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Short dental implants (5 mm) versus Long dental implants (10 mm) in combination with sinus floor elevation: A Randomized Clinical Trial

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Short dental implants (5 mm) versus Long dental implants (10 mm) in combination with sinus floor elevation: A Randomized Clinical Trial

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In partial fulfillment of the M.S. in Periodontics

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INTRODUCTION

List of Abbreviations:

Implant placement (IP)

Marginal Bone level changes (MBL)

Probing pocket depth (PPD)

Bleeding on Probing (BOP)

Group Short (GS): Experimental Group

Group Long (GL): Control Group

BACKGROUND and SIGNIFICANCE

Edentulism is a condition of being toothless, which impacts the patient's ability in performing some daily tasks and affects their esthetic appearance and self-confidence (Misch, 2007). Prostheses supported by dental implants can improve patients' quality of life by providing a pleasant appearance as well as comfort in speaking and chewing (Sargozaie et al., 2017). After extraction, the bony socket undergoes significant horizontal and vertical resorption especially in the maxillary posterior area (Chappuis et al., 2017). These changes often lead to more complex and time-consuming procedures, such as a lateral or transcrestal sinus lift, for placing implants in the area. Despite the reliability of these techniques, providers are faced with challenges such as elevated cost, higher morbidity, and more intra- and post-surgical complications. These challenges may be overcome by utilizing less invasive procedures such as short implants. However, the definition of a short dental implant remains a topic of controversy. According to Striezel & Reichart, an implant with a length of ≤11 mm is considered short (Strietzel and Reichart, 2007) whereas some authors consider a short implant to be <10 mm (Mezzomo et al., 2014, Telleman et al., 2014) or <8 mm (Fan et al., 2017). Additionally, an implant with a length of ≤6.5 mm has been defined as extra-short (Anitua et al., 2014, Anitua et al., 2015) . During the last decade, short implants have shown to be a reliable and effective alternative solution for patients with bone atrophies (Pieri et al., 2017). Indeed, it has been demonstrated that unfavorable crown to implant (C/I) ratio is not related to increased biological complications or implant failure (Garaicoa-Pazmino et al., 2014). However, prevalence of peri-implantitis could present a greater concern due to the limited length, especially for people with previous history of periodontitis. A recent meta-analysis on short implants versus standard implants in the posterior jaw that included 13 studies with 1269 patients and 2631 implants showed no significant difference in implant survival, marginal bone loss, complications, or prosthesis failure. Nevertheless, it was

concluded that short implants with <8 mm should be used with caution because they present a higher risk of failure as compared to standard-length (≥8mm) implants (Lemos et al., 2016). In a systematic review based on the evaluation of 8 randomized controlled clinical trials (RCTs), the European Academy of Osseointegration (EAO) Consensus Conference in 2015 noted that longer dental implants in the augmented sinus caused a higher number of biological complications, increased morbidity, costs and surgical time. Therefore, shorter dental implants may be the preferred treatment alternative (Thoma et al., 2015). A recent multicenter, randomized, controlled clinical trial found that short implants (6 mm) for single-tooth restorations in the posterior maxilla were a viable solution versus longer implants (≥10mm) in combination with sinus lift. After three years of follow-up and with a residual ridge height of 5–7 mm, no implants were lost in both groups and no statistically significant difference in prosthetic complications were reported (Pohl et al., 2017). All these studies excluded patients with a previous history of periodontitis.

OBJECTIVES OF THE STUDY

The purpose of this study is to evaluate clinical and radiological parameters of 5 mm short implants (GS) compared to longer implants (GL) (10 mm) placed in sinus-grafted sites.

Null Hypothesis (H_0): There are no statistically significant clinical or radiographic outcome differences between the two groups, GS and GL.

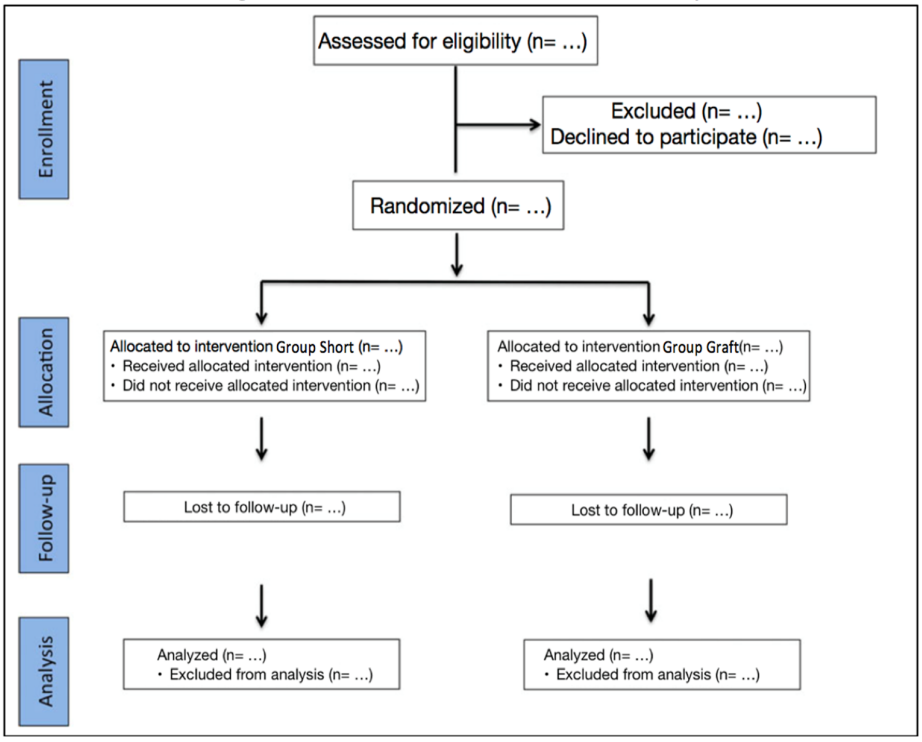
Alternative Hypothesis (H_1): There are statistically significant clinical or radiographic outcome differences between the two groups, GS and GL.

STUDY DESIGN

The present study will be a parallel, randomized single center clinical trial performed according to the CONSORT statement (http://www.consort-statement.org/).

Two different treatment modalities, GS and GL, will be compared in this randomized clinical trial. GS subjects will receive a short dental implant (5 mm in length) with no sinus lift whereas GL subjects will receive a 10 mm long implant after sinus lifting with allograft. The flow chart of the study is presented in Fig. 1.

Fig. 1 CONSORT flow chart of the study



The Institutional Review Board (IRB) for the Medical Sciences at the University of Michigan, Ann Arbor, MI, must review and approve this study before enrollment of participants begins. It is the responsibility of the investigator to assure that all aspects of the institutional review are conducted in accordance with current Federal Regulations. A letter with IRB approval for the protocol must be received by the Principal Investigator before the initiation of the study. Amendments to the protocol will be subject to the same requirements as the original protocol. At each annual protocol renewal, an updated report of the numbers of samples and any adverse events will be provided to the IRB.

After completion or termination of the study, the investigator will submit a final report to the IRB. This report should include any deviations from the protocol, the number of patients evaluated, adverse events, and a conclusion summarizing the results. This study will also be registered on ClinicalTrials.gov. In addition, the study will be conducted according to the principles outlined in the Declaration of Helsinki on experimentation involving human subjects, as revised in 2000. Partially edentulous patients requiring an implant to replace a missing tooth in the maxillary premolar, 1st molar, or 2nd molar area with bone crest height more than 5 mm but less than 8 mm will be recruited for this trial. Up to 50 patients will be enrolled (half randomized for each group) in the Periodontics and Oral Medicine clinic at the University of Michigan School of Dentistry, Ann Arbor, Michigan.

A signed, written informed consent must be obtained from each subject before he or she enters the study after he or she has been given verbal and written information describing the nature and duration of the study. Subjects will be consented in a private cubicle inside the Periodontics and Oral Medicine clinic. An investigator or study coordinator will give the consent document to the potential subject and answer any questions the subject has before and after they read the consent document. Subjects will be given ample time to read the form and ask questions before they sign. The signed informed consent will be retained with the study records. Each subject will also be given a copy of his/her informed consent.

Patients that meet the inclusion/exclusion criteria and consent to the research study will receive a dental implant at no cost and an implant crown at reduced cost to replace their missing tooth. Research subjects will be followed for 24 months (± 1 month) after implant placement, for a total of 23-26 months (see Appendix A: Schedule of Events) for the entire study. Subjects will complete 10 research visits as described in the Study Procedures.

Primary and secondary endpoints

Primary endpoint: Comparing mesial-distal (M-D) bone loss between the two groups (Radiologic outcome)

Secondary endpoints: Clinical outcomes and Patient reporting outcomes

1. Determine the survival rate and success rate of the Group Short (GS) and Group Long (GL) group.
2. Compare incidence and types of surgical and prosthetic complications between groups
3. Compare the number of sites with bleeding on probing (BOP)
4. Compare the cost of both procedures and the cost of the prosthetic complications
5. Compare the probing pocket depth (PPD)
6. Determine the pain after treatment: Visual analog score (VAS)
7. Compare patient satisfaction
8. Compare surgical time

Participants

50 patients satisfying the following inclusion criteria will be recruited:

- Age 20 years or older at enrollment
- Able to provide informed consent
- Systemically healthy patients

- Full-mouth plaque score and full-mouth bleeding score ≤ 30% (measured at four sites per tooth)
- Missing one premolar, 1st molar, or 2nd molar in the maxillary arch (Minimum healing time after extraction: ≥4 months)
- One neighboring tooth or implant restoration must be present to the implant site.
- Presence of natural tooth/teeth, partial prosthesis and/or implants in the opposite jaw in contact with the planned crown/s deemed by the investigator as likely to present an initially stable implant situation
- Residual bone height under the maxillary sinus more than 5 mm but less than 8 mm and a width of at least 7 mm, as measured on cone beam computer tomography (CBCT) scans.

Exclusion criteria are:

- Unlikely to be able to comply with study procedures
- Uncontrolled pathologic processes in the oral cavity
- History of allergic reactions to dental local anesthetics
- History of head and neck chemotherapy or radiation within 5 years prior to surgery
- Systemic or local disease or condition that could compromise post-operative healing and/or osseointegration, such as HIV infection, Paget's disease, osteoporosis, etc.
- Uncontrolled diabetes mellitus (HbA1c >8)
- Patients taking corticosteroids, IV bisphosphonates, or any other medication that could influence post-operative healing and/or osseointegration
- Smokes more than 10 cigarettes/day
- Present alcohol and/or drug abuser (self-reported)
- Pregnant, unsure pregnancy status, or lactating females (self-reported), or planning to become pregnant within 1 year of study enrollment
- Any medical conditions that may affect the outcome of the study.

INVESTIGATIONAL PRODUCT OVERVIEW

Implants

- *GS* - T3 Short External Hex with DCD 5.0 mm Length Implants; Zimmer Biomet (Zimmer, Palm Beach Gardens, Florida, US)
- *GL* - T3 with DCD External Hex Parallel Walled x 10 mm Length Implants; Zimmer Biomet (Zimmer, Palm Beach Gardens, Florida, US)

STUDY PROCEDURES

Clinical measurements

1) The following measurements will be taken for each treated implant by a blinded, calibrated examiner at the implant placement (surgery V2), at the time of prosthetic placement (5-month post-op V6), 12-month follow-up (V8), and 24-month follow-up (V10).

- Marginal bone level (MBL): It will be calculated based on standardized radiographs using registered bite-block with a Rinn (Dentsply Rinn, Elgin, IL, USA) film holder and expressed as the distance from the implant shoulder to the most coronal bone-to-implant contact (BIC) on the mesial and distal side of the implant. The mean values will be calculated for each implant at the time of implant placement, at the time of prosthetic placement (5-month post-op V6), 12-month follow-up (V8), and at 24-month follow-up (V10). In the case that the bone levels around the study implants are hidden or difficult to read, new radiographs will be taken. Peri-implant marginal bone levels will be measured using the ImageJ software* (ImageJ, U. S. National Institutes of Health, Bethesda, Maryland, USA) (Schneider et al., 2012). The software will be calibrated for every single image using the known implant length or the length of the implant collar. Measurements of the mesial and distal bone crest level adjacent to each implant will be rounded to the nearest 0.1 mm. Implants with bone up to the coronal margin of the implant collar will be given a value of zero. Mesial and distal measurements of each implant are averaged, and a mean calculated at patient level and then at group level.
- PPD and BOP: It will be assessed at 4 sites per implant (mesial, distal, buccal, and palatal) with a measurement stent using a periodontal probe (UNC, Hu-Friedy, Chicago, IL, USA). PPD are measured from the distance of the mucosal margin to the bottom of the probable pocket in mm. BOP is recorded using the following scoring method: 0) no bleeding 1) an isolated bleeding spot is visible, 2) blood forms a confluent red line on margin, and 3) heavy or profuse bleeding.
- Plaque: The level of oral hygiene will be evaluated using the Modified gingival index (Lobene et al., 1986) (Scores 1-4).

  0 = Absence of inflammation

  1 = Mild inflammation or with slight changes in color and texture but not in all portions of gingival marginal or papillary

  2 = Mild inflammation, such as the preceding criteria, in all portions of gingival marginal or papillary

3 = Moderate, bright surface inflammation, erythema, edema and/or hypertrophy of gingival marginal or papillary

4 = Severe inflammation: erythema, edema and/or marginal gingival hypertrophy of the unit or spontaneous bleeding, papillary, congestion or ulceration.

- Prosthesis failure: Planned prosthesis which could not be placed due to implant failure(s), loss of the prosthesis secondary to implant failure(s), or replacement of the definitive prosthesis for any reason.
- Implant failure: It will be defined as implant mobility (assessed from force applied with two hand instrument), pain, or neuropathy.
- Implant success: It will be defined as 1) Absence of persistent subjective complaints such as pain, foreign body sensation and/or dysesthesia 2) Absence of a peri-implant infection with suppuration 3) Absence of mobility 4) Absence of a continuous radiolucency around the implant and 5) Absence of any biological or prosthetic complications (Buser et al., 2012)
- Peri-implantitis: It will be defined as detectable radiographic bone loss beyond the initial biological bone remodeling.

2) The following measurements will be taken for each treated implant by a blinded, calibrated examiner after implant placement, 12-month follow-up, and 24-month follow-up.

- Bone thickness (BT): It will be determined based on CBCT and expressed as the distance from the most coronal bone-implant contact to the outer surface of the buccal plate. The mean values will be calculated for each implant.

3) The following measurements will be taken for each treated implant by a blinded, calibrated examiner at prosthetic placement, 12-month follow-up, and 24-month follow-up.

- Crown to implant ratio: The height of the crowns will be measured on the radiographs from the implant-abutment interface to the most coronal point on the crown. The anatomical crown-to-implant ratio (anatomical C/I ratio) will then be calculated dividing the anatomical crown by the length of the implant.4)

4) ISQ (Implant stability quotiant) will be measured at the time of healing abutment placement.

Intra-operatory measurements

- Subjective evaluation of the bone type (Lekholm & Zarb 1985) during implant site preparation will be performed by the surgeon.
  - Type 1: Almost entirely comprised of homogeneous compact bone

  - Type 2: thick layer of compact bone surrounding a core of dense trabecular bone
  - Type 3: thin layer of cortical bone surrounding a core of dense trabecular bone
  - Type 4: Thin layer of cortical bone surrounding a core of low-density trabecular bone coupled with the surgeon's tactile perception
- Thickness of soft tissues will be measured with a 1.0-mm marked periodontal probe (UNC, Hu-Friedy, Chicago, IL, USA) on the top of bone crest in the center of future implant placement. This will ensure direct visibility of mucosal thickness during measurement.
- Patient phenotype: Classification of the patient's phenotype will be thin, medium, thick, or very thick by using the Colorvue biotype probe (Hu-Friedy).
- Chair time of the surgical procedure will be recorded from the end of local anesthesia until the completion of sutures.
- The time required for placement of one single implant, with both treatments (short implants and sinus floor elevation with placement of longer implants) will be calculated as follows: the time required for the entire surgical procedure (from anesthesia to sutures) will be assessed for each patient and divided by the number of installed fixtures. The ratio of the time required for placement of a single short implant to the time required for a sinus floor elevation procedure in combination with a longer implant will be calculated and expressed as a percentage.
- A wireless magnetic-based Osstell Mentor RF Analyzer (Ostell USA, Linthicum, MD, USA) will be used to assess primary implant stability. The designated transducer (SmartPeg) will be hand-tightened per the manufacturer's instructions to the fixture. ISQ values will be taken immediately after implant placement and measured in triplicate and averaged to yield the mean baseline ISQ value for each implant.

Clinical measurement to monitor early healing

- At the 2-week post-op suture removal visit (± 2 days after surgery) clinical photographs will be taken. In addition, data on soft tissue complications (edema, bleeding), general discomfort, pain (measured by VAS from 0 to 100) (Appendix A) and patient satisfaction (Appendix B) will also be collected at the 2-week post-op visit.

Demographic data and patient questionnaires

At the pre-surgical visit, age, gender, smoking habits (number of cigarettes/day) will be recorded.

At the 2-week post-op visit, data on post-operative pain during the first day and possible side

effects or complications of the first three days will be registered. Patient discomfort will be measured by VAS scale and number of post-operative pain medication quantified. Patients will receive 3 sheets containing the VAS scale to be filled out daily. In case of drop out, the related reason will be registered (Appendix B).

Furthermore, all patients will be asked at the 2-weeks, 12-month, and 24-month follow-up to give their perception of the received therapy by completing a questionnaire concerning function, esthetics, cleaning of the implant-supported restorations, satisfaction, and cost (Appendix C).

Screening & Pre-surgical procedures

The medical history and vitals (heart rate and blood pressure) will be taken. In addition, clinical photographs and one standardized periapical radiograph will be completed. A CBCT scan will be taken before implant placement for screening eligibility, and impressions will be taken for surgical guide preparation. The CBCT scan may be scheduled separately due to availability of the CBCT machine.

Randomization and masking of examiners

The randomization of the patients to either the test (5-mm implant) or control group (10-mm implant) is determined using a computer-generated randomization list (www.random.org). After administration of a local like 2% Lidocaine with 1:100k epinephrine, sulcular incisions at the adjacent teeth and a midcrestal incision will be performed, allowing reflection of a full-thickness flap. At this stage, the randomization concealment will be broken, and the surgical site will be prepared according to the manufacturer's instructions.

Surgical procedures

The medical history and vitals (heart rate and blood pressure) will be taken prior to the surgical procedure. In addition, clinical photographs will be taken during the surgical procedure. An implant surgical guide for partially edentulous patients will be fabricated according to procedure previously described by Shotwell (Shotwell et al. 2005).

Experimental group (GS)

5.0 mmL x 5.0mmD Zimmer T3 Short Ex Hex With Discrete Crystalline Deposition (DCD) implants:

1. Crestal incision and flap elevation

2. ACT Short Pointed Started Drill will be used to penetrate the cortical bone to the first depth mark on the drill. The recommended drill speed is 1200-1500 rpm. Copious irrigation with sterile saline solution is planned to prevent overheating of the bone during high speed drilling.
3. 2.0 mm ACT Short Twist Drill will be to drill to the bottom of the depth mark for 5.0 mm length implants. The recommended drill speed is 1250 rpm.
4. The direction and position of the preparation is verified by inserting the narrow end of the direction indicator into the osteotomy. A suture will be threaded through the hole to prevent accidental swallowing.
5. After proper alignment is verified using the Direction indicator, the 3.25 mm ACT Short Twist Drill will be used to drill until the bottom of the depth mark for 5 mm implants with a speed 1250 rpm.
6. Once the coronal aspect of the osteotomy has been prepared the 3.85mm ACT Short Twist Drill will be used to Drill to the bottom of the depth mark for 5.0mm. The recommended drill speed is 1250 rpm.
7. The 3.85 mm Short Shaping Drill with a yellow band indicating that it is for use with a 5.0mmD T3 Short Implants. The recommended drill speed is 1250 rpm.
8. Tapping Step for dense bone (Type I) using the Handpiece Connector advancing the tap into the prepared site at approximately 15-20 rpm. Final seating of the Short Dense bone Tap may require the use of the Ratchet Extension and the Ratchet Wrench.
9. The implant will be placed into the prepared site at approximately 15-20 rpm. Final seating of the implant may require the use of a Ratchet Extension and Ratchet Wrench.
10. To remove the implant mount, Open End Wrench will be placed onto the mount. The screw is loosened at the top of the mount with a Large Hex Driver or Large Hex Driver Tip inserted into the Right-Angle Driver or Low Torque Indicating Ratchet Wrench and rotate counter-clockwise. After the screw is completely loosened, the Open End Wrench will be rotated counter-clockwise slightly before removing the mount. The mount can be carried from the mouth with the Open End Wrench.
11. Cover Screw from the No-Touch Implant Tray with the Small Hex Driver (PHD00N) is placed onto the implant at no more than 10 Ncm.
12. Soft-tissue flaps will be secured and repositioned with sutures.
13. Final periapical radiograph is taken.

Control group (GL)

10 mmL X 5.0mmD Zimmer T3 with DCD Ex Hex Parallel Walled implants

1. A midcrestal incision is made, with full thickness flap reflection. Then sutures will be used to assist flap reflection both on the buccal and palatal sides.
2. Implant sites are marked with a 2.0mm round bur drill and prepared to a depth of 1.0 mm from the sinus floor with first 2 osteotome drills (up to 2.8 mm wide).
3. 2.8 mm reamer (SCA kit, Neobiotech, Seoul, South Korea) will then be inserted with different stoppers until the sinus membrane wall is fractured.
4. After the sinus membrane wall is fractured, a gauge will then be applied to check sinus wall surrounding to ensure membrane is lifted from the sinus wall.
5. Subsequently, bone graft (human allograft) small particle (size 250µm to 850 µm) will be inserted into the osteotome sites then slowly tapped into the sinus floor either by bone inserter/spreader (SCA kit, Neobiotech, Seoul, South Korea) or osteotome instrument by mallet. These instruments should not enter the sinus cavity.
6. The sinus floor should be elevated to at least 2 mm height longer than the desired implant length due to bone shrinkage occurring after healing.
7. Implant osteotome drills will be used to drill the osteotome site to the final diameter size according to the manufacturer's guideline, but only to the level of remaining bone height. Again, the instruments should not enter the sinus cavity to avoid any potential perforation.
8. 10mm length of Zimmer T3 with DCD Ex Hex Parallel Walled implant will be placed into the prepared hole.
9. Cover Screw is placed onto the implant at no more than 10 Ncm.
10. Soft-tissue flaps will be secured and repositioned with sutures.
11. Final periapical radiograph is taken.

All surgeries will be performed under local anesthesia using one or more of the following medications:

- Lidocaine with epinephrine, (Xylocaine 2%®-Epinephrine 1:100,000 and 1:50,000, Dentsply Pharmaceutical, York, PA, USA).
- Articaine (Septanest 4%®-Epinephrine 1:100,000, Dentsply Pharmaceutical, York, PA, USA).
- Mepivacaine (Polocaine 2%®-Levonordefrin 1:20,000, Dentsply Pharmaceutical, York, PA, USA)."

Post-surgical instructions

All subjects will be prescribed and instructed to take the following oral antibiotics after surgery: 500 mg amoxicillin (GlaxoSmithkline) three times per day for 7 days, or 300 mg clindamycin (if allergic to penicillin) four times per day for 7 days. In addition, 600 mg of ibuprofen (Brufen; Abbott S.R.L., Latina, Italy) as needed, and chlorhexidine mouthwashes 0.12% twice daily for 2 weeks. Subjects with a removable prosthesis will be instructed to not wear them during the healing phase. The sutures will be removed after 2 weeks. Any surgical complication will be recorded such as infection, pain, and other adverse events.

Prosthetic placement

After 4 months of submerged healing, exposure of the implant and placement of a healing abutment is performed. After 2 weeks, the sutures are removed. After 5 months of submerged healing, impressions via pick-up impression copings are taken either using a polyether material (Impregum 3M/ESPE, Neuss, Germany) and/or a digital scan (TRIOS, 3Shape, Denmark). Within 1 to 3 weeks, definitive screw-retained metal-ceramic or metal-resin restorations are delivered.

Follow-up evaluation visits

Follow-up evaluation (2 weeks)

- Clinical photographs
- Suture removal
- VAS on pain
- Patient satisfaction
- Implant mobility
- Plaque index

Follow-up evaluation (4 months) for stage 2 implant (Installment of abutment)

- Clinical photographs
- Standarized Periapical Radiograph
- ISQ
- Implant mobility
- Plaque index

Follow-up evaluation (4 months and 2 weeks) for post-op and impression

- Post-op stage 2 implant, remove suture
- Implant mobility
- Plaque index

Follow-up evaluation (5 months) for post-op and impression

- Impression definitive crown
- Implant mobility
- Plaque index

Follow-up evaluation (5 months and 2 weeks) for crown placement and maintenance

- Implant maintenance
- Definitive Crown placement
- Clinical photographs and standardized periapical radiographs.
- Implant mobility
- Plaque index

Follow-up evaluation (6 months after crown placement)

- Clinical measurements evaluation
- Implant maintenance
- Clinical photographs and standardized periapical radiographs.
- Patient satisfaction
- Implant mobility
- Plaque index

Follow-up evaluation (12 months after crown placement)

- Implant maintenance
- Implant mobility
- Plaque index

Follow-up evaluation (18 months after crown placement)

- Clinical measurements evaluation
- Clinical photographs and standardized periapical radiographs.
- Patient satisfaction
- Implant maintenance
- Implant mobility
- Plaque index

DATA MANAGEMENT

Data reflecting participant experience with the protocol under investigation will be reported to the Principal Investigator and the data recorded on Case Report Forms (CRF). CRF will be signed and

dated by the investigator or a designated representative and filled out in black ink. If an entry on a CRF requires change, the correction will be made as follows:

a. A single line will be drawn through the incorrect entry.

b. The date will be entered and the change initialed. White-out or erasure on CRFs will not be permitted under any circumstance.

All fields and blanks must be completed. The following abbreviations will be used when values or answers cannot be provided: NA=not applicable; ND=not done, UNK=not known. Completed original CRF's will be collected by the Principal Investigator. CRF must be submitted for each subject. Database entry will proceed directly from the CRF for analysis. The data, as well as group/subject identification, will be made available to the investigator at the conclusion of the study.

The study coordinator will audit all CRFs and corresponding portions of School of Dentistry records. The monitoring will provide the Principal Investigator the opportunity to evaluate the progress of the study and to verify the accuracy and completeness of the CRFs; assure that all protocol requirements, applicable FDA regulations and investigator's obligations are being fulfilled, and to resolve any inconsistencies in the study records. The Principal Investigator may stop the study if it is observed that the protocol or sound clinical practices are not being followed. The Principal Investigator may exclude subjects from the study if review of their records indicates violations of the protocol or if there were other reasons to believe that their inclusion would jeopardize the validity of the study.

All research records will be labeled "confidential" and kept in a locked room in a locked cabinet with limited access or in a password protected computer program. Only those directly involved with this research study will have access to the research records and password. A description of this clinical trial will be available on http://www.clinicaltrials.gov/, as required by U.S. Law. This Web site will not include information that can identify the patient.

The study coordinator and investigator will make an accurate and adequate written progress reports to the IRB at appropriate intervals not exceeding one year. The investigator will make an accurate and adequate final report to the IRB within 3 months after completion or termination of the study. The investigator will make an accurate and adequate special report to the IRB on any serious unexpected or life-threatening adverse event or death occurring in relationship to the study whether regarded as study-related or not.

On completion of the study, the investigators will prepare a final report of the study results.

STATISTICAL CONSIDERATIONS

The study will be powered to detect a minimum clinically significant difference in bone loss of 0.5 mm using $\alpha = 0.05$, a power $(1- \beta) = 80\%$. Considering possible dropouts, the number of patients will also be increased by 10% for each arm. On the basis of this data, the minimum needed number of patients to be enrolled in this study is 17 with for the test group (GS) and 17 for the control group (GL). Mean values, standard deviations, and medians will be calculated for the clinical parameters. The association between crown-implant ratio and final bone loss as well as prosthetic complications will be examined. Changes of the parameters over time within the two groups as well as differences between groups will be analyzed using repeated measure of analysis of variance (ANOVA).

PATIENT SAFETY AND COMPLIANCE

Deviations

The investigator will not deviate from the protocol without obtaining written approval from the IRB. Any other changes or deviation in the protocol will be made as an amendment to the protocol and must be approved by the IRB before being implemented.

Risks associated with dental x-rays

In this study, patients will have about eight standard dental x-rays and two CBCT scans. They should experience no more discomfort related to the x-rays than they would with x-rays taken during regular dental visits. The only discomfort may be related to the x-ray film or film holder pressing on the soft tissues.

The biologic effect of radiation is termed “effective dose” (EF) and is expressed in milliSieverts (mSv). The amount of radiation for one dental x-ray is about 0.005 mSv and 5.3mSv for CBCT scan. This is considered to be a very small risk. The average radiation exposure that includes the natural background radiation an individual receives is about 3.1 mSv per year and about 0.008 mSv per day. The total amount of radiation exposure to patients from this study is minimal.

The researchers will try to minimize these risks by providing a lead apron that will be mandatory to wear during x-rays.

Risk associated with surgery

Subjects will be assigned to a treatment program by chance. The treatment they receive may prove to be less effective or to have more side effects than the other study treatment(s) or other available treatments. The likelihood that the patient will be assigned a treatment that will be less effective than other study treatments or other available treatments is unknown. Both surgery methods are the standard of care. Mild to moderate pain and swelling is expected for both groups. There is a very low risk of uncontrolled bleeding that may occur with subjects that are in general good health and not taking medications that are classified as a blood-thinner. In some cases, subjects may feel some temporary sensitivity with the teeth next to the implant.

Implant Related Risks

1) Implant Failure
2) Biologic complications such as sinus membrane perforations, persistent bleeding, sinusitis (or acute sinus infection), rupture of sinus membrane, soft tissue (graft) dehiscence, abscess, pus, pain, swelling, peri-implant mucositis (heavily inflamed soft tissue without bone loss), or peri-implantitis (bone loss around the implant).
3) Prosthetic complications such as fixed prosthetic device detachment, loosening of abutment screws or healing caps, and fracture of the screw, framework, or occlusal material.

Risk of Sinus Lift

A major risk of a sinus augmentation is that the sinus membrane could be pierced or ripped. There are other risks involved including infection, inflammation, hematoma, pain, graft failure, sinusitis, and hemorrhage.

Risk of Bone Graft

Donor bone (allograft) will be used during this study. This material has been used for more than 30 years. Any pieces in the bone that may cause a reaction have been removed when it was made. There has been no report of people getting an infection from the donor bone. However, that does not mean an infection or reaction will not happen to the subjects. There is a low chance that the bone graft may get infected or the body may reject the bone graft, which would result in removal of the graft.

The researchers will try to minimize these risks by taking a CBCT prior to surgery. All of these risks are possible for any implant placed and are standard of care risks.

Adverse Events (AE)

One of the following determinations will be used to document the relationship of any adverse events to the study test material:

- NOT RELATED
- POSSIBLE
- PROBABLE

ANY SERIOUS AND UNEXPECTED ADVERSE EVENT INCLUDING HOSPITALIZATON OR DEATH DUE TO ANY CASE, WHICH OCCURS DURING THIS INVESTIGATION, WHETHER OR NOT RELATED TO THE STUDY, MUST BE REPORTED IMMEDIATELY (WITHIN 24 HOURS) TO THE PRINCIPAL INVESTIGATOR. Reports of serious or unexpected adverse events will be made immediately to: Dr. Tae-Ju Oh, Phone number: (734) 647-3320 or Dr. Andrea Ravidà, Phone number: (734) 730-9678.

This telephone report or fax must be followed within 5 days by a written summary fully documenting the event in order to permit the Principal Investigator to file a report, which satisfies regulatory guidelines. All serious and unexpected adverse events associated with the use of the study test material will be immediately reported to the IRB by the Principal Investigator. Adverse events reporting will proceed according to the University of Michigan guidelines for standard AE reporting.

Withdrawing Participation

Taking part in this study is strictly voluntary. Patients do not need to participate if they do not want to, and are free to leave the study at any time. In addition, their care will not be affected by not taking part in this study. Patients may have other options to replace their missing tooth at their own cost.

The researchers may also need to end a subject's participation in the study even if they want to continue to participate. For instance, a subject may be withdrawn if the researcher believes that it is not in their best interest to stay in the study, if they become ineligible to participate, if their condition changes and they need treatment that is not allowed while taking part in the study, or if the subject does not follow instructions from the researchers.

If a subject leaves the study before it is finished, there will be no penalty to them. They will not lose any benefits to which they may otherwise be entitled. There would be no harm to the patient if they decide to leave this study before it is finished. If they leave the study before the crown is made, no money will be given to them and they will receive no free cleanings.

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Appendix A: Schedule of Events Table

Visit	Screening & Pre-Surgical Visit (V1)	Surgery (V2)	2 weeks post-op (V3)	4 months post-op (V4)	4 months post-op (V5)	5 months post-op (V6)	5 months post-op (V7)	6 months post-crown delivery (V8)	12 months post-crown delivery (V9)	18 months post-crown delivery (V10)
Window		Baseline (BL)	± 2 days	± 1 month	2 weeks after V4 ± 2 days	± 1 month	± 1 month	± 1 month	± 1 month	± 1 month
Informed consent (*Inclusion & exclusion criteria)	*X									
Medical History	X	X	X	X	X	X	X	X	X	X
Adverse Events		X	X	X	X	X	X	X	X	X
CBCT scan (*May be scheduled separately)	*X									X
Vitals (blood pressure & heart rate)	X	X								
Maintenance							X	X	X	X
Implant crown placement (definitive)							X			
Radiograph (*Standardized)	*X	X and *X		*X			*X	*X		*X
Suture removal			X		X					
Impression	X					X				
Photographs	X	X	X	X	X		X	X		X
Clinical measurement		X		X			X	X		X
Subject pain assessment			X							
Patient satisfaction			X					X		X

Appendix B

Subject:_____

Rating Scales for Pain Measurement

Line Scale:

Please rate the level of your pain by placing an "X" on the following line.

No Pain **Worst pain imaginable**

_____

Box Scale:

Rate the level of your pain by circling one number on the scale, where 0 means "no pain" and 10 means "worst pain imaginable."

1	2	3	4	5	6	7	8	9	10

Verbal Rating Scale:

Circle the phrase that best describes your pain

Not Painful	Slightly Painful	Moderately Painful	Very Painful	Extremely Painful

How much ibuprofen (or other painkiller) did you take today? _____

Appendix C

Subject:_____

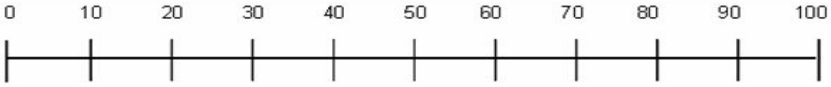
Patient Evaluation of Implant Treatment

Please answer the following five questions. Place an "X" on the line indicating your satisfaction from 0 "not satisfied at all" to 100 "fully satisfied".

1. **DOES MY IMPLANT-SUPPORTED RESTORATION(S) FUNCTION WELL?**

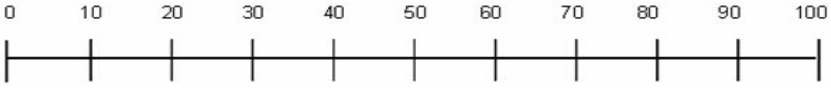
Not satisfied at all — Fully satisfied

2. **DO I FEEL SECURE BITING/CHEWING ON MY IMPLANT-SUPPORTED RESTORATION?**



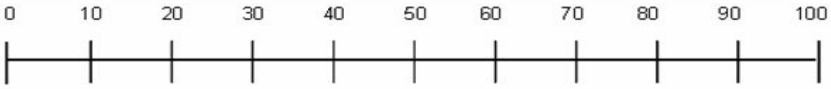
Much less secure — Much more secure

3. **AM I PLEASED WITH THE ESTHETIC RESULT?**



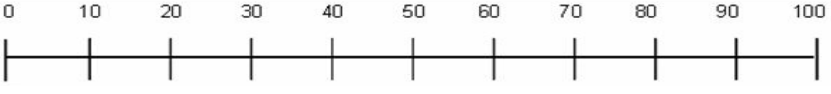
Not satisfied at all — Fully satisfied

4. **CAN I CLEAN MY IMPLANT-SUPPORTED RESTORATION(S) WELL?**



Extremely unlikely — Extremely likely

5. **AM I SATISFIED WITH THE TREATMENT?**

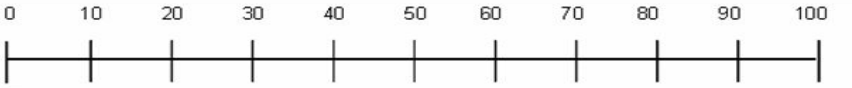


Not satisfied at all — Fully satisfied

6. **WOULD I UNDERGO THIS TREATMENT AGAIN, IF REQUESTED?**

Extremely unlikely Extremely likely

7. **WOULD I RECOMMEND THIS TREATMENT TO A RELATIVE/FRIEND?**



Extremely unlikely Extremely likely