to validate radiological modalities in the assessment of occult and suspect hip fractures, statistical analyses with linear weighted kappa (κ) for observer agreement in imaging was performed to provide information about the "reliability" and "repeatability" of imaging diagnosis. "Reliability" measures to what extent repeated readings under unchanged conditions by different observers (inter-observer) agree and "repeatability" to what extent repeated readings under the same conditions by the same observer (intra-observer) agree [192]. A reliable and repeatable method should produce good agreement when used by knowledgeable observers and an ideal system should not have any observer discrepancies [193]. In clinical praxis kappa (κ) values of above 0.8 are considered almost perfect or perfect and may be implemented in a clinical trial [183]. Even if a reliable method is more likely to be accurate in ruling in or out fractures, it is vital not to conclude the "accuracy" of the readings from observer agreement only [192]. This can further be emphasized by that κ has shown to be different from accuracy as measured by the area under the receiver operating characteristic curve (ROC). Taplin et al included 31 radiologists who read 120 mammograms and studied agreement and accuracy of single- and double-reading of mammograms for breast cancer by using the mean area under the ROC. They showed that double reading resulted in better agreement but not in better accuracy [194].

The term "accuracy" in radiological readings tells us to what degree the diagnoses represents a "true fracture status" in the cases included as well as the freedom from both random and systematic reading errors. Surgical treatment is frequently used as clinical outcome of radiographically occult or suspect (non-displaced) hip fractures but as surgical management predominantly is performed with closed reduction with internal fixation techniques under fluoroscopy, it is to a large extent influenced by a non-verifiable radiological diagnosis. On the other hand, MRI is considered extremely accurate in fracture diagnosis with sensitivity of 100% and specificity of between 93% and 100% and is considered "gold standard" for assessment of occult and suspect fractures [23].

Perusal of the literature has not revealed any intra- or interobserver variation analyses with a large material and good design of either conventional radiography or computed tomography of patient with hip trauma. Agreement analyses in this thesis were performed in purpose to assess the reliability of radiography, CT and MRI in diagnosing occult or suspect hip fractures.

Bone bruise

It is well documented that MRI is extremely sensitive in hip fracture diagnoses due to the high water content with high proton density in trabecular bone [195]. When an occult or suspect fracture is present, areas of increased proton density in trabecular bone are accumulated as oedema and haemorrhage and can easily be recognized as changes in signal patterns, even for less experienced interpreters [196, 197]. In **paper I**, the observer agreement at MRI was almost perfect for all interpreters, regardless of experience.

A typical appearance of fracture at MRI is a black line on T1-sequences surrounded by high signal changes on inversion recovery or fat-saturated T2-sequences. Differently sized poorly defined areas of decreased signal intensity in the trabecular bone on T1-weighted images and increased signal intensity on fat-saturated T2-weighted or STIR images is commonly referred to as "bone bruise", and best visualized on images produced from STIR-sequences.

The term "bone bruise" in traumatic skeletal lesions is not clearly defined and there are several synonyms in the literature such as bone contusion, acute bone lesion and bone marrow oedema [198-200]. Bone bruise can also be seen in primary bone marrow oedema syndrome, which is a self-limiting disease of uncertain aetiology, presumably without foregoing trauma [196].

Few studies have been conducted on the histopathology of bone bruising on human subjects, with no reports on human femoral neck or trochanteric region. Rangger et al [201] evaluated histopathological and cryosection investigations of five cases of bone bruises of the knee. They described microfractures of cancellous bone as well as oedema and haemorrhage in fatty marrow. Other findings were fatty marrow necrosis due to impacted hyaline cartilage mixed with fragmented bony trabeculae. In a juvenile porcine cadaver model femoral neck fractures were produced through a mechanical apparatus. MRI images were compared to histological sections. The MRI signals were attributed to trabecular fractures only as there was neither haemorrhage nor oedema in the cadaver specimens [202]. In another study, six proximal tibiae in three anesthetized piglets were subjected to trauma and sacrificed after MRI examination and had ensuing histological study. In five tibiae there were varying signal changes at MRI which at histological examination turned out to be hemorrhage and edema and in two there were also trabecular fractures [203]. These experimental data indicate that we cannot differ between trabecular fractures, oedema and hemorrhages. Furthermore, distinguishing non-traumatic “bone marrow oedema” from traumatic bone marrow oedema (bone contusion, acute bone lesions and bone bruise) at MRI is difficult and must be aided by the clinical history of an associated trauma. Thus, it is important to note that all patients included in this thesis had suffered low-energy trauma to the hip prior to the MRI imaging. At observer agreement analysis for MRI in **paper I**, the few cases with diagnostic discrepancies were mainly attributed to differences in the interpretation of bone bruise; either as disagreement of fracture location due to a bone bruise on both sides of the capsular attachment, extending from the femoral neck into the intertrochanteric region, or either as obscured signal changes (due to age-related changes with demineralisation of trabecular bone) overlooked by the least experienced observers.

Fracture extension

Seemingly isolated fractures of the greater trochanter may be a part of a larger fracture into the intertrochanteric region [204-206]. Two previous reports on eight and 17 radiographically occult or suspect fractures propose that incomplete trochanteric fractures can only be diagnosed with MRI [40, 41]. In this regard, we tried to assess the intertrochanteric fracture extension for radiography, CT and MRI. In **paper I**, when avulsions of the greater trochanter were excluded from the study protocol the observer agreements in terms of linear weighted kappa (κ) for both radiography and CT were considerably reduced from 0.69-0.71 to 0.43-0.52 and from 0.91-0.97 to 0.59–0.76 respectively, while agreements for MRI remained almost perfect. The findings support that radiography and CT have their greatest strength in diagnosing cortical disruptions but are less reliable in determining the intertrochanteric fracture extension due to limitations of these modalities in detecting acute bony lesions (bone bruise) in cancellous bone. Even if CT has the ability to detect bone bruises as an increased density (attenuation) in cancellous bone and can strengthen the fracture diagnosis on the basis of these findings [95], the diagnostic performance of CT was clearly inferior to MRI in depicting solely trabecular lesions.

DETAILED DISCUSSION

Paper I

The study population in paper I on observer agreement comprises 170 patients examined with MRI, which by far exceeds previous reported materials on 23, 24 and 33 patients, respectively [70, 207, 208]. In the article by Verbeeten et al there was complete agreement between two senior observers but a kappa (κ) value of 0.75 registered between senior and junior observers. In the study conducted by Frihagen et al the agreement between senior observers was 0.78 and between seniors and an inexperienced resident 0.66. The kappa (κ) of 0.85 reported by Dominguez et al cannot be evaluated as the composition of the study population is not clearly stated. Our kappa (κ) values between 0.93 and 0.97 are most likely more robust than in the earlier reports and should be large enough for robust statistical analysis regarding consistency in diagnoses and to assess to what extent experience is influential in the diagnostics. The reliability of our study should not be influenced by the retrospective design. Our study was performed by three knowledgeable observers and it is not surprising that it showed very good observer agreement and should be able to test the diagnostic consistency of MRI.

Cortical disruptions and dislocations are the most obvious fracture signs at radiography and CT and observer agreement should be reached. However, agreement may be difficult to reach on subtle signs of fracture, e.g. trabecular disruption, discrete impactions, bone bruise and capsular distension. Osteoporotic and osteoarthritic changes my cause suspicion of fracture. The diagnostic discrepancies at radiography between the observers with varying degree of experience reflect that occult and suspect fractures cannot be diagnosed with radiography. Also, the least experienced observer diagnosed twice as many suspect cervical fractures than the experienced reviewers. Experienced observers are more decisive in confirming or ruling out fractures. However, for CT and MRI there was almost perfect agreement between all observers, in slight favor for MRI.

The only factor varying in *intraobserver* analysis is the observer. Perusal of the literature has not revealed any report on intraobserver analyses for occult hip fractures. Our study showed good intra-observer reproducibility for CT and MRI and inferior reproducibility for radiography. The kappa values for intraobserver variation were almost same as for the interobserver agreement results.

In the same material as in **paper I** we performed a study on 193 patients examined with CT after negative or equivocal radiography for suspicion of hip fracture and concluded that CT can detect almost all radiographically occult and suspect fractures and is highly accurate in ruling out cases needing surgery [72]. Thus, the high kappa values for inter- and intraobserver *reliability* at knowledgeable review for CT in **paper I** seemed closely related to the clinical management of these cases**.** In another study, on partly the same material, on 231 patients examined with CT for occult and suspect hip fracture, ancillary signs such as bone bruise and joint effusion were shown to strengthen the fracture diagnosis at CT [95]. Even if the studies lacked an imaging gold standard for all cases the studies indicated no false-positive cases and a CT sensitivity of 95%, judged by available outcome measures.

Paper II

In **Paper II**, the clinical utility of experienced review in diagnosing radiographically occult or suspect fractures was assessed. Furthermore the possible value of discriminating between occult and suspect fractures was assessed. Diagnostic differences in terms of accuracy between the general radiologists in the primary reports could not successfully be analyzed statistically due to the vast heterogeneity in experience among the observers. However, even if primary reports from the clinical situation were compared with consensus diagnoses by two musculoskeletal radiologists in a study situation with special interest in hip fracture diagnoses a feature of the study is that experienced observers are more accurate in diagnostics and more determined in confirming or ruling out fractures. This was underscored by that the percentage of suspect fractures that were confirmed after MRI were higher for the reviewers (73%) than for primary reporting (53%) and the percentage of negative cases that were changed to definite fractures were almost twice as high for primary reporting (37%) compared to review (21%). Also, at review there were half as many suspect diagnoses and half as many false negative diagnoses after MRI and all definite fractures at review were confirmed at MRI. Also, the clinical follow-up revealed no missed fractures at MRI. The higher number of confirmed fractures after MRI among the suspect cases, for both primary report and review were statistically significant. The tendency is that when subtle signs of fracture exist, experienced observers tend to upgrade occult fractures to suspect fractures and suspect fractures into definite fractures which can reduce the cases needing further imaging. The findings suggest that experience is of great importance in diagnosing radiographically occult and suspect fractures as well as in discriminating between these entities, and that all non-fractured trauma cases should benefit by control by an experienced radiologist.

Paper III

In a previous report we concluded high clinical utility of CT in detection of radiographically occult or suspect hip fractures with only two false negative studies in 86 normal cases of totally 193 patients with 109 hip fractures [72]. In another study on 65 patients 20% fractures were found with no missed fractures at clinical follow-up [74]. In a recent study by Thomas et al, on 1443 patients with trauma to the hip, 209 had inconclusive radiographs [96]. Of these, 199 underwent subsequent examination with CT of which 48 hip fractures were diagnosed. The study concluded that patients found to have either no fracture or conservatively managed fractures had an uneventful clinical course at 4 months follow up. Thus, judged by available outcome measures the authors claimed an accuracy of 100% for CT. It is noteworthy that the prevalence of occult hip fractures in their study was 15%, which is higher than previously reported in the literature [71, 77, 94, 209]. Thus the inclusion criterion of occult hip fractures in their study may be questioned. As the authors emphasized in their discussion, an explanation for the remarkable high accuracy may be the thin axial slices (0.625 mm) used. The findings underscore that CT has the ability to detect most occult hip fractures. However, in rare cases, the CT examination is inconclusive and remaining clinical suspicion of hip fracture necessitates further imaging with gold standard MRI. In order to compare the diagnostic performance of CT with MRI, we conducted a trial on 44 patients examined with both CT and MRI. Even if a thorough evaluation of the CT images were performed for presence of ancillary signs, such as bone bruise and lipoheamarthrosis, the sensitivity and specificity of CT came out inferiorly compared to MRI. The study had a retrospective nature, and only patients with inconclusive CT and subsequent examination with MRI for elucidation of possible fractures were included. The study design implies that the CT cases were the most difficult to diagnose during the study period. Patients with evident fractures at CT as well as patients with normal CT and decreasing symptoms were not further examined with MRI and thus excluded from the study.

At CT review there were no equivocal diagnoses while all primary reports were scored as either negative or suspect for fracture. The diagnostic disagreements at CT between primary reporting and review (k=0.11 and 0.13) should mainly be attributed to the careful evaluation by knowledgeable observers with special interest in hip fracture diagnostics who had almost perfect agreement (k=0.87).

As high observer agreement reflects high reliability, the large diagnostic discrepancies between “almost perfect” agreement after CT review and “perfect” agreement after “gold standard” MRI is remarkable since the reviewed CT diagnoses were changed in one third of the patients after MRI (for both reviewers). Thus, the findings in **paper III** underscores that reliability is different from accuracy and that high reliability in terms of high observer variation is different from correct diagnostics.

The literature reveals no reports on occult fractures appearing after normal MRI and all patients in this thesis with normal MRI had an uneventful clinical course. Contrarily, the study in **paper III** implies that the accuracy of hip fracture diagnoses at CT in the study population is low for general radiologists. Perusal of the literature reveals four previous studies on the same subject. The studies describe inconsistencies on fracture diagnoses between CT and MRI in totally 13 of 29 occult hip fractures (45%) overlooked by CT [46-49]. The findings in these reports were similar to our study and demonstrate an inferior accuracy for CT in fracture diagnosis compared to MRI.

It has previously been shown that ancillary signs of fracture, such as bone bruise and lipoheamarthrosis can strengthen the diagnosis of occult or suspect hip fractures in CT [95]. Even if ancillary signs were assessed in **paper III** and facilitated the fracture diagnosis in a few cases, MRI diagnostics came out superior compared to CT. The major advantage of CT is that it is fast and has the capability to exclude or verify most fractures with inconclusive radiography [72, 96]. However, CT may sometimes be difficult to interpret, especially for less experienced radiologists. MRI, on the other hand, is time consuming, has contraindications and is not always immediate available, but is easy to interpret, even for less experienced radiologists.

Paper IV

In our previous papers I-III, on partly the same material, a substantial number of pelvic fractures as well concomitant hip and pelvic fractures were noted in patients with occult or suspect hip fracture after low-energy trauma. It is well known that MRI is highly accurate in detection of hip and pelvic fractures [69, 71] and also has the capability to address soft tissue lesions such as oedema, haemorrhage and accompanying muscle injuries around the hip as well as malignancies [69, 71, 210, 211]. The current thesis, is however, focused on skeletal lesions only.

Perusal of the literature revealed five previous studies with conflicting results regarding the prevalence of concomitant hip and pelvic fractures. Two reports on respective 106 and 98 patients suggest that hip and pelvic fractures are mutually exclusive [69, 212]. In three reports frequencies of between two and 11 percent were noted [101, 210, 213]. In a study from 1995 on 70 patients with radiographically occult hip fractures there were six cases with concomitant pelvic fractures at MRI [101]. In a recent article two of 113 retrospectively reviewed patients had concomitant occult fractures of the proximal femur and the pelvic ring [210]. Another recent retrospective review on 102 patients for suspect occult hip fractures reported 11 concomitant pelvic and proximal femur fractures [213]. These five articles have fairly similar inclusion criteria and patient material as in paper IV, consisting of average elderly patients subjected to low-energy trauma with suspicion of occult hip fracture. In another study on 145 patients with diagnosis of insufficiency fractures it was noted that two or more insufficiency fractures were present as well as concomitant fractures of pelvis and proximal femur [214]. Thus, exclusively pelvic and concomitant fractures in the femur and pelvis have been reported at MRI both in normal elderly and in osteoporotic patients. Our study on 316 patients is by far the largest of any comparable study and should provide more robust statistics. All patients in paper IV were referred to MRI for clarification of radiographically occult or suspect hip fractures, thus no patients were referred for pelvic fractures. The frequency of concomitant hip and pelvic fractures was 9% and there were an equal proportion of normal cases (23%) and exclusively pelvic fractures (26%). Even if concomitant hip and pelvic fractures are rare, the findings in **paper IV** demonstrate that these fracture combinations can occur at a single low-energy trauma. Thus, patients with inability to bear weight after a fall with evidence of pubic rami fractures only (on either side of the trauma) at primary radiography should not be dismissed without second-line investigations.

LIMITATIONS

From the material in this thesis, collected during nine consecutive years, it was impossible to calculate the exact prevalence of occult and suspect hip fractures since surgically treated displaced fractures after index radiography or discharged patients with normal findings were excluded from the studies (**paper I-IV**). Accordingly, a few specific sources of bias concerning the retrospective study design of this thesis should be mentioned. Firstly, only patients with clinical suspicion of hip fracture underwent second-line investigation with CT and/or MRI, thus inaccurately high approximations of occult fractures were likely to be present. If all patients with inconclusive radiography were referred for subsequent examinations, the incidence of occult or suspect fractures would probably be even lower (selection bias). Secondly, since occult and suspect hip fractures are non-displaced and typically treated with minimally invasive techniques, surgical confirmation of the actual fracture status is rarely or never obtained and MRI as reference standard becomes its own "gold standard", i.e. circular logic (incorporation bias). Thirdly, the feature of overlapping cohorts in this thesis might have introduced recall biases even if the data collections for the studies (paper I-IV) as well as the reviews were performed more than one year apart and there were no other information available at image review than age, gender and name. Also, the vast number of patients with the shared property of non-displaced fractures makes recollection difficult.

CONCLUSIONS

Paper I: At radiography, the least experienced observer was less decisive and scored twice as many equivocal fractures than as the other two observers. Patient age did not significantly influence the results. Observer agreements for CT and MRI for *fracture* diagnosis were almost perfect when used by knowledgeable observers, but the intertrochanteric *fracture extension* could not successfully be assessed with CT, regardless of experience. MRI in occult and suspect hip fractures is easy to interpret, even for less experienced observers.

Paper II: Compared to experienced review, general radiologists tend to downgrade definite radiographic signs of fracture to equivocal findings. MRI detected a significantly higher proportion of fractures among radiographically suspect than among negative cases, both at primary reporting and review. Thus, experienced review of radiography can with statistical significance reduce the number of patients possibly needing further imaging. The results suggests that radiographically occult or suspect fractures are different entities and that suspect fractures should benefit from experienced review. MRI in occult and suspect hip fractures is easy to interpret regardless of radiological experience. At clinical follow-up, no missed fractures at MRI were revealed.

Paper III: There were a high proportion of discrepancies between clinical symptoms of hip fracture and the CT findings. At primary reporting MRI changed the majority of the CT diagnoses. Even at experienced review of CT, with almost perfect observer agreement, MRI changed the CT diagnoses in one third of the cases. Thus, high interobserver reliability for the musculoskeletal radiologists at CT did not reflect high diagnostic accuracy. Clinical follow-up revealed no missed fractures at MRI.

Paper IV: All patients were referred to MRI for occult or suspect hip fracture. About half of the patients were dismissed from the emergency department with either no signs of fracture or exclusively pelvic fracture after MRI. The other half of the patients had evidence of hip fracture at MRI, of which one fifth had concomitant hip and pelvic fractures. The study confirms that concomitant fractures of the hip and pelvic fractures are not mutually exclusive.

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