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Bone remodeling around short-stemmed hip prostheses

Degree Project in Medicine

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Abstract

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BACKGROUND

Total hip arthroplasty generally provides excellent results. During the last decades, prostheses with a shorter stem has emerged as an alternative to conventional prostheses. Short-stemmed prostheses are believed to reduce stress shielding and consequently reduce the loss of bone mineral density (BMD) in the proximal femur. Easier revision surgery and improved functional level are also proposed as benefits.

AIM

The aim of this study was to evaluate the change of BMD around two designs of short-stemmed hip prostheses with the use of two conventional prostheses as controls.

METHODS

The first study evaluated the CFP (Collum Femoris Preserving) stem and the second one the Fitmore stem. DXA (Dual-energy X-ray absorptiometry) scans were performed after surgery and at 3, 6, 12 and 24 months. The BMD was measured in regions of interests (ROIs) according to Gruen zones 1-7. Differences in change in BMD compared to baseline was calculated at 2 years as primary outcome.

RESULTS

At 2 years follow-up, BMD values for the CFP stem was inferior in all ROIs compared to the control. The difference was statistically significant in region 1, 6 and 7. The Fitmore stem was

inferior in ROIs 1, 2 and 4 but superior in ROIs 3, 5, 6 and 7. The difference was statistically significant in ROIs 1, 2 and 5.

CONCLUSION

The CFP stem was found to be inferior in all ROIs with large decrease in BMD in the proximal regions, indicating larger degree of stress shielding compared to the control. The Fitmore stem was observed with larger decrease in BMD in the lateral ROIs, but lesser decrease in the medial ROIs. Moderate differences between the Fitmore stem and the control indicates that the Fitmore stem is not an inferior alternative with respect to stress shielding and especially in younger patients.

KEYWORDS

Total hip arthroplasty, short stem, CFP, Fitmore

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List of Abbreviations

BMD	Bone mineral density
CFP	Collum femoris preserving
DXA	Dual-energy X-ray absorptiometry
ROI	Regions of interest
THA	Total hip arthroplasty
VAS	Visual analog scale
CLS	CementLess Spotorno
WOMAC	Western Ontario & McMaster Universities Osteoarthritis Index
RSA	Radio stereometric analysis
IQR	Interquartile range
EQ VAS	EuroQol Visual analog scale

Background

From the earliest hip arthroplasty until today

The first arthroplasty surgery took place in Germany in 1891, when professor Themistocles Glück used ivory to replace hip-joints damaged by tuberculosis. Other early attempts of arthroplasty were made with different tissues to replace damaged or lost cartilage. During the 1920s, experiments were made with glass as a replacement for the damaged cartilage on the femur head. Complications quickly arose, when the glass shattered under the massive strains that occurred in the hip joint. In the 1950s, the first stainless steel prosthesis was used, which provided greater durability. [1]

The hip prostheses of today have much in common with those developed in the 1960s. The early modern prostheses were composed of a stem made out of metal and a cup in polyethylene, both fixed with acrylic cement. Acrylic bone cement had its origin among dentists, but was found useful in arthroplasty surgery as well. The cemented total hip arthroplasty (THA) quickly gained popularity, which led to other types of prostheses falling out of the spotlight. The metal stem with a metal head combined with a polyethylene cup showed good results and became the dominating concept, which still is widely used, with minor modifications and improvements. [1]

Failures of early designs due to loosening and osteolysis, which during the 1980s was believed to be caused by the cement, generated an increase in uncemented fixation. Uncemented prostheses rely on initial stability provided by a tight fit to the bone. The implants are typically made of a titanium alloy, titanium or tantalum or a combination of these materials, where the surface coating is made of titanium or tantalum and the underlying cup-shell or stem is made of titanium alloy. An additional coating with hydroxyapatite may be used. With use of these modern implant, osseous fixation will occur in a reproducible way by

in- or ongrowth of bone tissue. The initial stability is crucial since micro movements larger than 150 micrometer could result in fibrous rather than bony fixation, which is important to reduce the risk of later clinical failure [2]. As indicated above, the concept of uncemented fixation emerged from the idea that failure was partially due to the bone cement, leading to "cement disease" [3]. The superiority of cemented or uncemented prostheses are still under debate with data indicating different strengths and weaknesses for the different methods as shown by Phedy et al in a meta-analysis [4]. The indication for cemented fixation increases with increasing age and decreasing bone quality [5, 6].

Another factor contributing to the risk of clinical failure was found in the wear particles, which were found to be a significant factor for development of bone resorption. Most wear particles in the artificial joint come from the polyethylene as a result of articulation, but any type of micro particles, e.g. from the cement or the metal, may initiate an inflammatory response. This inflammatory response will initiate bone resorption, osteolysis, which often end up in clinical loosening [7].

Modern arthroplasty and stress shielding

Modern THA generally provides excellent results. In Sweden, 10 years prosthesis survival was 97.8% based on data from 2006-2016 [8]. Patient reported outcome measured by VAS (visual analog scale) on pain and overall satisfaction was evaluated on patients who underwent THA in Sweden 2013-2015. Pain VAS, where 0 is no pain and 100 is worst possible pain, showed a decrease from 64 preoperatively to 13 postoperatively. EQ VAS, where 0 is the worst health the patient can imagine and 100 is the best health the patient can imagine, increased from 58 preoperatively to 76 postoperatively [9].

Despite the good results, there are some inherent complications needed to be addressed in order to optimize the procedure further. When fitted with a prosthetic hip, the head and neck

of the femur is removed and replaced with a prosthesis. This alters the force load on the femur, shifting load forces from the proximal femur further distally. Reduced load of the proximal femur results in remodeling of the bone. With time, the proximal areas of the femur tend to become osteoporotic and in the distal parts the bone density will increase [10].

To determine bone mineral density (BMD), dual x-ray absorptiometry (DXA) is considered the gold standard [11, 12]. The scan provides a two-dimensional image, but uses two x-ray beams of different energy. Due to different absorption in the tissues it will become possible to calculate the BMD [13]. DXA scans after THA is usually divided into 7 regions according to the Gruen classification, where region 1 is the most lateral and proximal region and region 2 and 3 follows further distally. Region 4 represents the bone at the tip of the prosthesis and region 5, 6 and 7 follows on the medial side with region 5 most distally and 7 most proximally (fig.1). A total net average is also provided representing the average of the 7 regions.

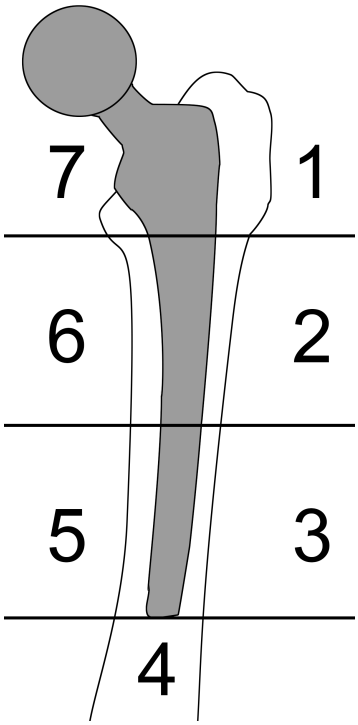

Figure 1 Gruen zones 1-7 in relations to the femur and the prosthesis

Redistribution of bone density after THA is known as stress shielding and occurs according to Wolff's law. Wolff's law states that bone is remodeled according to the strains put upon it, where higher load results in higher BMD and vice versa [14]. When loading force is distributed in a less physiological way, i.e. after THA, demineralization occurs in the bone where the load forces are decrease. When fitted with a prosthesis, the heavy load on the proximal femur becomes distributed further distally due to design and stiff material of the prosthesis [15]. When the proximal femur is under less mechanical stress, i.e. stress shielding, it undergoes remodeling and over time decreases in BMD and might even become more or

less completely resorbed and disappear. As a result of stress shielding and demineralization, revision surgery might become increasingly difficult. Lack of bone will jeopardize the fixation of a new implant and there is less bone tissue left to support the new prosthesis.

Another important complication with THA is aseptic loosening of the prosthesis. In Sweden 68.8% of revision surgery performed on patients, who had been operated with THA between 1979-2015 was due to aseptic loosening [9]. The cause of aseptic loosening could be due to several different factors. When the prosthesis is not properly fixated, micro-movements causes bone remodeling leading to demineralization of the bone, loosening its structural integrity and leads to prosthesis failure.

The loss of BMD in proximal regions of the femur after THA is very well documented. R. Zügner et al. [10] showed in their 23-years follow up of the Madreporic Lord stem, a marked decrease in BMD in the proximal regions of the femur with a gradual increase in the distal regions. Similar results were found by Merle et al. [16] in a 17 years follow-up of the CLS stem. The largest decrease of BMD occurs in the first 6-12 month after THA, the bone remodeling then reaches a plateau stage. A slow decrease in BMD is, however, usually observable over time [17, 18].

The short stem

Attempts have been made to reduce the decrease of BMD after THA. Bisphosphonates have been used trying to maintain periprosthetic bone stock. Studies have, however, shown moderate evidence of its efficacy [19]. Another approach to reduce the loss of bone stock is by the development of prostheses with shorter stems. These prostheses reduce the amount of proximal femur needed to be removed when inserting the prosthesis. A more conservative bone resection proximally and use of short stem prostheses are believed to facilitate proximal loading and reduce stress shielding [20]. Development of shorter stems has been carried out

since the 1980s [21], resulting in the diversity of stem designs present today.

A traditional hip prosthesis is approximately 150 mm, whereas a short stem is considered to be <120 mm [22]. Short stemmed prostheses (fig. 2) have, as earlier mentioned, been around since the 1980s, but have gathered more interest more recently. A traditional prosthesis is anchored into the femoral canal and provides fixation relatively distal in the femur. This provides good stability and fixation but may cause problems if they need to be removed during a revision. Today the 15 years survival of hip prostheses in males and females reaches 88.6% (CI: ±0.4%) and 92.03% (CI: ±0.3%), according to the Swedish Hip Arthroplasty Register Annual report 2016. Even if these results can be regarded as good, the large quantities of THA preformed every year leads to an increasing amount of revision surgery needed to be performed. Furthermore, revision surgery is associated with an increased risk of further revisions and often within in a comparatively short time period [8]. The consequences may be increased suffering for the patients, increased costs and strained surgical schedule for the clinics. This becomes a greater concern with younger patients, since they are more likely to outlive the lifespan of their prostheses. Also, since total life expectancy is still increasing, a larger portion of patients who undergoes THA will eventually need revision in the future.

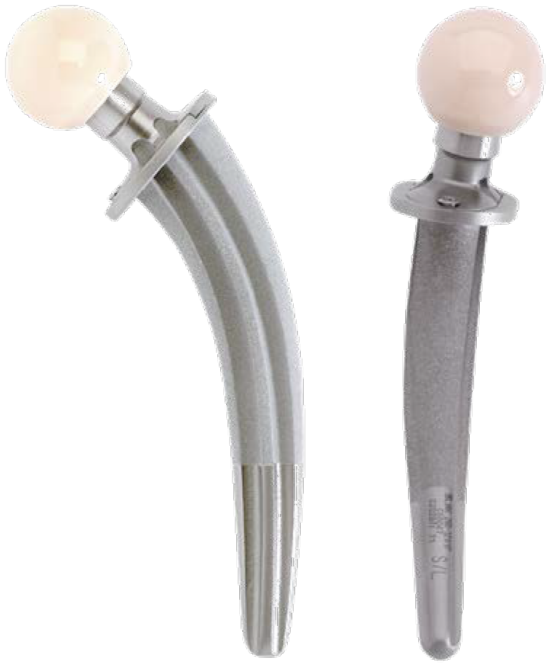

Figure 2 Short stemmed prosthesis (The CFP stem, copyright: Link)

The short stem depends on a metaphyseal fixation, leaving the femoral canal more intact compared to the traditional stem. The possible benefits from a shorter stem is the ability to perform minimal invasive surgery and revision surgery when needed, with less traumatic

damage on the femur. Shorter stems are also believed to be able to transfer the load forces more proximally compared to traditional stems, possibly leading to less stress shielding, and thus higher BMD and less risk of aseptic loosening [22]. Another theoretical advantage is potential faster rehabilitation and higher level of function, since the short stem requires less trauma to soft tissue at insertion, providing possibility for better muscle function post-operatively [23].

Studies performed on short stems have showed good results regarding patient reported outcome. In patient reported questionnaires, short stemmed prostheses have received similar results as prostheses of traditional type. A meta-analysis by Hou et al. compared results in terms of Harris Hip Score (6 studies) and Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC, 5 studies), where the majority of the studies had a follow up of more than 1 year. This meta-analysis found strong evidence supporting no difference between the two stem designs. 3 studies included analysis of thigh pain after THA, with a follow up ranging from 3.3-4.8 years, found less thigh pain for the short stem design compared to the traditional design [24].

A randomized controlled trial by Salemyr et al. [25] compared ultra-short stems to conventional stems with a follow up of 2 years. Primary outcome was periprosthetic bone demineralization in Gruen zone 1 and 7. The trial showed a significant lower decrease in bone mineralization for the ultra-short stem compared to the conventional stem. Zone 1 showed a mean difference of -18%, zone 7 showed a mean difference of -5% in comparison between the two stem designs. The authors conclude that the stem provided excellent results with low BMD decrease and reduced thig pain for the ultra-short stem design.

Present study

In this study, 4 types of prostheses are used. The first trial compares the CFP (collum femoris preserving) stem with the Corail stem. The Corail stem is a well-documented prosthesis of conventional type produced by DePuy Orthopedics, Inc., USA. It became available in 1986 and has since then been subject of minor updates. The clinical record of the Corail stem is to be considered excellent [26], and is one of five stems included in the control group at the Swedish Hip Arthroplasty Register with a survival rate at 98.5% at 10 years [8]. The CFP stem (Link, Germany) was introduced in 1987 and offers a shorter stem and a more curved design. As the name indicates, it requires less of the femoral neck to be resected during insertion. Clinical experience indicates good results [27], however, follow-up data have indicated an increased risk of aseptic loosening with this stem[28].

The second trial compares the Fitmore stem to the CLS stem. Both stems are manufactured by Zimmer, Inc, USA. The CLS stem was introduced in 1984, and has been frequently used with good clinical results. It has in several studies showed excellent results at long term follow-up [26, 29, 30] and is also included in the control group at the Swedish Hip Arthroplasty Register with a survival rate at 98% at 10 years [8]. The Fitmore stem was introduced more recently and shares similarities in design with the CLS stem, but is significantly shorter; a 129 mm tall Fitmore stem corresponds to 190 mm tall CLS stem. There are less clinical experiences using the Fitmore stem, but studies have shown promising results [23, 31].

Aim

Our hypothesis was that a shorter stem would reduce stress shielding and thus to a larger extent preserve BMD in the proximal femur. Our aim was to evaluate if a shorter stem (the CFP stem and the Fitmore stem) was associated with less loss of BMD around the implants

compared to a traditional stem (the Corail stem and the CLS stem respectively) up to 2 years after THA.

Material and Methods

Two different trials were set up in order to evaluate the hypothesis: the CFP-trial and the Fitmore-trial.

The primary outcome for both of the separate trials was level of pain and satisfaction with the prosthesis after one year.

Secondary outcomes were:

1) Proximal/distal migration of caput femoris measured with radio stereometric analysis (RSA) postoperatively to 2 years after the operation.
2) Abduction range at gait on a flat surface (gait analysis).
3) Loss of BMD in region 7, 2 years post-operatively.

The primary outcome for this sub-analysis of both trials were change in BMD in region 1-7 after 24 months.

The CFP-trial

In the CFP-trial, a prosthesis of collum femoris-preserving design (CFP) was compared with a conventional type of prosthesis (Corail). Patients who sought the orthopedic clinic at Sahlgrenska University Hospital, Mölndal, and were accepted to undergo THA as a result of hip disease in one or both hips were asked to participate in the study. Only cases operated on one side the same day were included. Inclusion took place from 2011 to 2015. Inclusion criteria were age 35-70 and well preserved collum femoris, with an anatomy suitable for the CFP stem. Exclusion criteria were joint disease predisposing for affected bone stock quality (e.g. inflammatory joint decease, osteoporosis, previous hip fracture) and predisposing

difficulties to participate in the study (e.g. substance abuse, language difficulties, severe associated diseases). Patients diagnosed with primary cox arthritis, secondary cox arthritis due to femoral head necrosis or mild hip dysplasia were included. Both men and women were asked to participate. All patients were given oral information about participating in the trial from a doctor or a specially trained nurse, as well as written information. All patients who choose to participate in the trial gave their written consent. 83 patients who met the inclusion criteria accepted to participate. Patients were randomized to either a CFP or a Corail stem with use of envelopes. All patients received the same uncemented cup (Delta-One TT, Lima, Italy). After surgery, the patients were instructed to bare as much weight on the operated leg as tolerated. 0-20 (mean 3) days after surgery, the patients underwent DXA scan. Follow-up with DXA was scheduled at 3, 6, 12 and 24 months. 7 patients did not participate in the postoperative and 6 patients failed to participate in the 24 months follow up, resulting in a total of 70 patients (34 CFP, 36 Corail) for the final analysis. For the analysis of change over time, 3 additional patients were excluded due to missing one or several scans 3-12 month after surgery resulting in a total of 67 patients (33 CFP, 34 Corail) with complete data (fig. 3).

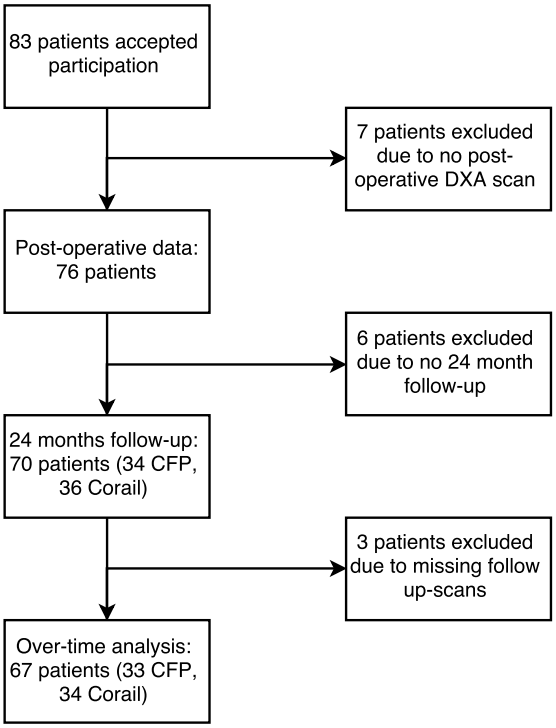

Figure 3 Flowchart of exclusion algorithm, CFP trial

Table 1 Age distribution at the time of surgery, CFP trial

Age at surgery	CFP	Corail
Median	61.5	58
Minimum	35	43
Maximum	73	73

Table 2 Gender distribution, CFP trial

Gender	CFP	Corail	Total
Male	24	22	46
Female	10	14	24

Table 3 Reported diagnoses leading to THA, CFP trial

Diagnosis	Frequency
M16.0 - *Coxarthritis [arthritis of hip]*	13
M16.1 - *Other primary coxarthritis*	62
M16.2 - *Coxarthritis resulting from dysplasia, bilateral*	2
M16.3 - *Coxarthritis resulting from dysplasia, bilateral*	3
M16.5 - *Other post-traumatic coxarthritis*	1
M870 - *Osteonecrosis: Multiple sites*	1
Missing diagnosis	1
Total	83

The Fitmore-trial

The Fitmore-trial compares a stem of conventional type (CementLess Spotorno, CLS) with a short stem (Fitmore), whose design is based on the CLS stem, but has a significantly shorter profile. The inclusion- and exclusion criteria for the Fitmore-trial was similar to the CFP-trial, with the exception that the patients suffer from bilateral hip disease. Medical history should have motivated bilateral insertion of prosthesis during the same occasion of surgery. Inclusion occurred from 2011 to 2016. All patients were given oral information about participating in the trial from a doctor or a specially trained nurse, as well as written information. 44 patients accepted participation and gave their written consent. The hip with the most severe symptoms or, if equal, the one with most pronounced degenerative changes on radiographs, was randomized to the Fitmore stem or the CLS stem. The contralateral hip was provided with the opposite stem type. Both sides were given the same type of cup (Trilogy, Zimmer, USA). 1-7 (mean 4) days after surgery, the patients underwent DXA scan to provide a baseline value for BMD. The patients were followed up at 3, 6, 12 and 24 months with DXA scan. One patient only underwent surgery on one hip because of blistering of the skin after the first operation

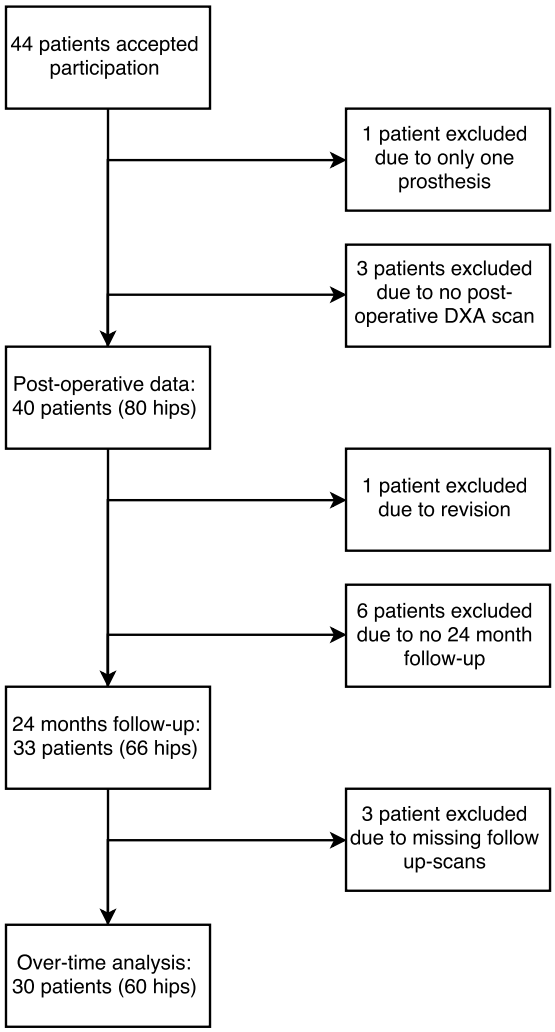

Figure 4 Flowchart of exclusion algorithm, Fitmore

and was therefore excluded from the analysis. 3 patients failed to participate in the post-operative DXA scan, resulting in a total number of 40 patients (80 hips). 1 patient underwent revision and was subsequently excluded. 6 patients had not met the 24 months follow up and were excluded from the final analysis, resulting in a total of 33 patients (66 hips). For the analysis of change over time 3 additional patients were excluded due to missing one or several scans 3-12 month after surgery resulting in a total of 30 patients (60 hips) for the analysis (fig. 4).

Table 4 Gender distribution, Fitmore trial

Gender	Fitmore	CLS	Total (Hips)
Male	15	15	30
Female	18	18	36

Table 5 Age distribution at the time of surgery, Fitmore trial

Age at surgery	Fitmore/CLS
Median	57
Minimum	43
Maximum	73

Table 6 Reported diagnoses leading to THA, Fitmore trial

Diagnosis	Frequency
M16.0, Coxarthritis [arthritis of hip]	39
M16.1, Other primary coxarthritis	2
M16.2, Other primary coxarthritis	1
M16.7, Other secondary coxarthritis	1
M870F, Osteonecrosis: Multiple sites	1
Total	44

Methods and statistics

All DXA scans were performed at Sahlgrenska University hospital, Mölndal by two different trained DXA-operators. Equipment used was a Hologic Discovery QDR DXA scanner, software Hologic Discovery Apex, version 12.7.3. Scan mode used was the metal removal program. To keep the variance of the scans to a minimum, the feet of the patients were

strapped to a support to keep the leg in a fixated, internal rotated position.

Analyses of the scans and extraction of the data was performed by the author. All analyses were performed using regions of interest (ROI) according to the Gruen zones 1-7. For the short stems, region 2-3 and 5-6 was reduced in height, instead of using the modified Gruen zones 1-5, to provide comparability with the conventional stem. Each hip was analyzed in a sequence to reduce variability of the ROIs. The size of the ROIs was customized for each hip and was kept with as little modifications as possible for the remaining scans for each hip.

For each scan, a value of BMD was generated for zone 1-7, as well as a total net average BMD, based on average of the 7 ROIs. The postoperative analysis was used as reference value for the subsequent analyses. The amount of change in BMD for each subsequent analysis (3, 6, 12 and 24 months) was calculated as a ratio of the postoperative value for each ROI as well as the net average value. Since a large quantity of the data did not meet the criteria of normality in both trials, nonparametric analyses were used. For the primary outcome, difference in change between each group after 24 months, Mann Whitney's test was used to calculate significance. All statistical analyses were performed with IBM© SPSS© Statistics, 25.0.

Ethics

Both trials were approved by the local ethics board in Gothenburg. The CFP trial was approved by the committee 2012-06-19, registration number 243-12. The Fitmore trial was approved by the committee 2010-11-17, registration number 617-10.

Results

All values are reported as medians and interquartile range (IQR) if not specified otherwise.

The CFP trial:

At 24 months, both groups had a reduction in net average BMD. In the CFP group the median value was -7.3% (IQR 0.1%) and in the Corail group -1.2 (IQR 0.1%, p=<0.001). The Corail stem had significantly smaller decrease in region 1, 6 and 7 compared to CFP. Both stems had the greatest loss of BMD in zone 7. In region 1, CFP had a decreased BMD at -10.2% (IQR 0.2%) whereas Corail had an increase of 1.6% (IQR 0.1%,) in medians (p=0.001). In region 7 a loss of BMD was observed for both stems, -21.7% (IQR 0.2%) and -9.4% (IQR 0.2%) in medians for CFP and Corail respectively (<p=0.0001). See table 7 for remaining regions.

Table 7 **Results, CFP. Change in BMD (%) 2 years post-operatively compared to baseline values.**

CFP:	**Net avg.**	**Region 1**	**Region 2**	**Region 3**	**Region 4**	**Region 5**	**Region 6**	**Region 7**
Median	-7.3	-10.2	-4.6	-1.1	0.5	1.4	-4.3	-21.7
Range	0.3	0.6	0.4	0.7	1.0	0.5	0.7	0..9
*IQR**	0.1	0.2	0.1	0.1	0.1	0.1	0.2	0.2
Corail:								
Median	-1.2	1.6	-1.4	0.8	0.6	2.6	3.2	-9.4
Range	0.3	0.9	0.5	0.3	0.2	0.3	0.6	1.2
*IQR**	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.2
Exact Sig. (2-tailed)	<0.001	0.001	0.235	0.371	0.636	0.208	0.016	<0.001

***IQR = Interquartile range.**

The changes of BMD over time in terms of medians, were compared for 3, 6, 12 and 24 months. No statistical analyses were performed on the change over time data. Compared to

the Corail stem, the change of net average BMD was numerically declining for the CFP stem. Region 1 and 7 was also observed with an increasing numeric decline. Region 6 was observed with a numeric difference of < 1% up to 12 months, but decreased to -4.11% at 24 months. Region 2 was observed with a numeric difference of < 1% up to 12 months, but decreased to -4.11% at 24 months. Region 3 and 5 was observed with numeric differences of < 2% in all measures. Region 4 was consistently observed with numeric differences < 1 %. Each region is presented in figure 5.

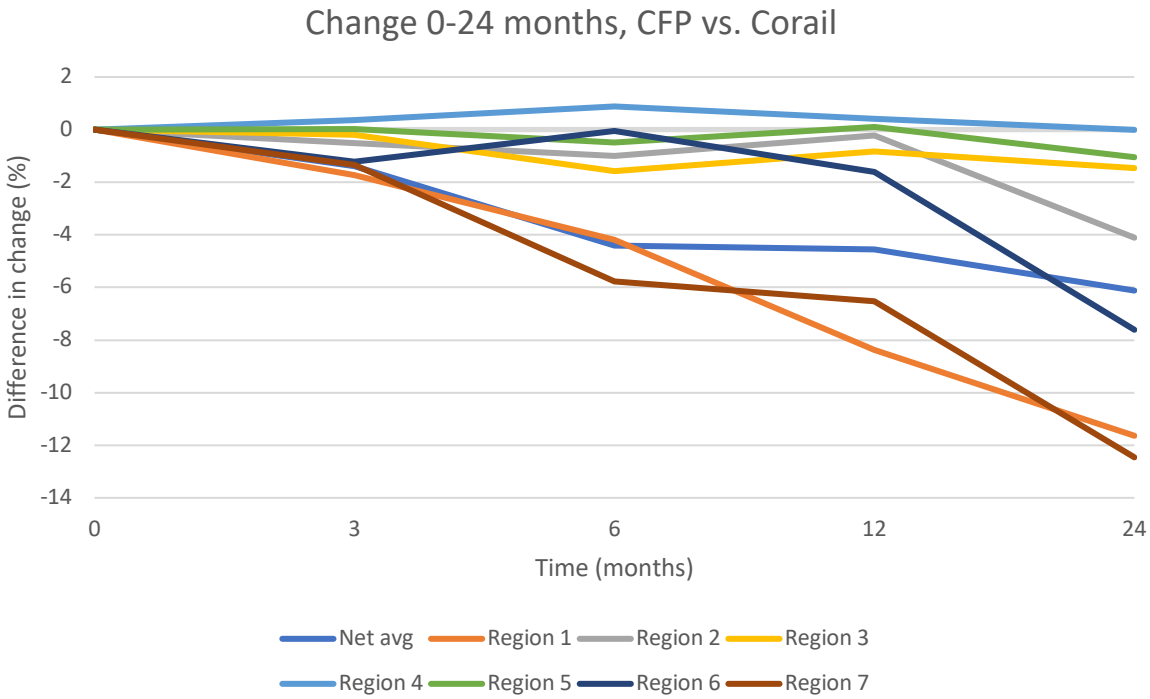

Figure 5 Difference in change compared to baseline at 3, 6, 12 and 24 months between the CFP stem and the Corail stem for each ROI and net avg. Negative value indicates lower BMD change value for CFP compared to Corail. Positive value indicates higher BMD change value for CFP compared to Corail.

The Fitmore trial:

Observations after 24 months showed similar net average BMD for both stems. A slight decrease was observed for Fitmore (median -1.4%, IQR 0.1%) and a slight increase for CLS (median 0.03%, IQR 0.1%), but no difference between the groups (p=0.184). In region 1, the Fitmore stems showed a decrease (median -5.2%, IQR 0.2%), whereas the mean value for the

CLS stems was almost unchanged (median 0.2%, IQR 0.2%) (p=0.012). There was a decrease for both stems in region 2 (Fitmore: median -6.7%, IQR 0.1%; CLS: median -1.5%, IQR 0.1%), which was more pronounced in the Fitmore group (p=0.016). In regions 3 and 4 there were no difference between the groups (p= 1.0 for both comparisons). In region 5, both stems showed an increase, which was higher for Fitmore stems (median 6.1%, IQR 0.1%) compared to the CLS (median 1.5%, IQR 0.1%, p=0.046). In region 6, there was a numerical increase, but no difference between the groups (p=0.3). Region 7 was observed with a pronounced numerical decrease for both stems, but no statistical difference between the groups (Fitmore: median -13.7%, IQR 0.2%; CLS: median -17.0%, IQR 0.3%, p=0.8). See table 8 for further information.

Table 8 Results, Fitmore. Change in BMD (%) 2 years post-operatively compared to baseline values.

Fitmore	**Net avg.**	**Region 1**	**Region 2**	**Region 3**	**Region 4**	**Region 5**	**Region 6**	**Region 7**
Median	-1.4	-5.2	-6.7	-0.9	0.8	6.1	5.9	-13.7
Range	0.2	0.6	0.6	0.3	0.2	0.4	1.0	0.6
*IQR**	0.1	0.2	0.1	0,1	0.1	0.1	0.2	0.2
CLS								
Median	0.03	0.2	-1.5	-1.7	1.5	1.5	2.8	-17.0
Range	0.2	0.9	0.3	0.3	0.2	0.7	0.5	0.5
*IQR**	0.1	0.2	0.1	0.1	0.1	0.1	0.1	0.3
Exact Sig. (2-tailed)	0.184	0.012	0.016	0.98	0.97	0.046	0.326	0.789

***IQR = Interquartile range.**

Similar to the CFP trial, comparisons for the changes of BMD over time in terms of medians

at 3, 6, 12 and 24 months were made for Fitmore trial. No statistical analyses were performed on the change over time data. The changes of BMD over time in terms of medians were compared for 3, 6, 12 and 24 months. Compared to the CLS stem, the numerical difference in change for total net average BMD was consistently within ±3 %. Region 5, 6 and 7 were all observed with a positive numerical change for the Fitmore stem compared to the CLS stem, and was higher at 24 months compared to 3 months. In contrast, region 1 and 2 were both observed with a negative numerical change for the Fitmore stem compared to the CLS stem, and was lower at 24 months compared to 3 months. In region 3, the numerical change was negative at 3, 6 and 12 months, but positive at 24 months, the values was however within ±4%. Region 4 was observed with a numerical difference within ±2 %. Each region is presented in figure 6.

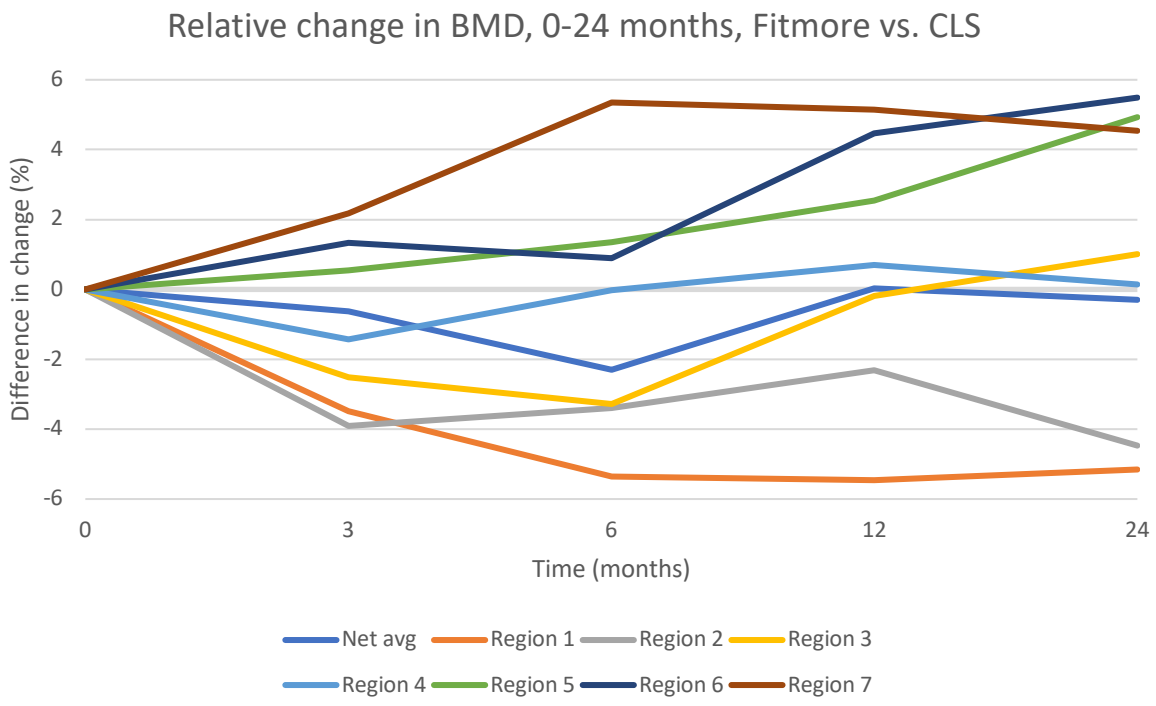

Figure 6 Difference in change compared to baseline at 3, 6, 12 and 24 months between the Fitmore stem and the CLS stem for each ROI and net avg. Negative value indicates lower BMD change value for Fitmore compared to CLS. Positive value indicates higher BMD change value for Fitmore compared to CLS.

Discussion

The main goal for this study was to evaluate whether a short femoral stem would be associated with less loss of BMD, when compared with a conventional stem. In order to not only cover one single implant, and, to a limited extent, account for differences in shape and design philosophy, this study includes two types of short stems. Two different conventional stems were used as controls, the Corail and CLS stem, both with a very thorough clinical documentation.

The CFP trial

The CFP stem was observed with a larger decrease of net average BMD compared to the Corail stem. The largest difference was observed in region 1 and 7, where the CFP stem had decreases of -10.2% and -21.7% in median respectively. The Corail stem had a considerably smaller decrease in these regions, -1.6% and -9.4% in median respectively. As compared to the hypothesized outcome, the CFP stem lost more bone mineral than expected. In the proximal regions, the short stem was hypothesized to prove better results compared to the conventional stem due to less stress shielding. Instead, a substantial loss was observed compared to Corail in these regions.

At the first follow up occasion there was a small difference, which increased substantially during the following 3 months in regions 1 and 7. Remaining regions were observed with smaller differences. Change in BMD then reached a plateau-like state up to the 1 year follow up. At the 2 years follow up there was an observed increase of the difference in regions 1 and 7, in favor of the Corail stem. In comparison of the 1 and 2 years follow up there was an increasing difference in the second most proximal regions (2 and 6), also in favor of the Corail stem. Although these changes were not statistically significant, it does not imply any decrease in stress shielding with use of the CFP stem, rather the opposite. With the use of the

CFP stem, more of the femoral neck is preserved, which means that parts of region 1 and 7 do not exist with the use of the Corail stem. Nonetheless, this part of the bone does, according to our observations, seem to be subjected to stress-shielding and less loading force than before removal of the femoral head. Findings of increased BMD in regions 4 and 5 support the theory that the CFP stems transfer load distally. Overall, our observations of BMD changes during the postoperative 2 years do not indicate any advantage of the CFP design as regards maintenance of BMD.

Lazarnis et al. [20] evaluated the CFP stem two years after insertion in 27 hips. The study showed similar results as our data with large decrease in BMD in the proximal regions and less losses in the distal regions. At 1 year, region 7 showed decrease in BMD of -31% with a small increase at 2 years to -28%. Region 6 was also observed with large decrease in BMD at -19% after 2 years. This study had however a somewhat different definition of ROIs compared to our study, making comparison difficult. In contrast to our findings, Lazarinis et al. found an almost complete remission to baseline values in region 1. Region 2 on the other hand remained with a significant decrease in BMD after 2 years. The difference from our findings was interesting, since we did not observe any increase in region 1 in our data. As mentioned, the definition of regions to be analyzed were not the same in their study and ours, which to a certain extent could be an explanation.

The Fitmore trial

The net average difference of BMD between the Fitmore and the CLS stems was small and slightly in favor of the CLS stem. A difference was observed in region 1, where the Fitmore stem had significantly larger decrease in BMD compared to the CLS stem. This difference was, however, relatively small compared to the CFP-trial. A noticeable difference compared

to the CFP trial was observed in region 2, where the Fitmore as well as the CLS stem had larger decrease in BMD than in region 1. Both stems showed similar tendencies in region 3 and 4 with small deviations from postoperative data, as was seen in the CFP-trial as well. The outcome in the distal regions was expected, as other studies has shown similar results [10, 20, 32].

Compared to the CFP trial, the Fitmore and CLS stems showed smaller changes over time. The CLS stem exhibit higher BMD values in the lateral regions (ROIs 1-3), whereas the Fitmore stem exhibited higher values in the medial regions (ROIs 5-7). The most distal region (ROI 4) exhibit small deviations from baseline for both stems. In conclusion, there were no substantial differences between the two designs. According to our observations, preservation of proximal bone stock that surround the prosthesis does not seem to be a valid argument for use of a shorter stem.

To our knowledge, previous studies of the Fitmore versus CLS have shown similar results as ours. Freitag et al [18] performed a randomized controlled trial including 138 patients completing 1-year follow up comparing the Fitmore stem to CLS stem. DXA scans showed a significant reduction in all ROIs 1 year after THA, except for region 3 in the short stem where there was a small increase. Similar to our findings, the study showed the most pronounced decrease of BMD for both stems in region 7, -17.2% and -16.7% in median for Fitmore and CLS respectively. In region 6, decrease in BMD was observed for both stems, but the short stem had significantly less loss in BMD compared to the conventional stem. In contrast to our findings, the study showed significant decrease for the Fitmore stem compared to the CLS stem in region 1. In summary, the findings of Freitag et al. is to a large extent similar to ours.

Strengths and limitations

This study has several strengths and weaknesses regarding the study design. Both studies are randomized control trials of similar size and distributions of gender and age in both the study and the control group. There are fewer women than men in the CFP trial, although the distribution between the groups is similar. Since no patient older than 75 years was included, this study cannot draw any conclusions regarding the effect of THA with short stems in an older population. The main purpose with the short stem is to provide a better alternative for younger patients, since they are most likely to undergo revision surgery in the future. Nevertheless, most patients who undergo surgery with THA is older, and since total life expectancy is steadily increasing [8], an increased proportion of older patients will need revision surgery as well. Patients above 75 years of age will in Sweden, more likely be operated with a cemented stem to reduce the risk of periprosthetic fracture and dislocation. Further on, in older patients with poor bone stock the possibility to achieve adequate primary fixation with the use of a short stem is limited.

The CFP trial has a traditional study design with a study group (the CFP stem) and a control group (the Corail stem). Since different patients is included in each group, there is an inherent risk of bias between the two groups. The Fitmore-trial has a different study design with each patient included in both the trial- and the control group. This design should exclude bias caused by skewed groups. The downside of this design is, however, the reduced number of included patients, making the impact of each patient that might skew the data greater. Since each patient is included in both groups, any bias should be applied on both groups, rendering the net effect relatively small. Further studies would preferably be performed with a larger study population.

An inherent difficulty with this type of studies is the matter of blinding. The patients have been randomly assigned to either of the prosthesis types, but the surgeons performing the insertion are not blinded. This is not possible to perform, since the physical appearance of the prostheses are different and also demands different surgical techniques. Furthermore, there is no blinding while analyzing the DXA scans, since different prostheses types have different appearances on the scans. Besides the risk of biased data from the scans, another problem with the DXA scans is different ROI sizes. Since the prostheses are different in length, width and shape, with different amount of the femoral neck preserved, there will be a systematic difference in regards of location and size of ROIs used. This is only partly accounted for by calculating the change in BMD, instead of absolute values, but the risk of remaining bias is still substantial. For further studies, constructing a system with more clearly defined and reproducible ROIs within different prostheses types could help to reduce this problem.

The bone remodeling process occurs mainly within 2-3 years after insertion of the prosthesis, after which it reaches a plateau stage [33]. These trials have a follow up of two years, which rather well corresponds to the most important period for bone remodeling. The bone-remodeling process does, however, continue and at present it is uncertain when it mainly mirrors the process of ageing. The changed stress distribution will most certainly have an influence for a longer period than two years, but the time point when an equilibrium is reached is not known. We think that our results provide a good benchmark of how these prostheses would affect bone remodeling over time. It is however desirable to preform studies with longer follow up. Both trials in this study is ongoing with a planned follow up of at least 10 years follow up and will hopingly reveal additional information about bone remodeling in the longer time perspective.

BMD is an important aspect regarding choices of prosthesis design. However, there are many more variables needed to take into consideration when concluding the superiority of one design over another. This study only evaluates BMD via DXA scans, but radiostereometric analysis is also highly valuable to detect micro movement and early signs of loosening due to much higher precision compared to conventional radiography [34]. It is also of great importance to include patient centered outcomes, usually measured by self-evaluation scales, such as Harris Hip Score, WOMAC and EQ-5D, to get a more comprehensive picture of the function of the prosthesis in the clinical environment.

All data in this study has been treated as non-normalized since several data points did not meet the criteria of normality. There are also several outliers in all groups. As a consequence, the statistical analyses were made with non-parametric tests. There are however no analyses preformed to explore the background to this distribution of data. Previous studies including about the same number of hips have shown a similar data distribution. It is plausible that the relatively small sample sizes in these studies and our could be the cause. If so, further studies with larger populations would yield more rigid statistical results. There is however a high individual variation of BMD in the population and probably also of bone turnover. It could also be that some of the patients included in studies suffer from not diagnosed metabolic disturbances or diseases which could be responsible for the observed scatter of data.

The short stem in the future

Is a short stem superior to a conventional stem? With the short stems potential advantages of improved function and if needed, easier revision surgery, it is conceivable that a short stem would be beneficial if it provided at least similar BMD profile as a conventional stem. If a

short stem also would provide less hip pain and generally more or equally satisfied patients, then the conclusion would be further extended, but these outcomes were not studied here.

Our findings regarding the CFP stem does not indicate that there are any advantages with this type of prosthesis. Compared to its control (the Corail stem), the BMD change was significantly higher in several regions and there was no evidence of reduced stress shielding. This could mean that even if this stem conserves more bone at insertion, this effect is counteracted by higher loss in BMD two years post-operatively. In conclusion, the CFP stem does not appear to be clinically superior compared to its conventional counterpart, especially taking in consideration the good clinical experiences from using the Corail stem.

The data for the Fitmore stem was much closer to its conventional counterpart (the CLS stem). Any reduction in stress shielding was, however, not observed for the short stem in this trial either. There was a significantly higher loss of BMD in region 1 and 2 in the Fitmore group, but on the other hand lower, although not significantly, loss in region 3, 5, 6 and 7. These uncertainties could possibly be reduced in a study with larger groups. The data does not support conclusions stating any advantages with the Fitmore stem over the CLS stem. Even so, the data is consistent enough to speculate if a shorter stem could provide a good complement for younger patients with a higher level of activity, who also are more likely to be needing revision surgery. To draw any firmer conclusions, further studies with larger patient groups are still needed.

Conclusions and Implications

Provided that the anatomy of the proximal femur design is compatible with use of the particular short stem design of interest, use of such stems could be favorable under certain conditions. The CFP stem was found to have a significantly larger decrease in BMD compared to the control. The Fitmore stem was found to present a somewhat different profile in change in BMD, but the overall differences were moderate.

Our findings do not allow us to conclude any advantages with short stems based on the DXA data. We did not find any support for the argument of reduced stress shielding with the use of a shorter stem. However, in a young and active population, the advantage of the shorter stem could compensate for minor difference in change in BMD. In such cases, the Fitmore stem could be a feasible option. To obtain basis for more firm conclusions, studies combining BMD data with long term follow up including patient reported outcome and risk for revision are needed. This is however outside of the scope of this study.

Populärvetenskaplig sammanfattning

Benombyggnad kring kortstammade höftproteser

Höftprotesoperationer ger i regel mycket goda resultat. I Sverige genomförs årligen ca 17 000 höftprotesoperationer och siffran stiger för varje år. Med ett ökat antal operationer kommer också ett ökat behov av om-operationer då proteser slits eller lossnar, ibland till följd av att bentätheten kring protesen minskat. För att minska förlusten av bentäthet kring höftprotesen har flera nya proteser utvecklats, ofta med kortare protesstam. Tanken är att den kortare protesen ska ge en mer naturlig belastning på lårbenet, vilket ska förhindra förlust av bentäthet samt underlätta vid en eventuell om-operation. En kort protes skulle även kunna erbjuda snabbare rehabilitering och bättre funktion, eftersom operationen innebär ett mindre ingrepp i höften och dess omkringliggande strukturer, jämfört med konventionella proteser.

Den här studien har undersökt två typer av korta proteser (CFP-protesen och Fitmore-protesen) och jämfört dessa med kontroller (Corail-protesen och CLS-protesen) av konventionell, längre typ. I CFP-studien ingick 83 patienter, som slumpvis valdes till en protes av CFP-typ eller Corail-typ. I Fitmore-studien ingick 44 patienter som erhöll höftproteser på båda sidorna, en av Fitmore-typ och en av CLS-typ. Kompletta data upp till 2 år var vid denna utvärdering tillgängliga för 67 respektive 30 patienter i CFP och Fitmore studien.

Efter två år visade bentäthetsmätningen att patienterna som erhållit CFP-protesen hade en signifikant minskad bentäthet kring protesen jämför med kontrollgruppen. Fitmore-studien visade efter 2 år ett mer blandat resultat, där vissa regioner uppvisade en större minskning, medan andra regioner uppvisade en mindre minskning i bentäthet jämfört med kontrollen. Skillnaderna i Fitmore-studien var dock relativt små.

Då CFP-stammen totalt sett uppvisade ett sämre resultat på alla mätpunkter jämfört med

Corail-stammen, tyder detta på att användning av denna protes inte kan försvaras på grunderna att den skulle kunna minska förlusten av benmineral och belasta benet mer fysiologiskt. Fitmore-protesen å andra sidan visade sig vara jämförbar med kontroll-protesen. Ingen av proteserna i studien uppvisar dock den minskade benförlusten som man i teorin skulle kunna förvänta sig.

Utifrån våra data kan man dra slutsatsen att hos vissa patientgrupper skulle Fitmore-protesen kunna vara ett bra alternativ. Fler studier behövs fortfarande för att undersöka vad som händer på längre sikt, då en protes idag förväntas ha en livslängd på över 15 år och patienterna i denna studie endast följts under två år. Dessutom behövs en sammanvägd bild av fler aspekter efter höftledsoperationer så som om-operationsfrekvens och patientupplevd funktion. Vår studie tyder på att med rätt design på protesen kan en kortstammad protes utgöra ett bra komplement till konventionella proteser, och för vissa patientgrupper möjligen innebära en fördel.

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Figures and Tables

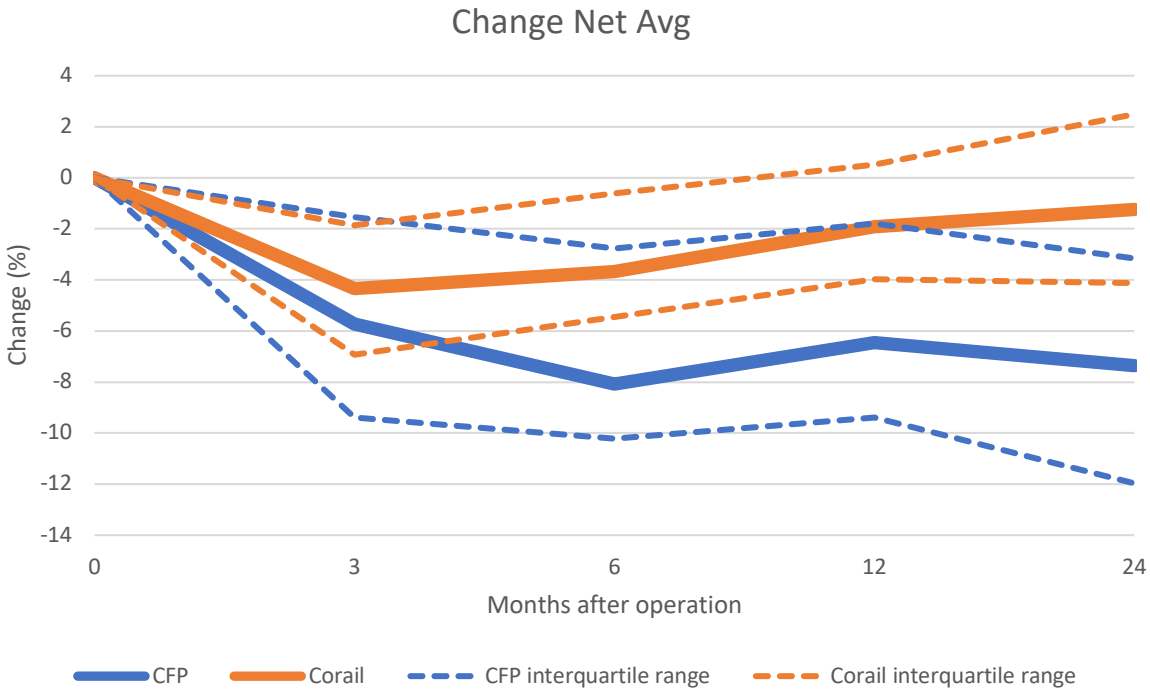

Figure 7 Change in net average BMD, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

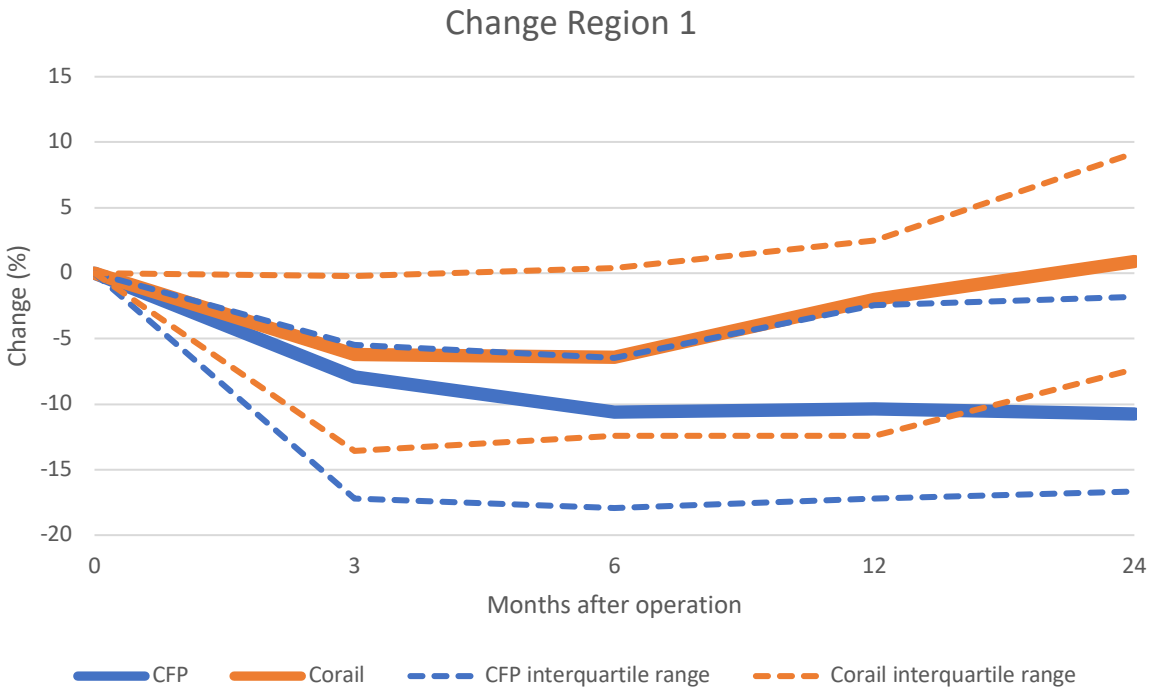

Figure 8 Change in BMD, region 1, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

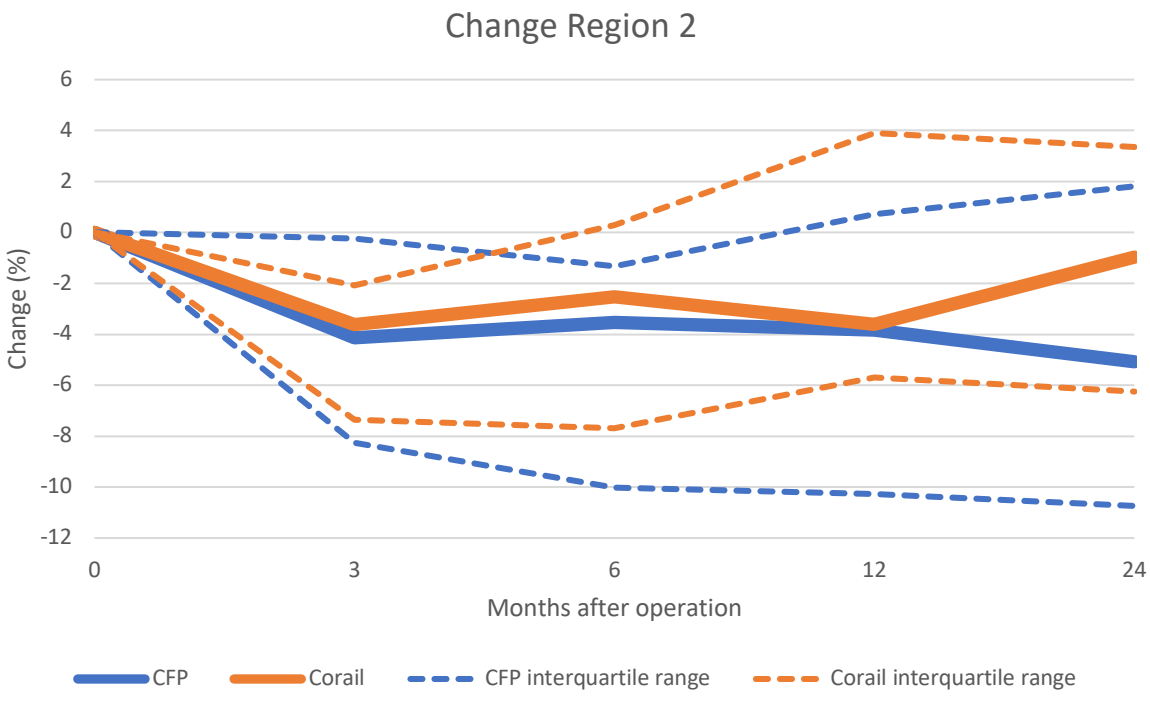

Figure 9 Change in BMD, region 2, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

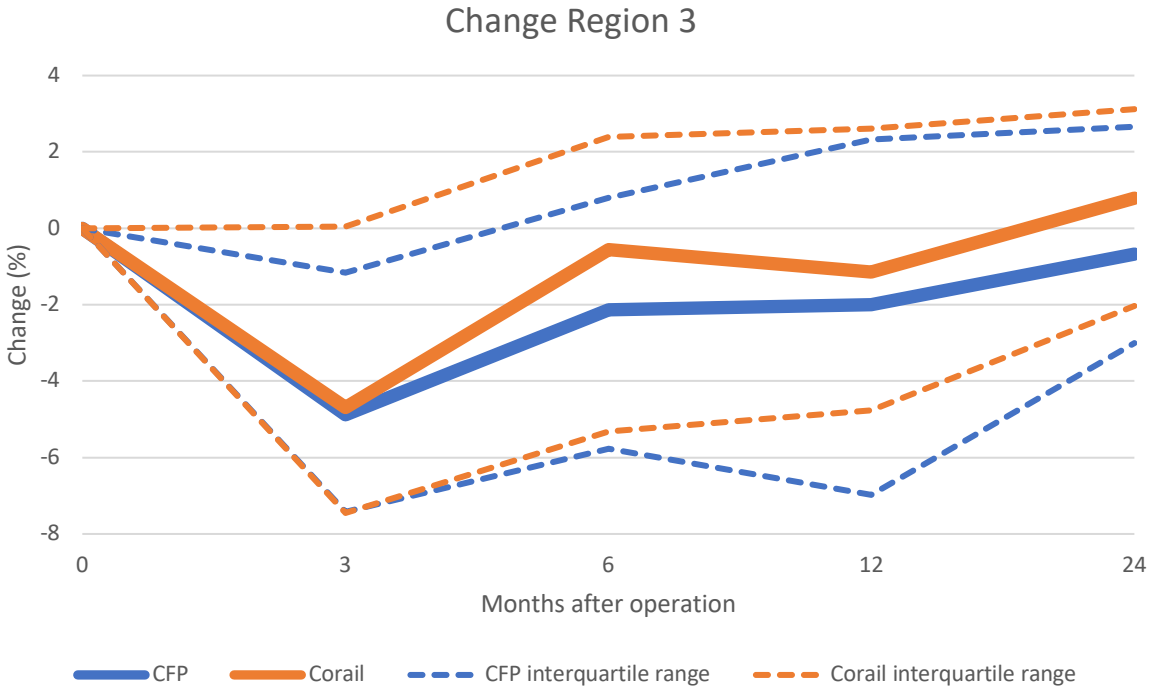

Figure 10 Change in BMD, region 3, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

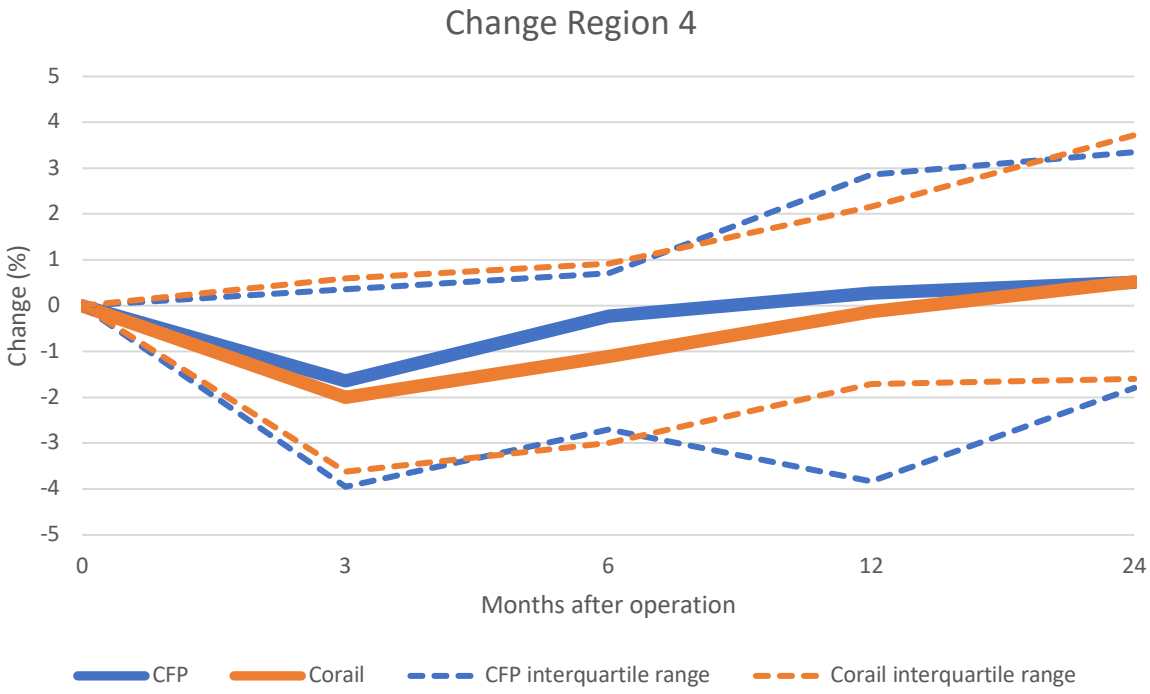

Figure 11 Change in BMD, region 4, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

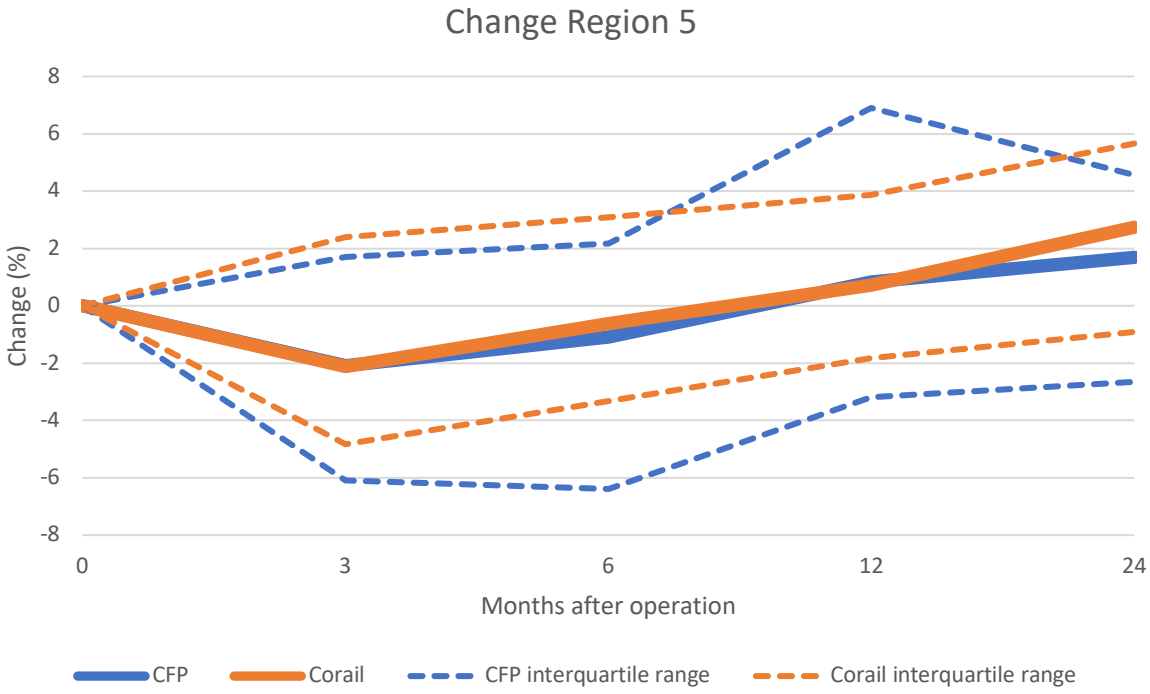

Figure 12 Change in BMD, region 5, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

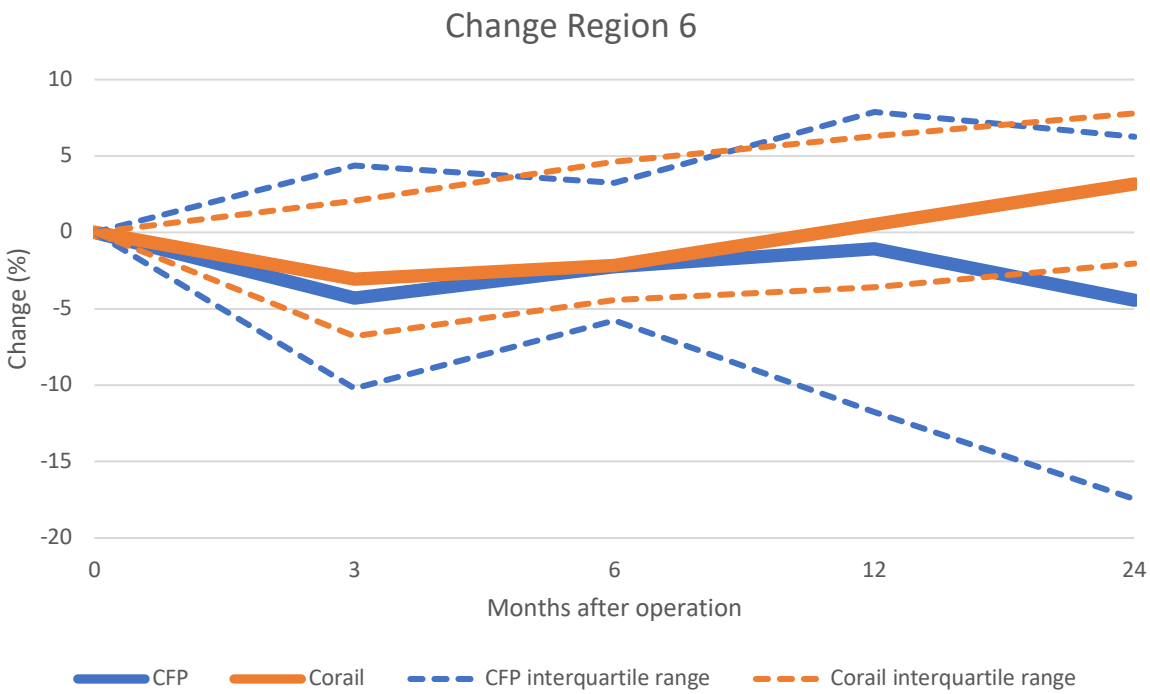

Figure 13 Change in BMD, region 6, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

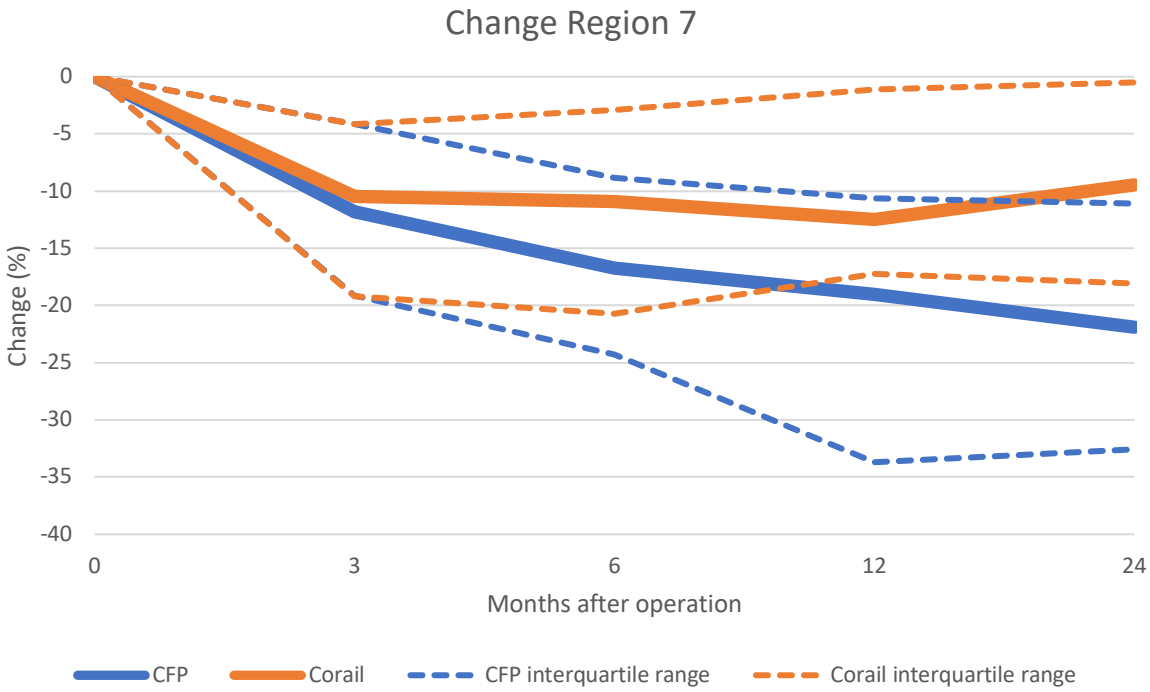

Figure 14 Change in BMD, region 7, compared to baseline at 3, 6, 12 and 24 months, the CFP trial

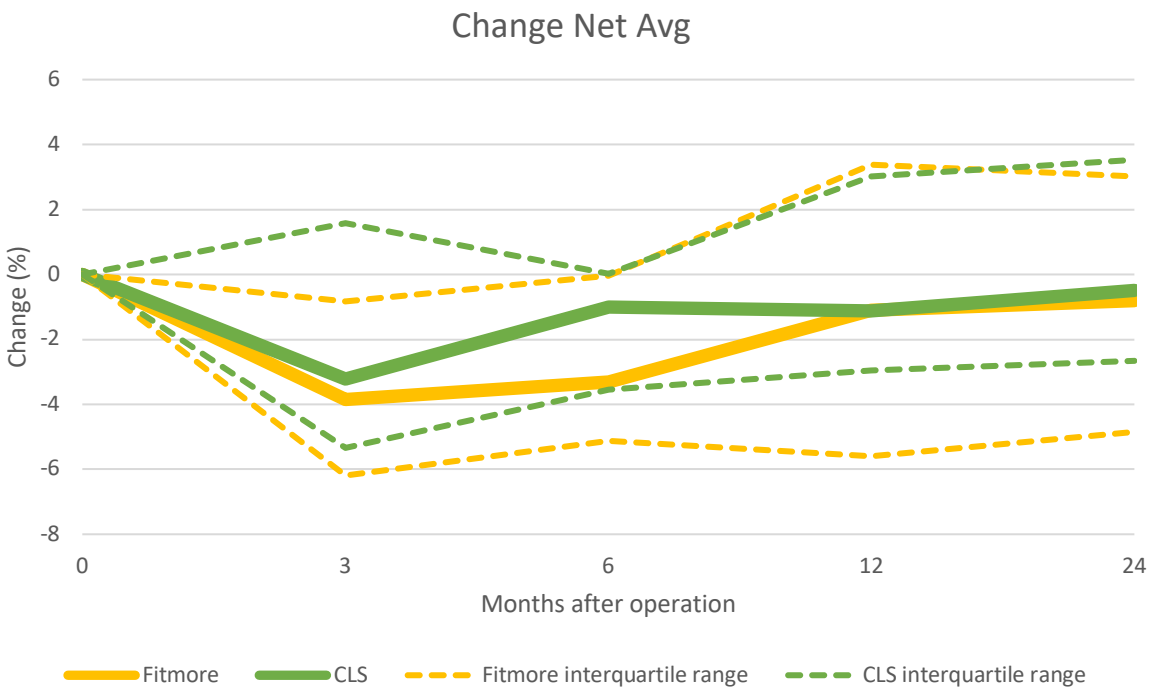

Figure 15 Change in net average BMD, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

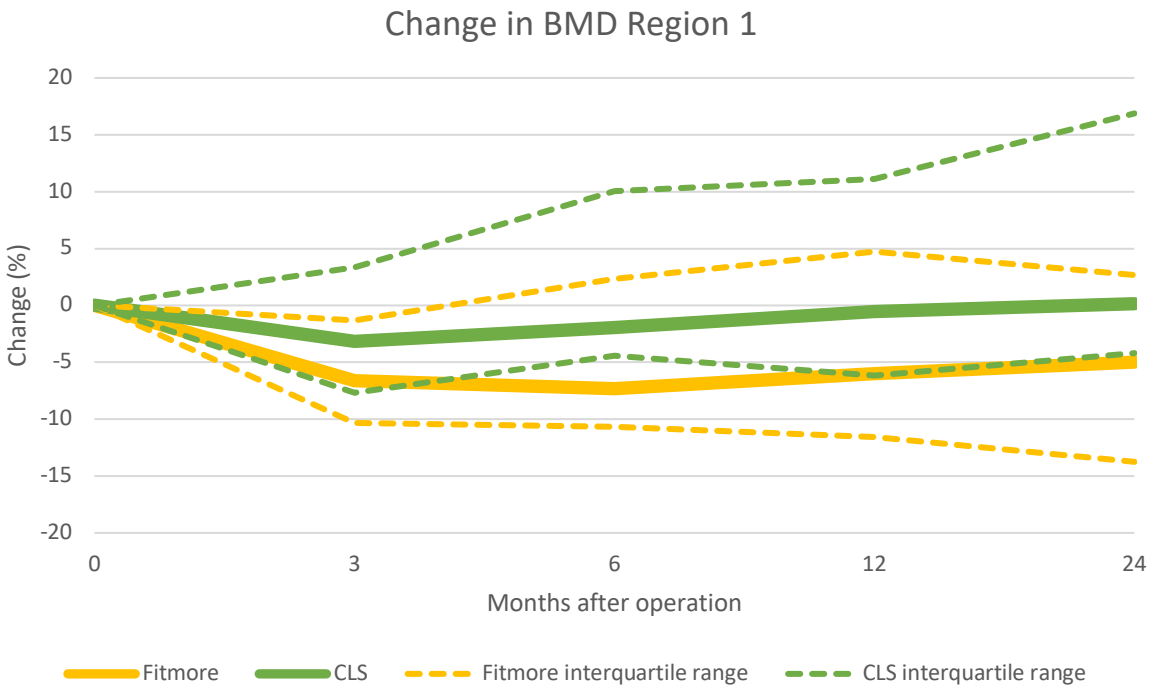

Figure 16 Change in BMD, region 1, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

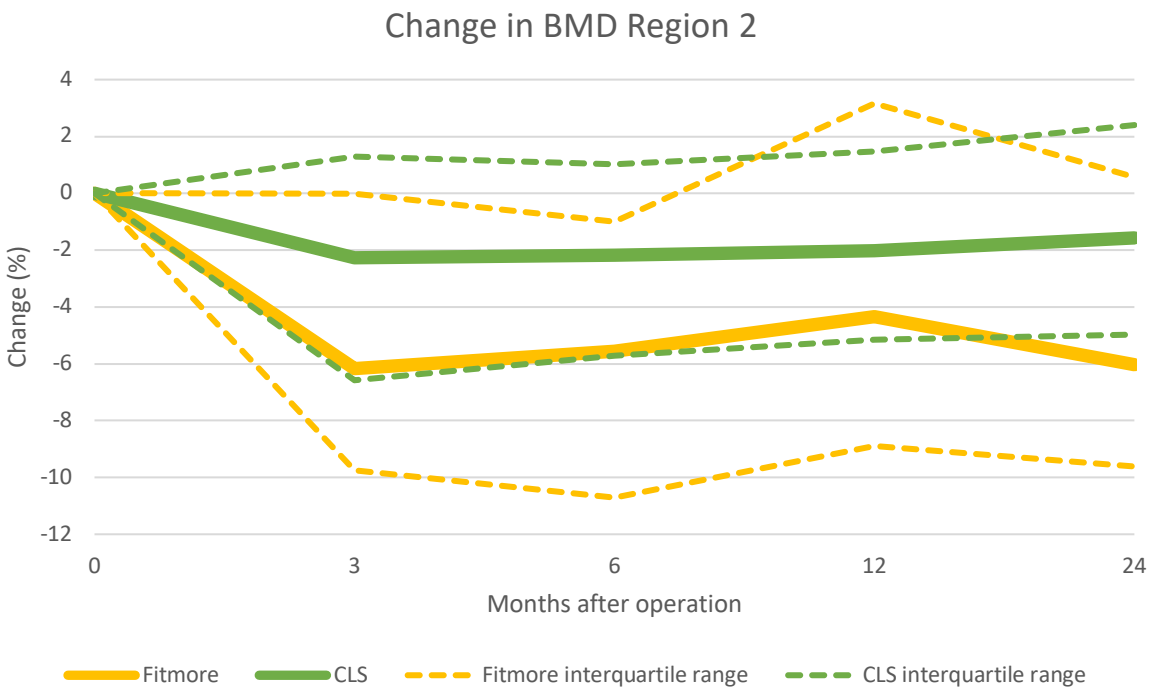

Figure 17 Change in BMD, region 2, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

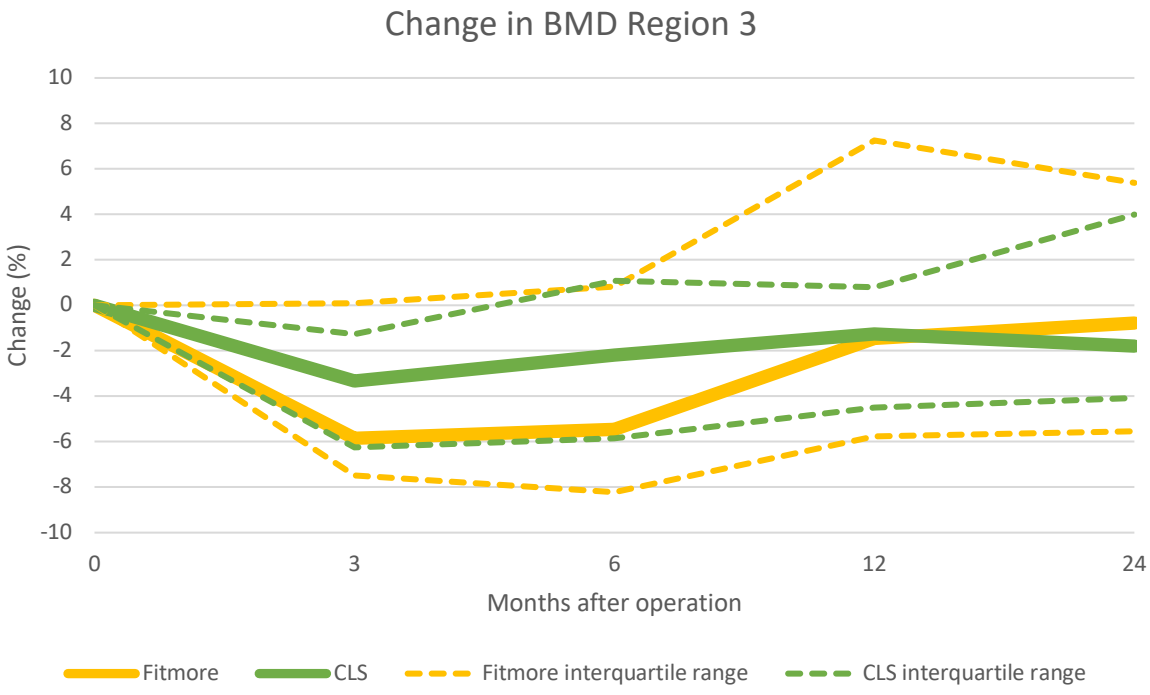

Figure 18 Change in BMD, region 3, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

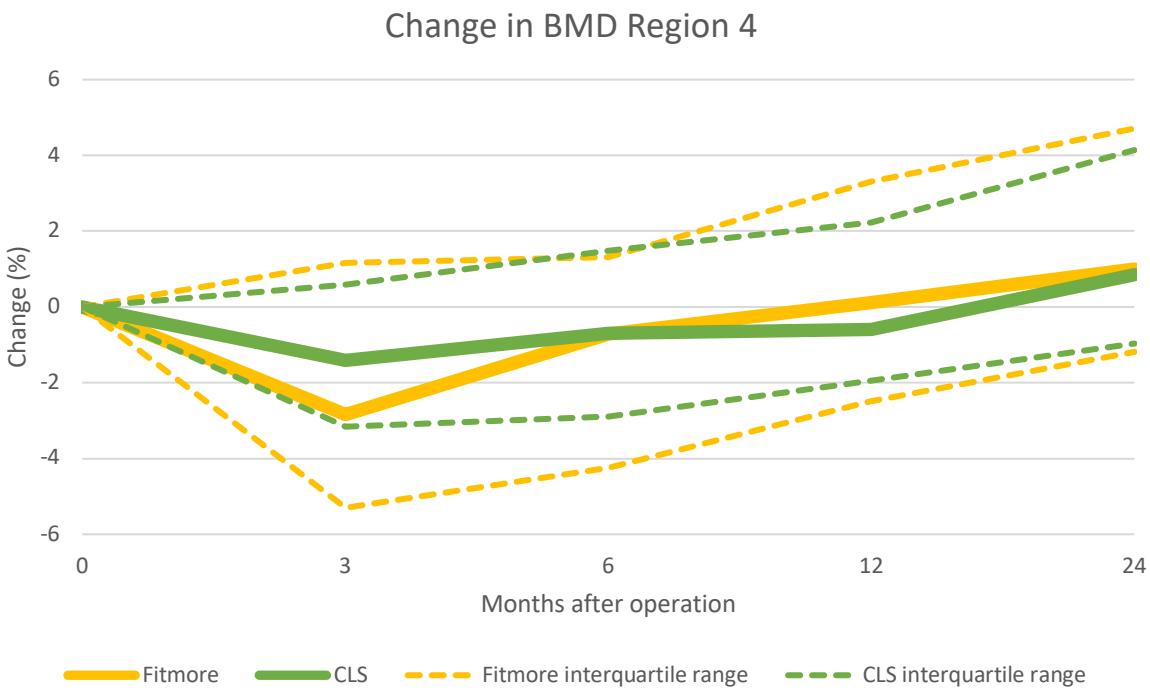

Figure 19 Change in BMD, region 4, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

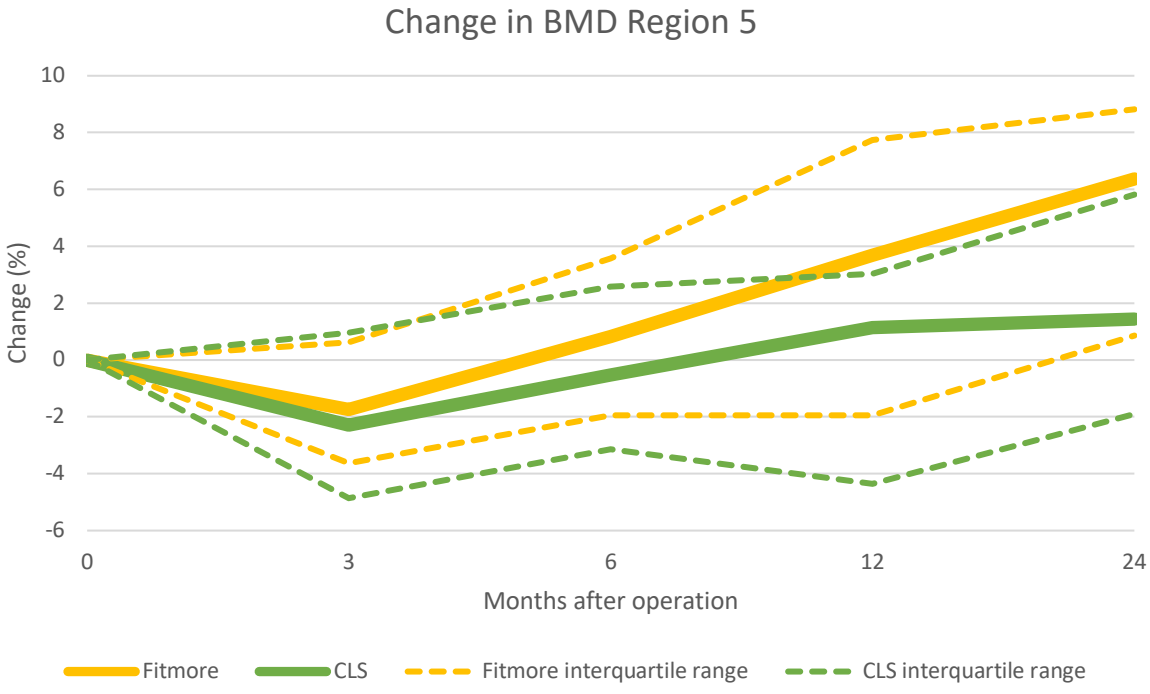

Figure 20 Change in BMD, region 5, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

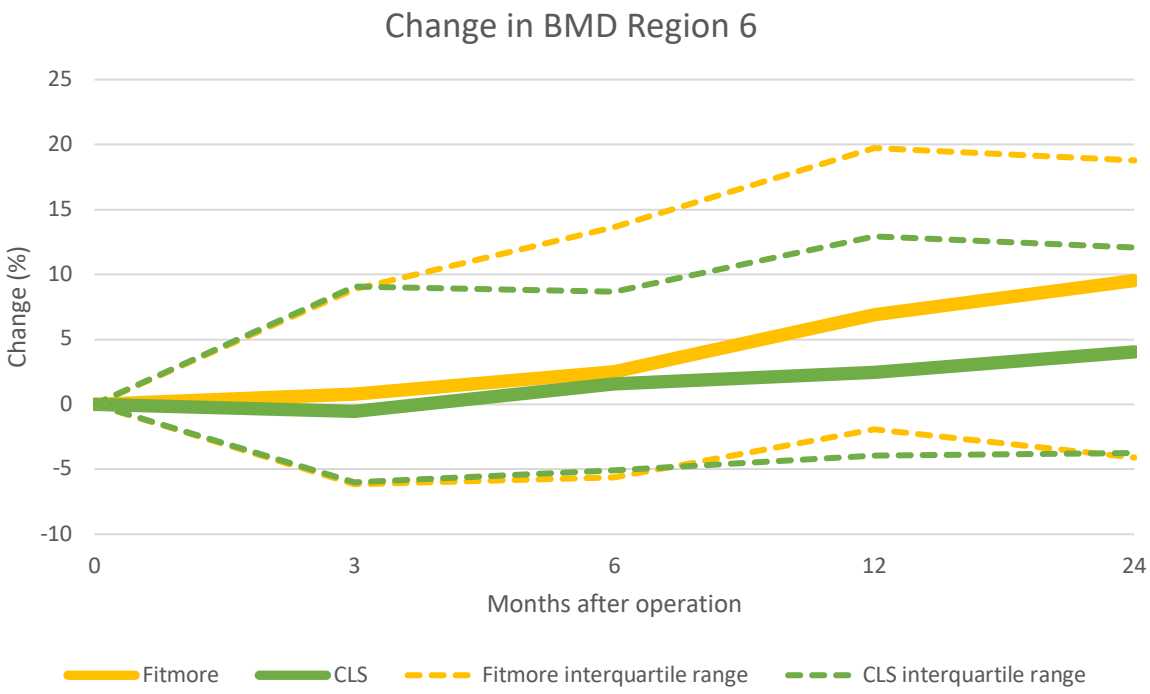

Figure 21 Change in BMD, region 6, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial

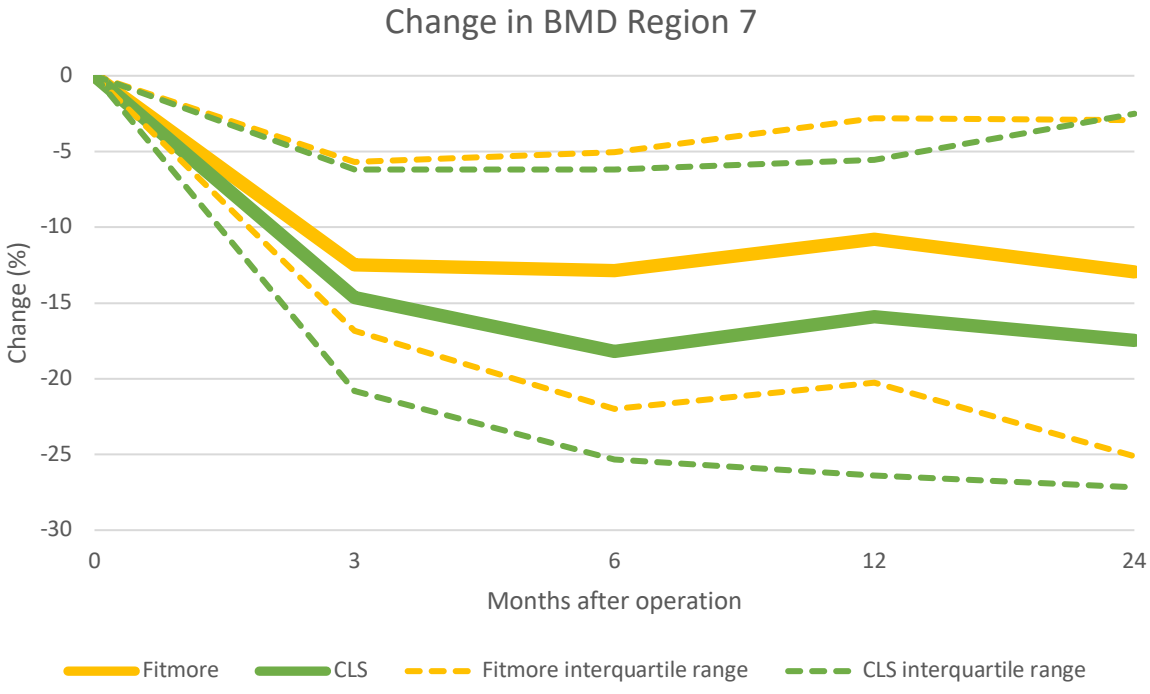

Figure 22 Change in BMD, region 7, compared to baseline at 3, 6, 12 and 24 months, the Fitmore trial