Imperial College London

‘The future of treatment for avascular necrosis of the femoral head: hip resurfacing arthroplasty health economics and surgical technology’

Supervisor: Prof. Justin Cobb

Co-supervisor: Dr. Richard Abel

Candidate: Zexin Zheng

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Department of Surgery and Cancer

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Originality Declaration

I hereby declare that all work contained in this thesis has been produced by me and that all else has been appropriately referenced.

Copyright Declaration

List of Abbreviations

THA	Total hip arthroplasty
HRA	Hip resurfacing arthroplasty
OA	Osteoarthritis
AVN	Avascular necrosis of femoral head
SARS	Severe Acute Respiratory Syndrome
AM	Additive manufacturing
3D	Three- dimensional
NJR	National joint registry
BHR	Birmingham hip resurfacing
CT	Computed tomography
STL	Stereolithography
CEA	Cost-effectiveness analysis
NICE	National Institute for Health and Clinical Excellence
GT	Greater Trochanter
LT	Lesser Trochanter
ICER	Incremental cost-effectiveness Ratio
PSA	Probabilistic sensitivity analysis
WTP	Willingness to pay
ICC	Intraclass Correlation Coefficient

Abstract

Introduction

Avascular necrosis of the hip (AVN) is a disease which causes a lack of blood supply in the femoral head, resulting in the bone death, and a subsequent biomechanical failure of the hip joint. Current treatment is mainly to seek for total hip replacement. However, the majority of these affected patients < 60 years of age, having total hip replacement will lose the ability to engage in massive physical work, or lower their life qualities. On the contrary, hip resurfacing arthroplasty (HRA), which is a femoral head preserving surgery, seems to be an ideal intervention for AVN patients because HRA does not change native hip anatomy and helps restoring hip joint. The present question when performing HRA on AVN patients is, surgeons do not know to what lesion extent can they perform such surgery. This thesis aims to review all aspects of AVN, to find out whether the HRA is more cost-effective than THA, to determine the maximum lesion extent to perform HRA, and to plan the surgery better.

Method

First, we did a comprehensive review on AVN's mechanism, treatments and staging systems. Second, we use a health economic model to simulate the benefits of performing HRA over THA. Third, we simulate a series of lesions with bone graft HRA in composite bone mechanical tests under healthy human walking load in the hip joint, and compare these lesions data to non-lesion data. From these data, we are able to summarise an indication table for AVN-HRA classification. Last, we develop a pre-operative planner to optimse HRA on AVN, and validate the planner's reliability and reproducibility. All these steps have never been fully studied before.

Results

First, the AVN prevalence rates in easter Asian countries were quite high, and the non-surgical treatment cannot cure AVN, as well as the lack of hip resurfacing AVN staging system. Second, the

health economic model (Markov model), specifically its Monte Carlo simulation showed a 60% probability that HRA was more cost-effective than THA during 10 years post-operatively. Third, the simulated lesions on HRA mechanical tests demonstrated that 10mm depth of lesion down from the tip of the prepared femoral head with autograft, were able to achieve initial stability. Any lesion depth deeper than 10mm is not recommended for hip resurfacing. Four, the inter-observer and intra-observer reliability and repeatability were all higher than 80% using our pre-operative planner, meaning that this planner is reliable enough to be a workhorse for AVN hip resurfacing pre-operative planning.

Conclusion

Overall, our results showed that HRA is more cost-effective than THA, and we found out that 10mm of lesion depth was on the margin of the safe HRA, with autograft to fill the defect cause by lesion. Finally, we created a reliable planner that helps planning AVN HRA preoperatively. Our results well matched the hypothesis mentioned above.

Contents

Chapter 1

Introduction

1.1 What is avascular necrosis of femoral head?

Avascular necrosis of femoral head (AVN), also known as osteonecrosis of femoral head (ONFH), is a major cause of hip disease leading to painful secondary osteoarthritis, best treated by hip arthroplasty. Approximately 0.73% of Chinese population (1) and 0.02% of Japanese population develop symptomatic AVN (2). In the UK, up to 40% of patients with sickle cell disease developed AVN (3). In the early stage, AVN patients are asymptomatic. When the disease progresses, femoral head has local sclerosis and cystic changes, some even have femoral collapse and deformation. These changes lead to hip pain and even a loss of ability to walk. Commonly, the condition presents late (4, 5). When significant collapse has occurred, no drugs or other preservation intervention cannot prevent the progression of necrosis, and hip arthroplasty is the only surgical option.

1.2 Is hip resurfacing a more cost-effective intervention for AVN patients than total hip replacement?

Compared to traditional total hip arthroplasty (THA), hip resurfacing (HRA) has many advantages, most prominent of which are significant lower dislocation rates, and a much higher range of motion and preserves much more femoral head bone stock (6, 7). Therefore, HRA is theoretically ideal for treating young and active AVN patients under the age of 60. Previous follow-up studies (8-18) proved that HRA was able to provide decent results, but we still do not know whether HRA is a more cost-effective option to THA. To achieve this, a health economic model (Markov model) was carried out to compare between total hip replacement and hip resurfacing for AVN.

1.3 To what AVN extent can surgeon perform hip resurfacing for patients?

The finite element analysis from Tai et al (19) indicated that a large AVN lesion size had no significant difference when compared to no lesion hip resurfacing in terms of bone-implant displacement. They simulated 4 levels of necrotic regions, range from 0°, 60° to 100°, 115°, the displacements were around 8 microns throughout the range. This suggests that hip resurfacing might be a viable option For AVN patients with large necrotic lesions. However, Yang (20)scanned 55 AVN hips and had different lesion location to Tai's experiment, that the lesions were not only limited to the weight-bearing area. Yang also analysed 28 necrotic hips and drew to a conclusion that the most common areas to fracture were the subchondral area and the deep necrotic portion adjacent to the necrotic-viable junction. Amstutz et al. (12) reported long-term follow-up results of hip resurfacing on AVN patients and they reckoned a deep lesion such as 1cm down the femoral head should also be indication for hip resurfacing surgery. However, such previous studies fail to answer the question to what lesion extent are surgeons willing to perform hip resurfacing surgery.

1.4 3D preoperative planning

In the past, surgeons used pre-operative template on patients' x-ray on the monitor, in order to measure and estimate intraoperative implant size (21, 22). However, such method would result in high errors when planning AVN on hip resurfacing surgery. This is because AVN's irregulate lesion shape and lesion extent. On the contrary, preoperative 3D planning generates 3D view of lesion and is much more accurate when predicting implant size results (21-23).

Despite these advantages, the repeatability and reliability of preoperative planning cannot be overlooked. Yasushi (23) , Carter (24) and Unnanuntana (25) reported that the reliability levels were higher than 70% when predicting implant sizes. In comparison, both Choi (26) Olsen et al (27) reported low reliable results of under 60% using x-ray.

1.5 Aims of this thesis

This thesis aims to explore four sections regarding hip arthroplasty surgery:

1: Summarise the cause, symptoms, diagnosis, treatment and staging of AVN.

2: The Markov economic model to compare HRA with THA.

3: The maximum lesion indicated for hip resurfacing.

4. An AVN-hip resurfacing staging system based on lab results

5.The repeatability and reliability of AVN hip planer for hip resurfacing.

Chapter 2

Literature Review

2.1 The mechanism and risk factors of avascular necrosis of femoral head

The mechanism of AVN has not been fully understood, most theories point to a pathomechanical condition of the femoral head (28), a damage or interruption to the blood supply (29).This causes partial death of bone cells and bone marrow components and leads to subsequent bone regeneration (30). This condition eventually progresses to bone tissue necrosis, resulting in structural changes and collapse of the femoral head, pain in the hip and functional disorders (31). The earliest pathological changes in the femoral head are the death of hematopoietic cells and adipocytes. Subsequently, oxygen deprivation caused by the lack of blood supply osteocyte death in the femoral head (32, 33). This is followed by bone repair process, which includes necrotic bone resorption and new living bone regeneration to replace dead bone (34). However, the faster speed of resorption than that of regeneration in the subchondral trabeculae, leads to fewer bone stock and the destruction of normal hip joint (34). It is clear that resorption itself causes subchondral fracture and hip joint incongruity rather than necrosis (35, 36).

Understanding such pathomechanical process, but what causes the ischemia in the femoral head? 3 main hypotheses: 1) Vascular interruption caused by trauma. 2) Thrombotic occlusion, caused by either intravascular coagulation, or alcohol-induced/steroid-induced fat emboli. 3) Extravascular compression (34).

Among all the causes, steroid administration is the most common factor (37-40). Steroid-induced cases account for up to 38% of all AVN cases (41). Also, steroid-induced AVN made up 10% of all the total hip replacements in the USA (42). As mentioned above, steroid induces fat emboli and leads to later ischemia in the femoral head, and causes necrosis eventually.

Steroid might be the last medicine to save those patients who are in critical ill, especially those have severe respiratory disease. A randomised control trial in finding treatments for COVID-19 from

Oxford University indicated that steroid could reduce the mortality rate by 1/3 among those dying patients (43). Despite such life-saving efficacy, however, steroid might cause AVN after long-term use (43). Take Severe Acute Respiratory Syndrome (SARS, caused by coronavirus) as an example, patients had steroid-induced, pathological bone necrosis (AVN), with incidence rates of up to 33% (44, 45). In the SARS related AVN, the vast majority of patients who had high-dose (accumulated dose>2000mg), intravenous injection of prednisone and oral prednisone (45). High steroid dose, along with long-term steroid use (>18 days) were high risk factors for AVN. AVN occurred within 6 months after initial steroid treatment on average, and most of them were observed at 3 months (44). This is to say that AVN cases would increase after coronavirus treating with steroid.

In addition to steroid use, AVN can also be induced by other factors. Chinese AVN Diagnosis and Treatment Guidelines (46) indicated that steroid use, alcohol abuse, sickle cell disease and systemic lupus erythematosus are the main risk factors for AVN.

2.2 The diagnosis of AVN

In general, the diagnosis of AVN is being made based on signs, symptoms, physical examination and imaging tests. The sign of AVN is tenderness around the hip joint, and the symptoms include pain in the groin, pain or buttock. However, these signs and symptoms may be only noticeable in the late stage of AVN, patients might not present any in the early stage. Because of limited range of motion from AVN, physical examinations focus on checking Shape test, Thomas Sign. These examinations are positive indicated the necrosis is severe in the ipsilateral femoral head and the affected patients cannot extend their hips. Last but not least, imaging tests are vital to confirm the diagnosis of AVN. Common imaging tests include X-ray plain film, CT scan and MRI scan, X-ray cannot detect bone changes in the early stage of AVN, both CT and MRI scan are able to show early bone changes in the femoral head (47).

In addition to those mentioned above, the history of trauma, steroid administration, as well as alcohol abuse provide evidence when making the diagnosis.

2.3 Current non-surgical treatments for AVN

Non-surgical interventions for AVN include bed rest, weight reduction, pharmacological therapy. Conservative management such as bed rest and weight reduction cannot reverse necrosis and the treatment successful rate was as low as 20% (32).

With regard to pharmacological therapy, case study from Agarwala (48) reported alendronate (a kind of bisphosphonate) was able to relieve pain and improve joint range of motion on AVN patients. Randomised control trials from Lai (49) and Chen (50) reported contradicted results, Lai's study had a significant lower femoral collapse rate in the alendronate treatment group than the placebo control group while Chen's alendronate group (50) had no significant difference compared to placebo control group in the progression of AVN. Ma (51) demonstrated that bisphosphonate would reduce bone tensile strength and Young's Modulus, and increase microcrack accumulation after long-term use. These findings suggested that bisphosphonate would reduce bone mechanical strength and might lead to AVN progression.

To summarise, the efficacy of treating AVN with bisphosphonate is still not confirmed, therefore bisphosphonate should not be routinely used on AVN cases (52).

2.4 Current surgical treatments for AVN

AVN patients are usually asymptomatic or a slightly lower range of motion in abduction and external rotation in the early stage, they have severe symptoms when femoral collapse happens in the middle to end stage. Pre-collapse might be the last chance for hip-preserving treatment for AVN. It is recommended that the pre-collapse should be considered as a dedicated stage, evaluating and guiding the selection of treatments (53). Biomedical regeneration surgery is mainly based on core decompression of the femoral head, or combined with other biomedical treatments based on it (54). A meta-analysis (55) showed that core decompression of the femoral head is a safe and effective surgical intervention for the treatment of early-stage AVN. It was also considered to be an effective intervention to treat early-stage femoral head osteonecrosis by Ficat (56). However, Kim (57) found that drilling into the femoral head destroyed a large number of native trabecular bone structures, decreased the mechanical stiffness of the femoral head and neck, and may lead to iatrogenic femoral head collapse. The results of a prospective study with a follow-up of 5 to 10 years reported by Hernigou (58), along with a randomized controlled trial by Zhao (59), demonstrated that core decompression cannot prevent the progression of femoral head collapse, therefore the core decompression in treating AVN was controversial. Despite such controversy, core decompression can be used for the treatment of ARCOI/II stage lesions in small and medium extent (15% lesion extent of the whole femoral head volume or Kerboul angle <200°), and most of these patients can be treated conservatively (60). Femoral head preservation rate after femoral collapse (Ficat Stage III) was only 23-35% in a published study (61). For the collapsed stage and post-collapse stage, core decompression combined with bone grafting can be used (62, 63), while at these stages, decompression alone was not recommended. Wang (64) used femoral neck decompression + debridement + autologous graft for AVN treatment with an average follow-up of 25 months. The results showed that the survival rates of hip preservation in patients with ARCO ⅡA, ⅡB, ⅡC, and ⅢA stages decreased when lesion progressed. Steinberg (65) reported that for the Steinberg Stage early III, autologous bone graft was able to reduce the demand for THA, which dropped from 82% to 23%, while the femoral head preservation rate of Steinberg Stage IV was only 50%. In conclusion, none of these femoral head preservative interventions can guarantee the treatment satisfaction. Once the disease progresses to end stage, the hip joint function is highly limited, artificial joint replacement can be only option to restore the hip joint function. However, the use of total hip replacement in young and active patients has disadvantages. They are as follows: 1) The young and active patients have a greater demand for strenuous exercise and therefore the implant wears much faster than the elderly patients, which shortens the implant longevity. 2) The extended reaming to the femoral canal during surgery and the post-operative long-term bone mass loss between the femoral shaft bone stock – femoral stem wear led to difficulty in revision surgery.

Table 2.1. The summary to the AVN interventions.

Intervention	Mechanism	Pros	Cons	References
Core decompression	Core decompression can improve the symptoms of patients with AVN by removing the necrotic bone in the femoral head and reducing the pressure in the medullary cavity	Core decompression is simple to perform, and the clinical outcome is satisfactory for the patients in the early-stage of AVN	Poor outcome for late-stage AVN	(66-68)
Core decompression combined with stem cell transplantation	Bone marrow stem cells implanted into the femoral head have the ability to regenerate new bone. Combined with	For patients in the early-stage, the outcome is good, and the postoperative hip preservation rate and hip joint function are	The stem cell extraction is complex and has high equipment requirement	(28, 69-73)

	core decompression, stem cells can be implanting when decompressing	better than core decompression alone		
Vascularised bone transplantation	The necrotic bone in the femoral head was removed and the vascularised bone flap was implanted to the defect	It provides effective mechanical support and new blood supply for the necrotic femoral head, and has good long-term outcome	Vascularised bone transplantation is not easy to perform, the surgical technique is difficult, and is also massively invasive	(74-79)
Tantalum rod implantation	Tantalum rod has high rigidity and porosity, which can provide mechanical support for the femoral head and promote the formation of new bone	Low surgical technique requirements and good clinical outcome for the early-stage AVN	Poor outcome for end-stage patients, and the hip preservation rate is low	(80-82)

	regeneration			
Osteotomy	By modifying the bearing area of the joint, the necrotic part of the femoral head could avoid bearing weight	osteotomy has a good mid-term outcome and can delay the progress of AVN	Osteotomy is not minimally invasive, and change of the normal anatomical structure of the femoral head, would lead to the difficulties for the later hip replacement surgery	(83, 84)
Total Hip replacement	Artificial joint used to replace the diseased hip joint to reconstruct the normal hip joint function	Great clinical outcome	THA is not suitable for patients with large demand for exercise or sports. The implant longevity is short and might need revision surgery	(85-88)

2.5 Current AVN staging systems and lesion shape

ARCO (Association Research Circulation Osseous) had renewed their staging system for AVN at 2019 (89). The main updates of 2019 version compared to the 1994 version are as follows:

Stage 0 deleted

The quantitative standard of necrotic extent was cancelled, and the 2019 staging system was no longer based on the size of necrotic extent.

According to the degree of femoral head collapse (≤2 mm, > 2 mm), the original three subtypes of stage III (femoral head collapse stage) were simplified into two subtypes.

The main AVN staging systems are as follows (Table 2.2):

Table 2.2 Mainstream staging systems for AVN.

<table>
<tr><th colspan="5">Current AVN Staging Systems</th></tr>
<tr><td>Features</td><td>Ficat
(90)</td><td>Steinberg
(91)</td><td>ARCO 1994
(92)</td><td>ARCO 2019
(89)</td></tr>
<tr><td>Pre-clinical</td><td>0</td><td>0</td><td>0</td><td>-</td></tr>
<tr><td>MRI change</td><td>I</td><td>I</td><td>I</td><td>I</td></tr>
<tr><td>X-ray or CT change</td><td>II</td><td>II</td><td>II</td><td>II</td></tr>
<tr><td>Subchondral Fracture</td><td rowspan="3">III</td><td rowspan="2">III</td><td rowspan="3">III</td><td>III</td></tr>
<tr><td>Femoral collapse≤2 mm</td><td>IIIA</td></tr>
<tr><td>Femoral collapse>2 mm</td><td>IV</td><td>IIIB</td></tr>
<tr><td>Joint space narrowing</td><td rowspan="2">IV</td><td>V</td><td rowspan="2">IV</td><td rowspan="2">IV</td></tr>
<tr><td>Progress to Osteoarthritis</td><td>VI</td></tr>
</table>

As shown in the table, that these most popular staging systems have not yet made any consensus, particularly on the collapse height and higher stage. This is because surgeons have different perspectives towards surgical interventions, which are popular in some countries whereas not in other countries. For example, Japanese surgeons are in favor of transtrochanteric osteotomy, but surgeons from other countries might not be pleased with this kind of iatrogenic change to the native hip anatomy. This intervention might lead to postoperative bone non-union and would increase the difficulty in later total hip replacement. Other interventions such as Core Decompression, can only be used on AVN patients in the early stage.

With regard to lesion shape, ARCO 1994 (92) termed the lateral lesion as 'Type C', which was also the largest lesion type. Type C lesion resembles to the simulated lesion in the Figure 4.4, chapter 4, and this is why we simulated the lesion like that.

2.6 Commonly used arthroplasty implants based on Joint Registries data

In the 2019 Australian Joint Registry Annual Report, they documented that the Exeter V40, CORAIL, and Polarstem were the most used femoral stems while the Trident (Shell), PINNACLE, and R3 were the most frequently used acetabular prostheses for primary total conventional hip replacement (93). Osteoarthritis was the major diagnosis (88.3%) for primary total hip replacement and had a lower revision rate (9.9%) at 18 years., while AVN was accounting for only 3.2% of primary total hip replacement and had a higher revision rate (11.9%) at 18 years. However, these revision rates had no significant differences between two interventions. Among all total hip replacements, over 60% used cementless fixation whereas cemented fixation dropped to only 3%.

On the contrary, the National Joint Registry (NJR) in England and Whales seemed to be in favor of cemented fixation. NJR reported lower dislocation rates in cemented fixation than cementless fixation for total hip replacements from 4 randomised control trials (94). With regard to bearing surfaces, long-term RCTs found that cross-linked polyethylene cup liners had lower revision rates than non-cross-linked polyethylene cup liners, and ceramic-on-ceramic head on cup liner bearing surface had lower incidence rate than a metal-on-polyethylene femoral head on cup liner bearing surface.

NICE guidelines (95) reported comparative RCT results of total hip replacement and hip resurfacing for osteoarthritis patients. No significant differences observed on Oxford Hip Score, Western Ontario McMaster Osteoarthritis Index score…etc. NJR's assessment group conducted a meta-analysis for 2 RCTs and reported that total hip replacement implant was more likely to be infectious than hip resurfacing implant 12-56 months postoperatively. 2 systematic reviews which included RCTs concluded hip resurfacing arthroplasty had higher revision rates than total hip replacement 10 years postoperatively. In addition, they also indicated that hip resurfacing arthroplasty was more likely to be complicated with component loosening.

Despite such disadvantages, hip resurfacing is better in terms of postoperative activity levels (6, 7), especially in younger patients (17). Past studies of AVN on hip resurfacing (8-18) also proved that resurfacing was robust treating AVN. The most common types of hip resurfacing implants are metal bearings, they are Conserve Plus (metal on metal, stem cemented or uncemented), Birmingham Hip Resurfacing (metal on metal, stem cemented), Corin Cormet 2000 (metal on metal, stem uncemented), Magnum (metal on metal, stem uncemented).

The biggest concern regarding hip resurfacing on AVN was its complication, component aseptic loosening (8-18). Strong level evidence of hip resurfacing on AVN is lacking, long-term RCTs are still needed to verify its efficacy.

To summarise, both total hip replacement and hip resurfacing arthroplasty provide ideal postoperative outcomes, although hip resurfacing arthroplasty has higher revision rates and complication rates. Hip resurfacing arthroplasty has higher postoperatively activity levels.

Chapter 3

Cost-effectiveness analysis comparing total hip arthroplasty and hip resurfacing for avascular necrosis based on published data

3.1 Abstract

Background: Avascular necrosis of the hip (AVN) is a common condition globally, resulting painful secondary osteoarthritis (OA) which is treated in the same way as primary OA. The purpose of this study was to use the published literature to compare the effectiveness of total hip arthroplasty (THA) and hip resurfacing arthroplasty (HRA) for this secondary OA and to conduct a cost-effectiveness analysis based upon this data.

Method: A systematic review was performed of all papers reporting the outcome of hip arthroplasty for AVN. Implant survivorship and revision rates were evaluated, matching mean age at index surgery and mean follow-up times. A Markov model was simulated using published cost data. Sensitivity analyses evaluated cohort age, utility values, failure probabilities, and treatment costs.

Results: 14 studies (985 hips) in the THA group and 14 studies (1069 hips) in the HRA group were included. The re-operation rates with the endpoint of revision for any reason were significant higher in THA (8.2%, 62 hips) than HRA (6.7%, 71hips) at a mean follow-up of 8 years. Mortality following THA was 4 times significantly higher than HRA. The Markov model and Monte Carlo simulation showed a 60% probability that HRA was more cost-effective than THA in the first ten years of Markov model simulation following surgery.

3.2 Introduction

The procedure of total hip arthroplasty (THA) is well established as a safe and effective intervention for osteoarthritis (OA), but the medical complications associated with AVN make THA significantly less cost-effective (96). Hip resurfacing arthroplasty (HRA) is a conservative alternative to THA enabling higher levels of activity (6, 7), with good long-term outcomes in younger patients (17), although patients with AVN experience a significantly higher revision rate compared with patients with primary osteoarthritis. The Australian Joint Registry reports a lower mortality rate for HRA when compared with THA at all-time points up to 15 years postoperatively (93). This is confirmed in a large study based upon data from the UK national joint registry and corrected for age and co-morbidity (94).

Despite these advantages, hip resurfacing remains controversial for two reasons. Firstly, there remain concerns regarding the release of metal ions from some devices, which have now been withdrawn (97, 98) leading to a more widespread opinion that resurfacing in general is unsafe. Secondly, a hip resurfacing can be revised to a dual mobility hip replacement relatively easily, while revision of a total hip replacement may be technically demanding, so the threshold for revision may differ substantially between the procedures (99). The use of a headline 'revision rate' to compare the two procedures when the thresholds for revision are so different may thus lead to perverse conclusions (100).

In this study, we sought to address 2 null hypotheses for patients with AVN:

(i) the two forms of arthroplasty are equally safe.

(ii) the two forms of arthroplasty are equally cost-effective.

3.3 Material and Methods

Search strategy

PubMed, Embase and Cochrane were systematically searched from their commencing dates to April 13, 2020. Reference checking and hand searching of these databases was then undertaken, and experts in relevant fields in NICE were identified. Possible data from conferences attended was also sought. Only publications in the English language were included. The protocol had been registered on Inplasy before searching, with a protocol number of 202040200 (see Appendix I). Mesh terms can also be seen at the Appendix I.

Inclusion Criteria

(i) For inclusion, a study should be a randomised controlled trial, cohort or observational study. (ii) Patients in the studies having total hip arthroplasty or hip resurfacing arthroplasty who were diagnosed with avascular necrosis of the femoral head. (iii) for inclusion, a study should compare groups of THA and HRA, or a single cohort of either THA or HRA patients. (iv) for inclusion, a study should report at least the end point of re-operation due to component failure for any reason.

Exclusion Criteria

Prior total hip replacement.

Validity and quality assessment

Two main reviewers (one surgeon and one physician, experienced with hip surgery) examined every paper, and a third reviewer (an expert in hip surgery) resolved any disagreements, and decided data to be extracted and terminology used in PubMed/Embase/Cochrane. All processes followed PRIMSA checklist (see Appendix II)

Data Abstraction

(i)All patients' demographic data and outcome variables in 2 interventions (THA and HRA) were abstracted. Two reviewers independently abstracted outcome data from the included studies, and disagreements were solved through consensus.

(ii)Costs and effectiveness

The costs of the two procedures, and their utilities were gathered from the recent literatures.

The Markov model ran a Monte Carlo simulation - probabilistic sensitivity analysis (PSA), with 1,000 iterations for 10 cycles (10 years). Model outputs include quality-adjusted life years gained (QALYs), the estimated probability of that either intervention is more cost-effective at a willingness to pay threshold of £ 20,000/QALY, and the incremental cost-effectiveness ratio (ICER) which determined the relative cost of QALYs obtained by HRA in comparison with their cost obtained by THA.

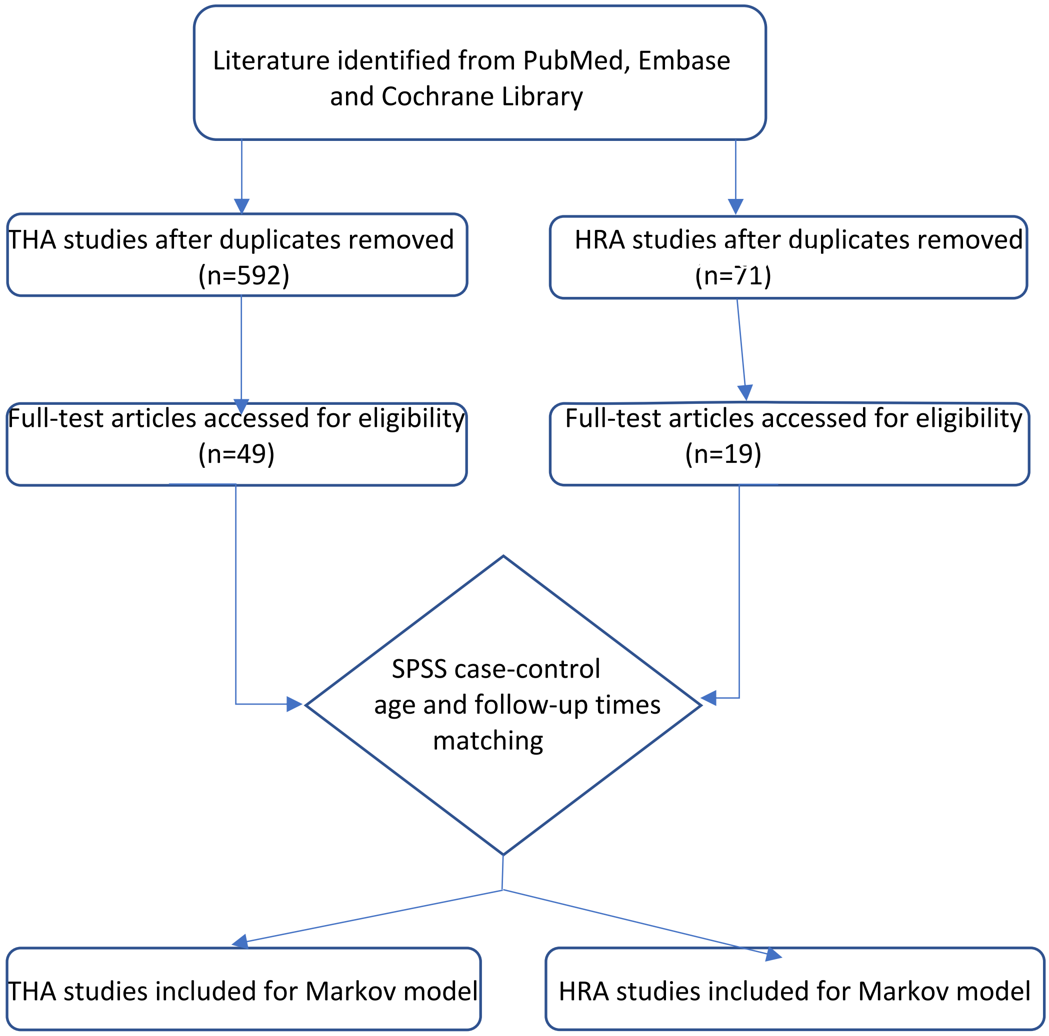
Matching

The studies were matched at 1:1 ratio between HRA and THA, using case control matching function in the SPSS. Variables to match on were Mean Age and Mean Follow-up Time. Match tolerances were set to 2 and 2, which mean 2 years of threshold both for Mean Age and Mean Follow-up Time. Group Indicator was set to Group (HRA/THA), Case ID was set to Study ID. Give priority to exact match and sampling without replacement. The reason we sought for 1:1 ratio was that a longer follow-up times would lead to higher mortality rates (101), the Australian Joint Registry reported significant incline of mortality rates from 23.2% (10 years postoperatively) to 52.5% (18 years postoperatively) for THA patients, and 3.7% (10 years postoperatively) to 12.2% (18 years postoperatively) for HRA patients. These higher mortality from THA might be the older ages having surgery, although co-morbidities may also lead to more deaths. Therefore, we decided to match mean age and mean follow-up times over other factor. We did try to match HRA to THA studies at 1:2 or 1:4 ratios, however, the follow-up times from THA were always longer, which had more deaths. Our Markov model is quite sensitive to deaths, so the HRA to THA at 1: 1 ratio was most suitable in this simulation.

Analysis

(i) Mortality rates and re-operation rates were calculated and from included studies, respectively. (ii) Studies matched mean age and mean follow-ups using SPSS 26.0 (IBM, New York, USA), publication bias and sensitivity analysis were calculated with STATA 16 MP (StataCorp, Texas, USA) (iii) Cost-effectiveness analysis (CEA) using Markov model was developed by Fitzpatrick (99) and repeated by others (100, 102, 103). The TreeAge Pro 2020 R2 (TreeAge Software LLC, Massachusetts, USA) was used to simulate 10 years of cost-effectiveness between THA and HRA after surgery in patients' fourth decade (between 40 and 49 years of age).

Figure 3.1. Study flowchart.



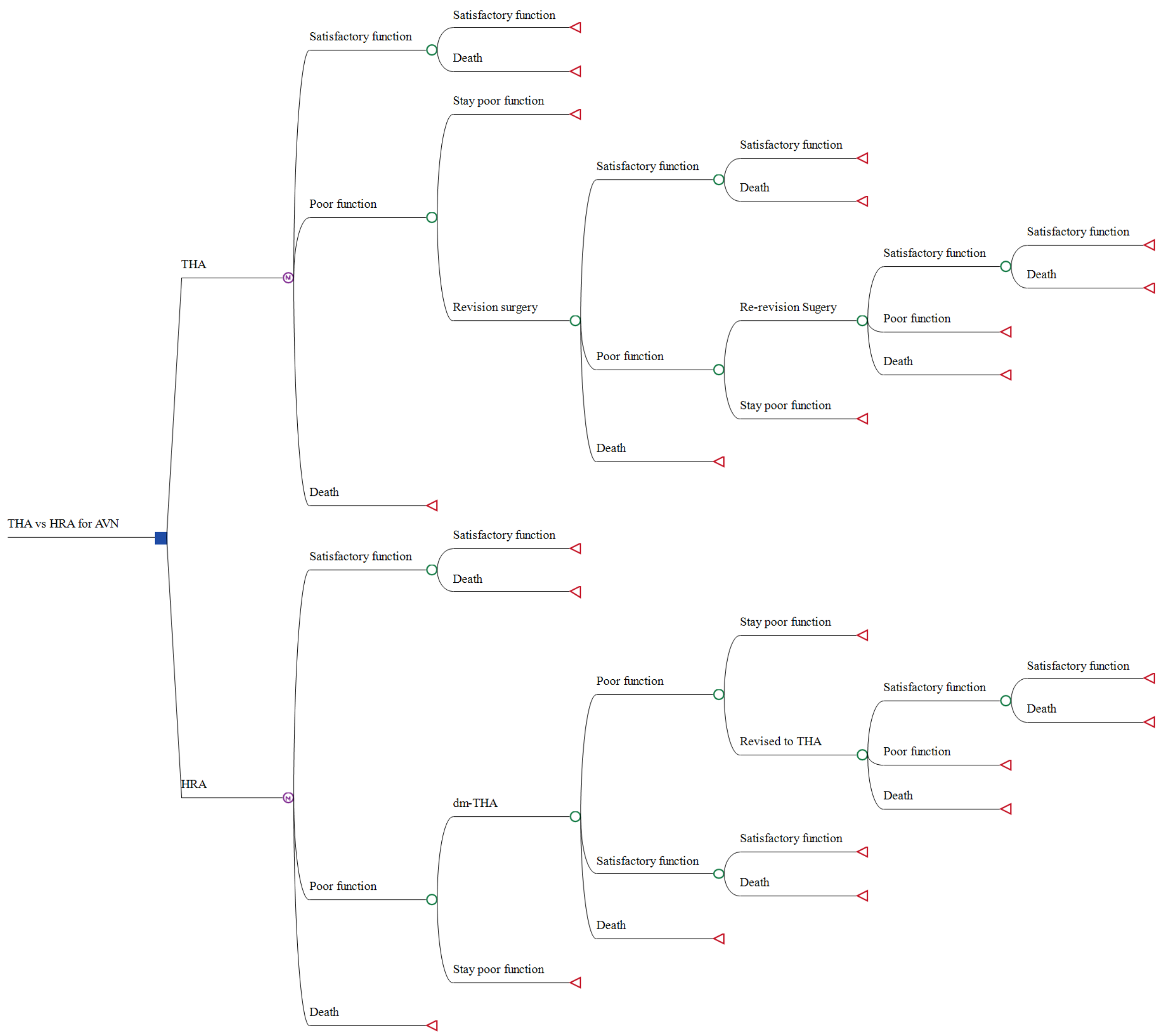


Figure 3.2. This shows how the whole Markov model runs: 3 health states exist after both primary THA and HRA surgery: satisfactory function, poor function and death. Deaths are attributed to the group with satisfactory function. Similarly, 3 health states exist after surgery: satisfactory function, poor function and death. A poorly functioning HRA may be left in situ or revised with a dual-mobility total hip arthroplasty, while a poorly functioning THA may also be left in situ or revised with a revision THA. All these events may result in 3 health states: satisfactory function, poor function and death. Poor function may be treated by revision, or left as a poorly functioning hip. A dual mobility THA may be revised to a revision THA, while a revision THA may be revised to a second revision THA.

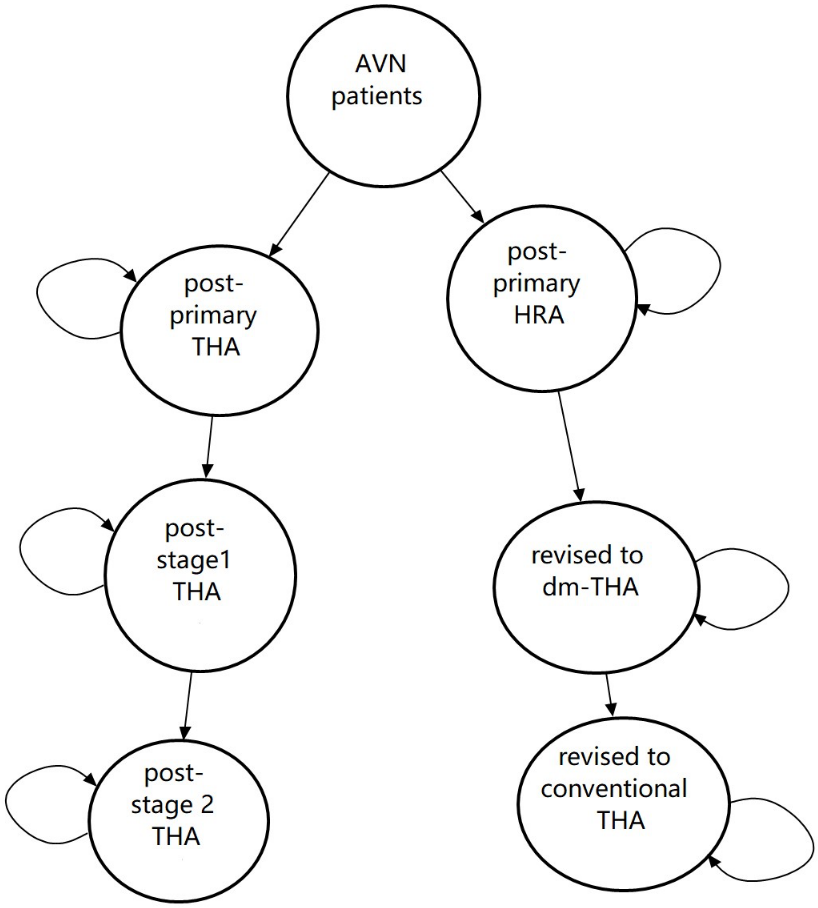


Figure 3.3 The simplified Markov model comparing total hip arthroplasty to hip resurfacing arthroplasty. In this model, the transition to the absorbing death state is only from satisfactory state (not shown in the figure). Each state is a 10-year tunnel (not shown in the figure). HRA, hip resurfacing arthroplasty; THA: total hip arthroplasty. AVN: avascular necrosis of femoral head. dm-THA: dual mobility total hip arthroplasty.

Table 3.1 Included studies in THA group

Author/year	Study type	Cement/cementless
Kim/2010 (85)	Case series	cementless
Osawa/2017 (104)	Cohort study	both
Kawasaki/2005 (105)	Cohort study	cementless
Hungerford/2006 (106)	Case series	cementless
Mont/2001 (107)	Cohort study	cementless
Chang/2013 (108)	Case series	cementless
Yuan/2009 (109)	Case series	cementless
Garino/1997 (110)	Case series	cementless
Fye/1998 (111)	Case series	cementless
Dastane/2008 (112)	Cohort study	both
Merschin/2008 (113)	Cohort study	cementless
Bedard/2013 (114)	Cohort study	cementless
Zhang/2008 (115)	Case series	cementless
Issa/2014 (116)	Cohort study	cementless

Table 3.2 Included studies in HRA group

Author/Year	Study type	cemented /cementless
Park/2020 (8)	Cohort study	cemented
Umemura/2018 (9)	Cohort study	cemented
Mont/2006 (18)	Cohort study	cemented
Inoue/2019 (10)	Cohort study	cemented
Woon/2012 (13)	Cohort study	cemented
Amstutz/2016 (12)	Case series	both
Amstutz/2010 (16)	Cohort study	cemented
Gross/2012 (14)	Cohort study	both
Li/2013 (117)	Cohort study	cemented
Aulakh/2010 (15)	Cohort study	both
Madhu/2011 (118)	Case series	cemented
O'Leary Group 1/2017 (11)*	Cohort study	cemented
O'Leary Group 2/2017 (11)*	Cohort study	cementless
Revell/2016 (17)	Case series	cemented

* This study had no overall data but 2 dedicated group and therefore treated as 2 studies when matching.

Table 3.3 Demographics and follow-up data from included studies.

AVN for	Total hip	Hip resurfacing	p
Patients	808	972	-
Hips	985	1069	-
Mean Age (SD) /years	43.2 (9.7)	42.4(9.9)	0.10
Mean follow-ups (SD) /years	7.8 (3.3)	8.0 (3.1)	0.16
Steroid/%	27.1%	32.5%	-
Alcohol/%	29.1%	10.1%	-
Trauma/%	9.2%	23.6%	-
Idiopathy/%	18.4%	35%	-
Revisions	63	71	-
Revision rates (SD)	8.2% (7.9%)	6.7% (3.7%)	<0.01
Deaths	45	14	-
Mortality rates (SD)	8% (11%)	2.4% (2.3%)	<0.01
Mechanical complications	110	54	-
Aseptic Loosening.	29	36	-
Dislocation	18	3	-
Medical Complications	70	9	-
Osteolysis	45	0	-
Infection	5	5	-
pain	7	1	-
DVT	12	0	-

AVN: avascular necrosis of femoral head. These demographic data came from systematic review early in this chapter.

Cost-effectiveness comparisons between THA and HRA

In the decision tree (Figure 3.2 and 3.3) we assume that 3 health states exist after both primary THA and HRA surgery: satisfactory function, poor function and death. As almost all authors in the included studies claimed that no patients died immediately following surgery or revision surgery, we attributed the deaths to the group with satisfactory function. Following revision surgery, again, 3 health states exist: satisfactory function, poor function and death. A poorly functioning HRA may be left in situ or revised with a dual-mobility total hip arthroplasty, while a poorly functioning THA may also be left in situ or revised with a revision THA. Once again, both these events may result in 3 health states: satisfactory function, poor function and death. Once again, poor function may be treated by revision, or left as a poorly functioning hip. A dual mobility THA may be revised to a revision THA, while a revision THA may be revised to a second revision THA.

The implant and other related costs were obtained from published data from the UK NHS supply chain (95) and are listed in Table 4. The model cycle length was one year, and we ran 10 cycles in total. The 1-year transition probability to death, effectiveness (satisfactory function) and 1-year mortality rate were obtained and converted from Table 3.2. The utilities of post primary surgery state were obtained from a PSA comparing the cost and utility of HRA and THA for OA undertaken in 2013 (119). The post revision surgery state utility for both THA and HRA were also derived from the same study (119), we assume the dual-mobility THA costs the same with primary THA. A 3.5% annual discount rate was applied according to NICE Guidance and NHS supply chain (95). The cost for revision surgery was derived from a recent financial analysis based once again on NHS costs (120). Half cycle correction was applied.

Table 3.4. Model inputs for the base case analysis of cost-effectiveness.

Inputs for	Total hip (SD)	Hip resurfacing (SD)	Distribution	Source
Implant /£	2571	2571	N/A	NHS Supply Chain (95)
Cement /£	0	164	N/A	NHS Supply Chain (95)
Surgery /£	2805	2805	N/A	NICE guidance (95)
Hospital stay/£	1687	1628	N/A	NICE guidance (95)
1-year follow-up /£	400 (240)	509(535)	Gamma	Edin (121)
Revision surgery /£	14857 (8373)	14857 (8373)	Gamma	Vanhegan(120)
Effectiveness [a]	0.918	0.933	Beta	Table 3.3
Transition probability [b]	0.003(0.001)	0.008 (0.005)	Gamma	Table 3.3
1-year mortality rate	0.008 (0.009)	0.004 (0.002)	Gamma	Table 3.3
Utility in the primary health state	0.810 (0.113)	0.818 (0.104)	Beta	Heintzbergen(119)
Utility in the revision health state	0.553 (0.113)	0.590 (0.103)	Beta	Heintzbergen(119)
Discount Rate	0.035	0.035	N/A	NICE guidance (95)

a. effectiveness = 1- Revision rate; b. transition probability = 1-year revision rate. Annual revision rates and annual mortality rates were divided by follow-up years respectively, these annual rates were calculated automatically by TreeAge Pro software.

3.4 Results

In the total hip group, 14 studies were included involving 985 hips. The mean age was 43.2 years (SD, 9.7 years) at index surgery, with a mean follow-up of 7.8 years (SD, 3.3 years). In the hip resurfacing group, 14 studies were included involving 106 hips. The mean age was 42.4 years (SD, 9.9 years) at index surgery, with a mean follow-up of 8.0 years (SD, 3.1 years) (Table 3.3). Most implants used in the total hip arthroplasty group were cementless whereas most implants in the hip resurfacing arthroplasty group had a cemented femoral component and cementless acetabular component.
There were 63 reoperations in 985 THA cases, and 71 reoperations in 1069 HRA cases. The most common cause for reoperation in both groups was aseptic loosening, (THA 29/985, HRA 36/1069) (Table 3.3). Medical complications appeared more prevalent in THA than HRA (110/808 vs 54/972). Deaths were also more common following THA (8%, 45/808 vs 2.4% 14/972) at 8 years of follow up. The CEA indicated that HRA was more cost-effective than THA, at a threshold of £20,000 (Figure 3.4). The cost-effectiveness acceptance curve suggested that HRA was more cost-effective than THA if the cost was higher than £ 1000 (Figure 3.5).

The Monte Carlo simulation indicates that HRA is the preferred strategy in 60% of simulations, while THA is preferred in 40% (Figure 3.6). This is illustrated in the Incremental Cost Effectiveness Ratio plot (Figure 3.7), where 60% of the points are below and to the right of the Willingness to Pay line of £20,000. While HRA cost £ 702 more than THA in this model (Table 3.5), the incremental effectiveness was 0.65, so the ICER was 1086 - much lower than the threshold of 20000, suggesting that HRA is a cost-effective strategy in the treatment of AVN. A cost-effectiveness scatterplot illustrates this further with HRA generally appearing at highest density to the right side indicating greater efficacy, and slightly above the red dots indicating greater expense. (Figure 3.8).

Sensitivity analysis demonstrated that this conclusion was sensitive to the input variables. The Tornado plot (Figure 3.9) illustrates that the mortality rate of THA was the dominant variable. The annual cost of HRA follow-up is a significant variable, followed by the mortality rate of HRA and annual cost of THA follow-up, while other input parameters were less sensitive (Figure 3.9).

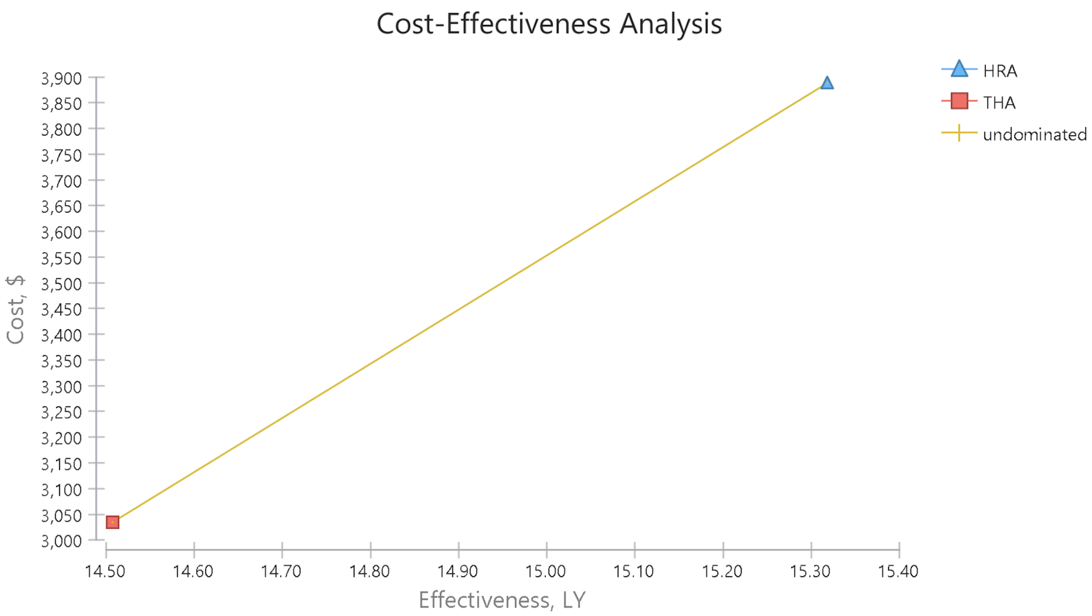


Figure 3.4 cost-effectiveness analysis at a threshold of 20,000 GBP.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty. WTP: willingness to pay.

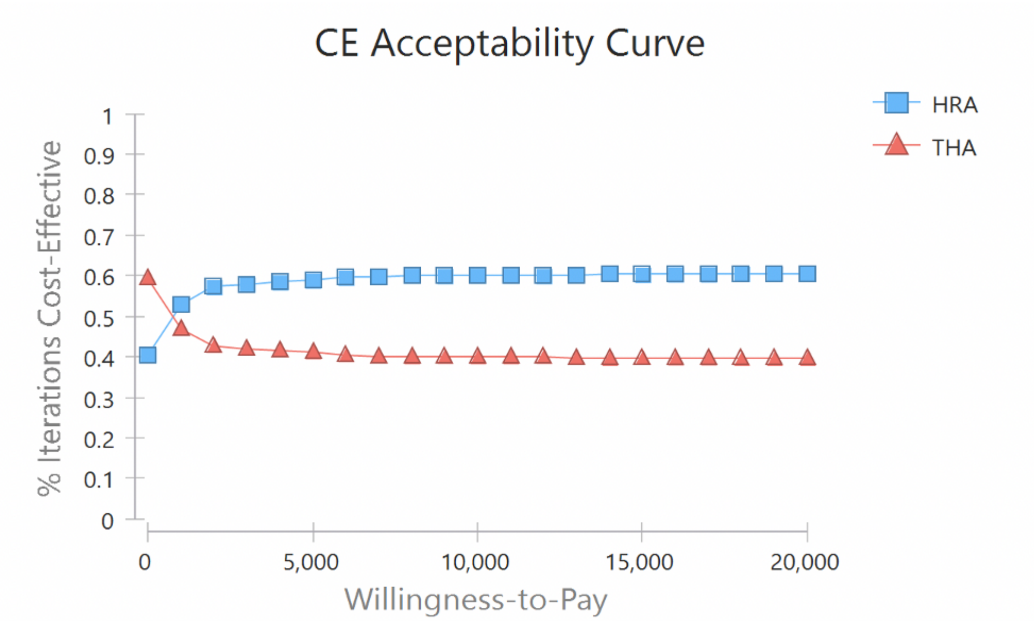


Figure 3.5 cost-effectiveness acceptance curve at willingness to pay at a threshold of 20,000 GBP.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty. CE: cost-effectiveness.

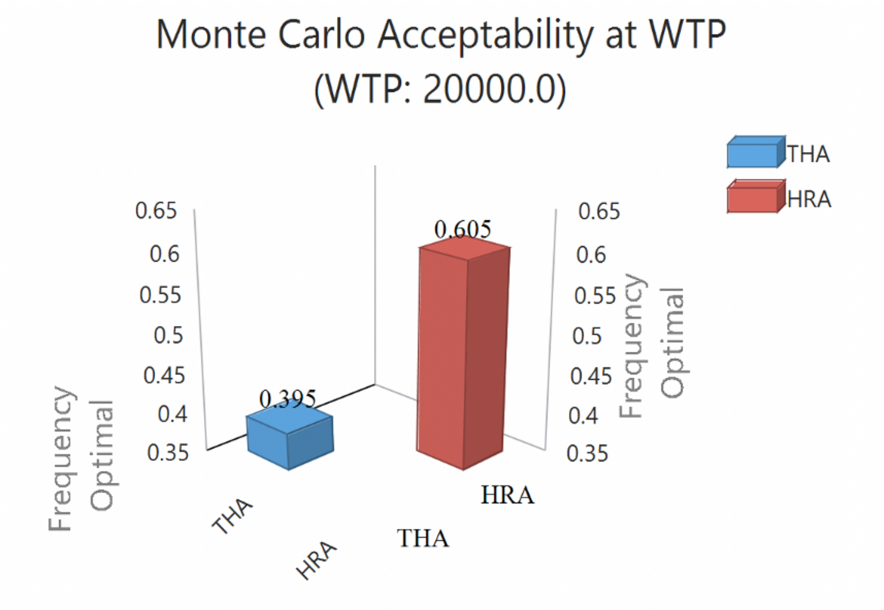


Figure 3.6 Monte Carlo acceptability at willingness to pay at a threshold of 20,000 GBP.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty. WTP: willingness to pay.

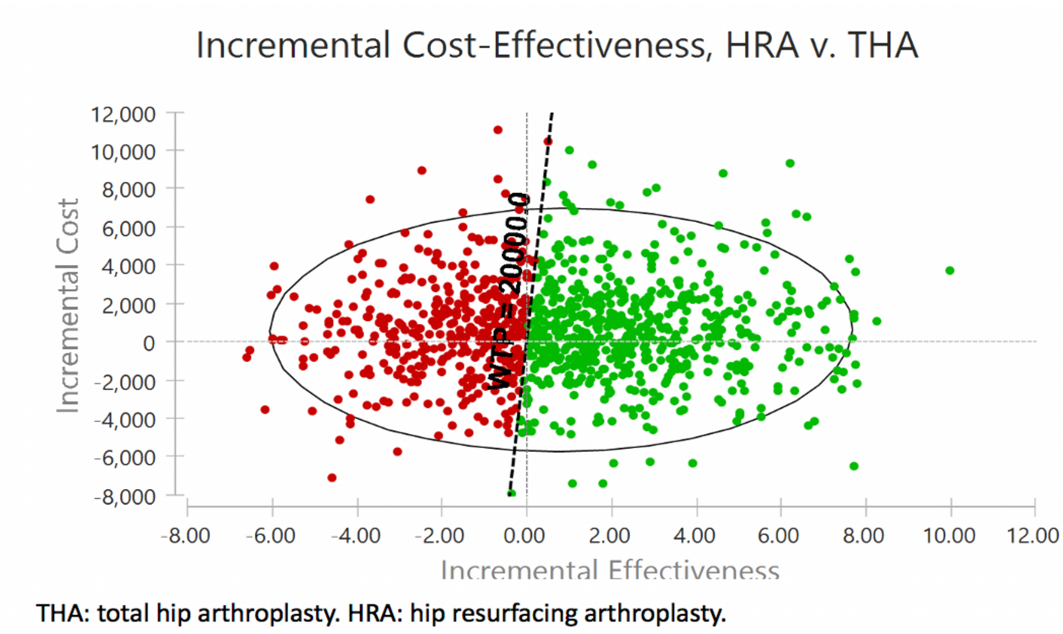


Figure 3.7. HRA dominates on the right half to the WTP dotted line in the scatterplot.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty.

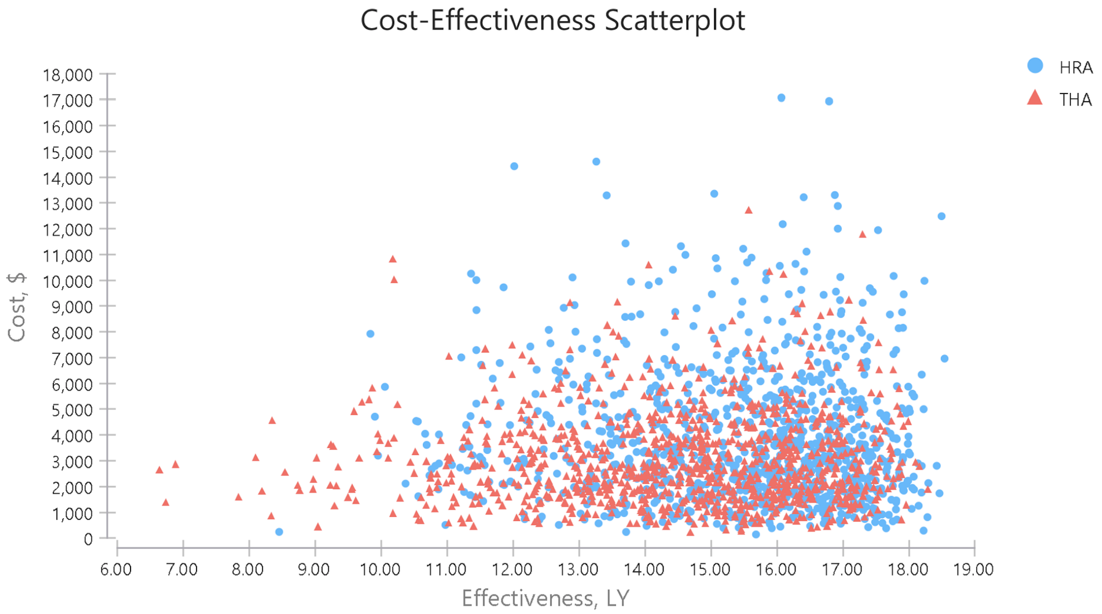


Figure 3.8. The plot shows possible cost-effectiveness scatter points.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty. Hip resurfacing scatters are more densely populated in the bottom right corner; this means hip resurfacing is more likely to be cost-effective.

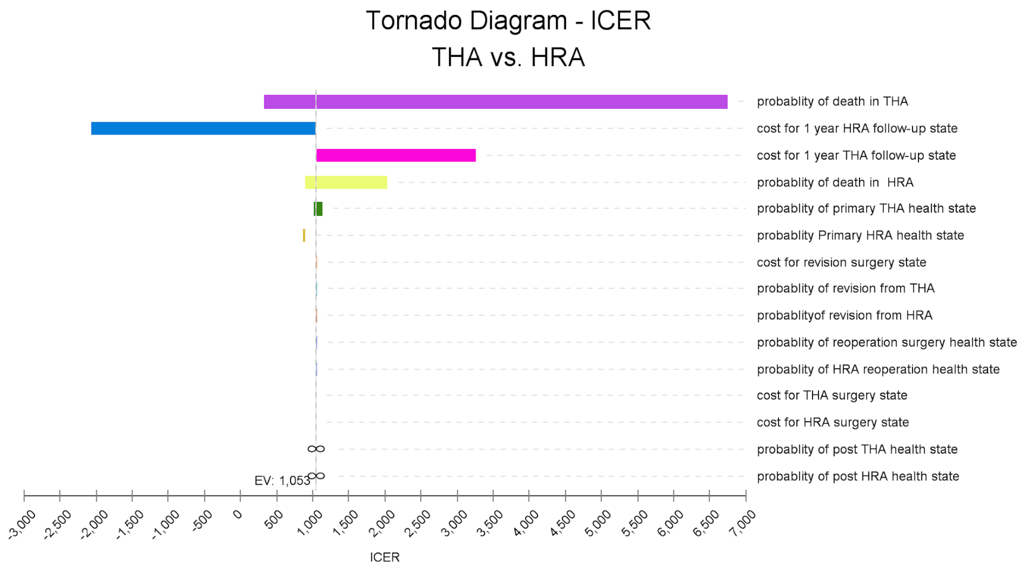


Figure 3.9. Sensitivity analysis of input parameters.

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty.

Table 3.5. Cost-effectiveness rankings

Parameters / Strategy	THA	HRA
Incremental cost	-	702
Incremental effectiveness	-	0.65
ICER	-	1086

THA: total hip arthroplasty. HRA: hip resurfacing arthroplasty. ICER: incremental cost to effectiveness ratio.

3.5 Discussion

This study set out to establish the relative costs and benefits of two forms of arthroplasty for Avascular Necrosis of the Hip. Our principal finding was unexpected: that hip resurfacing was more cost-effective than total hip arthroplasty for AVN patients, despite a higher headline revision rate for the two procedures in primary osteoarthritis. There are a number of limitations which temper our confidence in this conclusion – principally that the datasets are retrospective and the lack of RCTs. Also, because we aimed to match the follow-up times and mortality rates, selection bias was inevitably existed, although we checked this bias with STATA. We used same cost value for revision surgery in this model because both THA and HRA were revised with THA and other CEAs used same value and no other values available. As discussed earlier in this chapter, the longer follow-up times, or the older age at index surgery might lead to higher mortality rates, which would result in less cost-effective results. The included studies were all cohort studies and case series, and had no clinical trials, it's too early to say that THA is less cost-effective. However, our results in this chapter are difficult to reverse. This is because Australian Joint Registry reported much higher mortalities and revisions after primary THA surgery, so did other registries for patients aged 40-50.

We had to match follow-up times and age at surgery to make a fair comparison between two interventions. Significant uncertainly must also exist in the longer term, as the revision rate for HRA increases after 10 years in patients with AVN in the published literature. Against this, the benefit claimed for HRA is modest in this model, and patient safety appears to be substantially better served by HRA where it is possible. The cost for revision surgery we assumed the same for both HRA and THA, this was because they both be revised with THA and previous Markov models did the same thing(102, 119, 121).

The motivation behind this study was the perceived demand from AVN patients, who sought a higher post-operative function, both for their work and daily lives, especially in their 40s and 50s, where THA revision rates in primary OA are similar to those for HRA, despite the differing thresholds for revision between the two procedures, and published lower mortality. To our knowledge, this study is the first cost-effectiveness analysis of the clinical results of the two forms of hip arthroplasty for AVN. This is also the first large-scale study reporting the post-operative mortality and medical complications specifically for AVN patients.

Revisions, mortality, and medical complications

Current study showed a revision rate of 8 % for THA on the basis of all included studies at a mean follow-up of 8 years, while the revision rate for HRA was a mean of 2.4% at 8 years. While this difference in revision rates is probably not clinically important, however, the much higher incidence of medical complications after THA is clinically important. This difference is statistically significant, and relevant both clinically and economically. Among those complications, osteolysis (45) and DVT (12) in the THA group and these were much higher than osteolysis (0) and DVT (0) in the HRA. Yang (122) reported a significant higher medical complication rates of AVN patients than OA patients within 2 years after THA, pulmonary embolism and renal complications were among the most prominent. Similarly, Lovecchio (96) also indicated that AVN patients, compared to non AVN patients had a much higher medical complication rate (20% vs 15%) and bleeding transfusion was most common (20%). What was more, the 30-day re-admission rate of AVN patients was twice likely to other patients following THA.

The mortality rate reported for THA was 2 times that recorded for HRA from included studies. This difference in mortality rate is close to the report from Australian Joint Registry, which reported the 15-year mortality of THA to be 43% compared with 9% for HRA when corrected for age and gender (101). There may well be residual confounding, but this difference is substantial. Berstock (123) reported a pooled mortality rate of 0.65% in only 90 days after THA. Brooks (124) also reported a relatively high mortality rate of 8.9% within 8 years following THA, in comparison, only 1.6% of HRA patients died during the same period. This mortality trend is quite close to our study in AVN patients. One of the reasons of the higher mortality rates after THA might probably be the higher incidences of cardiovascular and cerebrovascular events. 12 DVT cases after THA and 0 case after HRA in our review indicated that the HRA would lead to fewer cardiovascular and cerebrovascular events.

Cost-effectiveness analysis between HRA and THA

The cost-effectiveness analysis in this present study suggests that a more conservative first procedure is both safe and cost-effective, promoting a stepwise therapeutic strategy for AVN patients. When the cost of implant, surgery and hospital stays are similar, as they are in the UK today, then the Monte Carlo simulation suggests that HRA is a cost-effective option. That probability (60%) for AVN patients of HRA being more cost-effective than THA was closely matched a cost-utility analysis asking the same question for patients with primary osteoarthritis between 40 and 50 years of age (61%) owing to the higher revision rate of THA for AVN (119). Another Markov cost-effectiveness model reported that HRA was more cost-effective than THA, but this was only true for a few selected HRA implants (125).

NICE guidance did accept that HRA was an option, but the revision rate was key to either procedure being cost-effective (95). From this analysis, because AVN has a higher revision rate with either procedure, there is a strong case for the tariff being higher, as it is with other diagnoses such as rheumatoid arthritis. This does not distract from the central message that HRA dominates THA in the ICER-- HRA is cheaper and more effective for patients presenting with AVN whose disease is suitable for HRA.

3.6 Conclusion

This conservative Markov Model of hip arthroplasty for AVN suggests that HRA is a cost-effective option, as it appears safer, and while the revision rate is higher than for other diagnoses, the correct comparison should be with THA for AVN, not with HRA for OA. Patient selection is key to long-term implant survivorship, encouraging surgeons and their patients to proceed early, rather than waiting for severe collapse to develop. A ladder of surgical interventions should be considered in this age group (40-60 years of age), from hip resurfacing arthroplasty to total hip arthroplasty, with the risk of progression up that ladder depending in part on disease severity at presentation.

Chapter 4

Finding the Maximum Lesion Extent Limit for Hip Resurfacing Arthroplasty

Abstract

Background: Although hip resurfacing arthroplasty (HRA) has been widely used on patients with osteoarthritis, HRA is not yet a mainstream choice for avascular necrosis of femoral head (AVN) patients. This is mainly because surgeons do not know to what lesion extent performing HRA is able to obtain initial bone-implant stability. In addition, most AVN-HRA studies were looking at cemented hip resurfacing, which might lead to thermal damage to the femoral head, and this thermal effect would eventually affect the bone regeneration on the femoral head.

Methods: 5th generation composite femur Sawbones were used to create post-operational models, simulating 3 different levels of necrotic extents (10mm, 15mm, 20mm) and the bone-implant displacements were compared to the intact femoral head Sawbones on Ceramic H1 implant. Same necrotic levels of Sawbones were also created, alternatively used Birmingham Hip Resurfacing implant and the bone-implant displacements were also recorded and analysed. The displacements were measured under the compression mode of Instron at the anatomical walking load of 1925N.

Results: The bone-implant displacements of intact femoral head, 10mm, 15mm, 20mm on H1 were 17um, 24um, 100um and um respectively, and the bone-implant displacements of intact femoral head, 10mm, 15mm, on BHR were 42um, 88um,112um respectively. According to the under 150um law, any displacement higher than which will fail to form bone regeneration between bone and implant, 15mm of necrotic extent is the maximum extent for a stable uncemented hip resurfacing.

Conclusion: a deep lesion extent is still suitable for a stable uncemented hip resurfacing.

4.1 Introduction

From previous studies from Nishii (126), Hernigou et al. (127) , Bassounas et al.(128) and Yang et al. (20), as well as the type C lesion shape from ARCO 1994, they indicated that the lesion shape was just like the shape in the Figure 4.4. Also, Amstutz (12) indicated that the lesion depth was the factor affecting long-term outcome of AVN hip resurfacing. Thus, we simulated the necrotic lesion and cut the femoral head in the Figure 4.1.

Speaking of the use of cement for simulation, we tended not to use cement. During the HRA surgery, necrotic bone tissue is removed, débride is done and the dead bone is replaced with bone cement. This, however, concerns rose. Hsieh (129) demonstrated that the peak heat emitted from bone cement was as high as 99 degrees and >50 degrees lasted for over 30 minutes, measured with a thermalcouple, which was securely attached to the bottom of necrotic lesion. The thicker cement used to fill the bone loss from the lesion, the higher temperature remained in the femoral head (temperature for a 2 to 5 mm of cement for fixation was 50-55 degrees). It's quite obvious that thicker cement needed to fill the lesion during hip resurfacing surgery and temperature might even rise higher. As such, bone death is inevitable (bone death occurs if temperature >50 degrees and lasts for over 1 minute) (130). Apparently, thermal damage to the healthy bone after débride cannot be overlooked because this will kill bone cells, affecting bone regeneration process, and might lead to unsatisfactory clinical outcome.

In addition, studies (131-134) have reported that replacement of necrotic bone with cement can cause changes in femoral strain. Tai et al (19) suggested valgus hip resurfacing would minimise stress shielding.

Digital Image Correlation

Digital Image Correlation (DIC) is a full-field image analysis method based on grey-scale digital images, which can determine the contour and displacement of objects in a three-dimensional space.

DIC is an optical process that coats the specific area of the sample with a high-contrast random speckle pattern that the whole process is recorded with a digital camera. Related software can be used to analysed the footage from the camera, calculating the absolute and relative displacement of rounded points or 'facets'. Subsequently, these loaded readings are compared to unloaded reference reading, the differences between them are strain (135, 136).

One of the main advantages of DIC is that it can be applied to irregular geometry components that made of a wide variety of materials. This makes it an ideal method for measuring biomechanical specimen's strain (137, 138).

The femoral rig used in this study was kindly provided by Alex Dickinson (139) who had validated his rig via DIC method, with a R^2 correlation of 0.8 between the simulation and test. The reproducibility and sensitivity of strain measurements were even better than other similar studies (140-142).

In this study, we aim to investigate that, to what lesion extent should surgeons perform hip resurfacing arthroplasty on AVN patients.

4.2 Materials and methods

The 5th generation SAWBONE units were placed in Ceramic H1 group and BHR group respectively. Sawbone installed with H1 component was prepared using H1 routine surgical technique and H1 came with a stem, no cement used in this cementless component. When preparing BHR on Sawbone, we followed the BHR surgical routine, the only difference was we did not use cement. The reason was Amstutz (12) reported great long-term results with cementless fixation in cemented components and he suggested it's safe not to cement the femoral stem for those femoral head component size larger than 48mm. He also suggested it's safe not to cement metal on metal femoral components (Conserve Plus, in his case) when the lesion depth was shallower than 1cm.Therefore, cementless 50mm BHR (also metal on metal) and Ceramic H1 (porous coated, uncemented) femoral components were chosen for our experiments and the simulated lesion started with 10mm (1cm). Then simulated lesion increased at 5mm interval to find the maximum lesion limit.

4 units were tested at each lesion level (Figure 4.1) in each group, made up a total of 32 units. Each unit was sectioned and potted in PMMA resin with 12° of flexion and 12° of adduction with the femoral rig (Figure 4.2). In this load and gait pattern, to apply force vertically with the single axis Instron machine, an abductor lever arm was set up to simulate abductor muscle forces. Meanwhile, femoral joint contact force was applied vertically. A 1925N load cell driven by Instron 5569 electromechanical test machine (Instron Corp., MA, USA) and the Instron was driven by BLUEHILL software (Instron Corp., MA, USA). The whole test setup can be seen in Figure 4.3.

Sawbone preparation

Each Sawbone model was tightly fixed to a lab bench, and a femoral guide wire was inserted at 5-10 degrees of valgus to its original femoral neck-shaft angle. This was followed by the reaming process, the femoral head was reaming using BHR reamer/ H1 reamer, a second BHR reamer, and a final BHR reamer which was a chamfer reamer used to do a final reaming to femoral head. H1 femoral head was prepared with only one H1 reamer, no second or third reamer needed. For bone graft, we cut the prepared femoral head in the way in the Figure 4.4 and graft back onto the femoral head. A trial femoral component was placed onto the prepared femoral head to check whether the femoral head was well matched (Figure 4.5). The final step was to install BHR femoral component/ H1 femoral component onto prepared Sawbone model with femoral impactor. No cement used during the whole process, regardless of the use BHR or H1 femoral component. The H1 used was a stemmed design.

Experimental setup

For displacement measurements, rounded points marked to the femoral component margin and the proximal femoral head, the central implant marker was determined by a horizontal line from greater trochanter marker to femoral component, another marker on the bone was made close to the implant marker (Figure 4.6). This speckle pattern was tested and gained satisfactory repeatability of displacements between marker, analyzing these displacements and checked their repeatability with GOM correlate from first 3 Sawbone models. Once the Sawbone mounted on the Instron machine, the displacements between points were recorded by SONY alpha 7R Mark III digital camera (SONY Corp., Tokyo, Japan) with Hasselblad Xpan 30mm aspherical lens (Hasselblad Corp., Göteborg, Sweden). The video settings were 3840 x 2160 pixels of resolution, 24 frames per second, in super35 mode in order to obtain sharpest and low distortion image possible. The recorded footages were post-processed in Final Cut Pro X (Apple Corp., San Francisco, USA) and the increased the contrast, cropped to 1080p when exporting new video. The edited footages were loaded into GOM Correlated 2020 software (GOM Gmbh., Schmitzstraße, Germany) and this software was used to calculate displacement and under loading. The camera was positioned at a distance of 50cm and the points marked (Figure 4.4) on the implant were used for calibration since the interval between points was 5mm. The displacements were the distance before points (Figure 5.7).

Compression physical tests were conducted via Instron. The vertical load was increased from 0 to 1925N. Each unit was tested both the anterior and posterior aspects, repeated 3 times at each aspect.

Finally, after all the displacement measurements were collected, the data at different lesion levels were compared to intact femoral head hip resurfacing data, using student t test. The comparison calculation level the p was set at 0.05 level.

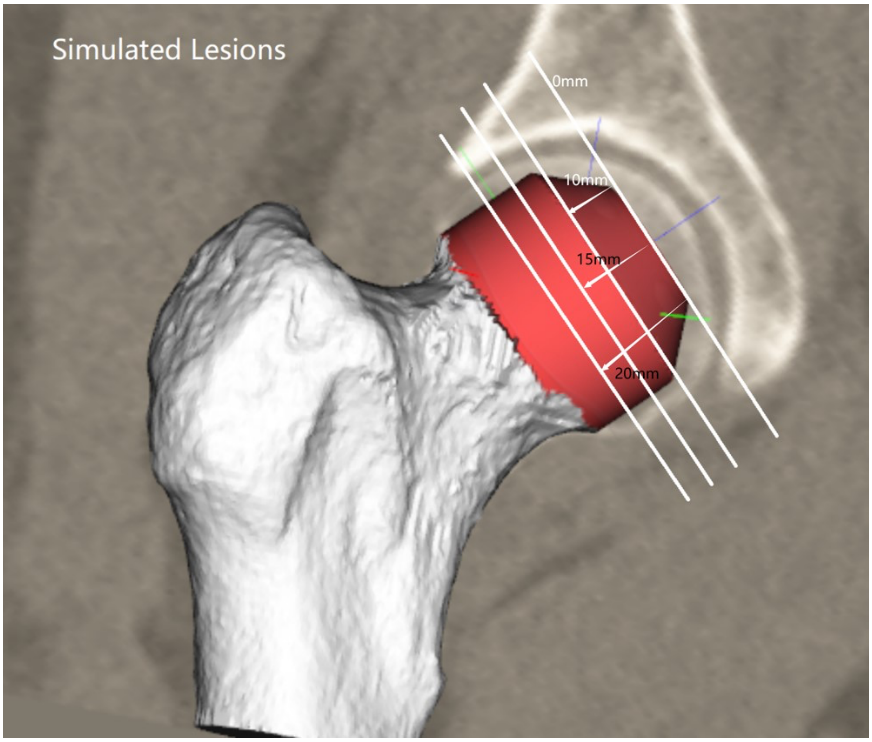


Figure 4.1 The simulated lesion levels.

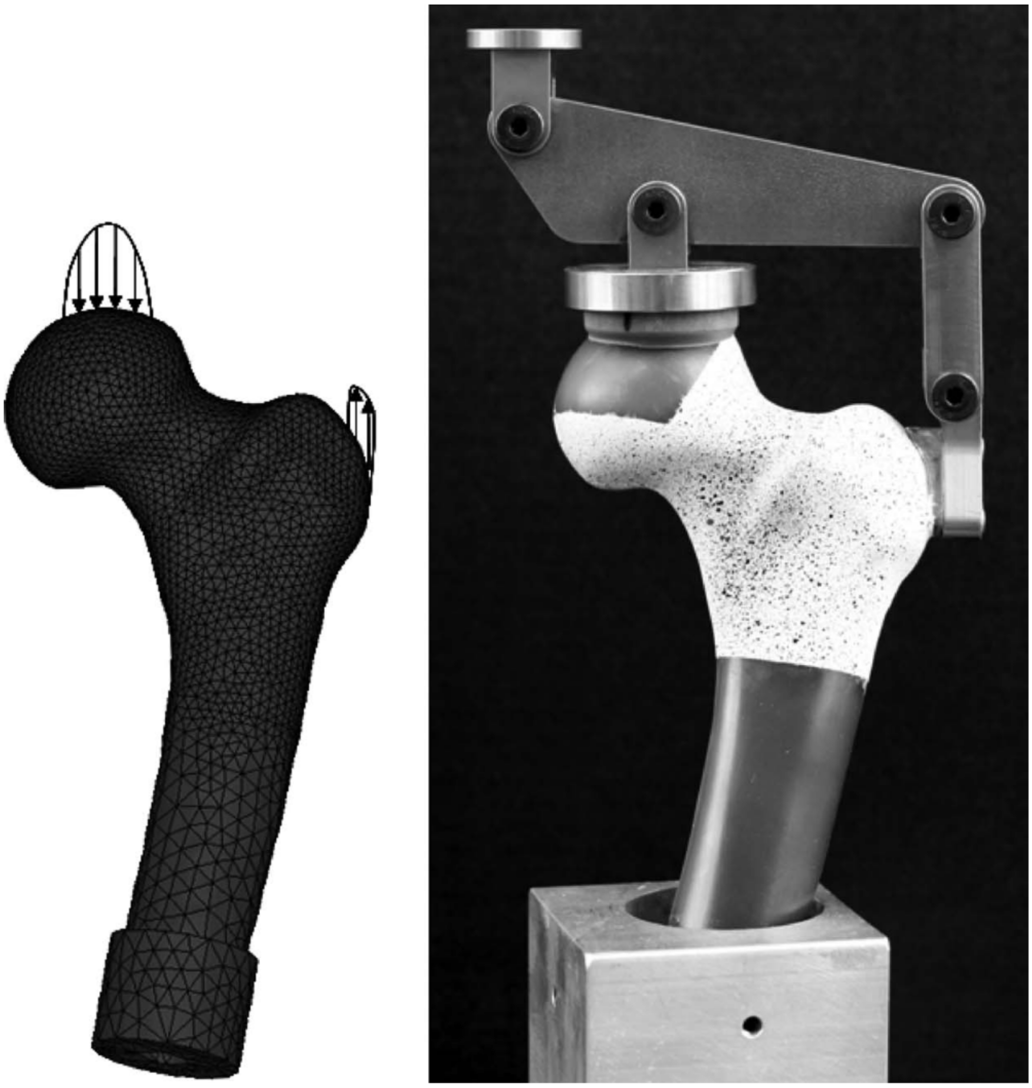


Figure 4.2 The femoral rig fixes Sawbone in 12° of flexion and 12° of adduction.

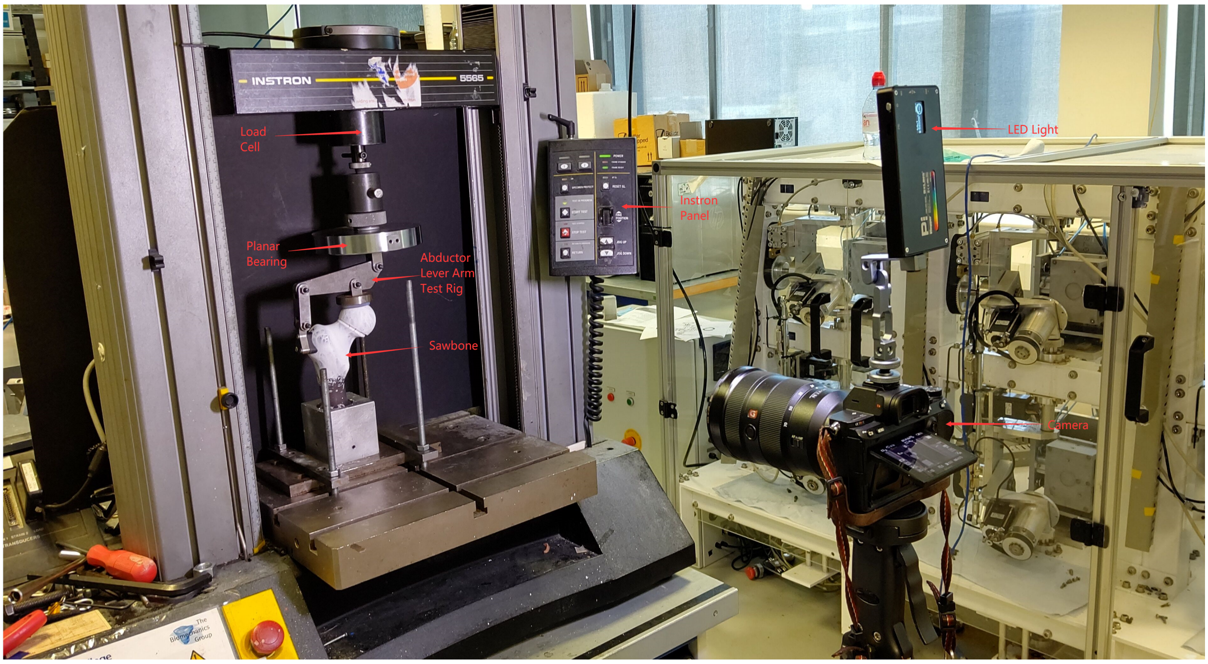


Figure 4.3 the test setup.

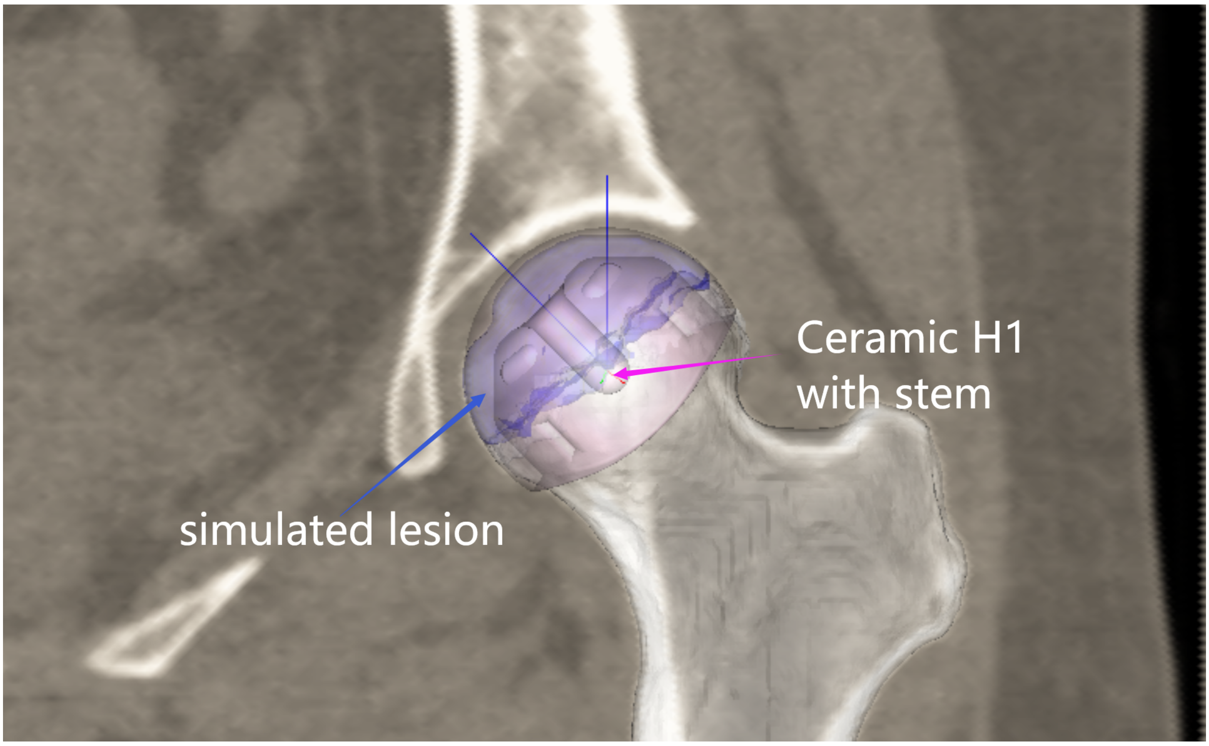


Figure 4.4 Bone graft (simulated lesion) were cut from intact Sawbone and used as graft (purple) back onto the femoral head. Then the femoral component was impacted into the femoral head in the press-fit way.

Figure 4.5 Use the H1 femoral component trial to check whether the femoral head was well prepared.

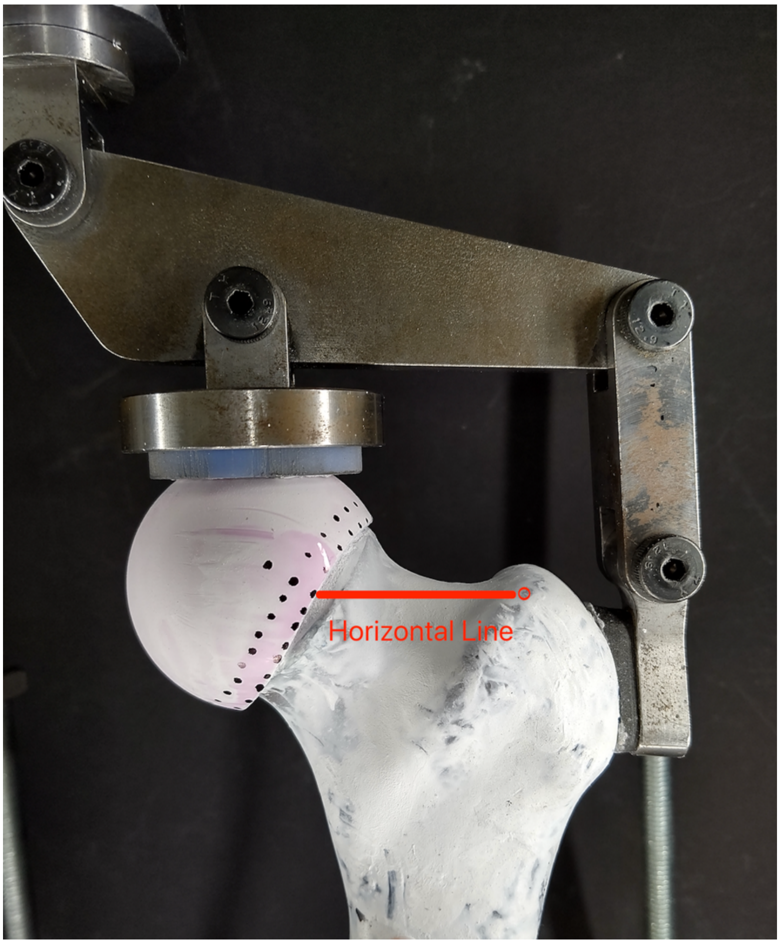


Figure 4.6 the marker on the femoral component was determined by the horizontal line, connecting greater trochanter and the implant.

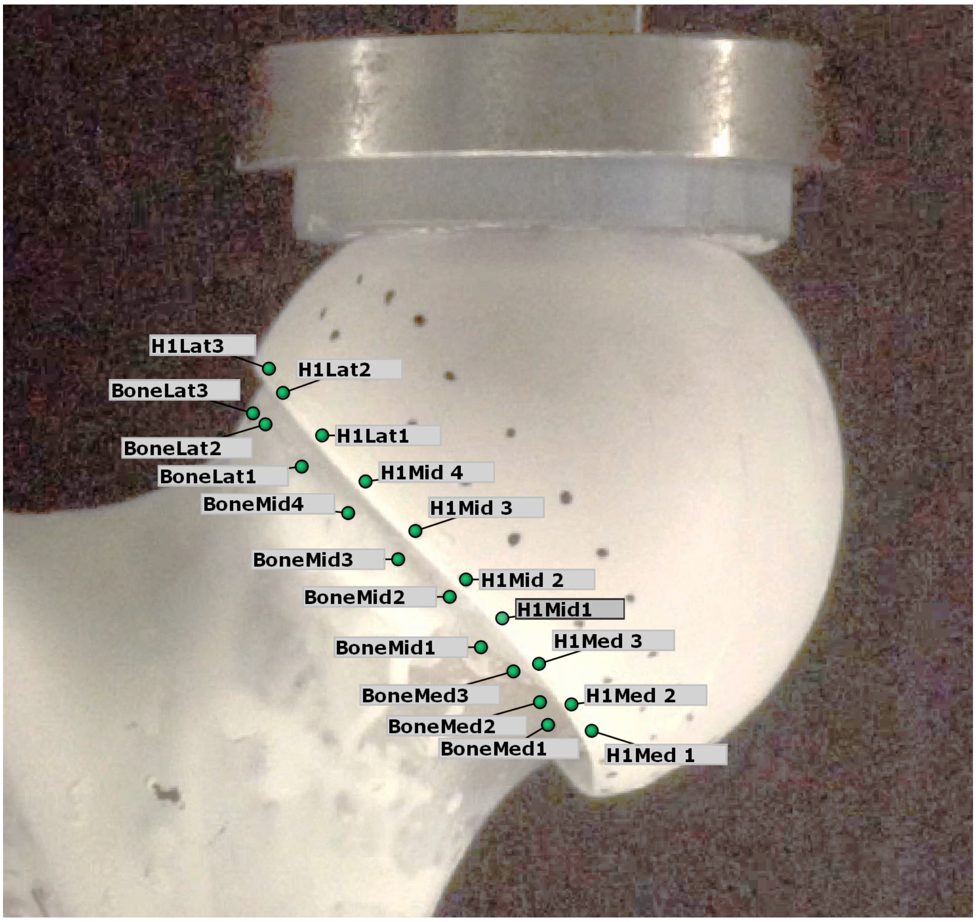


Figure 4.7 The markers on the implant and the bone.

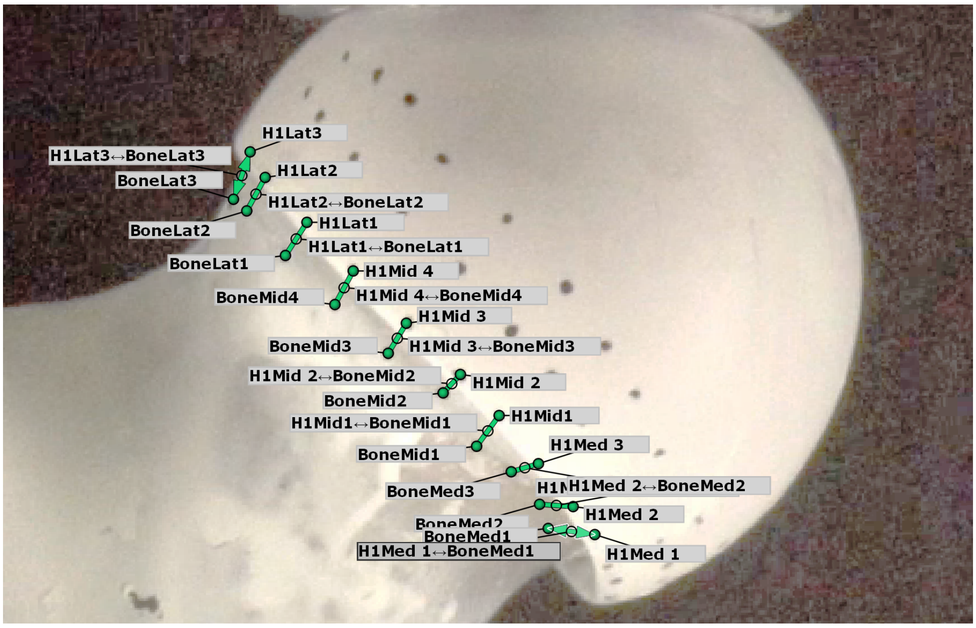


Figure 4.8 The change in distance between bone and implant is the displacement.

4.3 Results

Overall, the displacement reports were generated from GOM Correlate (Figure 4.10), and the displacement patterns in both Ceramic H1 and BHR group were relatively similar, the displacements increased when the lesion grew larger. The displacements on BHR femoral component were 42μm (SD, 35μm) in 0mm lesion extent, 66μm (SD, 31μm) in 10mm lesion extent, 112μm (SD, 35μm) in 15mm lesion extent, respectively. Meanwhile, those from H1 were 16μm (SD, 5μm) in 0mm lesion extent, 25μm (SD, 4μm) in 10mm lesion extent, 104μm (SD, 5μm) in 15mm lesion extent and 665μm (SD, 858μm) in 15mm lesion extent, respectively. The increase was both prominent when the lesion simulation between 15mm to 20mm.

In terms of displacements between BHR and H1, they were all significant larger in all necrotic lesion levels on BHR femoral components (Table 4.1).

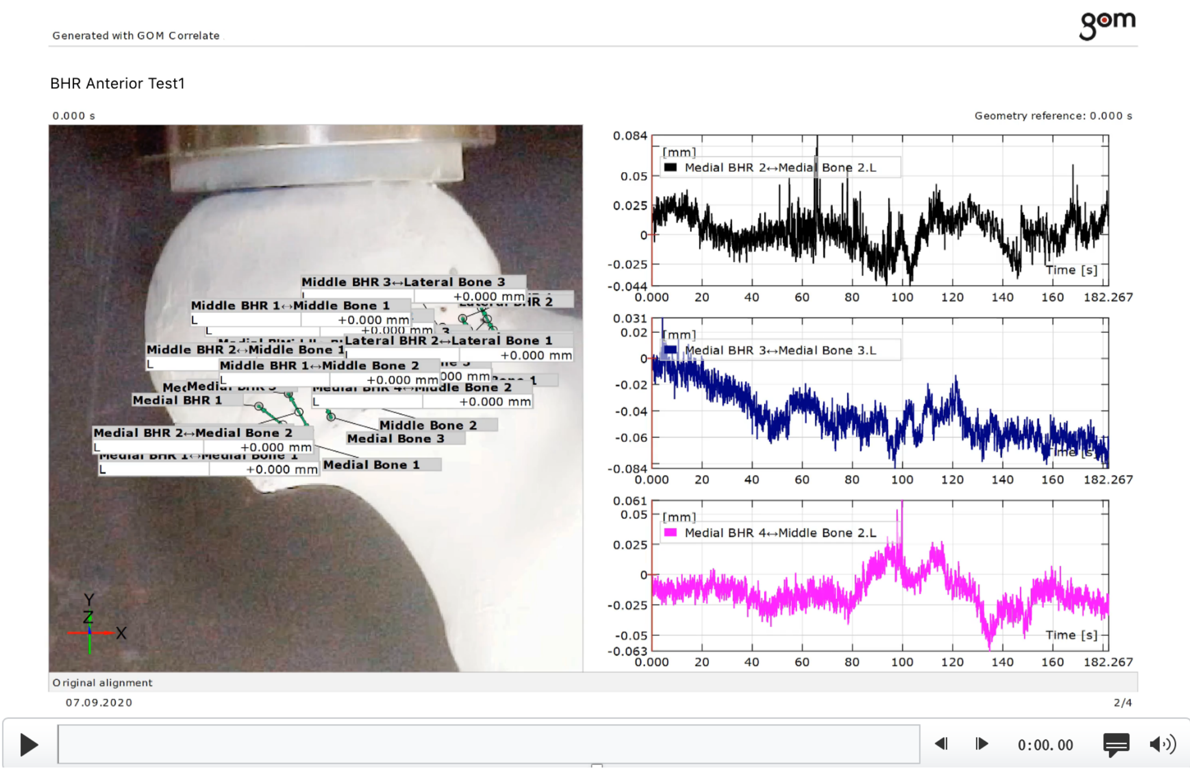


Figure 4.10 The displacements report exported from GOM Correlate software.

Table 5.1 Results of Sawbone bearing tests

	LESION LEVEL			
IMPLANT	Intact/µm Mean (SD)	10mm/µm Mean (SD)	15mm/µm Mean (SD)	20mm/µm Mean (SD)
BHR	42(35)	66(31)	112(35) ‡	Unable to complete test
H1	16(5)	25(4) †	104(5) †	665(858) †
P*	<0.05	<0.05	<0.05	-

*: the p values compared the displacements between BHR and H1 under the same necrotic lesion.

BHR: Birmingham Hip Resurfacing.

‡: the displacement of that lesion level was significantly larger than that of intact BHR.

†: the displacement of that lesion level was significantly larger than that of intact H1.

4.4 Discussion

Our results of H1 showed that all micromotion of lesions not deeper than 15 mm was smaller than 150µm(143). This means the implant initial stability was achieved within 15mm of lesion depth. Itayem et al. (144) reported that the bone-implant mean micromotions were smaller than 46 µm in 20 OA patients having BHR 2 months postoperatively. Compared Itayem's results to our BHR results without lesion, mean values were relatively close, indicating BHR component might be great in the short-term even without cement among no lesion patients. Bitsch et al. (145) reported a significant lower mean micromotion of 17 µm between bone and 31 cadaveric cases of ASR cemented femoral component, they stressed that no cement penetration or cement thickness relation to the micromotion. They also found out that a strong correlation between femoral head bone density and micromotion because hip resurfacing femoral component highly depended on cancellous bone fixation. This is why cementing femoral component is such important for cemented design hip resurfacing femoral component. In this theory, the press-fit design of cementless component, such as Ceramic H1, is able to achieve great initial stability once strong connection to the cancellous bone established.

Despite above results, our study had some limitations. First, we only used composite bone for testing, animal experiments, or even clinical trial are also important to verify our conclusion. Second, we only tested the static loading, but human hip joint moves while walking or running. Therefore, dynamic tests are still needed. Last, we hadn't test smaller femoral components (<48mm), whose stem was considered to be cemented (12).

Charing Cross Hospital AVN-HRA Staging System

Based on the Ceramic H1 data we have in this study, and also because we initiated this project in the Charing Cross Hospital, we would like to introduce a brand new AVN staging system with hip resurfacing arthroplasty - Charing Cross Hospital AVN-HRA Staging System. The indication for AVN hip resurfacing is as follows in the table.

Table 4.2 Charing Cross Hospital Cementless hip resurfacing – AVN staging system

Charing Cross Hospital Hip Resurfacing Arthroplasty – AVN Staging System (cementless only)		
Lesion Depth	Stage	Hip Resurfacing Arthroplasty
0~10mm	I	√ Indicated for Hip Resurfacing
10~15mm	II	—Not recommended
15~20mm	III	× Contraindicated
>20mm	IV	× Contraindicated

1) Any lesion depth within 0~10mm lesion depth (10mm down from the top of the femoral head after Chamfer reaming), is able to gain initial implant-bone stability.

2) Any lesion depth within 10~15mm lesion depth (10~15mm down from the top of the femoral head after Chamfer reaming), might be able to gain initial implant-bone stability. In clinical practise, such lesion depth dealt with H1 component cannot guarantee 100% of strong fixation because the peak micromotion might exceed 150mm, therefore we are not recommending patients with such lesion depth to receive hip resurfacing arthroplasty at the moment.

3) Any lesion depth is deeper than 15mm lesion depth (15mm down from the top of the femoral head after Chamfer reaming), is not able to obtain initial stability, under this tests' setting.

From 1-3 above, we can conclude that 10mm lesion involved in the prepared femoral head is indicated for hip resurfacing arthroplasty. 10~15 mm of lesion depth is the maximum lesion limit we sought for. Amstutz (12) shared a similar opinion, which he reckoned the lesion was not exceeding the margin of chamfer (the lesion depth was not deeper than 1cm) to be safe for cementless hip resurfacing.

Our staging system still has room to improve. First, this staging system is based on bench experiment, we need to verify through animal experiments, and even clinical trial if animal results come out great. Second, will there be an upscaling or downscaling strategy if the bone continues to be necrotic or regenerated after surgery in clinical practise? Third, is this staging system also true when it comes to cemented hip resurfacing on AVN?

Chapter 5

The Validation of a Novel Pre-operative Planner for Hip Resurfacing Arthroplasty on Avascular Necrosis of the Femoral Head Patients.

5.1 Abstract

Background: Avascular necrosis of the femoral head (AVN) has been proved to be treated effectively with hip resurfacing arthroplasty, and the maximum lesion for such surgery has also been determined. Therefore, the demand for pre-operative planning might see a significant increase in the future. The aim of this study was to investigate whether inter-and intra-observer agrees on preoperative implant planning using computed tomographic (CT) segmented 3D hip models loaded into a novel planner.

Method: Intraclass correlation coefficient (ICC), along with Bland- Altman method was carried out. 19 consecutive patients who diagnosed with ARCO Stage III and IV AVN were involved in this study. Pre- operative CT Dicom images were used to segment 3D hip joint models. 2 observers (1 attending hip surgeon and 1 engineer) performed a blinded review of preselected radiographs and 3D CT hip models. Inter- and intra-observer agreement was assessed with femoral component size, femoral neck-shaft angle, femoral neck length, as well as native hip measurements such as horizontal offset, anterior offset and head-shaft anteversion.

Results: The inter-observer and intra-observer agreements for femoral component size were 100% and 100% with exact size respectively. Interobserver ICC for anterior offset was 0.904, and 0.95 for intra-observer reliability. Interobserver ICC of the horizontal offset was 0.846, and 0.917 for intraobserver reliability. Interobserver ICC of the head-shaft relative anteversion was 0.99, and 1.0 for intra-observer reliability.

Conclusion: CT-based 3D preoperative planning for AVN hip resurfacing is a reliable tool.

5.2 Introduction

The initial implant stabilization of hip resurfacing arthroplasty is highly associated with lesion size or depth. This stabilization can be affected by inappropriate implant size, implant malposition, and malalignment. Pre-operative planning is increasingly important especially on AVN hip resurfacing, because the pre-operative planning is not only about outcome, but also determined whether the AVN patient suits hip resurfacing or not. Therefore, the reliability and repeatability of the preoperative planning for AVN hip resurfacing are relatively crucial.

2-Dimensional (2D) pre-operative planning used to be a well reproduceable method for hip surgery (146), because of its fast and simple way measuring femoral parameters. Traditionally, surgeons only need to place a pre-operative template on an anterior-posterior x-ray, and then femoral canal parameters obtained, as well as implant sizes. Such advantages from 2D planning were also reported in previous studies (21, 22).

Despite those advantages, however, it’s not the case when planning AVN hip resurfacing. The reason is mainly due to AVN’s irregulate lesion and lesion extent. Today, CT-based 3D planning is much popular than ever before, and such planning method is able to give accurate implant size results (21-23). Specifically, CT planning enables surgeons to estimate the implant orientation and alignment in a 3D view, where the 2D view lacks of. This is even more important for AVN hip resurfacing, because of its unevenly distributed nature in the femoral head. Only in this way, can we surgeons predict component sizes precisely.

Therefore, I (ZZ) explained my concept of this planner to EmBody (London, UK) and they made this planner come true with their greatest effort. EmBody designed the planner’s graphical interface, defined implant’s coordinate system and fixed bugs. We joint to optimise and fine-tune the planner and eventually we have this Version 2.2.0 AVN Hip Planner.

5.3 Material and Methods

19 hips from 19 patients (14 males and 5 females) with no known hip surgery involved. In order to balance efficiency and accuracy, in accordance to previous methods (24, 25), a sample size of 19 was chosen. The mean age of the patients was 40 years (range 39-59 years, SD 10 years). All hips were classified as ARCO stage III or IV, which were in the end-stage of AVN.

3D hip joint digital models of the femoral head were obtained using 120 slice CT (Siemens, Germany). Every patient was in supine position and hip neutral position. The scanning range was from the proximal end of the femoral head to 2 cm below the lesser trochanter. The scanning settings were: 1 mm of layer thickness, 4.5 mm of pitch, 100 kV of voltage, 50 Ma of current, 2000 Hu of width, 125 Hu level, 512 × 512 of matrix.

The CT scanning imaging data were saved in DICOM format. The three-dimensional reconstruction of proximal femur and necrotic area was performed by Mimics research 21.0 (Materialise, Belgium). The necrotic extents were segmented by 2 clinicians whom had previous hip anatomy training respectively (ZZ and XF). The non-necrotic bone tissue and necrotic tissue of the femoral head were identified as masks and segmented on the coronal, sagittal and transverse planes.

All hip models loaded into Zexin AVN Hip Planner V2.2.0 (Figure 5.1), and each model was repeated planning by each observer respectively.

Figure 5.1 The main panel of Zexin AVN Hip Planner. It is co-engineered with Embody company.

Bony landmarks when planning

In the planner,

1) place markers on the femoral head in order to fit a sphere femoral head (Figure 5.2).
2) place 3 land markers on the femur, namely Greater Trochanter, Lesser Trochanter and

Intertrochanteric Line (Figure 5.3).

3) place marker in the femoral neck center (Figure 5.4) and place markers on the internal surface of

the femoral canal (Figure 5.5).

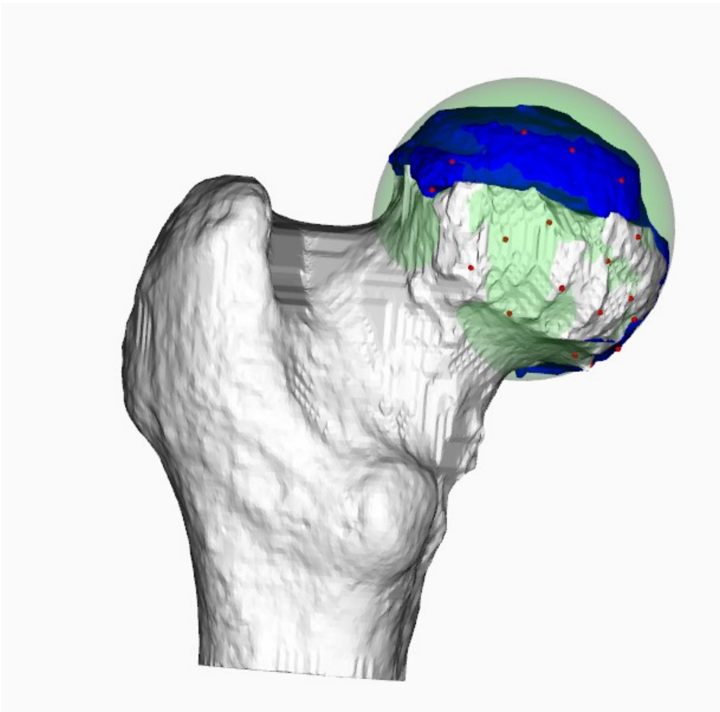


Figure 5.2 Markers (red dots) on the femoral head so as to fit a sphere shape.

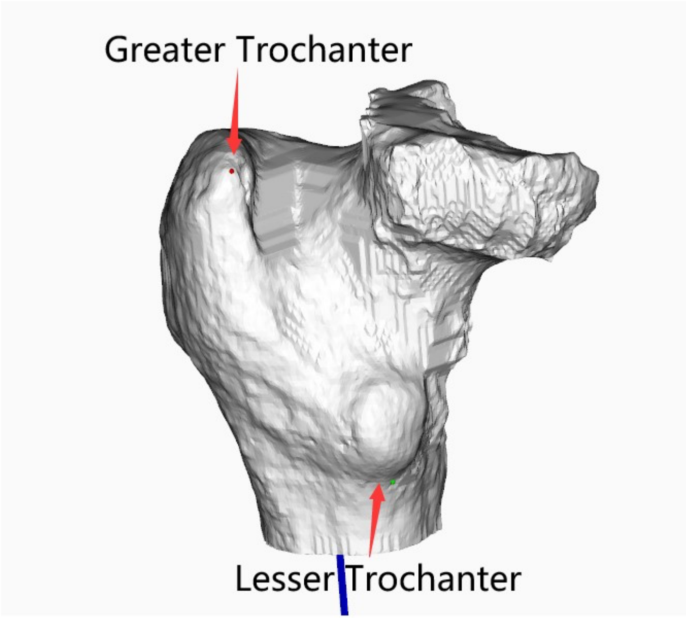


Figure 5.3 We need GT and LT to find the femoral neck center.

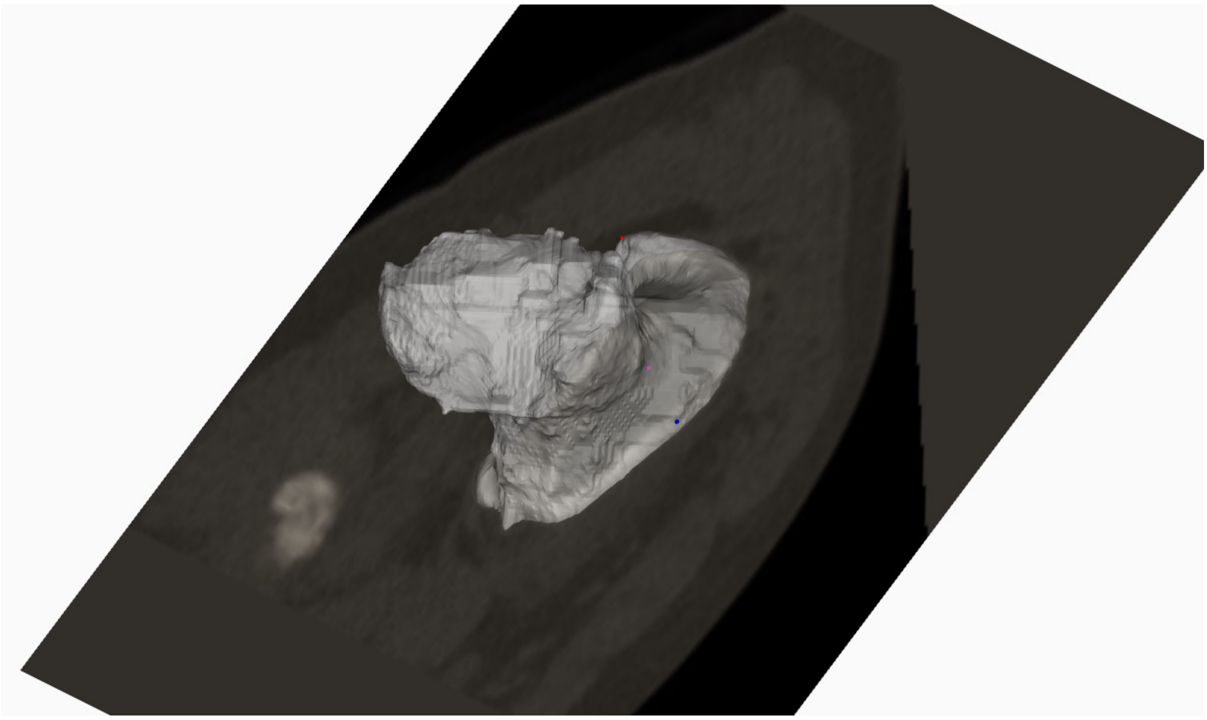


Figure 5.4 Place the purple dot in the center of the femoral neck.

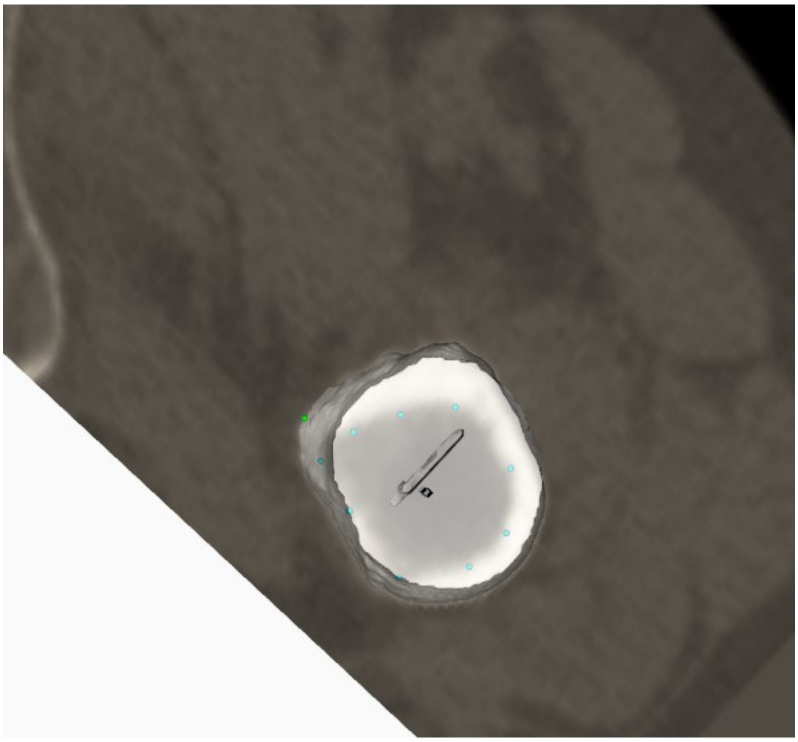


Figure 5.5 Place blue dots on the internal surface of the femoral canal.

Finally, the intraclass correlation coefficients (ICC) and Bland-and -Altman charts were recorded from the planning panel (Figure 5.6). The ICCs were applied to determine the relative reliability of Intra-observers' measurements (single measurements) and inter-observers' measurements (average measurements), and well repeated by researchers (147, 148). Bland-Altman plot was used to check measurement variations (repeatability) between observers and intra-observers (147). The recorded data included auto generated femoral component size, femoral neck-shaft angle, femoral neck length, as well as native hip measurements such as horizontal offset, anterior offset and head-shaft anteversion.

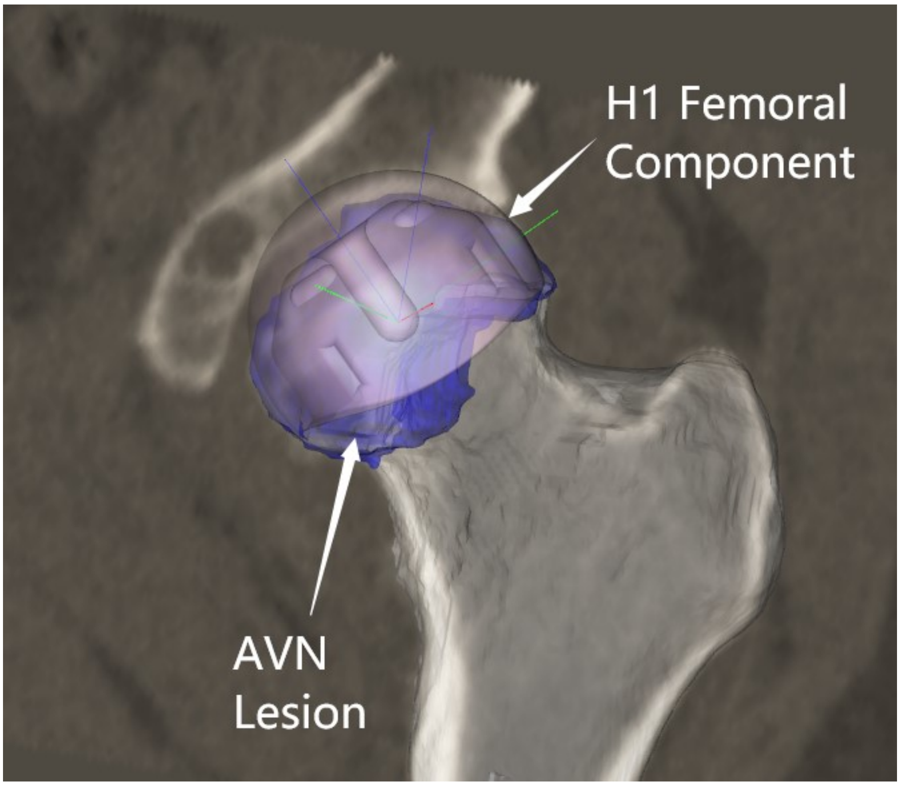


Figure 6.6 The planning panel contains component and native hip measurement data.

Statistical Analysis

The percentage agreement with the exact femoral component size, was assessed using the intraclass correlation coefficient (ICC), both for intra-observer and inter-observer reliabilities. We used Landis scoring system, any result higher than 0.81 indicates a ultra-high reliability. ICC was performed using reliability Analysis (kappa) from SPSS 26.0 (IBM, Chicago, USA), single measures represented the intra-observser's measures and average measures represented inter-oberver's measures. Bland-Altman test plotted with MedCalc software (MedCalc Software, Ltd, Ostend, Belgium). A P-value <0.05 was considered to be statistically significant.

5.4 Results

Anterior offset measurements

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.1 below, and the Bland-Altman plot was in the Figure 5.7. The ICCs of intra-observer and inter-observer was 90.4% and 95% respectively. The Bland-Altman plot well matched the ICCs.

Table 5.1 The intraclass correlation coefficient results of anterior offset.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.904[a]	.824	.949	19.411	37	37	.000
Average Measures	.950	.903	.974	19.411	37	37	.000

Two-way random effects model where both people effects and measures effects are random.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

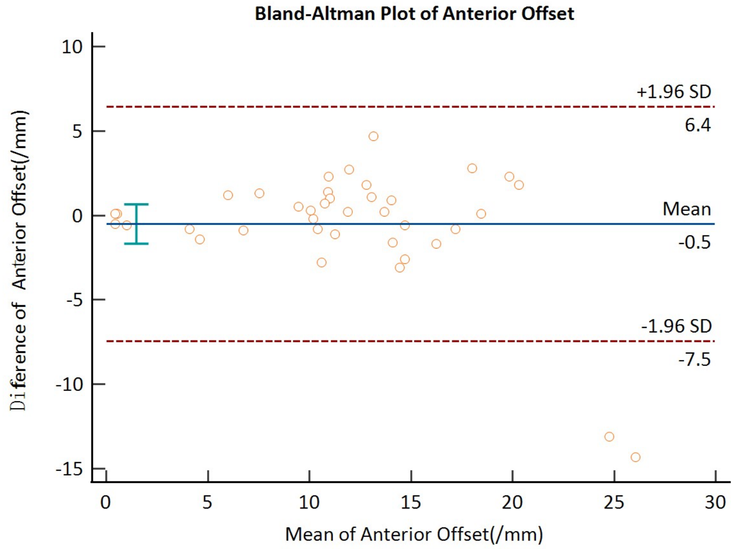


Figure 5.7 The Bland-Altman plot of anterior offset.

Horizontal offset measurements

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.2 below, and the Bland-Altman plot was in the Figure 5.10. The ICCs of intra-observer and inter-observer was 84.6% and 91.7% respectively. The Bland-Altman plot well matched the ICCs.

Table5.2 The intraclass correlation coefficient results of horizontal offset.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.846[a]	.724	.917	11.919	37	37	.000
Average Measures	.917	.840	.957	11.919	37	37	.000

Two-way random effects model where both people effects and measures effects are random.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

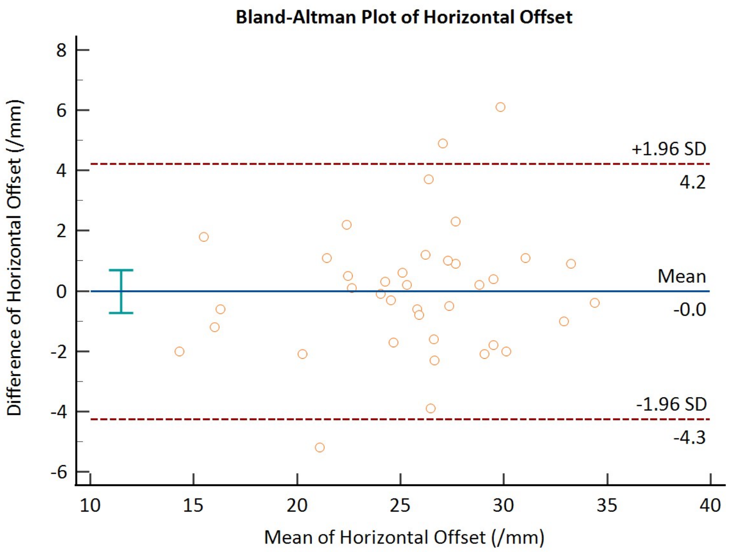


Figure 5.8 The Bland-Altman plot of Horizontal offset.

Head-shaft relative anteversion measurements

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.3 below, and the Bland-Altman plot was in the Figure 5.8. The ICCs of intra-observer and inter-observer was 99.7% and 99.8% respectively. The Bland-Altman plot well matched the ICCs.

Table 5.3 The intraclass correlation coefficient results of head-shaft relative anteversion.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	.997[a]	.994	.998	640.175	37	37	.000
Average Measures	.998	.997	.999	640.175	37	37	.000

Two-way random effects model where both people effects and measures effects are random.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

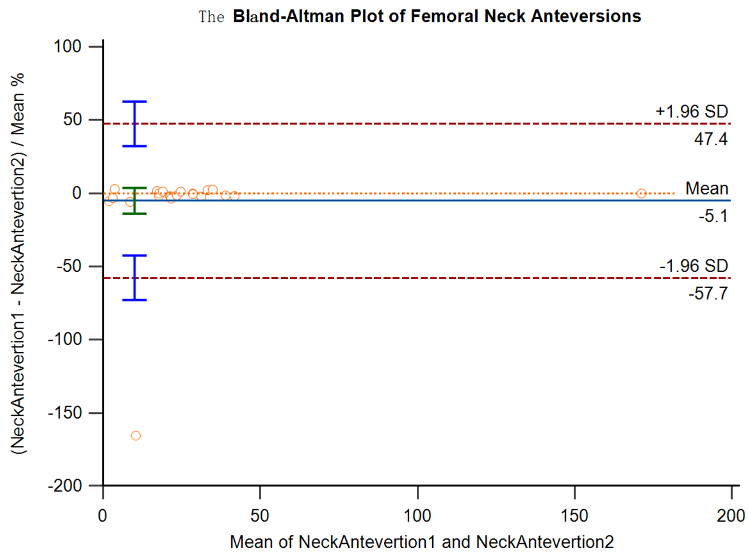


Figure 5.8 The Bland-Altman plot of head-shaft relative anteversions.

The implant preoperative-related measurements

Implant size

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.4 below, and the Bland-Altman plot was in the Figure 5.9. Both the ICCs of intra-observer and inter-observer were 100%. The Bland-Altman plot well matched the ICCs.

Table 5.4 The intraclass correlation coefficient results of implant size.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	1.000[a]	.	.	.	37	.	.
Average Measures	1.000[c]	.	.	.	37	.	.

Two-way mixed effects model where people effects are random and measures effects are fixed.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

c. This estimate is computed assuming the interaction effect is absent, because it is not estimable otherwise.

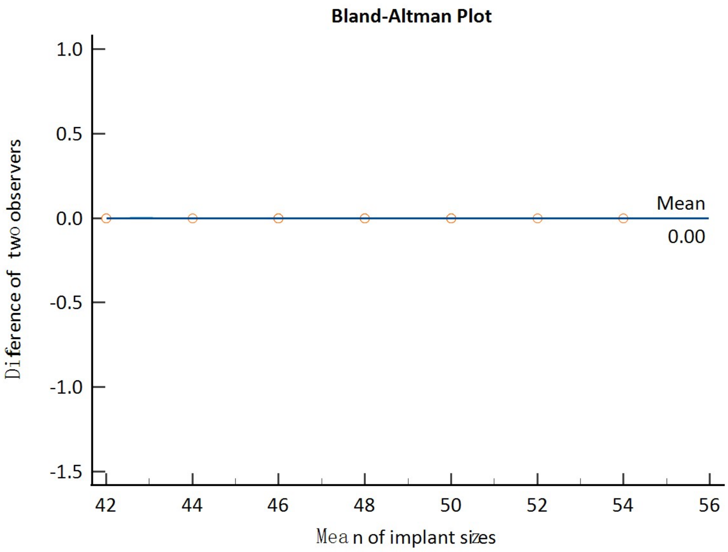


Figure 5.9 The Bland-Altman plot of implant size.

Neck anteversion

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.5 below, and the Bland-Altman plot was in the Figure 5.10. Both the ICCs of intraobserver and inter-observer were 100%. The Bland-Altman plot well matched the ICCs.

Table 5.5 The intraclass correlation coefficient results of femoral neck anteversion.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	1.000[a]	1.000	1.000	2150578.13	37	37	.000
Average Measures	1.000[c]	1.000	1.000	2150578.13	37	37	.000

Two-way mixed effects model where people effects are random and measures effects are fixed.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

c. This estimate is computed assuming the interaction effect is absent, because it is not estimable otherwise.

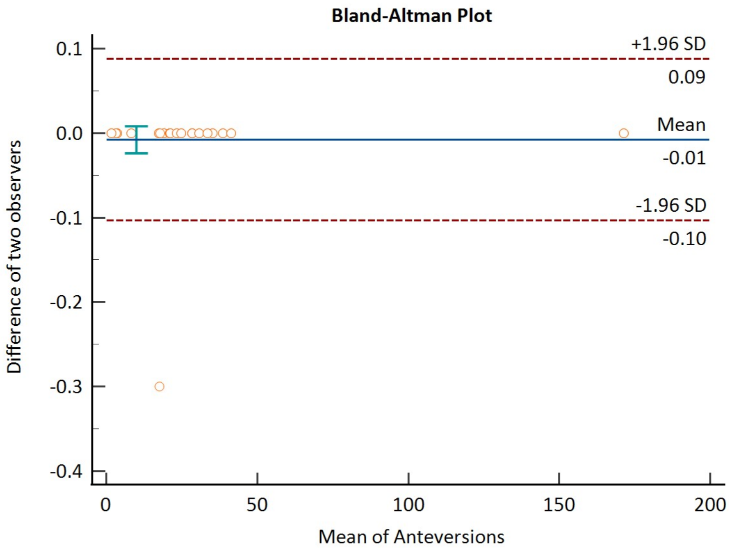


Figure 5.10 The Bland-Altman plot of femoral neck anteversion.

Femoral component neck length

The intra-observer (single measures) and inter-observer results (average measures) of ICCs were in the table 5.6 below, and the Bland-Altman plot was in the Figure 5.11. Both the ICCs of intraobserver and inter-observer were 100%. The Bland-Altman plot well matched the ICCs.

Table 5.6 The intraclass correlation coefficient results of femoral neck length.

Intraclass Correlation Coefficient

	Intraclass Correlation[b]	95% Confidence Interval		F Test with True Value 0			
		Lower Bound	Upper Bound	Value	df1	df2	Sig
Single Measures	1.000[a]	.	.	.	37	.	.
Average Measures	1.000[c]	.	.	.	37	.	.

Two-way mixed effects model where people effects are random and measures effects are fixed.

a. The estimator is the same, whether the interaction effect is present or not.

b. Type A intraclass correlation coefficients using an absolute agreement definition.

c. This estimate is computed assuming the interaction effect is absent, because it is not estimable otherwise.

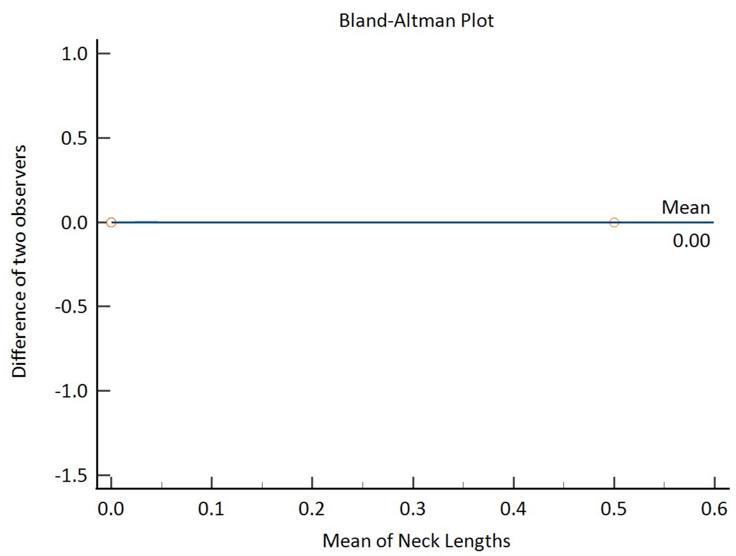


Figure 5.11 The Bland-Altman plot of femoral neck length.

5.5 Discussion

This is an interobserver and intraobserver reliability and reproducibility study of 3D preoperative planning software for AVN hip resurfacing arthroplasty using Ceramic H1 implant. To our knowledge, this study is also the first report on the preoperative planner, which is designed for AVN hip resurfacing.

The main finding of this study is that, this preoperative planner enables users to have a reliable and repeatable pre-operative planning, all measurements are in high agreement levels (> 80%). Such agreements are most prominent (100%) in the femoral component planning parameters, which include component size, component neck length and component anteversion. These 3 parameters play a crucial part in choosing the intraoperative component. Meanwhile, the rest part measuring femoral head and neck showing that, the agreements from them are not bad (>84%), although some measurement errors existed between observers and intra-observers.

Comparing to previous studies investigating preoperative hip surgery planning, our planner seems to give higher agreement results. Yasushi's study on AVN THA reported of 93% intraobserver agreement of stem size and 84% of femoral neck anteversion, and their intraobserver results were 93% and 60% respectively (23). With regard to cementless femoral component, both Carter (24) and Unnanuntana (25) reported that the agreements were lower than 70% for femoral components.

There are only limited studies on preoperative planning for hip resurfacing. Choi (26) reported a relatively low reliable results of under 60% using x-ray. Their reliability highly relied on surgeon's experience. Another study from Olsen et al (27) reported a 54% of agreement in femoral component 2D preoperative planning. No known studies on AVN hip resurfacing preoperative, nor any studies of 3D planning on hip resurfacing have been identified.

Despite some agreement advantages, however, there are some limitations on our study. First, the sample size in this study is small, which can be improved in subsequent large-scale trial. Second, the number of observers was only 2, the repeatability might be lower if the observers involved. Third, the perspective on the margin of AVN lesion varies from one person to another, and this might lead to lesion volume changes when segmentizing 3D models, thus, the measurement errors in the planner will increase as well. Fourth, such preoperative planning prediction accuracy should also be tested with intraoperative actual component use in clinical use.

5.6 Conclusion

In conclusion, the Zexin AVN Hip Planner is a useful and reliable preoperative planning tool for AVN hip resurfacing arthroplasty. The intraobserver and interobserver agreements from this planner are high enough in planning femoral component.

Chapter 6

Summary

The main findings of this thesis, are: 1) High AVN prevalence rates in East Asian countries. No intervention can guarantee to cure AVN except arthroplasty. 2) Hip resurfacing arthroplasty is more cost-effective than total hip arthroplasty for the AVN patients age 40-50 years. 3) HRA is a potential alternative to THA for patients who need intensive working/sporting levels, under 60 years of age. 4) The maximum simulated lesion depth to achieve initial stability between composite bone and cementless femoral component is 10mm of depth down from the top of femoral head, based on strain tests in lab. 5)A lab data based, cementless hip-AVN staging system was created, lesion depth <10mm was classified into ‘indicated for surgery’ category, whereas the 10-15mm and >15mm lesion depth into ‘not recommend for surgery’ and ‘contraindicated for surgery’ respectively. The preoperative planning for AVN hip resurfacing arthroplasty through our AVN planner is reliable and reproducible.

Current concepts treating avascular necrosis of the femoral head are polarized, those preserving intervention such as core decompression, osteotomy cannot guarantee a thorough necrotic bone removal. Meanwhile, although total hip replacement is able to remove all necrotic bone and provides satisfactory long-term implant survival rate, AVN patients might lose some benefits from this surgery compared to hip resurfacing arthroplasty. The reason for this should be something more important than simply chasing high implant survival rates. Something really matters should not be overlooked, especially the demands for attending high levels of intensive work and sports, considering their ages. These demands could be met by use of hip resurfacing arthroplasty.

Although our composite bone hip resurfacing bearing weight results went much further than all present AVN classifications, and we draw to a conclusion that 10mm of necrotic lesion depth can be dealt with autograft alone. There’s still room to improve, for example, is there any chance to gain hip resurfacing femoral component initial stability when the lesion depth is deeper than 15mm? And whether alternative materials could replace autografts, in order to obtain a stronger connection between bone and implant, although human native bone is always less rejected by their body?

As such, repeating simulated lesion in vivo experiments, or even experimenting new add-on materials to check if bony structure grows onto implant is essential in the foreseeable future. Only in this way we will be able to know whether this method can be used in clinical practice or not. If all these results live up to our expectation, clinical trial should be carried out. Only through double blinded clinical trials, will we be able to know how much hip resurfacing improve patients' postoperative life quality and how long the implant lasts before revision surgery.

In addition, pre-operative planning plays an important role in the stage before performing surgery. The planner gives an intuitive view to the lesion extent, depth and its location, and it also enables surgeons to do their planning work with a much higher accuracy, although its accuracy should be further tested from more observers.

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Appendix I: Review Registration

International Platform of Registered Systematic Review and Meta-analysis Protocols

INPLASY PROTOCOL

To cite: Zheng et al. A systematic review and meta-analysis to compare the survivorship of total hip arthroplasty and hip resurfacing for avascular necrosis. Inplasy protocol 202040200. doi: 10.37766/inplasy2020.4.0200

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Corresponding author:
Justin Cobb

j.cobb@imperial.ac.uk

Author Affiliation:
MSk Lab, Imperial College London

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None.

A systematic review and meta-analysis to compare the survivorship of total hip arthroplasty and hip resurfacing for avascular necrosis

Zheng, Z[1]; Zhao, H[2]; Cobb, J[3]; Abel, R[4].

Review question / Objective: **1. For patients with avascular necrosis of the femoral head, is hip resurfacing arthroplasty a safer procedure than Total Hip Arthroplasty? 2. For patients with avascular necrosis of femoral head, is hip resurfacing more cost-effective than total hip arthroplasty? 3. Is revision surgery for patients with avascular necrosis of the femoral head more successful following resurfacing than total hip arthroplasty?**
Rationale: **Patients with avascular necrosis of the femoral head are those young and active between 20 to 50 years of age, hip resurfacing arthroplasty is able to provide higher post-operative functional outcome and lower mortality rate than conventional total hip arthroplasty.**

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2020 and was last updated on 28 April 2020 (registration number INPLASY202040200).

INTRODUCTION

Review question / Objective: **1. For patients with avascular necrosis of the femoral head, is hip resurfacing arthroplasty a safer procedure than Total Hip Arthroplasty? 2. For patients with avascular necrosis of femoral head, is hip resurfacing more cost-effective than total hip arthroplasty? 3. Is revision surgery for patients with avascular necrosis of the femoral head more successful following resurfacing than total hip arthroplasty?**

Rationale: **Patients with avascular necrosis of the femoral head are those young and active between 20 to 50 years of age, hip resurfacing arthroplasty is able to provide**

higher post-operative functional outcome and lower mortality rate than conventional total hip arthroplasty.

Condition being studied: There are no known drugs available to cure avascular necrosis of femoral head(AVN). Commonly, the condition presents late, when significant collapse has occurred, and arthroplasty is the common treatment. The procedure of total hip arthroplasty (THA) is well established as a safe and effective intervention, but a large scale matched cohort study from American College of Surgeon's database indicated AVN patients had significantly higher medical complication rate than osteoarthritis(OA) patients. The Australian Joint Registry and UK Joint Registry also reported that much higher mortality rates of total hip arthroplasty to that of hip resurfacing 15 years postoperatively. Hip resurfacing arthroplasty (HRA) is a conservative alternative to THA, for AVN patients. This kind of surgery will not remove the necrotic lesion only. Hip resurfacing is not only less invasive and causes fewer postoperative complications than THA, but also provides patients with better postoperative functional outcomes. However, hip resurfacing remains controversial for two reasons. Firstly, the release of metal ions from some devices, which have now been withdrawn. Secondly, a hip resurfacing can be revised to a THA very easily, while revision of a THA can be very demanding, so comparison based upon revision rates alone may be misleading.

METHODS

Search strategy: #1. Search ((((((Femur Head Necroses[mh]) OR (Femur Head Necroses) OR (Head Necrosis, Femur) OR (Necrosis, Femur Head) OR (Aseptic Necrosis of Femur Head) OR (Necrosis, Aseptic, of Femur Head) OR (Ischemic Necrosis Of Femoral Head) OR (Femoral Head, Avascular Necrosis Of) OR (Avascular Necrosis Of Femoral Head, Primary) OR (Avascular Necrosis of Femur Head) OR (Necrosis, Avascular, of Femur Head) #2.Search ((((((Arthroplasties, Replacement, Hip[mh]) OR (Arthroplasty, Hip Replacement) OR (Hip Prosthesis Implantation) OR (Hip Prosthesis Implantations) OR (Implantation, Hip Prosthesis) OR (Implantations, Hip Prosthesis) OR (Prosthesis Implantation, Hip) OR (Prosthesis Implantations, Hip) OR (Hip Replacement Arthroplasty) OR (Replacement Arthroplasties, Hip) OR (Replacement Arthroplasty, Hip) OR (Arthroplasties, Hip Replacement) OR (Hip Replacement Arthroplasties) OR (Hip Replacement, Total) OR (Replacement, Total Hip) OR (Hip Replacements, Total) OR (Replacements, Total Hip) OR (Total Hip Replacements) OR (Total Hip Replacement) #3. Search ((((((Estimate, Kaplan-Meier[mh]) OR Kaplan-Meier Test) OR Kaplan Meier Test) OR Test, Kaplan-Meier) OR Product-Limit Method) OR Method, Product-Limit) OR Methods, Product-Limit) OR Product Limit Method) OR Product-Limit Methods) OR Kaplan-Meier Analysis) OR Analysis, Kaplan-Meier) OR Kaplan Meier Analysis) OR Curves, Kaplan-Meier Survival) OR Kaplan Meier Survival Curves) OR Survival Curves, Kaplan-Meier) #4. Search ((((((Follow Up Studies[mh]) OR (Follow-Up Study) OR (Studies, Follow-Up) OR (Study, Follow-Up) OR (Followup Studies) OR (Followup Study) OR (Studies, Followup) OR (Study, Followup) #5. Search #3 or #4 #6. Search #1 and #2 and #5.

Participant or population: People with AVN; any age, any gender and any severity of AVN. Population not restricted to the UK.

Intervention: People who have been admitted to hospital with AVN, who have received total hip arthroplasty or hip resurfacing.

Comparator: 1. Total hip arthroplasty for AVN patients with hip resurfacing for AVN patients. 2. Hip resurfacing for AVN patients and for osteoarthritis.

Study designs to be included: Including RCTs and observational/cohort studies.

Eligibility criteria: 1. Survival rates came without 95% confidence interval. 2. All surgeries done after the year of 1990. 3. Reliable design implants.

Information sources: PUBMED/MEDLINE; COCHRANE LIBRARY DATABASE; EMBASE; Reference checking and hand searching of these database. Contacting experts in relevant fields in DOH/BTS/NICE Identifying possible data from conferences attended.

Main outcome(s): Findings will suggest that a ladder of surgical interventions should be advocated, from femoral head preserving surgery, to hip resurfacing arthroplasty, with total hip arthroplasty kept for revision and those with severe disease.

Data management: Data extraction form in Word document Endnote to be used to keep track of references Reviewer number 1 (ZZ) will review first, followed by reviewer number 2 (HZ), which will be done independently. If necessary reviewer number 3 will review if there are any disparities between the two initial reviews.

Quality assessment / Risk of bias analysis: 1. Protocol will define the method of literature critique/ appraisal use, and will use PRISMA tool for relevant content and methodology used in the each of the papers to be reviewed. 2. Use STATA built-in bias analysis.

Strategy of data synthesis: Narrative synthesis will be done alongside any meta-analysis and will be carried out using a framework which consists of four elements; 1. Developing a theory of how the intervention works, why and for whom 2. Developing a preliminary synthesis of findings of included studies 3. Exploring relationships within and between studies 4. Assessing the robustness of the synthesis

Subgroup analysis: Each group will be subgrouped by the post-operative follow-up years.

Sensibility analysis: Use the STATA builit-in sensibility analysis and PRISMA tool.

Language: English only.

Country(ies) involved: China, UK.

Keywords: Avascular necrosis of femoral head, hip resurfacing, total hip arthroplasty, mortality rate, revision rate.

Contributions of each author:

Author 1 - Zexin Zheng - Author 1 define search strategy, manage literatures, do statistical analysis, draft the manuscript.

Author 2 - Hongyan Zhao - Author 2 define search strategy, manage literatures, do statistical analysis, draft the manuscript.

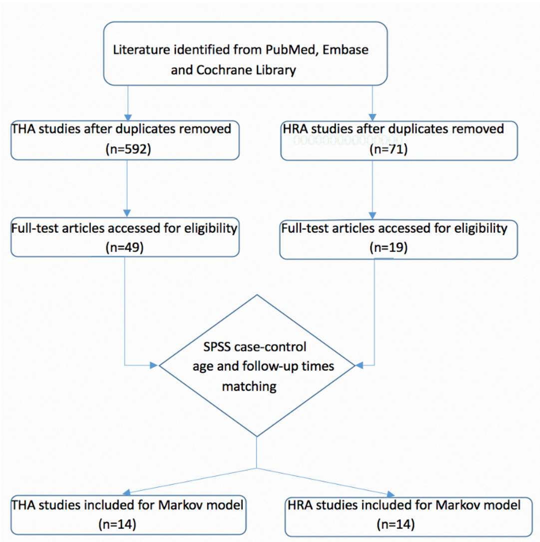
Author 3 - Justin Cobb - Author 3 supervises the review method and stastistical method, revises manuscript.

Author 4 - Richard Abel - Author 4 supervises the review method and stastistical method, revises manuscript.

Appendix II: PRIMSA Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Cost-effectiveness analysis comparing total hip arthroplasty and hip resurfacing for avascular necrosis based on published data	22
ABSTRACT			
Structured summary	2	Abstract Background: Avascular necrosis of the hip (AVN) is a common condition globally, resulting painful secondary osteoarthritis (OA) which is treated in the same way as primary OA. The purpose of this study was to compare the implant survival rate of total hip arthroplasty (THA) to the one of hip resurfacing arthroplasty (HRA). Method: A systematic review was performed of all papers reporting the outcome of hip arthroplasty for AVN. Implant survivorship and revision rates were evaluated, matching mean age at index surgery and mean follow-up times. Results: 14 studies (985 hips) in the THA group and 14 studies (1069 hips) in the HRA group were included. The re-operation rates with the endpoint of revision for any reason were significant higher in THA (8.2%, 62 hips) than HRA (6.7%, 71hips) at a mean follow-up of 8 years. Conclusion: Hip resurfacing arthroplasty is able to provide equally great outcome compared to total hip arthroplasty. Key words: Hip resurfacing arthroplasty, total hip arthroplasty, survival rate, revision rate.	22
INTRODUCTION			
Rationale	3	Patients with avascular necrosis of the femoral head are those young and active between 20 and 60 years of age, hip resurfacing arthroplasty is able to provide higher post-operative functional outcome and lower mortality rate than conventional total hip arthroplasty	23
Objectives	4	1. For patients with avascular necrosis of the femoral head, is hip resurfacing arthroplasty a safer procedure than Total Hip Arthroplasty? 2. For patients with avascular necrosis of femoral head, is hip resurfacing more cost-effective than total hip arthroplasty? 3. Is revision surgery for patients with avascular necrosis of the femoral head more successful following resurfacing than total hip arthroplasty?	23
METHODS			
Protocol and registration	5	INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 28 April 2020 and was last updated on 28 April 2020 (registration number INPLASY202040200).	24
Eligibility criteria	6	1. Survival rates came without 95% confidence interval. 2. All surgeries done after the year of 1990. 3. Reliable design implants.	24
Information sources	7	PubMed, Embase and Cochrane were systematically searched from their commencing dates to April 13, 2020.	24
Search	8	Reference checking and hand searching of these databases was then undertaken, and experts in relevant fields in NICE were identified. Possible data from conferences attended was also sought. Only publications in the English language were included.	24
Study selection	9	(i) For inclusion, a study should be a randomised controlled trial, cohort or observational study. (ii) Patients in the studies having total hip arthroplasty or hip resurfacing arthroplasty who were diagnosed with avascular necrosis of the femoral head. (iii) for inclusion, a study should compare groups of THA and HRA, or a single cohort of either THA or HRA patients. (iv) for inclusion, a study should report at least the end point of re-operation due to component failure for any reason.	24
Data collection process	10	(i)All patients' demographic data and outcome variables in 2 interventions (THA and HRA) were abstracted. Two reviewers independently abstracted outcome data from the included studies, and disagreements were solved through consensus.	24
Data items	11	Participant or population: Patient with AVN; any age, any gender and any severity of AVN. Population not restricted to the UK. Intervention: People who have been admitted to hospital with AVN, who have received total hip arthroplasty or hip resurfacing. Comparator: The survival rates of total hip arthroplasty for AVN patients with hip resurfacing for AVN patients.	24
Risk of bias in individual studies	12	1. Protocol will define the method of literature critique/ appraisal use, and will use PRISMA tool for relevant content and methodology used in the each of the papers to be reviewed. 2. Use STATA built- in bias analysis	25
Summary measures	13	Implant survival rates should be measured between total hip arthroplasty and hip resurfacing arthroplasty on AVN patients.	25
Synthesis of results	14	Narrative synthesis will be done alongside any meta- analysis and will be carried out using a framework which consists of four elements; 1. Developing a theory of how the intervention works, why and for whom 2. Developing a preliminary synthesis of findings of included studies 3. Exploring relationships within and between studies 4. Assessing the robustness of the synthesis	25

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Selection bias in the THA group because this group involved much more studies.	25
Additional analyses	16	Use the STATA builit-in sensibility analysis	25
RESULTS			

Study selection	17		27
Study characteristics	18	In the total hip group, 14 studies were included involving 985 hips. The mean age was 43.2 years (SD, 9.7 years) at index surgery, with a mean follow-up of 7.8 years (SD, 3.3 years). In the hip resurfacing group, 14 studies were included involving 1069 hips. The mean age was 42.4 years (SD, 9.9 years) at index surgery, with a mean follow-up of 8.0 years (SD, 3.1 years).	35
Risk of bias within studies	19	Selection bias and publication bias	40
Results of individual studies	20	There were 63 reoperations in 985 THA cases, and 71 reoperations in 1069 HRA cases. The most common cause for reoperation in both groups was aseptic loosening, (THA 29/985, HRA 36/1069) (Table 1). Medical complications appeared more prevalent in THA than HRA (110/808 vs 54/972). Deaths were also more common following THA (8%, 45/808 vs 2.4% 14/972) at 8 years of follow up.	32
Synthesis of results	21	The 8 years implant survival rates were higher in THA (8.2%) group than HRA group (6.7%)	32

Risk of bias across studies	22	Both selection bias and publication bias passed STATA built- in bias analysis	40
Additional analysis	23	Use the STATA built-in sensibility analysis	40
DISCUSSION			
Summary of evidence	24	The 8 years implant survival rates were higher in THA (8.2%) group than HRA group (6.7%), with mean age at surgery and follow-up time matched. The mortality rates from THA (8%) were also higher those from HRA (2.4%)	40
Limitations	25	The main limitation is only small proportion of THA studies involved because of the match of mean age at surgery and follow-up time matched.	40
Conclusions	26	Hip resurfacing arthroplasty was more cost-effective to total hip arthroplasty from published data.	42
FUNDING			
Funding	27	Support: Uren foundation – NCN011	-

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(6): e1000097. doi:10.1371/journal.pmed1000097

For more information, visit: **www.prisma-statement.org**.

Appendix III

Avascular necrosis of femoral head CT/ MRI slides sharing agreement

Title of Agreement	Avascular necrosis of femoral head CT/ MRI slides sharing agreement
Date of Request	11/03-2019

An update of an earlier extract ☐ New application ☑

Date Access to Begin: ________01/04/2019___

Date Access Ends: ______01/04/2021__________

Details of Requesting Organisation	
Name of Requesting Organisation: Please note that the Data Access Agreement will be immediately returned unless the requesting organisation has signed section H.	
Name of Authorised Officer /PI	Prof. Justin Cobb
Position/Status	Chair of Orthopaedics
Address Postcode	MSk Lab, Charing Cross Hospital, Fulham Palace Road, London W8 6RF
Sector of the requesting organisation e.g. Voluntary, Public, Private etc	Department of Surgery & Cancer
Telephone Number	+44 (0)20 3311 7687
Email Address	j.cobb@imperial.ac.uk
Name and Telephone Number of Organisation's Personal Data Guardian/Caldicott Guardian	Wayne Murrel +44 20 7594 7284

DATA ACCESS AGREEMENT

I CONFIRM THAT:

1. The Beiliu people's Hospital
consents to the disclosure of the data specified, to the organisation identified in Section B of this form.

Signed: Zhang chao Jin *(Trust internal use)*
(Information Governance)

Signed: Zhang Chao Jin
(Personal Data Guardian) OR (Senior Information Risk Owner SIRO)

Date: 22.04.2019