Taperloc Complete Microplasty vs Taperloc Complete Standard: Randomized Controlled Study on Bone Mineral Density

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Table of Contents

STUDY SUMMARY

TITLE Taperloc Microplasty vs. Taperloc Standard: Randomized Controlled Study on Bone Mineral Density

DESIGN Multi-Center Comparative Two Armed Randomized Controlled Study (Centralized Randomization run by Sponsor)

PURPOSE The primary purpose of this study is to measure the postoperative changes in bone mineral density, comparing the Taperloc Complete Reduced Distal Microplasty stem and the standard length Taperloc Complete Reduced Distal stem.

OUTCOME MEASURES The primary outcome measures are the change in bone mineral density in the Gruen zones surrounding the stem measured by DEXA and incidence of thigh pain.

The secondary outcome measures are the assessment of leg length and femoral offset, to determine the suitability of the implant size range and neck geometry, standard clinical scores (i.e. modified Harris Hip Score), complications, and survivorship analysis.

POPULATION 100 Patients:

50 with Taperloc Complete Reduced Distal stem.

50 with Taperloc Complete Reduced Distal Microplasty stem

Up to four sites will be used to enroll patients into this study

ELIGIBILITY To be included in the study, a patient must be prescribed a primary total hip arthroplasty with the Taperloc system. The Taperloc system is to be used in accordance to the indications for use and contraindications detailed in the approved labeling of the device.

DURATION 1 year recruitment, and 5 years follow up

STUDY SPONSOR Zimmer Biomet

1. INTRODUCTION

1.1. BACKGROUND

The Taperloc Microplasty cementless stem is designed to transmit load to the proximal femur, thereby preserving bone density, and preventing long term instability and loosening secondary to proximal bone resorption. The primary aim of this study is therefore to compare the postoperative changes in bone density with the Taperloc Microplasty stem, using the standard length Taperloc stem as a control.

In addition, the Taperloc stem has historically had a neck angle of 138°. There have been criticisms that this neck angle is too high for the typical Korean population. The newer Taperloc Complete system (both Microplasty and standard length) has a neck angle of 133°. A secondary aim is occurrence ratio of thigh pain difference between Microplasty and standard stem in Korean population

1.2. DEVICE DESIGN AND DESCRIPTION

The Taperloc stem is designed after the philosophy of a flat tapered wedge. It has evolved to incorporate the Reduced Distal and Microplasty stems to better address all patient anatomies, and facilitate multiple surgical techniques.

The Flat Tapered Wedge Geometry enhances proximal loading, preserves bone, and provides rotational stability. Standard and lateralized options reproduce various patient anatomies without lengthening the leg

The stem is manufactured from Titanium Alloy Ti-6AL-4V, which allows for stress transfer to preserve cortical density. Titanium alloy porous plasma spray coating allows for initial scratch-fit stability and bone fixation. The Reduced Distal Stem Option allows the stem to be used in femoral canals with proximal/distal mismatch

The Microplasty Stem has a stem length reduced by 35 mm. This accommodates a minimally invasive approach, preserves soft tissues and bony structures, and ensures proximal stress transfer.

Product codes for the stems to be used in this study are listed below:

Full Length, Reduced Distal		
Size	Standard Offset	High Offset
5x130	51-100050	51-101050
6x132	51-100060	51-101060
7x134	51-100070	51-101070
8x136	51-100080	51-101080
9x137	51-103090	51-104090
10x140	51-103100	51-104100
11x142	51-103110	51-104110
12x144	51-103120	51-104120
13x146	51-103130	51-104130
14x148	51-103140	51-104140
15x150	51-103150	51-104150
16x152	51-103160	51-104160
17x154	51-103170	51-104170
18x156	51-103180	51-104180
20x160	51-103200	51-104200
22x164	51-103220	51-104220
24x167	51-103240	51-104240

Microplasty		
Size	Standard Offset	High Offset
5x95	51-108050	51-109050
6x97.5	51-108060	51-109060
7x99	51-108070	51-109070
8x101	51-108080	51-109080
9x102.5	51-106090	51-107090
10x105	51-106100	51-107100
11x107.5	51-106110	51-107110
12x109	51-106120	51-107120
13x111	51-106130	51-107130
14x113	51-106140	51-107140
15x115	51-106150	51-107150
16x117	51-106160	51-107160
17x119	51-106170	51-107170
18x121	51-106180	51-107180
20x125	51-106200	51-107200
22x129	51-106220	51-107220
24x132	51-106240	51-107240

1.3. RATIONALE FOR CURRENT STUDY

Stress shielding in cementless hip replacement leads to bone resorption. Not only does that increase the likelihood of long term aseptic loosening, but the reduction in bone stock could compromise the outcome of revision surgery. This is particularly important considering that cementless components are frequently used preferentially in young patients. Not only is the revision risk for a given implantation time higher with young patients, but life expectancy is higher as well. This means that young patients are much more likely to need revision surgery in their lifetime. Preservation of bone stock in order to keep revision options open is therefore a very important consideration.

One way to preserve the bone stock and to reduce stress-shielding bone resorption of the proximal femur is by removing the distal stem of the femoral component and providing metaphyseal fixation. Alternatively, reducing the size of the distal stem could also encourage metaphyseal fixation. The questions arise which is most effective at encouraging proximal load

transfer, and whether it is possible to obtain strong and long-lasting fixation of the femoral component without diaphyseal anchoring.

The rationale for this study is therefore to determine whether radiographic results and stress shielding are similar between the short and conventional length cementless femoral components with identical metaphyseal design.

1.4. STUDY PURPOSES

The main objectives of the study are to:

- Compare the postoperative changes in bone density with the Taperloc Microplasty stem, using the standard length Taperloc stem as a control.
- Compare and confirm the stability and fixation of short and standard Taperloc hip implants.
- Compare clinical scores in patients receiving the short and standard Taperloc stems.
- Collect survivorship data
- Determine whether the geometry and options available with the Taperloc Complete hip system can accurately reconstruct leg length and offset in this patient population.

2. STUDY DESIGN

2.1. OVERALL DESIGN

This study is a multi centre, prospective two-way randomized comparative study, involving 100 patients, recruited among up to 2 centers (approximately 50 patients from each site). Patients will be randomized at the time of surgery into two groups, as detailed below.

2.2. STUDY GROUPS/TREATMENTS

The first group will receive a Taperloc Complete Reduced Distal standard length stem, and the second group will receive a Taperloc Complete Reduced Distal Microplasty stem.

2.3. NUMBER OF SITES AND SUBJECTS/PROCEDURES

The total sample size is 100 hips in 100 patients recruited from up to two sites.

2.4. EFFICACY AND/OR SAFETY HYPOTHESES

There will be no difference of BMD change between both groups.

2.5. PRIMARY AND SECONDARY ENDPOINTS

Primary Endpoints:

- Change in bone mineral density around the implant
- Incidence of thigh pain

Secondary Endpoints:

- Postoperative restoration of femoral offset and leg length
- Radiographic measurements of stability and fixation
- Overall Survivorship
- Harris Hip Score
- Complications

2.6. ASSESSMENT PROCEDURE

2.6.1. ASSESSMENT TIMELINES/SCHEDULE

	Pre-op	Intraop	Immediate Post-op	6 weeks	6 months	1 year	2 years	5 years
Operative Form		X						
Standard Radiographs	X			X		X	X	X
DEXA			X			X	X	X
Modified Harris Hip Score	X				X	X	X	X
Thigh pain	X			X	X	X	X	X
Complications		Any Time						

2.6.2. ALLOWED WINDOW OF EACH SCHEDULE

Follow-up Time Point	Allowed Window
Immediate Post-Op	+ 1 Week
6 weeks	1-2 Months
6 months	+/- 1 Month
1 Year	+/- 2 Months
2 Year	+/- 3 Months
5 Year	+/- 6 Months

2.7. STUDY DURATION

The estimated study duration is 6 years with 1 year allotted for site and patient enrollment and 5 years of active follow-up.

3. SELECTION AND WITHDRAWAL OF SUBJECTS

Inclusion/exclusion criteria are identical to those indications and contraindications stated in the package insert of Taperloc hip Implants.

3.1. INCLUSION CRITERIA

Patients suitable for primary Total Hip Replacement

Patients with degenerative joint disease (inflammatory or non-inflammatory) or any of the composite diagnoses of:

a. Osteoarthritis
b. Avascular necrosis
c. Legg Perthes
d. Rheumatoid arthritis
e. Diastrophic variant
f. Fused hip
g. Sequelae of slipped capital epiphysis
h. Traumatic arthritis
i. Patients aged over 20

j. Patients must be able to understand instructions and be willing to return for follow-up

3.2. EXCLUSION CRITERIA

Absolute contraindications include: infection, sepsis, and osteomyelitis.

Relative contraindications include:

a. Uncooperative patient or patient with neurologic disorders who are incapable of following directions
b. Small femoral canal
c. Severe osteoporosis (patients over 65 years old)
d. Metabolic disorders which may impair bone formation
e. Osteomalacia
f. Distant foci of infections which may spread to the implant site
g. Rapid joint destruction, marked bone loss or bone resorption apparent on roentgenogram
h. Vascular insufficiency, muscular atrophy, or neuromuscular disease
i. Pregnancy
j. Fracture of the pelvis
k. Subcapital fractures

3.3. SUBJECT WITHDRAWAL

It is recognized that the subject's participation in this study is entirely voluntary, and that she/he may refuse to participate and may withdraw from participation at any time without jeopardy to any future medical care. It is also recognized that the investigator, at his/her discretion, may withdraw a subject from this study based upon his/her professional judgment. In event of subject withdrawal, applicable local procedures should be followed.

If a patient is withdrawn or rescinds their consent, a "Lost to Follow-up" case report form (CRF) should be completed detailing the reason for the patient withdrawal. If the patient has not yet reached the primary endpoint, the study Sponsor should be contacted to discuss whether or not the patient should be replaced. The site should also notify their Institutional Review Board (IRB) if applicable. If a patient is withdrawn from the study by the investigator, the patient should be notified of their removal by a letter from the site.

It is required that patients return within the defined follow-up period to complete all study assessment forms and radiographs. Patients that miss or will not return for follow-up are not considered "protocol deviations" or "lost to follow-up."

4. PROTOCOL DEVIATION MANAGEMENT AND REPORTING

Any deviation from the protocol should be documented on the "Protocol Deviation" CEF. Protocol Deviations should be reported to the study Sponsor within ten days of knowledge of the reported event.

5. ADVERSE EVENT MANAGEMENT AND REPORTING

Any adverse event, according to definitions section 18, should be documented on the "Complication" CRF. A record of all adverse events, including details of the nature, onset, duration, severity, relationship to the device, relationship to the operative procedure and outcome, will be made on the relevant section(s) of the subject's CRF.

Complications should be reported to the study Sponsor within ten days of knowledge of the reported event. If the event is considered an unanticipated adverse event, it should be reported to the study Sponsor within 5 days of knowledge of the reported event.

6. DATA ANALYSES

6.1. SAMPLE SIZE JUSTIFICATION

We performed a sample size calculation based on detecting a difference in the incidence of postoperative thigh pain between the 2 study groups, assuming an overall α error (2 sided) of 5% with a statistical power of 80% (β error = .20). We assumed that the incidence of thigh pain in the conventional femoral implant group would be 15% compared to 5% in the short anatomical femoral implant group at 2-year follow-up. With these assumptions, approximately 40 patients per study group were needed.

6.2. DESCRIPTION OF STATISTICAL ANALYSES

Significance Levels

The Type I error rate for the primary study analysis will be 0.05.

Comparisons for secondary, exploratory, and safety analyses will use $\alpha = 0.05$, with no adjustment for multiple comparisons.

Models for Continuous Measures

Comparisons of study groups with regard to continuous baseline and secondary outcomes will be performed using standard statistical tests and will be chosen as appropriate for the scale and distribution of the measures being analyzed. For example, a t-test, Wilcoxon test, or one-way ANOVA (as appropriate) can be performed to assess differences.

Categorical Data Analyses

Comparisons of study groups with regard to categorical baseline, secondary and safety outcomes will be performed using standard statistical tests and will be chosen as appropriate for the scale and distribution of the measures being analyzed.

Exploratory Analyses

Exploratory Analyses described below will be carried out if possible, depending on the data. If empty cells exist or models do not converge, these analyses will not be performed.

Repeated measures ANOVA models will be developed for each of the Gruen Zones to determine the effect of visit (time), treatment and baseline value of BMD on the BMD results. Baseline factors may also be included. To determine whether a factor has an effect on the BMD results, a Type 3 analysis of effects based on the F test will be conducted. Hypothesis testing will use $\alpha = 0.05$.

7. DATA COLLECTION, HANDLING AND RETENTION

7.1. SOURCE DOCUMENT REQUIREMENTS

Source documentation for this study will be maintained to document the treatment and study course of a subject and to substantiate the integrity of the study data. Source documentation may include, but not be limited to, worksheets, hospital and/or clinic or office records documenting subject visits including study and other treatments or procedures, medical history and physical examination information, laboratory and special assessments results, pharmacy records, device accountability records, and medical consultations (as applicable).

Before the study starts, a record of the source document for each endpoint will be recorded and kept at the site and with the Sponsor. If for any reason this source document changes, the record will need updated, and communicated to the Sponsor.

7.2. CASE REPORT FORMS

Data for this study will be collected and documented on the subject Case Report Forms (CRFs) provided which may be in paper form or in an electronic form. Authorized study site personnel will complete CRFs only. CRFs must be reviewed for completeness and accuracy, and signed by the investigator or his/her designees.

Since there is a potential for errors, inaccuracies, and misinterpretation in transcribing data onto the CRFs, the following documents must be available at all times for inspection and comparison to the CRFs by the study monitor when appropriate:

- data query forms
- originals and photocopies/certified copies of all relevant records and reports
- copies of test results

Sample CRFs to be used with this study are provided in Appendix 2.

7.3. ELECTRONIC DATA ENTRY

When using electronic data handling and/or remote electronic data systems, the Sponsor should:

- Ensure and document that the electronic data processing system(s) conforms to the Sponsor's established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e. validation).
- Maintain SOPs for using these systems.
- Ensure that the systems are designed to permit data changes in such a way that the data changes are documented and that there is no deletion of entered data (i.e. maintain an audit trail, data trail, edit trail).
- Maintain a security system that prevents unauthorized access to the data.
- Maintain a list of the individuals who are authorized to make data changes.
- Maintain adequate backup of the data.
- Safeguard the blinding, if any (e.g. maintain the blinding during data entry and processing).

7.4. STUDY DOCUMENT RETENTION

Study documents should be retained for a season after the study is complete as required by local, state, national, or international health authorities.

8. DATA REPORTING

The site will provide study progress and data summary reports to the Sponsor per frequency agreed by both parties.

9. MONITORING PLAN

The Sponsor of this study may monitor the data collection to ensure that the study is being conducted consistent with the protocol. The following describes the monitoring activities, which may take place during the course of the study.

9.1. FREQUENCY

Pre-Study Visit/Conference:

Prior to initiation of the study, the study manager will provide the investigator with all the necessary information to enable him/her to carry out his/her responsibilities. This prepares the site with an in-depth training on the protocol, CRFs, and data collection process for the length of the study. The study manager will also train the site on using the Sponsor's Joint Assist database.

Monitoring of the Data

Monitoring of the data will occur at least annually, and as often as monthly. Times when this may be appropriate include:

- Monthly Invoicing
- Quarterly Review
- Annual Reports
- While performing data analysis for marketing material or publication.

9.2. SAMPLING PLAN

All data will be monitored for completeness and accuracy on at least an annual basis.

9.3. MONITORING TASKS

The Sponsor will continually monitor the progress of the study. These activities include:

- Tracking of patient enrollment
- Review of all electronic patient data forms received for completeness

- Tracking of patients to ensure follow-ups are being completed at appropriate intervals
- Review of all adverse reactions
- Maintaining open communication with all investigational sites in order to ensure the quality of the study.
- In-house audits as needed

Upon completion of any type of monitoring, the site is responsible for resolving all discrepancies found in a timely manner. All discrepancies found within the Joint Assist database will be queried and sent directly to the site. Delays in resolving queries are to be avoided at all costs; this provides the study with the most accurate data, prevents delay in reporting procedures & publication, and safeguards in the event of an audit by the relative regulatory authority in the region.

9.4. STUDY CLOSE-OUT

When a site has completed their data collection, a visit may be necessary by a Sponsor's monitor to ensure all data has been obtained. Data will be reviewed for completeness, and monitored to ensure that all discrepancies have been resolved.

10. LABELING

The devices and products will be used in accordance with their instructions for use and/or approved labeling. The package insert for the device(s) in this study is included in the Investigator Binder.

11. ETHICAL AND REGULATORY REQUIREMENTS*

12.1. CODE OF CONDUCT

The investigator will ensure that the clinical study is conducted in accordance with

1. Protocol
2. Regulatory and IRB requirements
3. ISO 14155, GCP

This study is for academic purposes and safety of the products will also be assessed.

12.2. INSTITUTIONAL REVIEW BOARDS

The investigator must obtain appropriate Institutional Review Board (IRB) approval before the study can be initiated. A copy of the written approval from the IRB and a copy of the approved informed consent form should be sent to the Sponsor. A list of the IRB members (including their institution affiliations, gender makeup, and occupations); or a statement from the IRB specifying that the membership comply with applicable regulations is to be provided to the Sponsor. This must be done on an annual basis and copies sent to the Sponsor as long as the study is open at the site.

Any changes to the protocol must be discussed and approved by the Sponsor in writing unless the change is made to assure the safety of the subject. In the non-emergent setting, after agreement on the changes has been reached, an amendment to the protocol will be provided by the Sponsor for submission to the IRB for review and approval prior to initiation of the change. Any change made emergently must be documented in the subject's medical record and reported to the Sponsor within the time period required by IRB and applicable regulations.

The investigator must immediately forward to the IRB any written safety reports or updates from the Sponsor.

The investigator must keep the IRB informed of the progress of the study as required by the IRB but at least annually.

12.3. INFORMED CONSENT

Subjects (or the subject's legally authorized representative) will be provided with an informed consent and patient information sheet in order to give ample opportunity to review the consent and ask questions. The signed informed consent will be obtained before any study procedures begin. If the subject agrees to participate in the study, the subject/representative must sign the informed consent form. The witness and the investigator must also sign the informed consent form. A copy of the informed consent form should be given to the subject/representative. All subjects who meet all of the entry criteria will be considered for inclusion in this study. Any subject meeting any of the exclusion criteria will be excluded from the study.

The informed consent form must be approved by the institution’s IRB.

Subjects will be informed of new information learned during the study, which may affect the subject’s decision to continue participation in the study.

An Informed Consent Log will be completed to document the existence of the signed informed consent form. The log will contain: Subject ID, date informed consent form signed, and the version signed. The monitor will initial and date the log once the executed informed consent form has been reviewed. Signed informed consent forms (or copies) are to be maintained in the study file and must be available for verification by monitors or inspectors.

12.4. SUBJECT CONFIDENTIALITY

The CRFs do not include any patient identifying information. Therefore, once the data is entered in the online database a patient can no longer be identified.

Once the site enters a patient into Joint Assist, the database will assign the patients an ID number. It is the responsibility of the investigator to maintain a list of patient identification and Joint Assist ID numbers throughout the course of the study. By assigning patients a unique ID number, their identity is protected in Joint Assist, the online database. The database is restricted, allowing an investigator to only view and enter data from his/her patients. User authentication is required to view research data. The data is transmitted to a centralized database through a secured (SSL) channel on the Internet. Data in transit is in 128-bit encryption. The access to the centralized database is limited to those who are responsible for maintaining the database.

12. INSURANCE AND INDEMNIFICATION

This arrangement will be negotiated by site in their investigator agreement.

13. APPENDICS

Appendix 1 Informed Consent Draft for Use in Submission to IRB

Appendix 2 Case Report Forms

Appendix 3 Regulatory Approval Info / Package Insert

Appendix 4 Surgical Technique & Product Brochures

GLOSSARY OF ABBREVIATIONS

DEXA: Dual Energy X-ray Absorptiometry