Early Loading of Titanium Dental Implants with an Intraoperatively Conditioned Hydrophilic Implant Surface: 3-Year Results of a Prospective Case Series Study

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Purpose: The hydrophilic implant surface (INICELL) is a chemical alteration of a sandblasted and thermally acid-etched surface that should lead to long-term osseointegration. This study investigated 3-year results after early loading of implants with a hydrophilic, moderately rough surface in occlusal contact. Materials and Methods: This prospective case series study was conducted in subjects with partially edentulous mandibles. Implants were placed on day 21 and loaded with a provisional reconstruction after at least 21 days of healing (baseline, day 0) if their implant stability quotient (ISQ) was ≥ 70 (mean of three measurements) and were replaced by definitive porcelain-fused-to-metal prostheses at the 6-month follow-up visit. Follow-up examinations were planned 1, 3, 6, 12, and 36 months after baseline. Results: A total of 20 implants were placed in 15 patients (mean age: 51 years, range: 32 to 67 years). After 36 months, all implants were osseointegrated, and no suppuration was recorded. Small changes of bone level were observed between 3 months and 36 months. At 36 months, the median values of the 20 implants were 0.25 (range: 0 to 0.5, SD: 0.17), 0.25 (range: 0 to 1, SD: 0.27), and 4 (range: 2 to 7.25, SD: 1.17) for the mean modified Plaque Index (mPI), mean modified Sulcus Bleeding Index (mSBI), and mean probing pocket depth, respectively. The pairwise analysis between 3 and 36 months showed an improvement in the mean mPI (P = .0126) and mean mSBI (P = .0059). After 36 months, all patients (n = 15) were fully satisfied with a mean of 9.43 (range: 8 to 10, SD: 0.678) at the visual analog scale. Conclusion: Early functional loading of implants with a hydrophilic, moderately rough outer surface in occlusal contact 21 days after healing appears to be a safe and feasible treatment option when placed in the posterior mandible of partially edentulous patients. Int J Oral Maxillofac Implants 2020;35:1013–1020. doi: 10.11607/jomi.8045

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Tooth replacement and oral rehabilitation with the aid of dental implants is considered to be a safe and reliable treatment option. Dental implants are used favorably as anchors for fixed dental prostheses (FDPs) as well as for removable prostheses.¹–⁴ New bone formation at the bone-to-implant contact area is required for a successful implant treatment and the osseointegration of an oral implant.⁵ To maintain the marginal bone level around implants, a healthy and tight peri-implant mucosa and, therefore, adequate oral hygiene are needed.

To improve the degree of osseointegration, different techniques (additive and subtractive) have been developed to enhance the implant surface topography. The goal is to increase the surface area and to improve direct bone apposition during healing compared with machined-only surfaces. A long-term study with rough dental implants with an additive surface modification such as the titanium plasma-sprayed (TPS) surface showed an implant survival rate of 89.5% after 20 years of function in partially edentulous patients.⁶ A subtractive method to change the surface topography is sandblasting with large particles and acid etching in a bath of HCl/H₂SO₄ (SLA surface).⁷ This procedure leads to a moderately rough surface, which is currently considered the standard roughness.⁸ Different studies have proven that the bone-to-implant contact of moderately rough surfaces is greater than around smoother or rougher surfaces. In a preclinical study, the

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bone-to-implant contact increased from 37.5% (TPS surface) to 55% (SLA surface).7 The superiority of the moderately rough surfaces has been shown in different clinical studies. In a study with more than 500 implants, the survival rate of implants with a sandblasted and acid-etched surface was 98.8%, and the success rate was 97.0% after 10 years of function.9 Another 10-year follow-up study showed survival rates of 95.1% for SLA implants supporting full-arch prostheses in the maxilla.10 However, the roughest TPS surfaces show higher failure rates, and the best results are achieved with anodized-surface implants according to a review from Wennerberg et al and studies by Wagenberg and Froum and Simonis et al.11–13

Further improvement of the implant surface may be achieved by chemical modifications of the surface. The main purpose of these modifications is to improve and accelerate the initial bone healing. Through an increase of the surface energy of hydrophilic implants, the binding of proteins and the differentiation and maturation of osteoblasts may be positively affected. Different in vitro studies showed clear effects of hydrophilic surfaces, including increased wettability, affinity of proteins, and adhesion of osteoblasts.14,15 Preliminary clinical trials of a hydrophilic implant surface (INICELL, Thommen Medical) suggested a favorable performance and reliability.16–20 The hydrophilic surface is a chemical modification and superhydrophilization of an established sandblasted and thermally acid-etched surface developed by the same manufacturer.21 Hydrophilization is achieved by a purely chemical process that consists of conditioning the implant intraoperatively using a dedicated device (APLIQUIQ) with 0.05-M NaOH solution (pH 12.4).22 As a result, the implant surface is changed from initial hydrophobic to the hydrophilic state. The surface energy and wettability are increased while preserving the topographic characteristics and the macrostructure and microstructure of the surface of the original implant. The prerequisite for a surface to be called superhydrophilic is that water (liquid) spreads on it completely (to a nearly zero apparent contact angle, < 5 to 10 degrees).23 A long-term study with hydrophilic implants from another manufacturer showed a very high implant success rate after early loading.24 However, there are also reports of no significant increase of late clinical results after using implants with hydrophilic surfaces.25 A retrospective study testing the same implant system as the one in the present study reported significantly higher early implant failure rates for hydrophobic implants than for hydrophilic implants.26

The aim of this report was to present the 3-year results of a prospective case series study conducted to investigate the efficacy of the early loading of implants with a hydrophilic, moderately rough surface in occlusal contact after 21 days of healing when placed in the posterior mandible of partially edentulous patients.

**MATERIALS AND METHODS**

**Study Design**

This single-center, prospective observational study was conducted at the School of Medicine, University of Bern, Switzerland, in patients with partially edentulous mandibles. Implants were placed in eligible patients 21 days before baseline (–21) and loaded with a provisional reconstruction after at least 21 days of healing (baseline, day 0) if their implant stability quotient (ISQ, Osstell) was ≥ 70 (mean of 3 measurements). Follow-up visits occurred at 1, 3, 6, and 36 months after baseline (functional loading). The provisional reconstructions were replaced by definitive porcelain-fused-to-metal prostheses at the 6-month follow-up visit. Results of this prospective study at 6 months were published earlier.27

Prior to the start of this study, the protocol was approved by the local ethics committee for clinical studies of the Medical Faculty of the University of Bern (approval number: 118/10). This prospective case series was designed and conducted in accordance with the ethical principles of the Declaration of Helsinki. Before any relevant study procedures were conducted, all patients signed the informed consent form after having ample time to reflect on their study participation.

**Patient Selection**

All patients were enrolled between April 2011 and February 2013. Patient eligibility was evaluated at least 1 day before implant placement based on clinical and radiographic examinations. The eligibility criteria were as follows:

**Inclusion criteria:**

- Age ≥ 18 and ≤ 75 years
- Partially edentulous with missing teeth in the posterior mandible (first premolar to second molar) and a healed site (at least 16 weeks after tooth extraction)
- Physical status 1 or 2 according to Physical Status Classification System of the American Society of Anesthesiologists
- Adequate native bone volume, quality, and quantity for an implant with a diameter of at least 4 mm with no need for guided bone regeneration
- Opposing dentition with natural teeth, or a tooth or implant-supported fixed restoration

**Exclusion criteria:**

- Women of childbearing potential with a positive urine pregnancy test
- Inadequate oral hygiene or persistent intraoral infection
Implant to prepare the provisional restoration were plants were placed after full-thickness flap reflection. Primary stability were included in the study. All implants were assessed by ISQ after implant placement. Only patients who received at least one implant with adequate primary stability were included in the study. All implants were placed after full-thickness flap reflection.

The procedures to check the position and fit of the implant to prepare the provisional restoration were already described in Hicklin et al²⁷: Prior to wound closure, the implant position was indexed using a screw-retained impression coping that was connected to the implant. After the visual check of the fit, this coping was bonded to the surgical stent using a resin material (Pattern Resin LS, GC Corporation). The implant was connected to the surgical stent, and the implant position was transferred to the planning model using an altered cast technique. On this cast, the provisional restoration was fabricated. Bite blocks were positioned, and standardized radiographs were taken after the application of the healing abutment and the wound closure.

Patients received antibiotic prophylaxis with 2 g amoxicillin/clavulanic acid (600 mg clindamycin in case of penicillin allergy) 2 hours before surgery and were instructed to follow standard postsurgical oral hygiene procedures for 2 weeks and to avoid hard food intake for several days.

Screw-retained titanium provisional restorations with acrylic veneering were placed and loaded 21 days after implant surgery if ISQ measurements were at least 70, and they were torqued with 15 Ncm. Shimstock foil (Coltène/Whaledent) was used to verify that all crowns had at least one occlusal contact to the maxilla. The criteria for preparing the definitive implant restoration were as follows:

- ISQ ≥ 70
- Absence of implant mobility
- Soft tissue conditions that do not preclude or make it unadvisable to proceed with the placement of the provisional restoration
- No complaints of pain or severe discomfort on palpation of the soft tissue and implant during the removal of the healing cap

**Radiographic Procedures**
Standardized radiographs were obtained directly after implant surgery, after inserting the provisional reconstruction, and during the 3-, 6-, and 36-month postloading follow-up visits. To ensure consistent projection geometries of radiographs across study visits, x-ray holders (Extension Cone Paralleling, Dentsply Rinn) were individualized before implant placement. To obtain this, bite blocks of the x-ray holders were modified using a polymethyl methacrylate material (Pattern Resin LS, GC Corporation) for each study implant site.

**Outcome Assessment**
The standardized radiographs were used to measure the distance between the implant collar and the bone crest (DIB) at the mesial and distal aspects of each implant to evaluate the crestal bone level changes. Radiographic data were obtained from images at the day of implant placement, at loading 21 days later (baseline),...
and at all scheduled study visits. The two measurements were pooled before statistical analyses. The following clinical measurements were conducted during all follow-up visits:

- Modified Plaque Index (mPI; according to Mombelli et al\textsuperscript{28})
- Modified Sulcus Bleeding Index (mSBI; according to Mombelli et al\textsuperscript{28})
- Probing pocket depth (PPD)

The parameters mPI, mSBI, and PPD were assessed mesially, distally, buccally, and orally. For analysis, the mean of these four points was used. Patient satisfaction was evaluated with the aid of a visual analog scale (VAS), with 1 point indicating the worst result and 10 points indicating the best result at the 6- and 36-month visits. Patients were actively asked to report unexpected events and pain, and the implantation site was checked for implant failure and infection.

The treatment was considered effective in the absence of implant mobility (tested by hand), any continuous peri-implant radiolucency judged on radiographs, recurrent peri-implant infection, continuous or recurrent pain, and structural failure of the implant. The implants were not torque tested.

**Statistical Analysis**

The raw data were collected using Excel (Microsoft) and were then imported by SAS Version 9.4 for statistical analysis. All available data from all patients in the database were considered in the analyses. Besides performing summary statistics, changes over time were analyzed by analysis of variance (ANOVA, SAS PROC NPAR1WAY). Pairwise analyses were performed using Wilcoxon rank sum tests.

**RESULTS**

Sixteen patients were screened during the recruitment period, and 15 of these patients (7 female and 8 male) met all eligibility criteria. There was one exclusion due to a screening failure. Detailed information on patient eligibility has already been published.\textsuperscript{26} Twenty implants were placed in the 15 subjects (1 implant in 11/15 patients, two implants in 3/15 patients, and three implants in 1/15 patients). Patients had a mean age of 52 years (range: 32 to 67 years, SD: 11.2) at the time of implant placement (day –21). According to the ethical committee, pregnancy testing was performed for women of childbearing potential. Most of the implants replaced the first mandibular molar (17/20, 85%), with only 2/20 (10%) implants replacing the second premolar and 1/20 (5%) implant replacing the first premolar. Implant platform diameters ranged from 4.5 to 6.0 mm. All 20 implants were placed according to the study protocol. The clinical assessment of the bone at the implant sites showed sufficient bone quantity to place an implant with a diameter of at least 4 mm (ridge width of at least 6 mm). Twenty-one days (range: 20 to 22 days) after implant placement, all study implants revealed an ISQ $\geq$ 70 and were provisionally restored per protocol with 18 single crowns and one FDP. There was no exclusion due to low ISQ. At the 6-month follow-up visit, the provisional reconstructions were replaced by definitive porcelain-fused-to-metal prostheses.

After 36 months, every implant was judged to be clinically stable, and no suppuration could be detected. Both implant survival and success rates were therefore 100% after 3 years of function (example in Fig 1). In addition, no failure of components was reported, and no screw loosening occurred. One crown showed a ceramic chipping at the 3-year visit, which could be polished with no need for replacement. This resulted in a survival rate of 100% and a success rate of 94.7% at the reconstruction level.

The results of the radiographic measurements between the implant shoulder and bone crest at different time points are shown in Table 1 and Fig 2. Crestal bone loss was noted during the first healing period of 21 days after implant placement and provisional reconstruction and the 3-month follow-up ($P < 0.0001$). Thereafter, just small changes of the peri-implant bone levels were noticed until the 36-month follow-up examination. Of the 20 implants placed, 6 showed a mean DIB of more than 1 mm. Therefore, the most coronal visible DIB stabilized in most of the implants at the junction between the machined collar and the moderately rough surface. The radiographs of a patient at the 6- and 36-month follow-ups are presented in Fig 1.

At 36 months, the median values of the 20 implants were 0.25 (range: 0 to 0.5, SD: 0.17), 0.25 (range: 0 to 1, SD: 0.27), and 4 (range: 2 to 7.25, SD: 1.17) for the mean mPI, mean mSBI, and mean PPD, respectively. An overview of the clinical parameters at implantation, loading, and follow-up is shown in Fig 3.

The pairwise analysis of the clinical parameters between 3 and 36 months showed an improvement in the mean mPI ($P = .0126$), the mean mSBI ($P = .0059$), and a stable mean PPD ($P = .2636$).

Patient satisfaction with treatment outcome as assessed by the VAS was high. The mean VAS score after 6 months ($n = 15$) was 9.47 (range: 8 to 10, SD: 0.743). After 36 months, all patients ($n = 15$) were still fully satisfied with a mean VAS of 9.43 (range: 8 to 10, SD: 0.678). The occlusal and buccal view of a study patient at the 36-month visit is shown in Fig 4.
DISCUSSION

The objective of this case series was to assess if early loading (21 days after placement) of implants with an intraoperatively conditioned surface in healed posterior sites of the mandible is a safe and efficient treatment modality. Thirty-six months after implant placement, all 20 implants were clinically stable and had been restored with porcelain-fused-to-metal reconstructions.

In order to shorten treatment periods and improve clinical outcomes, new implant surfaces that offer faster osseointegration are paramount.

The development of moderately rough implant surfaces, which are currently considered as the gold standard, is crucial. The findings from this study support the feasibility and effectiveness of early loading in selected cases, providing a viable alternative for patients seeking accelerated treatment protocols.
standard, was a major step toward reaching this goal. In addition, changes in the surface chemistry have enhanced the process of osseointegration. One way to change the physicochemical properties of implant surfaces is to improve their wettability. As the procedure of osseointegration is accelerated by the use of modern hydrophilic surfaces, early and full functional loading becomes safer. One of the procedures to obtain a hydrophilic surface is to condition the titanium implant with a solution containing hydroxide ions before inserting it into the bone. A study conducted in the mandibles of minipigs, where unconditioned and conditioned implant surfaces were compared, demonstrated a trend toward early bone formation around the hydrophilic implants. The same trend was observed in several other animal studies.

This prospective case series study in patients has also demonstrated the safety and efficacy of an intraoperatively hydrophilized titanium implant with a moderately rough surface: All 20 implants were restored and functionally loaded 3 weeks after implant insertion. In detail, all implants in the present study were judged to be integrated at the 36-month follow-up examination as reflected in the peri-implant tissue conditions with an implant survival rate of 100%. These results are consonant with other clinical studies that tested hydrophilic implant surfaces from other manufacturers, which also reported 3-year survival rates of 100% and 96.7%.

In the present report, the machined collar height of the implants was 1 mm. In all implants, the border between the machined shoulder and the rough surface
was placed from 0.5 to 1 mm below the level of the bone crest during surgery. Therefore, it was expected that a first remodeling of the surrounding bone would occur during the initial healing phase. After several weeks of healing, the bone-to-implant contact was located in most of the cases at the mentioned border. The mean distance between the implant shoulder and bone crest was 0.76 mm after 36 months. These results are comparable to those observed in other studies, which tested hydrophilic implant surfaces. Tonetti et al reported an initial bone remodeling between the time point of crown insertion and the 12-month follow-up (no statistical significance) and stable bone levels thereafter over 36 months for delayed placed implants. The implants used had the same surface but a machined collar height of 1.5 mm. Nicolau et al reported a mean bone level alteration of 0.57 ± 0.83 mm in the early loading group for tissue-level implants with a different neck design. The reported bone loss was slightly higher than in another study with the same implant, which reported changes in the crestal bone levels of 0.12 mm between implant placement and the 36-month follow-up in relation to the platform. These differences might be explained by the fact that the implants in the study by Nicolau et al were inserted deeper, which may lead to more initial bone remodeling around the implant shoulder.

The incidence of technical complications after a study period of 3 years in the present report is low, with no screw loosening occurring during the observation period. In a systematic review, the reported frequency of screw loosening was 8.8% after 5 years. Also, the ceramic chipping rate was low: Only one reconstruction presented a small fracture of the veneering ceramic, which could be polished. This is in accordance with the cumulative incidence of ceramic chipping of 4.5% after 5 years reported in an earlier systematic review.

The examined clinical parameters revealed well-maintained oral hygiene over time and, therefore, healthy peri-implant tissues and low mSBI values.

The technique used to take the impression during implant placement and the 21-day early-loading protocol with provisional reconstructions had no negative impact on outcomes. The digital technologies available today may even make it possible to produce the definitive reconstruction with no need for a provisional crown or FDP. This can lead to a more time- and cost-saving way to replace posterior teeth with implant-supported reconstructions.

CONCLUSIONS

Within the limitations of this prospective observational study, eg, the exclusion of the potential risk factors bruxism and heavy smoking, the following conclusions can be drawn for this 3-year postloading follow-up: (1) early functional loading of implants with a hydrophilic, moderately rough endosseal surface in occlusal contact 21 days after healing appears to be a safe and reliable treatment option when placed in the posterior mandible of partially edentulous patients; (2) success (ie, no implant loss, minimal crestal bone changes) was observed in all implants; (3) no complications except for one case with ceramic chipping were reported; (4) the radiographic marginal bone level (DIB) remained stable at the border between the machined implant collar (height of 1 mm) and the structured implant surface.

Comparative clinical trials (hydrophilic vs hydrophobic surfaces) with a higher number of cases, a prolonged follow-up period, and involving the maxilla are necessary to confirm these results.

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