The 10-year follow-up of the Delta-TT trial:
Stability of the Delta-TT cup with Polyethylene insert compared to the Delta-TT cup with Ceramic insert.

RESEARCH PROTOCOL

Versie 1.1: 15-07-2024

PROTOCOL TITLE 'The 10-year follow-up of the Delta-TT trial:
Stability of the Delta-TT cup with Polyethylene insert compared to the Delta-TT cup with Ceramic insert.'

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Coordinating investigator/project leader	***Sigrid Vorrink, PhD, Research coordinator*** [redacted] ***Drs. A. D. Klaassen, Orthopaedic researcher*** [redacted] ***Department of Orthopaedics, OLVG***
Researcher	***Drs. O. Hoonhout, Orthopaedic researcher*** [redacted] ***Department of Orthopaedics, OLVG***
Principal investigator(s) (in Dutch: hoofdonderzoeker/ uitvoerder)	***Prof. dr. R.W. Poolman, MD*** ***Orthopaedic surgeon*** ***Department of Orthopaedics*** ***OLVG*** ***Postbus 95500*** ***1090 HM Amsterdam, the Netherlands*** [redacted]
Sponsor (in Dutch: verrichter/opdrachtgever)	***Limacorporate spa*** ***Via Nazionale 52*** ***33038 Villanova di San Daniele (Udine)*** ***Italy***

Subsidising party	*Limacorporate spa* *Via Nazionale 52* *33038 Villanova di San Daniele (Udine)* *Italy*
Independent expert (s)	*Dr. D.F.P. van Deurzen, MD* *Orthopedic surgeon* *OLVG Postbus 95500* *1090 HM Amsterdam* *The Netherlands* [redacted]

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LIST OF ABBREVIATIONS AND RELEVANT DEFINITIONS

ABR	General Assessment and Registration form (ABR form), the application form that is required for submission to the accredited Ethics Committee; in Dutch: Algemeen Beoordelings- en Registratieformulier (ABR-formulier)
AP	Anteroposterior X-ray
BMI	Body Mass Index
CCMO	Central Committee on Research Involving Human Subjects; in Dutch: Centrale Commissie Mensgebonden Onderzoek
CV	Curriculum Vitae
Delta- TT Cup	A cementless press fit hemispheric cup with a trabecular structure made out of Titanium alloy
DSMB	Data Safety Monitoring Board
EC	Ethical Committee
EQ5D-3L	Euro Quality of Life 5D-3L
EQ5D-5L	Euro Quality of Life 5D-5L
EU	European Union
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation; in Dutch: Algemene Verordening Gegevensbescherming (AVG)
H MAX S stem	A uncemented stem with Corail design philosophy in Titanium alloy with a Hydroxyapatite coated macro-textured surface
HOOS-PS	Hip disability and Osteoarthritis Outcome Score-Physical function Short form
IB	Investigator's Brochure
ICF	Informed patient Consent Form
LAT	Lateral X-ray
METC	Medical research ethics committee (MREC); in Dutch: medisch-ethische toetsingscommissie (METC)
NRS	Numeric (Pain) Rating Scale
PROMs	Patient-Reported Outcome Measures
RSA	RadioStereomatic Analysis
(S)AE	(Serious) Adverse Event
Sponsor	The sponsor is the party that commissions the organisation or performance of the research, for example a pharmaceutical

	company, academic hospital, scientific organisation or investigator. A party that provides funding for a study but does not commission it is not regarded as the sponsor, but referred to as a subsidising party.
SUSAR	Suspected Unexpected Serious Adverse Reaction
THA	Total Hip Arthroplasty
TT	Trabecular Titanium
WMO	Medical Research Involving Human Subjects Act; in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen

SUMMARY

Rationale: Aseptic loosening of the acetabular component of hip implants in total hip arthroplasty (THA) remains one of the main causes of long-term implant failure and revision surgery. Aseptic loosening is often induced by wear of polyethylene liners, causing osteolysis around the implant. Highly cross-linked polyethylene liners have been developed to reduce wear. Ceramic-on-ceramic (CoC) shows even lower wear rates compared to ceramic on polyethylene CoP. However, the inelasticity of a CoC bearing might cause increased micromotion and thereby affect implant stability in press-fit THA.

The Delta TT cup and H MAX S stem have been developed aiming to optimize initial stability and osseointegration of the implant. In our initial Delta TT RSA study, the migration of Delta-TT cups with a H MAX S stem was compared, using Radiostereometric Analysis (RSA) between ceramic and polyethylene liners. The results at 2- and 5-years after the operation showed good stabilization of the implant, regardless of liner type. A trend towards increased migration was observed in Delta TT cups combined with ceramic liners, but the between-group effects were small and not statistically significant.

Objective: The primary objective of this 10-year follow-up study is to investigate long-term migration patterns of the Delta-TT cup, comparing outcomes between ceramic and polyethylene liners. Similar to the 2- and 5-years results, good stability is hypothesized at 10-years postoperatively, regardless of liner type.

The secondary objectives are to measure migration of the H MAX S stem at 10-years postoperatively, to evaluate implant survival, signs of osteolysis, clinical outcomes and patient-reported outcome measures (PROMs) for the Delta-TT cup and H MAX S stem, comparing outcomes between the ceramic and polyethylene group.

Study design: This is a long-term follow-up of a randomized control trial comparing migration patterns of the Delta-TT cup between ceramic and polyethylene liners.

Study population: Patients included in the initial Delta TT randomized study, will be invited to participate in this 10-year follow-up study. At the time of inclusion, patients were male or non-pregnant female, between 18 and 75 years of age, who provided informed consent for the initial Delta TT study and underwent uncemented total hip arthroplasty.

Study parameters/endpoints: the primary endpoint of this study is the long-term (10-year) stability of the Delta-TT cup, compared between a ceramic and polyethylene liner. This is

measured in 3D translations and rotations via RSA X-rays en mean migration results will be compared between the 2 groups.

Secondary endpoints include long-term (10-year) stability of the H MAX S stem, measured in 3D translations and rotations via RSA X-rays. Besides, implant survival and radiographic signs of osteolysis will be investigated for the Delta TT cup and H MAX S stem. Additionally, clinical outcomes such as squeaking and PROMs will be collected using questionnaires, including EuroQol 5D-5L (EQ5D-5L), Hip disability and Osteoarthritis Outcome Score-Physical function Short form (HOOS-PS), Numeric (Pain) Rating Scale (NRS) and Oxford Hip Score. Finally, we will compare the survival data at 10-years postoperatively with the predicted survival at 2-years postoperatively using the thresholds presented in the literature. The aim is to quantify how well RSA analysis at 2-years predicted survival for the uncemented press-fit components used in this study, based on migration and surival results of individual patients.

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Patients have already been randomized in the initial study between a polyethylene and cermic liner and are being evaluated by means of RSA imaging and PROMs. There are, in our view, no risks associated with participation in this study. The added effective radiation dose for this study is 0.27 mSv. This is negligible when compared to the natural annual exposure of 2.9 mSv. There is no guarantee that patients will personally benefit from inclusion in this study. Patients undergo a more thorough screening than non-study patients and may benefit from this increased surveillance. Information gathered in this study may benefit others undergoing THA with uncemented components.

1. INTRODUCTION AND RATIONALE

Aseptic loosening of the acetabular component of hip implants in total hip arthroplasty (THA) remains one of the main causes of long-term implant failure and revision (LROI, 2023; NJR, 2023; NJRR, 2023). Aseptic loosening is often induced by wear of polyethylene liners, causing osteolysis around the implant. Highly cross-linked polyethylene liners have been developed to reduce the risk of wear. Ceramic has a higher stiffness and ceramic-on-ceramic (CoC) shows even lower wear rates compared to ceramic on polyethylene. However, the inelasticity of a CoC bearing might hamper a natural load transfer to the bone, potentially causing increased micromotion and thereby affect implant stability in press-fit THA (Small et al., 2013; van Loon et al., 2023).

The Delta-TT cup and H MAX S stem have been developed,aiming to optimize initial stability and osseointegration of the implant (LimaCorporate, Villanova San Daniele del Friuli, Italy). Radiostereometric Analysis (RSA) is a very accurate measurement technique to determine micromotion of the implant relative to inserted tantalum markers in the surrounding bone and has been the recommended means in evidence-based phased introduction of new implants (Swierstra et al., 2011). It is believed that early RSA migration patterns at 2 years postoperatively can predict implants at risk for long-term aseptic loosening(Nieuwenhuijse, Valstar, Kaptein, & Nelissen, 2012; Pijls et al., 2012; Streit et al., 2016)

In our initial Delta-TT study, we used RSA imaging to compare early migration patterns of the Delta-TT cup and H MAX S stem between polyethylene and ceramic liners. A trend towards increased migration was observed in Delta TT cups combined with ceramic liners, however between-group effects were small and not statistically significant. The 2-year results showed stabilization of Delta-TT cups within 6 months, regardless of liner type (Klaassen et al., 2022). Similarly, the 5-year results showed comparable migration patterns of the Delta TT cup and H MAX S stem between ceramic and polyethylene liners. These results indicate that after initial migration, implants in both groups showed secondary stabilization, which is promising for long-term survival of the implant.

In this study, we will investigate the long-term migration patterns of the Delta-TT cup and compare these outcomes between polyethylene and ceramic liners. Similar to the 2- and 5-years results, good stability is hypothesized at 10-years postoperatively, regardless of liner type. The secondary objectives are to determine migration of the H MAX S stem at 10-years postoperatively and to evaluate implant survival, signs of osteolysis, clinical outcomes and patient-reported outcome measures (PROMs) for the Delta-TT cup and H MAX S stem, comparing outcomes between the ceramic and polyethylene group.

Finally, we will compare the survival data at 10-years postoperatively with the predicted survival at 2-years postoperatively using the thresholds presented in the literature (Nieuwenhuijse et al., 2012; Pijls et al., 2012; Streit et al., 2016). The aim is to quantify how well RSA analysis at 2-years predicted survival for the uncemented press-fit components used in this study.

This will be the first study to evaluate long-term migration patterns of uncemented components, compared between ceramic and polyethylene liners. Besides, this study will investigate long-term stability and survival of the Delta-TT cup and H MAX S stem. The results will contribute to the understanding of long-term survival of uncemented components.

2. OBJECTIVES

Primary Objective:

- To compare long-term stability of the Delta TT cup between ceramic and polyethylene liners, by means of RSA at 10-years postoperatively.

Secondary Objectives:

- To compare long-term stability of the H MAX S stem between ceramic and polyethylene liners, by means of RSA at 10-year postoperatively.
- To measure implant survival rates, reasons for revision and radiographic signs of osteolysis and compare these outcomes between ceramic and polyethylene liners.
- To compare clinical outcomes and patient-reported outcome measures (PROMs) for the Delta TT cup with H MAX S stem, between the ceramic and polyethylene group.
- To compare the survival data at 10-years postoperatively with the predicted survival at 2-years postoperatively using the thresholds presented in the literature. The aim is to measure the predictive value and quantify how well RSA analysis at 2-years predicted survival for the uncemented press-fit components used in this study.

3. STUDY DESIGN

This study is a long-term follow-up of the Delta-TT trial, in which 52 patients who underwent unilateral primary hip arthroplasty were randomized between a polyethylene liner (n = 25) and a ceramic liner (n = 27). The initial study included RSA imaging at baseline (within 3 days postoperative before weight bearing) and at 6 weeks, 3 months, 6 months, 1 year, 2 years and 5 years postoperatively. At these same timepoints PROMs were documented, including EuroQol 5D-3L (EQ5D-3L), Hip disability and Osteoarthritis Outcome Score-Physical function Short form (HOOS-PS), Numeric (Pain) Rating Scale (NRS) and Oxford Hip Score. At 5-years follow-up, 1 patient was withdrawn from the study, the remaining 51 patients will be invited to participate in the RSA-10 follow-up study.

In this 10-year follow-up, 3D translations and rotations by means of RSA X-rays are used to determine the long-term stability of the Delta-TT cup and the H MAX S stem for the polyethylene and ceramic liner group. Implant survival is determined through revision rates. Furthermore radiographic signs of aseptic loosening will be investigated for both the cup and stem, by evaluating radiolucency on anteroposterior (AP) and lateral (LAT) X-rays. The acetabular zones will be evaluated as described by DeLee and Charnley and the zones around the stem will be evaluated using the Gruen zones (DeLee & Charnley, 1976; Gruen, McNeice, & Amstutz, 1979; Zicat, Engh, & Gokcen, 1995). PROMs will be collected to determine long-term functional outcome of the implants. Instead of EQ5D-3 the more recent EQ5D-5L will be used, because it shows a reduced ceiling effect compared to the EQ5D-3L version (Feng, Devlin, & Herdman, 2015; Herdman et al., 2011). To compare these EQ5D-5L scores to the values of the initial study they will be translated to the EQ5D-3L scores (van Hout et al., 2012). In addition, clinical outcomes such as squeaking of the hip will be collected. An overview of the 10-year follow-up measurement methods is provided in table 1.

Table 1: timeline of measurements.

Outcome measurements 10-year postoperatively
RSA röntgenanalysis
Survival
AP and LAT X-rays
Numeric (Pain) Rating Scale (NRS)
EQ-5D-5L
HOOS-PS
Oxford Hip Score
Other clinical outcomes

All patients were included in the initial study, between October 2014 and February 2016 and will therefore reach the 10-year mark between October 2024 and February 2026. An overview of the study timeline is provided in table 2.

Table 2: study timeline.

Study phase	2024				2025				2026			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
Preparation												
Patient inclusion and data collection												
Data analysis and reporting												

4. STUDY POPULATION

4.1 Population (base)

All participants in this study were already enrolled in the initial Delta-TT trial, between October 2014 and February 2016. All patients were included in the OLVG hospital (Amsterdam, the Netherlands) and will be contacted to participate in the follow-up trial. Patients will be informed about the results of the 2- and 5-year follow-up and the study specifics for the 10-year follow-up. They will also be given the opportunity to ask questions and to take time to think about their decision. If patients do not wish to participate and are willing to share their reason why, this will be recorded in the screening log.

4.2 Inclusion criteria

The inclusion criteria for the initial Delta-TT study were:

A. Patients scheduled to undergo primary total hip replacement.

B. Patient is able to understand the meaning of the study and is willing to sign the ethical committee (EC) approved, study-specific Informed Patient Consent Form (ICF).

C. Ability and willingness to follow instructions and to return for follow-up evaluations.

D. The subject is a male or non-pregnant female between 18 and 75 years of age.

We anticipate that some of the patients from the initial study, whether in the ceramic insert group or the polyethylene group, may have subsequently undergone a THA revision. The frequency of THA revisions holds significant importance as an outcome measure for this study. These patients will therefore also be requested to provide written informed consent. If consent is given, these patients will be included in the study but will not be eligible for RSA imaging and X-rays. All other data will be collected.

4.3 Exclusion criteria

The exclusion criteria for the initial Delta-TT study were:

A. The subject is morbidly obese, defined as Body Mass Index (BMI) of > 40.

B. The subject will be operated bilaterally.

C. Patients having a deformity or disease located in other joints than the hip that needs surgery and is limiting their ability to walk.

D. The subject has an active or suspected latent infection in or about the hip joint.

E. Patient who is expected to need lower limb joint replacement for another joint within one year.

F. The subject has a neuromuscular or neurosensory deficiency, which would limit the ability to assess the performance of the device.

G. The subject has a systemic or metabolic disorder leading to progressive bone deterioration.

H. The subject's bone stock is compromised by disease or infection which cannot provide adequate support and/or fixation to the prosthesis.
I. Female patients planning a pregnancy during the course of the study.

For the 10-year follow-up study only the following exclusion criteria will be checked again:

J. The patient is unable or unwilling to sign the ICF specific to this study.
K. Subject deemed unsuitable for participation in the study based on the investigator's judgement.

4.4 Sample size calculation

RSA studies have a high degree of sensitivity and accuracy of measurements (Valstar et al., 2005). Therefore, relatively small patient groups are sufficient to detect between group differences. Sample size calculations in the initial study are based on a standard deviation of 0.3mm translation and 0.8° rotation for the uncemented cup (Baad-Hansen et al., 2011). At 10 years, we aim to include all 51 patients that were still included in the previous study at 5-years follow-up. Using Cohen's d, a difference of 1SD can be detected with 80% power and alfa 0.05, based on 16 patients in each group (https://www.sealedenvelope.com/power/continuous-superiority/).

5. TREATMENT OF SUBJECTS

< This chapter is only applicable for intervention studies>

Not applicable

6. INVESTIGATIONAL PRODUCT

6.1 Name and description of investigational product(s)

Delta-TT cup : a cementless press fit hemispheric cup with a TT structure made out of Titanium alloy. In the current study, this cup will be used with a standard highly cross linked polyethylene insert (UHMWPE X-Lima, LimaCorporate), as well as a ceramic insert (CeramTec GmbH, Plochingen, Germany).
https://limacorporate.com/repo/storage/834/file/B-5552-83-012-1_091900_FLY_DELTA-TT_EN_V2.pdf

H-MAX S femoral stem: a uncemented stem with Corail design philosophy in Titanium alloy with a Hydroxyapatite coated macro-textured surface. The stem is straight for a fast and effective osteointegration.
https://limacorporate.com/repo/storage/321/file/B-4250-83-000-1_111500_FLY_H-MAX-S_EN.pdf

A 32 mm ceramic head will be used (CeramTec GmbH, Plochingen, Germany).
https://www.ceramtec-medical.com/fileadmin/user_upload/Medical/Dokumente/Infocenter/Downloads-for-Health-Professionals/Product-Information/BIOLOXdelta-Quick-Reference-Guide.pdf

6.2 Summary of findings from non-clinical studies

The Delta-TT cup has been made with Trabecular Titanium (TT), which has osseointegration-promoting characteristics (Bondarenko et al., 2018; Massari et al., 2017). The porosity and pore size of the TT technology enhances vascularisation and mineralisation favouring new bone formation (Frosch et al., 2004; Karageorgiou & Kaplan, 2005). Besides, stem cells grown in TT scaffold have shown to adhere, proliferate and differentiate into osteoblastst (Benazzo et al., 2014; Gastaldi et al., 2010). The H MAX S stem has a hydroxyapatite coating for an effective osteointegration (Rokkum, Reigstad, & Johansson, 2002).

6.3 Summary of findings from clinical studies

Clinical studies have shown promising short- and mid-term outcomes of the Delta-TT cup in terms of bone incorporation without bone loss due to stress shielding (Massari et al., 2017). Besides, both the 2-year and 5-year results of our initial trial, showed stabilization of the Delta-TT cup and H MAX S stem (Klaassen et al., 2022).

6.4 Summary of known and potential risks and benefit

There is no guarantee that patients will personally benefit from inclusion in this study. Patients undergo a more thorough screening than non-study patients and may benefit from this added follow-up moment at 10-years postoperatively. Information gathered in this study may benefit others undergoing THA with uncemented components. Patients have already been randomized in the initial study and will only be evaluated by means of RSA imaging and questionnaires. There are, in our view, no risks associated with participation in this study. The effective radiation dose per RSA-radiograph is 70 µSv and is only administered at 1 follow-up moment. The additional annual radiation dose is negligible if the natural annual exposure of 2.5 mSv is considered and will do the patient no harm (Lewis, Blake, & Fogelman, 1994). The International Commission on Radiological Protection categorizes the corresponding level of risk qualitative due to radiation as "trivial" with a quantitative risk of about one in a million or less. The required level of benefit should be related to "only increase knowledge" (http://ec.europa.eu/energy/nuclear).

7. NON-INVESTIGATIONAL PRODUCT

<This chapter is applicable for any other product that is used in the study, like challenge agents or products used to assess end-points in the trial. This can be a medicinal product or a food product or a chemical compound or stable isotope or other product.

Not applicable

8. METHODS

8.1 Study parameters/endpoints

In general, data will be summarized by treatment group. For parameters represented by continuous variables, the summaries will consist of the mean and 95% confidence intervals,. Continuous outcome variables will be analysed with parametrical statistical techniques, unless the normality assumption does not seem reasonable for the data, in which case non-parametric techniques will be considered.

For categorical variables, the number and percent in each category will be presented and will be analysed. Descriptive statistics for demographic, efficacy, and safety variables will be provided in tables. A two-sided 0.05 alpha level will be used.

8.1.1 Main study parameter/endpoint

The primary outcome in this study is long-term migration patterns of the Delta TT cup combined with the H-MAX S stem and compared between a ceramic and polyethylene liner, measured in 3D translations and rotations by means of RSA X-rays at 10-years postoperatively.

8.1.2 Secondary study parameters/endpoints

Secondary endpoints at 10-years postoperatively are:

- Long-term migration patterns of the H-MAX S stem, expressed in 3D translations and rotations (Method: RSA X-rays).

8.1.3 Other study parameters

- Implant survival of the Delta TT cup and H-MAX S stem (Method: Revision yes / no; reason for revision; survival in years). Survival data will be collected from the Dutch Arthroplasty Register (LROI).
- Radiographic signs of osteolysis around the cup and the stem (Method: Radiolucent lines at X-ray, acetabular zones as described by DeLee and Charnley and Gruen zones around the stem. Orthopaedic surgeons will be blinded for liner type while evaluating the X-rays. Before the evaluation, the researcher will obscure the liner (and head) section on the X-rays.
- Clinical outcomes, obtained through Patient reported outcome measures (PROMs):
    - Pain at rest (NRS);
    - Pain during weight-bearing (NRS);
    - Quality of life (EuroQol 5-dimensions EQ5D-5L);

- Hip function by means of the Hip Disability and Osteoarthritis Outcome Score – Physical function Short form (HOOS-PS) and the Oxford Hip Score (OHS);
- Self-reported squeaking

- Survival data at 10 years postoperatively will be related to the predicted survival at 2-years postoperatively, using the thresholds presented in the literature: Proximal cup translation on the Y-axis ≥ 1.0 mm at 2 years and for the stem subsidence ≥ 2.7mm at 2-years postoperatively (Nieuwenhuijse et al., 2012; Pijls et al., 2012; Streit et al., 2016).

8.2 Randomisation, blinding and treatment allocation

Not applicable

8.3 Study procedures

RSA procedure:

The RSA set-up consist of two synchronized roentgen tubes positioned approximately 1.5 meter above two roentgen cassettes (35 X 43 cm) at a 20° angle to the vertical. Both roentgen tubes simultaneously expose the roentgen film (Figure 2). A calibration box is used to calibrate the experimental set-up.

The baseline RSA X-ray which was taken within three days after surgery and before weight bearing is used as baseline. Since the tantalum balls are fixed in the bone around the implants, the position of the implant relative to the bone can be calculated. Taking these bone markers as reference points, the spatial translations and rotations of the component during follow-up can be calculated (Kaptein, Valstar, Spoor, Stoel, & Rozing, 2006; Valstar et al., 2005). The bone markers need to be well fixated in the bone. Bone markers are defined unstable when they move more than 0.3 mm with respect to the other bone markers. Unstable markers will be excluded from analysis (Garling, Valstar, & Nelissen, 2005).

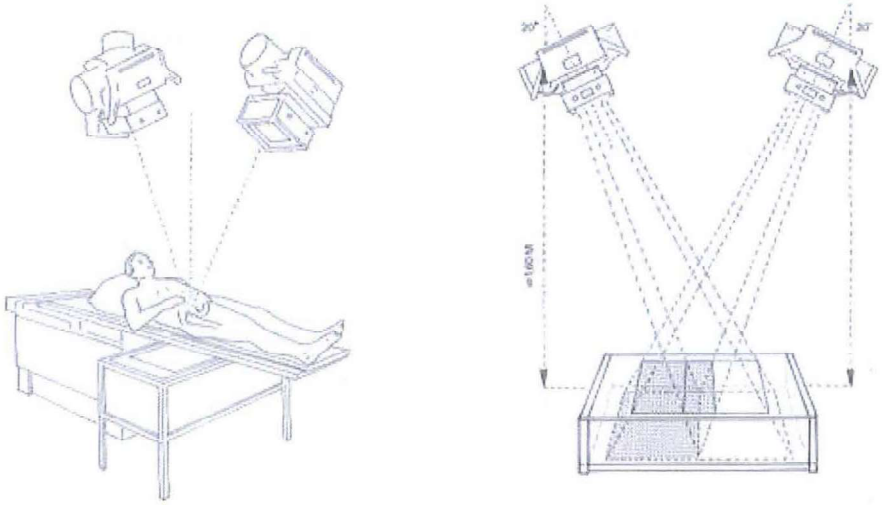

Figure 1: A uniplanar RSA arrangement. Two X-ray tubes are focused on the joint under examination. A calibration cage is placed underneath the X-ray table. It holds two X-ray films positioned next to each other.

The 10-year RSA X-rays will ideally be completed within 20 weeks after reaching date of 10-years postoperatively. An independent party, RSA*core* of the Department of Orhopaedics of LUMC will be responsible for the analysis of the RSA images. The anonymous RSA images can be directly uploaded to the secure website of the RSA*core*. RSA*core* will perform the RSA related data analysis and provide a report after completion of the study.

8.4 Withdrawal of individual subjects

Subjects can leave the study at any time for any reason if they wish to do so without any consequences. The investigator can decide to withdraw a subject from the study for urgent medical reasons.

8.5 Replacement of individual subjects after withdrawal

Since this is a long term follow-up study, patients who withdraw from the study cannot be replaced.

8.6 Follow-up of subjects withdrawn from treatment

Not applicable; this study does not include treatment.

8.7 Premature termination of the study

The investigator will notify the accredited Medical research Ethical Committee (METC) of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's visit which is estimated March 2026. The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action. In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature termination. Within one year after the end of the study, the

investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

9. SAFETY REPORTING

9.1 Temporary halt for reasons of subject safety

In accordance to section 10, subsection 4, of the WMO (in Dutch: Wet Medisch-wetenschappelijk Onderzoek), the sponsor will suspend the study if there is sufficient ground that continuation of the study will jeopardise subject health or safety. The sponsor will notify the accredited METC without undue delay of a temporary halt including the reason for such an action. The study will be suspended pending a further positive decision by the accredited METC. The investigator will take care that all subjects are kept informed.

9.2 AEs, SAEs and SUSARs

All participants in this study had THA 10 years ago and received a Delta TT cup with ceramic head and either a ceramic- or a polyethylene liner and a H-MAX S stem. They were followed for adverse events up until 5-year follow-up or until lost to follow-up. Adverse events as defined in the protocol of the initial study and were reported in toetsingonline. This 10-year follow up study has a cross-sectional design and includes only one single follow-up moment and visit to the hospital. Prior to this visit, patients will be queried about any medical procedures performed on either the affected and unaffected hip joint. These data will be utilized for data analyses, but will not be reported as a serious adverse event (SAE) because these events did not occur during the study. Following the visit, participants will not be followed up.

10. STATISTICAL ANALYSIS

In general, data will be summarized by treatment group. For parameters represented by continuous variables, the summaries will consist of the mean and 95% confidence intervals. Continuous outcome variables will be analysed with parametrical statistical techniques, unless the normality assumption does not seem reasonable for the data, in which case non-parametric techniques will be considered.

For categorical variables, the number and percent in each category will be presented and will be analysed. Descriptive statistics for demographic, efficacy, and safety variables will be provided in tables. A two-sided 0.05 alpha level will be used.

Descriptive statistics and statistical comparisons for important demographic, efficacy, and safety variables will be provided in tables. A two-sided 0.05 alpha level will be used.

To assess cup and stem migration a mixed model analysis will be performed, with bearing (PE vs. CE) as the primary independent value of interest. Primary outcome will be the effect of bearing over the 10-year follow-up period on implant migration. Group differences will be separately analysed at each time point including time as a categorical factor variable and a time-by-group interaction term. Differences are considered significant for p-values below 0.05.

10.1 Primary study parameter(s)

The main study parameter is migration of the Delta TT cup compared between a polyethylene and ceramic insert by means of RSA imaging at 10 years postoperative. RSA data will be analyzed using mixed model analysis with bearing (CE vs PE) as a primary independent value of interest.

10.2 Secondary study parameter(s)

- Migration of the H-MAX S stem compared between a polyethylene and ceramic insert by means of RSA imaging at 10 years postoperative. RSA data will be analysed using mixed model analysis with bearing (CE vs PE) as a primary independent value of interest.

10.3 Other study parameters

- 10-year implant survival rates will be investigated for both the Delta TT cup and H MAX stem. We hypothesize that survival for both components is >95% at 10 years

postoperatively. Since this study is not powered for survival analysis, the differences between the groups will be reported, but not statistically tested.

- For determining radiological signs of aseptic loosening, radiolucent lines (RLs) are examined on lateral and anteroposterior X-rays. Around the cup, RLs are assessed in the three zones defined by DeLee and Charnley (DeLee & Charnley, 1976). Around the stem, RLs are examined in the seven zones defined by Gruen (Gruen et al., 1979). An RL is defined as such if the maximum width is equal to or greater than 1 mm, similar to previous studies (Carli, Warth, de Mesy Bentley, & Nestor, 2017; Hasler et al., 2021; Oishi et al., 2021). A Chi-square test is used to compare the number of cases with one or more RLs between the polyethylene liner group and the ceramic liner group, for both the acetabular cup and the femoral stem. If there are fewer than 10 observed cases with one or more RLs in one of the two groups, the Fisher's exact test is used, which is valid for all sample sizes (Kim, 2017).
- Patient reported outcomes up until 10 years postoperatively will be presented with means and 95% confidence intervals and visually presented in graphs.
- Survival data at 10-years postoperatively will be compared with the predicted survival at 2-years postoperatively using the thresholds presented in the literature. The aim is to measure the predictive value and quantify how well RSA analysis at 2-years predicted survival for the uncemented press-fit components used in this study.

11. ETHICAL CONSIDERATIONS

11.1 Regulation statement

The study will be conducted according to the principles of the Declaration of Helsinki (2013) and in accordance with the Medical Research Involving Human Subjects Act (WMO) and Good Clinical Practice guidelines.

11.2 Recruitment and consent

Eligible participants are not currently under treatment but have previously consented to participate in the initial Delta TT trial. Patients included in the initial trial who were still included at 5-years follow-up will be invited by the treating orthopaedic surgeon to participate in the 10-year follow up trial (RSA-10). The eligible participant will be provided with the EC approved patient information letter and ICF and given at least one week to contemplate participating in the study. Patients will be given the opportunity to ask questions about the study. All patients will be requested to provide written consent prior to any research related procedures.

11.3 Benefits and risks assessment, group relatedness

The participants have previously been randomized in the initial study and are only being re-evaluated at 10-years follow up. There are no risks for the study subjects associated with participation in this study. In our opinion, a separate study subject insurance for participation in this study will not be necessary and dispensation will be requested of the METC.

11.4 Compensation for injury

The sponsor has an insurance which is in accordance with the legal requirements in the Netherlands (Article 7 WMO). This insurance provides covers for damage to research subjects through injury or death caused by the study. The insurance applies to the damage that becomes apparent during the study or within 4 years after the end of the study.

12. ADMINISTRATIVE ASPECTS, MONITORING AND PUBLICATION

12.1 Handling and storage of data and documents

Questionnaire data will be collected using Castor EDC. Imaging will be conducted by the radiology department of OLVG hospital and stored on a local server. All subject data will be anonymized by assigning study numbers to each subject. A new study number will be generated using Castor EDC. The study numbers are not based on the patient initials or birth-date. The key to these study numbers is only available to the coordinating investigator and research assistant(s) and will be kept in the secured research location on Sharepoint. Outcome data, anonymised, is only accessible for the coordinating investigator, principal investigators, statistical analysers and authorized research personnel of the Joint Research group at OLVG Amsterdam. Data will be collected and stored for a period of 15 years. An encrypted file with contact information is already made for the initial study. Data without identifiable patient variables will be processed and stored in SPSS. Security requirements: Data input capabilities are limited to the coordinating investigator. Data processing capabilities are limited to the coordinating investigator, statistical analysers, the principal investigators and authorized research staff. The handling of personal data will comply with the Dutch General Data Protection Regulation (Algemene Verordening Gegevensbescherming, AVG).

12.2 Monitoring and Quality Assurance

A monitoring plan will be developed and conducted locally by a dedicated monitor in OLVG.

12.3 Amendments

Amendments are changes made to the research after a favourable opinion by the accredited METC has been given. All amendments will be notified to the METC that gave a favourable opinion.

12.4 Annual progress report

The sponsor/investigator will submit a summary of the progress of the trial to the accredited METC once a year. Information will be provided on the date of inclusion of the first subject, numbers of subjects included and numbers of subjects that have completed the trial and amendments.

12.5 Temporary halt and (prematurely) end of study report

The investigator will notify the accredited METC of the end of the study within a period of 8 weeks. The end of the study is defined as the last patient's last visit which is estimated March 2026. The sponsor will notify the METC immediately of a temporary halt of the study, including the reason of such an action. In case the study is ended prematurely, the sponsor will notify the accredited METC within 15 days, including the reasons for the premature

termination. Within one year after the end of the study, the investigator/sponsor will submit a final study report with the results of the study, including any publications/abstracts of the study, to the accredited METC.

12.6 Public disclosure and publication policy

Our intention is to publish the results of this study in a relevant scientific journal after the last patient is measured and the data is analysed.

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