**KEY WORDS**
Immediate loading, Non-occlusal loading, Partial edentulism

Randomized controlled trial

# IMMEDIATE LOADING OF OCCLUDING DEFINITIVE PARTIAL FIXED PROSTHESES *VERSUS* NON-OCCLUDING PROVISIONAL PROSTHESES: 10-YEAR POST-LOADING RESULTS FROM A MULTICENTRE RANDOMIZED CONTROLLED TRIAL

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**PURPOSE.** To compare the clinical outcomes of dental implants restored with definitive occluding partial fixed prostheses within one week after implant placement *versus* immediate loading with non-occluding provisional restorations replaced by definitive prostheses after four months.

**MATERIALS AND METHODS**. Forty partially edentulous patients treated with one to three dental implants, of length at least 8.5 mm and width 4.0 mm and inserted with a torque of at least 35 Ncm, were randomized to two groups of 20 patients each. Patients from one group received one definitive screw-retained metal-ceramic prosthesis in occlusion within one week after placement (occlusion group), while those in the other group received one non-occluding provisional acrylic reinforced prosthesis within 24 hours after implant placement (non-occlusion group); after four months, provisional prostheses were replaced by definitive ones. The follow-up for all patients was 10 years post-loading. Outcome measures were prosthesis and implant failures, any complications, peri-implant marginal bone level changes, aesthetics, patient satisfaction, chairside time and number of visits to the clinic from implant placement to delivery of definitive restorations.

**RESULTS.** At 10-year follow-up, nine patients had dropped out, four from the non-occlusion group and five from the occlusion group. Two implants from the latter, along with their definitive prostheses, failed early (difference in proportions = 0.1; 95% CI = -0.08 to 0.26; P = 0.487). Five patients from the occlusion group were affected by seven complications *versus* five patients (five complications) in the non-occlusion group, with no statistically significant difference in proportions (difference in proportions = -0.01; 95% CI = -0.28 to 0.26; P = 1). Ten years after loading, patients subjected to occlusal loading lost an average of 0.94 mm of peri-implant bone *versus* 0.90 mm in patients initially restored with non-occluding provisional prostheses. There were no statistically significant differences in marginal bone level changes between the two groups (mean difference = 0.17 mm; 95% CI -0.25 to 0.58; P = 0.416). Likewise, there were no significant differences in either pink aesthetic scores (5.32 *versus* 4.45; P = 0.496) or patients' satisfaction with aesthetics (Fisher's exact probability test P = 1), and all patients in both groups declared being fully satisfied with function. However, patients immediately loaded with a definitive prosthesis required significantly less chairside time (mean difference -38.00; 95% CI -58.96 to -17.04; P = 0.001) and fewer visits (mean difference -2.15; 95% CI -2.77 to -1.53; P <0.001).

**CONCLUSIONS.** Although unable to provide a definitive conclusion due to the insufficient sample size, the results do suggest that immediate loading in occlusion with definitive partial fixed prostheses is not only a viable therapeutic option for patients, but requires fewer appointments and less chairside time.



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## INTRODUCTION

Nowadays, there is ample evidence to suggest that dental implants can be successfully loaded immediately after their placement[1], instead of waiting for 3 to 4 months in mandibles and 6 to 8 months in maxillae as was common practice before the turn of the millennium[2]. Furthermore, immediate-loading procedures save time, cost and patient discomfort. However, immediately loaded implants might be at greater risk of early failure, and various strategies have been proposed to mitigate this risk, among which insertion of implants with torques greater than 30 Ncm and, whenever possible, avoiding occlusion of the provisional prostheses during the osseointegration phase. Nonetheless, while there is clear evidence that a torque greater than 30 Ncm can minimize failures in immediately loaded implants[3,4], the issue of avoiding direct occlusal loading during bone-to-implant healing remains controversial. In fact, only two randomized controlled trials (RCTs) have set out to test this hypothesis, and neither yielded any conclusive evidence[5,6]. In one trial investigating immediately loading single implants with provisional crowns in occlusion the total failure rate was 10%, with two out of 24 patients in the occlusally loaded group experiencing implant failure *versus* three out of 24 in the non-occlusally loaded group[5]. The second trial yielded similar results: the total failure rate was 12.5%, with two out of 20 patients in the non-occlusally loaded group and three out of 20 patients in the occlusally loaded group experiencing implant failure[6]. If we took these results at face value, it would not be necessary to keep immediately loaded single implants out of occlusion; however, the sample sizes were too small for a definitive answer, and the conclusion was that trials with larger samples sizes would be required.

That being said, the limited and preliminary evidence available on the subject does not preclude immediate loading of dental implants with definitive prostheses in occlusion, thereby saving time and costs. Hence, the aim of this randomized controlled trial (RCT) was to provide more data, comparing the clinical outcomes of dental implants restored with definitive partial fixed prostheses in occlusion within one week of implant placement *versus* immediate loading with non-occluding provisional restorations replaced by definitive prostheses after four months. The RCT was designed to run for ten years, and this paper presents the results up to 10 years post-loading from four of the five centres originally involved in the study. Previous publications reported the data from five centres at 4 months[7] and 3 years after loading, respectively[8]. The data is reported following CONSORT statement guidelines for improving the quality of reports of parallel-group randomized trials (http://www.consort-statement.org/).

## MATERIALS AND METHODS

### Study design and patient selection

The study was designed as a multicentre randomized controlled trial of parallel-group design with blind assessment, where possible.

Any partially edentulous patient aged 18 years or older, able to understand and sign informed consent, lacking up to four adjacent teeth, and having sufficient bone volumes to house implants at least 8.5 mm long and 4 mm wide was eligible for this trial. Only implants inserted

with a torque greater than 35 Ncm and immediately loaded (within one week) were considered. Post-extraction sites were left to heal for at least three months before implantation. Only one prosthesis per patient was included. Minor bone augmentation procedures using anorganic bovine bone granules (Endobon, ZimVie Dental, Palm Beach Gardens, FL, USA) and/or resorbable barriers (OsseoGuard, ZimVie Dental) at implant placement were allowed. Preoperative radiographs were used to quantify the amount of available bone.
Exclusion criteria were:

- general contraindications to implant surgery;
- irradiation of the head and neck area;
- immunosuppression or immunodepression;
- previous or ongoing treatment with intravenous aminobisphosphonates;
- untreated periodontitis;
- oor oral hygiene and motivation;
- uncontrolled diabetes;
- regnancy or nursing;
- known substance abuse;
- psychiatric problems or unrealistic expectations;
- lack of opposing occluding dentition in the area intended for implant placement;
- participation in other trials precluding proper adherence to the research protocol;
- referral for implant placement alone;
- unavailability for follow-up for 10 years after loading;
- aesthetic areas deemed at risk of unpredictable aesthetic outcome (at the discretion of the operator);
- bruxism or clenching;
- acute infection (abscess) or suppuration at the site intended for implant placement;
- implants placed with an insertion torque of 35 Ncm or less.

Patients who were included were categorised into three groups based on the number of cigarettes they declared smoking daily: non-smokers, moderate smokers (up to 10 cigarettes per day) and heavy smokers (11 or more cigarettes per day).
Patients were initially recruited and treated by five operators at five centres in five different countries. However, one centre only provided data to 4 months post-loading. The remaining data has been published previously[7], but is not included in the present article, which reports data from the four centres that provided 10-year post-loading data, namely Greece (Implant Clinic and Graduate Prosthodontics Clinic, School of Dentistry, National and Kapodistrian University of Athens, c/o Prof. Papavasiliou), Ireland (Dublin University Dental Hospital, c/o Dr Grufferty), Germany (private practice in Morsbach-Lichtenberg, c/o Dr Heinemann) and Poland (private practice in Wrocław, c/o Prof. Dominiak). All operators used similar and standardized procedures, and were experienced with immediate loading.
The principles outlined in the Declaration of Helsinki on clinical research involving human subjects were adhered to, and the study was approved by the ethics committees of the University of Dresden (EK 283092012), the National and Kapodistrian University of Athens (Protocol number 2.10.21/3/13), the SJH/AMNCH in Dublin (REC Reference: 2012/12/10) and the University of Wroclaw. All patients received a thorough explanation, confirmed that they had understood, and signed informed written consent prior enrolment in the trial. After implant placement, eligible patients were randomized to immediately receive either a definitive prosthesis in slight contact with the opposing dentition or a provisional prosthesis without no contacts either in occlusion or during lateral excursion.

## Clinical procedures

All patients underwent at least one session of oral hygiene instructions and debridement when required in the ten days prior to implant placement. One hour prior to implant placement, all patients received a single dose of prophylactic antibiotic therapy: either 2 g amoxicillin, or 600 mg clindamycin if allergic to penicillin. Patients rinsed with 0.2% chlorhexidine mouthwash for one minute prior to implant placement, and were treated under local anaesthesia using articaine with adrenaline 1:100,000. Surgical stents could be used. After crestal or slightly lingual incision and flap elevation, implant sites were prepared according to the implant manufacturer's instructions using 3.25-mm, 4-mm and, when needed, 5- and 6-mm diameter Quad Shaping Drills.

Bone quality was subjectively assessed at drilling as either "hard", "medium" or "soft"[9]. Implant sites with "medium" and "soft" bone quality were underprepared using, respectively, a drill of diameter one or two less than that suggested in the attempt to obtain an insertion torque greater than 35 Ncm. The surgical motor was set at a torque of 35 Ncm, and implants placed with an insertion torque up to 35 Ncm were not included in the study. T3 Certain Tapered Prevail (BNPTXX) implants (ZimVie Dental) with internal connection and a dual acid-etched and blasted surface up to the top of the neck were used. Operators chose implant lengths (8.5, 10.0, 11.5 or 13.0 mm) and diameters (4, 5 and 6 mm) based on bone anatomy. Bicortical implant engagement was sought in maxillae when the remaining bone height was less than 9 mm. The neck of the implants was placed at the level of the surrounding bone.

After all implants were placed with a torque above 35 Ncm, the sequentially numbered envelope corresponding to the patient enrolment number was opened, and the operator was thereby informed whether to load the implants immediately with either an occluding screw-retained metal-ceramic definitive restoration (occlusion group) within one week (**FIGS. 1A-E**) or a non-occluding screw-retained reinforced acrylic provisional restoration (non-occlusion group) within 24 hours.

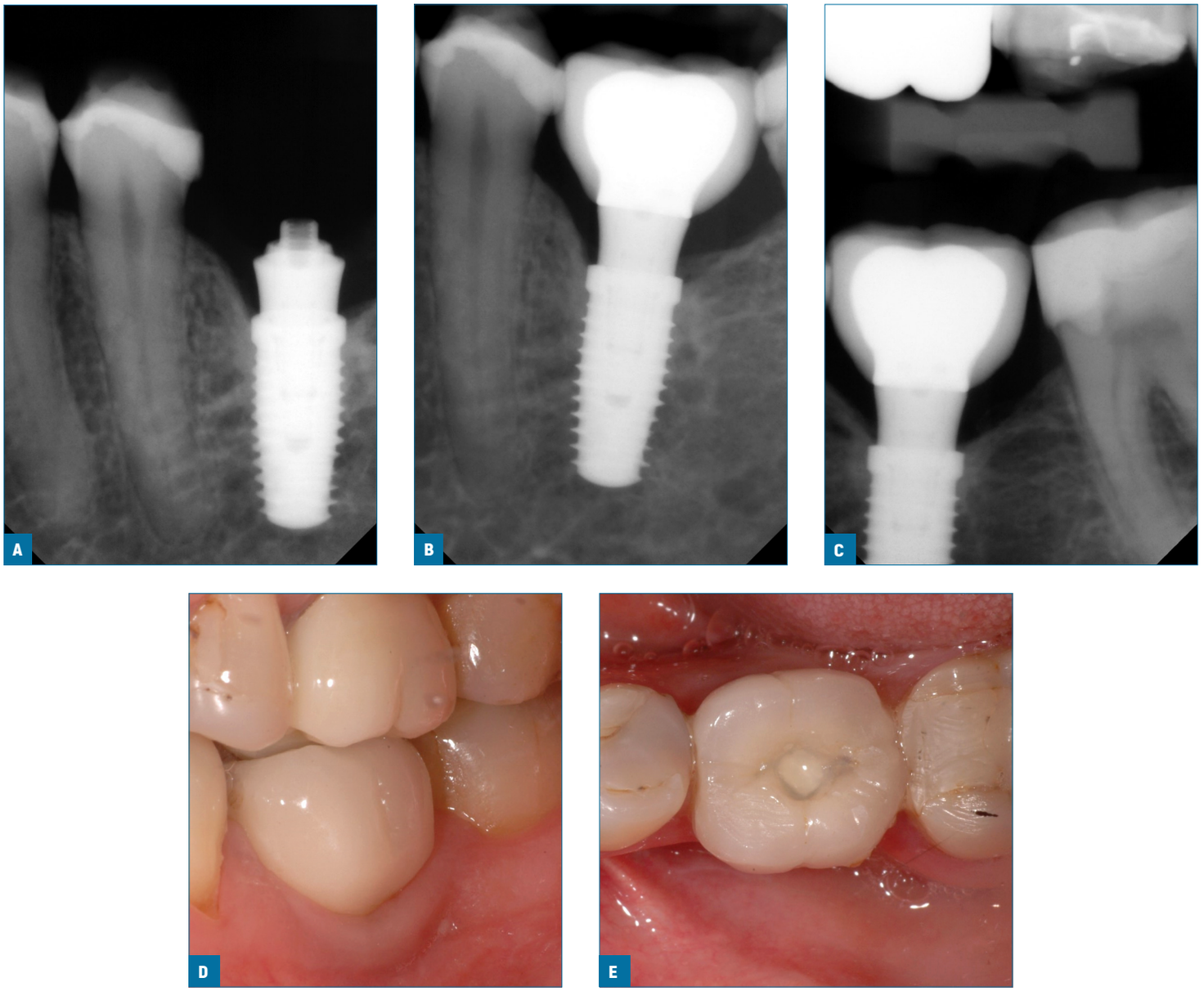
Depending on the soft tissue height, Final Low-Profile Abutments (ZimVie Dental), of height 1 to 3 mm were placed and tightened with a 15 Ncm force. Impressions were taken with Low-Profile Impression copings and Low-Profile analogues. Baseline periapical radiographs were taken of the study implants, and repeated if the peri-implant marginal bone levels were not measurable. Temporary abutments were placed in the non-occlusion group and healing abutments in the occlusion group.

Ibuprofen 400 mg (or 1 g paracetamol for patients with gastric problems or allergic to ibuprofen) was prescribed to be taken 2 to 4 times a day during meals, as long as required, but patients were advised not to take analgesics in the absence of pain. They were instructed to rinse with 0.2% chlorhexidine mouthwash twice a day for 2 weeks, to follow a soft diet for 2 weeks, and to avoid brushing and trauma to surgical sites. After one week, sutures were removed and patients received detailed oral hygiene instructions.

In the non-occlusion group, screw-retained provisional reinforced acrylic restorations were fitted within 24 hours on non-hexed Temporary Low Profile PreFormance Abutments.

Occlusion was carefully checked in both groups, but the provisional prostheses randomized to non-occlusion loading were carefully ground out from static and dynamic occlusion.

Definitive prostheses rigidly joining multiple implants were fitted onto Final Low-Profile Gold Cylinder Abutments (LPCGC2) (Non Hexed) either one week (occlusion group) or four months (non-occlusion group) after implant placement. Occlusal surfaces were in light contact with the opposing dentition when biting hard, and lateral contacts were slight. Cantilevers were allowed, with a minimum of two implants. Joining of implant-supported




**FIGS. 1A-E:** *Treatment sequence of one of the patients randomly allocated to immediate loading of a definitive prosthesis in occlusion (treated by Dr Papavasiliou): periapical baseline radiographs at placement of one implant in position 36 (A); fitting of the definitive crown (B); 10 years post-loading. In this case no evident bone loss occurred over the entire follow-up period (C); vestibular (D) and occlusal (E) views at 10 years post-loading. These pictures were used for the aesthetic evaluation by a blinded dentist.*

prostheses and natural dentition was not allowed. Patients were enrolled in an oral hygiene programme with recall visits every 6 months.

Four months, and 1, 3 and 10 years after implant placement, implants were manually tested for stability by the blinded outcome assessors; periapical radiographs and vestibular and occlusal clinical pictures of the study implants were taken; and patient satisfaction was evaluated.

## Outcome measures

This study tested the null hypothesis that there would be no differences between the two procedures against the alternative hypothesis that there would.

Outcome measures were the following.

- *Prosthesis failure*: when prosthesis placement was not possible due to implant failure or secondary to implant failure, or replacement of the definitive prosthesis for any reasons.
- *Implant failure*: implants that were mobile or removed due to progressive marginal bone loss or implant body fracture, or any other mechanical complication rendering the implant unusable. Implant stability assessments were performed at 4 months, and t 1, 3 and 10 years after placement by tightening the individual abutment screws with 25 Ncm torque or, for single implants only, by manual checking the crown stability using the handles of two metal instruments.
- *Any biological or prosthetic complications*.
- *Peri-implant marginal bone level changes*: evaluated on periapical radiographs taken with the paralleling technique at implant placement, and at 4 months, and 1, 3 and 5 years after placement. If the radiograph did not allow measurement, it was taken again. The distance between the marginal bone level and implant-abutment junction was measured at both mesial and distal sides and averaged. Bone level changes at single implants were averaged at patient level and then at group level. Non-digital radiographs were scanned into TIFF format with a 600 dpi resolution, and stored on a desktop computer. Peri-implant marginal bone levels were measured using Image J (version 1.49, National Institutes of Health, USA Image) software, which was calibrated for every single image using the known height of the implant collar. 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 most coronal margin of the implant collar and the most coronal point of bone-to-implant contact.
- *Aesthetic assessment*: performed on a computer screen using clinical pictures taken 4 months after implant placement (after delivery of the definitive prostheses) and at 1, 3 and 10 years after loading. Vestibular and occlusal views had to include one tooth on each adjacent side. Aesthetic assessment was performed using the pink esthetic score (PES)[10]. In brief, seven variables were evaluated: mesial papilla, distal papilla, soft tissue level, soft tissue contour, alveolar process deficiencies, and 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. The score was evaluated at each crown, and then averaged per patient and per group.
- *Patient satisfaction*: patients were asked the following questions at 4 months (after fitting of the definitive prostheses), and at 1, 3 and 10 years after loading:
  1) are you satisfied with the function of your implant-supported tooth/prosthesis? Possible answers were "yes, absolutely", "yes, partially", "not sure", "not really", or "absolutely not";
  2) are you satisfied with the aesthetic outcome of your implant supported tooth/prosthesis? Possible answers: "yes, absolutely", "yes, partially", "not sure", "not really", or "absolutely not";
  3) would you undergo the same treatment again? Possible answers: "yes" or "no".
- *Number of visits to the dental office* from implant placement to fitting of definitive restorations. This outcome was reported in the previous publications.
- *Chairside time in minutes* from implant placement to definitive prosthesis fitting. This outcome was reported in the previous publications.

## Blinding

Implant stability and patient satisfaction were evaluated by blinded dentists at each centre. One experience outcome assessor (Dr Anna Trullenque-Eriksson up to the third year of fol-

low-up and Dr Erta Xhanari for the 10-year follow-up) evaluated blindly peri-implant marginal bone levels and aesthetics on the clinical pictures. Complications, number of patient visits and chairside time were recorded by the treating patients with seven implants dentists, who were not blinded.

### Statistical analysis

The sample size was calculated for the primary outcome measure (implant failure) based on findings from a similar trial[5]: a two-group continuity-corrected chi-squared test with a 0.050 two-sided significance level will have 90% power to detect the difference between a proportion of 0.999 and a proportion of 0.920 for patients experiencing at least one implant failure (odds ratio of 0.0012) when the sample size in each group is 154. However, it was decided to recruit 25 patients in each group since but only 10 patients per centre were the number of patients we could realistically enroll..

The study was designed as a pragmatic multicentre randomized controlled trial of parallel-group design. Five restricted randomisation lists were computer generated, and only one investigator (Prof. Marco Esposito), who was not involved in the selection and treatment of the patients, knew the randomization sequence and had access to the randomization list, which was stored on a password-protected laptop computer. The randomization codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened sequentially only if implants were placed with an insertion torque greater than 35 Ncm. Therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

All data analysis was performed according to a pre-established analysis plan by a dentist with expertise in biostatistics (Dr Anna Trullenque-Eriksson up to the 3-year follow-up and Prof. Jacopo Buti for the 10-year evaluation), who analysed the data without knowing the group codes. The patient was the statistical unit of the analyses. Between-group differences in the proportions of patients with prosthesis failures, implant failures and complications (dichotomous outcomes) were compared using Fisher's exact probability test. Between-group differences in patient-level means for marginal peri-implant bone levels, aesthetics (PES), number of visits, and chairside time (continuous outcomes) were compared by using t-tests. marginal peri-implant bone level measurements made at 4 months and 1, 3 and 10 years were respectively compared with baseline measurements using paired tests to detect any changes. Comparisons between groups and among centres of peri-implant bone level changes (outcome variable) at 4 months and 1, 3 and 10 years were estimated using analysis of covariance with the baseline value as a covariate. The Mann–Whitney U test was used to compare the medians of the two groups' patient satisfaction, or Fisher's exact probability test when only two categories of responses were available. Differences in PES among centres were analysed using the Kruskal–Wallis test. All statistical comparisons were conducted at the 0.05 level of significance.

## RESULTS

Only the results from the four centres who provided the data up to 10 years after loading are reported here. All four centres enrolled the agreed number of patients; a total of forty-five patients were initially screened for eligibility, but five could not be included in the trial due to the following reasons: bruxism in three, insufficient bone volume in one, and inability to afford the definitive prosthesis in one. Hence, forty eligible patients were consecutively enrolled in the trial. All patients were treated according to the allocated interventions. Nine drop-outs occurred up to 10-year post-loading: four patients with four implants from the non-occlusal

group (three patients become unreachable after the 3-year evaluation and another after the 8-year evaluation) and five patients with seven implants from the occlusal group (two patients become not reachable, one before 1 year and the other after 3 years of follow-up; one patient was no more willing to attend after the 3-year visit and two patients become unreachable after the 8 year of follow-up). In addition, one patient from each group, who were originally scored as drop-outs, attended the 10-year follow-up appointment.

No major deviations from the original research protocol occurred, but there were three minor events in three patients from the non-occlusion group and one from the occlusion group. Specifically, in the non-occlusion group one out of three placed implants was immediately loaded even though inserted with a torque of less than 35 Ncm, and two definitive prostheses were fitted after a one-month delay. In the occlusion group, two 15-mm-long implants were inserted in one patient, when the maximum length allowed by the protocol was 13 mm.

Patients were recruited and treated between March 2013 and April 2014. The follow-up of all patients was to around 10 years post-loading. The main baseline patient characteristics are

**TABLE 1** PATIENT AND INTERVENTION CHARACTERISTICS

| | Occlusal (n = 20) | Non-occlusal (n = 20) |
|---|---|---|
| Females | 9 (45%) | 12 (60%) |
| Mean age at implant insertion (range) | 42.8 (18–62) | 44 (18–65) |
| Smokers + heavy smokers | 3 (15%) + 0 | 6 (30%) + 1 (5%) |
| Bone augmentation procedures | 0 | 1 (5%) |
| Number of implants | 34 | 38 |
| Implant length 8.5 mm | 5 (14.7%) | 6 (15.8%) |
| Implant length 10 mm | 8 (23.5%) | 14 (36.8%) |
| Implant length 11.5 mm | 13 (38.2%) | 10 (26.3%) |
| Implant length 13 mm | 6 (17.6%) | 8 (21.1%) |
| Implant length 15 mm | 2 (5.9%) | 0 |
| Implant diameter 4 mm | 19 (55.9%) | 21 (55.3%) |
| Implant diameter 5 mm | 15 (44.1%) | 17 (44.7%) |
| Implant diameter 6 mm | 0 | 0 |
| Soft bone quality | 2 (5.9%) | 0 |
| Medium bone quality | 26 (76.5%) | 33 (86.8%) |
| Hard bone quality | 6 (17.6%) | 5 (13.2%) |
| Upper incisors | 0 | 0 |
| Upper canines | 0 | 1 (2.6%) |
| Upper premolars | 7 (20.6%) | 8 (21.1%) |
| Upper molars | 2 (5.9%) | 1 (2.6%) |
| Lower incisors | 0 | 0 |
| Lower canines | 0 | 0 |
| Lower premolars | 7 (20.6%) | 7 (18.4%) |
| Lower molars | 18 (52.9%) | 21 (55.3%) |

**TABLE 2** DISTRIBUTION OF FAILURES AND COMPLICATIONS ACROSS STUDY CENTRES

| Dentist (number of patients) | Prosthesis failures Occlusion group | Prosthesis failures Non-occlusion group | Patients with implant failures Occlusion group | Patients with implant failures Non-occlusion group | Patients with complications Occlusion group | Patients with complications Non-occlusion group |
|---|---|---|---|---|---|---|
| Greece (10) | 0 | 0 | 0 | 0 | 1 | 1 |
| Ireland (9) | 1 | 0 | 1 | 0 | 1 | 2 |
| Germany (10) | 0 | 0 | 0 | 0 | 1 | 1 |
| Poland (9) | 1 | 0 | 1 | 0 | 2 | 1 |
| Total (38) | 2 | 0 | 2 | 0 | 5 | 5 |

presented in **TABLE 1**. There were no apparent significant baseline imbalances between the two groups, with exception of more smokers in the non-occlusion group.
The main results are summarised in **TABLE 2**.
Outcome measures were as follows.
Implant and prosthesis failures: two implants failed in the occlusion group *versus* no implant in the non-occlusally loaded group. This caused failure of the respective definitive prostheses in both cases. The difference in implant/prosthesis failure rate between the two groups was not statistically significant (difference in proportions = 0.1; 95% CI = -0.08 to 0.26; P = 0.487). Both implants were placed in first lower molar positions in non-smoking patients and were lost at 6 and 8 weeks after loading, respectively.
Five patients from the occlusion group were affected by seven complications *versus* five patients (five complications) in the non-occlusion group. The difference in proportions was not statistically significant (difference in proportions = -0.01; 95% CI = -0.28 to 0.26; P = 1). In the occlusally loaded group, 3 days post-operatively one patient experienced buccal wound dehiscence, exposing the underlying bone, in position 35–36; it took up to 10 days to close by secondary intention healing. Vestibuloplasty was performed to correct the resulting missing attached gingiva: the mucosa was incised at a distance of about 3 mm from the implants, and the flap was apically displaced and sutured to the periosteum; the open periosteum was closed using a collagen membrane matrix (Mucograft Geistlich Pharma, Wolhusen, Switzerland). Another patient in the occlusion group complained of pain at the implant site (position 46) for 3 weeks, starting from the third week after implant placement; the implant was found to be mobile and was removed. At 2 months post-loading, another patient experienced screw loosening at a single crown (position 25); this was retightened. In a fourth patient, the retaining screw was found to be mobile at the 1-year follow-up, and was retorqued accordingly. In the fifth occlusion-group patient to experience complications, both implants (46 and 47) were found to be affected by peri-implantitis at the 3-year follow-up. Surgery was scheduled and one tablet of 100 mg doxycycline was administered once a day for 7 days, starting one hour before the intervention; flaps were raised, the implant surface was treated with Er-YAG laser, and guided bone regeneration was performed using anorganic bovine bone (Bio-Oss, Geistlich Pharma) and a collagen resorbable membrane (BioGide, Geistlich Pharma). Two months later, an attempt was made to increase the keratinised mucosa: the prosthesis was unscrewed but both connecting screws fractured and the procedure was aborted. A new episode of peri-implantitis occurred at the same implants at year 5, and was treated via non-surgical debridement. In the non-occlusion group, one patient complained of prolonged postoperative pain at

**TABLE 3** MEAN RADIOGRAPHIC PERI-IMPLANT MARGINAL BONE LEVELS AND CHANGES BETWEEN GROUPS AND TIME POINTS

| | Occlusion group N / Mean / (SD) | Non-occlusion group N / Mean / (SD) | Difference (SE) / 95% CI of the difference | P-value |
|---|---|---|---|---|
| Implant placement | 19 / 0.62 / (0.60) | 20 / 0.43 / (0.34) | 0.19 (0.16) / -0.13 to 0.52 | 0.230 |
| 4 month afters placement | 19 / 1.14 / (0.79) | 20 / 1.05 / (0.83) | 0.09 (0.26) / -0.44 to 0.61 | 0.732 |
| 1 year after placement | 18 / 1.45 / (0.96) | 18 / 1.26 / (0.93) | 0.19 (0.32) / -0.45 to 0.83 | 0.548 |
| 3 years after placement | 18 / 1.49 / (1.15) | 18 / 1.20 / (1.03) | 0.29 (0.37) / -0.45 to 1.04 | 0.428 |
| 10 years after placement | 14 / 1.57 / (1.26) | 16 / 1.36 (1) | 0.21 (0.42) / -0.66 to 1.07 | 0.626 |
| Placement to 4 months (SE) ** | 19 / 0.52 / (0.23) | 20 / 0.62 / (0.21) | 0.05 (0.13) / -0.22 to 0.32 | 0.719 |
| 95% CI of the difference | 0.04 to 0.99 | 0.19 to 1.06 | | |
| P-value | 0.034* | 0.007* | | |
| Placement to 1 year (SE) ** | 18 / 0.83 / (0.26) | 18 / 0.81 / (0.25) | 0.10 (0.16) / -0.23 to 0.43 | 0.545 |
| 95% CI of the difference | 0.28 to 1.39 | 0.29 to 1.33 | | |
| P-value | 0.006* | 0.004* | | |
| Placement to 3 years (SE) ** | 18 / 0.88 / (0.34) | 18 / 0.75 / (0.27) | 0.19 (0.18) / -0.19 to 0.56 | 0.313 |
| 95% CI of the difference | 0.15 to 1.60 | 0.19 to 1.32 | | |
| P-value | 0.021* | 0.012* | | |
| Placement to 10 years (SE)** | 14 / 0.94 / (0.42) | 16 / 0.90 / (0.30) | 0.17 (0.20) / 0.25 to 0.58 | 0.416 |
| 95% CI of the difference | 0.03 to 1.84 | 0.26 to 1.54 | | |
| P-value | 0.043* | 0.009* | | |

**Statistically significant difference; **Analysis of Covariance. The radiograph at baseline of the failed implant was not provided by the centre and could not be assessed. Please note that all values presented in this table up to the 3-year follow-up have been re-analysed due to an error in the direction of signs that occurred at baseline and 4-month data collection. This error did not change any statistical test significance, and therefore both the results and conclusions previously published remain unaltered.*

the site in position 24. In another patient, loosening of the retaining screw occurred 4 months after loading, and was retorqued. In a third patient, the abutment at a posterior lower molar showed through the mucosa because it was too long (position 46), causing aesthetic discomfort for the patient; the prosthesis was adjusted for aesthetic reasons. In the final two patients, minor chipping of the ceramic lining occurred at 9 and 10 years, respectively, but required no treatment.

Peri-implant marginal bone level changes: at implant placement, there was no statistically significant between-group difference in marginal bone levels: 0.62 mm in the occlusion group and 0.43 mm in the non-occlusion group (difference = 0.19; 95% CI: -0.13 to 0.52; P = 0.230; **TABLE 3**). However, ten years after loading both groups had gradually lost a highly statistically significant amount of marginal peri-implant bone (P = 0.043 in the occlusion group and P = 0.009 in the non-occlusion group; **TABLE 3**), with patients in the occlusion group having lost an average of 0.94 mm *versus* 0.90 mm in the non-occlusion group. However, there was no statistically significant difference between the two groups in peri-implant bone level change (mean difference = 0.17 mm; 95% CI -0.25 to 0.58; P = 0.416; **TABLE 3**).

Pink esthetic scores (PES): there were no statistically significant between-group differences in average PES score at either 4 months (7.36 in the occlusion *versus* 7.15 in the non-occlusion group; P = 0.826, **TABLE 4A**), 1 year (5.51 *versus* 6.01; P = 0.668, **TABLE 4B**), 3 years (7.09 *versus* 6.90; P = 0.873, **TABLE 4C**) or 10 years (5.32 *versus* 4.45; P = 0.496, **TABLE 4D**).

**TABLE 4A** PES SCORES AT 4 MONTHS AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAIN (SD IN PARENTHESES)

| | Mesial papilla | Distal papilla | Soft tissue level | Soft tissue contour | Alveolar process deficiencies | Soft tissue colour | Soft tissue texture | Total PES score |
|---|---|---|---|---|---|---|---|---|
| Occlusion group (N = 18) | 1.31 (0.69) | 1.12 (0.67) | 1.44 (0.75) | 0.94 (0.84) | 0.71 (0.78) | 0.98 (0.43) | 0.85 (0.58) | 7.36 (2.84) |
| Non-occlusion group (N = 20) | 1.19 (0.64) | 0.88 (0.66) | 1.37 (0.74) | 0.96 (0.76) | 0.85 (0.75) | 0.95 (0.48) | 0.96 (0.74) | 7.15 (3.01) |
| Difference | 0.11 | 0.25 | 0.08 | -0.01 | -0.14 | 0.03 | -0.11 | 0.21 |
| P-values | 0.599 | 0.261 | 0.749 | 0.958 | 0.582 | 0.834 | 0.628 | 0.826 |

**TABLE 4B** PES SCORES AT 1 YEAR AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAIN (SD IN PARENTHESES)

| | Mesial papilla | Distal papilla | Soft tissue level | Soft tissue contour | Alveolar process deficiencies | Soft tissue colour | Soft tissue texture | Total PES score |
|---|---|---|---|---|---|---|---|---|
| Occlusion group (N = 18) | 0.94 (0.66) | 0.82 (0.71) | 1.11 (0.83) | 0.61 (0.72) | 0.75 (0.81) | 0.72 (0.55) | 0.55 (0.60) | 5.51 (3.60) |
| Non-occlusion group (N = 19) | 0.92 (0.71) | 0.79 (0.56) | 1.19 (0.62) | 0.71 (0.77) | 0.83 (0.79) | 0.77 (0.68) | 0.89 (0.76) | 6.01 (3.43) |
| Difference | 0.02 | 0.03 | -0.08 | -0.10 | -0.08 | -0.05 | -0.35 | -0.50 |
| P-values | 0.918 | 0.870 | 0.735 | 0.688 | 0.754 | 0.809 | 0.134 | 0.668 |

**TABLE 4C** PES SCORES AT 3 YEARS AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAIN (SD IN PARENTHESES)

| | Mesial papilla | Distal papilla | Soft tissue level | Soft tissue contour | Alveolar process deficiencies | Soft tissue colour | Soft tissue texture | Total PES score |
|---|---|---|---|---|---|---|---|---|
| Occlusion group (N = 17) | 1.26 (0.43) | 1.00 (0.66) | 1.16 (0.83) | 0.75 (0.80) | 0.91 (0.86) | 1.07 (0.71) | 0.95 (0.80) | 7.09 (3.29) |
| Non-occlusion group (N = 19) | 1.10 (0.70) | 0.85 (0.58) | 1.34 (0.72) | 0.96 (0.79) | 0.98 (0.79) | 0.88 (0.74) | 0.89 (0.83) | 6.90 (3.52) |
| Difference | 0.16 | 0.15 | -0.19 | -0.21 | -0.07 | 0.19 | 0.06 | 0.19 |
| P-values | 0.428 | 0.500 | 0.501 | 0.450 | 0.799 | 0.457 | 0.846 | 0.873 |

Patient satisfaction: regarding function at 4 months, the 20 patients in the non-occlusion group and 16 patients from the occlusion group declared that they were completely satisfied. Two patients from the occlusion group declared that they were partially satisfied, one was uncertain and one was not really satisfied. As for aesthetics, 16 patients in the occlusion group and 17 patients in the non-occlusion group declared full satisfaction. In the oc-

**TABLE 4D** PES SCORES AT 10 YEARS AFTER LOADING BY GROUP AND BY DIFFERENT AESTHETIC DOMAIN (SD IN PARENTHESES)

| | Mesial papilla | Distal papilla | Soft tissue level | Soft tissue contour | Alveolar process deficiencies | Soft tissue colour | Soft tissue texture | Total PES score |
|---|---|---|---|---|---|---|---|---|
| Occlusion group (N = 13)* | 0.96 (0.56) | 0.59 (0.61) | 1.08 (0.86) | 1.04 (0.72) | 0.35 (0.43) | 0.85 (0.77) | 0.54 (0.75) | 5.32 (3.53) |
| Non-occlusion group (N = 16) | 0.81 (0.54) | 0.55 (0.49) | 1 (0.71) | 0.83 (0.76) | 0.58 (0.73) | 0.34 (0.60) | 0.41 (0.61) | 4.45 (3.12) |
| Difference | 0.15 | 0.04 | 0.08 | 0.21 | -0.23 | 0.50 | 0.13 | 0.86 |
| P-values | 0.467 | 0.857 | 0.798 | 0.463 | 0.307 | 0.068 | 0.613 | 0.496 |

**The photograph of one patient were taken with the wrong angle and could not be evaluated*

clusion group, two patients were partially satisfied, one was uncertain and one patient was not really satisfied. In the non-occlusion group, three patients were partially satisfied. Nevertheless, there were no statistically significant between-group differences in satisfaction with either function or aesthetics (Mann-Whitney U test P = 0.289 and 0.738, respectively). All but one patient (from the occlusion group) declared that they would undergo the same procedure again (Fisher's exact probability test P = 1).

At 1 year, 16 patients from the occlusion group were completely satisfied with the function of their implant-supported prosthesis, as compared to 18 patients in the non-occlusion group. In the former group, two patients were only partially satisfied and one was not really satisfied, while in the latter, one patient was partially satisfied. Regarding the aesthetics, 16 patients in each group were fully satisfied; in the occlusion group, two patients were partially satisfied and one was not really satisfied, whereas in the non-occlusion group three were partially satisfied. There was no statistically significant difference in satisfaction with either the function or aesthetics between groups (Mann-Whitney U test P = 0.583 and 0.977, respectively). All but one patient (from the occlusion group) declared that they would undergo the same procedure again (Fisher's exact probability test P = 1)

At 3 years, 16 occlusion-group patients were completely satisfied with function *versus* 17 patients in the non-occlusion group. In the occlusion group, one patient was partially satisfied, one patient was uncertain, and one patient was not really satisfied, while in the non-occlusion group, one was partially satisfied. Regarding aesthetics, 15 patients in each group were completely satisfied. In the occlusion group, three patients were partially satisfied and one patient was not really satisfied, while in the non-occlusion group 3 patients were partially satisfied. There were no statistically significant between-group differences in satisfaction with either the function or aesthetics (Mann-Whitney U test P = 0.578 and 0.799, respectively). All but two patients (one from each group) declared that they would undergo the same procedure again (Fisher's exact probability test P = 1). At 10 years, all patients in each group declared that they were completely satisfied with the function of their implant-supported prosthesis. As regards the aesthetics, however, only 12 patients from the occlusion group and 14 patients from the non-occlusion group were completely satisfied, whereas two patients from each group were only partially satisfied. Nonetheless, there were no statistically significant differences between groups in terms of satisfaction with aesthetics (difference in proportions = 0.02; 95% CI = -0.24 to 0.28; Fisher's exact probability test P = 1). All patients declared that they would undergo the same procedure again.

**TABLE 5** COMPARISONS FOR CONTINUOUS OUTCOMES BETWEEN THE FOUR CENTRES AT 10 YEARS POST-LOADING

| Outcome | Centre 2 Greece | Centre 3 Ireland | Centre 4 Germany | Centre 5 Poland | P-value (across groups) |
|---|---|---|---|---|---|
| Bone loss from placement to 10 years (N Mean SE)* | 7 / 0.72 / (0.35) | 3 / 0.53 / (0.80) | 10 / 0.45 / (0.50) | 10 / 1.64 / (0.40) | 0.449 |
| PES total (N Mean SD)** | 7 / 5.28 / (4.39) | 3 / 8.5 / (3.88) | 10 / 4.44 / (2.88) | 9 / 3.72 / (1.84) | 0.290 |

*'Analysis of Covariance' ** Kruskal-Wallis test*

Number of visits to the dentist: on average, a significantly greater number of visits was required for patients subjected to non-occlusal loading than occlusal loading (5.00 visits *versus* 2.85 visits; mean difference -2.15; 95% CI -2.77 to -1.53; P < 0.001).

Chairside time: on average, significantly more chairside time was required for patients subjected to non-occlusal loading than occlusal loading (179.50 minutes *versus* 141.50 minutes; mean difference -38.00; 95% CI -58.96 to -17.04; P = 0.001).

Comparisons among the four centres are presented in **TABLE 2** (dichotomous data) and **TABLE 5** (continuous data). There were insufficient failures and complications for statistical tests to be applied. However, at 10 years there were no statistically significant differences among centres in either peri-implant marginal bone level changes or PES scores.

## DISCUSSION

This trial was designed to determine whether it would be clinically feasible to immediately load implants with a definitive prosthesis in occlusion. The hypothesis was generated based on the results of two previous similar RCTs[5,6], which revealed no statistically significant differences nor trends in favour of non-occlusally loaded implants. Although no statistically significant differences were observed for primary outcome measures in this trial, the results it yielded differed somewhat. In fact, 10% of the definitive prostheses restored in direct occlusion failed early *versus* none of the provisional prostheses not placed in direct occlusion. If these results are truly representative of what really happens, then it may be speculated that larger trials with much larger sample sizes would show such a difference. In that case, the most important clinical implication would be that care should be taken when immediately loading the implants, avoiding occlusal contacts in static and dynamic occlusion whenever possible.

Indeed, since all implants but one were inserted with insertion torques greater than 35 Ncm, parameters other than a high insertion torque[3,4] are likely to play a determinant role in the success of immediate loading, at least with partial fixed prostheses supported by up to three implants. One of these factors may be to avoid direct prostheses occlusion at loading, although on the basis of available evidence this should be considered a plausible hypothesis rather that a fact.

Apart from the abovementioned RCTs[5,6], there have been no other trials evaluating this hypothesis. However, several trials have investigated immediate loading of single implants, albeit with conflicting results. Some trials reported high failure rates for immediate loading[3,5,6,11], while others reported few or no implant failures[12-20], as did studies that included partially edentulous patients in which most received single implants[21-23].

That being said, it did become abundantly clear that the chairside time and the number of visits needed to complete rehabilitation were, as might be expected, substantially lower with the more direct option, i.e. fitting the definitive prostheses directly in occlusion with the op-

posing dentition. Moreover, no significant differences in aesthetics between the two options were noticed by either the patients or by blinded outcome assessors using a subjective aesthetic score[10]. That being said, 3 years post-loading total PES scores were not particularly high: 7.1/14 in the occlusion group and 6.9/14 in the non-occlusion group. By 10 years, PES scores had further deteriorated (5.32/14 for the occlusion group *versus* 4.45/14 for the non-occlusion group). However, it should be noted that the latter scores were assigned by a different another outcome assessor, and there is a great deal of subjectivity in this type of assessment, which allows only crude quantification of subjective aesthetic variables.

Despite the low aesthetics scores, the average peri-implant marginal bone loss after 10 years was below 1 mm in both groups, which is a remarkably positive result. When checking the data, we noticed that an error in the direction of signs for some imputed values had occurred at baseline and at 4 months. Therefore, all bone-loss statistics were recalculated, and are presented in **TABLE 3**. Fortunately, this error did not alter any statistical test significance, and both the results and conclusions of the previous publications therefore remained unaltered.

The main limitation of the present investigation was the small sample size. Only 25 patients per group were originally included. In addition, one centre did not deliver any data after the 4-month follow-up, further decreasing the sample size. Such a small sample size is insufficient to disclose a possible significant difference, if any. However, all treated patients were accounted for with no exclusions. In addition, peri-implant bone levels as well as aesthetic assessments were performed by centralized blinded assessors. Furthermore, both procedures were tested und real clinical conditions and patient inclusion criteria were rather broad, and it should therefore be possible to generalize the results of the present trial to a wider population with similar characteristics. Moreover, one of the aspects that makes this trial of particular interest is the long duration of its follow-up. Only a few RCTs with such a long-term follow-up have been published, but together they provide essential and reliable information on the prognosis of implant-supported rehabilitation. Looking at this specific multicentre trial, it can be concluded that the rate of both biological and mechanical complications over the 10-year of follow-up is particularly low.

## CONCLUSIONS

Although unable to provide a definitive conclusion due to the insufficient sample size, the results do suggest that immediate loading in occlusion with definitive partial fixed prostheses is not only a viable therapeutic option for patients, but requires fewer appointments and less chairside time. Larger trails are, however, needed to confirm these findings.

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