

A Prospective Noninterventional Study to Evaluate Survival and Success of Reduced Diameter Implants Made From Titanium-Zirconium Alloy

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Narrow diameter implants may be at increased risk of overload due to occlusal forces; therefore, implants with higher fatigue strength may be beneficial. The aim of this observational study was to evaluate survival and success of narrow diameter (Ø 3.3 mm) TiZr alloy (Roxolid, Institut Straumann AG, Basel, Switzerland) implants for 2 years in daily dental practice. This was a prospective, non-interventional, multicenter study; no specific patient inclusion or exclusion criteria were applied. Each patient received at least one TiZr implant; the treatment plan, including implant loading and final restoration, was at the investigator's discretion. The primary outcome was implant survival and success after 1 year. Secondary outcomes included 2-year survival and success and marginal bone level change. A total of 603 implants were placed in 357 patients. Cumulative survival and success rates were 97.8% and 97.6%, respectively, after 1 year and 97.6% and 97.4%, respectively, after 2 years. Bone levels remained stable in the majority of patients, and soft tissue remained stable up to 2 years. Within the limitations of a non-interventional study design, TiZr implants showed excellent survival and success with minimal bone loss up to 2 years in daily dental practice. The results compare favorably with those of small-diameter implants in controlled clinical trials.

Key Words: titanium-zirconium (TiZr), Roxolid, non-interventional, narrow diameter implants, SLActive surface

INTRODUCTION

Predictability of dental implant treatment has been amply demonstrated in clinical studies in a variety of indications, ranging from single-tooth replacement to restoration of the fully edentulous jaw.¹⁻⁵ Implant survival and success is often reported in literature as proof of effectiveness of dental implants over the long term (ie, 5 years and longer).⁶ These clinical studies usually consist of randomized controlled trials in which the implants are used in specific indications according to a strict treatment protocol. Rigorous patient inclusion and exclusion criteria are often applied, which may limit the applicability of the results to a narrowly defined subject population. Further, patients enrolled in a controlled

study may be treated by experienced specialists in a dedicated research facility, as opposed to a busy dental office. Due to the design of these trials, patients may receive more attention by their clinicians, including additional clinical measurements and follow-up visits. In contrast, most patients receiving dental implants present with a wide range of dental situations, risk factors, and additional concomitant challenges that must be addressed. For these reasons, the design of controlled clinical trials may increase the risk of bias toward favorable outcomes, and the results may not apply to the general population, especially in terms of implant survival and success.⁷

Non-interventional studies can be useful in overcoming some of the aforementioned criticisms, as they are designed to contribute to the overall evaluation of the device in a real-world clinical practice. In such studies, the study population reflects all patients eligible to receive the device, as opposed to a narrow population selected by inclusion and exclusion criteria. The device (eg, dental implants) is used according to the approved indications, and patients are followed according to the standard practice of each participating clinician as opposed to a defined study protocol. Although there is more freedom in treatment decisions with an observational study, the systematic documentation of the device usage and clinical outcomes

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DOI: 10.1563/AAID-JOI-D-13-00149

provides an overall assessment on how the device performs in clinical practice.

The material composition and implant surface characteristics of dental implants are key success factors in modern implantology.^{8–12} Both have an important influence on implant strength and osseointegration, as demonstrated in several studies.^{13–15} A new implant material of titanium (Ti) and zirconium (Zr)—two materials known to be highly biocompatible—was recently developed. This TiZr alloy has been shown to have significantly increased biomechanical strength in dynamic fatigue strength testing.¹⁶ Unlike other Ti alloys, such as aluminium and vanadium (Ti6Al4V), a chemically modified hydrophilic SLA surface (SLActive, Institut Straumann AG, Basel, Switzerland) can be produced with TiZr. This surface has been shown to have faster osseointegration than the normal SLA surface,^{17,18} and preclinical data have demonstrated similar osseointegration with this surface on TiZr compared to Grade IV Ti.^{19–21}

Implants with a reduced endosseous diameter have proven to be extremely useful in a number of challenging indications, such as narrow edentulous ridges or single-tooth gaps in narrow interdental spaces.^{22,23} However, narrow diameter implants may also be subject to a potentially increased risk of failure or overload in some cases due to higher occlusal forces.^{24,25} The new TiZr alloy was developed to increase the fatigue strength of reduced diameter implants and proposed that the combination of faster osseointegration with higher mechanical strength may allow implants made from the TiZr alloy to be used in a wider range of indications, including the use of narrow (eg, 3.3 mm) implants in more demanding situations.^{16,26} It has been shown in clinical studies that the outcomes obtained with these implants are comparable to those obtained with titanium Grade IV implants.²⁶

The aim of the present study was to evaluate the survival and success of TiZr implants used for tooth replacement for up to 2 years following implant placement and, as a secondary objective, radiographic evaluation of the change in marginal bone level.

MATERIALS AND METHODS

This was a non-interventional, multicenter, prospective cohort study to evaluate the success and survival rates of TiZr implants. The study was planned to run for 3 years; 1- and 2-year outcomes are reported here. Patients were recruited from October 2008 to June 2010. The study was performed in 40 centers, mainly private practices, in 7 countries (Table 1). The study was approved by the Independent Ethics Committee of the Principal Investigator (and subsequent centers if considered applicable), before the start of the study. All research was carried out in accordance with the World Medical Association Declaration of Helsinki (1964) and subsequent amendments.

Patients and implants

All patients gave written informed consent to the study. Due to the non-interventional nature of the study, no specific patient inclusion or exclusion criteria were applied. Patients were eligible for this study if their general medical condition was

| | No. of Centers |
|---------------|----------------|
| All centers | 40 |
| Germany | 12 |
| Great Britain | 4 |
| France | 5 |
| Spain | 8 |
| Sweden | 2 |
| Portugal | 1 |
| USA | 8 |

sufficient to allow an oral surgical procedure, if there were no contraindications for dental implant placement, and if dental implants were indicated for tooth restoration. Each patient's dental situation was assessed, as well as the oral hygiene score and risk factors (eg, history of periodontitis, smoking, radiotherapy, bisphosphonates, etc). The anatomical situation, implant sites, implant types, augmentation procedures, healing procedure (eg, trans- or submucosal), primary implant stability, and any complications were recorded. A periapical radiograph was taken after implant placement according to the center's standard procedure, as per the study protocol.

Each patient received at least one Roxolid implant of 3.3 mm endosseous diameter made of TiZr alloy (Institut Straumann AG). The implants were inserted according to each center's normal treatment protocol and based on the manufacturer's standard surgical guidelines. The initial surgical protocol proposed elevation of a subperiosteal flap under local or general anesthesia and a round bur to mark the implant position, followed by a 2.2 and 2.8 drill for implant bed preparation. A profile drill, as well as tapping for final crestal preparation, were recommended. Either submerged or transmucosal healing were possible. All types of final restorations were allowed, including single crowns, bridges, and partial or full dentures; all loading concepts, including immediate and early loading, were allowed. The choice of implant procedure and loading protocol was the responsibility of the investigator based on the patient's clinical situation.

Clinical and radiographic parameters

At final restoration, implant success and survival was documented, complications and soft tissue were evaluated, and the type of the final restoration was recorded. The primary outcome parameter was implant success and survival after 1 year. Secondary parameters were implant success and survival after 2 years, radiographic evaluation of marginal bone level change, implant distribution in the jaws, dentist satisfaction with the procedure, and success and survival by loading protocol, implant position, and augmentation procedures.

Implant success was defined in 1990 according to Buser et al²⁷ as having the possibility for restoration and the absence of: (1) persistent pain, foreign body sensation, or dysesthesia; (2) recurrent peri-implant infection with suppuration; (3) tactile implant mobility; and (4) continuous peri-implant radiolucency. Implant survival was defined as the implant being in place at the 12- and 24-month follow-up visits. Marginal bone level

| | No. of Patients (%) |
|-----------------------------------|---------------------|
| All patients | 359 |
| Gender | |
| Female | 233 (64.9) |
| Male | 126 (35.1) |
| Age range | |
| <20 | 14 (3.9) |
| 20 < 30 | 19 (5.3) |
| 30 < 40 | 44 (12.3) |
| 40 < 50 | 68 (18.9) |
| 50 < 60 | 97 (27.0) |
| 60 < 70 | 74 (20.6) |
| 70 < 80 | 30 (8.4) |
| ≥80 | 13 (3.6) |
| Oral hygiene | |
| Excellent | 49 (13.6) |
| Good | 203 (56.5) |
| Satisfactory | 95 (26.5) |
| Poor | 12 (3.3) |
| Risk factors | |
| Previous periodontitis | 99 (28.5) |
| Radiotherapy | 3 (0.9) |
| Bisphosphonates | 4 (1.1) |
| Heavy smoker (>10 cigarettes/day) | 25 (7.2) |
| Other | 23 (6.7) |
| Dental history | |
| Existing implants | 85 (23.7) |
| Missing teeth | 339 (94.4) |
| Tooth extraction at implantation | 89 (24.8) |

change was assessed at both mesial and distal sites by the local investigator using available peri-apical radiographs. Due to the restrictions of the x-ray evaluation method with nonstandardized parameters, bone remodeling was categorized in steps of 1 mm (ie, no bone loss, < 1 mm, 1 ≤ 2 mm, 2 ≤ 3 mm, 3 ≤ 4 mm, > 4 mm, and unable to determine). The soft tissue condition was rated by the local investigator with respect to form (normal/swollen), color (pink/white/white-necrotic), and mucosal attachment (flexible/movable/not determined).

Statistical methods

Data acquisition was performed using an electronic case report form transmitted to a remote data capture system (Marvin,

| Time Between Tooth Loss and Implantation | No. of Implants | % |
|--|-----------------|------|
| Type 1* | 80 | 13.3 |
| Type 2† | 25 | 4.1 |
| Type 3‡ | 88 | 14.6 |
| Type 4§ | 410 | 68.0 |

*Implant placement immediately following tooth extraction and as part of the same surgical procedure.

†Complete soft tissue coverage of the socket (typically 4–8 weeks).

‡Substantial clinical or radiographic bone – fill of the socket (typically 12–16 weeks).

§Healed site (typically more than 16 weeks).

| Bone Volume Situation | No. of Implants | % |
|---|-----------------|------|
| Bone grafting necessary with an implant diameter larger than 3.3 mm | 327 | 54.2 |
| Bone grafting not necessary with an implant diameter larger than 3.3 mm | 150 | 24.9 |
| Augmentation was performed | 126 | 20.9 |

XClinical, Munich, Germany). A rigid follow-up plan and close central monitoring of the remote data capture system with feedback to the local centers was employed to reduce loss to follow-up as a critical source of bias.

The main study population consisted of all patients who had completed the 1- and 2-year follow-up visits. The data were analyzed descriptively using frequencies for categories and mean values for continuous variables. Data were analyzed for survival rates after 1 and 2 years, with additional analysis of implant success and correlation of certain loading protocols and anatomical or surgical parameters. Implant survival is shown in survival tables (Tables 5 and 6). All statistical analyses are descriptive.

RESULTS

Patients and implants

A total of 359 patients were enrolled, with 357 undergoing surgery. The main demographics and risk factors are summarized in Table 2. A total of 603 TiZr implants were placed; most patients (68.8%) received only TiZr implants, while 31.2% also received additional titanium implants (Institut Straumann AG). The TiZr implants were of Standard, Standard Plus, Tapered Effect, or Bone Level types ranging from 8 to 14 mm in length (Figure 1). The majority of implants were 12 or 10 mm long (47.6% and 38.3%, respectively); 14 mm (10.3%) and 8 mm (3.8%) long implants were also used. Figure 2 shows a typical case of a Bone Level TiZr 3.3 mm diameter implant restored with a cemented single crown up to two years after implant placement.

Most implants (68%) were placed in healed sites (Table 3). Bone sufficiency at the implant site and the necessity for grafting procedures are described in Table 4. For cases when bone grafting was not necessary for placement of the implant with 3.3 mm diameter, the investigator was asked to evaluate if bone augmentation would be necessary with an implant diameter larger than 3.3 mm. Transmucosal healing was performed in 56.1% of cases, while submerged healing was performed in 43.9% of cases.

One year after surgery, 259 patients with 446 implants were available for evaluation; after 2 years, 233 patients with 409 implants could be evaluated.

Implant final loading was performed between 3 and 6 months (conventional loading) in most cases (44.8%); 29.4% of cases were loaded after 6 months (delayed loading), and 22.8% were early loaded (between 48 hours and 3 months). Only 3.0%

TABLE 5
Cumulative implant success and survival rates at different visit time points

| Visit | Survival Data | | | | | | |
|-----------------------|------------------|-------------------------|---------------------------|----------------------|--------------------------|--|----------------------------|
| | Implants at Risk | No. of No-Show Implants | No. of Implants Evaluated | No. of Lost Implants | No. of Survived Implants | No. of Any Other Unsuccessful Implants | No. of Successful Implants |
| Final restoration (%) | 603 | 62 | 541 | 9 | 532 (98.3) | 3 | 529 (97.8) |
| 1 year follow-up (%) | 603 | 157 | 446 | 1 | 445 (97.8) | 1 | 444 (97.6) |
| 2 year follow-up (%) | 603 | 194 | 409 | 0 | 409 (97.6) | 1 | 408 (97.4) |

of implants were immediately loaded (within 24 hours of implant surgery). A temporary restoration was placed before the final restoration in only 30.1% of cases, of which 54% were placed out of occlusion and 46% were placed in occlusion. The majority of restorations were cemented (58.8%); of these, most were single crowns (68.1%), while 31.9% were fixed partial dentures (FPDs). Of the screw-retained restorations, 34.2% were overdentures, 31.5% were FPDs, 25.1% were single crowns, and 9.1% were removable partial dentures.

Clinical parameters

Normal soft tissue was assessed in 98.5% of cases at final restoration; the amount of normal soft tissue remained stable at 1 year (98.4%) and 2 years (96.6%). Soft tissue color was pink in the vast majority of cases at all time points (Table 5); no white-necrotic tissue was observed at any time point. In terms of mucosal attachment, the percentage of fixed soft tissue was

92.9% at final restoration (with 3.2% movable and 3.9% unknown). The percentage of fixed soft tissue increased slightly over time to 95.3% after 1 year and 96.8% after 2 years (with 0.9% and 2.2% movable, respectively).

Implant success and survival

Cumulative survival and success data at the different time points are shown in Table 5. Cumulative survival and success rates were 97.8% and 97.6%, respectively, after 1 year and 97.6% and 97.4%, respectively, after 2 years. A total of 10 implants were lost: 9 before final restoration and 1 before the 1-year follow-up. Cumulative survival rates after 1 and 2 years in relation to tooth region, implant type, augmentation situation, bone quality, and implant length are shown in Table 6. None of these factors appeared to have an influence on implant failure. Of the 10 implant losses, 5 were Bone Level implants and 5 were Tissue Level implants.

TABLE 6
Cumulative implant survival rate 1 and 2 years after implant placement

| | 1 Year Follow-up | | | 2 Year Follow-up | | |
|--|------------------------------|--------------------------|---------------------------|------------------------------|--------------------------|---------------------------|
| | No. of Survived Implants (%) | No. of Lost Implants (%) | Total no. of Implants (%) | No. of Survived Implants (%) | No. of Lost Implants (%) | Total no. of Implants (%) |
| All implants | 445 (97.8) | 10 (2.2) | 455 (100) | 409 (97.6) | 10 (2.4) | 419 (100) |
| Tooth region | | | | | | |
| Front | 222 (96.9) | 7 (3.1) | 229 (100) | 205 (96.7) | 7 (3.3) | 212 (100) |
| Premolar | 173 (99.4) | 1 (0.6) | 174 (100) | 155 (99.4) | 1 (0.6) | 156 (100) |
| Molar | 50 (96.2) | 2 (3.8) | 52 (100) | 49 (96.1) | 2 (3.9) | 51 (100) |
| Implant Type | | | | | | |
| Bone level | 282 (98.3) | 5 (1.7) | 287 (100) | 242 (98.0) | 5 (2.0) | 244 (100) |
| Standard | 19 (95.0) | 1 (5.0) | 20 (100) | 17 (94.4) | 1 (5.6) | 18 (100) |
| Standard plus | 127 (98.4) | 2 (1.6) | 129 (100) | 134 (98.5) | 2 (1.5) | 136 (100) |
| Tapered effect | 17 (89.5) | 2 (10.5) | 19 (100) | 16 (88.9) | 2 (11.1) | 18 (100) |
| Bone volume situation for placement of a Ø 3.3 mm TiZr Implant | | | | | | |
| Sufficient bone available | 349 (98.3) | 6 (1.7) | 355 (100) | 321 (98.2) | 6 (1.8) | 327 (100) |
| Not sufficient bone available | 96 (96.0) | 4 (4.0) | 100 (100) | 88 (95.7) | 4 (4.3) | 92 (100) |
| Bone quality* | | | | | | |
| I | 23 (95.8) | 1 (4.2) | 24 (100) | 22 (95.7) | 1 (4.3) | 23 (100) |
| II | 172 (96.6) | 6 (3.4) | 178 (100) | 167 (96.5) | 6 (3.5) | 173 (100) |
| III | 210 (99.1) | 2 (0.9) | 212 (100) | 182 (98.9) | 2 (1.1) | 184 (100) |
| IV | 40 (97.6) | 1 (2.4) | 41 (100) | 38 (97.4) | 1 (2.6) | 39 (100) |
| Implant length | | | | | | |
| 8 mm | 20 (95.2) | 1 (4.8) | 21 (100) | 20 (95.2) | 1 (4.8) | 21 (100) |
| 10 mm | 175 (97.2) | 5 (2.8) | 180 (100) | 164 (97.0) | 5 (3.0) | 169 (100) |
| 12 mm | 206 (98.6) | 3 (1.4) | 209 (100) | 178 (98.3) | 3 (1.7) | 181 (100) |
| 14 mm | 44 (97.8) | 1 (2.2) | 45 (100) | 47 (97.9) | 1 (2.1) | 48 (100) |

*Bone Quality: I = Almost homogeneous compact bone, II = A thick layer of compact bone surrounding a core of dense trabecular bone, III = A thin layer of compact bone surrounding a core of low density trabecular bone, IV = A thin layer of compact bone surrounding a core of low density trabecular bone.

| TABLE 5 | | | |
|-------------------|---------|----------------|---------|
| Extended | | | |
| Soft Tissue Color | | | |
| Pink | White | White-necrotic | Unknown |
| 520 (97.7) | 8 (1.5) | 0 (0) | 4 (0.8) |
| 440 (98.9) | 2 (0.4) | 0 (0) | 3 (0.7) |
| 409 (100) | 0 (0) | 0 (0) | 0 (0.0) |

Radiographic parameters

Marginal bone levels were stable in the majority of patients. Changes in marginal bone level at 1 and 2 years are shown in Figure 3. After 1 year, no bone loss was observed at 77.3% of implants (77.3% of both mesial and distal implant sites), and marginal bone loss of <1 mm was seen at 13.8% of implants (13.5% and 14.2% of mesial and distal sites, respectively). Only 5.4% of implants showed bone loss ≥1 mm. After 2 years, no bone loss was observed at 81.2% of implants (80.4% and 81.9% of mesial and distal sites, respectively), and bone loss of <1 mm was observed at 11.2% of implants (12.2% and 10.3% of mesial and distal sites, respectively).

Clinical satisfaction

Clinician satisfaction with the outcomes was high after 2 years; on a scale of 1–6 (1 being the highest), clinicians rated their satisfaction with the surgical outcome as 1 or 2 in 70.8% and 23.2% of cases. Satisfaction with the prosthetic outcomes after 2 years was rated as 1 or 2 in 63.1% and 30.5% of cases, respectively.

DISCUSSION

The purpose of this non-interventional study was to evaluate the survival and success of TiZr implants used for tooth replacement in all approved indications for up to 2 years following implant placement. The results indicated excellent performance of the implant in daily dental practice. Cumulative survival and success rates after 2 years were 97.6% and 97.4%, respectively, with no or very little (<1 mm) bone loss in the vast

majority of cases. The survival rate of the TiZr implants compared favorably with those of narrow diameter implants in more strictly controlled clinical trial settings.^{26,28,29}

The prevalence of previous history of periodontitis in this patient population was lower than that previously reported by some authors.^{30,31} In this study population, 71.5% of the subjects had no previous history of periodontitis. Recent evidence has suggested that there is a trend toward a lower prevalence of periodontal disease in recent years.³² In addition, prevalence rates vary according to country and population³⁰ and have proven difficult to define due to important differences in how periodontal disease is defined.³¹ It is also important to note that some data indicate that patients with a history of periodontitis may be a greater risk for developing peri-implant disease, but the evidence is weak³³ and may be heavily influenced by other factors, such as smoking³⁴ or preventive maintenance.³⁵ Indeed, recent studies have suggested that patients with a history of periodontitis can be successfully treated with implants, with no significant adverse influence on implant failure.³⁶ In addition, the observation time (up to 2 years) may not be sufficient to detect evidence of peri-implant disease in periodontitis-susceptible patients.

Implants with a reduced endosseous diameter (eg, 3.3 mm vs 4.1 or 4.8 mm, in the case of Straumann implants) are often used in challenging indications where the interdental space or the width of the alveolar ridge is insufficient for the placement of implants of a normal diameter.^{23,24} In the latter situation, the placement of narrow diameter implants can help to avoid augmentation procedures, which are more invasive and can have disadvantages in terms of longer overall treatment time and greater risk of complications, such as donor site morbidity in the case of autogenous bone^{37,38} or increased risk of recession due to insufficient thickness of the buccal bone. In addition, clinical evidence shows that implants placed in augmented sites may be at greater risk of implant failure than implants placed in native bone.³⁹ One possibility is that this may be due to an increase in marginal bone loss if graft stiffness is reduced, according to a finite element analysis (FEA) study.⁴⁰ Insertion torque has also been demonstrated to be significantly lower in grafted compared to nongrafted bone.⁴¹ Given that higher occlusal forces may themselves be a risk factor for failure or overload of narrow diameter implants, it would seem that the best practice would be to avoid augmentation or, if augmentation is necessary, to use implants

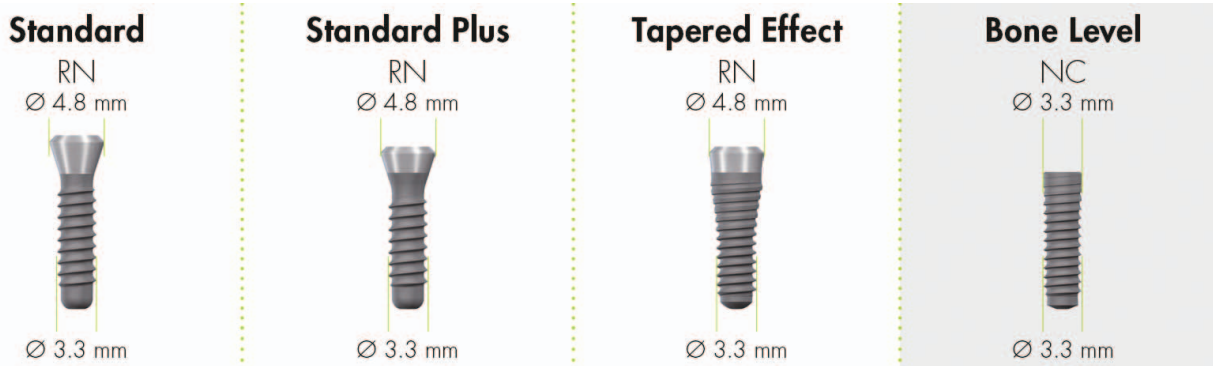
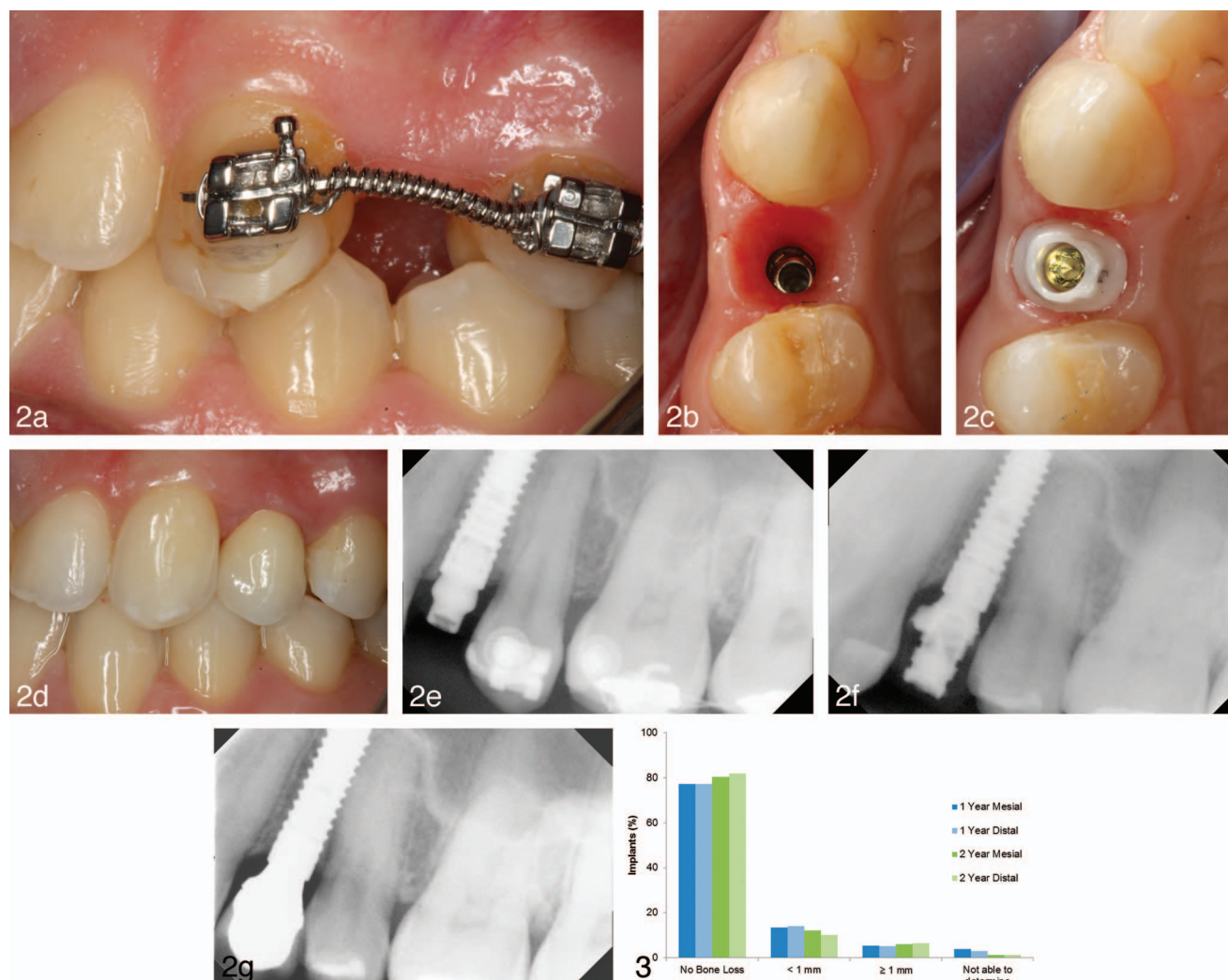


FIGURE 1. Types of implants used in this study.



FIGURES 2 AND 3. FIGURE 2. A clinical case (provided by Dr J. Tondela) of a Bone Level Narrow CrossFit TiZr 3.3 mm diameter implant restored with a cemented zirconia single crown at position 12. (a) Frontal view before implant placement. (b) Soft tissue emergence profile. (c) Zirconium abutment. (d) Lateral view at the 2-year follow-up. (e) Intra-oral radiograph after dental implant placement (day 0). (f) Intra-oral radiograph at the 1-year follow-up. (g) Intra-oral radiograph at the 2-year follow-up. **FIGURE 3.** Marginal bone level changes mesial and distal after 1 and 2 years.

made of a stronger material than pure titanium. In the current study, it was found that the use of narrow diameter implants (3.3 mm) could avoid the need for augmentation in more than half (54%) of cases that would otherwise require it (Table 4).

Implants with a reduced diameter have a reduced surface area for osseointegration; this may increase the stress in the crestal bone and consequently increase the risk of crestal bone loss and implant failure. In a recent FEA investigation on the effects of stress distribution on the alveolar crest around implants, mean and peak stresses were highest for implants of 3.3 mm diameter and 10 mm length, and these were significantly greater than implants of 4.1 mm or 4.8 mm.⁴² Previous investigations have also suggested that tensile and compressive stress decreases as the implant diameter increases.⁴³ In addition to the increased peri-implant bone stress associated with narrow diameter implants, the biomechanical strength of titanium may be somewhat limited in certain circumstances.^{44,45} This is an especially important point for

narrow diameter implants. The load resistance of narrow diameter implants was evaluated in a biomechanical study under standardized laboratory conditions. Fracture resistance was found to be significantly lower for implants with 3 or 3.3 mm diameters compared to those of 4.1 mm diameter, and there was a further significant difference for implants of <3 mm diameter. The authors suggested that narrow diameter implants may be at higher risk of fracture in clinical situations.²⁴ Titanium alloys have been used to increase the fracture and tensile strength, one of the most common being an alloy with aluminum and vanadium (TiAl64V), which has also been extensively used in the orthopedic field. However, fractures have also been reported with Ti alloy implants,^{46,47} possibly as a result of the increased stress forces at the implant-bone interface.⁴⁸

Titanium alloys containing zirconium have been shown to have better fatigue strength and tensile strength than pure titanium.⁴⁵ The biocompatibility of such alloys is similar to that

of Ti, as demonstrated by the similar behavior of osteoblast-like cells on the material surface and osteoblast proliferation.⁴⁴ In comparison with Ti or Zr, an alloy of both was shown to have lower tissue response scores and no sensitization response after implantation in rats for 8 months, indicating greater biocompatibility.⁴⁴ A recent biomechanical and histological study in minipigs compared implants of the TiZr alloy used in the current clinical study with Ti implants, both with the same surface properties. The results indicated similar osteoconductive properties for both, but a significantly higher peri-implant bone area for TiZr implants. Bone-to-implant contact was similar for both, but the removal torque was significantly higher for the TiZr implants.⁴⁹

The greater biomechanical strength of the TiZr material suggest that narrow implants made of this material may have advantages in more challenging clinical indications, especially where occlusal forces may be higher. In the current study, 62 implants were placed in molar positions. Despite this, the implant survival rate for implants in the molar region (96.2% and 96.1% after 1 and 2 years, respectively) was similar to that observed for implants in the anterior or premolar positions (Table 6).

The current study was of a non-interventional nature, meaning that the products or materials evaluated in such a study are intended to be used according to their approved use. Treatment is not defined by a strict protocol, as is the case in most controlled clinical trials, but by the clinician according to the patient's particular situation. The patient is treated according to the clinician's standard clinical practice, but the assessment of outcomes and follow-up evaluations are systematically documented and subsequently analyzed. Such trials are slowly becoming more common, and have been used for contrast agents,⁵⁰ carcinoma treatment,⁵¹ hemoglobin control,⁵² or treatment for osteoarthritis and osteoporosis.⁵³ In dental implantology, therefore, non-interventional trials of this nature can complement the external validity of the results obtained in controlled clinical trials and assess the performance and effectiveness of a device in daily dental practice. One of the drawbacks of this type of study, however, is that the patient dropout rate may often be much higher than in controlled trials, despite methods to retain them in the study and include them in follow-up evaluations.⁵⁴ This can be seen in the current study, where only 233 patients with 409 implants remained after 2 years from an initial total of 357 treated patients with 603 implants. This may be for a number of reasons, including patients moving away, patients not attending scheduled follow-up visits, patients being referred to other dentists (eg, for specialist prosthetic treatment), or because the clinician has been unable to contact the patient. In addition, due to the nature of this type of study, patient data may sometimes be missing or incomplete.⁵⁵ In the current study, the rate of patient attrition was unfortunately rather high at almost 35%; in a formal randomized controlled trial, the possibility of bias is a concern if the patient attrition rate is more than 20%.⁵⁵ However, in large non-interventional trials, the risk of bias may be substantially reduced because of the more heterogeneous indications and patient population. Another limitation with this type of study is the difficulty in regard to standardizing any procedures or assessments among participating centers, such

as collecting standardized radiographs. However, despite these limitations, non-interventional studies have great scientific validity, as they are the only trials that can evaluate a treatment or intervention in daily dental practice in a prospective manner without the risk of bias toward more favorable outcomes that may occur in more formal randomized controlled trials.⁷

CONCLUSION

Within the limitations of this single-arm study design and a rather short follow-up time, TiZr implants showed excellent survival and success rates and little or no bone loss up to 2 years in daily dental practice. Survival and success rates after 2 years were 97.6% and 97.4%, respectively, which compare favorably with the survival rates of narrow diameter dental implants in strict randomized controlled clinical trials.

ABBREVIATIONS

FEA: finite element analysis
FPD: fixed partial denture

ACKNOWLEDGMENTS

The investigators received financial support for the study from Institut Straumann AG, Basel, Switzerland. The authors also wish to acknowledge the assistance of Colin McKinnon and Eveline Ackermann (both Institut Straumann AG, Basel, Switzerland) in the preparation of the manuscript.

REFERENCES

- Lang NP, Pun L, Lau KY, Li KY, Wong MC. A systematic review on survival and success rates of implants placed immediately into fresh extraction sockets after at least 1 year. *Clin Oral Implants Res.* 2012;23:39–66.
- Pjetursson BE, Tan WC, Zwahlen M, Lang NP. A systematic review of the success of sinus floor elevation and survival of implants inserted in combination with sinus floor elevation. *J Clin Periodontol.* 2008;35:216–240.
- Misch CE, Perel ML, Wang HL, et al. Implant success, survival and failure: the International Congress of Oral Implantologists (ICOI) Pisa Consensus Conference. *Implant Dent.* 2008;17:5–15.
- Koller B, Att W, Strub JR. Survival rates of teeth, implants, and double crown-retained removable prostheses: a systematic literature review. *Int J Prosthodont.* 2011;24:109–117.
- Mangano C, Mangano F, Shibli JA, Ricci M, Sammons RL, Figliuzzi M. Morse taper connection implants supporting “planned” maxillary and mandibular bar-retained overdentures: a 5-year prospective multicenter study. *Clin Oral Implants Res.* 2011;22:1117–1124.
- Bhatavadekar N. Assessing the evidence supporting the claims of select dental implant surfaces: a systematic review. *Int Dent J.* 2008;58:363–370.
- Bhatavadekar N. Helping the clinician make evidence-based implant selections. A systematic review and qualitative analysis of dental implant studies over a 20 year period. *Int Dent J.* 2010;60:359–369.
- Hansson HA, Albrektsson T, Branemark PI. Structural aspects of the interface between tissue and titanium implants. *J Prosthet Dent.* 1983;50:108–113.
- Palmquist A, Omar OM, Esposito M, Lausmaa J, Thomsen P. Titanium oral implants: surface characteristics, interface biology and clinical outcome. *J R Soc Interface.* 2010;7(suppl 5):S515–S527.
- Wennerberg A, Albrektsson T. On implant surfaces: a review of current knowledge and opinions. *Int J Oral Maxillofac Implants.* 2010;25:63–74.

11. Schwarz F, Wieland M, Schwartz Z et al. Potential of chemically modified hydrophilic surface characteristics to support tissue integration of titanium dental implants. *J Biomed Mater Res B Appl Biomater*. 2009;88:544–557.
12. Rompen E, Domken O, Degidi M, Pontes A, Piattelli A. The effect of material characteristics, of surface topography, and of implant components and connections on soft tissue integration: a literature review. *Clin Oral Implants Res*. 2006;17:55–67.
13. Rautray TR, Narayanan R, Kwon TY, Kim KH. Surface modification of titanium and titanium alloys by ion implantation. *J Biomed Mater Res B Appl Biomater*. 2010;93:581–591.
14. Yamazoe J, Nakagawa M, Matono Y, Takeuchi A, Ishikawa K. The development of Ti alloys for dental implant with high corrosion resistance and mechanical strength. *Dent Mater J*. 2007;26:260–267.
15. Elias CN, Meirelles L. Improving osseointegration of dental implants. *Expert Rev Med Devices*. 2010;7:241–256.
16. Barter S, Stone P, Brägger U. A pilot study to evaluate the success and survival rate of titanium-zirconium implants in partially edentulous patients: results after 24 months of follow-up. *Clin Oral Implants Res*. 2012;23:873–881.
17. Lang NP, Salvi GE, Huynh-Ba G, Ivanovski S, Donos N, Bosshardt DD. Early osseointegration to hydrophilic and hydrophobic implant surfaces in humans. *Clin Oral Implants Res*. 2011;22:349–356.
18. Buser D, Brogini N, Wieland M, et al. Enhanced bone apposition to a chemically modified SLA titanium surface. *J Dent Res*. 2004;83:529–533.
19. Saulacic N, Bosshardt DD, Bornstein MM, Berner S, Buser D. Bone apposition to a titanium-zirconium alloy implant, as compared to two other titanium-containing implants. *Eur Cell Mater*. 2012;23:273–286.
20. Thoma DS, Jones AA, Dard M, Grize L, Obrecht M, Cochran DL. Tissue integration of a new titanium-zirconium dental implant: a comparative histologic and radiographic study in the canine. *J Periodontol*. 2011;82:1453–1461.
21. Grandin HM, Berner S, Dard M. A review of titanium zirconium (TiZr) alloys for use in endosseous dental implants. *Materials*. 2012;5:1348–1360.
22. Sohrabi K, Mushantat A, Esfandiari S, Feine J. How successful are small-diameter implants? A literature review. *Clin Oral Implants Res*. 2012;23:515–525.
23. Klein MO, Schiegnitz E, Al-Nawas B. Systematic review on success of narrow diameter dental implants. *Int J Oral Maxillofac Implants*. 2014;29(suppl):43–54.
24. Allum SR, Tomlinson RA, Joshi R. The impact of loads on standard diameter, small diameter and mini implants: a comparative laboratory study. *Clin Oral Implants Res*. 2008;19:553–559.
25. Quek CE, Tan KB, Nicholls JL. Load fatigue performance of a single-tooth implant abutment system: effect of diameter. *Int J Oral Maxillofac Implants*. 2006;21:929–936.
26. Al-Nawas B, Brägger U, Meijer HJ, et al. A double-blind randomized controlled trial (RCT) of titanium-13zirconium versus titanium grade IV small-diameter bone level implants in edentulous mandibles – results from a 1-year observation period. *Clin Implant Dent Relat Res*. 2012;14:896–904.
27. Buser D, Weber HP, Lang NP. Tissue integration of non-submerged implants. 1-year results of a prospective study with 100 ITI hollow-cylinder and hollow-screw implants. *Clin Oral Implants Res*. 1990;1:33–40.
28. Bergkvist G, Sahlholm S, Nilner K, Lindh C. Implant-supported fixed prostheses in the edentulous maxilla. A 2-year clinical and radiographic follow-up of treatment with non-submerged ITI implants. *Clin Oral Implants Res*. 2004;15:351–359.
29. Zarone F, Sorrentino R, Vaccaro F, Russo S. Prosthetic treatment of maxillary lateral incisor agenesis with osseointegrated implants: a 24-39-month prospective clinical study. *Clin Oral Implants Res*. 2006;17:94–101.
30. König J, Holtfreter B, Kocher T. Periodontal health in Europe: future trends based on treatment needs and the provision of periodontal services – position paper 1. *Eur J Dent Educ*. 2010;14:4–24.
31. Burt B; Research, Science and Therapy Committee of the American Academy of Periodontology. Position paper: epidemiology of periodontal diseases. *J Periodontol*. 2005;76:1406–1419.
32. Hugoson A, Nordeyrd O. Has the prevalence of periodontitis changed during the last 30 years? *J Clin Periodontol*. 2008;35:338–345.
33. Renvert S, Persson GR. Periodontitis as a potential risk factor for peri-implantitis. *J Clin Periodontol*. 2009;36:9–14.
34. Heitz-Mayfield LJ, Huynh-Ba G. History of treated periodontitis and smoking as risks for implant therapy. *Int J Oral Maxillofac Implants*. 2009;24:39–68.
35. Costa FO, Takenaka-Martinez S, Cota LO, Ferreira SD, Silva GL, Coste JE. Peri-implant disease in subjects with and without preventive maintenance: a 5-year follow-up. *J Clin Periodontol*. 2012;39:173–181.
36. Gianserra R, Cavalcanti R, Oreglia F, Manfredonia MF, Esposito M. Outcome of dental implants in patients with and without a history of periodontitis: a 5-year pragmatic multicenter retrospective cohort study of 1727 patients. *Eur J Oral Implants*. 2010;3:307–314.
37. Esposito M, Grusovin MG, Felice P, Karatzopoulos G, Worthington HV, Coulthard P. Interventions for replacing missing teeth: horizontal and vertical bone augmentation techniques for dental implant treatment. *Cochrane Database Syst Rev*. 2009;4:CD003607.
38. Cosyn J, Eghbali A, Hanselaer L, et al. Four modalities of single implant treatment in the anterior maxilla: a clinical, radiographic, and aesthetic evaluation. *Clin Implant Dent Relat Res*. 2013;15:517–530.
39. Clementini M, Morlupi A, Canullo L, Agrestini C, Barlattani A. Success rate of dental implants inserted in horizontal and vertical guided bone regenerated areas: a systematic review. *Int J Oral Maxillofac Surg*. 2012;41:847–852.
40. Inglam S, Suebnukarn S, Tharanon W, Apatanon T, Sittiseripratip K. Influence of graft quality and marginal bone loss on implants placed in the maxillary grafted sinus: a finite element study. *Med Biol Eng Comput*. 2010;48:681–689.
41. Johansson B, Bäck T, Hirsch JM. Cutting torque measurements in conjunction with implant placement in grafted and nongrafted maxillas as an objective evaluation of bone density: a possible method for identifying early implant failures? *Clin Implant Dent Relat Res*. 2004;6:9–15.
42. Ding X, Liao SH, Zhi XH, Zhang XH, Zhang L. Effect of diameter and length on stress distribution of the alveolar crest around immediate loading implants. *Clin Implant Dent Relat Res*. 2009;11:279–287.
43. Bourauel C, Aitlhrach M, Heinemann F, Hasan I. Biomechanical finite element analysis of small diameter and short dental implants: extensive study of commercial implants. *Biomed Tech (Berl)*. 2012;57:21–32.
44. Ikarashi Y, Toyoda K, Kobayashi E, et al. Improved biocompatibility of titanium-zirconium alloy (Ti-Zr): tissue reaction and sensitization to Ti-Zr alloy compared with pure Ti and Zr in rat implantation study. *Mater Trans*. 2005;46:2260–2267.
45. Kobayashi E, Matsumoto S, Doi H, Yoneyama T, Hamanaka H. Mechanical properties of the binary titanium-zirconium alloys and their potential for biomedical materials. *J Biomed Mater Res*. 1995;29:943–950.
46. Eckert SE, Meraw SJ, Cal E, Ow RK. Analysis of incidence and associated factors with fractured implants: a retrospective study. *Int J Oral Maxillofac Implants*. 2000;15:662–667.
47. Nagasawa S, Hayano K, Niino T, et al. Nonlinear stress analysis of titanium implants by finite element method. *Dent Mater J*. 2008;27:633–639.
48. Kong L, Sun Y, Hu K, et al. Bivariate evaluation of cylinder implant diameter and length: a three-dimensional finite element analysis. *J Prosthodont*. 2008;17:286–293.
49. Gottlow J, Dard M, Kjellson F, Obrecht M, Sennerby L. Evaluation of a new titanium-zirconium dental implant: a biomechanical and histological comparative study in the mini pig. *Clin Implant Dent Relat Res*. 2012;14:538–545.
50. Palkowitsch P, Lengsfeld P, Stauch K, et al. Safety and diagnostic image quality of iopromide: results of a large non-interventional observational study of European and Asian patients (IMAGE). *Acta Radiol*. 2012;53:179–186.
51. Lencioni R, Kudo M, Ye SL, et al. First interim analysis of the GIDEON (Global Investigation of therapeutic Decisions about hepatocellular carcinoma and Of its treatment with sorafenib) non-interventional study. *Int J Clin Pract*. 2012;66:675–683.
52. Heidenreich S, Leistikow F, Zinn S, et al; SUPRA Study Group. Monthly administration of a continuous erythropoietin receptor activator provides efficient haemoglobin control in non-dialysis patients during routine clinical practice: results from the non-interventional, single-cohort, multicenter, SUPRA study. *Clin Drug Invest*. 2012;32:99–110.
53. Ringe SD, Schäfer S, Wimmer AM, Giesecke T. Use of OROS hydromorphone in the treatment of osteoarthritis and osteoporosis: a pooled analysis of three non-interventional studies focusing on different starting doses. *Wien Klin Wochenschr*. 2012;124:25–31.
54. Booker CL, Harding S, Benzeval M. A systematic review of retention methods in population-based cohort studies. *BMC Public Health*. 2011;11:249.
55. Dumville JC, Torgerson DJ, Hewitt CE. Reporting attrition in randomised controlled trials. *BMJ*. 2006;232:969–971.