

Stepwise introduction of a bone-conserving osseointegrated hip arthroplasty using RSA and a randomized study

II. Clinical proof of concept—40 patients followed for 2 years

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Background We have developed a bone-conserving commercially pure titanium hip replacement system using osseointegration principles: a metaphyseal loading proximal femoral component affixing into the retained neck and metaphysis only, leaving the femoral canal untouched. The acetabular cup closely fits a dual-geometry cavity, avoiding stress protection at the dome.

Patients and methods After extensive laboratory and clinical pilot trial investigations, the surface-engineered implants were submitted to a prospective randomized controlled clinical trial involving 40 patients (40 hips), in which they were compared to the cemented Spectron femoral component and cementless Trilogy cup as control implant. The following clinical measures were used to monitor progress at regular intervals for the first 2 postoperative years: radiostereometric analysis (RSA), Harris Hip Score, pain score, WOMAC, and SF-36.

Results After 2 years of follow-up, no statistically significant differences were seen between the groups concerning rotation or translation along the cardinal axes. The patients receiving the Gothenburg osseointegrated titanium (GOT) system had significantly higher Harris Hip Score at 6 months, suggesting more rapid recovery. WOMAC, SF-36 and pain analysis were similar for the first 2 postoperative years.

Interpretation Our RSA data suggest that osseointegration was achieved for all patients receiving the GOT hip system. This bone-conserving prosthesis may pro-

vide a good alternative, especially for young and active patients. ■

Treatment of young, active patients with osteoarthritis of the hip is problematic. Conventional arthroplasty will probably not last the lifetime of the patient as a result of loosening, wear and osteolysis. There is increasing interest in hip replacement with less aggressive bone resection than in conventional stemmed femoral arthroplasties. Bone-sparing devices such as surface replacements may lack adequate fixation, and subcapital fractures have been reported (Amstutz et al. 2004, Beaulé et al. 2004, Stem et al. 2004, Sharma et al. 2005) that compromise the long-term results. Uncemented proximally fixed femoral components have been developed which resurface the femoral head with adjunctive fixation within the neck or with a side plate (Huggler et al. 1993, Scholtz and Grundeir 1996). The results of these prostheses are still not well documented.

Our research group developed a bone-conserving hip arthroplasty that fulfills the criteria of osseointegration, including proximal loading by a metaphyseal-fixed femoral component and reduced stress shielding of both acetabulum and proximal femur.

The 6 criteria for osseointegration are (Albrektsson et al. 1981, Brånemark 1985, Zarb and Albrektsson 1991): a biocompatible material (c.p. titanium), implant design (threaded), implant surface (rough-blasted and etched), state of host bed (bone-sparing surgery), surgical technique (accurate bone-implant fit) and loading conditions (biomechanically favorable design). After testing in pilot studies and a previous randomized study with earlier prototypes (Albrektsson et al. 1998, Macdonald et al. 1999, Carlsson et al. 2006 (pages 549–558 of this issue)) our data now suggest that the Gothenburg osseointegrated titanium (GOT) hip arthroplasty which resects minimal bone stock, achieves initial stable fixation and makes revision easy should that be necessary. Experimental studies have indicated that more physiological loading is imposed, and thus that remodeling does not jeopardize long-term stability (Macdonald et al. 2002). Our preliminary results (Carlsson et al. 2006) show that long-term stability based on osseointegration is possible in the retained neck with a threaded c.p. titanium implant. In that study, however, early failures due to migration were experienced in some cases. We believed that these failures were caused by excessively smooth surfaces, suboptimal thread design and bone support due to implant design and surgical technique. Technical and design improvements made to the Mk. I system components included flared geometry just inferior to the collar (to better engage the endosteal femoral neck), rougher blasting and fluoride treatment of the bone contacting surfaces to enhance bone reaction (Ellingsen 1995, Wennerberg et al. 1998, Ellingsen et al. 2004), and an altered transition between the 2 threaded diameters, which would strengthen and stiffen the implant. Changes to surgical instrumentation were also introduced, to improve the initial apposition to bone.

We present the results after optimizing these factors by changing the prototype design and instrumentation. In the present study, the Gothenburg hip arthroplasty Mk. II was compared to the cemented Spectron stem (Smith and Nephew Richards, Warsaw, IN) and the uncemented Trilogy cup (Zimmer, Warsaw, IN). The primary objective of this study was to compare implant migration by radiostereometric analysis (RSA), and the secondary objective was to examine overall function and

quality of life. We present the clinical outcome and migration results during the first 2 postoperative years using RSA.

Patients and methods

40 patients with osteoarthritis were randomly allocated to receive either the osseointegrated GOT hip arthroplasty or the cemented Spectron stem and Trilogy uncemented acetabular cup. The study started in 2001, after receiving approval from the Ethics Committee of Sahlgrenska University Hospital.

Description of the implants

The GOT femoral component is made of commercially pure titanium (c.p. Ti) and incorporated the changes suggested by the previous clinical trial (Carlsson et al. 2006).

The control system included the Spectron femoral component (Smith and Nephew Richards), as used in the previous trial. The Trilogy porous-coated cup (Zimmer) is effectively the same as the Harris-Galante II cup with improved liner retention, and these were inserted in a 1-mm underreamed acetabular bone bed. Two self-tapping titanium bone screws were used to augment the initial fixation stability to improve bone ingrowth.

Surgical techniques for both systems were as described in the first trial (Carlsson et al. 2006).

Patients

Inclusion and exclusion criteria were the same as described for the previous clinical study.

Mean age was 58 (43–72) years for patients in the test group and 60 (45–72) for the control group. There were 9 women and 11 men in the GOT group and 7 women and 13 men in the control group. The GOT patients' mean weight was 80 (57–96) kg; corresponding values for the control group were 84 (67–99) kg. Sex distribution and weight were similar between the groups. Using the minimization method (Pocock 1983), the patients were randomized by a call-center just before surgery to receive either the GOT or the Trilogy/Spectron arthroplasty.

To date, the patients have been followed for a minimum of 24 months. Annual follow up will be



Appearance of the implanted Gothenburg osseointegrated titanium arthroplasty Mk. II.

performed for up to 10 years. 4 surgeons undertook the surgery, working in an ultraclean air tent using exhaust gowns. Patients were prepared for operation with spinal anesthesia, prophylactic antibiotics and low molecular weight heparin. Weight bearing as tolerated using 2 crutches was required for the first 6 weeks after surgery.

Clinical evaluation was performed preoperatively, postoperatively and at 3, 6, 12 and 24 months using a standard data form sheet. An independent physiotherapist, unaware of prosthesis type or radiographic appearance, performed all the follow-up clinical examinations. Harris Hip Score was determined preoperatively and at 12 and 24 months postoperatively. Visual analog scales for pain (VAS) at rest and during activity were used to describe pain (0 = no pain, 100 = unbearable pain) in addition to that of the Harris score. Outcome analysis with WOMAC questionnaires (Bellamy et al. 1988) and SF-36 (Ware and Sherbourne 1992, Sullivan et al. 1995) were performed. The WOMAC index grades pain (5 items), stiffness (2 questions) and function (17 questions) on a scale of zero (no symptoms/no limitation) to 10 (maximal symptoms/limitation) (Bellamy et al. 1992), while the SF-36 items are scaled from 0 (maximal symptoms/limitation) to 100 (no symptoms/limitation) (Ware et al. 1997).

During the operation, 8–12 tantalum balls 0.8 mm in diameter were inserted into the proximal femur and around the acetabulum (Figure). The prostheses had been marked preoperatively with

1-mm tantalum balls. These markers were used for RSA, with the center of the head as an additional point. Due to the different forms of the components, the only truly comparative feature was the spherical center of the head, and because of the different migratory motions of the two implants, maximal total point motion (MTPM) of the femoral head was the most meaningful measure of stem translations. Preoperative radiographs of whole A-P pelvis, and true anteroposterior and lateral views of the hips were taken. This was repeated immediately postoperatively and after 3, 12 and 24 months. Due to the high precision of RSA, only radiolucencies and ectopic calcification were evaluated on the conventional radiographs. Evaluation of radiographs was performed by an independent radiologist. The interface of the femoral implant was divided into Gruen zones for the control device and 12 zones for the test implant.

Migration and wear of both implants was measured with RSA as described by Kärrholm and co-workers (Kärrholm and Snorrason 1992, Kärrholm et al. 1994a). Precision of RSA was checked by double examinations in the previous study (Carlsson et al. 2006). Mathematical calculations of the reliability of marker scattering were performed by the software and given as condition number. A condition number of less than 120 was used in all cases (points of extreme uncertainty were not used in the calculations). Clinical monitoring by RSA enables reliable prediction of long-term results after only 2 years of follow-up with patient numbers as low as 15 per group (Selvik 1974, Kärrholm 1989, Valstar et al. 2005); for the present study, 20 patients per group was considered adequate for statistical power.

Statistics

The descriptive statistics for the values measured for pain with Visual Analog Scale (VAS), Harris Hip Score, WOMAC and SF-36 at each visit and changes from the baseline (first postoperative assessment) were noted (Table 1). The hypothesis that there was no change from baseline values was tested using the Wilcoxon signed rank test within each treatment group. The hypothesis that the change was equal between the 2 implant groups was tested by means of the Wilcoxon rank sum test (normal approximation).

Table 1. Descriptive statistics for clinical evaluation parameters; mean (range)

	GOT			Control		
	Preop.	12 months	24 months	Preop.	12 months	24 months
HHS ^a	44 (21–68)	97 (91–100)	98 (91–100)	47 (21–65)	96 (80–100)	97 (80–100)
WOMAC						
pain	11 (4–15)	1 (0–7)	1 (0–10)	11 (5–15)	1 (1–5)	2 (0–10)
function	38 (18–51)	10 (7–38)	7 (5–39)	37 (19–50)	8 (2–20)	7 (5–27)
stiffness	5 (2–7)	2 (1–6)	1 (0–6)	5 (2–7)	1 (2–4)	1 (0–5)
Pain (VAS)						
at rest	47 (15–75)	0 (0–3)	1 (0–6)	42 (6–91)	1 (0–13)	1 (0–5)
on movement	69 (25–91)	2 (0–15)	2 (0–13)	73 (43–94)	2 (0–14)	2 (0–18)
SF-36 pain	31 (12–74)	82 (52–100)	81 (22–100)	25 (0–52)	74 (22–100)	86 (41–100)

^a HSS at 6 months: GOT 88 [9.1] (74–100) and Controls 78 [16] (45–100)

The Wilcoxon rank sum test and ANOVA were used for statistical testing of the RSA results.

Results

Clinical evaluation

No patients were lost to follow-up, although 1 patient (control implant) could not attend the 2-year follow-up because of complications after surgery unrelated to the implant; he has now recovered and will be checked at the 3-year follow-up. Preoperatively, all patients had moderate or severe hip pain. At the 2-year follow-up the highest VAS value for pain on movement was 15 for the GOT group and 14 for the control group. The clinical improvement for both groups was statistically significant for pain and all parameters in the outcome analysis using Harris Hip Score, WOMAC and SF-36 ($p < 0.001$) (Table 2). Harris Hip Score was above 90 (“excellent”) for all patients but 1 in the control group (score of 80). At the 6-month follow-up, the Harris Hip Score was statistically significantly higher for the test group. No other differences were observed between the 2 groups regarding function or pain.

Complications

1 patient in the test group experienced a nonfatal pulmonary embolus and 1 patient in the control group suffered a deep vein thrombosis. There were no infections or other serious complications in either group.

Table 2. Statistical results: hypothesis tests for no change from baseline (Wilcoxon signed rank test) and that the changes in both groups are equal (Wilcoxon rank sum test), p-values

	Change from baseline		Changes equal at	
	GOT	Control	1 year	2 years
HHS	< 0.001	< 0.001	0.3	0.5
WOMAC				
pain	< 0.001	< 0.001	0.8	0.3
function	< 0.001	< 0.001	0.9	0.3
stiffness	< 0.001	< 0.001	0.9	0.8
Pain (VAS)				
at rest	< 0.001	< 0.001	0.4	0.3
on movement	< 0.001	< 0.001	0.7	0.9
SF-36 pain	< 0.001	< 0.001	0.3	0.3

Radiostereometric analysis

Valid RSA data were not available for 4 cups in the GOT group, and in the control group for 6 at 1 year and 8 at 2 years, because too few tantalum markers were visible on the radiographs. All examinations for stem migration but 1 in each group were successful.

Stem rotation after 2 years was similar for the GOT hip and the Spectron prosthesis (Table 3). Migration (MTPM) of the center of the head for the GOT femoral component Mk. II was 0.41 mm at 1 year and 0.38 mm at 2 years, and corresponding figures for the Spectron component were 0.58 mm and 0.62 mm; there were no statistically significant differences between the groups (Table 4). These values are well within the threshold of 1.2 mm allowable migration and predict stable outcomes at 10 years (Kärrholm et al. 1994 a, b).

Table 3. RSA measurements of femoral component rotation around the x-, y- and z-axes for the GOT and Specron components; in degrees, mean (SD)

		3 months	1 year	2 years
GOT	x	0.2 (0.17)	0.3 (0.04)	0.3 (0.06)
	y	0.5 (0.38)	0.5 (0.07)	0.7 (0.21)
	z	0.1 (0.07)	0.2 (0.04)	0.2 (0.06)
Control	x	0.2 (0.17)	0.2 (0.06)	0.2 (0.06)
	y	0.4 (0.20)	0.5 (0.10)	0.6 (0.15)
	z	0.1 (0.06)	0.1 (0.02)	0.1 (0.03)

Table 4. RSA measurements of migration of the center of the head. Individual components and maximal total point motion (MTPM, the vector sum of the 3 axial migrations); in mm, mean (SD)

		3 months	1 year	2 years
GOT	x	0.10 (0.08)	0.16 (0.11)	0.14 (0.17)
	y	0.17 (0.14)	0.20 (0.15)	0.24 (0.14)
	z	0.23 (0.22)	0.28 (0.30)	0.33 (0.33)
	MTPM	0.35 (0.20)	0.44 (0.27)	0.48 (0.33)
Control	x	0.13 (0.11)	0.17 (0.11)	0.27 (0.18)
	y	0.18 (0.12)	0.21 (0.18)	0.22 (0.15)
	z	0.40 (0.31)	0.51 (0.55)	0.53 (0.60)
	MTPM	0.50 (0.28)	0.64 (0.52)	0.70 (0.56)

Table 5. RSA measurements of cup rotation for the GOT and Trilogy implants; in degrees, mean (SD)

		3 months	1 year	2 years
GOT	x	0.3 (0.01)	0.22 (0.10)	0.3 (0.10)
	y	0.5 (0.20)	0.68 (0.25)	0.3 (0.10)
	z	0.6 (0.30)	0.80 (0.37)	0.3 (0.10)
Control	x	0.4 (0.10)	0.33 (0.10)	0.3 (0.10)
	y	0.4 (0.10)	0.52 (0.15)	0.5 (0.10)
	z	0.2 (0.10)	0.31 (0.08)	0.4 (0.10)

The cup rotations at 2 years varied between 0.27° and 0.31° for the test group and between 0.33° and 0.52° for the control group (Table 5). No statistical differences were found between the 2 groups. Wear and cold flow (proximal penetration of head into liner) during the first 2 postoperative years measured with RSA showed maximal migration of the center of the head relative to the rigid body of the

cup of 0.3 (0.1–0.5) mm for the GOT prosthesis and 0.3 (0.2–0.8) mm for the control. No significant difference was found between the 2 groups at 2 years ($p = 0.9$, Wilcoxon rank sum test).

Radiographic evaluation

Except for minor resorption under the collar of femoral components in both test and control groups, no radiolucencies were observed. One patient in the test group developed myositis ossificans grade 3 according to Brooker et al. (1973). However, this patient also displayed a major calcification in the quadriceps muscle after an earlier minor trauma, and was probably prone to develop myositis ossificans.

Discussion

Failures after total hip arthroplasty are mainly due to aseptic loosening and occur more frequently in younger patients. Revisions for both cemented and uncemented arthroplasties are difficult and show poorer results than primary procedures. A bone-conserving alternative is therefore desirable. We have presented results from such a procedure in our previous study (Carlsson et al. 2006). Although that study showed that it was possible to achieve stable fixation in the retained neck, the reproducibility of the procedure was unacceptable. We noted several features that could be improved to increase the reproducibility. These included flared geometry just inferior to the collar, rougher blasting (to an Ra of about 2 μm) and fluoride treatment of the bone-contacting surfaces to enhance bone reaction (Ellingsen 1995, Wennerberg et al. 1998), and a strengthened and stiffened transition between the 2 threaded diameters. The use of c.p. titanium was retained due to its proven superior bone reaction (Johansson 1991, Han et al. 1998, Johansson et al. 1998). Changes to surgical instrumentation were also introduced to improve the initial apposition to bone.

The design of the implants in this study is based on data from experimental studies (animal and bench) as well as computer simulations. The first prototype of our implant was used in 1992 in pilot studies, and further improvements have been introduced over the years and tested using RSA. We now

have an implant (Mk. II) which seems to fulfill the criteria of bone-conservative resections, proximal loading (avoiding stress shielding) and stable fixation, indicative of osseointegration in all cases. We have introduced these hip replacement implants in a stepwise manner and believe that alternative implants should only be introduced when the clinical results are as good as or better than those of existing designs (Malchau 1995).

Our results with the improved Mk. II GOT prosthesis are encouraging. Radiostereometric analysis showed very low migration rates for the femoral component, indicating that osseointegration had been achieved. Our previous study (Carlsson et al. 2006) and other migration studies (Mjöberg et al. 1986, Freeman and Plante-Bordeneuve 1994, Kärholm et al. 1994 a, b, Ryd et al. 1995) have shown that components with low migration at 2 years are highly likely to remain stable in the long term. Although the follow-up was short and the number of patients was small, it is justified to report the results at this early stage because RSA is such an accurate and good prognostic instrument as early as 2 years after surgery (Valstar et al. 2005).

The reproducibility of results for the GOT arthroplasty is now excellent. In the previous study of the Mark I prosthesis, we observed a radiolucency along the proximal part of the implant in 14 of 24 patients. In the present study, no such radiolucencies were detected in any of the patients. This seems to indicate that the rougher blasting and fluoride treatment enhanced the bone apposition in this region, and that the changes in instrumentation ensured that the components were implanted more securely endosteally (as intended), and were less prone to micromotion. In some cases, there was minimal resorption just beneath the collar which extended no further than 3 mm. Similar resorption is common for both cemented and uncemented conventional femoral components under the collar, even if the neck has been resected.

2 cups in the GOT group displayed rotation of more than 1° in all directions at 3 months, but the migration rate between 3 and 12 months was low and well below 1°. This may mean that the implant was not fully and finally seated at operative impaction, but that under postoperative mobilization the implant moved to a more stable position. The acetabular component displayed stability similar

to that of the Trilogy cup (measured by migration rate). However, osteolysis and wear-through may be less of a problem, as adjunctive screw fixation was not used for the GOT cup. Furthermore, a much thicker polyethylene component can be used—as the GOT c.p. titanium acetabular shell is only 1 mm thick at the dome.

The results of this study demonstrate osseointegration of a metaphyseal fixed prosthesis. The migration rate is no different from that of a cemented conventional stem (Spectron), which has shown a very good survival rate in the Swedish registry (Malchau et al. 2000). Proximal loading of the prosthesis will prevent stress shielding of the diaphysis (Macdonald et al. 2002), reducing the risk of future femoral shaft fractures. Several of the complications in cemented and uncemented conventional prosthesis may be eliminated or reduced with the use of a threaded implant fixed in the retained neck. This includes perioperative femoral fractures, stress shielding and thigh pain, osteolysis of the shaft, reduced bleeding and microembolism.

These trials have not proven that the GOT device achieved osseointegration according to the original definition (Albrektsson et al. 1981). This could only be proven by histology, which is obviously impractical in a clinical study of living patients. However, Zarb and Albrektsson (1991) outlined a functional definition of osseointegration in 1991 because the same difficulty of histological proof of osseointegration applied with dental patients. What these trials have proven is that a biocompatible material (c.p. Ti) in an implant of form and finish conforming to the principles of osseointegration—when inserted accurately as dictated by osseointegration theory—achieves initial and longer-term stability as good as a conventional cemented stemmed implant. The RSA results predict that the GOT implants will remain stable in the long term, and it is implicit in this stability (and that at 2 and 3 years) that an intimate bone-implant contact has been achieved and maintained. Comparable stability in the cemented Spectron stem does not imply similar osseointegration: cemented stability is achieved by the invasion of a non-biocompatible material (bone cement) into the interstices of the cancellous bone, where it is tolerated but with a fibrous tissue interface. Conversely, c.p. Ti is biocompatible so the initial intimate bone-biomaterial

contact will probably be improved by bone apposition into the micro-irregularities of the titanium surface. Ultimately, the real proof of osseointegration of this system awaits histological specimens and the actual long-term results.

Revision of this device should be easy with conventional designs of primary implants. This has been demonstrated at revision of previous prototypes (Carlsson et al. 2006), and the outcome of these revisions was comparable to those with primary arthroplasties.

The current study shows that it is possible to achieve osseointegration of a commercially pure titanium implant in the retained neck. Secure fixation in the neck with further support in the lateral cortex reduces the risks of aseptic loosening and neck fractures reported for surface replacements. This bone-conserving procedure seems to be an attractive choice for the younger and active patient especially. Furthermore, this implant may be a superior choice for patients with old malaligned, subtrochanteric fractures where a conventional stemmed femoral component is not suitable. Although the GOT device is intriguing, a longer follow-up with more patients is needed. Based on the knowledge gained from this study, we now believe that it is justified to test the implants in a larger multicenter study.

Contributions of authors

LVC, TA, CMJ and WM were principal investigators involved in the design and testing of the system components before clinical trials, experimental design and implementation of the clinical trial including surgical implantation and data interpretation, and preparation of the manuscript. BEJA, BGA, LR, TR, LRW were associate investigators providing consulting advice during system development and clinical trial preparation and interpretation, and surgical implantation as participants in the clinical trials. LR made and interpreted the RSA analysis.

Clinical Trial Management and monitoring were undertaken independently by Clinical Data Care of Lund, Sweden, and RSA determinations were performed independently by the Orthopaedic Department, Sahlgrenska Sjukhuset, Göteborg. System development was undertaken at the Department of Biomaterials Research, University of Göteborg, independent of but with support from Astra Tech AB.

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