gabri.grusovin@tiscali.it; r_pistilli@libero.it; fguali@tin.it; leest007@daum.net; anyridge@imegagen.com; holeonemedical@libero.it; sian.matthews@megagen.org; h.maghaireh@yahoo.co.uk; periopkb@imegagen.com; j.buti@ucl.ac.uk

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Dental implants with internal versus external connections: 10-year post-loading results from a pragmatic multicenter randomised controlled trial

Marco Esposito, Hassan Maghaireh, Roberto Pistilli, Maria Gabriella Grusovin, Sang Taek Lee, Federico Gualini, Jacopo Buti

Marco Esposito, DDS, PhD

Free lance researcher and Associated Professor, Department of Biomaterials, The Sahlgrenska Academy at Göteborg University, Sweden

Hassan Maghaireh, BDS, MFDS, MSc

Associate Professor, Dental Implants & Oral Surgery, College of Medicine & Dentistry University, Birmingham, and private practice in Leeds, UK

Roberto Pistilli, MD

Resident, Oral and Maxillofacial Unit, San Camillo Hospital, and private practice in Rome, Italy

Maria Gabriella Grusovin, DDS

Private practice in Gorizia, Italy

Sang Taek Lee, DDS

Private practice in Suncheon, South Korea

Federico Gualini, MD, DDS, MSD

Private practices in Lovere and Bergamo, Italy

Jacopo Buti, DDS, PhD, MPerio RCSEd

Associate Professor, Unit of Periodontology, UCL Eastman Dental Institute, London, UK

Correspondence to: Dr Marco Esposito, Casella Postale 34, 20862 Arcore (MB), Italy. E-mail: espositomarco@hotmail.com

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Abstract

Purpose: To compare the effectiveness of identical implants with internal or external connections.

Materials and Methods: One-hundred-twenty patients with any type of edentulism (single tooth, partial and total edentulism) requiring one implant-supported prosthesis were randomly allocated in two equal groups to receive either implants with external connection EC) or implants of the same type but with internal connection (IC) (EZ Plus, MegaGen Implant, Gyeongbuk, South Korea) at four centres. Due to slight differences in implant design/components IC implants were platform switched while EC were not. Patients were followed for 10 years after initial loading. Outcome measures were: prosthesis/implant failures, any complication, marginal bone level changes assessed by blinded outcome assessors, when possible.

Results: Sixty patients received 96 EC implants and 60 patients 107 IC implants. Eight patients dropped-out from the EC group and nine from the IC group, but all remaining patients were followed up to 10-year post-loading. Two EC patients experienced implant and

prosthetic failures versus three IC patients (P = 0.631, diff = 0.02, 95% CI: -0.07 to 0.11). Fifteen complications occurred in 13 EC patients versus 13 complications in 11 IC patients (P = 0.720, diff. = -0.03, 95% CI: -0.19 to 0.13). There were no statistically significant differences for prosthesis and implant failures and complications between the different connection types. Ten years after loading, there were no statistically significant differences in marginal bone level estimates between the two groups (diff. = 0.07 mm, 95% CI: -0.41 to 0.54 mm, P (ancova) = 0.782) and both groups lost bone from implant placement in a statistical significant way: 1.01 mm for the EC implants and 1.27 mm for the IC implants.

Conclusions: Within the limitations given by the difference in neck design and platform switching between EC and IC implants, 10-year postloading data did not show any statistically significant differences between the two connection types, therefore clinicians could choose whatever they prefer.

Conflict of interest statement: This trial was partially funded by MegaGen Implant, Gyeongbuk, South Korea, the manufacturer of the implants evaluated in this investigation, however data belonged to the authors and by no means did the manufacturer interfere with the conduct of the trial or the publication of the results.

INTRODUCTION

Implant-supported prostheses are an effective and reliable treatment for replacing missing dentition. The success of implant-supported prostheses is mainly based on the "integration" of dental implants in newly formed bone(1). This process is generally known as "osseointegration". Literally thousands of new dental implant design, materials and surface technologies are continuously developed to further improve the outcome of implant therapy, many of them claiming superiority over competitors. There are many randomised controlled

trials (RCTs) comparing different dental implant made of various materials and having different design, and surface characteristics(2). Most of the dental implants used nowadays have a connection which allows a stable and more or less rigid connection to an abutment or directly to the dental prosthesis. There are connections allowing the retention via a screw of the abutment/prosthesis and others in which the abutment is permanently cemented in the implant. Connections usually have various shapes (such as triangles, hexagons, octagons, etc.) and other mechanisms to minimise the risk of movements and screw loosening.

The connections more commonly used are the screw-retained ones, since abutments can be removed, if needed. Screw-retained connections can be divided in two major groups: external and internal connections. The external connection is characterised by a mechanism on the top of the screw to block rotation movements which favours unscrewing. The most widely used external connection is the "external hexagon" originally used on the Brånemark implant system(1). The external hexagon connection can be considered the "gold-standard" with many manufacturers who adopted it, thought there are other types of external connections. The internal connection is characterised by the presence of the connection mechanism inside the implant body. There are many different types of internal connections with and without anti-rotating mechanism and a gold standard here is not easy to identify, though the so-called 'conometric' connections have many estimators.

The implant-abutment connection is believed to play an important role in the outcome of the implant therapy and almost each dental implant manufacturer developed its own unique connection. These connections are subjected to an aggressive marketing campaign with many manufactures and clinicians claiming the superiority of one connection over the others. Interesting to say, despite that osseointegrated dental implants have been in use for almost half century, not a single well designed and conducted RCT has been conducted to specifically investigate the role, if any, of different implant connections, by evaluating

implants where the only difference is their connections(2). Since there are no yet any valid evidence-based clinical data evaluating whether one implant connection could be superior to the others and whether if and how the different connection types could influence the clinical outcome of implant-supported rehabilitations in terms of complications, peri-implant marginal bone loss, aesthetics and easy to use; it would be desirable to have RCTs evaluating these aspects. It would also be interesting to evaluate whether the preferable connection type could be different depending on the numbers of implants supporting the same prosthesis (single crown, two to three implants or more than three implants supporting the same prosthesis).

The aim of this pragmatic multicentre RCT of parallel group design was to compare the outcomes of identical implants with internal or external connections. This is the third report on this study presenting clinical outcome at 10-year post-loading. One(3) and 5(4) years data were previously published. The present article is reported according to the CONSORT statement for improving the quality of reports of parallel-group randomised trials (http://www.consort-statement.org/).

MATERIALS AND METHODS

The study was designed as a multicentre randomised controlled trial of parallel group design with two arms with blind outcome assessments.

Any patient requiring one implant-supported prosthesis, supported by one or more implants, being 18 years or older, and able to understand and sign a written informed consent form was eligible for this trial. Only one prosthesis per patient was to be considered for this trial which could only be supported by the type of implants dictated by the randomization procedure. This trial was designed as a pragmatic trial in order to be as close as possible to the clinical reality. Broad inclusion criteria were used including, for instance, any type of bone quality,

any jaw location and whether or not patients were heavy smokers. Clinicians were allowed to choose the treatment option they considered to be the optimal for the patient to be rehabilitated (for instance flapless implant placement, immediate post-extractive implants, minor augmentation procedures at implant placement, immediate, early or delayed loading, submerged or non-submerged techniques, etc.) at their discretion.

Pre-operative radiographs (intra-oral, panoramic, CT scans or other radiographic examinations at the discretion of the operators) together with clinical inspection were used to determine bone volumes. Exclusion criteria were:

- general contraindications to implant surgery
- irradiation in the head and neck area
- immunosuppressed or immunocompromised patients
- treated or under treatment with intravenous amino-bisphosphonates
- untreated periodontitis
- poor oral hygiene and motivation
- uncontrolled diabetes
- pregnancy or nursing
- substance abusers
- psychiatric problems or unrealistic expectations
- lacking antagonistic occlusal surfaces for the implant-supported prosthesis at implant loading
- acute/purulent infection in the area intended for implant placement
- unrestorable with a retrievable prosthesis to allow individual implant stability assessment (with exceptions of single implants)
- participation in other studies, if the present protocol could not be properly followed
- referred only for implant placement

- unable to commit to 10-year follow-up.

All patients received thorough explanations and signed a written informed consent form prior to being enrolled in the trial to document that they understood the scope of the study (including procedures, follow-up evaluations, and any potential risks involved), were allowed an opportunity to ask questions pertaining to this study, and were apprised of treatment alternatives. The study was open to qualifying patients without regard to sex or race.

Patients were categorised in three groups according to what they declared: non-smokers, moderate smokers (up to 10 cigarettes per day), and heavy smokers (more than 10 cigarettes per day). For patients needing more than one implant-supported prosthesis, the operator could choose which one to include in the study at the screening visit.

Originally ten centres agreed to participate in the study but two centres did not provide any data whereas one centre provided data non compatible with the random allocation procedure and did not provide the periapical radiographs, therefore was not considered in the study. The remaining seven centres provided the 1 year after loading data, however two centres never supplied the intra-oral radiographs(3). Only four centres delivered the 5- and 10-year post-loading data, therefore only data from these latter four centres are presented below. Three of the four remaining practices were located in Italy (Drs Grusovin, Gualini and Pistilli) and in South Korea (Dr Lee). Each dentist treated 30 patients. All the follow-up visits were done at the respective treating centres.

The investigational devices were commercially available tapered titanium screw-shaped EZ Plus dental implants (MegaGen Implant, Gyeongbuk, South Korea) with sand-blasted acid-etched surface up to the neck either with external (**Fig 1a-d**) or internal (**Fig 2a-c**) connection. The external connection was the standard external hexagon of the Brånemark System (**Fig 1a-c**), whereas the internal connection was an 11° morse taper connection (**Fig 2a-c**) that produces a conical seal forming a cold welding between the abutment and the implant. The

only differences between the two implants apart the connections are the presence of a bevel at the implant neck of the IC (designed to allow platform mis-matching) which is not present in the EC design (**Figs 1a** and **2a**) and a different neck design for the implants with external connection of 3.3 mm diameter (**Fig 1d)**. The neck was designed differently in order to adapt the standard external hexagon on a small diameter implant. The other difference involved the abutment shape since those designed for the IC group had to be platform switched (**Figs 3a-c and 4a-c**). Operators were free to choose implant lengths (7, 8.5, 10, 11.5, 13 and 15 mm) and diameters (3.3, 4, 4.5 and 5.5 mm) according to clinical indications and their preferences.

Clinical procedures

Patients received prophylactic antibiotic therapy: 2 g of amoxicillin (or 600 mg of clindamycin if allergic to penicillin) one hour prior to surgery and rinsed for one minute with 0.2% chlorhexidine. All patients were treated under local anaesthesia. Tooth extractions, when needed, were performed as atraumatically as possible attempting to preserve the buccal alveolar bone. Extraction sockets were carefully cleaned from any remains of granulation tissue. The decision to elevate or not the flap was left to the individual clinician. The standard implant site preparation procedure as recommended by the implant manufacturer was used. In case of soft bone a final drill of one smaller size than the conventional procedure was used to underprepare the implant site. During implant site preparation bone quality was subjectively assessed and divided into hard, medium and soft. Once the implant site preparation was completed, the operator was informed whether the implant to be placed had to be with external or internal connection, according to a parallel-group study design with two arms, by opening a sequentially numbered sealed envelope corresponding to the patient recruitment number. Implants were placed with the neck flush to the crestal bone level with the exception of post-extractive implants that were placed about two mm below the palatal bone level and more palatally.

Clinicians were free to decide whether to load the implants immediately, early or conventionally, to submerge or to leave them non-submerged for the healing period they decided but they had to ensure that both groups were treated in a similar way, meaning that for instance the healing time for implants of both groups was similar, etc. Just after implant placement, intraoral radiographs (baseline) were made with the paralleling technique. If bone levels around the study implants were hidden or difficult to estimate, a second radiograph was made. Ibuprofen 400 mg was prescribed to be taken 2 to 4 times a day during meals, as long as required. Patients were instructed to use 0.2% chlorhexidine mouthwash for one minute twice a day for two weeks and to avoid brushing and trauma on the surgical sites. Postoperative antibiotics were only prescribed to patients subjected to bone augmentation procedures: 1 g of amoxicillin twice a day for six days. Patients allergic to penicillin were prescribed 300 mg of clindamycin twice a day for six days. Within one week all patients were recalled and checked.

Clinicians were also free to choose screw-retained or cemented restorations with provisional cement, to load the implants directly with definitive restorations, and whether to use metal-ceramic or metal-composite restorations (single crowns could be also in full ceramic). Overdentures could also be used.

Patients were enrolled in an oral hygiene program 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 were no differences in the clinical outcomes between the two connection types against the alternative hypothesis of a difference. Outcome measures were:

- Prosthesis failure (primary outcome measure): whether it will not be possible to place the prosthesis due to implant failures, secondary to implant losses or remake of a definitive prosthesis for any reasons.
- Implant failure (primary outcome measure): implant failure was defined as 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 with a wrench delivering a torque of 20 Ncm or by assessing the stability of single crowns using the handles of two instruments at initial loading, 1-, 5- and 10-year after loading.
- Any complications and adverse events (primary outcome measure) were recorded and reported by connection types directly by the operators.
- Peri-implant marginal bone level changes (secondary outcome measure) evaluated on intraoral radiographs taken with the paralleling technique at implant placement, initial loading, 1-, 5- and 10-year after loading. Non-digital radiographs were scanned in TIFF format with a 600 dpi resolution, and stored in a personal computer. Peri-implant marginal bone levels were measured using the UTHSCSA Image Tool 3.0 (The University of Texas Health Science Center, San Antonio, USA) software. The software was calibrated for every single image using the known implant neck diameter. Measurements of the mesial and distal bone crest level adjacent to each implant were made to the nearest 0.01 mm and averaged at patient level and the at group level. The measurements were taken parallel to the implant axis. 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.

At each center a local blind outcome assessor evaluated implant stability. The implant type was not recognizable when assessing implant stability of single crowns. One dentist (Dr. Maghaireh) not involved in the treatment of the patients performed all radiographic assessments without knowing group allocation, however IC implants could be identified on radiographs due to the presence of the neck bevel and of platform switched abutments.

Methodological aspects

No sample size calculation was attempted. It was originally decided to include 30 patients at each of the 10 planned centres for a total of 300 patients, 150 patients randomised to each group.

Ten computer generated restricted random lists were created. Only one investigator (Dr. Esposito), who was not involved in the selection and treatment of the patients, knew the random sequence and had access to the random list stored in a pass-word protected portable computer. The random codes were enclosed in sequentially-numbered, identical, opaque, sealed envelopes. Only after the implant sites were prepared, the envelope corresponding to the patient recruitment number was opened and the clinician knew whether to place an implant with internal or external connection. Therefore, treatment allocation was concealed to the investigators in charge of enrolling and treating the patients.

All data analyses were carried out according to a pre-established analysis plan. A dentist with expertise in statistics (Dr. Buti) analysed the data. Differences in the proportion of patients with prosthesis failures, implant failures and complications (dichotomous outcomes) were compared between groups using the Chi-squared test or Fisher Exact test (when cell count <5). Differences of means at patient level for continuous outcomes (bone levels) between groups were compared by t-tests. Comparisons between each time points and the baseline measurements were made by paired t-tests, to detect any changes in marginal peri-implant bone levels. An analysis of covariance was used to compare the mean radiographic values at

loading, 1-, 5- and 10-year, with the baseline value as a covariate. Differences among centres for dichotomous outcomes were calculated using the chi-squared test or the Freeman-Halton extension of Fisher Exact test (when cell count <5). Between-centres differences in mean radiographic values at 5-years were calculated using an analysis of covariance with the baseline value as a covariate. All statistical comparisons were conducted at the 0.05 level of significance.

RESULTS

The four centres screened 221 patients for eligibility but 101 patients were not included for the following reasons: 57 patients did not want to participate into a clinical trial, 26 patients were referred only for implant placement; seven patients unable to commit to a 10 years follow-up; five patients because were treated or were under treatment with oral bisphosphonates, four patients had the implant to be connected to other implant types; two patients for poor oral hygiene/motivation. All 120 patients had their sites treated according to the allocated interventions. Seventeen patients with 30 implants dropped-out before the completion of 10-year post-loading follow-up, eight from the EC group (11 implants) and nine from the IC group (19 implants).

Drop-out from the EC group:

- Patient #10 with one implant was severely depressed and unable to attend both 5- and 10-year visits but she reported that everything was fine (Dr. Pistilli).
- Patient #7 with two implants was sick and unable to attend both 5- and 10-year visits (Dr. Gualini).
- Patient #21 with one implant, had a serious accident and was unable to attend the 5- and 10-year visits, last seen at the 3-year follow-up (Dr. Lee).

- Patient #2 with one implant, did not want to attend the 10-year follow-up, she reported no problem; last seen at 5-year postloading (Dr. Pistilli).
- Patient #27 with two implants moved away and is followed by another dentist. No problems reported up to 10 years after loading; last seen at 5-year follow-up (Dr Gualini).
- Patient #10 with one implant become unreachable, last seen at 5-year follow-up (Dr. Lee).
- Patient #23 with one implant died of lung cancer 6 years after loading (Dr. Lee).
- Patient # 20 with two implants died for ictus 6 years and 4 months after loading (Dr. Gualini).

Drop-out from the IC group:

- Patient #25 with two implants had economical problems and was depressed and did not attend any follow-up after prosthesis delivery but reported no problem for the implant-supported prosthesis (Dr. Grusovin).
- Patient #16 with one implant died for lung carcinoma just after the 1 year follow-up (Dr. Gualini).
- Patient #1 with two implants did not want to attend the 5- and 10-year visits (Dr. Gualini).
- Patient #6 with two implants was very sick and unable to attend the 5- and 10-year visits (Dr. Gualini).
- Patient #4 with four implants become severely ill, last seen at 5-year, sent orthopantomograph at 10 year and reported no complication (Dr. Pistilli).
- Patient #21 with one implant did not come for health reasons, last seen at 5-year follow-up (Dr. Pistilli).

- Patient #25 with three implants become unreachable, last seen at 5-year follow-up (Dr. Pistilli).
- Patient #8 with one implant was unable to attend the 10 years visit, last seen at 5 years. Reported no problems (Dr. Grusovin).
- Patient #24 with three implants promised to come to the 10-year follow-up but did not, last seen at 5 years (Dr. Gualini).

One patient from Dr. Pistilli from the IC group, who was unreachable at the 5-year follow-up, attended the 10-year follow-up.

The data of all remaining patients were included in the statistical analyses. The main protocol deviations are summarised in **Table 1.** An additional protocol deviation was that Dr Lee did not record the number and reasons of those patients screened as potential candidates for the trial but did not match the inclusion criteria, and excluded patients of 'old age'.

Patients were recruited and implants were inserted from February 2009 to June 2010. The follow-up for all patients was 10-year post-loading.

The main baseline patient and intervention characteristics, divided by study group, are presented in **Table 2**. There were no apparent significant baseline imbalances between the two groups. There were 60 patients in each group and 96 EC and 107 IC implants were placed.

Prosthesis failures: Two prostheses failed in the EC group (one of the two supporting implants failed due to peri-implantitis one year and half after loading; a single implant failed for peri-implantitis at 8 years after loading) versus three prostheses (one not delivered due to implant failures and the other failed 5 and 8 years after loading due to peri-implantitis) of the IC group. There was not statistically significant difference for patients experiencing prosthesis failures between groups (P = 0.631, diff = 0.02, 95% CI: -0.07 to 0.11).

Implant failures: Two implants failed in two patients of the EC group versus four implants in three patients of the IC group. There was not statistically significant difference for patients experiencing implant failures between groups (P = 0.631, diff = 0.02, 95% CI: -0.07 to 0.11). The following implant failures occurred at EC implant group:

- One non-smoker male (#22 of Dr. Gualini), had one of the two implants affected by peri-implantitis 1 year after loading. The implant in position 35 (10 x 4 mm) was treated with open flap debridement but failed 5 months after.
- One non-smoker male (#18 of Dr. Grusovin), presented with the implant replacing 36 (11.5 x 4 mm), mobile 8 years after loading. Apparently it was lost for peri-implantitis.

The following implant failures occurred at IC implants:

- One female patient, smoking more than 10 cigarettes per day (#8 of Dr. Gualini), received two implants (10 x 4 mm and 11.5 x 4 mm) in hard bone in position 46 and 47. The surgery was painful and pain persisted postoperatively. After 2 weeks, the bone was exposed and necrotic at both implants, which were removed. These implants replaced two implants which failed previously and were not replaced.
- One non-smoker female (#19 of Dr. Gualini) had one of the two implants affected by peri-implantitis 3 years after loading. The implant in position 16 (13 x 4 mm) was treated with open flap debridement but failed 2 years after**.** The implant was successfully replaced.
- One smoker male (#13 of Dr. Grusovin) showed up with implant replacing 21 (13 x 4 mm) mobile at 8 years after loading with no apparent signs of inflammation. The patient had previously lost another implant in the same position and then he had a cystic formation treated one year before placing the presently failed study implant.

Complications: thirteen EC patients were affected by 15 complications versus 11 IC patients who were affected by 13 complications, the difference being not statistically significant (P = 0.720, diff. = -0.03, 95% CI: -0.19 to 0.13). The following complications occurred at patients who received EC implants (different complications that occurred in the same patient are numbered):

- 1) Loosening of one healing abutment after one week which was retightened. 2) Loosening of the abutment at 6 years after loading which was retightened.
- The abutment screw become loose once at single implants carrying provisional crowns in three patients. Crowns were drilled and screws retightened.
- 1) The abutment screw become loose once at a single implant one month after delivery of a definitive screw-retained crown. The screw was retightened at 30 Ncm. 2) It loosened again at 7 years post-loading and was retightened.
- The contact point between the implant-supported prosthesis and the adjacent natural tooth was lost in three patients. Prostheses were unscrewed and reshaped in the laboratory.
- One implant out of two in the same patient, replacing 35, was affected by peri-implantitis at 1 year post-loading. It was surgically treated but subsequently it failed.
- Peri-implantitis at 3 years post-loading at implant replacing 46 treated with prosthesis removal and surgical debridement plus systemic antibiotics. It recurred at 6 years and was retreated surgically.
- Peri-implantitis at 8 years post-loading at implant replacing 15, treated surgically.
- Peri-implantitis at 8 years post-loading at implant replacing 36, The patient did not come to regular check-ups, the implant was mobile and was therefore removed.

- Peri-implantitis at 9 years post-loading at implant replacing 26 treated with non-surgical debridement and with a chemical desiccant (HybenX, EPIEN Medical, St. Paul, MN, USA), stable situation.

Patients with IC implants were affected by the following complications:

- Post-operative infection with bone exposure leading to failure of two implants in one patient.
- An abutment screw become loose once at a single implant carrying a provisional crown. The crown was drilled and the screw retightened.
- Loosening of one definitive crown after three months. The screw was retightened at 30 Ncm.
- Loosening of one partial fixed prosthesis after 3 months. Screwed again with the manual torque wrench at 30Ncm.
- Peri-implantitis at 3 years post-loading at implant replacing 16, treated with surgical debridement but the implant failed at 5 years post-loading.
- Peri-implantitis at 4 years post-loading at both mandibular implants supporting one overdenture. The patient was previously hospitalized and did not come to checkups. Since she refused surgical cleaning, a non-surgical debridement was delivered plus systemic antibiotics. The problem was temporarily solved but the patient did not manage to attend regular maintenance visits. Recurrence at 10 years post-loading, patient now also affected by Alzheimer, continuous inflammation, the problem is ongoing.
- Peri-implantitis at single implant replacing 43 at 4 years and 6 months after loading treated with flap surgery and maintenance also with local antibiotics. Implant still in function at 10 years but with purulent secretion.

- 1) Peri-implantitis at two implants replacing 37 and 47 at 5-year post-loading, treated with debridement and local antibiotics. 2) Screw-loosening at implant replacing 45 10 years post-loading, retightened.
- Peri-implant mucositis at two implants replacing 34 and 36, noticed at 5-year post-loading, and successfully treated with local antibiotics and antiseptics.
- Loosening of the contact point with the adjacent natural tooth causing food impaction noticed at 5-year post-loading. The prosthesis was unscrewed and reshaped in a dental laboratory.
- Peri-implantitis at single implant replacing 26 at 10 years post-loading, treated non surgically, inflammation resolved.

Peri-implant marginal bone levels: At baseline (implant placement), there was no statistically significant difference (P = 0.092; diff. = -0.11 mm; 95% CI: -0.24 to 0.02). Both groups gradually lost marginal peri-implant bone in a highly statistically significant way at to 10-year after loading (P < 0.001; **Table 3**). Ten-year after loading, patients with EC implants lost an average of 1.01 mm peri-implant bone versus 1.27 mm for patients with IC implants (**Table 3**).

When considering baseline bone level as a covariate, no statistically significant differences were found between the two groups for estimated peri-implant bone levels at loading (diff. = 0.07 mm, 95% CI: -0.17 to 0.31 mm, P (ancova) = 0.566; **Table 4**), and 10 years after loading (diff. = 0.07 mm, 95% CI: -0.41 to 0.54 mm, P (ancova) = 0.782; **Table 4**).

The comparison between the four centres is presented in **Tables 5 and 6**. There were no statistically significant differences between centres for complications (P=0.567), for implant failures (P=0.084) and for prosthesis failures (P = 0.084) (**Table 5**). Regarding marginal bone loss, significantly more bone loss was observed at Dr. Gualini and Dr. Grusovin centres

compared to Dr. Lee (P = <0.001); and at Dr. Gualini compared to Dr Pistilli (P = 0.037) (**Table 6**).

DISCUSSION

Ten-year post-loading, no statistically significant differences or even trends could be observed comparing similar implants with internal and external connections. In order to perform a reliable comparison regarding the role of the type of connection, only the type of connection has to be different, all other implant characteristics (implant material, surface characteristics and implant shape) remaining exactly the same. The EZ Plus implant system was chosen because it almost had all the required characteristics (the main differences are the bevel present at the coronal portions of IC implants (**Fig 2a**) and the different neck of the 3.3 mm diameter EC implants (**Fig 1d**). Another reason for choosing the EZ plus systems was that the implant manufacturer was glad to sponsor an independently conducted trial to evaluate the clinical outcome of different implant connections.

Some comments could be done on those complications which might be related specifically to the connection type. Five EC implants in five patients were affected by peri-implantitis versus seven IC implants in five patients (plus another patient having two implants treated for peri-implant mucositis). The number are too small for drawing any conclusions, however they do not support the myth created by marketing of external connections being more prone to peri-implantitis because of a poorer seal allowing an enhanced bacterial leakage. The four early abutment screw loosening (three in the EC and one in the IC group) reported by Dr. Pistilli at single implants with provisional crowns can be explained by the habit of the operator to screw manually the abutment screws holding provisional crowns with torques below 10 Ncm. When placing definitive crowns the surgeon applied a torque of 25 Ncm and no more screw loosening occurred.

No differences were observed for marginal bone level changes between the two groups despite that IC implants were designed to allow platform switching. In the present study no advantages could be observed at platform switched IC implants. Regarding platform switching, contradictory results have been presented by different authors: some RCTs showed significantly less bone loss of about 0.3 mm at 1 year post-loading at platform switched implants,(5, 6) whereas other RCTs did not show any difference(7, 8).

The comparisons between the four centres yielded an intriguing observation with three times more bone loss at two centres compared to another centre. We do not have any tentative explanation or a convincing hypothesis for this difference, but some differences between treatment protocols could have been present.

According to the present findings, operators can choose the connection type, according to their preferences. It could be also hypothesised that internal connections are more user-friendly when single implants or prosthesis supported by two or three implants are used. On the contrary, it may be that in the presence of multiple implants, as when rehabilitating an edentulous jaw, the external connection could be more forgiving at impression taking than an internal one. However, these are simply hypotheses that need to be verified.

It is also interesting to observe that despite clinicians were left the option to choose the time of implant loading, only one and two patients were subjected to immediate or early loading procedures, respectively. This may suggest that immediately loading procedures for single implants or short partial fixed prostheses are not so commonly performed.

There are no other published randomised controlled trials comparing internal versus external connections alone without changing the collar design of the implants,(2) so meaningful comparisons with other similar RCTs cannot be made at the present stage.

The main limitations of the present trial are: i) the design of the two evaluated implants was not identical but additional platform switching features were present at IC implants which

may have slightly favoured IC implants; ii) the low number of patients available at the 10-year post-loading follow-up.

Regarding the generalisation of these results, due to the pragmatic nature of the present study design, similar results should be obtained by other operators treating patients with similar procedures.

CONCLUSIONS

Acknowledging that implants with internal connection had a slight modified neck due to the presence of a minor bevel, no statistically significant differences were observed in clinical outcomes between implants with internal or external connections, therefore the choice of the type of connection can be simply based on clinician preference.

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Table 1 Summary of protocol deviations by centre up to 10-year after loading (N = number of patients).

	EC (N=60)	IC (N=60)
Pistilli (N=30)	0	2 (took panoramic instead of periapical rx at 1-year) 1 (took panoramic instead of periapical rx at 10-year)
Grusovin (N=30)	2 (used Ex-Feel implants) 1 (patient refused to make 5-year rx) 1 (patient refused to make 10-year rx) 1 (took readable panoramic instead of periapical rx at 10-year)	2 (used 3 Ex-Feel implants) 1 (still wearing provisional resin crown at 5-year for financial reasons) 1 (patient refused to make 10-year rx) 1 (10-year rx not taken at patient with frank peri-implantitis and Alzheimer)
Gualini (N=30)	2 (missing periapical rx at 1 year after loading) 1 (took unreadable panoramic instead of periapical rx at 1 year)	1 (missing periapical rx at loading and 1-year)
Lee (N=30)	3 (prosthesis attached to other implant types having the same connection) 2 (used Ex-Feel implants with correct connection instead)	1 (prosthesis attached to other implant types having the same connection)
Total (N=120)	13	10

Table 2 Patient and intervention characteristics.

	EC [N=60]	**IC [N=60]**
Females (%)	37 (61.7%)	36 (60%)
Mean age at implant insertion (range)	50.4 ± 13.8 (25-74)	54 ± 13.4 (20-79)
Smoking up to 10 cigarettes/day (%)	6 (10%)	10 (16.7%)
Smoking more than 10 cigarettes/day (%)	9 (15%)	9 (15%)
Number of implants placed	96	107
Implants in upper jaws (%)	38 (39.6% impls)	40 (37.4% impls)
Implants in lower jaws (%)	58 (60.4% impls)	67 (62.6% impls)
Implants in incisor position	2 (2.1% impls)	6 (5.6% impls)
Implants in canine position	0	8 (7.5% impls)
Implants in premolar position	36 (37.5% impls)	34 (31.8% impls)
Implants in molar position	58 (60.4% impls)	59 (55.1% impls)
Implants in hard bone	20 (20.8% impls)	25 (23.4% impls)
Implants in medium bone	61 (63.5% impls)	70 (65.4% impls)
Implants in soft bone	15 (15.6% impls)	12 (11.2% impls)
Implants with 3.3 mm diameter	13 (13.5% impls)	8 (7.5% impls)
Implants with 4 mm diameter	44 (45.8% impls)	63 (58.9% impls)
Implants with 4.5 mm diameter	1 (1% impls)	0
Implants with 5 mm diameter	38 (39.6% impls)	36 (33.6% impls)
Implants 7 mm long	0	0
Implants 8.5 mm long	18 (18.8% impls)	16 (15% impls)
Implants 10 mm long	23 (24% impls)	35 (32.7% impls)
Implants 11.5 mm long	34 (35.4% impls)	35 (32.7% impls)
Implants 13 mm long	21 (21.9% impls)	21 (19.6% impls)
Post-extractive implants (%)	9 (15%)	7 (11.7%)
Implants in augmented sites (%)*	19 (31.7%)	23 (38.3%)
Implants inserted flapless (%)	0	0
Patients with implants submerged (%)	44 (73.3%)	51 (85%)
Single crowns (%)	30 (50%)	26 (43.3%)**
Partial fixed prostheses (%)	30 (50%)	31 (51.7%)**
Cross-arch fixed prostheses (%)	0	0**
Overdentures (%)	0	2 (2.3%)**
Patients with immediately loaded implants (within 1 week) (%)	0 (0%)	1 (1.7%)
Patients with early loaded implants (between 1 week and 2 months) (%)	2 (2.3%)	0 (0%)
Patients with conventionally loaded implants (after 2 months) (%)	58 (96.7%)	58 (96.7%)**

*Including augmented post-extractive sites at implant placement

**Two implants on the same patient of Dr. Gualini were removed 2 weeks after placement due to infection, so the patient could not be rehabilitated, therefore the prosthesis is not accounted for in this table.

Table 3 Implant placement, loading, 1-, 5- and 10-year values for mean radiographic peri-implant marginal bone levels and their within-group changes in mm.

	EC Implants			IC Implants		
	N	**Mean (SD)**	**95% CI**	**N**	**Mean (SD)**	**95% CI**
Implant Placement	60	0.21 (0.45)	[0.10; 0.33]	60	0.1 (0.24)	[0.04; 0.16]
Loading	60	0.79 (0.62)	[0.63; 0.95]	58	0.65 (0.73)	[0.46; 0.84]
Change	60	0.58 (0.66)	[0.41; 0.75]	58	0.56 (0.67)	[0.38; 0.74]
P-value	<0.001*			<0.001*		
	N	**Mean (SD)**	**95% CI**	**N**	**Mean (SD)**	**95% CI**
Implant placement	60	0.21 (0.45)	[0.10; 0.33]	60	0.1 (0.24)	[0.04; 0.16]
1-year	57	1.23 (0.93)	[0.98; 1.48]	58	1.03 (0.87)	[0.80; 1.26]
Change	57	1.00 (1.03)	[0.73; 1.28]	58	0.94 (0.84)	[0.72; 1.16]
P-value	<0.001*			<0.001*		
	N	**Mean (SD)**	**95% CI**	**N**	**Mean (SD)**	**95% CI**
Implant placement	60	0.21 (0.45)	[0.10; 0.33]	60	0.1 (0.24)	[0.04; 0.16]
5-year	56	1.36 (1.04)	[1.08; 1.64]	54	1.28 (1.11)	[0.98; 1.58]
Change	56	1.13 (1.24)	[0.80; 1.46]	54	1.21 (1.09)	[0.92; 1.51]
P-value	<0.001*			<0.001*		
	N	**Mean (SD)**	**95% CI**	**N**	**Mean (SD)**	**95% CI**
Implant placement	60	0.21 (0.45)	[0.10; 0.33]	60	0.1 (0.24)	[0.04; 0.16]

10-year	48	1.26 (0.95)	[0.98; 1.53]	48	1.35 (1.30)	[0.98; 1.73]
Change	48	1.01 (1.15)	[0.67; 1.34]	48	1.27 (1.30)	[0.89; 1.64]
P-value	<0.001*			<0.001*		

*All changes from baseline (paired t-test) statistically different (P<0.001). SD = Standard deviation; CI = Confidence interval.

Table 4 Mean radiographic peri-implant marginal bone level estimates with baseline bone level as covariate per group at different times.

	Baseline-loading* N Mean (SE)	Baseline-1 year* N Mean (SE)	Baseline-5 years* N Mean (SE)	Baseline-10 years* N Mean (SE)
EC implants	60 0.76 (0.09)	57 1.21 (0.12)	56 1.39 (0.15)	48 1.27 (0.17)
IC implants	58 0.69 (0.09)	58 1.05 (0.12)	54 1.25 (0.15)	48 1.34 (0.17)
Difference (SE); 95% CI	0.70 (0.12); -0.17 to 0.31	0.17 (0.17); -0.17 to 0.50	0.14 (0.21); -0.28 to 0.56	0.07 (0.24); -0.41 to 0.54
P-value (ancova)	0.566	0.332	0.505	0.782

*Analysis of covariance at loading, 1-, 5- and 10-year after loading with baseline as a covariate.

Table 5 Comparisons between study centres for the various outcome measures expressed at patient level (N = number of patients) at 10-year post-loading.

	Pistilli	Grusovin	Gualini	Lee	Total (103)	P-value
Patients with prosthesis failures (N=103)	0 out of 25	2 out 28	3 out 23	0 out of 27	5	0.084[a]
Patients with implant failures (N=103)	0 out of 25	2 out 28	3 out 23	0 out of 27	5	0.084[a]
Patients with complications (N=104)	5 out of 26	9 out 28	5 out 23	5 out of 27	24	0.567[b]

[a]Freeman-Halton extension of Fisher Exact test; [b]Chi-Square test

Table 6 Mean radiographic peri-implant marginal bone level estimates with baseline bone level as covariate per centre at 10 years (N = number of patients).

	Mean in mm (SE) 95%CI
Pistilli (N = 25) b c	1.12 (0.21) [0.71; 1.53]
Grusovin (N = 23) a b	1.74 (0.22) [1.31; 2.16]
Gualini (N = 21) a	1.95 (0.22) [1.51; 2.40]
Lee (N = 27) c	0.61 (0.20) [0.21; 1.00]

Ordered Differences Report

Centre Comparison		Mean Diff.	(SE)	95%CI	P-Value
Gualini	Lee	1.35	(0.30)	[0.57; 2.13]	<0.001*
Grusovin	Lee	1.13	(0.29)	[0.36; 1.90]	<0.001*
Gualini	Pistilli	0.83	(0.31)	[0.04; 1.63]	0.037*
Grusovin	Pistilli	0.62	(0.30)	[-0.17; 1.41]	0.176
Pistilli	Lee	0.51	(0.28)	[-0.23; 1.25]	0.279
Gualini	Grusovin	0.22	(0.31)	[-0.59; 1.03]	0.897

Statistically significant difference between centres (P-value (ancova) P<0.001).
Levels not connected by the same letters are statistically significant different.
Tukey's Test for Post-Hoc Analysis was used.
*Statistically significant difference

Figures

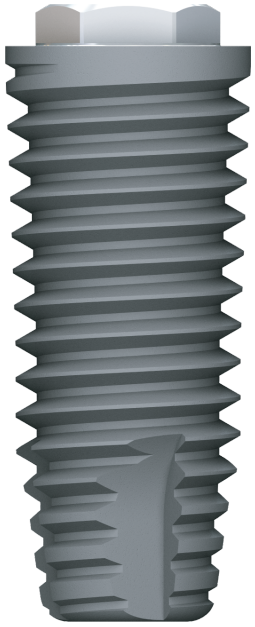

Fig 1a

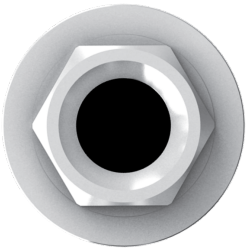

Fig 1b

Fig 1c

Fig 1d

Fig 1a-d: EZ Plus implant with external connection: a); sagittal view; b) occlusal view of the external connection; c) sagittal section showing the external connection; d) the 3.3 mm diameter has a different neck design to have the same connection and it is represented here with the implant mount.

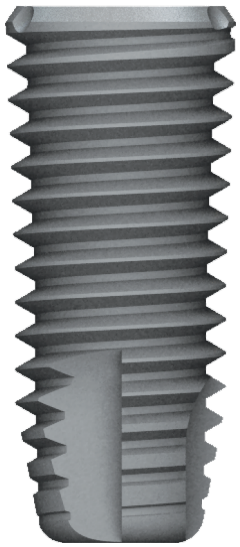

Fig 2a

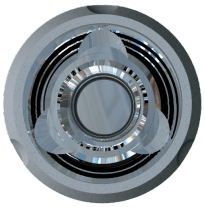

Fig 2b

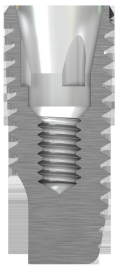

Fig 2c

Fig 2a-c: EZ Plus implant with internal connection: a); sagittal view; b) occlusal view of the internal connection; c) sagittal section showing the internal connection.

Fig 3a-c: Sequence of periapical radiographs of one of the patients treated with Ez Plus implants with external connection (EC) included in this study (courtesy of Dr. Pistilli): a) implant placement; b) initial loading; c) 10-year after loading; while peri-implant bone levers are maintained, a distal caries and calculus can be noticed at tooth 44

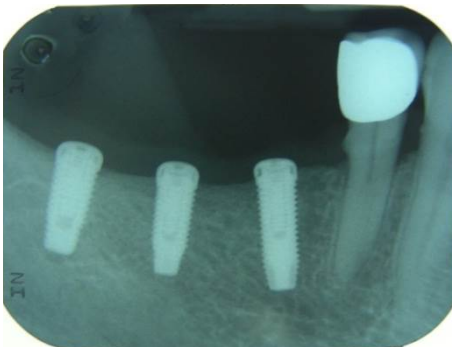

Fig 3a

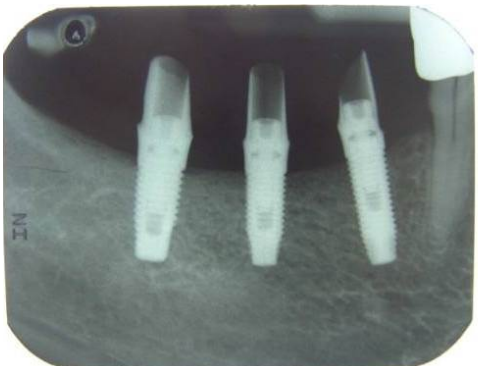

Fig 3b

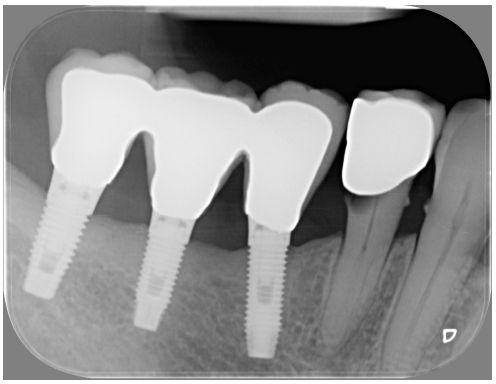

Fig 3c

Fig 4a-c: Sequence of periapical radiographs of one of the patients treated with Ez Plus implant with internal connection (IC) included in this study (courtesy of Dr. Pistilli): a) implant placement; b) initial loading; c) 10-year after loading. Please note that IC implants had to be platform-switched due to the implant design.

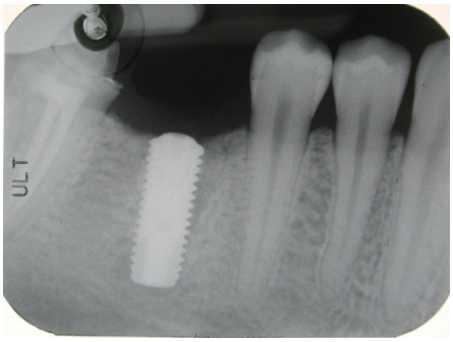

Fig 4a

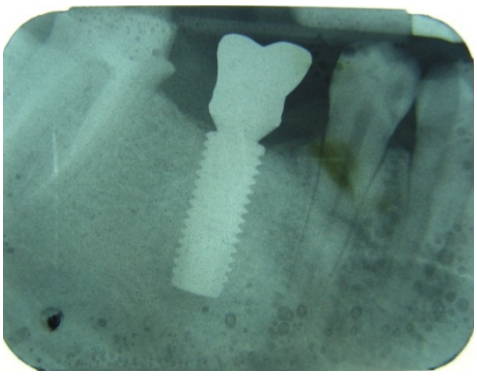

Fig 4b

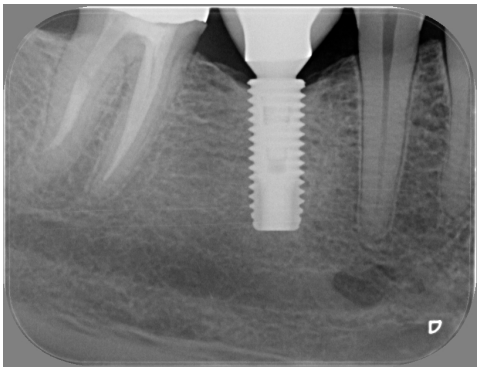

Fig 4c