Comparison of two Early Loading Protocols in Full Arch Reconstructions in the Edentulous Maxilla using the Cresco Prosthetic System. A 3-arm parallel group Randomised Controlled Trial.

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Running head: Early loading of implants with Cresco components for suprastructure

Abstract

Objectives: Appraise the feasibility of interchanging conventional components of a fixed dental prosthesis (FDP) with those of Cresco in two different early loading protocols. **Material and methods:** In five centers patients with an edentulous, fully healed maxilla were recruited to partake in a three-arm blinded randomized controlled trial (RCT). Each patient received 5/6 implants using a single-stage surgery approach to support a 10/12-unit FDP. The implants used were SLA solid screw two-part implants. In test groups 1 and 2 components from Cresco were used and the implants loaded 10 days or 6-8 weeks post-implant placement. Group 3 received their FDP fabricated with conventional components 6-8 weeks post-implant placement. Patients were followed up 3 years. **Results:** Of 36 patients 30 remained after 3 years. The adjusted means and ranges of changes in crestal bone levels were -0.65 mm, -0.5 mm and -0.40 mm in groups 1,2 and 3 respectively. The change from baseline was statistically significant in all treatment groups. Adjusting for the difference in implant depth, there was an expected additional change in bone level of -0.29 mm by each 1 mm the implant was placed deeper. There was no significant difference between the 6-8 weeks post-implant placement loading Cresco group versus the control group or between the two Cresco groups. **Conclusions:** The vertical placement has more effect on bone loss than the fabrication technique used for the suprastructure and whether the implants were loaded after 10 days versus 6 to 8 weeks.

The principles of modern implant treatment established some 30-40 years ago were based on adopting a two-stage procedure with a 4-6 month interval between implant placement and implant loading (Brånemark et al. 1977). This precautionary principle was applied based on the assumption that loading a newly placed implant too early would compromise or even completely inhibit the osseous healing around the implant (osseointegration). Other contemporary research teams advocated alternative approaches such as immediate postextraction implant placement with or without immediate implant loading using a one-stage surgical procedure (Linkow & Cherchéve 1970; Schröder et al. 1976 ; Ledermann 1979). The intensive research activity since then has generated a better understanding of bone healing, physiology and remodeling processes with regard to osseointegration and dental implants (Jokstad 2009).

Just before the turn of the millennium innovative approaches with a focus on immediate loading and function of implant-supported prostheses emerged (Szmukler-Moncler et al. 2000). The perceived advantages of immediate loading were that the patient would be able to resume oral functions and appearance more quickly post surgery and also avoid subsequent surgery sessions. Moreover, a fixed provisional prosthesis would potentially reduce the risks of excessive forces being applied to the non-osseointegrated implants by placing the occlusal forces in controlled physiological ranges. A few years later some 350 clinical trials had been conducted on immediate and early loading; however, a distinct minority of these were randomized clinical trials and none had a primary focus on time-to-loading of full jaw maxillary fixed prostheses (Roccuzzo et al. 2001; Gatti & Chiapasco 2002; Romeo et al. 2002; Tawse-Smith et al. 2002; Prosper et al. 2003; Rocci et al. 2003a, 2003b; Payne et al. 2003; Schropp et al. 2003; Esposito et al. 2004).

A critical element in implant-based prosthodontics is to fabricate a suprastructure that fits accurately to the implants with the assumption that poor fit is associated with increased risk of technical and biological complications (Brunski 1999; Sahin & Cehreli 2001). Other investigators have hypothesized that an improved fit of the suprastructure would subject the supporting implants to less micromotion and thereby allow implant loading earlier than usual (Ericsson & Nilner 2002). Conventional casting of alloys without creating distortions is a very technique-sensitive procedure, especially for non-precious or titanium alloys. Various fabrication techniques and position transfer devices have therefore been developed to optimize the fit of fixed partial dentures made from different alloys. Single-block milling concepts and laser-welded methods are new avenues in this respect and a system in the latter category for fabricating close-fitting suprastructures is the Cresco concept (Helldén et al. 1999; Helldén et al. 2003). In summary, the scientific documentation at the turn of the century based on data from clinical trials and laboratory experiments indicated that implants could have the potential to predictably osseointegrate even if loaded early under the condition that a close-fitting suprastructure was being used.

This study was designed to appraise the feasibility of interchanging conventional components of a fixed dental prosthesis (FDP) with those of Cresco in two different early loading protocols by comparing implant survival and vertical loss of crestal bone. The study hypothesis was that there would be no difference in bone loss between implants in the two Cresco-component FDPs versus implants supporting the FDPs made conventionally. A second hypothesis was that there would be no difference between the two Cresco groups when using a 10 day versus a 6-8 weeks post-healing loading protocol.

Materials and methods

The study protocol and patient information documentation were approved by the regional ethics institutional boards in Norway (#S-04162) and in Sweden (Dnr M102-04). Patient confidentiality procedures adhered to the national regulatory standards in Norway and Sweden. Necessary approval from the Norwegian Patient privacy ombud was acquired (#11123). The ClinicalTrials.gov identification number is: NCT00922935.

The study progress and case report form recordings (CRFs) were monitored by the study sponsor, who was responsible for collecting all original CRFs and radiographs and eventual adverse event forms, in accordance with ISO 14155 guidelines. Data, progress and compliance with the protocol were reviewed annually. A clinical research organization (Analytica intl., Lörrach, Germany) was responsible for the randomization allocation.

Seven public dental health clinical centres in Sweden and one university clinic in Norway familiar with the Straumann implant system committed to recruit patients after having participated in joint protocol development and calibration meetings.

Patient Population

Patients with an edentulous, fully healed maxilla with bone ridge width ≥ 7 mm and bone height ≥ 8 mm and who desired a 10- to 12-unit maxillary fixed dental prosthesis were recruited. Each patient was informed of the overall requirements and procedures of the study, the nature of the planned treatment, alternative procedures and the potential risks, possible complications and benefits of the proposed treatment. Several inclusion and exclusion criteria were applied (Table

1). Additional exclusion criteria applied during or after implant surgery were: 1. lack of primary stability of ≥ one implant(s) at surgery; 2. insufficient bone; or, 3. inability to place implants according to protocol requirements. In these instances the patient was withdrawn from the study.

All patients had read, understood and signed the written informed consent form at least 7 days before implant surgery. Patients could withdraw from the study at any time without prejudice and would be offered an appropriate alternative treatment. Patients were advised of the need for the prescribed follow-up visits for their ongoing care and well-being and for the collection of relevant study data as shown in Fig. 1.

Pre – prosthodontic and surgical procedures

Procedures at the pre-treatment visits included clinical examinations, appropriate medical history, determination of concomitant medication usage, and appropriate panoramic radiographs.

Each patient received five or six implants symmetrically placed with a spread to support a 10- to 12-unit fixed prosthesis. The most distally placed implants were in the 15 and 25 regions, in accordance with national health insurance standard of care protocols.

The implant surgeries were performed under sterile conditions in an outpatient environment or a dental practice. Prophylactic antibiotic therapy was given at the surgeon's discretion according to each centre's standard practice. Single-stage implant surgery was performed under local anaesthesia using a reflected full-thickness mucoperiosteal flap. To avoid unnecessary soft-tissue damage, surgical retractors were not typically used. Careful ridge alveoloplasty was usually performed to achieve a flat bone surface of sufficient width. In situations with a narrow ridge crest, reduction was permitted to obtain the necessary width of at least 7 mm in a palatinal-buccal direction.

The implants used were SLA solid screw two-part implants (Institut Straumann AG, Basel, Switzerland) with diameters of 3.3 mm (lengths 8-14 mm) or 4.1 mm (lengths 6-14 mm). Standard Plus implants were predominantly used, but the use of Standard implants was also allowed, provided that only one implant type was consistently used in each patient.

The surgeons followed the implant manufacturer's guidelines for standard procedures relating to bone excavation, bone preparation and placement of the implants. Drilling procedures were performed with light hand pressure and sink depth controlled with a depth gauge. The recipient site was flushed with sterile saline and the implant placed using an insertion device, with a hand ratchet or motor drive for the final torque step. Insertion torque was recorded and primary implant stability was immediately assessed by hand testing. Any lack of primary stability at this stage led to exclusion of the patient from the study. The implant site was closed and sutured with the implant head exposed as per the manufacturer's recommended protocol.

Following implant placement, standard open tray impression copings were screwed onto the implant heads and the soft tissues were sutured. The surgical stent was used as an impression tray, as described by other investigators (Colomina 2001; Becker et al. 2003). The pre-existing prosthesis was duplicated and modified by trimming the palatal anterior flange, allowing the duplicate to be used as a surgical template and as an impression tray. After lingual reduction, impression copings could be accommodated without interfering with the duplicate in its correct position, as ascertained by a maxilla-mandibular index. The open tray impression materials were either a poly-vinyl-siloxane or a polyether elastomer (Fig. 2a-f). The opaque envelope containing the randomisation code was opened only after the impression was completed.

Depending on the study arm allocation, the patient received either an implant closure screw or a healing cap. If any implant turned on tightening of the healing screw then the implant was considered to have failed the primary stability test and the patient was withdrawn from the study.

Patients were instructed not to brush in the treated area, and to rinse twice daily for one minute with chlorhexidine digluconate for plaque control. Analgesics were given as required for pain control and prophylactic antibiotic coverage, as previously described.

Randomization

Each patient was allocated to one of three groups following a randomisation list generated by an independent statistician. Each patient was assigned a unique participant number and was allocated treatment according to a sealed numbered randomisation opaque envelope from the study sponsor. The opaque envelope was opened first after the impression taking and was maintained as source document, in accordance with the study protocol.

If a removable prosthesis was opposite the study implants the patient was advised to not use the opposing prosthesis for 2 weeks after surgery. At approximately 10 days the patients were recalled for suture removal.

Prosthodontic procedures

The three restorative protocols were as follows:

Test Group1: loading 10 days post-implant placement using Cresco (Cresco Ti Systems, Sarl, Lausanne, Switzerland) components

A permanent screw-retained FDP was placed within 10 days following implant placement. Further adjustments to the FDP could be done up to 14 days post implant-placement, but if not completed by this time, the patient was withdrawn.

Test Group 2: loading 6-8 weeks post-implant placement using Cresco components
The minimum healing period was 4 weeks, and the implants were loaded with a permanent screw-retained FDP within 42-56 days (6 to 8 weeks) of implant placement surgery.

Control Group: loading 6-8 weeks post-implant placement using conventional components
The minimum healing period was 4 weeks, and the implants were loaded with a permanent screw-retained FDP within 42-56 days (6 to 8 weeks) of implant placement surgery.

All patients wore a relined denture with teeth in full functional occlusion during the interim healing period. The FDP was also placed in full functional occlusion at the time of loading. A maximum of one unit cantilever on either quadrant was incorporated, in accordance with national health insurance standard of care guidelines. Functional occlusion was tested by clear resistance to dragging a 6 micrometer Shimstock through the teeth in normal occlusion. Temporary measures (use of acrylic) to build up the temporary removable prosthesis were permitted, to avoid the patient being without the prosthesis for a long period.

Dental Laboratory procedures

In the Cresco study arms the permanent FDPs were made using regular components selected from the Cresco catalogue range in combination with the appropriate All-Parts-Included (API) set from Straumann. The FDP was fabricated by a Cresco accredited laboratory according to the manufacturer's guidelines. In the control group the FDP was constructed using the standard prosthetic components from Straumann in accordance to the manufacturer's instructions.

Each of the clinical centres cooperated with only one laboratory throughout the study to reduce heterogeneity. The centres were also given the opportunity to choose whether the conventionally made FDPs were to be made by their customary dental laboratory or by the licensed Cresco laboratory.

Baseline

Baseline was considered as the time of implant loading with the fixed dental prosthesis. Before loading, implant mobility was tested by direct finger manipulation around the implants with or without evaluating the tapping sound made with a hand instrument.

Rinn XCP film-holders (Dentsply Rinn, Elgin, IL, USA) were customised to each patient by adapting the film-holders to the occlusal surface of the FDP using a heavy body elastomer while ensuring a position of the film tangential to the indicator arm. Film-holders were marked and kept for future recordings, enabling subsequent repeat standardized periapical x-rays.

Radiographs were taken with the film placed parallel to the implants and the x-ray beam directed perpendicular to the implants to include at least two coronal implant threads.

Recalls

Patients were followed up throughout the study at 3 and 6 months, and 1, 2, and 3 years from baseline. Standard clinical examinations, including assessment of periodontal health were performed. Mobility was measured indirectly by movement of the FDP, radiographic radiolucency or clinical signs and symptoms around the implant. If mobility was detected the FDP was removed to test whether the prosthesis or any of the implants appeared to be mobile.

Oral hygiene was assessed using sulcus bleeding, plaque index and oral hygiene criteria (Mombelli et al. 1987). If indicated, the FDP was cleaned of plaque or calculus and oral hygiene maintenance was reinforced.

Patient satisfaction was determined by using a questionnaire containing questions about the perceived appearance, ability to chew, comfort, general satisfaction and ability to taste, ranked as excellent, good, fair or poor. All patient complaints or any complications resulting from a change in health status from baseline or any implant-related complications such as pain, paresthesia or peri-implant infection were recorded and monitored.

Radiographic measurements

Periapical radiographs using the customized film holders were taken at all examinations. The same type of film was used throughout the study for consistency. Individual radiographs were digitized using a digital camera (Nikon Coolpix 995, Melville, NY, USA) mounted on a copy stand at 8” distance and subsequently measured using public domain software (ImageJ, U.S. National Institutes of Health, USA).

Bone level measurement was blinded and performed independently by an investigator unrelated to the study. The assessor was calibrated with the lead author and repeat measures were done until the intraclass correlation was > 95%. Mean values were used and repeated if the two measurements deviated more than 0.5 mm. Vertical distances in millimeters from the implant shoulder to the most apical initial point of first visible bone contact (depth of implant bone contact; DIB) were measured for both proximal sites using the measurement tool function of the software. Eventual misalignments of the film planes relative to the implant long axis were accounted for by calibrating the software for each measurement to the known thread pitch of the implants.

Evaluations

Changes in crestal bone levels between the baseline and 1, 2, and 3 years post loading was measured on the digitized periapical radiographs. All occurrences of technical and biological complications and adverse events were noted, including implant mobility, peri-implant radiolucency, peri-implant recurrent infection, structural failure of the implant and framework adverse events.

Statistical analyses

Two different statistical analytical approaches were used, one where all implants were taken into account and the other where only one implant was taken as representative of all. In the first analysis with multiple implants, the patients build the clusters in the dataset. For the second analysis both a mixed model and a cumulated logit model was applied.

The distribution of the continuous responses was appraised by applying the Kolmogorov-Smirnov test and graphical presentation of the distribution with special emphasis on symmetry, outliers and skewness. The outcome of this test suggested that premises were adequate for using a “mixed model with random cluster-specific effect and fixed effects TIME, GROUP and TIME x GROUP”. In addition, two-factorial nonparametric analysis of variance (Friedman test) was applied as a further check.

The dependent response in both types of analysis was the change of bone level over time, specifically the difference in bone level between the three groups, i.e. the response of a matched pair design, evaluated by paired t-test.

The statistical ANOVA type model was used, especially a mixed model with random effect “patient” and fixed effects GROUP (3 levels), TIME, TIME x GROUP. The main effect to be tested was GROUP and sample size considerations were focused on this effect.

Sample size considerations

Sample sizes were calculated for a two-sided test to compare two independent groups with one implant each by the two-sample t-test (analysis 2), as well as for six implants per patient (analysis 1). For the minimum sample sizes to detect differences in mean bone level it is necessary to take into account the estimated standard deviation. In previously published clinical trials the standard deviation (SD) of bone level varies from 0.1 to 0.3 mm (6-16). Anticipating an SD of 0.2 mm and considering a mean difference of 0.1 mm bone loss between groups 1 and 2 and the control group (3) at 1 year as clinically significant, a study with 80% power with an overall significance level of $p = 0.05$ indicated a minimum of 22 patients per group.

All statistical analyses were done using SPSS statistical software (SPSS Inc., Chicago, IL, USA).

Results

In total, 43 patients were assessed for participation eligibility and 40 participants in the period between October 2004 and May 2006 received treatment before the trial was closed for further recruitment.

At the time of surgery four patients were not included in the study due to insufficient bone, while 36 patients received implants and were subsequently randomly allocated to one of three study arms. The three study groups were similar regarding clinical and demographic characteristics apart from gender, bone quality and size as well as average depth of implant placement (Table 2).

The types of implants favored by the surgeons were rather limited, i.e, only six out of the approximately twenty eligible implants of the standard and standard plus types were used, of which the ø=4.1 x 12 mm standard plus implant was preferred (Fig. 3).

Four patients received their allocated intervention although not per protocol, either due to the inability to place, or obtain primary stability of all six implants (Fig. 4). All four patients were examined at the 1- and 3-year follow-up examination.

Three patients in the Cresco 6-8 weeks post-loading group were withdrawn from the study prior to the first follow-up examination at 6 months. One patient failed to show-up for further treatment after having received the implants. The two others were excluded as satisfactory osseointegration was not achieved for one and the Cresco components could not be used for the other. One patient in the same group died before the 12-month examination. The

final withdrawal in this group was a patient who due to phonetic and functional problems replaced the Cresco-made FDP with a new bridge after 2.5 years. In the 10 days postloading group one patient died before the 12-month examination.

A single occurrence of a localized peri-implantitis at approximately 2.8 years was treated uneventfully by penicillin. No other implant-related complications occurred during the 3 years. Prosthodontic complications and failures were rare. In the Cresco groups one patient required a correction immediately after receiving the supra-structure and a second patient required a fracture repair after approximately 3 years. In the control group three patients experienced multiple repeat repairs due to tooth fractures and/or loosening.

Periodontal indices such as plaque index, peri-implant pocket probing depth and sulcus bleeding did not differ significantly per implant surface distal, buccal, lingual and mesial or per implant in sum (Fig. 5). Patient satisfaction scores were high in all three study groups regarding general satisfaction, comfort, satisfaction with appearance and ability to chew and taste . No further calculations were performed to elucidate statistical relationships due to the relatively small study sample size.

The vertical implant placement depth varied markedly, ranging between having the first implant thread situated 0.6 mm above the bone crest to 4.2 mm below (Fig. 6).

The bone level changes between baseline and 12 months were normally distributed as assessed by the Kolmogorov-Smirnov test, so a mixed model analysis for change in bone level could be made with subject as random effect. Significant effects for the implant depth at baseline ($p = < 0.001$) and implant position (most posterior, most anterior or middle, $p = 0.021$) were identified. Implant type, bone form and the implant position * treatment group interaction were

borderline significant. Treatment group, center, bone quality, crest width, available bone height, treatment group * centre interaction and the treatment group * implant type interaction were all not significant. After removing non-significant effects from the model, the borderline significant effects also became non-significant and the implant position became only borderline significant ($p = 0.07$). Therefore, a final model with treatment group, implant depth at baseline and implant position as independent parameters was chosen. The adjusted means and ranges of changes in crestal bone levels were -0.65 mm (-1.07 to -0.24), -0.5 mm (-0.68 to -0.32) and -0.40 mm (-0.62 to -0.19) in the 10 days post-implant placement loading Cresco group, 6-8 weeks post-placement Cresco and cast FDP groups respectively. The change from baseline was statistically significant in all treatment groups. As expected from the non-significant global p-value, the comparisons between the treatment groups were not significant. Assuming a non-inferiority margin of 0.3 mm, clinically relevant superiority of the Cresco groups compared to the control group could be excluded, but inferiority of the Cresco groups compared to the control group could not be excluded. Adjusting for the difference in implant depth, there was an expected additional change in bone level of -0.29 mm by each 1 mm the implant was placed deeper. Without adjusting for implant depth, there was a significant difference between the 10 days post-implant placement loading Cresco group versus the control group, but there was no significant difference between the 6-8 weeks post-implant placement loading Cresco group versus and the control group or between the two Cresco groups.

The average bone loss over 3 years amongst the six implants supporting the double-sided single-unit cantilever suprastructure was 0.5 mm (SD 0.9) for the medial pair, 0.9 (SD 1.1) for the two implants in the cuspid regions and 0.5 mm (SD 0.9) for the two most distal implants. The respective bone loss for these implants in the three study groups were 0.9 – 1.3 – 0.6 mm for

the Cresco 10 days postloading group; 0.3 – 0.8 – 0.7 mm for the Cresco 6-8 weeks postloading group and 0.4—0.5 – 0.3 mm for the conventional bridge 6-8 weeks postloading group. Thus, the cantilever did not seem to accelerate bone loss on the most distally placed implants.

Discussion

The protocol of this multicentre randomised controlled trial was designed in accordance with the EC directive 2001/20/EC on medical devices and also followed the current ISO14155 guidelines. Data, progress and compliance with the protocol were reviewed annually and involved even an external clinical research organization. The estimates of the sample sizes to reach 80% power indicated that 22 patients would be needed in each study arm. Seven public dental health clinical centres in Sweden and one university clinic in Norway familiar with the Straumann Dental Implant system committed to recruit patients after having participated in joint protocol development and calibration meetings. An unforeseen difficulty was that the Swedish national health insurance regulations requiring funding pre-approval could not be aligned with simultaneous screening of patients for trial inclusion. Three Swedish clinical centers had therefore to withdraw from this study and the remaining centres were challenged with accruing enough participants to compensate for the loss. A strategic decision was therefore made in the spring of 2006 to close the patient recruitment period and report on the accumulated findings. It was reasoned that although the study has a lower power than planned, the findings would be of scientific value due to the high internal validity of this clinical trial. Moreover, if the hypothesis for the study was to be rejected, at least a trend towards more positive outcomes associated with the Cresco 10 days implant placement postloading group should be expected.

The randomisation process resulted in fairly equal groups apart from gender, bone quality and form. (Table 2). The gender imbalance in the control group is probably coincidental and may or not be correlated with the unequal bone quality distributions. Moreover, in the control group the higher proportion of knife-form should be linked with the higher proportion of crest widths less than 7 mm, which signify that the clinicians in these situations reduced the heights to obtain the necessary width of at least 7 mm in a palatinal-buccal direction.

The implant placement depth seemed to differ between the 10 days group versus the two other study groups. This difference can partly be explained to be a consequence of the fact that the timing of the baseline radiographs differed between 10 days post-implant placement versus 6-8 weeks post-implant placement. There is limited information about how bone loss progress in this early phase following implant placement, but it has been proposed that it is more pronounced during the first and second months with estimates of about 0.4-0.6 mm (Brägger et al. 1992; Brägger 1998) and even more if the implant is placed deeper into the bone (Hämmerle et al. 1996).

At the time of the protocol development for the current study the study arms were defined as early and delayed loading. However, the terminology used to describe the time-to loading of dental implants has since changed. Currently, the favoured interpretation of the term “early loading” seems to be defined as being between 1 week and 2 months subsequent to implant placement (Weber et al. 2009). The debate will probably not abate since the current terms are defined more by consensus rather than by some operational criteria determined by clinical or biological parameters. For this reason the terms immediate, early, conventional and delayed loading have been avoided in this report in favour of using the terms 10 days respectively 6-8 weeks post-implant placement.

The interface space between a fixed suprastructure and its supporting implants is measurable and can be assessed using a range of methods (Kan et al. 1999). Different terms are being used to describe this interface space such as “misfit” or “gap” or “distortion” or “microgap” or “level of passive fit”. Nevertheless, the consensus on what constitutes acceptable level of misfit with regards to clinical significance remains speculative and controversial. Proposals for acceptable maximum margins have ranged between 10 цm (Brånemark et al. 1977) and 100 цm (Jemt & Book 1996) and rationale based on alleged increased risks of biological and/or technical complications beyond these limits. Focus has specifically been on accelerated bone loss and higher incidence of screw loosening, with or without taking into account functional forces (Sahin et al. 2002). The alleged correlation between degree of misfit and biological and/or technical complications is further obfuscated by the possibilities of localized cyclic microgaps developing during occlusal loading. Relevant variables in this regard are the implant-abutment design and the masticatory and dynamic functional loads and force vector directions as a function of the three-dimensional suprastructure-abutment-implant configuration (Hecker & Eckert 2003; Zipprich et al. 2004).

While some animal studies suggest that peri-implant crestal bone around two-piece implants may be associated with the size of the microgap between components (Hermann et al. 1997; Broggini et al. 2006) at least one well designed human clinical study over 5 years does corroborate such findings (Heijdenrijk et al. 2006). Although based on low number of observations in a retrospective study it has been proposed that a certain degree of non-passive fit between the components does not influence bone loss (Jemt & Book 1996). The current randomized controlled trial seems to support this hypothesis.

The alleged association between degree of misfit and long-term effects on screw preload is also unclear (16). While torque and detorque values are relatively easy to measure in an

artificial laboratory environment and mathematical models can be hypothesized, such theoretical models are not necessarily replicated in vivo in general (Sahin et al. 2002) or specifically to the Cresco system (Schmitt et al. 2009). The latter clinical study reported that within the first 3 months the screw-joint stability between implants and the suprastructure decreased in average approximately 30%. Moreover, the decrease was not influenced by manufacturing technique, i.e. Cresco-manufactured or conventional cast, nor implant system, i.e., Straumann or Brånemark implants (Schmitt et al. 2009).

That the clinical performance of the implants supporting suprastructures made using the Cresco components are comparable to those supporting FDPs made by conventional methods using manufacturer components has also been demonstrated in two retrospective studies over 5 to 8 years involving Brånemark implants (Hedkvist et al. 2004) and 3 years involving Brånemark and Astra (Hjalmarsson & Smedberg 2005) implants.

The 3-year clinical results for the Cresco 10 days post-implant placement group from this multicentre study is slightly better than a relatively comparable study employing similar implants and treatment indications (Nordin et al. 2007). The difference between the two studies was that the former combined implants placed in extraction sockets and healed bone in an approximately 2:1 ratio to support the suprastructure while the current study required at least 3 months healing.

Conclusion

The null hypothesis of this study could not be confirmed. The data generated from this RCT suggest that the vertical placement of the implant has a more direct effect on bone loss over the first 3 years than the fabrication technique used for the suprastructure and whether the implants were loaded at 10 days or at 6 to 8 weeks.

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References

Becker, W., Becker, B.E. & Huffstetler, S. (2003) Early functional loading at 5 days for Brånemark implants placed into edentulous mandibles: a prospective, open-ended, longitudinal study. *Journal of Periodontolology* 74: 695-702.

Broggini, N., McManus, L.M., Hermann, J.S., Medina, R., Schenk, R.K., Buser, D. & Cochran, D.L. (2006) Peri-implant inflammation defined by the implant-abutment interface. *Journal of Dental Research* **85**: 473-478.

Brunski, J.B. (1999) In vivo bone response to biomechanical loading at the bone/dental-implant interface. *Advances in Dental Research* **13**: 99-119.

Brånemark, P.I., Hansson, B.O., Adell, R., Breine, U., Lindström, J., Hallén, O. & Ohman, A. (1977) Osseointegrated implants in the treatment of the edentulous jaw. Experience from a 10-year period. Pp. 1-132. Stockholm: Almqvist & Wiksell International.

Brägger, U., Burgin, W., Fourmousis, I. & Lang, N.P. (1992) Image processing for the evaluation of dental implants. *Dentomaxillofacial Radiology* **21**: 208-212.

Brägger, U. (1998) Use of radiographs in evaluating success, stability and failure in implant dentistry. *Periodontolology 2000* **17:** 77-88.

Colomina, L.E. (2001) Immediate loading of implant- fixed mandibular prostheses: a prospective 18-month follow-up clinical study – preliminary report. *Implant Dentistry* **10**: 23–29.

Ericsson, I. & Nilner, K. (2002) Early functional loading using Brånemark dental implants. *International Journal of Periodontics and Restorative Dentistry* **22**: 9-19.

Esposito, M., Worthington, H.V. & Coulthard, P. (2004) Interventions for replacing missing teeth: different times for loading dental implants (Cochrane Review). In: *The Cochrane Library,* Issue 2. Chichester, UK: John Wiley & Sons, Ltd.

Gatti, C. & Chiapasco, M. (2002) Immediate loading of Brånemark implants: a 24-month follow-up of a comparative prospective pilot study between mandibular overdentures supported by conical transmucosal and standard MKII implants. *Clinical Implant Dentistry and Related Research* **4**: 190-199.

Hecker, D.M. & Eckert, S.E. (2003) Cyclic loading of implant-supported prostheses: changes in component fit over time. *Journal of Prosthetic Dentistry* **89**: 346-351.

Hedkvist, L., Mattsson, T. & Hellden, L.B. (2004) Clinical performance of a method for the fabrication of implant-supported precisely fitting titanium frameworks: a retrospective 5- to 8-year clinical follow-up study. *Clinical Implant Dentistry and Related Research* **6**: 174-180.

Heijdenrijk, K., Raghoebar, G.M., Meijer, H.J., Stegenga, B. & van der Reijden, W.A. (2006) Feasibility and influence of the microgap of two implants placed in a non-submerged procedure: a five-year follow-up clinical trial. *Journal of Periodontolology* **77**: 1051-1060.

Helldén, L., Ericson, G., Elliot A., Fornell, J., Holmgren, K., Nilner, K. & Olsson, C.O. (2003) A prospective 5-year multicenter study of the Cresco implantology concept. *International Journal of Prosthodontics* **16**: 554-562.

Helldén, L.B., Dérand, T., Johansson, S. & Lindberg, A. (1999) The CrescoTi Precision method: description of a simplified method to fabricate titanium superstructures with passive fit to osseointegrated implants. *Journal of Prosthetetic Dentistry* **82**: 487-491.

Hermann, J.S., Cochran, D.L., Nummikoski, P.V. & Buser, D. (1997) Crestal bone changes around titanium implants. A radiographic evaluation of unloaded nonsubmerged and submerged implants in the canine mandible. *Journal of Periodontology* **68**: 1117-1130.

Hjalmarsson, L. & Smedberg, J.I. (2005) A 3-year retrospective study of Cresco frameworks: preload and complications. *Clinical Implant Dentistry and Related Research* **7**:189-199.

Hämmerle, C.H., Brägger, U., Bürgin, W. & Lang, N.P. (1996) The effect of subcrestal placement of the polished surface of ITI implants on marginal soft and hard tissues. *Clinical Oral Implants Research* **7**: 111-119.

Jemt, T. & Book, K. (1996) Prosthesis misfit and marginal bone loss in edentulous implant patients . *International Journal of Oral and Maxillofacial Implants* **11**: 620-5

Jokstad, A. (2009) Osseointegration and Dental Implants. Pp. 1-418. Ames, Iowa: Wiley Blackwell.

Kan, J.Y., Rungcharassaeng, K., Bohsali, K., Goodacre, C.J. & Lang, B.R. (1999) Clinical methods for evaluating implant framework fit. *Journal of Prosthetic Dentistry* **81**: 7-13.

Ledermann, P.D. (1979) Stegprothetische Versorgung des zahnlosen Unterkiefers mit Hilfe von plasmabeschichteten Titanischraubenimplanten. *Deutsche Zahnärztliche Zeitung* **34**: 907–911.

Linkow, L.I., Cherchéve, R. (1970) In: Theories and techniques of oral implantology. Volume I, Pp.74-76. St Louis: CV Mosby Company.

Mombelli, A., van Oosten, M.A., Schurch, E. Jr & Lang, N.P. (1987) The microbiotica associated with success of or failing osseointegration of titanium implants. *Oral Microbiology and Immunology* **2**: 145-151.

Nordin, T., Graf, J., Frykholm, A. & Helldén, L. (2007) Early functional loading of sand-blasted and acid-etched (SLA) Straumann implants following immediate placement in maxillary extraction sockets. Clinical and radiographic result. *Clinical Oral Implants Research* **18**: 441-451

Payne, A.G., Tawse-Smith, A., Thompson, W.M. & Kumara, R. (2003) Early functional loading of unsplinted roughened surface implants with mandibular overdentures 2 weeks after surgery. *Clinical Implant Dentistry and Related Research* **5**: 143-153.

Prosper, L., Gherlone, E.F., Redaelli, S. & Quaranta, M. (2003) Four-year follow-up of larger-diameter implants placed in fresh extraction sockets using a resorbable membrane or a resorbable alloplastic material. *International Journal of Oral and Maxillofacial Implants* **18**: 856-64.

Rocci, A., Martignoni, M. & Gottlow, J. (2003) Immediate loading in the maxilla using flapless surgery, implants placed in predetermined positions, and prefabricated provisional restorations: a

retrospective 3-year clinical study. *Clinical Implant Dentistry and Related Research* 5 Suppl 1: 29-36.

Rocci, A., Martignoni, M. & Gottlow, J. (2003) Immediate loading of Brånemark System TiUnite and machined-surface implants in the posterior mandible: a randomized open-ended clinical trial. *Clinical Implant Dentistry and Related Research* 5 Suppl 1: 57-63.

Roccuzzo, M., Bunino, M., Prioglio, F. & Bianchi, S.D. (2001) Early loading of sandblasted and acid-etched (SLA) implants: a prospective split-mouth comparative study. *Clinical Oral Implants Research* **12**: 572-578.

Romeo, E., Chiapasco, M., Lazza, A., Casentini, P., Ghisolfi, M., Iorio, M. & Vogel, G. (2002) Implant-retained mandibular overdentures with ITI implants. *Clinical Oral Implants Research* **13**: 495-501.

Sahin, S., Cehreli, M.C. & Yalçin, E. (2002) The influence of functional forces on the biomechanics of implant-supported prostheses--a review. *Journal of Dentistry* **30**: 271-282.

Sahin, S. & Cehreli, M.C. (2001) The significance of passive framework fit in implant prosthodontics: current status. *Implant Dentistry* **10**: 85-92.

Schmitt, J., Holst, S., Eitner, S., Schlegel, A., Wichmann, M. & Hamel, J. (2009) Prosthetic screw detorque values in implants retained as cast bar superstructures or bars modified by the Cresco Ti Precision technique--a comparative in vivo study. *International Journal of Prosthodontics* **22**: 193-200.

Schropp, L., Kostopoulos, L. & Wenzel, A. (2003) Bone healing following immediate versus delayed placement of titanium implants into extraction sockets: a prospective clinical study. *International Journal of Oral and Maxillofacial Implants* 2003; **18**: 189-199.

Schröder, A., Pohler, O.M. & Sutter, F. (1976) Gewebsreaktion auf ein Titan Hohlzylinder implant mit Titan-spritzschichtoberfläche. *Schweizerische Monatsschrift für Zahnheilkunde* **86**: 713-716.

Szmukler-Moncler, S., Piattelli, A., Favero, G.A. & Dubruille, J.H. (2000) Considerations preliminary to the application of early and immediate loading protocols in dental implantology. *Clinical Oral Implants Research* **11**: 12-25.

Tawse-Smith, A., Payne, A.G., Kumara, R. & Thomson, W.M. (2002) Early loading of unsplinted implants supporting mandibular overdentures using a one-stage operative procedure with two different implant systems: a 2-year report. *Clinical Implant Dentistry and Related Research* **4**: 33-42.

Weber, H.P., Morton, D., Gallucci, G.O., Roccuzzo, M., Cordaro, L. & Grutter, L. (2009) Consensus statements and recommended clinical procedures regarding loading protocols. *International Journal of Oral and Maxillofacial Implants* 24 Suppl:180-183.

Zipprich, H., Weigl, P., Fischbach-Sedlatschek, S. & Lauer, H-C. (2004) Failure mode of implant-abutment connections after horizontal cyclic loading. *International Poster Journal of Dental and Oral Medicine* **6(30)** Poster 238.

Legend to figures.

Fig. 1. Progress of the study over 36 months for the three study groups.

Fig. 2. The duplicate of the original prosthesis is used as a surgical stent (upper left) before being converted to an open-impression-tray in a pre-determined maxilla-mandibular jaw relation. Upper right picture show the impression copings placed on the implant platforms following suturing. The following pictures show the elastomer impression, in this case Impregum contained within red wax, and the copings contained in the impression. The bottom pictures show left, the implant with the cover screws and right the original prosthesis relined with a soft-liner, in this case GC Soft Reline.

Fig. 3. Distribution of implant types used in the trial.

Fig. 4. Flow of participants through each stage of the study.

Fig. 5. Average sulcus bleeding index over 36 months. Line with triangles are the control group, squares the Cresco 6-8 weeks and diamonds the Cresco 10 days postloading group. (Score 0: no bleeding when a periodontal probe is passed along the gingival margin adjacent to the implant, score 1: isolated bleeding spot visible, score 2: blood forms a confluent red line on margin and score 3: heavy or profuse bleeding).

Fig 6. Examples of high, medium and deep vertical placement of SLA solid screw implants. Left graphic display of implant for illustrative purpose. Implant apex width is ø=4.1 mm; platform width is ø=4.8 mm; cervical polished neck is 1.8 mm; the distance between threads is 1.25 mm.

Fig. 1.

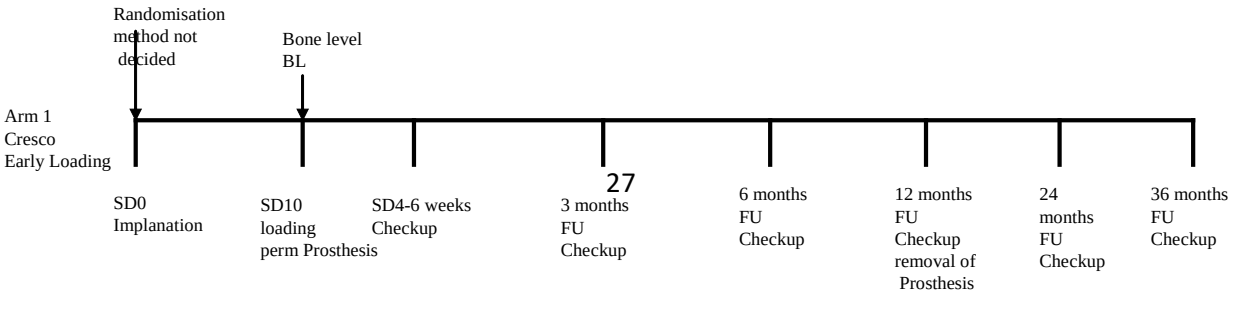

Fig. 2.

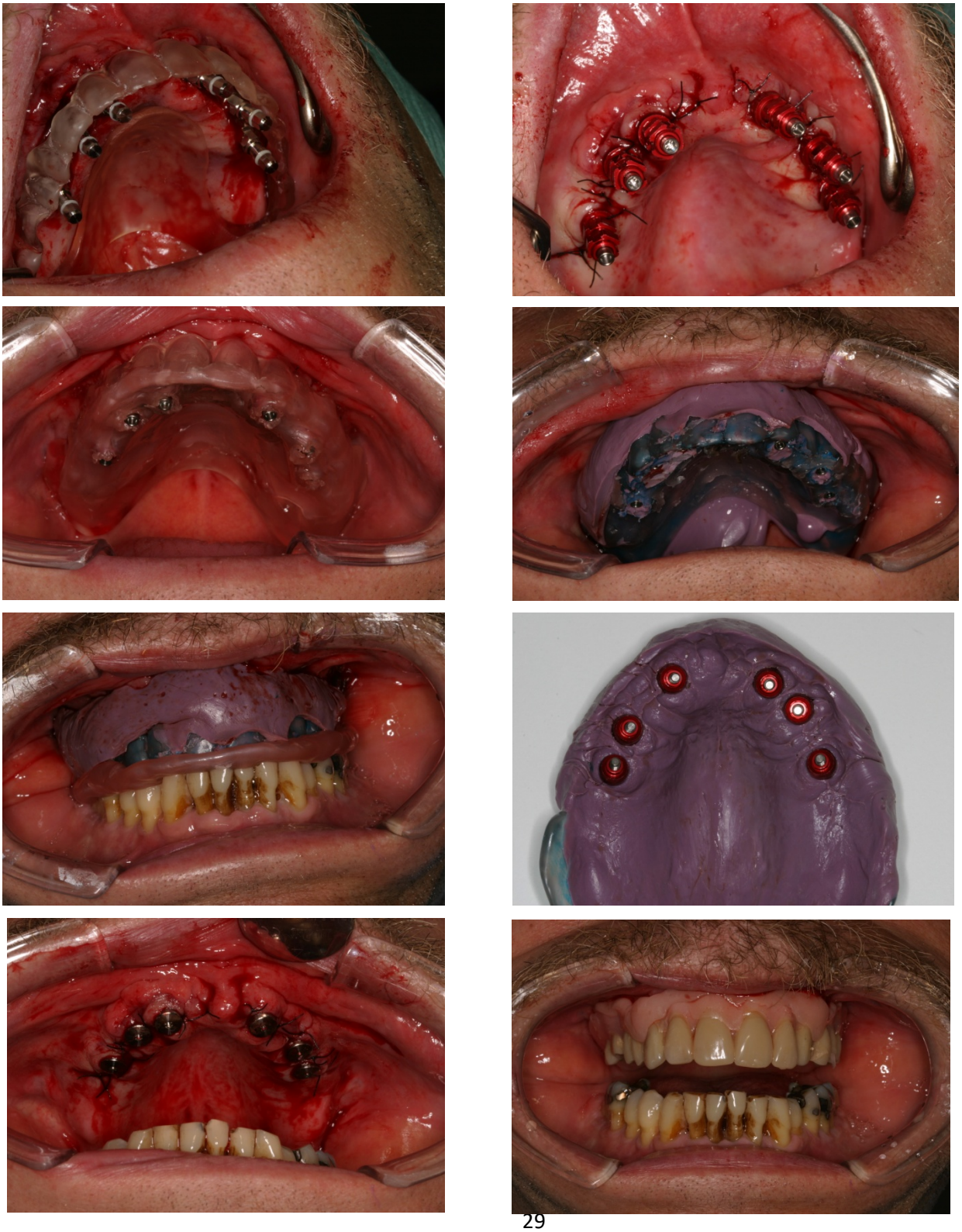

Fig. 3.

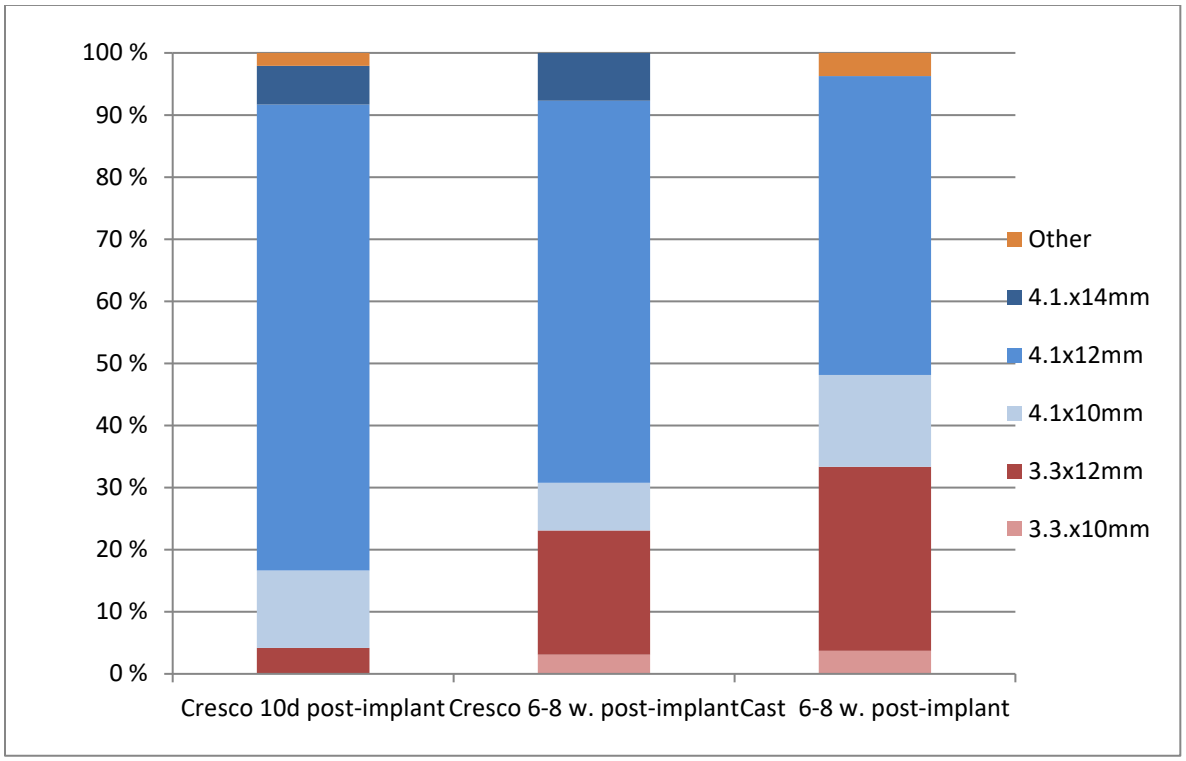
100 %
90 %
80 %
70 %
60 %
50 %
40 %
30 %
20 %
10 %
0 %
Other
4.1.x14mm
4.1x12mm
4.1x10mm
3.3x12mm
3.3.x10mm
Cresco 10d post-implant
Cresco 6-8 w. post-implant
Cast 6-8 w. post-implant

Fig. 4.

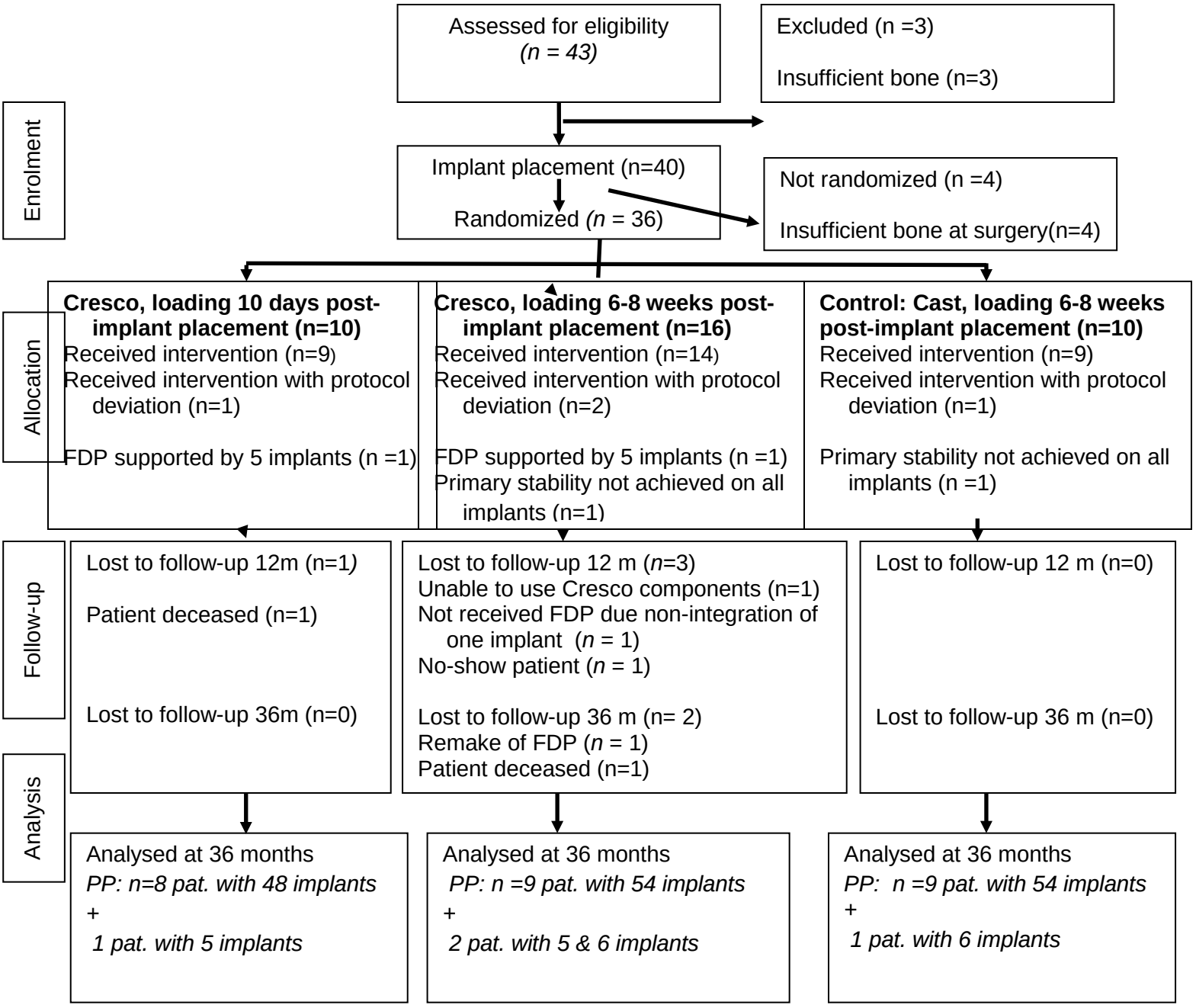
Assessed for eligibility
(n = 43)
Excluded (n =3)
Insufficient bone (n=3)
Enrolment
Implant placement (n=40)
Randomized (n = 36)
Not randomized (n =4)
Insufficient bone at surgery(n=4)
Allocation
Cresco, loading 10 days post-implant placement (n=10)
Received intervention (n=9)
Received intervention with protocol deviation (n=1)
FDP supported by 5 implants (n =1)
Cresco, loading 6-8 weeks post-implant placement (n=16)
Received intervention (n=14)
Received intervention with protocol deviation (n=2)
FDP supported by 5 implants (n =1)
Primary stability not achieved on all implants (n=1)
Control: Cast, loading 6-8 weeks post-implant placement (n=10)
Received intervention (n=9)
Received intervention with protocol deviation (n=1)
Primary stability not achieved on all implants (n =1)
Follow-up
Lost to follow-up 12m (n=1)
Patient deceased (n=1)
Lost to follow-up 36m (n=0)
Lost to follow-up 12 m (n=3)
Unable to use Cresco components (n=1)
Not received FDP due non-integration of one implant (n = 1)
No-show patient (n = 1)
Lost to follow-up 36 m (n= 2)
Remake of FDP (n = 1)
Patient deceased (n=1)
Lost to follow-up 12 m (n=0)
Lost to follow-up 36 m (n=0)
Analysis
Analysed at 36 months
PP: n=8 pat. with 48 implants
+
1 pat. with 5 implants
Analysed at 36 months
PP: n =9 pat. with 54 implants
+
2 pat. with 5 & 6 implants
Analysed at 36 months
PP: n =9 pat. with 54 implants
+
1 pat. with 6 implants

Fig. 5.

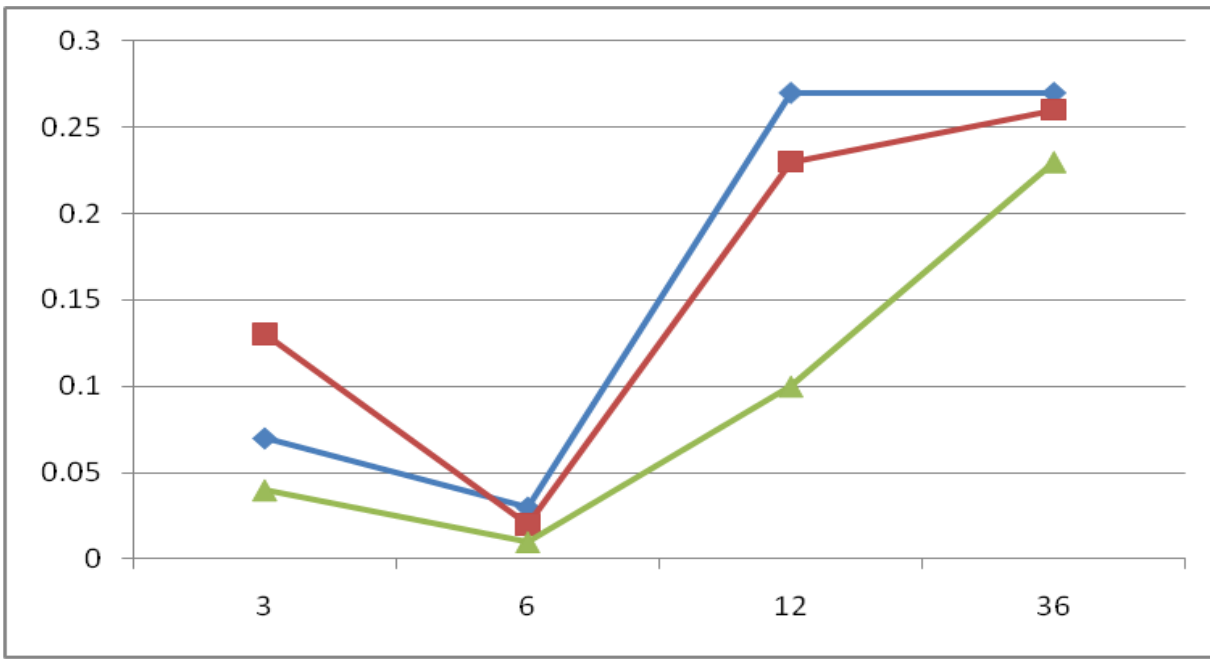

Fig. 6.

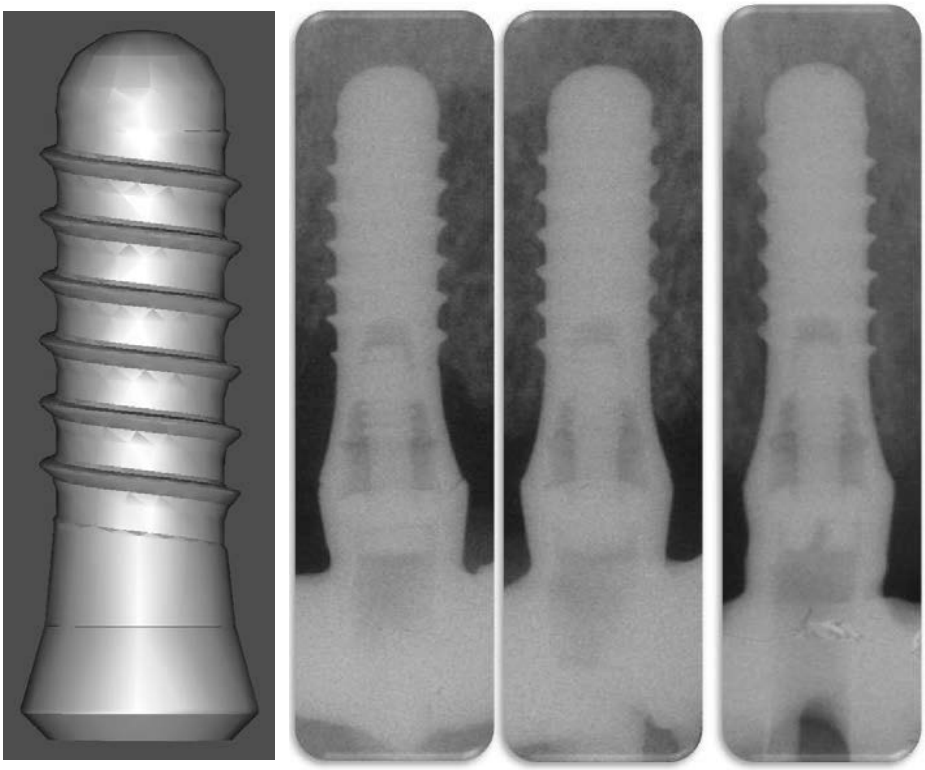

Table. 1. Inclusion and exclusion criteria.

Inclusion criteria	**Exclusion criteria**
• Aged ≥ 18 years • Edentulous maxilla (at least 3 months before date of surgery) and request for implant-supported screw-retained FDP • GBR/GTR completed ≥ 6 months before implant surgery • Adequate bone quality and quantity for placement of 3.3/4.1 mm implants without bone augmentation • Agreement to participate in study up to 3 years follow-up	*Systemic* • Conditions requiring chronic antibiotic prophylaxis • Conditions requiring prolonged steroid use • History of leukocyte dysfunction or deficiency, bleeding disorders, neoplastic disease, renal failure, uncontrolled endocrine disorders • Metabolic bone disorders • Physical handicaps that may affect oral hygiene maintenance • Use of investigational drugs ≤ 30 days prior to implant surgery • Alcoholism or drug abuse • HIV infection • > 10 cigarettes or cigar or chew tobacco equivalents per day • Any conditions that may prevent study participation or interfere with analysis of results in the investigator's opinion *Local* • Inflammation, including untreated periodontitis • Mucosal diseases • History of irradiation therapy • Osseous lesions • Unhealed extraction sites • Bone surgery • Severe bruxism/clenching • Persistent intraoral infection • Inadequate oral hygiene

Table 2. Baseline data (ITT: intention to treat group, n=32 patients; PP: Per protocol group, n=26 patients)

	Cresco framework - loading 10 days post-implant placement		Cresco framework - loading 6-8 weeks post-implant placement		Cast framework - loading 6-8 weeks post-implant placement	
	Patient withdrawal (n=1)	PP (n= 8 patients, 48 implants)	Patient withdrawal (n=5)	PP (n= 9 patients, 54 implants)		PP (n= 9 patients, 54 implants)
Gender males (%)	1(100)	5 (63)	3(60)	6 (55)		1 (11)
Mean patient age (SD)	68	64 (12)	65	64 (11)		67 (7)
Clinical team (1 – 5): patients (n)	team1: 1patient	1:3 - 2:1 - 4:3 – 5:1	team2: 2patients team 4: 1 patient team5: 2patients	1:3 - 2:1 – 3:2 – 4:3		1:3 – 2:3 – 4:2 - 5:1
Bone quality (I – IV) (%)	II	II: 37 – III: 50 – IV: 13	II/III & III & 2:III/IV &IV	II: 20 – III: 62 – IV: 18		II: 0 – III: 56 – IV: 44
Bone form: knife (K) – parallel (P) – taper (T) – undercut (U) (%)	P	K: 0 – P: 65 – T: 29 – U: 6	P & T & 3:T/P	K: 2 – P: 71 – T: 20 – U: 8		K: 28 – P: 50 – T: 11 – U: 11
Crest width: <5 mm - 6 -7 - 8 >8 mm (%)	4-8mm	0 – 4 – 17 – 69 - 10 - 0	3:7mm & 7-8 mm & 7-9 mm	3 - 5 – 8 – 56 – 5 – 6		11 – 13 – 11 -50 – 13 – 2
Bone height: <10 mm – 10/11 -12/13 >13 mm (%)	10-13 mm	15 – 15 – 54 - 17	2: 8 mm & 10-12 mm & 12 mm & 12-13 mm	2 – 12 – 73 - 23		13 – 17 – 69 – 2
Implant depth* (mm) (SD) (min – max)	3.6 mm	2.9 (0.7) (1.3 – 4.2)	3: no radiographs & 1.9 mm & 2.2 mm	2.1 (0.6) (-0.3 – 3.3)		1.7 (0.9) (-0.6 – 1.9)

* distance between cortical bone level and first implant thread