

## Clinical Research Protocol



# **A PROSPECTIVE MULTI CENTER RANDOMIZED CONTROLLED TRIAL TO EVALUATE G7 Acetabular System with CoC ARTICULATION COMPARED TO EXCEED ABT Acetabular System with CoC ARTICULATION IN TOTAL HIP ARTHROPLASTY**

**PROTOCOL NUMBER (Study ID): ORTHO.CR.GH42**

**PROTOCOL VERSION: FINAL v.6.0 (08<sup>th</sup> February, 2018)**

**Amendment 2**

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## GENERAL INFORMATION

### Investigators

Name	Site	Contact (i.e. Postal address, Phone Number)	Role (Principal or co-investigator)
Seung-Beom Han	Korea University Medical Center	+82 2 920 5692	Principal Investigator
Jeong-Joon Yoo	Seoul Nat'l University Hospital	+82 2 2072 1994	Principal Investigator
Young-Soo Chun	Kyunghee University Hospital at Gangdong	+82 2 440 6155	Principal Investigator
Seung-Jae Lim	Samsung Medical Center	+82 2 3410 1228	Principal Investigator

### Study Sponsor(s)

Zimmer Biomet

### Project Leader(s)/Monitor

Anna Lee

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## STUDY SUMMARY

<b>TITLE</b>	Prospective Multi Center Randomized Controlled Trial to evaluate G7 Acetabular System with CoC articulation compared to Exceed ABT Acetabular System with CoC articulation in Total Hip Arthroplasty
<b>DESIGN</b>	Prospective Randomized Controlled Trial
<b>PURPOSE</b>	Evaluate the safety and effectiveness of patients who received G7 Acetabular system in conjunction with Ceramic on Ceramic articulation and Taperloc Complete Microplasty stem compared to patients who received the Exceed ABT Acetabular system with the same combination
<b>OUTCOME MEASURES</b>	160 patients (80 per group)
<b>POPULATION</b>	
<b>ELIGIBILITY</b>	Approved Indications for Use for G7 Acetabular System, Exceed ABT Acetabular System and Taperloc Complete Microplasty stem in Total Hip Arthroplasty
<b>DURATION</b>	All patients will be followed at 6 months, 1, and 2 years postoperatively. Assuming the enrolment will be completed in one year, the total duration of the study is 3 years.

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## 1. INTRODUCTION

### 1.1. BACKGROUND

The Biomet G7™ Acetabular System has been designed to provide more options to surgeons for treatment of patients needing total hip arthroplasty, while concurrently simplifying the surgical process with well-designed, modular components and corresponding instruments. The G7™ Acetabular System includes three liner types; ArComXL highly-crosslinked or E-1 Vitamin E-infused polyethylene and a Biolox Delta (Ceramtec, Plochingen, Germany) ceramic liner.

The Exceed ABT Acetabular System has been designed for cementless fixation and consists of an acetabular shell and an acetabular insert. The acetabular insert/bearing includes a tapered outer geometry that matches the inner geometry of the acetabular shell and an inner hemispherical geometry to suit the varying modular head diameters. Inserts/bearings are inserted into the acetabular shell intra-operatively and are available in varying sizes to match the acetabular shell diameters. The insert/bearings are available in Biolox Delta ceramic (CeramTec AG).

G7 is a new acetabular system and to support its launch and ensure it continues to perform as intended, clinical evidence is required to be collected. There is also a need to collect clinical data on Exceed ABT to continue supporting marketing.

### 1.2. DEVICE DESIGN AND DESCRIPTION

#### **The Biomet G7™ Acetabular System**

The Biomet G7 Acetabular System is a modular acetabular system, offering two types of acetabular shells. The shells are available in either a solid shell design, with an apical plug, or a limited hole with an apical plug and optional screw holes. Components are available in numerous designs and sizes intended for both primary and/or revision applications.

All patients that consent to the study will be operated by either posterior-lateral or antero-lateral incision approach which are standard incision approaches for treatment of patients needing total hip arthroplasty.

#### Cup materials

Acetabular Shells are made of porous coated (PPS) titanium alloy. Screw hole and apical hole plugs are also made of titanium alloy. It contains options to use acetabular screws.

The acetabular shell is designed to be used with multiple bearings.

In the current study, the ceramic on ceramic articulation will be used.

#### Ceramic materials

Ceramic Acetabular Liners are made of zirconia-platelet toughened alumina (ZPTA)

#### **The Biomet Exceed ABT Acetabular System**

In the current study, the ceramic on ceramic articulation will be used.

#### Cup materials

Acetabular Shell: Titanium alloy Biolox® delta Ceramic Inserts Toughened alumina

Acetabular Screws: Titanium alloy

PPS porous plasma spray coating

#### **Taperloc Complete Microplasty stem.**

Biomet® Taperloc™ Complete stems are intended for uncemented biological fixation. They are offered in several sizes in both a standard and high offset design. The Taperloc™ Complete hip stems can be used for total hip arthroplasty.

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Stem materials:

Femoral Stems	Titanium Alloy
Porous Coating	Titanium Alloy

All the sites will use the Taperloc Complete Microplasty stem designed for ease of insertion with an posterior hip approach

- Stem length reduced to 35 mm from standard length stem
- Bone conserving stem option
- High offset options will also be available for the study

## 1.3. RATIONALE FOR CURRENT STUDY

To insure G7 Acetabular system and Exceed ABT Acetabular system perform as they are intended, clinical evidence is required to be collected.

## 1.4. PURPOSES

The purpose of the study is to evaluate the safety and effectiveness of patients who received G7 Acetabular system in conjunction with Ceramic on Ceramic articulation and Taperloc Complete Microplasty stem in primary total hip arthroplasty compared to patients who received the Exceed ABT Acetabular system with the same combination.

# 2. STUDY DESIGN

## 2.1. OVERALL DESIGN

This study will be a multi-center randomized controlled study. Eligible patients will be randomly assigned to receive a combination of G7 Acetabular system with CoC articulation and Taperloc Complete Microplasty stem or Exceed ABT Acetabular system with CoC articulation and Taperloc Complete Microplasty stem. Patient demographics, preoperative clinical outcomes, operative information, postoperative clinical outcome, radiographic assessment, incidence of squeaking, incidence of dislocation, implant survivorship and adverse events will be collected prospectively.

## 2.2. NUMBER OF SITES AND SUBJECTS/PROCEDURES

This is a multi-center study to be conducted in Korea at a maximum of 4 sites

## 2.3. EFFICACY AND/OR SAFETY HYPOTHESES

This study is designed to evaluate any difference in terms of patient reported clinical outcome (i.e. OHS, HHS) postoperatively in patients who received one of the abovementioned combinations of total hip systems.

## 2.4. PRIMARY AND SECONDARY ENDPOINTS

Primary endpoint is Harris Hip Score (HHS) at 1 year follow-up.

Secondary endpoints include

- Harris Hip Score at 2 years postop
- Oxford Hip Score at 6 months, 1 and 2 years postop
- Radiographic Assessment at Immediate post-op, 6 months, 1 and 2 years postop
- Incidence of squeaking at different follow-up visits
- Dislocation rate at different follow-up visits
- Survivorship

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## 2.5. ASSESSMENT PROCEDURE

### 2.5.1. ASSESSMENT PARAMETERS AND METHODS

#### Medical History and Demographic Data

Demographic information will be collected which will include but is not limited to gender, age at surgery, height, weight, primary diagnosis & medical history

#### Clinical Assessments

Clinical assessments will include functional scores, radiographic analysis.

An operative record will be completed upon the surgery. The operative record will include but are not restricted to date of surgery, surgical approach, implant components (part number).

#### Radiographic Assessments

Standardized antero-posterior pelvis radiographs and true lateral hip radiographs will be taken at each follow-up period. Femoral and acetabular implant position will be measured and the presence of signs of loosening will be analyzed. Radiographs will also be assessed for all time points using Gruen zone analysis of the femoral component and Charnley-DeLee zone analysis of the acetabular system

### 2.5.2. ASSESSMENT TIMELINES/SCHEDULE

Clinical and Radiographic Exams						
Data Collection item	Pre-operative	Intra-operative	Immediate Post-operative	6 Months	1 Year	2 years
Demographic and Medical History	X					
Operative Record		X				
Clinical Evaluation – OHS, HHS	X			X	X	X
Radiographic assessment			X	X	X	X
Squeaking, Dislocation			X	X	X	X
Adverse events including revisions			As required			

### 2.5.3. ALLOWED WINDOW OF EACH SCHEDULE

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Allowed Window of Each Prospective Visit Schedule:

- 6 months (+/- 2 weeks)
- 1 year (+/- 2 months)
- 2 years (+/- 3 months)

Each follow-up visit time point will be determined based on the date of surgery.

## 2.6. DURATION OF THE STUDY

All cases will be followed up to 2 years. It is expected that the enrollment will be completed in 1 year; the total duration of the study is 3 years.

## 3. SELECTION AND WITHDRAWAL OF SUBJECTS

All subjects, regardless of sex, race, or geographic location, must fit into the scope of the Inclusion/Exclusion criteria to be eligible for the study. If required per applicable regulations, all participants must sign an Informed Consent to be enrolled into the study.

### 3.1 INCLUSION CRITERIA

Patients will be included in this study to receive G7 Acetabular System, Exceed ABT Acetabular System, Ceramic on Ceramic articulation and Taperloc Complete Microplasty stem per the approved indications for use:

1. Non-inflammatory degenerative joint disease, including osteoarthritis and avascular necrosis.
2. Rheumatoid arthritis.
3. Correction of functional deformity.
4. Treatment of non-union, femoral neck fracture, and trochanteric fractures of the proximal femur with head involvement, unmanageable by other techniques.
5. Revision of previously failed total hip arthroplasty.
6. age over 20 years old

### 3.2 EXCLUSION CRITERIA

Exclusion Criteria for this study should comply with the stated contraindications on package inserts of G7 Acetabular System, Exceed ABT Acetabular System, Ceramic on Ceramic bearing and Taperloc Complete Microplasty stem. These indications are stated below:

Absolute contraindications include: infection, sepsis, and osteomyelitis

Relative contraindications include:

- 1) uncooperative patient or patient with neurologic disorders who are incapable of following directions,
- 2) osteoporosis,
- 3) metabolic disorders which may impair bone formation,
- 4) osteomalacia,
- 5) distant foci of infections which may spread to the implant site,
- 6) rapid joint destruction, marked bone loss or bone resorption apparent on roentgenogram, and
- 7) vascular insufficiency, muscular atrophy, or neuromuscular disease.

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### 3.3. SUBJECT WITHDRAWAL

It is recognized that the subject's participation in this trial 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

### 3.4. Subject withdrawal

Subjects may be withdrawn from the trial at any time for any of the following reasons:

- At subject's own request
- Death of subject
- Failure to return for follow-up
- Removed from evaluation – a written explanation by the investigator is required.

#### 3.3.1 Early Termination of Clinical Investigation

The clinical investigation can be discontinued at the discretion of the Chief Investigator or of Sponsor in the case of any of the following:

- Inefficacy of the study device.
- Occurrence of adverse events unknown to date with respect to their nature, severity and duration or the occurrence of known adverse events with unexpected frequency.
- Acquisition of new scientific knowledge during the conduct of the study which shows that the sense or ethical claim of the study is no longer valid.

If the subject is withdrawn for any reason at any time a final evaluation form will be completed and the Sponsor will be notified.

## 4. PROTOCOL DEVIATION MANAGEMENT AND REPORTING

Protocol deviations are unplanned and unintentional events. Any changes in the research protocol during the period, for which IRB approval has already been given, may not be initiated without submission of an amendment for IRB review and approval.

Any protocol deviations occur during the trial will be reported to any necessary institutions to manage. And that information also is reported to IRB and Sponsor.

## 5. ADVERSE EVENT MANAGEMENT AND REPORTING

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 and provide to the Sponsor. The subject will be questioned about any adverse event(s) at each subsequent follow-up assessment visit. Serious Adverse Events that are related to the device should be reported to the Ethical Committee and Sponsor as soon as possible. These include any untoward medical occurrences that result in death, are life threatening, require in patient hospitalization, or prolongation of existing hospitalization, result in persistent or significant disability/incapacity, or resulted in a congenital anomaly/birth defect.

***“Any general adverse events that are not related to hip, will be reported once symptomatic diseases are administered and confirmed by other departments.”***

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## 6. STATISTICAL ANALYSIS PLAN

### 6.1 SAMPLE SIZE CALCULATION

This is a multi-center, randomized controlled study to compare G7 Acetabular System /CoC articulation/Taperloc Complete Microplasty stem with Exceed ABT Acetabular System /CoC articulation/Taperloc Complete Microplasty stem. The primary endpoint is Harris Hip Score at 1 year postop. Study sample size is determined assuming the use of an independent, two-sided, two-sample pooled t-test for differences in mean Harris Hip Score.

Assumptions:

$\alpha = 0.05$	Probability of Type I Error
$\beta = 0.20$	Probability of Type II Error
$sd = 12$	Estimated standard deviation of the differences based on current Exceed ABT CoC study in Korea

Based on the assumptions above, a mean difference in Harris Hip Score of 5.8 points between groups can be detected with 68 cases in each group. If 15% dropout/lost to follow-up is assumed this will give n=80 in each group.

A total of 160 cases will be enrolled in the study.

#### Randomization

In this study, patients will be randomized to G7 Acetabular System with CoC articulation and Taperloc Complete Microplasty stem or Exceed ABT Acetabular System with CoC articulation and Taperloc Complete Microplasty stem in 1:1 randomization scheme. The randomization will occur via a random number generator (manual or computer) by Sponsor using block randomization procedure (block size of 4). The doctor or other health care professional does not choose the participants for each group. For patients satisfying inclusion criteria, randomization will occur by retrieving the next randomly generated group assignment. Sites will control randomization assignment.

### 6.2 HANDLING OF MISSING AND INCOMPLETE DATA

Attempt will be made to ensure that patients come back for scheduled follow-up evaluations. In case of missing data, for clinical outcome scores, Last Observation Carried Forward will be used to impute the missing data. For survivorship analysis, the data including implant in situ collected in the next follow-up will be used to calculate survivorship

### 6.3 DATA ANALYSES

The following analyses will be performed:

Primary endpoint is Harris Hip Score (HHS) at 1 year follow-up.

Secondary endpoints include

- Harris Hip Score at 2 years postop
- Oxford Hip Score at 6 months, 1 and 2 years postop
- Radiographic Assessment at Immediate post-op, 6 months, 1 and 2 years postop
- Incidence of squeaking at different follow-up visits
- Dislocation rate at different follow-up visits
- Survivorship

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## Primary and Secondary Endpoint Analysis

Analysis for primary and secondary endpoints will use patient population which consists of those cases with complete data for one or more of the primary and secondary endpoints. Analysis is based on intention to treat principle.

## **7. DATA COLLECTION, HANDLING AND RETENTION**

### **7.1 SOURCE DOCUMENTATION 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 data. Source documentation will 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).

### **7.2. CASE REPORT FORMS**

Data for this clinical trial 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 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 where appropriate:

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

### **7.3. ELECTRONIC DATA ENTRY**

When using electronic trial data handling and/or remote electronic trial 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 (see 4.1.5 and 4.9.3).
- 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 after the study is complete as required by local, state, national, or international health authorities. IRB shall store all documents required to be stored under relevant law and IRB policy without charge. After such period, IRB may charge a reasonable and customary storage fee if Sponsor requests that IRB continue to store documents related to the Study.

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## 8. DATA REPORTING

### 8.1 INTERIM REPORT

An interim report will be provided after each follow-up period.

### 8.2 FINAL REPORT

Final report will be provided after 2 yrs follow-up period.

## 9. MONITORING PLAN

The Sponsor of this study may monitor the data collection to ensure that the investigation 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-Investigational Visit/Conference:

Prior to initiation of the study, the study manager will provide the Investigator with all the necessary information to enable him to carry out his responsibilities. This prepares the site with an in-depth training on the protocol, case report forms, 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:

- Quarterly Invoicing
- Quarterly Review(every 3 months)
- Annual Reports
- Adverse Event 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 clinical trial. These activities include:

- Tracking of patient enrollment
- Review of all electronic patient data forms received by Sponsor 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 clinical trial.
- 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. These will be sent to the site with an audit report by the study manager. All discrepancies found within the Joint Assist

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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. ETHICAL AND REGULATORY REQUIREMENTS

### 10.1. CODE OF CONDUCT

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

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

### 10.2. INSTITUTIONAL REVIEW/ETHICS COMMITTEE

If required, the Investigator must obtain appropriate Independent Ethics Committee (IEC) approval before the study can be initiated. A copy of the written approval from the IEC and a copy of the approved informed consent form should be sent to the Sponsor.

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 IEC 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 local SOPs and applicable regulations.

The Investigator must immediately forward to the IEC any written safety reports or updates from the Sponsor.

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

### 10.3. 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 trial. Any subject meeting any of the exclusion criteria will be excluded from the trial.

The informed consent form must be approved by the institution's IEC. Subjects will be informed of new information learned during the study, which may affect the subject's decision to continue participation in the study.

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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.

### **10.4. SUBJECT CONFIDENTIALITY**

To ensure study patients' privacy, all patients will be identified by unique identification numbers. All case report forms will only include subject IDs. It is the responsibility of the investigator to maintain a list of patient identification and Joint Assist.

Further the Joint Assist database is restricted, allowing a doctor to only view and enter data from his own 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.

The Sponsor will maintain the confidentiality of the identity of subjects enrolled in the study and the information contained in their study records. The Sponsor will also instruct the study investigators in the importance of maintaining the confidentiality of study records. The records will be made available as required for review by governing regulatory agency such as FDA and a reviewing IEC/IRB, however to the extent possible; the subject's identity will not be disclosed.