KEY WORDS
dental implant, immediate loading, keratinised mucosa, peri-implant marginal bone levels, repeated abutment disconnections

Randomised controlled trial

THE IMPACT OF REPEATED ABUTMENT CHANGES ON PERI-IMPLANT TISSUE STABILITY: FIVE-YEAR POST-LOADING RESULTS FROM A MULTICENTRE RANDOMISED CONTROLLED TRIAL

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PURPOSE. To evaluate the impact of at least three abutment disconnections on hard and soft tissues around conventionally loaded implants *versus* definitive immediately non-occlusally loaded abutments in implants. A secondary aim was to evaluate whether the presence of less than 2 mm of keratinised mucosa is associated with increased soft tissue recession and/or peri-implant marginal bone loss.

MATERIALS AND METHODS. Eighty patients requiring one single crown or one fixed partial prosthesis supported by a maximum of three implants were randomised, after implant placement at greater than 35 Ncm, according to a parallel-group design to receive either definitive immediately loaded abutments (definitive abutment or immediate loading group) or transmucosal abutments which were loaded after a delay of 3 months and removed at least three times. Patients were treated in four centres, and each patient contributed to the study with only one prosthesis, which was followed up for 5 years after initial loading. Outcome measures were: prosthesis failures, implant failures, complications, pink aesthetic score (PES), buccal recessions, patient satisfaction, peri-implant marginal bone-level changes and height of the keratinised mucosa.

RESULTS. Forty patients were randomly allocated to each group according to a parallel-group design. Seven patients from the definitive abutment group *versus* six from the repeated disconnection group dropped out or died. No patient from the definitive group had implant failures *versus* three patients who lost five implants in the repeated disconnection group (difference = 9.1%; CI95%: -0.7% to 18.9% to; P = 0.227). Nine patients from the repeated disconnection group lost or had to have their prosthesis remade (four provisional and five definitive prostheses) *versus* one provisional prosthesis failure in the definitive abutment group; this difference was statistically significant (difference = 23.5%; CI95%: 7.6% to 39.4%; P = 0.017), but was due to the erroneous use of non-indexed abutments in indexed implants in patients from the repeated disconnection group alone. Seven patients from the definitive abutment group *versus* nine patients from the repeated disconnection group were affected by complications (difference = -5.9%; CI95%: -26.0% to 14.2%; P = 0.775), the difference being not statistically significant. PES scores assessed at 5 years post-loading were 12.1±1.8 for the definitive abutment group and 11.9±1.7 for the repeated abutment changes group (difference = 0.2; CI95%: -0.7 to 1.1; P = 0.615); however, there was a statistically significant difference of 0.20 out of a maximum score of 2 in favour of the definitive abutment group for soft tissue contour alone (P = 0.045). Buccal recessions at 5 years post-loading amounted to -0.19±0.77 mm for the definitive abutment group and -0.07±1.24 mm for the repeated abutment changes group (difference = 0.12 mm CI95%: -0.42 to 0.66; P = 0.662). All patients declared being very satisfied or sati-

sfied with the function and aesthetics of their prosthesis and would undergo the same procedure again. Mean peri-implant marginal bone loss 5 years after loading was 0.11±0.30 mm for the definitive abutment group and 0.48±0.73 mm for the repeated abutment change group (difference = -0.37 [SE=0.14] mm; CI95%: -0.66 to -0.09; P = 0.012), the difference being statistically significant. The height of keratinised mucosa at 5 years post-loading was 2.81±1.46 mm in the definitive abutment group and 2.83±1.84 mm in the repeated abutment change group (difference = -0.02 mm; CI95%: -0.85 to 0.80; P = 0.956), and there were no significant differences in marginal bone loss (difference = 0.00 mm; CI95%: -0.32 to 0.32, P = 0.990) or buccal recession (difference = 0.05 mm, CI95%: -0.43 to 0.54, P = 0.826) at implants having less than 2 mm of keratinised mucosa at loading compared to those having more than 2 mm of keratinised mucosa.

CONCLUSIONS. Five-year post-loading data show that at least three repeated abutment disconnections significantly increased bone loss by 0.37 mm when compared to no disconnection, but this difference may not be clinically significant. While it might be advisable to avoid unnecessary abutment disconnection whenever possible, if disconnections are required, no clinically significant side effects may be expected. Immediately non-occlusally loaded dental implants are a viable alternative to conventional loading, and no increased bone loss or buccal recessions were noted even at implants with less than 2 mm of keratinised mucosa.

CONFLICT OF INTEREST STATEMENT. This trial was partially funded by Dentsply Sirona, the manufacturer of the implants and other products evaluated in this investigation; however, all data belonged to the authors and by no means did the manufacturer interfere with either the conduct of the trial or the publication of the results, with exception of rejecting a proposal to change the protocol, to allow the use of indexed abutments, after the trial was begun.

INTRODUCTION

Implant supported prostheses are an effective and reliable treatment for replacing missing teeth. Their success is based mainly on the ability of the bone to integrate and stabilise dental implants[1], a process known as "osseointegration". Implants can be submerged unloaded for the duration of the healing period, being exposed after several months to connect healing or provisional abutments for the period necessary to complete the restorative procedures. Depending on the procedures used, healing or temporary abutments may have to be disconnected and reconnected several times; the results of an experimental study performed on five dogs[2], in which five abutment disconnection-reconnection cycles were performed, show that 0.7 mm more marginal peri-apical bone loss occurred at implants subjected to repeated abutment disconnection. If this observation is correct, then it would be better to minimise the number of abutment disconnections in clinical practice, by placing a definitive abutment immediately and preferably not removing it thereafter. However, there might be clinical situations in which it could be a disadvantage to place a definitive abutment immediately since it is not always possible to predict the amount of soft tissue shrinkage. Therefore, it would be helpful to retain the option of changing abutments, when necessary, without causing too much disruption of the peri-implant tissues.

One randomised controlled trial[3] reported 0.2 mm higher peri-implant marginal bone levels when definitive abutments were not detached from immediate post-extraction implants during the 3 years after loading, a statistically significant difference. This procedure was therefore termed the "one abutment at one time" concept. From a clinical point of view, a statistically significant mean difference of 0.2 mm may not be clinically noticeable, and should not discourage clinicians from changing abutments if needed, or even from using healing and/or provisional abutments. Another controlled but non-randomised study tested the same hypothesis[4] in posterior edentulous mandibles and found no statistically significant difference in marginal bone loss three years after placement of implants treated according to the "one abutment at one time" concept *versus* abutments disconnected four times. However, two RCTs by the same group[5,6] reported 0.3 and 0.5 mm greater bone loss after 1 year for implants whose abutments were disconnected multiple times, both differences being statistically significant, while no significant differences were observed in another RCT[7].

Another interesting aspect of rehabilitation with implant-supported prostheses is the possibility of loading implants immediately, without waiting for bone healing around the implants. This procedure has important advantages, especially for the patients, who can have fixed prostheses on the same day as implant placement if the risk of implant failure is not increased. There is substantial evidence that immediate loading can be as effective as delayed loading[8] if implants are inserted with a sufficient insertion torque[9,10]; however the efficacy of immediate loading procedures still needs to be fully evaluated, especially in partially edentulous patients.

To add to this body of knowledge, the aims of this multicentre randomised controlled trial (RCT) of parallel-group design were to compare both hard and soft tissue changes between immediately non-occlusally loaded implants which had definitive abutments placed at implant placement and never removed *versus* conventionally loaded implants which had provisional abutments changed at least three times, specifically:

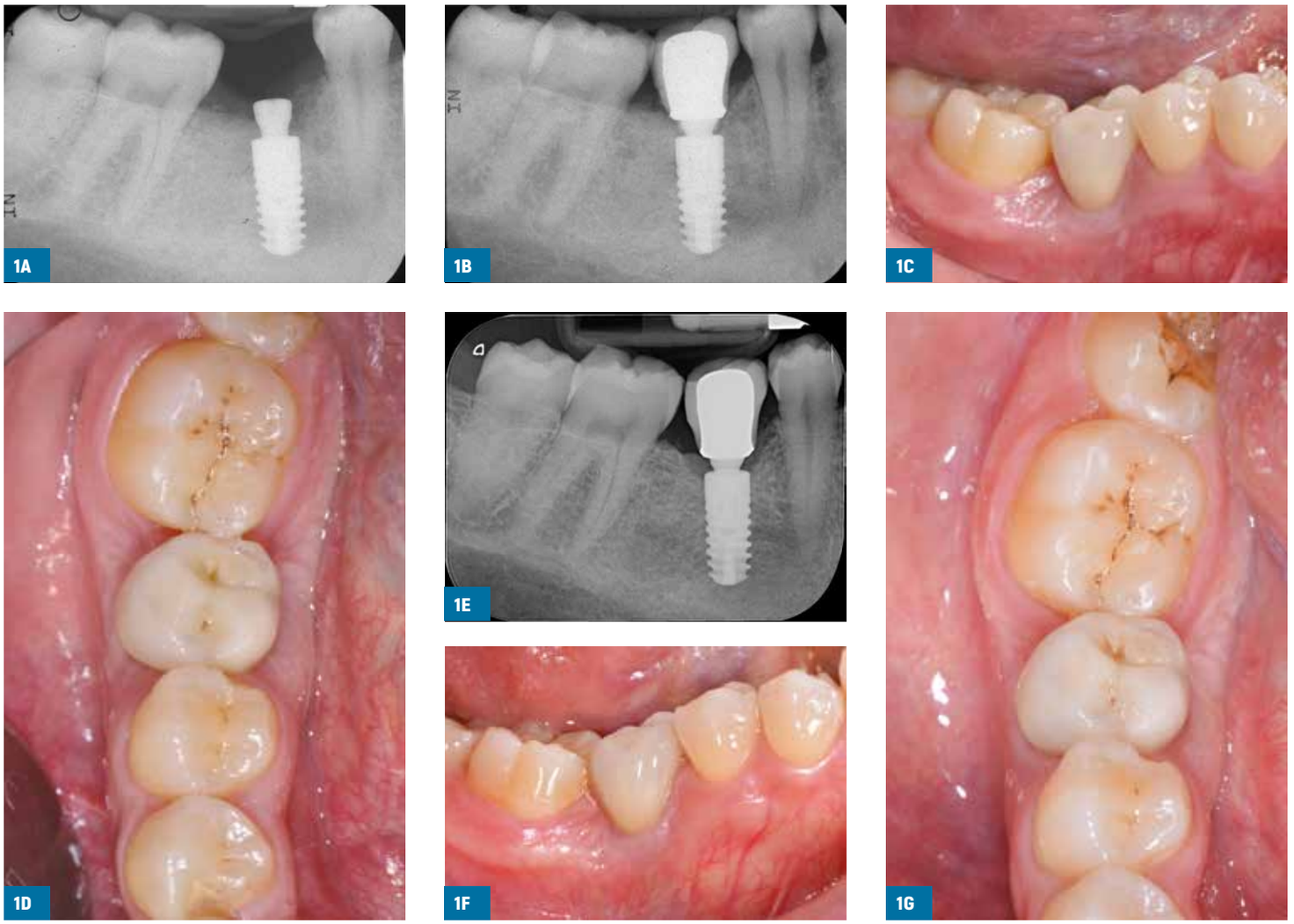
- at impression taking, 3 months after implant placement;
- when checking the zirconium core on titanium abutments for single crowns or the fitting of the prostheses' metal structure;
- a delivery of the definitive crowns/prostheses.

A secondary aim was to explore whether the presence of less than 2 mm of buccal keratinised peri-implant mucosa could be associated with increased buccal recession and peri-implant marginal bone loss.

This is the fourth report in a series. It presents the clinical outcomes at 5 years post-loading, following the previous publication of data at 4 months[11], 1 year[12] and 3 years[13] post-loading. Further reports on this study will be published upon completion of 7- and 10-year follow-up. This article is reported according to the CONSORT (Consolidated Standards of Reporting Trials) statement for improving the quality of reports on parallel-group randomised trials (http://www.consort-statement.org/).

MATERIALS AND METHODS

The trial was designed as a multicentre randomised controlled trial of parallel-group design with two arms. One arm consisted of patients having implants which received abutments that were removed at least three times and were conventionally loaded after 3 months of unloaded healing (**FIGS. 1A-G**). Patients from the other arm received definitive abutments immediately after implant placement, and these were immediately loaded with a provisional acrylic fixed temporary prosthesis, without removing the abutments (**FIGS. 2A-G**).

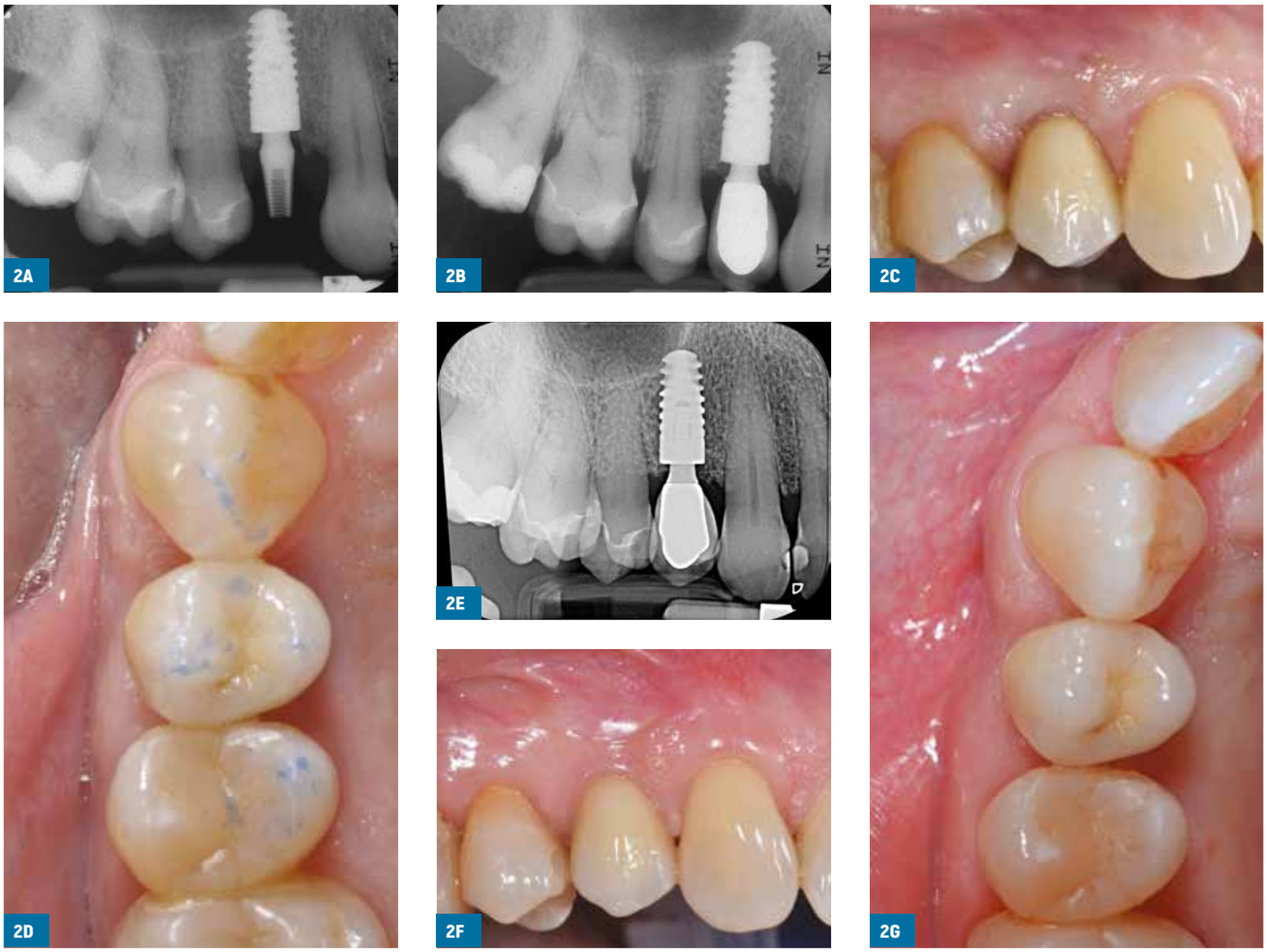


FIGS. 1A-G: *Treatment sequence of a patient randomly allocated to the repeated abutment disconnection group (Dr. D'Avenia): periapical radiograph at placement of implant in position 46 (A); periapical radiograph (B); vestibular (C) and occlusal (D) clinical view 4 months after loading at delivery of the definitive crown; periapical radiograph (E); vestibular (F) and occlusal (G) clinical views at 5 years post-loading.*

Any partially edentulous patient requiring one fixed prosthesis supported by a maximum of three implants, being 18 years old or older, and able to understand and sign a written informed consent form was eligible to be included in this trial. Only one prosthesis per patient was considered in the study, to be supported by implants inserted with an initial insertion torque of at least 35 Ncm, as assessed using a manual ratchet. Implants not achieving this level of torque were not included in the study.

Preoperative radiographs (periapical, panoramic, computed tomography (CT) scans or other radiographic examinations, at the discretion of the operators) together with clinical inspections were used to determine bone volumes and anatomical landmarks. Patients were not included in the study if any of following exclusion criteria was present:

- General contraindications to implant surgery;
- Previous irradiation in the head and neck area;
- Immunosuppression or immunocompromised;
- Past or ongoing treatment with intravenous aminobisphosphonates;



FIGS. 2A-G: *Treatment sequence of a patient randomly allocated to the definitive abutment group (Dr. D'Avenia): periapical radiograph at placement of implant in position 14 (A); periapical radiograph (B); vestibular (C) and occlusal (D) clinical view 4 months after loading at delivery of the definitive crown; periapical radiograph (E); vestibular (F) and occlusal (G) clinical views at 5 years post-loading.*

- Untreated periodontitis;
- Poor oral hygiene and poor motivation;
- Uncontrolled diabetes;
- Pregnancy or breastfeeding;
- Substance abuse;
- Psychiatric issues;
- Full edentulism;
- Post-extraction sites with buccal bone loss greater than 3 mm in relation to the palatal wall;
- Need for bone augmentation at implant placement, with the exception of use of a bone substitute in post-extraction sites;
- Lack of opposing occluding dentition/prosthesis in the area intended for implant placement;
- Acute infection in the area intended for implant placement;

- Impossibility of immediate non-occlusal loading;
- Inability to use a retrievable prosthesis to allow individual implant stability assessment (with the exception of single implants);
- Implants which did not achieve an insertion torque of at least 35 Ncm;
- Implants that could not be restored with standard straight or angulated titanium Ankylos (Dentsply Sirona Implants, Manheim, Germany) abutments;
- Patient participation in other studies if precluding proper adherence to the present protocol;
- Patients' inability to commit to 10-year follow-up.

The study was approved on 17 December 2009 by the University of Naples, Federico II, Ethics Committee (protocol number 187/09) for up to 3 years, and then again up to 10 years by the same Ethics Committee (protocol number 719/19 on 23rd May 2019). The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were adhered to. All patients received thorough explanation and signed an informed written consent form prior to being enrolled in the trial in order to document that they understood the scope of the trial (including procedures, follow-up evaluations, and any potential risks involved); all were provided an opportunity to ask questions pertaining to this research, and were apprised of treatment alternatives. The trial was open to qualifying patients, with no consideration given to sex or race. For patients who had more than one eligible implant site, the operator was free to choose the site to be included in the study at the screening appointment.
Patients were recruited and treated by experienced operators (Dr. Luongo, D'Avenia, Bressan and Grusovin) in four Italian private practices; each dentist treated 20 patients. Originally six centres agreed to participate in the trial, but two centres had to be excluded because one centre never recruited any patients and the other centre supplied incomplete data without any evidence in the case report forms that the planned abutment removal procedures were ever implemented.
Patients were categorised into three groups according to their declarations: non-smokers, moderate smokers (up to 10 cigarettes per day) and heavy smokers (more than 10 cigarettes per day).
The devices used were Ankylos C/X titanium dental implants with internal connection (Dentsply Sirona Implants). Operators were free to choose implant lengths (8, 9.5, 11 and 14 mm) and diameters (3.5, 4.5 or 5.5 mm) according to clinical indications and their preferences. Restorations were to be on standard straight or angulated Ankylos C non-indexed titanium abutments. However, it rapidly became apparent that the selection of non-indexed abutments for indexed implants was not ideal, given that while removing and reconnecting the abutment, it could be repositioned in a slightly different position, which would require adjustments or even necessitate the prosthesis being remade. As soon as the problem was brought to the attention of the trial advisor, it was proposed that the research protocol be modified by using indexed abutments, but this proposal was rejected by the sponsor.

Clinical procedures

Patients received prophylactic antibiotic therapy, namely 2 g of amoxicillin (or clindamycin 600 mg if allergic to penicillin), one hour prior to surgery, and rinsed for one minute with chlorhexidine 0.2%. All patients were treated under local anaesthesia using 1% articaine 40mg/ml with epinephrine 1:200,000 (Alfacaina, Dentsply Sirona). Tooth extractions, when needed, were performed with as little trauma as possible in order to preserve the buccal alveolar bone. Extraction sockets were carefully cleaned of any residual granulation tissue. Flapless implant

placement was also allowed, and the decision to raise the flap or not was left to the individual clinician. The standard implant site preparation procedure, as recommended by the implant manufacturer, was used; in brief, a round bur or lance drill was used to prepare the cortical insertion point, and was followed by the drills of increasing diameters. Bone quality was subjectively recorded as hard, medium or soft. Tapping was performed only in the presence of hard bone. Implants were placed 1 mm subcrestal to the palatal wall. The insertion torque was assessed manually using an Ankylos ratchet. Implants not achieving an insertion torque of at least 35 Ncm or placed at angles which did not allow the use of standard straight or angulated Ankylos titanium abutments were not included in the study. Implants that were not properly seated using a manual force of 35 Ncm were removed and the site was tapped. A bone substitute (Symbios Algipore, Dentsply Sirona) could be used to fill the gap in the event that post-extraction implants had a buccal wall loss of up to 3 mm when compared to the palatal wall and in the presence of an implant–bone gap. After implants were placed, the sealed envelope containing the group allocation code was opened, thereby informing the surgeon whether to place the definitive abutment(s), which were not to be removed, or transmucosal healing abutment(s), to be removed at least 3 times. Flaps were repositioned and sutured around the abutments. Healing abutments were to have their coronal portion at the level of or 1 mm above the soft tissues. Fixed full acrylic non-occluding provisional prostheses were prepared and connected onto the definitive abutments within 24 h in the immediate loading group. The immediate provisional prostheses were not in contact with the opposing dentition (non-occlusal loading), either in static occlusion or lateral movements.

Just after implant placement, periapical radiographs (baseline) were taken using the paralleling technique. The amount of keratinised mucosa was measured at the buccal site at each implant. Four hundred milligrams of ibuprofen was prescribed to be taken two to four times a day during meals for as long as required. Patients were instructed to use 0.2% chlorhexidine mouthwash for one minute twice a day for 2 weeks, and to avoid brushing and trauma to the surgical sites. Postoperative amoxicillin 1 g twice a day for 6 days was prescribed to patients treated with a bone substitute, or in cases of long and complicated surgery. Patients allergic to penicillin were prescribed clindamycin 300 mg twice a day for 6 days. Within 1 week all patients were recalled and checked.

Implants from the repeated abutment disconnection group were left to heal unloaded for three months. During the healing period, operators were allowed to use different types of provisional dentures or prostheses. Possible options were: no use of provisional prosthesis; removable provisional prostheses not pressing on soft tissues, or provisional prostheses fixed to the adjacent dentition. At the end of the healing period, the healing abutments were removed, the copy transfer inserted, impressions (Aquasil Ultra, Dentsply Sirona) taken at implant level, and the healing abutments were repositioned. The stability of individual implants was also tested by applying a 20-Ncm rotational force.

Healing abutments were removed three time as described below.

1. When taking the impression at implant level.
2. When testing the fit of the metal core for single crowns or the titanium framework for fixed prostheses; the healing abutments were positioned after checking the suitability of the prosthetic components.
3. During delivery of the definitive metal-ceramic prostheses. Here the stability of individual implants was checked again by applying a 20-Ncm rotational force.

In the definitive abutment group, the stability of individual implants was tested after 3 months with the provisional prosthesis in situ by applying a 20-Ncm rotational force, and an im-

pression was taken at the abutment level, without removing the definitive abutments, using Aquasil Ultra. Within 1 month after the definitive impression, implants in both groups were tested for stability by applying 20 Ncm of torque; contemporaneously, retrievable metal-ceramic prostheses were delivered (with the exception of crowns) and intraoral radiographs were taken of the study implants. Patients were enrolled in an oral hygiene programme with recall visits planned at least every 6 months for the entire duration of the study.

Outcome measures

This study tested the null hypothesis that there would be no differences in clinical outcomes between immediately placed definitive abutments supporting non-occluding provisional restorations *versus* connecting healing abutments disconnected three times before definitive prosthesis delivery and loaded after 3 months, against the alternative hypothesis of a difference.
Primary outcome measures were the following.

- Prosthesis failure: when it was not possible to place the prosthesis due to implant failures or secondary to implant losses, or replacement of a prosthesis for any reason.
- Implant failure: implant mobility and/or any infection dictating implant removal, or any mechanical failure rendering the implant unusable, such as implant fracture or deformation of the implant-abutment connection. The stability of each implant was measured manually by tightening the abutment screw at delivery of the definitive prostheses. One, 3 and 5 years after loading, partial prostheses were removed to assess implant stability, whereas single crowns were rocked with the metal handles of two dental instruments.
- Any complication or adverse event was recorded and reported, with the exception of poorly fitting crowns determined by the use of non-indexed abutments; these were classed as prosthesis failures when the crown had to be remade, and were assessed and treated by the operators.

Secondary outcome measures were the following.

- Buccal peri-implant tissue recession: assessed by a blinded outcome assessor (Dr. Sbricoli) on plaster models created from alginate impressions taken at delivery of the definitive prostheses (baseline) and 1, 3 and 5 years after initial loading. Measurements were made vestibularly from an occlusal reference point perpendicular to the marginal gingiva. For incisors, the reference point was the middle of the incisal margin; for canines and premolars it was the tip of the cuspid; and for molars it was the deepest occlusal vestibular margin between the two cusps. Values were averaged at patient level and then at group level.
- Aesthetic evaluation of the vestibular and occlusal clinical pictures, including the two adjacent teeth, at 4 month and 1, 3 and 5 years after loading (**FIGS. 1C, D, F, G, 2C, D, F, G**), performed on a computer screen. The aesthetic evaluation was carried out blind by an outcome assessor (Dr. Sbricoli) using the pink aesthetic score (PES)[14]. In brief, seven variables were evaluated: mesial papilla, distal papilla, soft tissue level, soft tissue contour, alveolar process deficiencies, soft tissue colour and texture. A 0-1-2 scoring system was used; 0 being the lowest and 2 being the highest value, with a maximum achievable score of 14 per implant.
- Patient satisfaction was assessed at definitive prostheses delivery, and at 1, 3 and 5 years after initial loading by the independent outcome assessors at each centre, who asked patients the following questions:

1. Are you satisfied with the function of your implant-supported prosthesis? Possible answers were: "yes, absolutely", "yes, partially", "not sure", "not really", and "absolutely not".
2. Are you satisfied with the aesthetic outcome of your implant-supported prosthesis? Possible answers were: "yes, absolutely", "yes, partially", "not sure", "not really", and "absolutely not".
3. Would you undergo the same treatment again? Possible answers were: "yes" or "no". Patients comments were also recorded.

- Peri-implant marginal bone level changes: assessed on periapical radiographs taken with the paralleling technique at implant placement (**FIGS. 1A, 2A**); 4 months after loading (**FIGS. 1B, 2B**), upon delivery of the definitive prosthesis; and at 1, 3 and 5 (**FIGS. 1E, 2E**) years after initial loading. In the case of unreadable radiographs, new radiographs were taken. A blind outcome assessor (Dr. Sbricoli) scanned the non-digital radiographs in TIFF format with a 600-dpi resolution, and stored the radiograph files on a personal computer. The assessor measured the peri-implant marginal bone levels blind using Scion Image (Scion Corporation, Frederick, MD, USA) software. The software was calibrated for each individual image using the known distance between two consecutive threads. Measurements of the mesial and distal bone crest levels adjacent to each implant were made to the nearest 0.01 mm. Reference points for the linear measurements were: the coronal margin of the implant collar and the most coronal point of bone-to-implant contact. Implants with bone up to the coronal margin of the implant collar were given a value of zero. Mesial and distal measurements of each implant were averaged, and a mean calculated per patient and per group.
- Height of the keratinised mucosa: measured blind, using a periodontal probe, in the middle of the buccal side of each study implant at loading of the definitive prosthesis, and at 1, 3 and 5 years after initial loading by the local outcome assessors; each measurement was rounded off to the nearest 0.5 mm.

At each centre there was a local outcome assessor who recorded implant stability, height of the keratinised mucosa and patient satisfaction blind. The local assessors were not calibrated.

Methodological aspects

The sample size was calculated for radiographic peri-implant marginal bone level changes. A sample size of 55 in each group had 90% power to detect a difference in mean changes in peri-implant marginal bone level of 0.300 mm, assuming that the common standard deviation is 0.480 using a two-group t-test with 0.05 two-sided significance level. We had planned to recruit 60 patients per arm, but unfortunately only data from 40 patients per arm were available since two centres did not contribute with any data; nevertheless, for n = 40 patients in each group, the power is still 78.8%.

Six computer-generated restricted randomisation lists were created. Only one investigator (Dr. Esposito), who was not involved in the selection and treatment of patients, knew the random sequence and had access to the list, which was stored on a password-protected laptop. The random codes were enclosed in sequentially-numbered, identical, opaque, sealed envelopes. Only after the implants were placed was the envelope corresponding to the patient recruitment number to be opened and the clinician informed whether to place a definitive or healing abutment. Therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

All data analysis was carried out according to a pre-established analysis plan, and was performed at the patient level unless otherwise specified. A biostatistician (Dr. Neumann) with

expertise in Dentistry, and a dentist (Dr. Buti) with expertise in Statistics analysed the data. Differences in the proportions of patients with prosthesis failure, implant failure and complications (dichotomous outcomes), as well as patient satisfaction, were compared using the chi-squared test or Fisher's exact test (for small cell sizes with expected values of less than 5), as appropriate. The differences between the two study groups in mean PES scores, radiographic peri-implant marginal bone level changes, buccal recession and amount of keratinised mucosa were compared using the t-test.

The differences between the different study centres were compared using ANOVA for metrical variables and the chi-squared test for count data. Changes in bone levels were tested in both groups using t-tests for paired samples. Mean buccal recession and peri-implant bone loss at 5 years post-loading were compared between implants with buccal keratinised mucosa height less and more than 2 mm using mixed effects models (with implants clustered within patients), in which baseline values were the covariate and the keratinised mucosa the factor. The level of significance was $\alpha = 0.05$. All statistical analyses were carried out using IBM SPSS Statistics Version 25.

RESULTS

Two of the six centres had to be excluded from the study, one because it never treated any patients, and the other because it supplied incomplete data, without any evidence in the case report forms that the planned abutment removal procedures were ever implemented. The four included centres treated 20 patients each (in total 80 patients) with 128 implants supporting 41 single crowns and 39 fixed partial prostheses.

Originally 142 patients were screened for eligibility, but 62 patients were not included in the trial for the following reasons: insufficient bone to place 8.0 x 3.5 mm implants (18 patients); not available for 10-year follow-up (15 patients); specifically requested an immediate loading procedure (12 patients); in need of bone augmentation procedure (excluding bone substitute in post-extraction sites, which was permissible) at implant placement (eight patients); need to use other implants in addition to implants already placed (four patients); implants placed with a torque of less than 35 Ncm (two patients); throat cancer prior to study initiation (one patient); insufficient oral hygiene (one patient); impossibility of performing immediate non-occlusal loading (one patient).

All patients had their sites treated according to the allocated interventions. Thirteen patients dropped out at 5 year follow-up; seven of these were patients from the definitive abutment group, specifically:

- One patient moved to another town after 4-month follow-up (Dr. D'Avenia);
- One patient died of a heart attack just before 1-year follow-up (Dr. Luongo);
- One patient stopped attending follow-up after the first year of follow-up because of a severe stroke (Dr. D'Avenia);
- One patient moved to another town after the first year of follow-up (Dr. D'Avenia);
- One patient died of cancer 2 years after loading (Dr. Bressan);
- One patient refused to attend the 3-year follow-up because she was affected by malaria contracted in Africa (Dr. Luongo), but returned for the 5-year follow-up, at which point she was no longer considered a drop-out;
- One patient died of cancer between years 3 and 5 of follow-up (Dr. Bressan);
- One patient moved to another town after the 4th year follow-up (Dr. Grusovin).

Six patients from the repeated disconnection group were also lost to follow-up, specifically:

- One patient moved to another town and was last seen at 2-year follow-up (Dr. Bressan);

- One very old female patient with walking problems was unable to attend and was last seen at 3-year follow-up (Dr. Luongo);
- One patient moved to another town and was last seen at 3-year follow-up (Dr. Grusovin);
- One patient died of a heart attack between years 3 and 5 of follow-up (Dr. Grusovin);
- One patient died of unknown causes between years 3 and 5 of follow-up (Dr. Luongo);
- One patient moved back to Romania after 3-year follow-up (Dr. Luongo).

Protocol deviations and reasons for missing data have been explained in a previous paper[13]. No more deviations or missing data had occurred at the 5-year time-point.

Main results

Patients were recruited and implants inserted from April 2010 to September 2012. The follow-up for all patients was at 5 years post-loading.

The main baseline patient and intervention characteristics, divided by study group, are presented in **TABLE 1**. There were no apparent significant baseline imbalances between the two groups.

- Prosthesis failures: nine prostheses from the repeated disconnection group had to be remade or were lost, specifically four provisional and five definitive prostheses, *versus* one provisional prosthesis lost in the definitive abutment group. The difference was statistically significant (difference = 23.5%; CI95%: 7.6% to 39.4%; P = 0.017); however, this imbalance was due to the erroneous use of non-indexed abutments in indexed implants, which affected only the patients in the repeated disconnection group, in which one definitive (Dr. D'Avenia) and four provisional crowns (Dr. Bressan) had to be remade because of poorly fitting crowns. One definitive crown had to be remade because it fractured 6 months after its delivery (Dr. Bressan). Another definitive prosthesis had to be remade because one of its three supporting implants fractured after almost 3 years in function (Dr. Bressan). Another partial prosthesis supported by three implants failed 3 years and 4 months after loading (Dr. Bressan) due to implant fracture in position 45. At 5-year follow-up, the implant in position 46 was also lost due to peri-implantitis. Another prosthesis (Dr. Bressan) was lost because peri-implantitis affected both the supporting implants in position 42 and 32 at 4 years after loading. Finally, one provisional crown (Dr. D'Avenia) from the definitive abutment group had to be remade about 10 weeks after loading because of repeated debondings.
- Implant failures: five implants in three patients from the repeated disconnection group failed *versus* none from the definitive group. There were no differences between the two groups in patients experiencing implant failures (difference = 9.1%; CI95%: -0.7% to 18.9% to; P = 0.227).
  - One implant in position 25 supporting a fixed partial prosthesis (together with two other implants) fractured after almost 3 years in function (Dr. Bressan) following multiple previous complications at the same implant, including prosthesis debonding, which may be indicative of an overload aetiology; it was replaced by a new implant in position 24 and a new prosthesis was made.
  - One patient had an implant in position 45 that fractured at 3 years and 4 months after loading (Dr. Bressan); a new implant was placed in position 42 to stabilise the prosthesis. At 5 years after loading, the other implant in position 46 was also lost due to peri-implantitis.
  - One patient had an implant in position 42 affected by peri-implantitis at 3 years and 5 months after loading; the second implant in position 32 was also affected by peri-im-

TABLE 1 PATIENT AND INTERVENTION CHARACTERISTICS

	Disconnected abutments n = 40	Definitive abutments n = 40
Females	24 (60%)	23 (58%)
Mean age at implant insertion (SD; range)	57.6 (12.9; 33-85)	55.6 (13.6; 30-81)
Smoking up to 10 cigarettes/day	9 (23%)	6 (15%)
Smoking more than 10 cigarettes/day	3 (8%)	2 (5%)
Implants in upper jaws	30/70 (43%)	21/58 (36.2%)
Implants in lower jaws	40/70 (57%)	37/58 (64%)
Implants at incisor position	7/70 (10%)	10/58 (17%)
Implants at canine position	4/70 (6%)	1/58 (2%)
Implants at premolar position	25/70 (36%)	23/58 (40%)
Implants at molar position	34/70 (49%)	24/58 (41%)
Implants in hard bone	17/70 (24%)	13/58 (22%)
Implants in medium bone	38/70 (53%)	31/58 (53%)
Implants in soft bone	15/70 (21%)	14/58 (24%)
Sites previously augmented with bone substitute	4 (10%)	2 (5%)
Implants of diameter 3.5 mm	47/70(67%)	36/58 (62%)
Implants of diameter 4.5 mm	21/70 (30%)	19/58 (33%)
Implants of diameter 5.5 mm	2/70 (3%)	3/58 (5%)
Implants of length 8 mm	29/70 (41%)	17/58 (29%)
Implants of length 9.5 mm	24/70 (34%)	23/58 (40%)
Implants of length 11 mm	14/70 (20%)	14/58 (24%)
Implants of length 14 mm	3/70 (4%)	4/58 (7%)
Implants inserted flapless	3 (8%)	9 (23%)
Post-extractive implants	1/70 (1%)	7/58 (12%)
Implants in simultaneously augmented sites	1/70 (1%)	6/58 (10%)
Single crowns	16 (40%)	25 (63%)
Prostheses supported by 2 to 3 implants	24 (60%)	15 (38%)

plantitis at 3 years and 8 months after loading. Despite the attempted treatment, both implants failed and the patient was rehabilitated using a removable prosthesis.

- Complications: seven patients from the definitive abutment group *versus* nine patients from the repeated disconnection group were affected by complications (difference = -5.9%; CI95%: -26.0% to 14.2%; P = 0.775), the difference not being statistically significant. All complications were resolved. The following patients from the definitive abutment group had complications:
  - One patient (Dr. D'Avenia) experienced three separate debondings of the provisional restorations on teeth 35 and 36 at 2, 5 and 10 weeks; a new provisional restoration was provided after the third debonding event;
  - Another patient (Dr. D'Avenia) had two separate debondings of single crowns in position 46 at 4 and 7 weeks after immediate loading. After re-cementation, no more debonding occurred;

- Another patient developed peri-implant mucositis with localized swelling and bleeding around implant 37 nine months after the delivery of the definitive restoration (Dr. D'Avenia); she was treated using local instrumentation and disinfection with chlorhexidine mouthwash, gel and rinses, together with oral hygiene instruction reinforcement. Improvements were observed at 1-year radiographic check-up;
- A definitive partial fixed prosthesis supported by implants in positions 24 and 25, bonded with provisional cement (TempBond, Kerr, Orange, CA, USA), debonded after 6 months (Dr. Bressan); it was bonded again with Harvard permanent cement;
- A definitive prosthesis supported by implants in positions 25 and 26 debonded 1 year and 10 months after delivery (Dr. Bressan), and was re-cemented with Harvard;
- A porcelain fracture was observed at a crown in position 47 three years and 1 week after loading (Dr. Grusovin), and was polished chairside;
- There was loosening of a crown at the 36 at 4 years and 2 months (Dr. Grusovin), which was re-cemented again with temporary cement.

Complications in the repeated disconnection abutment group were:

- One case of alveolar infection (Dr. D'Avenia) at an implant in position 47, noticed one week after placement of an immediate post-extraction implant together with Symbios Algipore bone graft; there was local oedema, and mucosal swelling and redness, together with spontaneous expulsion of part of the graft material. The infection was treated using local irrigation with an antimicrobial solution (rifamycin) associated with the removal of the infected graft still in situ, which resulted in the almost total removal of the graft. The infection was completely resolved within one week. At 4 years and 7 months after loading, the same patient had an acute episode of peri-implant infection at the 46; this was treated with 1g Augmentin 3 times a day for 7 days plus local antimicrobial therapy (three applications of air-abrasive glycine powder plus diode laser). At 5-year follow-up, clinical parameters were within the norm;
- A palatal wound dehiscence on implant 23 healed spontaneously (Dr. Bressan). The same patient experienced debonding of a provisionally cemented definitive prosthesis 1 week after its delivery; it was bonded again with Harvard definitive cement (Harvard Dental International, Hoppegarten, Germany). However, 22 months after loading peri-implantitis developed at implant 25, which was surgically treated the following month via open flap debridement and anorganic bovine bone with added collagen. Unfortunately, however, the implant fractured at the 3-year follow-up;
- One definitive crown fractured 6 months after its delivery (Dr. Bressan) and was replaced by a new crown;
- A fistula was present at definitive crown placement (Dr. Grusovin), but disappeared within 1 week after disconnecting and cleaning the definitive abutment. In the same patient, the definitive abutment became loosened one week after delivery and re-screwed in place, and again the crown debonded 35 months after loading and was cemented with temporary cement;
- Peri-implantitis was observed at the 42 at 3 years and 5 months after loading, and at the 32 at 3 years and 8 months after loading (Dr. Bressan). Both implants were treated via scaling but failed, and a removable prosthesis was delivered instead;
- Peri-implantitis was observed at the 36 three years and 6 months after loading (Dr. D'Avenia); it was surgically treated using air-abrasive glycine powder, apical repositioning of the flap and antibiotic therapy (Augmentin 1 g twice a day for 7 days). Good healing was achieved;

- Loosening of a definitive crown at 4 years and 8 months after loading (Dr. D'Avenia); this was re-cemented;
- Peri-implantitis was observed at the 46 five years after loading (Dr. Bressan); the implant failed;
- Fracture of the resin prosthesis lining on the 24–25 noticed at the 5-year follow-up (Dr. Grusovin); this was repaired chairside.

- Pink aesthetic score (**TABLE 2**): 5 years after loading, the average PES score was 12.1±1.8 for the definitive group and 11.9±1.7 for the repeated abutment changes group, the difference being not statistically significant (difference = 0.22, 95% CI: -0.65 to 1.09; P = 0.615, **TABLE 2**). When evaluating the single aesthetic domains, a statistically significant difference was observed in only one. This was recorded for the soft tissue contour at implants from the definitive abutment group, which scored a mean of 1.9 out of a maximum of 2, which was significantly better than implants from the disconnected abutment group, whose mean was 1.7 (P = 0.045).
- Buccal recession (**TABLE 3**): Buccal recessions at 1-year post-loading, with the delivery of the definitive prostheses as baseline, amounted to 0.07±0.35 mm for the definitive abutment group and 0.12±0.65 mm for the repeated abutment changes group. These figures correspond to a slight growth in buccal soft tissues in both groups. There were no statistically significant differences between the two groups (difference = 0.05 CI95% -0.19 to

TABLE 2 MEAN PES SCORES A 5 YEARS AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAINS; STANDARD DEVIATION IS IN PARENTHESIS

	Mesial papilla	Distal papilla	Soft tissue level	Soft tissue contour	Alveolar process deficiencies	Soft tissue colour	Soft tissue texture	Total PES score
Disconnected abutments (N = 31)	1.58 (0.56)	1.48 (0.57)	1.90 (0.30)	1.71 (0.46)	1.71 (0.46)	1.74 (0.45)	1.74 (0.45)	11.9 (1.7)
Definitive abutments (N = 33)	1.61 (0.50)	1.39 (0.61)	1.88 (0.33)	1.91 (0.29)	1.73 (0.52)	1.70 (0.47)	1.88 (0.33)	12.1 (1.8)
Difference	-0.03	0.09	0.02	-0.20	-0.02	0.05	-0.14	-0.22
P-value	0.849	0.544	0.758	0.045*	0.886	0.694	0.170	0.615

**Statistically significant difference*

TABLE 3 MEAN RECESSION BETWEEN GROUPS AND TIME PERIODS IN MM

	1 year after loading				3 years after loading				5 years after loading			
	N	Mean	(SD)	95% CI	N	Mean	(SD)	95% CI	N	Mean	(SD)	95% CI
Disconnected abutments	30	-0.07	(1.23)	-0.53 to 0.39	37	-0.12	(1.15)	-0.50 to 0.27	30	-0.07	(1.23)	-0.53 to 0.39
Definitive abutments	28	-0.19	(0.77)	-0.49 to 0.11	30	-0.13	(0.76)	-0.41 to 0.16	28	-0.19	(0.77)	-0.49 to 0.11
Difference		0.12		-0.42 to 0.66		0.01		-0.48 to 0.50		0.12		-0.42 to 0.66
P-value		0.659				0.965				0.658		

0.29; P = 0.659). Buccal recessions at 3-year post-loading amounted to -0.1±0.8 mm for the definitive abutment group and -0.1±1.2 mm for the repeated abutment changes group. These figures correspond to a slight loss of buccal soft tissues in both groups. Once again, there were no statistically significant differences between the two groups (difference = 0.01 CI 95% -0.48 to 0.50, P = 0.965). Buccal recessions at 5 years post-loading amounted to -0.19±0.77 mm in the definitive abutment group and -0.07±1.23 mm in the repeated abutment changes group, with no statistically significant difference between the two (difference = 0.12 mm CI95%: -0.42 to 0.66; P = 0.658).

- Patient satisfaction: five years after loading, there were no statistically significant differences in patient satisfaction between the two groups as regards either function or aesthetics. Thirty-two out of 33 patients (97.0%; CI95%: 84.2% to 99.9%) from the definitive abutment and 31 out of 32 (96.9%; CI95%: 83.8% to 99.9%) patients from the disconnected abutment group were very satisfied with the functional outcome (P = 1), and 32 (97.0%; CI95%: 84.2% to 99.9%) from the definitive abutment and 31 (96.9%, CI95%: 83.8% to 99.9%) from the disconnected abutment group (P = 1) were very satisfied with the aesthetic outcome. All other patients were satisfied with both functional and aesthetic outcomes. All patients would undergo again the same treatment.
- Marginal bone level changes (**TABLES 4, 5**): at implant placement there was a statistically significant difference (though not clinically relevant) of 0.08 mm between the two groups;

TABLE 4 MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVELS BETWEEN GROUPS AND TIME PERIODS

	Implant placement	4 months after loading	1 year after loading	3 year after loading	5 years after loading
	N Mean (SD) 95% CI	N Mean (SD) 95% CI	N Mean (SD) 95% CI	N Mean (SD) 95% CI	N Mean (SD) 95% CI
Disconnected abutments	40 0.11 (0.19) 0.05 to 0.16	40 0.20 (0.30) 0.10 to 0.29	40 0.33 (0.53) 0.16 to 0.50	39 0.61 (1.0) 0.28 to 0.94	31 0.55 (0.81) 0.25 to 0.84
Definitive abutments	40 0.03 (0.11) 0.00 to 0.06	40 0.11 (0.20) 0.05 to 0.17	38 0.09 (0.20) 0.03 to 0.16	34 0.11 (0.2) 0.04 to 0.17	33 0.15 (0.29) 0.04 to 0.25
Difference	0.08 (SE=0.03) 0.01 to 0.14	0.09 (SE=0.06) -0.03 to 0.20	0.24 (SE=0.09) 0.06 to 0.42	0.50 (SE=0.17) 0.17 to 0.84	0.40 (SE=0.15) 0.09 to 0.71
P-value	0.015*	0.167	0.011*	0.004*	0.014*

**Statistically significant difference*

TABLE 5 MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVEL CHANGES BETWEEN GROUPS AND TIME PERIODS

	Difference, placement-4 months	Difference, placement-1 year	Difference, placement-3 years	Difference, placement-5 years
	N Mean (SD) 95% CI	N Mean (SD) 95% CI	N Mean (SD) 95% CI	N Mean (SD) 95% CI
Abutment disconnection	40 -0.09 (0.20) -0.16 to -0.03	40 0.23 (0.49) 0.07 to 0.38	39 0.50 (0.93) 0.20 to 0.80	31 0.48 (0.73) 0.22 to 0.75
Definitive abutments	40 -0.08 (0.16) -0.13 to -0.03	38 0.06 (0.12) 0.02 to 0.10	34 0.07 (0.18) 0.01 to 0.13	33 0.11 (0.30) 0.00 to 0.22
Difference	-0.01 (SE=0.04) -0.09 to 0.07	0.16 (SE=0.08) 0.00 to 0.33	0.43 (SE=0.16) 0.13 to 0.74	0.37 (SE=0.14) 0.09 to 0.66
P-value	0.97	0.046*	0.007*	0.012*

**Statistically significant difference*

bone levels were 0.11 mm in the repeated abutment changes group and 0.03 mm in the definitive abutment group. There was no statistically significant difference in peri-implant bone levels (mean difference = 0.09 mm; CI95%: -0.03 to 0.20, P = 0.167) between the two groups at 4 months post-loading, but at 1, 3 and 5 years, the difference was statistically significant (mean difference = 0.24 mm; CI95%: 0.06 to 0.42, P = 0.011, mean difference = 0.50 mm; CI95%: 0.17 to 0.84, P = 0.004, and mean difference = 0.40 mm; CI95%: 0.09 to 0.71, P = 0.014, respectively, **TABLE 4**). There was no difference in bone loss at 4 months post-loading (mean difference = -0.01 mm; CI95%: -0.09 to 0.07, P = 0.97) but at 1, 3 and 5 years, the repeated abutment changes group had lost significantly more bone (mean difference = 0.16; CI95%: 0.00 to 0.33; P = 0.046, mean difference = 0.43 mm; CI95%: 0.13, 0.74; P = 0.007, and mean difference = 0.37 mm; CI95%: 0.66 to 0.09; P = 0.012, respectively, **TABLE 5**). Both groups gradually lost statistically significant amounts of marginal peri-implant bone up to 5 years post-loading: 0.11 mm (P = 0.044) in the definitive abutment and 0.48 mm (P = 0.001) in the repeated abutment changes group (**TABLE 5**).

- Keratinised mucosa: the mean buccal keratinised mucosa at definitive prosthesis delivery (4 months after loading) was 2.8±1.8 mm in the disconnected abutment group and 2.9±1.4 mm in the definitive abutment group. One year after loading it was 2.8±1.7 mm in the disconnected abutment group and 2.8±1.5 mm in the definitive abutment group, while three years after loading it was 2.8±1.6 mm in the disconnected abutment group and 2.8±1.3 mm in the definitive abutment group. Five years after loading, it was 2.8±1.8 mm in the disconnected abutment group and 2.8±1.5 mm in the definitive abutment group. There were no statistically significant differences in mean buccal keratinised mucosa heights at either 4 months (difference = 0.1 mm; CI95%: -0.7 to 0.8; P = 0.865), or at 1 year (difference = -0.0 mm; CI95%: -0.8 to 0.7 mm; P = 0.966) or 3 years post-loading (difference = 0.03 mm; CI95%: -0.67 to 0.73; P = 0.926). Mean buccal keratinised mucosa heights were also statistically similar at 5 years post-loading (difference = -0.02 mm; CI95%: -0.85 to 0.80; P = 0.956).
- Mixed models analysis could not find any association at implant level between having less or more than than 2 mm of keratinised mucosa height at delivery of the definitive prostheses (4 months after loading) and either peri-implant marginal bone loss (difference [<2 mm - ≥2 mm] = 0.00, CI95%: -0.32 to 0.32, P = 0.990; **TABLE 6A**) or buccal recession (difference [<2 mm - ≥2 mm] = 0.05, CI95%: -0.43 to 0.54, P = 0.826; **TABLE 6B**) at 5 years after loading. In the definitive abutment group, the keratinised mucosa height at loading was <2 mm in 9 out of 40 patients (22.5%, CI95%: 10.8% to 38.5%), while in the repeated abutment changes group it was <2 mm in 13 out of 40 patients (32.5%, CI95%: 18.6% to 49.1%), a difference that was not statistically significant (difference = -10.0%, CI95%: -29.4% to 9.4%, P = 0.453).
- A comparison between the four centres at 5 years after loading is presented in **TABLE 7**. There were statistically significant differences between centres in the number of patients with remade/failed prostheses (P = 0.006), failed implants (P = 0.018) and experiencing complications (P = 0.048), as well as pink aesthetic score (P = 0.043), peri-implant marginal bone loss (P <0.001) and keratinised mucosa height (0.023). However, there were no differences between centres in terms of buccal recession (P = 0.053) or patient satisfaction (P = 0.261 for functional and P = 0.357 for aesthetic outcomes).

DISCUSSION

The study was designed to evaluate whether an approach involving immediate non-occluding loading and no abutment disconnections could play a clinically significant role in maintaining bone levels, as compared to conventional loading and repeated abutment disconnection.

TABLE 6A MIXED MODEL FOR RECESSION CHANGES AT 5 YEARS AFTER LOADING

Fixed Effects Parameter Estimates

				95% Confidence Interval				
Names	**Effect**	**Estimate**	**SE**	**Lower**	**Upper**	**df**	**t**	**p**
(Intercept)	(Intercept)	8.7637	0.1736	8.423	9.104	20.9	50.472	< .001
KT Loading >=2mm (1 = yes)1	1 - 0	0.0544	0.2473	-0.430	0.539	84.5	0.220	0.826
Rec Baseline	Rec Baseline	0.8497	0.0537	0.744	0.955	85.4	15.816	< .001

Random Components

Groups	**Name**	**SD**	**Variance**	**ICC**
# pat	(Intercept)	0.558	0.311	0.261
Residual		0.939	0.881	

Note. Number of Obs: 91 , groups: # pat , 20

TABLE 6B MIXED MODEL FOR MARGINAL BONE LOSS (MBL) AT 5 YEARS AFTER LOADING

Fixed Effects Parameter Estimates

				95% Confidence Interval				
Names	**Effect**	**Estimate**	**SE**	**Lower**	**Upper**	**df**	**t**	**p**
(Intercept)	(Intercept)	0.46424	0.104	0.260	0.668	22.5	4.4597	< .001
MBL Bas	MBL Bas	2.03882	0.408	1.239	2.839	93.4	4.9945	< .001
KT Loading >=2mm (1 = yes)1	1 - 0	0.00206	0.164	-0.319	0.323	90.9	0.0126	0.990

Random Components

Groups	**Name**	**SD**	**Variance**	**ICC**
# pat	(Intercept)	0.296	0.0874	0.160
Residual		0.676	0.4574	

Note. Number of Obs: 97 , groups: # pat , 20

However, with the exception of 0.37 mm bone loss and 0.20 difference in PES score for soft tissue contour, in favour of implants receiving definitive abutments and no further disconnections, there were no other significant differences observed at 5 years post-loading. As mentioned, there was a difference between the two groups in terms of prosthesis failures, but this should not be considered since it was caused by the use of the wrong abutment components.

While the differences observed are indicative of some biological impact on the peri-implant tissues, they had no perceived or visible consequences for the patients. Given that no clinically significant differences were actually observed, clinicians should feel free to choose the procedure they prefer. That being said, there was a tendency to see more implant failures in the repeated disconnection group, in which three implants were lost due to peri-implantitis

TABLE 7 COMPARISON BETWEEN DIFFERENT CENTRES AT 5 YEARS POST-LOADING.

	Luongo (n = 16)	D'Avenia (n = 17)	Bressan (n = 16)	Grusovin (n = 18)	P-value
Patients with remade/failed prostheses	0 (0%)	5 (29.4%)	5 (31.3%)	0 (0%)	0.006*
Patients with implant failures	0 (0%)	0 (0%)	3 (18.7%)	0 (0%)	0.018*
Patients with complications	0 (0%)	6 (35.3%)	6 (37.5%)	4 (22.2%)	0.048*
Pink aesthetic score (PES)	11.5 (1.8)	12.7 (1.8)	11.1 (1.9)	12.3 (1.2)	0.043*
Buccal recession in mm**	0.33 (1.48)	-0.43 (1.02)	-0.60 (0.55)	0.11 (0.74)	0.053
Patient satisfaction with function (very satisfied/satisfied)	16/0	17/0	14/2	17/1	0.261
Patient satisfaction with aesthetics (very satisfied/satisfied)	16/0	17/0	15/1	18/0	0.357
Patients willing to undergo same treatment again	100%	100%	100%	100%	Not available
Bone loss in mm	0.85 (0.82)	0.19 (0.42)	-0.01 (0.19)	0.11 (0.21)	<0.001*
Keratinised mucosa height in mm	1.9 (0.4)	2.6 (1.6)	3.6 (2.3)	3.2 (1.4)	0.023*

**Statistically significant differences*
***Positive values correspond to a reduction in recession*

and two due to implant fracture. This finding may be indicative of the inferior performance of implants subjected to repeated disconnections, and should be further explored by additional trials to understand whether this was just a coincidence or is actually evidence of the superior performance of implants not subjected to abutment changes.

Another important finding of this trial was that immediate loading procedures did not negatively affect the implant success, in agreement with that reported in a Cochrane systematic review[8].

Finally, neither increased peri-implant marginal bone loss nor buccal recession was observed at implants with less than 2 mm of keratinised mucosa height. This observation is in line with the findings of another study[15] in which no statistically significant association was observed between the presence of peri-implant keratinised mucosa at the time of delivery of the definitive prosthesis and changes in bone levels and bleeding on probing after 5 years; in that study[15], when keratinised mucosa height was analysed as a dichotomous variable (present or absent), implants with keratinised mucosa at both vestibular and lingual aspects at delivery of the definitive prosthesis tended to bleed less on probing (estimate = -0.8 ; 95%CI -1.69 to 0.08; P = 0.0741), but displayed statistically significant greater marginal bone loss as compared to implants in which keratinised mucosa was only present at one site (estimate = 0.18; 95%CI -0.1 to 0.3; P = 0.0041). This prompted the conclusion that while the height of the keratinised mucosa does not seem to alter clinical outcomes, its presence at both vestibular and lingual sites may be associated with increased marginal bone loss with respect to implants having at least one side without keratinised mucosa. Both observations, from that study[15] and the present appear to contradict the general belief, and once again reinforce the urgent need to properly study the actual role of the keratinised mucosa in terms of long-term soft-tissue health. We therefore suggest that trials be conducted to evaluate the actual effectiveness of soft tissue augmentation procedures to prophylactically increase the keratinised mucosa with a view to preventing possible future bone loss and soft tissue recession.

Our results contrast slightly with those of another controlled but non-randomised trial in

which the same implant, but non-indexed, was used[4] that found no statistically significant difference in marginal bone loss 3 years after placement of implants in posterior mandibles. Our results were also in slight disagreement with a small RCT including only 16 patients[7], in which, again, no differences were noted. However, other RCTs using different implant systems have respectively reported statistically significant differences of 0.2(3), 0.3(5) and 0.5(6) mm in favour of those implants whose abutments were not disconnected, which are in line with findings from the present trial. From a clinical point of view, differences in bone loss of from 0.2 to 0.5 mm may not have a clinically significant impact, and clinicians should therefore not be discouraged from changing abutments when necessary, although the empirical rule that the less an abutment is handled the better still appears to be valid.

Comparison between centres revealed multiple statistically significant differences, some of which may have a clinical impact. For instance, two centres had to remake or lost more prostheses than the other two. Nevertheless, it is important to note that the need to make new crowns in one of the centres was mostly due to the specific prosthetic procedures used by that centre for rehabilitating single implants in the repeated disconnection abutment group; the use of the correct type of indexed abutments would have minimised, if not eliminated, this problem. That being said, there were also differences between centres observed in bone loss, and a variation in PES score of 1.6 out of a maximum score of 14 between the best and worst performing centres, which may have a clinical impact. It is difficult to explain such differences, but they may be indicative that these procedures can be operator-dependent.

The main limitations of the present trial are the small sample size and the used of non-indexed abutments on indexed implants. Unfortunately, the planned sample size could not be reached due to the loss of two centres, though the sample size was large enough to detect some statistically, albeit perhaps not clinically, significant differences between the two procedures at 5 years post-loading (peri-implant marginal bone loss and soft tissue contour). As for the issue of using non-indexed abutments on indexed implants, this presented a problem only if abutments were removed, since it was difficult to reposition them in exactly the same position. In ordinary clinical practice this problem is easily avoidable by using the correct, dedicated indexed abutments.

Another limitation was the invalidation of the allocation concealment procedure at one of the centres, as described in detail in the previous publications stemming from this trial[11-13]. Despite receiving verbal and written instructions and explanations on why not to open the envelopes to find out the randomisation code before implant installation, some clinicians still did it. On a wider scale, this problem may be underestimated, since in distant centres it is difficult to check when sealed envelopes, used to conceal allocation, are actually opened. Therefore, centrally computerised random allocation concealment after patients' data is entered onto digital case report forms would be preferable.

Finally, in the present study, implants were loaded at different time points in the two groups (immediately and after three months), which could be a confounding factor. In a Cochrane systematic review comparing immediate *versus* conventional loading, this issue was considered and it was found that patients with conventionally loaded implants lost 0.1 mm more peri-implant marginal bone than patients subjected to immediate loading procedures[8]. While this difference was found to be statistically significant, from a clinical point of view its importance is likely negligible.

With regard to the generalisation of the present results, if operators use the correct abutment types on indexed implants they could obtain better results, in terms of fewer remakes of prostheses, than those reported in this study.

CONCLUSIONS

Five-year post-loading data show that at least three repeated abutment disconnections significantly increases bone loss by 0.37 mm when compared to no disconnection, but this difference may not be clinically significant. Hence, it might be advisable to avoid, whenever possible, unnecessary abutment disconnections, though no clinically relevant side effects may be expected if disconnections are, in fact, required. Furthermore, immediately non-occlusally loaded dental implants are a viable alternative to conventional loading, and no increased bone loss or buccal recessions were noted at implants with less than 2 mm of keratinised mucosa, as compared to those having more than 2 mm of keratinised mucosa.

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