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Dental implants with internal versus external connections: 5-year post-loading results from a pragmatic multicenter randomised controlled trial

Key words complication, dental implant, external connection, internal connection

Purpose: To evaluate advantages and disadvantages of identical implants with internal or external connections.

Materials and methods: One hundred and 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 an external connection (EC) or implants of the same type with an internal connection (IC) (EZ Plus, MegaGen Implant, Gyeongbuk, South Korea), at four centres. Due to slight differences in implant design and components, IC implants were platform-switched while EC were not. Patients were followed for 5 years after initial loading. Outcome measures were prosthesis/implant failures, any complication, marginal bone level changes and clinician preference, assessed by blinded outcome assessors.

Results: Sixty patients received 96 EC implants and 60 patients received 107 IC implants. Three patients dropped out with four EC implants and five patients with ten IC implants, but all remaining patients were followed up to 5-year post-loading. One prosthesis supported by EC implants and two by IC implants failed ($P = 0.615$, difference = -0.02 , 95% CI: -0.08 to 0.04). One EC implant failed versus three IC implants in two patients ($P = 0.615$, difference = -0.02 , 95% CI: -0.08 to 0.04). Ten complications occurred in 10 EC patients versus nine complications in 9 IC patients ($P = 1.000$, difference = 0.01 , 95% CI: -0.13 to 0.15). There were no statistically significant differences for prosthesis and implant failures and complications between the different connection types. Five years after loading, there were no statistically significant differences in marginal bone level estimates between the two groups (difference = 0.14 mm, 95% CI: -0.28 to 0.56 , P (ancova) = 0.505) and both groups lost bone from implant placement in a statistically significant way: 1.13 mm for the EC implants and 1.21 mm for the IC implants. Two operators had no preference and two preferred IC implants.

Conclusions: Within the limitations given by the difference in neck design and platform switching between EC and IC implants, 5-year post-loading data did not show any statistically significant differences between the two connection types, therefore clinicians could choose whichever they preferred.

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■ 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 bone¹. This process is generally known as “osseointegration”. Literally thousands of new dental implant designs, 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 comparing different dental implants made of various materials and having different designs, and surface characteristics². 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 and prosthesis and others in which the abutment is permanently cemented. 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 into 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 favour unscrewing. The most widely used external connection is the “external hexagon” originally used on the Branemark implant system¹. The external hexagon connection can be considered the “gold-standard” with many manufacturers who adopted it, though 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 mechanisms 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 manufac-

turer developed its own unique connection. These connections are subjected to an aggressive marketing campaign with many manufacturers and clinicians claiming the superiority of one connection over the others. Interestingly, despite the fact osseointegrated dental implants have been in use for almost half a century, not a single well designed randomised controlled trial (RCT) has been conducted to specifically investigate the role, if any, of the different implant connections, by evaluating implants where the only difference is their connections². Since there are not 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 ease of 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 evaluate advantages and disadvantages of identical implants with internal or external connections. This is the second report on this study presenting clinical outcome at 5-year post-loading. One-year data were previously published³. The authors also planned to publish the 10-year follow-up data. The present article is reported according to the CONSORT (Consolidated Standards of Reporting Trials) 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 multicenter controlled trial of parallel group design with blind outcome assessments.

Any patient requiring one implant-supported prosthesis, being 18 years old 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 randomisation 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 at their discretion (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).

Preoperative radiographs (intraoral, panoramic, computed tomography [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 aminobisphosphonates;
- 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 or purulent infection in the area intended for implant placement;
- unrestorable with a retrievable prosthesis to allow individual implant stability assessment (with the exception 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 informed 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 noncompatible 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 post-loading data, however two centres never supplied the intraoral radiographs³. Only four centres delivered the 5-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 clinician 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 (Figs 1a to 1d) or internal (Figs 2a to 2c) connections. The external connection was the standard external hexagon of the Brånemark System (Figs 1a to 1c), whereas the internal connection was an 11° morse taper connection (Figs 2a to 2c) that produces a conical seal forming a cold welding between the abutment and the implant. The only differences between the two implants apart from the connections are the presence of a bevel at the implant neck of the IC (designed to allow platform mismatching), which is not present in the EC design (Figs 1a and 2a) and a different neck design for the implants with an 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-

Fig 1 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.

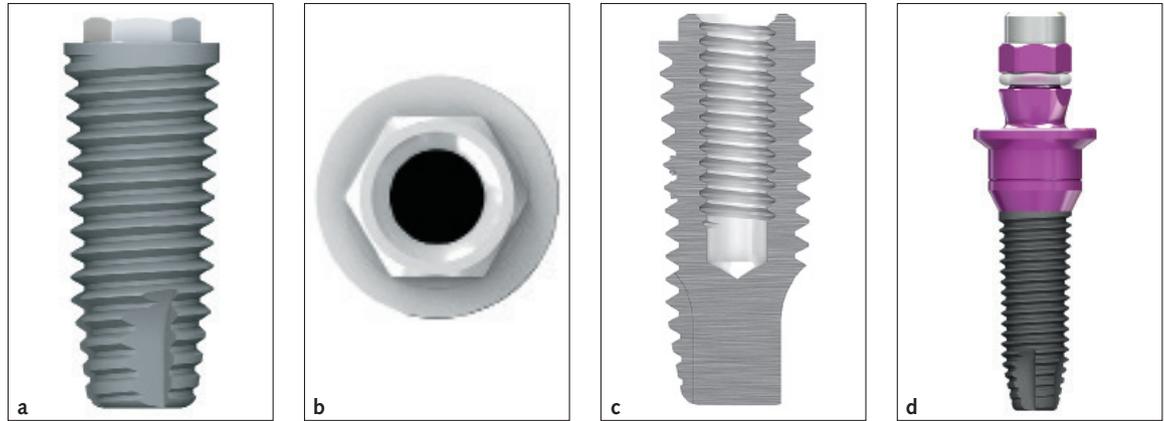
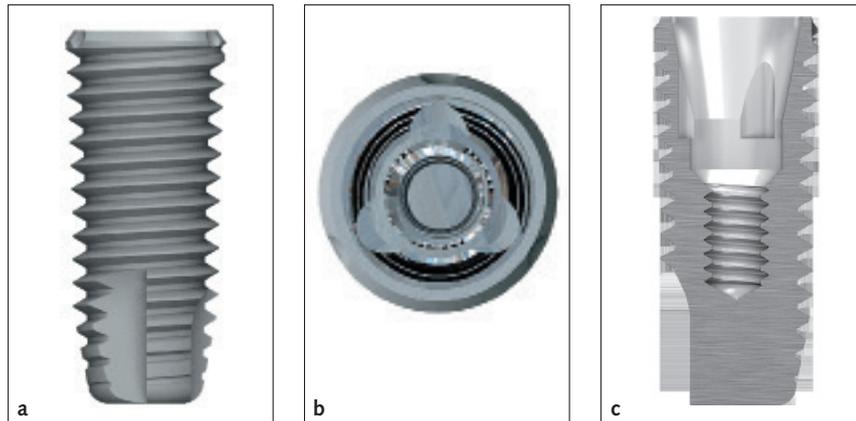


Fig 2 EZ Plus implant with internal connection: a) sagittal view; b) occlusal view of the internal connection; c) sagittal section showing the internal connection.



switched (Figs 3a to 3d and 4a to 4d). Operators were free to choose implant lengths (7.0, 8.5, 10.0, 11.5, 13.0 and 15.0 mm) and diameters (3.3, 4.0, 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) 1 h prior to surgery and rinsed for 1 min 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 whether or not to elevate 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 one size smaller than the conventional procedure was used to underprepare the implant site. During im-

plant 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 an 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 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. 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

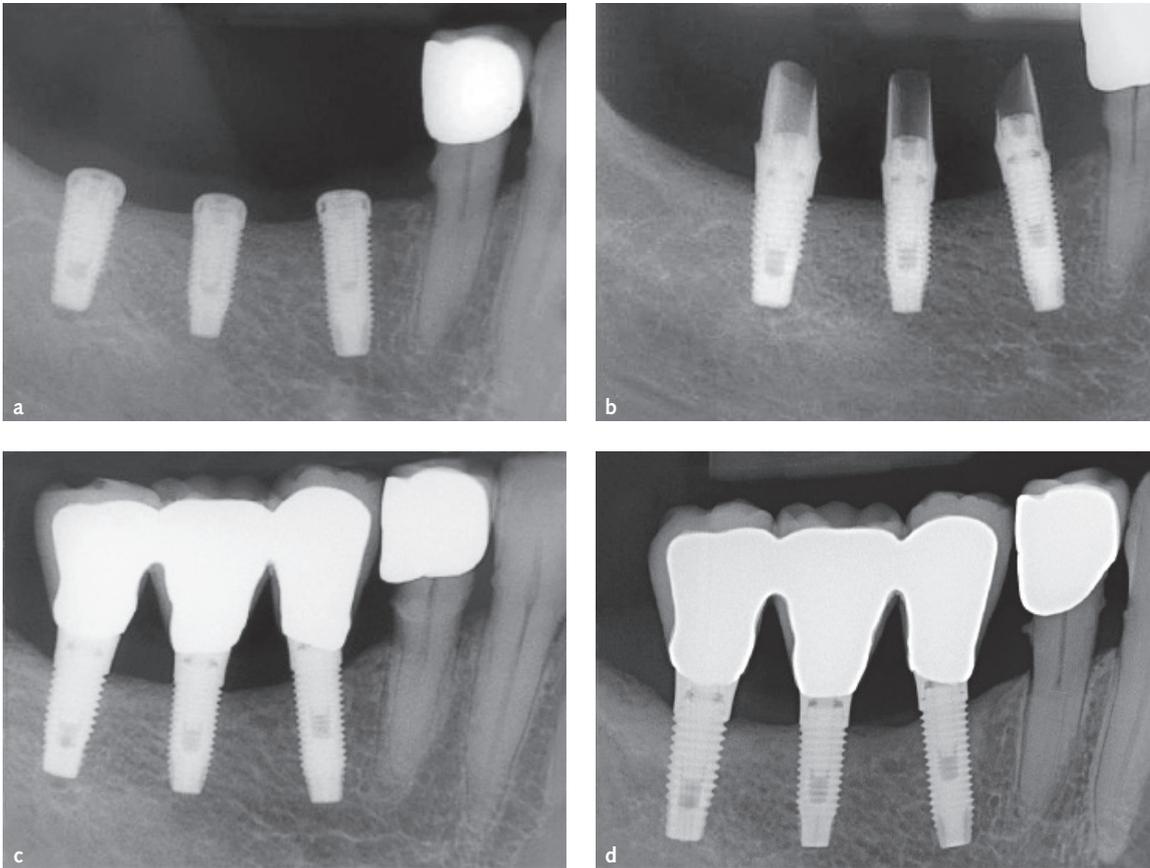


Fig 3 Sequence of periapical radiographs of one of the patients treated with EZ Plus implants, with an external connection (EC) included in this study (courtesy of Dr Pistilli): a) implant placement; b) initial loading; c) 1 year after loading; d) 5 years after loading.

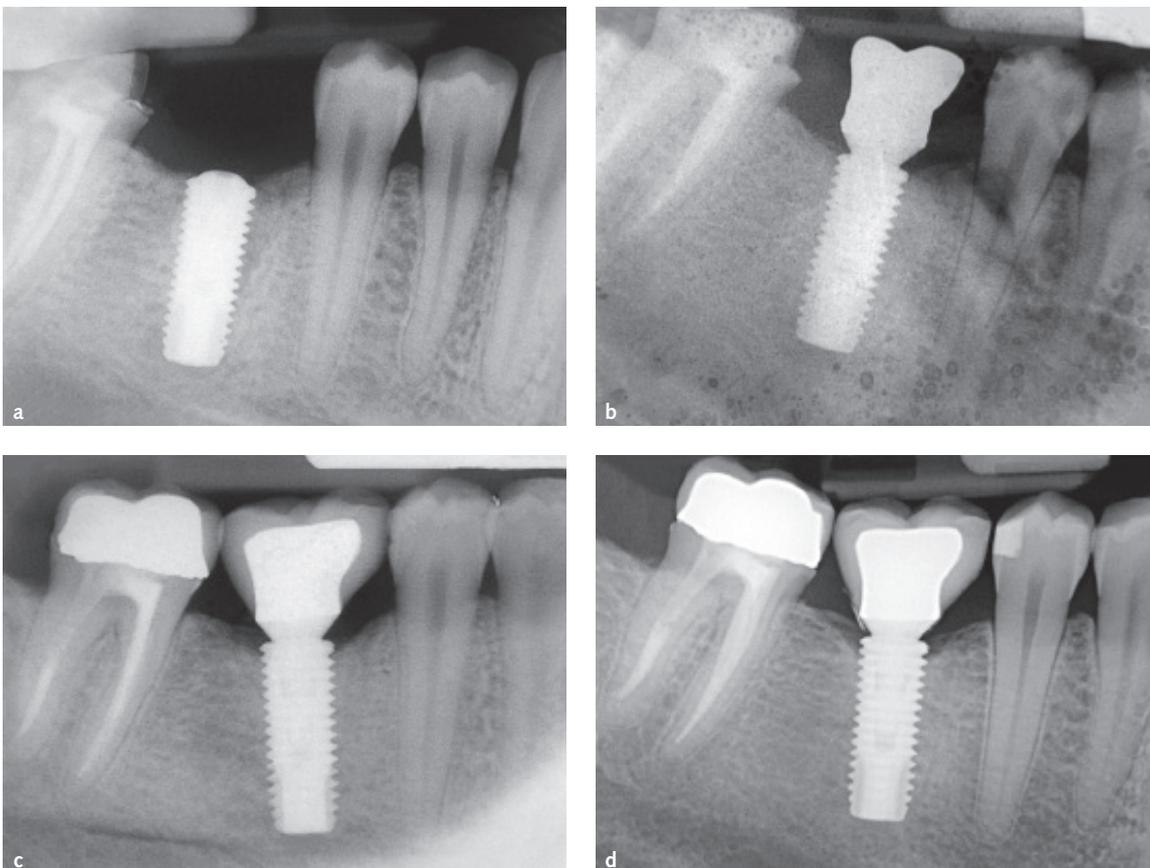


Fig 4 Sequence of periapical radiographs of one of the patients treated with EZ Plus implant, with an internal connection (IC) included in this study (courtesy of Dr Pistilli): a) implant placement; b) initial loading; c) 1 year after loading; d) 5 years after loading. Please note that IC implants had to be platform-switched due to the implant design.

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 1 min twice a day for 2 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 6 days. Patients allergic to penicillin were prescribed 300 mg of clindamycin twice a day for 6 days. Within 1 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 also be in full ceramic). Overdentures could also be used.

Periapical radiographs of the study implants were also taken at initial loading, 1 and 5 years after loading and individual implants were tested for stability: prostheses connecting more than one implant was removed and a torque of 20 Ncm was applied to the individual implants, whereas stability of implant-supported crowns was tested using the handles of two instruments.

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 and 5 years after loading.

- Any complications and adverse events (primary outcome measure) were recorded and reported by connection types.
- Peri-implant marginal bone level changes (secondary outcome measure) evaluated on intraoral radiographs taken with the paralleling technique at implant placement, at initial loading, 1 and 5 years after loading. 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, Texas, 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 then 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 the bone-to-implant contact.
- Operator preference (secondary outcome measure) for the connection type was recorded at delivery of the definitive prostheses and 1 year after loading. It was expressed in the following way: i) internal connection; ii) external connection; iii) no preference. Reasons for preference were recorded.

At each center a local blind outcome assessor evaluated implant stability. The implant type was not recognisable when assessing implant stability. One clinician (Hassan 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 the platform-switched abutments.

■ Methodological aspects

No sample size calculation was attempted. It was originally decided to include 30 patients at each of

Table 1 Summary of dropouts by centre, up to 5 years after loading, with the reasons for dropping out in parentheses (N = number of patients).

	Pistilli (N = 30)	Grusovin (N = 30)	Gualini (N = 30)	Lee (N = 30)	Total (N = 120)
EC (N = 60)	1 (sick)	0	1 (sick)	1 (sick)	3
IC (N = 60)	1 (not reachable)	1 (depression)	1 (died) 1 (sick) 1 (not willing to attend)	0	5

the 10 planned centres for a total of 300 patients, 150 patients randomised to each group.

Ten computer-generated restricted randomisation lists were created. Only one investigator (Marco 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 password-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 an internal or external connection. Therefore, treatment allocations were 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 clinician with expertise in statistics (Dr Anna Trullenque-Eriksson) analysed the data. Differences in the proportion of patients with prosthesis failures, implant failures and complications (dichotomous outcomes) were compared between groups using the Fisher's exact probability test. Difference of means at patient level for continuous outcomes (bone levels) between groups were compared by t-tests at baseline. Comparisons between each time point 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, at 1 and 5 years, with the baseline value as a covariate. Differences amongst centres for dichotomous outcomes were calculated using the chi-squared test. Differences between centres in terms of 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 in a clinical trial; 26 patients were referred only for implant placement; seven patients were unable to commit to a 10-year follow-up; five patients because were they treated or were under treatment with oral bisphosphonates; four patients had to have the implant connected to other implant types; two patients for poor oral hygiene and motivation.

All patients had their sites treated according to the allocated interventions. Eight patients with fourteen implants dropped out before the completion of the 5-year post-loading follow-up (Table 1). Dropouts from the EC group:

- One patient with one implant was sick and unable to attend the 5-year visit but reported that everything was fine (Dr Pistilli).
- One patient with two implants was sick and unable to attend the 5-year visit (Dr Gualini).
- One patient with one implant had a serious accident and was unable to attend the 5-year visit (Dr Lee).

Dropouts from the IC group:

- One patient 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).
- One patient with one implant died due to lung carcinoma just after the 1-year follow-up (Dr Gualini).
- One patient with three implants could not be contacted at 5 years (Dr Pistilli).
- One patient with two implants did not want to attend the 5-year visit (Dr Gualini).

Table 2 Summary of protocol deviations by centre up to 5 years after loading (N = number of patients).

	EC (N = 60)	IC (N = 60)
Pistilli (N = 30)	0	2 (took panoramic and not periapical radiographs at 1 year after loading)
Grusovin (N = 30)	2 (used Ex-Feel implants with correct connection instead) 1 (patient refused to make 5-year radiograph)	1 (prosthesis attached to other implant types having the same connections) 1 (still wearing provisional resin crown at 5 years after loading for financial reasons)
Gualini (N = 30)	2 (missing periapical radiograph at 1 year after loading) 1 (took unreadable panoramic instead of periapical radiograph at 1 year)	1 (missing periapical radiograph at loading)
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)	11	6

- One patient with two implants was very sick and unable to attend the 5-year visit (Dr Gualini).

The data of all remaining patients were included in the statistical analyses. The main protocol deviations are summarised in Table 2. 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 5-years post-loading.

The main baseline patient and intervention characteristics, divided by study group, are presented in Table 3. There were no apparent significant baseline imbalances between the two groups. There were 60 patients in each group, with 96 EC and 107 IC implants placed.

One prosthesis failed in the EC group (one of the two supporting implants failed due to peri-implantitis 1.5 years after loading) versus two prostheses (one not delivered due to implant failures and the other failed 5 years after loading due to peri-implantitis at one of the two supporting implants) in the IC group. There was no statistically significant differences for patients experiencing prosthesis failures between groups ($P = 0.615$, difference = -0.02, 95% CI: -0.08 to 0.04).

One implant failed in the EC group versus three implants in two patients of the IC group (Table 4).

There was no statistically significant difference for patients experiencing implant failures between groups ($P = 0.615$, difference = -0.02, 95% CI: -0.08 to 0.04). The following implant failure occurred in the EC implant group:

- One non-smoker patient 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.

The following implant failures occurred for IC implants:

- One patient, smoking more than 10 cigarettes per day, received two implants (10.0 x 4 mm and 11.5 x 4 mm) in hard bone in positions 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 patient 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.

Ten complications occurred in 10 EC patients versus nine complications in 9 IC patients (Table 5).

Table 3 Patient and intervention characteristics.

	EC [n = 60]	IC [n = 60]
Females (%)	37 (61.7%)	36 (60.0%)
Mean age at implant insertion (range)	50.4 ± 13.8 (25-74)	54 ± 13.4 (20-79)
Smoking up to 10 cigarettes/day (%)	6 (10.0%)	10 (16.7%)
Smoking more than 10 cigarettes/day (%)	9 (15.0%)	9 (15.0%)
Number of implants placed	96	107
Implants in the maxilla (%)	38 (39.6% implants)	40 (37.4% implants)
Implants in the mandible (%)	58 (60.4% implants)	67 (62.6% implants)
Implants in incisor position	2 (2.1% implants)	6 (5.6% implants)
Implants in canine position	0	8 (7.5% implants)
Implants in premolar position	36 (37.5% implants)	34 (31.8% implants)
Implants in molar position	58 (60.4% implants)	59 (55.1% implants)
Implants in hard bone	20 (20.8% implants)	25 (23.4% implants)
Implants in medium bone	61 (63.5% implants)	70 (65.4% implants)
Implants in soft bone	15 (15.6% implants)	12 (11.2% implants)
Implants with 3.3 mm diameter	13 (13.5% implants)	8 (7.5% implants)
Implants with 4.0 mm diameter	44 (45.8% implants)	63 (58.9% implants)
Implants with 4.5 mm diameter	1 (1.0% implants)	0
Implants with 5.0 mm diameter	38 (39.6% implants)	36 (33.6% implants)
Implants 7.0 mm long	0	0
Implants 8.5 mm long	18 (18.8% implants)	16 (15.0% implants)
Implants 10.0 mm long	23 (24.0% implants)	35 (32.7% implants)
Implants 11.5 mm long	34 (35.4% implants)	35 (32.7% implants)
Implants 13.0 mm long	21 (21.9% implants)	21 (19.6% implants)
Post-extractive implants (%)	9 (15.0%)	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 (85.0%)
Single crowns (%)	30 (50.0%)	26 (43.3%)
Partial fixed prostheses (%)	30 (50.0%)	31 (51.7%)
Cross-arch fixed prostheses (%)	0	0
Overdentures (%)	0	2 (2.3%)
Patients with immediately loaded implants (within 1 week) (%)	0	1 (1.7%)
Patients with early loaded implants (between 1 week and 2 months) (%)	2 (2.3%)	0
Patients with conventionally loaded implants (after 2 months) (%)	58 (96.7%)	58 (96.7%)

*Including augmented post-extractive sites at implant placement.

Table 4 Summary and comparisons expressed at patient level (N = number of patients), of implant failures up to 5 years after loading, by groups.

	Pistilli (N = 28)	Grusovin (N = 29)	Gualini (N = 26)	Lee (N = 29)	Total (N = 112)
EC (N = 56)	0 (N = 14)	0 (N = 15)	1 (N = 14)	0 (N = 14)	1 (N = 57)
IC (N = 55)	0 (N = 14)	0 (N = 14)	2* (N = 12)	0 (N = 15)	2 (N = 55)
P-value ^a	1.000	1.000	0.580	1.000	0.615

^aFisher's exact test used at patient level.

*One of the two patients lost two implants.

Table 5 Summary and comparisons expressed at patient level (N = number of patients), of complications up to 1 year after loading, by groups.

	Pistilli (N = 28)	Grusovin (N = 29)	Gualini (N = 26)	Lee (N = 29)	Total (N = 112)
EC (N = 57)	3 (N = 14)	3 (N = 15)	1 (N = 14)	3 (N = 14)	10 (N = 57)
IC (N = 55)	1 (N = 14)	3* (N = 14)	3* (N = 12)	2* (N = 15)	9 (N = 55)
P-value ^a	0.596	1.000	0.306	0.651	1.000

^aFisher's exact test used at patient level.

*One patient had two implants affected by complications.

There was no statistically significant difference for patients experiencing complications between groups ($P = 1.000$, difference = 0.01, 95% CI: -0.13 to 0.15). The following complications occurred for patients who received EC implants:

- Loosening of one healing abutment after 1 week which was retightened.
- The abutment screw became loose once at single implants carrying provisional crowns in three patients. Crowns were drilled and screws retightened.
- The abutment screw became loose once at a single implant 1 month after delivery of a definitive screw-retained crown. The screw was retightened at 30 Ncm.
- 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, in position 35, was affected by peri-implantitis at the 1-year follow-up. It was surgically treated but subsequently it failed.
- Peri-implantitis after the third year at an implant in position 46, successfully treated with prosthesis removal and surgical debridement plus systemic antibiotics.

Patients with IC implants were affected by the following complications:

- Postoperative infection with bone exposure leading to failure of two implants in one patient.
- An abutment screw became loose once at a single implant carrying a provisional crown. The crown was drilled and the screw retightened.
- Loosening of one definitive crown after 3 months. The screw was retightened at 30 Ncm.

- Loosening of one partial fixed prosthesis after 3 months. It was screwed again with the manual torque wrench at 30 Ncm.
- Peri-implantitis at third year at implant in position 16, treated with surgical debridement, but the implant failed 5 years after loading.
- Peri-implantitis at fourth year at both mandibular implants supporting one overdenture. The patient was previously hospitalised and did not attend checkups. Since she refused surgical cleaning, a non-surgical debridement was delivered plus systemic antibiotics. The problem was solved but the patient is still unable to attend the regular maintenance visits.
- Peri-implantitis at two implants in positions 37 and 47 at 5-year follow-up, treated with debridement and local antibiotics.
- Peri-implant mucositis at two implants in positions 34 and 36, observed at the 5-year follow-up, and successfully treated with local antibiotics and antiseptics.
- Loosening of the contact point with the adjacent natural tooth causing food impaction observed at the 5-year follow-up. The prosthesis was unscrewed and reshaped in a dental laboratory.

Regarding radiographic peri-implant marginal bone levels, at baseline (implant placement), there was no statistically significant difference ($P = 0.092$; difference = -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 5 years after loading ($P < 0.001$; Table 6). At loading, patients with EC implants lost an average of 0.58 mm peri-implant bone versus 0.56 mm for patients with IC implants (Table 6). One year after loading, patients with EC implants lost an average of 1 mm peri-implant bone versus 0.94 mm for patients with IC implants (Table 6).

Table 6 Implant placement, loading, 1- and 5-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	0.10 (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	0.10 (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	0.10 (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*		

*All changes from baseline (paired t-test) which were statistically different ($P < 0.001$). SD = standard deviation; CI = confidence interval.

Table 7 Mean radiographic peri-implant marginal bone level estimates with baseline bone level as covariate per group, at different times.

	Baseline-loading*			Baseline-1 year*			Baseline-5 years*		
	N	Mean	(SE)	N	Mean	(SE)	N	Mean	(SE)
EC implants	60	0.76	(0.09)	57	1.21	(0.12)	56	1.39	(0.15)
IC implants	58	0.69	(0.09)	58	1.05	(0.12)	54	1.25	(0.15)
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		
P-value (ancova)	0.566			0.332			0.505		

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

Five years after loading, patients with EC implants lost an average of 1.13 mm peri-implant bone versus 1.21 mm for patients with IC implants (Table 6).

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 (difference = 0.70 mm, 95% CI: -0.17 to 0.31 mm, P (ancova) = 0.566; Table 7), 1 year after loading (difference = 0.17 mm, 95% CI: -0.17 to 0.50 mm, P (ancova) = 0.332; Table 7), and 5 years after loading (difference = 0.14 mm, 95% CI: -0.28 to 0.56 mm, P (ancova) = 0.505; Table 7).

With regard to operator preference, two operators (Dr Pistilli and Dr Gualini) showed no preference between the two connections and two operators

preferred the IC connection (Dr Grusovin and Dr Lee). The reason they preferred the IC connection was that it was 'simpler to handle at abutment connection procedures'.

The comparison between the four centres is presented in Table 8. There were no statistically significant differences between centres in terms of complications. However, there was a statistically significant difference for implant failures ($P = 0.017$) and prosthesis failures ($P = 0.017$), with all failures occurring with Dr Gualini. Regarding the marginal bone loss, significantly more bone loss was observed at Dr Grusovin ($P = 0.006$) and Dr Gualini ($P = 0.001$) centres, compared to Dr Lee, with the former two centres losing about double the amount of peri-implant marginal bone (Table 9).

Table 8 Comparisons between study centres for the various outcome measures expressed at patient level (N = number of patients), at 5-year post-loading.

	Pistilli (N = 28)	Grusovin (N = 29)	Gualini (N = 26)	Lee2 (N = 29)	Total (111)	P-value
Patients with prosthesis failures (N = 112)	0	0	3	0	3	0.017 ^a
Patients with implant failures (N = 112)	0	0	3	0	3	0.017 ^a
Patients with complications (N = 112)	4	6	4	5	19	0.924 ^a

^aChi-square test**Table 9** Mean radiographic peri-implant marginal bone level estimates, with baseline bone level as covariate per centre at 5 years (N = number of patients).

	Mean (SE) 95% CI
Pistilli (N = 28)	1.19 (0.19) [0.81; 1.56]
Grusovin (N = 28)	1.63 (0.19) [1.26; 2.01] ^a
Gualini (N = 25)	1.81 (0.20) [1.42; 2.21] ^b
Lee (N = 29)	0.72 (0.19) [0.36; 1.09] ^{a,b}

Statistically significant difference between centres (*P*-value (ancova) < 0.001).^a *P* = 0.006; ^b *P* = 0.001

■ Discussion

Five years after 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, with 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 different implant connections.

Some comments could be made on the complications which might be related specifically to the connection type. Only two EC implants in two patients were affected by peri-implantitis versus five IC

implants in three patients (plus another patient having two implants treated for peri-implant mucositis). The numbers are too small for drawing any conclusions, however they do not support the myth created through the marketing of external connections, as being more prone to peri-implantitis because of a poorer seal allowing an enhanced bacterial leakage, considering also that the IC abutments had to be platform-switched. 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 routine habit of the operator to screw the abutment screws manually, 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 the fact 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 failures clustered in a single centre and there was 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.

Two operators had no preference with regard to the internal or external connection types, whereas

two operators preferred IC implants. The numbers were too low to allow for a statistical analysis, however two clinicians pointed out that their preference was justified by easier prosthetic procedures with the internal connection, which is understandable. Actually, 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 prostheses supported by two or three implants are used. On the contrary, it may be that in the presence of multiple implants, 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 the fact that clinicians were left the option to choose the time of implant loading, only one or two patients were subjected to immediate or early loading procedures, respectively. This may suggest that immediate loading procedures for single implants or short partial fixed prostheses are not commonly performed.

There are no other published randomised controlled trials comparing internal versus external connections², 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 5-year post-loading follow-up, also taking into consideration that three centres that provided at least partial 1-year data did not provide the agreed 5-year data.

Regarding the generalisation of these preliminary 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 an internal connection had a slightly 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 type of connection can be simply based on clinician preference.

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