A prospective, controlled clinical trial evaluating the clinical and radiological outcome after 3 years of immediately placed implants in sockets exhibiting periapical pathology

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Key words: bone regeneration, dental implantation, endosseus, human, immediate implant placement, periapical pathology, treatment outcome, controlled clinical trial, prospective study
Abstract:

Objectives: The aim of the present study was to compare the clinical and radiological outcome of immediately placed implants in sockets with or without periapical pathology 3 years after implant placement.

Materials and methods: 29 patients with immediate implant placement were clinically and radiologically followed 3 years after implant placement (test-group: 16 patients without periapical pathology, control-group: 13 patients with periapical pathologies). Clinical (FMBS, FMPS, CAL, width of keratinized mucosa buccally of the implant) and radiological parameters (IS-BIC) were assessed. Both 95% confidence intervals, as well as results of statistical tests (one-sample, two-sample, paired t-test) were provided.

Results: The implant survival rate was 100% for all 29 implants after 3 years. The clinical and radiological parameters showed no statistically significant difference between the test- and the control-group at 3 years (two-sample t-test). The vertical distance from the implant shoulder to the first bone-to-implant contact (IS-BIC) was between 1.54±0.88 mm (mesial, test) and 1.69±0.92 mm (distal, test). Between the 1- and 3-year visit the IS-BIC increased in both groups significantly on one side of the implant: 0.30±0.37 mm (mesial, test) and 0.33±0.43 mm (distal, control) (one-sample t-test). None of the 13 examined radiographs of implants immediately placed in sockets with periapical pathologies revealed retrograde periimplantitis after 3 years.

Conclusion: It is concluded within the limitations of this study, that after careful debridement of the extraction socket, immediate placement of implants into sites with periapical pathologies can be a successful treatment modality for at least 3 years with no disadvantages in clinical and radiological parameters to immediately placed implants into healthy sockets.
**Introduction:**

Implant placement immediately after tooth extraction is a widely accepted procedure revealing high survival rates ranging from 93.9-100% (De Rouck et al. 2008; den Hartog et al. 2008; Esposito et al. 2007; Ferrara, et al. 2006; Kan et al. 2003). This technique aimed originally at preserving the pre-extraction contours of the alveolar process, (Anneroth et al. 1985; Lazzara 1989; Schulte & Heimke 1976), since a marked resorption of the buccal bone plate after tooth loss was observed. However, dimensional ridge alterations could not be prevented when implants were immediately placed into fresh extraction sockets (Araujo & Lindhe 2005; Botticelli et al. 2004). Clinical studies demonstrated advantages to preserve the interproximal papilla, whereas the midfacial gingival tissues can be more problematic since bone remodeling and changes of the gingival margin will occur irrespective of the timing of the implant placement (De Rouck et al. 2008). In the last years the interest in treatment success has moved from implant survival rate to the evaluation of additional radiological, esthetic and clinical parameters.

Today’s literature provides information on different factors influencing the success of implants placed immediately after tooth extraction. These factors range from implant position, the use of grafting material, the soft tissue biotype, up to the use of soft tissue augmentation (Chen et al. 2005; Evans & Chen 2008; Grunder et al. 2005). An additional factor, which has been discussed controversially, is the presence or absence of periapical pathologies. Several studies advise against the immediate placement of implants in the presence of periapical pathologies (Barzilay 1993; Tolman & Keller 1991). Furthermore, the term retrograde periimplantitis got recently introduced as radiolucencies around the most apical part of an osseointegrated implant. They might be provoked by remaining scar or granulomatous tissue after immediate implant placement into extraction sockets (Quirynen et al. 2005). In contrast to these findings, more recent studies have shown in animal experiments, that implants placed
in artificially induced periapical lesions osseointegrate as well as implants placed in healthy sites (Marcaccini et al. 2003; Novaes et al. 2003; Novaes et al. 1998; Papalexio et al. 2004). In a previously published study by our group it could be shown in a prospective, controlled clinical trial, that immediate implant placement in sites with or without periapical pathology did not lead to an increased rate of complications, more interproximal bone loss or worse clinical parameters (Siegenthaler et al. 2007). Similar conclusions were found in a prospective, randomized study with 50 patients revealing no disadvantages for implants placed directly after extraction of teeth exhibiting periapical pathologies (Lindeboom et al. 2006). In both studies a follow-up evaluation was conducted at 1 year after implant placement. Hence, studies with longer follow-up periods are needed to determine the safety of this procedure.

The aim of the present study was to assess whether immediately placed implants in sockets with or without periapical pathology show any differences regarding survival rates, clinical parameters and interproximal bone levels after 3 years following implant placement. Another purpose was to look for residual or newly formed radiolucencies (retrograde periimplantitis) around the tip of the implants as previously described in the literature.
Material and methods:

Study design and patients:

In the present controlled clinical trial, patients with immediate implant placement were clinically and radiologically followed after 3 years following implant placement. All patients had been treated at the Department of fixed and removable prosthodontics and dental material science at the University of Zurich, Switzerland and were part of a former study evaluating the early events and the 1-year follow up (Siegenthaler et al. 2007). The local ethical committee approved all procedures and the patients obtained informed consent. All of the 29 patients included in the present 3-year follow-up data collection belonged to either one of the following treatment-groups: test-group including 13 patients without periapical pathologies, control-group with 16 patients showing periapical pathologies. These pathologies included pain, periapical radiolucencies >1mm, suppuration or a combination of these findings. In 11 patients the reason for extraction was endodontic failure. One patient lost his tooth because of root fracture and one patient presented with endodontic failure in combination with root caries. 6 patients of the test-group showed a buccal fistula with suppuration. Another 4 patients showed localized suppuration from the gingival sulcus of the tooth to be extracted due to an endodontic lesion that drained over the periodontal ligament. None of the patients lost the respective tooth because of periodontal reasons. All but two patients suffered from symptoms like chronic pain or pain on pressure. In order to categorize the lesions radiographically, periapical radiographs taken before tooth removal were scanned. The perpendicular distance between the biggest in the radiograph visible extent of the pathology and the root surface was measured according to the magnification of the x-ray.

The control-group consisted of patients in need of tooth replacement with an implant but showed no periapical pathology. Implant sites were limited to incisors, canines and premolars and bone regeneration was performed according to standard clinical procedures (Hammerle et al. 1998; Lang et al. 1994). All of the patients were in good general health and had no history
of periodontal disease. In the test-group 2 patients were smokers and in the control-group one patient was a smoker. The mean age of the patients in the test-group was 48 years (range 26-85 years) whereas that of the control-group was 58 years (range 26-80 years) at the time of the 3-year follow-up visit. There were no dropouts between the 1-year and the 3-year examination and all of the 29 patients could be examined.

**Treatment protocol:**

The surgical procedure has been described in detail in the previous study (Siegenthaler et al. 2007). In brief, after raising a full mucoperiosteal flap, the tooth was extracted in a gentle way to minimize damage to the bony housing. After thoroughly removing all granulation tissues an implant (Standard Plus or Tapered Effect, Straumann Dental Implant System, Straumann AG, Basel, Switzerland) with dimensions best suited to obtain primary stability was placed immediately in an optimal prosthetic position. GBR was performed using deproteinized bovine bone mineral (Bio-Oss spongiosa particles, Geistlich-Pharma, Wolhusen, Switzerland) and a resorbable collagen membrane (Bio-Gide, Geistlich-Pharma, Wolhusen, Switzerland). All of the patients received penicillin antibiotics (Clamoxyl 750 mg 1-1-1) for 5 days and rinsed with a 0.2 % chlorhexidine digluconate solution. After transmucosal or semisubmerged healing, implants were loaded at 3 months after placement.
3-year follow-up data collection:

Clinical parameters:

At the 3-year follow-up visit clinical photographs were taken and the following clinical data were collected:

- Full-mouth bleeding score (FMBS) (Lang et al. 1986)
- Full-mouth plaque score (FMPS) (O’Leary et al. 1972)
- Buccal and lingual/palatal interproximal clinical attachment level measurements (CAL) at the tooth-sides of the adjacent teeth facing the site of the implant. In order to compare the CAL to the data collected at the 1-year follow-up, the two lingual/palatal and the two buccal CAL measurements were averaged to one value.
- Buccal width of keratinized mucosa (KM) at the site of the implantation.

Radiological parameters:

Standardized radiographs of the implant and the adjacent teeth were taken using the same individual bite block as in the previous study (Siegenthaler et al. 2007). The radiographs were scanned and examined in the way as in the former publication at a 10 times magnification using an image-processing program (Image J64, Version 10.2). Vertical measurements were taken from the mesial and distal shoulder of the implant to the first bone-to-implant contact level in an axis parallel to the implant (IS-BIC). All distance measurements were recorded in pixels and subsequently converted to millimeters. To adjust each radiograph for distortion the distance between the tips of three threads of the implant was additionally assessed and the vertical measurements were multiplied by the ratio between the manufacturer-specified thread pitch of 0.8 mm (TE Implant), 1.25 mm (Standard Plus Implant, Regular Neck) and 1.0 mm (Standard Plus Implant, Narrow Neck) and the observed distance.

Two observers aiming for agreement regarding the first bone-to-implant contact performed the radiographic assessment. In cases of disagreement, an author of the previous study was
involved until consent was reached. Furthermore the periapical area of the implant was observed thoroughly by two of the authors for possible residual or newly formed periapical radiolucencies.

**Statistical analysis**

A power calculation was carried out to determine the sample size using the implants as the statistical unit. Primary outcome was the increase of the vertical distance from the implant shoulder to the first bone-to-implant contact between 1 and 3 years. A possible bone resorption of 0.2 mm annually was considered clinically relevant after the first year of loading. Consequently, relevant changes between the 1- and 3-year visit should be bigger than 0.4 mm.

One-sample t-test: To detect with 80% power a relevant difference of the primary outcome of delta = 0.4 (change between 1- and 3-year visit in mm) with a standard deviation of sigma = 0.4, a sample size of 10 is needed.

Not only the changes in measurements between the 1- and 3-year visit within the test- and control-group separately are of interest. But also the differences of these changes in this 2-year time-span between the test- and control group are important. Therefore, a difference of 0.5 mm is considered clinically relevant.

Two-sample t-test: To detect with 80% power a relevant difference of the primary outcome of delta = 0.5 with a standard deviation of sigma = 0.4, a sample size of 11 is needed for each (test and control) group.

The values of IS-BIC mesial/distal, FMBS, FMPS, CAL mesial/distal and the width of keratinized mucosa were computed at 3 years and descriptive statistics (mean, standard deviation, range) were provided. Because of small sample sizes in each group, medians were computed to give the reader an impression of symmetry or asymmetry of the data.

Kolmogorov-Smirnov test was applied to check if the assumption of approximately normal
sampling distribution does not hold. The results showed no significance (p>0.157). Consequently, a two-sample t-test was applied to investigate the differences in these parameters between test- and control-group.

Changes in IS-BIC mesial/distal, FMBS, FMPS, CAL mesial/distal and the width of keratinized mucosa between 1 and 3 years were calculated. Kolmogorov-Smirnov test was applied to check if the assumption of approximately normal sampling distribution does not hold. Significance was found only for the difference in width of keratinized gingival between 36 and 12 months (p=0.035). All other variables showed no significance (p>0.185). Therefore we used nonparametric methods (Wilcoxon signed rank test for the paired test and Mann-Whitney test for comparison between test- and control-group) for analysis of this variable. Otherwise parametric techniques were applied. Means, standard deviations and medians were computed. One sample t-test was applied to the differences for control and test group separately (It is equivalent to the paired t-test). Moreover, the corresponding 95% confidence intervals (95% CI) were provided. A two sample t-test was applied in order to disclose differences in IS-BIC mesial/distal, FMBS, FMPS, CAL mesial/distal and the width of keratinized mucosa between test- and control-group. Mean differences between groups together with the corresponding 95% confidence intervals were provided. For statistical analysis SPSS Version 17.0 was used. Results of the tests with p-values less than 5% were reported to be statistically significant. Since 28 tests were applied in this study an increased false-positive rate of the significant results could be expected. Therefore in addition Bonferroni correction was performed, rendereing only results with a p-value smaller than 0.00179 (0.05 divided by 28) to be considered statistically significant.
Results:
Of the original 34 patients (17 with and 17 without periapical pathologies) 5 patients had to be withdrawn from the study because primary implant stability could not be achieved. Four of these belonged to the test- and one to the control-group. There was no statistically significant difference regarding the early exits between the groups (Siegenthaler et al. 2007). Of the remaining 29 patients all could be recruited for a 3-year follow-up visit (13 in the test group and 16 in the control group). The size of the periapical pathology in the present study was 1.1 mm to 3.0 mm in the test-group, measured as the maximal width of the radiolucency projected by the pathology on the root surface in the radiograph. The implant survival rate was 100% for all 29 implants after 3 years.
Two patients of the control-group refused to take X-ray pictures at the 3-year follow-up visit, rendering 13 patients in the test- and 14 patients in the control-group for radiographic evaluation.

Clinical measurements at 3 years (test: n=13; control: n=16)
At the 3-year follow-up visit the full-mouth bleeding score (FMBS) was 11±7% (test) and 12±9% (control) (Table 1). The full-mouth plaque score (FMPS) was 21±18% (test) and 14±6% (control). The results for the clinical attachment levels (CAL) were: CAL mesial of the implant site in the test-group 2.7±1.0 mm (range from 1 to 5mm) and 3.4±1.3 mm (range from 2 to 7.5 mm) in the control-group. CAL distal of the implant site was 2.7±0.9 mm in the test-group (range from 1.5 to 4.5 mm) and 3.6±1.3 mm (range from 2 to 7 mm) in the control-group. The width of the keratinized mucosa buccaly of the implant site was 3.5±1.7 mm in the test-group (range from 2 to 7 mm) and 3.0±1.3 mm in the control-group (range from 1 to 5 mm). There was no statistically significant difference between the two groups at 3 years.
Table 1. Clinical measurements excluding early exit cases at 3 years

<table>
<thead>
<tr>
<th>Clinical measurements</th>
<th>Test, n= 13</th>
<th>Control, n=16</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>FMBS (%)</td>
<td>11(7); 8</td>
<td>12(9); 10</td>
<td>0.832</td>
</tr>
<tr>
<td>FMPS (%)</td>
<td>21(18); 17</td>
<td>14(6); 13</td>
<td>0.180</td>
</tr>
<tr>
<td>CAL mesial (mm)</td>
<td>2.7(1.0); 3</td>
<td>3.4(1.3); 3</td>
<td>0.150</td>
</tr>
<tr>
<td>CAL distal (mm)</td>
<td>2.7(0.9); 2.5</td>
<td>3.6(1.3); 3.3</td>
<td>0.078</td>
</tr>
<tr>
<td>KM site (mm)</td>
<td>3.5(1.7); 3.0</td>
<td>3.0(1.3); 3.0</td>
<td>0.428</td>
</tr>
</tbody>
</table>

FMBS: full-mouth bleeding score; FMPS: full-mouth plaque score; CAL mesial/distal: interproximal clinical attachment level at the tooth-sides of the adjacent teeth facing the site of the implantation, the buccal and oral values were averaged to one value; KM site: width of keratinized mucosa buccally of the site of implantation; p-value*: two-sample t-test, statistically significant difference <0.05; SD: standard deviation