Protocol Title: Short vs Long Dental Implants for the Fixed Rehabilitation of the Fully Edentulous Mandible

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Background, Significance, and Rationale

The clinical use of dental implants in the rehabilitation of totally and partially edentulous patients represents to date a long-term well documented and highly predictable procedure (for review see Cochran 1996, Esposito et al. 1998a, b). Historically, surgeons aimed for placement of the longest possible implants, in order to reach high bone-to-implant contact rates with the machined implants available at that time. The use of modern "rough" implants has been demonstrated to positively correlate with bone-to-implant contact rate and bone anchorage, leading to a significant enlargement of clinical indications for implant-supported rehabilitations (Gotfredsen et al. 1992; Cooper et al. 2000; Ivanoff et al. 2001; Shalabi et al. 2006).

The available amount of bone still remains the main limitation for implant placement. In cases of reduced bone height, standard length fixtures could be inserted only after advanced surgical treatments, such as vertical ridge augmentation, mandibular nerve transposition, and maxillary sinus lift. Patients often refuse such invasive procedures, ending up renouncing implant rehabilitation. For this reason, the possibility of using short implants is particularly fascinating, since it provides reliable solutions also in the numerous cases of reduced bone height, significantly expanding clinical indications for implant treatment. The use of short implants, moreover, presents also "absolute" benefits for patients in terms of limited foreign body, less invasive surgery (less biological tissue replacement), and reduced risk of damaging anatomical structures.

For "short" implants we refer to fixtures with an intraosseous length ≤ 8 mm (Renouard & Nisand 2006).

Short implants historically have been associated with higher failure rates than longer ones. On the other hand, a number of studies have failed to find differences in the survival rate of short and long implants (for review see Renouard & Nisand 2006, Morand & Irinakis 2007).

The discrepancies between these two groups of studies may relate to different factors such as the implant surface employed, the surgical protocol adopted in relation to the local bone density, the type of edentulism, and the prosthetic technique chosen.

Well-designed randomized controlled clinical trials demonstrating the efficacy of short implant rehabilitations are lacking to date.

The clinical performance of short and long implants should be compared at the level of areas having a good and comparable bone quality, the same bone height (this assumes the installation of short implants in sites able to receive longer ones), and for the resolution of the same type of edentulism by means of an identical prosthetic solution.

A reliable option is represented by 5 implants positioned in the interforaminal region of edentulous mandibles having bone height sufficient to receive standard-length implants, supporting a fixed full-arch prosthesis. The anterior mandibular region is usually characterized by high bone quality. Furthermore, the above-mentioned type of full-arch implant-supported rehabilitation possesses the best evidence of long-term success (Ekelund et al. 2003; Bryant et al 2007), being historically the first one performed and, to date, the most predictable too.

Specific Aims and Hypotheses

The aim of the present study is to evaluate the efficacy of 6 mm short implants compared with 11 mm long implants in comparable anatomic, surgical (no need for bone augmentation procedures), and prosthetic (fixed full-arch mandibular prosthesis) conditions. In particular, the null hypothesis is that there is no difference in terms of marginal bone level change (MBLc) between short and longer implants from prosthetic installation to 5 years of follow-up.

Study design and general information

This study has been designed as a multicenter parallel-group randomized controlled clinical trial (RCT) with a 1:1 allocation ratio. Three italian centers will be involved to the study. It will be reported according to the

CONSORT statement (http://www.consort-statement.org/). The Declaration of Helsinki principles will be followed, and all patients will sign a written informed consent form. The research protocol has been approved by the ethical committee of the University of Campania "Luigi Vanvitelli" (Aut. N. 13/2010).

Primary and secondary outcomes

The primary outcome will be the radiographic MBLc expressed as the change of MBL from prosthetic installation to the follow-up.

The secondary outcomes will include: (i) implant survival rate, (ii) prosthesis survival rate, (iii) biological or technical complications. Surviving implant or prosthesis will be considered those still in function at the follow-up. Biological complications included peri-implant mucositis, defined as a reversible inflammation of the soft tissues surrounding an implant in function with no loss of supporting bone, and peri-implantitis, defined as an inflammatory process affecting the tissues around an osseointegrated implant in function resulting in loss of supporting bone (Zitzmann & Berglundh 2008. Technical complications will be categorized in minor and major complications. The formers require only chair side repair and included screw loosening, and veneer material fracture. The latter require additional laboratory procedures and/or replacement components and included prosthesis or framework fracture, screw fracture, implant fracture, extended wear requiring veneer renewal.

Sample size calculation

Sample size calculation revealed that group sample sizes of 13 per group achieved 80% power to detect non-inferiority using a two-sample, one-sided test. The margin of non-inferiority (δ), that is the threshold value judged as clinically relevant, was 1.0 mm. The true difference between the means was assumed to be 0.0. In consideration of the one-tail nature of the non-inferiority test, the significance level (alpha) was set at 0.025. The data were drawn from populations with standard deviations of 0.9 and 0.9. Such a value was based on the long-term marginal bone loss data from the population of mandibular edentulous patients rehabilitated with Toronto bridges supported by conventionally loaded inter-foraminal long implants (Ekelund, Lindquist, Carlsson, & Jemt, 2003). Fifteen patients per group will be recruited to compensate for possible drop-outs.

Patient enrollment

Inclusion criteria will be age between 18 and 75 years, total mandibular edentulism for at least 8 months, sufficient amount of native bone (no previous bone augmentation procedures) in the inter-foraminal area to host 11 mm-long and 4 mm-wide implants with ≥1 mm of bone at the buccal and lingual aspects and ≥ 3 mm of inter-implant distance (determined by computed tomography), systemic health and compliance with good oral hygiene. Exclusion criteria will be any disease, medication or drug that could jeopardize healing, osseointegration or treatment outcome, severe bruxism or other parafunctional habits, and unrealistic aesthetic demands. Smoking habit will be registered as heavy smoker (≥10 sig./day), light smoker (<10 sig./day), nonsmoker or former smoker. Patient eligibility in terms of bone dimensions will be determined on computer tomography (CT) scans, with the aid of an implant planning software.

Preparing and planning phase

Eligible patients received a complete anamnestic and clinical examination; hopeless teeth will be extracted and remaining teeth will be periodontally and restoratively treated, if needed. A 15% cut-off for full-mouth plaque score and full-mouth bleeding score will be requested for dentate patients. The prosthetic project will be accurately planned on cast models mounted in an articulator. When possible, the previous denture will be used as a reference.

Randomization and allocation concealment

The randomization and the allocation concealment will be carried out using a computer-generated randomization list and sealed sequentially numbered opaque envelopes by a person not otherwise involved in the study. Envelopes will be consecutively opened at the leading center and communicated to the surgeon at the first surgery.

First surgical phase

Implant positioning will be performed by expert clinicians, following the same shared surgical protocol. A computer-aided bone-supported pilot surgical guide will be used during implant placement. All patients will be treated under local anesthesia using mepivacaine or articaine with adrenaline 1:100,000. A full-arch crestal incision, with distal releasing incisions if needed, will be performed and full thickness flaps will be raised. The mental nerves will be visualized and isolated. Five parallel implant sites will be prepared by calibrated burs and five 4 mm-wide implants (OsseoSpeed TX, Astra Tech Implant System, Dentsply Sirona Implants, Mölndal, Sweden) will be installed anterior to the mental foramens following the outline described by the manufacturer. 6 mm-long implants and 11 mm-long implants in the test and control groups will be placed, respectively. A minimum of 3 mm of inter-implant distance and 1 mm of bone at the buccal and lingual aspects will be required, with no need for augmentation procedures (if augmentation will be required, the patient would have been excluded from the study). If needed, an osteoplasty of the alveolar ridge will be done by means of a carbide cutting bur mounted on a straight surgical handpiece. The implant head will be placed flash to the bone. At the end of the surgical procedure cover screws will be positioned and a careful adaption of the flaps by means of an accurate suture will be assured in order to obtain primary closure and full periosteal coverage.

Postoperative care

The patients will be instructed to rinse with a chlorhexidine 0.12% mouthwash twice a day for 2 weeks and to avoid using the denture. Liquid and semisolid food will be prescribed for the first postoperative week, after which the sutures will be removed. Two weeks after the surgery, the denture will be properly relined avoiding direct contact with the fixture until the second-stage surgery. Patients will be controlled at 4, 8, and 12 weeks.

Second surgical phase and prosthetic procedures

After 3 months of healing all implants will be exposed by separated linear incisions, cover screws will be removed and replaced by healing abutments. After 1 week, the final abutment (Uni-abutment, Astra Tech Implant System, Dentsply Sirona Implants, Mölndal, Sweden) will be screwed on each implant and an abutment-level impression will be registered. Expert clinicians will follow all the prosthetic phases. All patients will receive a fixed screw-retained full-arch prosthesis with distal cantilevers. The length of the bridge cantilevers will be calculated to minimize implant overloading (Mericske-Stern, Taylor & Belser, 2000). All prosthetic procedures will be made according to the Astra Tech Implant System procedures and products manuals.

Supportive peri-implant therapy

Patients will be instructed in proper hygiene measures, suitably designed and based on their individual needs, including tooth brushing, interdental brushing, flossing, and rinsing with an antiseptic mouth. Patients will be recalled every six months for a control visit and professional supragingival ultrasonic debridement and polishing.

Baseline and follow-up examinations

Radiographs and clinical examinations will be performed, together with primary and secondary outcome assessment, at baseline (final restoration placement), and after 1, 3 and 5 years of loading.

Clinical examination will include visual inspection to detect signs of inflammation as well as the occurrence of technical complications. Peri-implant probing depth, the presence of visible plaque and bleeding/suppuration on probing around implants will be also evaluated.
Peri-apical radiographs will be taken with Rinn Universal Collimator (Dentsply RINN, York, PA, USA) to limit exposure levels and Rinn film holders (XPC Extension Cone Paralleling System, Dentsply RINN, York, PA, USA), for correct positioning. Film-holder's position will be noted down for each implant site to increase reproducibility. The MBL will be determined (ImageJ 1.48a, National Institutes of Health, Bethesda, MD, USA) as the distance between the top of the micro-thread implant region and the most coronal level of the bone-to-implant contact, using inter-thread distance for calibration. All the radiographic measurements will be performed by an experienced examiner not otherwise involved in the study, who will be kept unaware of the implant length by duly masking the radiograms. Mesial and distal MBL will be measured at each fixture and the MBLc from the baseline will be calculated at each follow-up (negative values in case of bone loss). Mean values will be calculated at the implant, patient and group level.

Statistical analysis plan
Descriptive statistics (means, standard deviations) of continuous variables and relative frequencies of discrete variables will be computed for each group separately using a statistical software program. Data will be analysed by an examiner blinded to the experimental groups using the patient as the statistical unit unless differently specified. Intention-to-treat (ITT) analysis will be adopted. The Fisher exact test for discrete inter-group variables and the one-sided Mann-Whitney U-test for MBLc values will be applied, because of the nature of the data. For primary outcome, statistical significance will be set at the alpha level of 0.025 using a one-sided test, while for two-sided tests statistical significance will be set at the alpha level of 0.05.

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