Evaluation of Triathlon

- a new total knee prosthesis system

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EVALUATION OF THE TRIATHLON KNEE SYSTEM

STUDY DESIGN SUMMARY PAGE

- Prospective, comparative, **randomised,** RSA series with 2-years follow-up.
- Primary total knee replacement surgery utilising the Triathlon Knee System
- A total of 300 patients will be included in the study, with 25 patients in each group of the sub studies.

- Clinical evaluations will be required pre-operatively, per-operatively, prior to discharge and at 3 months +/-2 weeks, 1 year +/- 2 months and 2 years +/- 2 months.

- RSA (Roentgen Stereophotogrammetric Analysis) evaluation will be required prior to discharge and at 3 months +/-2weeks, 1 year +/- 2 months and 2 years +/- 2months.
- Radiographic evaluation will be required to be completed pre-operatively, prior to discharge and at 1 year +/- 2 months and 2 years +/- 2months.

- Patient outcomes assessments (KOOS and KSS) will be required to be completed pre-operatively and at 3 months +/-2 weeks, 1 year +/- 2 months and 2 years +/- 2 months

Evaluation	Pre-op	Per-op	Prior to Discharge	3 Months	1 Year	2 Years
Medical History	✔					
Operative Details		✔				
RSA			✔	✔	✔	✔
Radiographs	✔		✔		✔	✔
Clinical	✔	✔	✔	✔	✔	✔
Outcomes	✔			✔	✔	✔

1. Introduction

Total Knee Arthroplasty (TKA) is the surgical reconstruction of the knee joint in order to relieve pain, restore function and correct deformity. It is a very common surgical procedure with figures showing more than 500.000 arthroplasties performed annually world wide. Total knee arthroplasty is considered one of the most successful types of joint reconstruction in that surgical results usually meet and even exceed expectations.

Efforts to improve the outcome of total knee replacement continue today, with issues such as implant design, material biocompatibility, wear resistance and instrument design being actively researched and refined. The role of implant design is particularly well documented in the literature. The patient's demands and the refinement of surgery have increased the demands, both on the implants and development of the surgical technique.

This clinical study proposes to evaluate a new knee prosthesis system, Triathlon.

The design for Triathlon prosthesis theoretically addresses the higher expectations and higher demands the patients of today have for their implants, especially with respect to the need for deeper knee flexion and greater ease of moving into deep flexion. This knee prosthesis is designed to allow for normal knee motion and stability through 150 degree or more of knee flexion. The design allows for correct balancing with stability and deep flexion, avoiding the gap and instability the prosthesis designs of today create during deep knee flexion. This instability is due to lack of contact between the femoral and tibia component. The Triathlon design also takes the Freeman/Pinskerova findings for the epicondylar axis during flexion in consideration. The tibia design of Triathlon is addressing this with the rotary arc for the tibial insert. The rotary arc provides the design with a possibility for smooth and consistent articulation with rotation throughout the range of motion during knee flexion, even deep.

The key features for the Triathlon design are a further improvement of the Duracon design with improved femoral posterior condyle flare and the rotary arc in insert. These features work together to provide possibility for, and help, rotation during deep knee

flexion. The Triathlon femur component has been designed for an improved anatomical fit. The anterior flange has been slightly steeper (7 degrees) which minimise the risk for anterior notching. The sizing and the femoral A/P and M/L dimensions minimize the risk for prosthetic overhang as the aspect ratio (M/L & A/P) both for the femur and the tibial component have been declined.

The Triathlon design is also focused on implant longevity by a precision locking mechanism. The aim with this is to reduce the micromotion of the poly insert related to the tibial tray even further. By reducing the micromotions, problems related to back-side wear could be reduced.

Cementless prosthetic fixations have enjoyed widespread use. It is generally agreed that careful site preparation (Toksvig-Larsen, 1994) and a precise fit between the implant and bone are required. The potential advantages of hydroxyapatite (HA) (Søballe 1993) are the shortening of the time needed to achieve adequate fixation strength and stability, and increasing the strength of the bone-Implant interface (Geesink, 1995, Søballe, 1993). Up to date the most used application is a plasma-sprayed coating technique using high temperatures (ceramics), but the technique is only feasible for rough or textured surfaces. This coating has been further developed to the Peri-Apatite coating technique which has the ability to coat all exposed surfaces of a three-dimensional porous in-growth structure. In the peri-apatite process the hydroxyapatite is formed at low temperature as a product of solution precipitation.

During the last decade, roentgen stereophotogrammetric analysis (RSA) has emerged as a way to assess prosthetic fixation (Selvik 1974). The method has been used extensively both in hip and knee arthroplasty (Kärrholm, 1989, Mjöberg, 1990, Nilsson, 1992, Ryd 1992, Nilsson, 1996, Ewald 2002). It has been shown that RSA can serve as a predictor of late mechanical loosening both for knee and hip prostheses (Ryd 1995, Kärrholm 1994).

2. Objective

The objective is to investigate the clinical, Radiographic, Roentgen Stereophotogrammetric behaviour and patient outcome when using the Triathlon total knee prosthesis in a prospective randomized clinical trial.

3. Number of Subjects

300 patients in six individually randomized sub-studies (25 patients in each randomized group) will be enrolled into the study over a 12 months recruitment period per sub-study.

Each investigator will perform at least 5-10 knee arthroplasties with the Triathlon CR (learning curve) before enrolling patients in the clinical study.

Patients will be randomly allocated to one of two equally sized groups in each sub-study. Please see section 5 of this protocol for study design and section 8.3 for randomisation.

4. Length of Study

A 2-year post-operative follow-up period for each patient is required.

5. Study Design

This is a prospective, comparative, randomised single centre clinical study. The Triathlon and the Duracon Knee Systems have to be implanted for evaluation in this study. Patients will be randomised to one of two equally sized groups within each sub study. Both knee systems are commercially available. Patellae will be resurfaced if needed. All patients included in the study will meet all inclusion criterias and none of the exclusion criterias.

Ethic Committee approval for the study will be obtained by the investigator prior to starting the inclusion of patients in the study.

Patients will be considered for enrolment according to the clinical findings and subject to gaining their suitable written informed consent (see Appendix II).

The principal evaluation parameter will be the RSA. Patient outcome will be assessed by the KOOS questionnaire and the KSS. Clinical evaluation will include the chair raise test, measurement of the extension strength, and a patella evaluation. The evaluation of the Triathlon system will be carried out in several steps, described as sub-studies all including RSA-technique.

Sub-studies:

a) Triathlon versus Duracon: The Triathlon system has a heritage in the well documented Duracon system, which has shown very good results in the Swedish Knee Register. The goal with this study is to get an indication of the long-term results of Triathlon. The evaluation is carried out by a prospective randomised RSA-study with Triathlon cemented knee prosthesis versus Duracon cemented knee prosthesis

b) Triathlon Cruciate Retaining (CR) versus Triathlon Posterior Stabilized (PS): During knee prosthesis surgery the surgeon many times need to make a judgement on if to keep a defect anatomical structure or if to replace it with knee prosthesis with a design that allows for adjustment of this defect. This sub study is aimed to evaluate which prosthetic choice to be made in respect of stability, long-term results and patient outcome.

c) Triathlon PA (HA-surface) versus Triathlon Pressfit design: The goal with the un-cemented technique is to reach a full integration between the bone and the prosthesis. During the last years the usage of prosthesis with hydroxyapatite surface within tooth-, mandibular-surgery, hips- and knee-joints, have increased significantly. It has been shown that a thin layer of hydroxyapatite stimulates the anchorage of the implant. The

goal with this sub study is to compare the stability of the fixation when using two different types of Triathlon un-cemented prosthesis designs. PA (HA-surface) versus Pressfit.

d) Triathlon implanted through computer assisted surgery versus conventional technique: Today's surgical technique within knee-arthroplasty has improved greatly with better instruments and more sophisticated equipment e.g. computer assisted surgery. The goal with this sub study is to evaluate if there are any advantages with computer assisted surgery together with Triathlon. The Triathlon knee system has been developed with instrumentation specifically prepared for computer assisted surgery.

e) Triathlon knee prosthesis implanted with MIS technique versus conventional technique: Today's surgical technique within knee arthroplasty is evolving towards smaller incisions and less traumatising techniques, so called Minimal Invasive Surgery (MIS). The goal with this sub study is to evaluate the advantages for the patient when using Triathlon-MIS-technique versus conventional surgical technique.

f) Triathlon Fixed versus Triathlon Mobile Bearing: This sub study is aimed to evaluate if Triathlon mobile bearing will give the patient any advantages over the Triathlon fixed bearing.

g) Triathlon Cruciate Retaining knee (CR) with a tibial keel of standard length randomised against Triathlon Cruciate Retaining knee (CR) with a tibial part with a short keel, both system will be used with cemented fixation. The short tibial keel is thought to facilitate the surgery due to easier access and better positioning possibilities. This sub-study is aimed at evaluating if the short tibial keel will have equal fixation and migration properties as the standard keel.

h) Triathlon Cruciate Retaining knee with cemented fixation randomised versus Triathlon Cruciated Retaining knee with uncemented fixation (Peri-Apatite). The aim with this sub study is to evaluate the uncemented PA knee fixation and migration properties versus the cemented version.

6. Inclusion and Exclusion criteria

6.1 Inclusion criteria

1. Patients suffering exclusively from OA, Stage II-V [Ahlbäck, 1968 #391] will be operated.

2. Patients requiring knee prosthesis, suitable for the use of Duracon and Triathlon knee system

3. Patients who understand the conditions of the study and are willing and able to comply with the post-operative scheduled clinical and radiographical evaluations and the prescribed rehabilitation.

4. Patients who signed the Ethics Committee approved Informed Consent Form prior to surgery.

6.2 Exclusion criteria

1. Previous major knee surgery

2. Other significant disabling problems from the muscular-skeletal system than in the knees

3. Obese patients where obesity is severe enough to affect subject's ability to perform activities of daily living (body mass index, kg/m^2: BMI $\geq$ 35).

4. Patients with active or suspected infection.

5. Patients with malignancy – active malignancy.

6. Patients with severe osteoporosis, Paget's disease, renal osteodystrophy.

7. Patients immunologically suppressed, or receiving steroids in excess of physiologic dose requirements.

8. The patient has a neuromuscular or neurosensory deficit which would limit the ability to assess the performance of the device or the patient has a neurological deficit which interferes with the patient's ability to limit weight bearing or places an extreme load on the implant during the healing period.

9. Female patients planning a pregnancy during the course of the study.

10. Patients with systemic or metabolic disorders leading to progressive bone deterioration.

11. Patients, who as judged by the surgeon, are mentally incompetent or are unlikely to be compliant with the prescribed post-operative routine and follow-up evaluation schedule.

12. Patients with other severe concurrent joint involvements, which can affect their outcome.

13. Patients with other concurrent illnesses, which are likely to affect their outcome such as sickle cell anaemia, systemic lupus erythematosus or renal disease requiring dialysis.

14. Patients under the protection of law (e.g. guardianship).

7. Prostheses

All components of the knee systems used in this study are CE marked and have been approved for sale and use throughout Europe. All prosthesis have chrome-cobalt femoral components and tibial trays. The polyethylene is relatively unconstrained. Both Triathlon and Duracon tibial trays have delta-shaped stems. When required a cemented polyethylene patellar component will be used.

Sub-studies

a) The prostheses inserted will be the Duracon total knee and the Triathlon total knee. Both prosthesis will be Cruciate Retaining design.

b) The second part of the study will include the Triathlon total knee in Cruciate Retaining (CR) and Posterior Stabilized (PS) version.

c) Triathlon PA (hydroxyapatite on a porous surface) and Triathlon Press-fit (porous coated), both in Cruciate Retaining design. The in-growth surface for both the femoral and the tibial component is a porous coated chrome-cobalt sintered bead surface for uncemented use. The porous coating is thicker than a single beads layer. The group studied with peri-apatite coating is an additional solution precipitated calcium phospated coating, 10-20 μm thick, which coat in between the sintered beads. This coating has been proved to improve the gap healing. This gap has been shown to be quite large in primary reconstructions [Toksvig-Larsen, 1994 #1131].

d) Triathlon Cruciate Retaining design.

e) Triathlon Cruciate Retaining design.

f) Triathlon Cruciate Retaining and Triathlon Mobile Bearing, Cruciate Retaining design.

g) Triathlon Cruciate Retaining cemented version with short keel and Triathlon Cruciate Retaining cemented version with statndard keel

h) Triathlon Cruciate Retaining cemented version and Triathlon Cruciate Retaining with PeriApatite (uncemented version)

8. Methods

8.1 Study design

The study is a prospective, randomised single centre trial with 25 patients in each group. The patients will be randomly allocated to one of two equally sized groups in each sub-study regarding different treatments and prosthesis designs.

8.2 Operative procedure

All patients will be operated at the Department of Orthopaedics in Hässleholm. The surgeries will be performed using the appropriate guide instruments and according to the surgical-technique manual supplied with the knee system. All femoral and tibial prosthetic components will be inserted according the protocol.

8.3 Randomisation procedure

The randomisation of the patients will take place when the surgeon decides that the patient can be included. The randomisation will be performed by opening a sealed envelope with 25 patients allocated to each group.

8.4 Post-operative mobilisation

Mobilisation will take place according to the ordinary clinical routines at the department of Orthopaedics in Hässleholm. Full weight-bearing is allowed postoperatively. The postoperative care and the mobilisation will be similar for all sub-groups.

8.5 Follow-up

The study period will be two years. Follow-ups will be performed at postoperatively, at 12 weeks and at 1- and 2 years. All assessment variables will be compiled preoperatively and at each follow-up. The patients will be followed indefinitely at 3 years intervals after completion of this protocol.

9. Assessment

Primary assessment variables will be

1. Roentgen stereophotogrammetric analysis (RSA) (Selvik, 1974).

Secondary assessment variables will be

2. Plain radiographs will be obtained for disease classification.

3. Clinical assessment according to the Knee Society Score (KSS) and KOOS score

4. At the post-op follow-up all plain radiographs will be obtained for the assessment of the component position. At the yearly radiographic follow up a weight-bearing investigation will be performed to assess wear, radiolucent zones and stress resorption. A patella sky view projection will be included in the postoperative x-ray and at the yearly controls

10. RSA

All cases will be prepared for RSA investigation by insertion of tantalum markers in the tibial polyethylene component and in the tibial metaphysis (Ryd, 1986).

11. Data analysis

11.1 Power - statistical considerations

From previous studies the migration during the first two years for cemented prostheses has been about 1.0 ± 0.5 mm (MTPM). Suppose this migration will decrease by 50% to 0.5 ± 0,5 mm. Considering an alpha level of 0.05 and a beta level of 0,20 (power ≈ 80%) this will require 17 cases in each group. With a ß of 0,75, 15 patients in each group will be needed. Continuous migration between the 1st and 2nd year follow-up has been found in up to 50% of the cases. Suppose that an improvement will have to yield a decrease in continuous migration to 10% in order to be clinic relevant. An alpha level of 0,05 and beta level of 0,20 (power = 80 %) would require 25 cases in each group.

11.2 Statistical analysis

All variable are considered continuous and measured on an interval scale, except migratory pattern, which is proportional. The difference between the two treatment groups will be evaluated with analysis of variance (ANOVA) for continuous variables at different time periods. Clinical scores will also be analysed using the analysis of covariance (ANCOVA) to compensate for different preoperative starting values. Continuous data which are not normally distributed will be analysed by non-parametric ranking tests and proportional values will be analysed by the chi-square test or the Fischer's exact test at low response frequencies.

11.3 Data management

The scientific collaborator will be responsible for the compilation and statistical treatment of data. Raw data and results will be kept available to the company at all times.

12. Publication of Results

Once the study has continued long enough to generate results of a good enough quality for publication, a review will be arranged at which results will be considered and an agreement for publication reached between the participating investigator and Stryker.

It is anticipated that the results of this study will be published in an international journal. In this context the results of the study are owned solely by the clinical investigator and the scientific collaborators, which decide on the final form of the report. The result of the study will be submitted to an international journal of orthopaedics within six months from the completion of the study. Before submission, Stryker will be informed regarding the manuscript. The results are not to be used for marketing or other purposes before the results have been accepted for publication of for presentation in an open scientific meeting.

12. Ethical considerations

12.1 Declaration of Helsinki

This study will follow the guidelines as laid down by the "Declaration of Helsinki" (Declaration of Helsinki, October 2000) (see Appendix I).

In accordance with the Declaration of Helsinki the Investigators must gain written Ethics Committee approval prior to enrolling patients in the study. Ethics Committee approval

must be gained either from the Ethics Committee that is local to the investigational site or from an adequately constituted [according to ICH GCP] independent Ethics Committee.

12.2 Informed Consent

The patient information sheet and informed consent documentation will be drawn up according to ICH GCP requirements. A patient information sheet will be given to each patient, in local language and written to an appropriate level of detail (see Appendix II).

12.3 Ethical committee

The study protocol will be subjected to and approved by the ethical committee of the Medical Faculty, Lund University, before the start of the study.

Amendment No. 2 to Evaluation of Triathlon - a new total knee prosthesis system

3. Number of Subjects

360 patients in six individually randomized sub-studies (30 patients in each randomized group) will be enrolled into the study over a 12 months recruitment period per sub-study.

Study Design Summary Page

- A total of 360 patients will be included in the study, with 30 patients in each group of sub-studies.

PROTOCOL TITLE:
EVALUATION OF THE TRIATHLON KNEE SYSTEM

Protocol addendum - Extended follow-up period with 5, 7 and 10 years follow-up visits

Protocol #: K-S-015
Revision: v1.0
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Study responsible doctor

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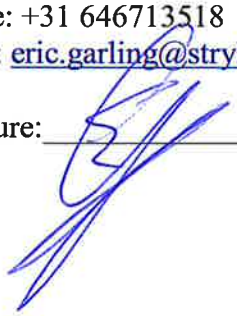

Introduction

The results of knee replacement surgery have continuously improved and operations are now highly cost effective from a social point of view and in terms of improved quality of life for the individual patient. However complications occur, especially in the long term as prosthetic loosening, wear, and infection. Extensive research is on-going to find improved prosthetic materials, better prosthetic design and surgical methods to manage these difficulties.

Adequate surgical expertise and the design of the artificial knee joint are among the most important factors in terms of outcome and long-term results. To evaluate these aspects for the Triathlon prosthesis, it is necessary to collect and analyse data from patients receiving this type of knee prosthesis. By collecting patient information, we can further evaluate some of the overall benefits of modern knee surgery, such as shorter rehabilitation time, generally faster recovery, more natural knee function and improved long-term outcomes. The Triathlon knee system is a further development of both the prosthesis and instrument design. The knee prosthesis design is better adapted to the wide variation of patient anatomy and size.

The Triathlon RSA study that is conducted in the orthopaedic clinic at Hässleholm's hospital have aimed at studying prosthesis fixation using accurate measuring techniques, so-called X-ray stereo photogrammetric technique (RSA). This method studies micro-motion of a prosthesis component in relation to the bone. All prosthetic components, cemented and uncemented have shown a micro mobility which later can be related to possible future prosthesis loosening. Thus it is of great importance to investigate the long term fixation of the Triathlon prosthesis and to present scientific results confirming that the prosthesis have excellent survival rate when implanted in patients. To reveal all possible aspects of the Triathlon prosthesis the Triathlon RSA study consists of a clinical and a radiographic part, including roentgen stereophotogrammetric analysis (RSA) of the knee prosthesis.

Examination procedure

The Triathlon RSA study was designed to evaluate the Triathlon knee system and to follow patients during the first two years after surgery. As the collected results are very promising and the study has a high scientific value it has been decided to extend the follow-up evaluation period and include a patient visit 5, 7 and 10 years after surgery to the original study design. Primary assessment variables will be similar as to the original study design:

1. Roentgen stereophotogrammetric analysis (RSA) (Selvik, 1974).

Secondary assessment variables will be:

2. Plain radiographs will be obtained for disease classification.
3. Clinical assessment according to the Knee Society Score (KSS), KOOS and EQ-5D score.

Data collection will be done by clinical evaluation, x-rays and patient evaluations collected in a separate folder at the clinic. Data is collected and processed by the research unit at the orthopaedic clinic in Hässleholm. The examinations will be conducted in the same manner as those already performed 1 and 2 years after surgery. During the patient visits an assessment of the knee function will be conducted (KSS) as well as answering patient questionnaires (EQ-5D, KOOS). The patient follow-ups will take place at the clinic in Hässleholm including RSA (stereophotogrammetric analyse) 5, 7 and 10 years after surgery.

Primary objective
To compare the clinical outcomes and long-term implant survival using RSA data including patient opinions about the function and quality of life after knee replacement surgery using the Triathlon knee prosthesis.

Secondary objective
To compare operative time, number of hospital days, blood loss, KSS results, KOOS (questionnaire about symptoms and activity level), EQ-5D (questionnaire about quality of life) unexpected events, radiographs / including RSA.

Extended evaluation schedule

Evaluation	Pre-op	Per-op	PTD	3 Months	1 Year	2 Years	5 Years	7 Years	10 Years
Medical History	X								
Operative Details		X							
RSA			X	X	X	X	X	X	X
Radiographs	X		X		X	X	X	X	X
Clinical	X	X	X	X	X	X	X	X	X
Outcomes (KSS, KOOS, EQ-5D)	X			X	X	X	X	X	X

- RSA (Roentgen Stereophotogrammetric Analysis) evaluation will be required prior to discharge and at 3 months +/-2weeks, 1 year +/- 2 months, 2 years +/- 2 months, 5 years +/- 2 months, 7 years +/- 2 months and 10 years +/- 2 months.

- Radiographic evaluation will be required to be completed pre-operatively, prior to discharge and at 1 year +/- 2 months, 2 years +/- 2 months, 5 years +/- 2 months, 7 years +/- 2 months and 10 years +/- 2 months.

- Clinical evaluations will be required pre-operatively, per-operatively, prior to discharge and at 3 months +/-2 weeks, 1 year +/- 2 months, 2 years +/- 2 months, 5 years +/- 2 months, 7 years +/- 2 months and 10 years +/- 2 months.

- Patient outcomes assessments (KOOS, EQ-5D and KSS) will be required to be completed preoperatively and at 3 months +/-2 weeks, 1 year +/- 2 months, 2 years +/- 2 months, 5 years +/- 2 months, 7 years +/- 2 months and 10 years +/- 2 months.