Marco Tallarico, Fulvio Gatti, Erta Xhanari, Leonardo Muzzi, Mircea Gheorghita, Andre de Waal, Elitsa Deliverska, Nicolas Widmer, Dario Melodia, Francesco Mattia Ceruso, Chang-Joo Park, Lukasz Zadrożny

KEY WORDS
Dental implants, Implant surface, Implant stability quotient

Randomized controlled trial

A SPLIT-MOUTH, MULTICENTRE RANDOMIZED CONTROLLED TRIAL COMPARING SINGLE SANDBLASTED ACID-ETCHED IMPLANTS WITH OR WITHOUT SURFACE MODIFIED WITH PH BUFFERING AGENT: RESULTS ONE YEAR AFTER LOADING

MARCO TALLARICO
School of Dentistry, University of Sassari, Sassari, Italy

FULVIO GATTI
University of Milan, Milan, Italy

ERTA XHANARI
Private practice, Tirana, Albania

LEONARDO MUZZI
Private practice, Siena, Italy

MIRCEA GHEORGHITA
Private practice, Craiova, Romania

ANDRE DE WAAL
Private practice, Stellenbosch, South Africa

ELITSA DELIVERSKA
Medical University, Sofia, Bulgaria

NICOLAS WIDMER
Private practice, Bern, Switzerland

DARIO MELODIA
School of Dentistry, University of Sassari, Sassari, Italy

FRANCESCO MATTIA CERUSO
School of Dentistry, Tor Vergata University of Rome, Italy

PURPOSE. To compare the clinical outcomes of single implants with sandblasted and acid-etched (SA, control group) surface *versus* implants with SA surface modified by pH buffering agent (SOI, test group).

MATERIALS AND METHODS. This study was designed as multicentre, split-mouth, randomized controlled trial in partially edentulous subjects requiring at least two single implant-supported crowns. A one-stage implant placement procedure was performed according to the manufacturer's instructions. Patients were randomized after implant site preparation. Eight weeks after implant placement, definitive impressions were taken. Four weeks later, definitive metal-ceramic or full-ceramic crowns were cemented or screw-retained, according to the investigator's preference. Outcome measures were prosthesis and implant failures, complications, peri-implant marginal bone levels, implant stability quotient (ISQ), bleeding on probing (BoP) and plaque index (PI).

RESULTS. Overall, 62 patients from nine centres were enrolled. Thirteen patients had dropped out at one year after loading so follow-up data from 49 patients with 98 implants were analysed. In the first 12 weeks of observation, two implants were lost, both in the SA group, this difference was not statistically significant (RR = 0.200 P = 0.296, 95% CI [0.0098, 4.0830]). No prosthesis failed up to one year after crown fitting. However, during the third and fourth weeks of measurement, loss of stability was observed in two implants in the SOI group and three implants in the SA group. Mixed-effects modelling revealed a statistically significant difference in implant stability between groups (P = 0.011) over time, with slightly lower ISQ values in the SOI group (-0.65; 95% CI -1.14 to -0.15). No statistically significant differences in marginal bone levels were found between the SA and SOI groups at either implant placement (P = 0.411), prostheses fitting (P = 0.917), or 1 year after loading (P = 0.617). Likewise, there was no statistically significant difference in marginal bone loss between groups at any time point. At one year follow-up, there were no statistically significant differences in bleeding on probing (P = 0.787) or plaque index (P = 0.638).

CONCLUSIONS. The results indicate that both implant types can be successfully loaded.

CONFLICT OF INTEREST STATEMENT
Implants used in this study were donated by Osstem Implant, Osstem Global, Seoul, South Korea, but the company had no influence on the study design or outcomes. No authors have any conflict of interest to declare.

CHANG-JOO PARK
Department of Dentistry, College of Medicine, Hanyang University, Seoul South Korea

ŁUKASZ ZADROŻNY
Faculty of Dental Medicine, Medical University of Warsaw, Warsaw, Poland

Correspondence to:
Dario Melodia
dariomld1@gmail.com

INTRODUCTION

Today dental implants are one of the most common and effective procedures available to restore missing teeth[1,2]. Implant failures occur predominantly during the first year after implantation[2], and current research is therefore focussing on rapid osseointegration and peri-implant bone loss prevention[3]. Several surgical and prosthetic procedures are being investigated with a view to reducing marginal bone loss and maintaining peri-implant soft tissue health. These include platform switching, sealed implant-abutment connections, micro- and macro-implant designs, and various loading protocols[2-6]. Conventional loading seems to be associated with a lower incidence of implant failure than immediate loading[3].

Several factors have been shown to significantly influence implant success rates and the degree of biological integration. These include surface roughness, which can be enhanced via various bioactive molecules, as well as sandblasting, acid-etching, anodizing or plasma-spraying[7-10]. In 1986, the American Academy of Implant Dentistry defined osseointegration as a "contact established without interposition of nonbone tissue between normal remodelled bone and an implant entailing a sustained transfer and distribution of load from the implant to and within the bone tissue"[11]. With a view to increasing the bone-to-implant contact during healing time, and potentially increase the survival rate of implant, recent research has been conducted on enhancing the surface characteristics of implants, focusing mainly on their micro- and nano-geometry[12-14].

Nowadays, it is possible to modify the implant surface through mechanical, chemical and physical means, either alone or in combination with each other[15]. Recently, Osstem Implant (Osstem Global, Seoul, South Korea) released an implant with a sandblasted acid-etched surface modified with a pH buffering agent to create a so-called SOI surface with the aim of improving the osseointegration process[16-18]. A preliminary report concluded that implants with SOI surface can be successfully loaded early[19].

The purpose of this split-mouth, multicentre, randomized controlled trial was to compare clinical and radiographic outcomes of TSIII (Osstem Implant) implants with sandblasted and acid-etched (SA) surface *versus* identical implants with SA surface (Osstem Implant) modified by a pH buffering agent (SOI) in the rehabilitation of single implant-supported crowns, one year after loading. These two implants are identical in terms of shape, dimensions and geometry, the only difference being the surface preparation. The SOI implant surface is hydrophilic, with higher wettability, compared to the SA surface. The null hypothesis was that there would be no difference between groups. This report was drafted according to the CONSORT statement guidelines for improving the quality of reports randomised trials (http://www.consort-statement.org/).

MATERIALS AND METHODS

This study was designed as a spilt-mouth, multicentre, randomized controlled trial with blind outcomes assessment, with the exception of complications and failures, which were evaluated by the treating dentists. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki for Biomedical Research Involving Human Subjects, as amended in 2018, and registered with clinicaltrial.gov as number NCT04073654. The research protocol received ethical approval from the coordinating centre, located in Albania (protocol number 1/2018). Before starting any treatment, all the patients were duly informed about the nature of the study, and an informed written consent form for surgical and prosthetic procedures was obtained. Patients were to be enrolled and treated in ten public and private centres in Europe and South Africa between September 2019 and June 2021.

Inclusion/exclusion criteria

Any partially edentulous subject requiring at least two single implant-supported crowns, being at least 18 years old, and able to sign informed consent was screened for eligibility. Any type of bone location was included. However, bone volumes had to be sufficient to allow placement of implants at least 8.5 mm long and 3.5 mm wide in the anterior sectors and a minimum diameter of 4.5 mm for molars, with a minimal insertion torque of 30 Ncm. Post-extraction sockets or augmented bone were allowed if at least 4 months had passed from the extraction or augmentation procedures. Smokers were categorized as moderate (up to 10 cigarettes/day) or heavy smokers (more than 10 cigarettes/day), according to their declaration.

Patients were not admitted to the study if any of the following exclusion criteria applied:

- general contraindications to implant surgery;
- less than 4 mm of keratinized gingiva at the implant sites;
- immunosuppression or immunocompromise;
- irradiation of the head and/or neck in the previous 5 years;
- uncontrolled diabetes;
- pregnancy or lactation;
- untreated periodontal disease;
- poor oral hygiene and motivation (full mouth bleeding and full mouth plaque index higher than 25%);
- addiction to alcohol or drugs;
- psychiatric problems and/or unrealistic expectations;
- acute infection or suppuration at the site intended for implant placement;
- the need for any form of tissue augmentation at implant placement;
- immediate post-extraction (implants could be placed after a 4-month healing period);
- current or ongoing treatment with intravenous aminobisphosphonates;
- referral only for implant placement and inability to follow up at the treatment centre;
- participation in other studies precluding adherence to the present protocol.

Preoperative radiographs (periapical and/or cone-beam computed tomographs) were obtained for every potentially eligible patient to quantify bone volumes at the planned implant sites. Patients having sufficient bone volumes to receive two single implants were invited to join the study and were duly informed. Only after they fully understood the nature of the study, including procedures, follow-up evaluations, and any potential risks involved, were they asked to join and sign informed written consent. In patients with more than two suitable implant sites, operators were free to choose those sites with the most similar characteristics at the screening appointment, preferably non-adjacent. The implant sites selected were then coded as number 1 (the lowest according to the FDI World Dental Federation notation) and number 2 (the highest).

Clinical procedures

About 10 days prior to implant placement, all patients attended a professional oral hygiene session. All patients received prophylactic antibiotic therapy, either 2 g of amoxicillin 1 hour prior to the intervention, or clindamycin 600 mg 1 hour before implant placement if allergic to penicillin. All patients rinsed with 0.2% chlorhexidine mouthwash for 1 minute prior to any surgical procedure, and were treated under local anaesthesia using articaine with epinephrine 1:100,000. Depending on the anatomy of the site and the clinician's preference, either flapless or minimally invasive flap (crestal flap without vertical incisions) approach was per-

formed (but the same in each patient). Implant sites were prepared during the same surgical session with taper drills (800-1200 RPM) and copious saline irrigation, following the drilling protocol recommended by the manufacturer (122 Taper kit, Osstem Implant), according to bone density; this was assessed during the drilling phase, and classed, based on the clinician's experience, as either hard, normal or soft. Operators were free to choose implant lengths according to the clinical indications and their preferences. If possible, the two implants in each patient had to be the same length and diameter. Tapered TSIII implants with sandblasted and acid-etched (SA) surface (SA group) or sandblasted and acid-etched surface modified with pH buffering agent (SOI group) were placed at bone level or slightly subcrestal, with a minimum insertion torque of 30 Ncm, following a one-stage protocol. If insertion torque was less than 30 Ncm, the implant was to be excluded for further ISQ measurements and left to heal undisturbed. In such case, the implant was submerged for 4 months.

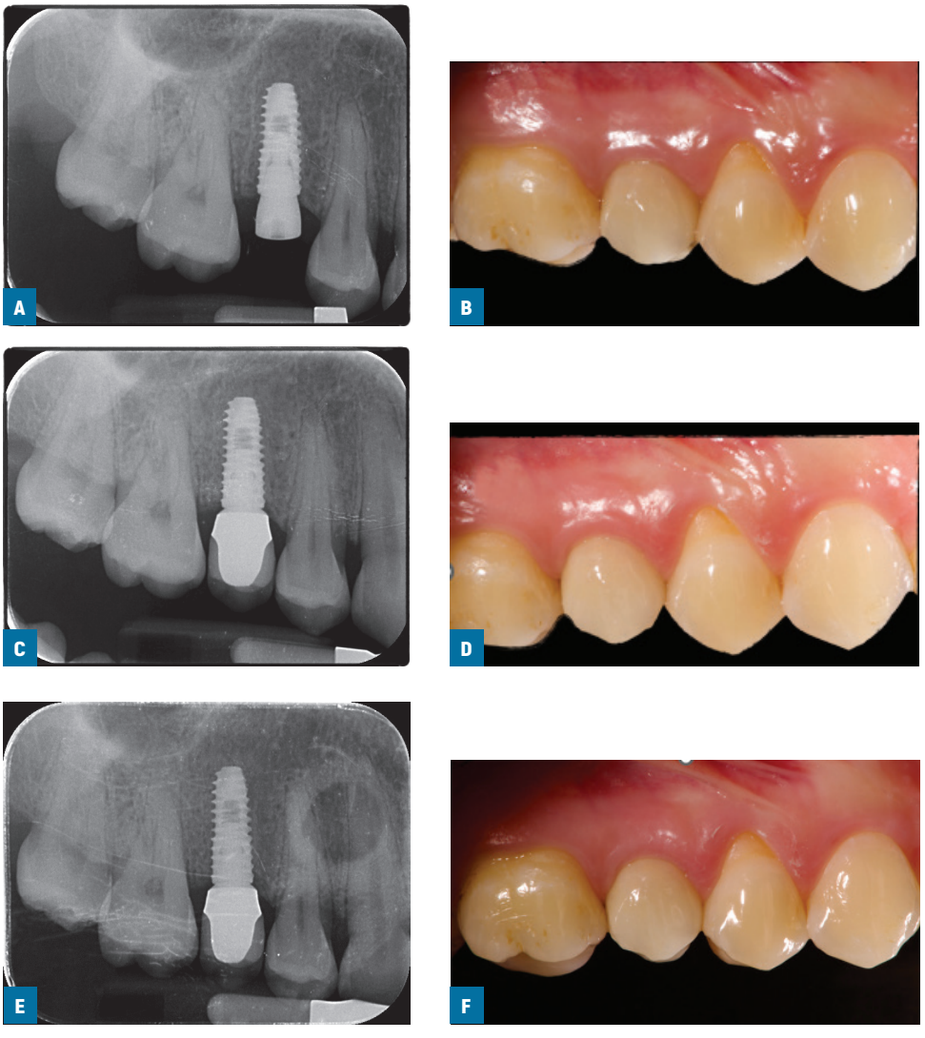
After implant placement, appropriate multipegs (Hiossen, Englewood Cliffs, NJ, USA) were connected to the implants, one at time, and the implant stability quotient (ISQ) was measured using resonance frequency analysis by means of IS3 Monitor device (Hiossen). Healing abutments were connected to the implants with a finger driver, and flaps were closed with sutures. Ibuprofen 600 mg was prescribed to be taken as needed. Antibiotics (1 g of amoxicillin or clindamycin 600 mg if patients were allergic to penicillin) were administered twice a day for 5 days. The ISQ measurements were continued weekly for 8 weeks after implant placement and at the twelfth week. At each time, the healing abutments were unscrewed, appropriate multipegs were attached to the implants, one at time, and two measurements were made, namely buccopalatal and mesiodistal. Finally, after disinfection with 0.2% chlorhexidine and ultrasonic cleaning, the healing abutments were screwed back in place with a finger driver. Eight weeks after implant placement, definitive impressions were taken. Twelve weeks after implant placement, definitive crowns were fitted. Implants were to be restored as single units. Investigators were free to deliver definitive metal-ceramic or full-ceramic crowns, which could be either cemented or screw-retained. Nevertheless, identical procedures and materials were to be used for both implants in each patient. Definitive crowns/abutments were screwed on according to the manufacturer's instructions, with a preload of 20 (mini platform implants) or 30 (regular platform implants) Ncm. After 10 minutes, crowns/abutments were tightened again at the same torque. Occlusion was checked and oral hygiene instruction reinforced, if necessary. Periapical radiographs and intraoral pictures were taken at implant placement, definitive crown fitting (**FIGS. 1A-D; 2A-D**) and 1 year after loading (**FIGS. 1E, F; 2E, F**).

Primary outcome measures were implant and prosthesis failures, any complications, and implant stability quotient (ISQ).

- Implant failure was defined as an implant rotating during abutment tightening/loosening, fracture, and/or any infection dictating implant removal or other mechanical complication rendering the implant unviable.
- Prosthesis failure was defined as crown replacement for any reason.
- Any biological (pain, swelling, suppuration, etc.) and/or mechanical (screw loosening, chipping of the ceramic materials, etc.) complication was also recorded.

Secondary outcome measures were, marginal bone levels (MBL), plaque index (PI) and bleeding on probing (BOP).

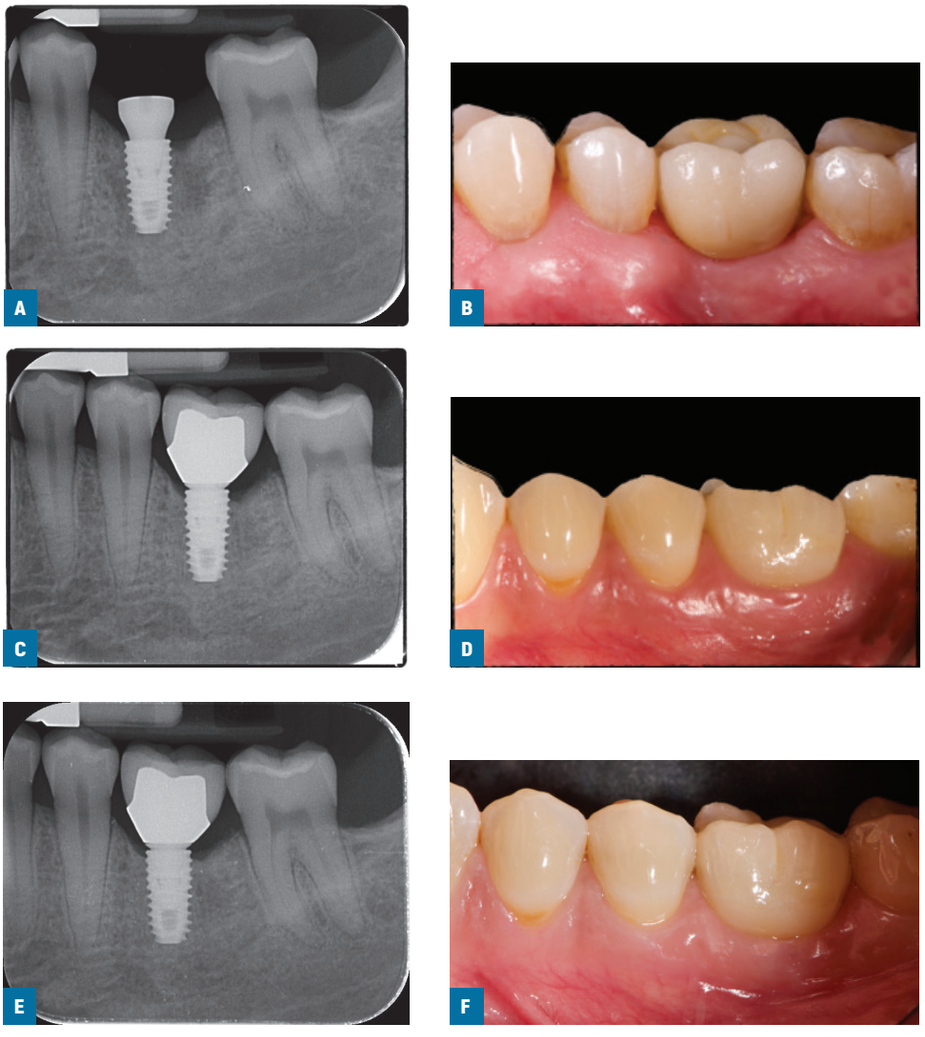
- Peri-implant marginal bone level changes were evaluated on digital intraoral radiographs taken with the paralleling technique at implant placement (baseline), initial loading, and one year after loading. In the event of unclear radiographs, new radiographs were to be taken. A trained centralized outcome assessor (FMC) measured peri-implant marginal



FIGS. 1A-F: *Implant placement (SOI group) (A); prosthesis fitting 3 months after implant placement (SOI group) (B); periapical radiograph at prosthesis fitting (SOI group) (C); 4-month follow-up (SOI group) (D); periapical x-ray one year after loading in SOI group (E); clinical photo one year after loading in SOI group (F)*

bone levels using dedicated software (DFW2.8 for windows, Soredex, Tuusula, Finland). The software was calibrated for every single image using the known implant length. If the full implant length was not displayed in the radiograph, the diameter at the implant neck was used for calibration. Measurements of the mesial and distal bone crest levels adjacent to each implant were made to the nearest 0.01 mm. Reference points for the linear measurements were the coronal margin of the implant collar and the most coronal point of bone-to-implant contact. Implants with bone up to the coronal margin of the implant collar were given a value of zero. Mesial and distal measurements of each implant were averaged, and means were calculated for each group.

ISQ values were recorded by blind outcome assessors using resonance frequency analysis. Buccopalatal and mesiodistal measurements were taken and averaged, with the result being displayed by the device in ISQ units, ranging from 1 to 100. The ISQ values were recorded at the time of implant placement (baseline), weekly up to the eighth week, and then at the twelfth week after implant placement at the time of definitive crown fitting.



FIGS. 2A-F: *Implant placement (SA Group) (A); prosthesis fitting 3 months after implant placement (SA group) (B); periapical radiograph at prosthesis fitting (SA group) (C); 4-month follow-up (SA group) (D); periapical x-rays one year after loading in SA group (E); clinical photo one year after loading in SA group (F)*

- Plaque index (PI), defined as plaque absent or present (0/1), and bleeding on probing (BoP), defined as absent or present (0/1), were recorded on six sites per tooth (three buccal and three oral sites) at one year after loading. Multiple implants were averaged at patient level and the data were expressed as percentages.

A blind outcome assessor collected the data at each centre. An independent assessor, not previously involved in the study, evaluated the MBL from all centres blind (FMC).

Data analysis

Based on a previous, similar study reporting ISQ values of 71.2±4.07 for the conventional surface and 74±4.68 for the modified surface[18] a sample size of 65 implants per group was estimated, given an effect size d = 0.6383489, α err prob 0.05, and power (1-ß err prob = 0.95). Due to the split-mouth design of the study, each patient provided both test (SOI) and control (SA)

implants. In order to avoid underpowered results due to possible drop-outs, 35 patients were added, taking the total sample size to 100 patients (200 implants). Each centre had therefore to place 10 test implants (SOI) and 10 control implants (SA) in 10 enrolled patients.

Hence, ten computer-generated restricted randomization lists were created. Only one person, not involved in the research, was aware of the randomization sequence and could have access to the randomization lists, which were stored on their password-protected laptop. The randomization codes were enclosed in sequentially numbered, identical, opaque, sealed envelopes. Envelopes were opened sequentially after both implant sites were prepared.

All data analysis was carried out according to a pre-established analysis plan by one of the investigators (DM) without knowing group allocation. Patient data were collected on an Excel spreadsheet (Microsoft Corporation, Redmond, Washington, USA). Implant failures, prostheses failures and complications (dichotomous outcomes) were compared between the groups using Fisher's exact probability test. Paired t-tests were used for continuous variables. A mixed-effects model was created to estimate differences among centres, considering patients as random effects and time and centre as fixed effects. The data are presented as mean ± standard deviation with 95% confidence interval (CI), and dichotomous variables are presented as frequency and percentage. P-values <0.05 were considered statistically significant.

RESULTS

Patients were to be recruited and treated at 10 different centres using similar procedures, and each centre was supposed to recruit and treat 10 patients (20 implants). However, one centre failed to recruit any patients (centre 5). The nine remaining centres were located as follows: three in Italy (MT, FG, LM), and one each in Albania (EX), Bulgaria (DE), Romania (MG), Switzerland (NW), South Africa (AdW) and Poland (LZ). Patients were assessed to establish their eligibility for the study, and only two centres (MT and EX) recruited 10 patients. Another centre (MG) recruited nine patients, two centres (NW and AdW) eight patients each, two centres (LM and LZ) six patients each, and the remaining two centres recruited three (DE) and two (FG) patients, respectively. Thus, a total of 91 patients were screened for eligibility, but only 62 participants were consecutively enrolled in the trial by the nine participating centres. Reasons for not including 29 patients were: patients refused frequent check-up visits (18 patients), and the need for guided bone regeneration (11 patients). Of the 62 patients in the final sample, 23 were males and 39 females.

Thirteen patients had dropped out by follow-up one year after loading (**TABLE 1**), so data from a total of 49 patients with 98 implants were analysed. Twenty-two deviations from the original protocol occurred at six centres, as reported in **TABLE 2**.

The mean age of the patients was 52.1±14.3 years. The majority, 66.1%, were non-smokers, with 27.4% smoking up to 10 cigarettes per day and 6.5% more than 10 cigarettes per day.

A total of 124 implants were placed, 55 in the upper and 69 in the lower jaw. The number of each size of implants is in the following study 19. All centres provided the same type of prostheses in all patients except for one (Patient 2 at Centre 3 received one screw- and one cement-retained crown). Materials were similar in both groups. The majority of protheses were screw-retained in both SA and SOI groups (69.4% and 68.1%, respectively), and 56.5% of crowns were metal-free in both groups.

Two implants from the SA group were lost (at Centres 7 and 10, respectively), while no implant failed in the SOI group up to one year after loading; the between-group difference was not statistically significant (P = 0.4948). Both implants were lost (mobility without pain) between the third and fourth week, and immediately replaced. At Centre 7, the patient's remaining (SOI)

TABLE 1 DROP-OUTS BY CENTRE

CENTRE 1	Patient 9 move to another city
CENTRE 2	None
CENTRE 3	None
CENTRE 4	None
CENTRE 6	Patient 3 did not return calls Patient 4 did not return calls
CENTRE 7	Patient 6 was non-compliant and eventually dropped-out due to Covid-19 (refused check-ups)
CENTRE 8	Patient 10 got tired of the follow-up
CENTRE 9	The centre originally enrolled six patients, but monitoring was less than optimal, and at the one-year follow-up only Patient 3 was examined
CENTRE 10	Patient 6 withdrew from the study due to one implant failure

TABLE 2 DEVIATIONS FROM THE ORIGINAL PROTOCOL

CENTRE 1	Patient 2: measurements at SA implant were suspended at week 4 (up to week 12) due to implant mobility (ISQ lower than 55) Patient 7: measurements at SOI implant were suspended at week 3 (up to week 12) due to implant mobility (ISQ lower than 55) Patient 9: measurements at both implants were suspended for 6 weeks at week 2 due to Covid-19 quarantine
CENTRE 2	None
CENTRE 3	Patient 2: received one screw- and one cement-retained crown Patient 5: measurements at both implants were suspended for 6 weeks at week 2 due to Covid-19 quarantine Patient 6: measurements at both implants were suspended for 6 weeks at week 2 due to Covid-19 quarantine
CENTRE 4	None
CENTRE 5	No patients recruited
CENTRE 6	None
CENTRE 7	Patient 6: measurements at SOI implants were suspended at week 1 (up to week 12) due to implant mobility (ISQ lower than 55) Patients 1, 2, 3, 7 and 8: measurements were not taken at week 12 due to the prostheses having already been fitted Patient 2: measurements were not taken at weeks 2 and 5 due to holidays Patients 4 and 6: measurements were stopped at weeks 3 and 1, respectively, due to Covid 19 quarantine Patient 5: measurements were stopped at week 1 due to IS3 malfunction
CENTRE 8	Patient 6: measurements at SOI implant were suspended at week 3 (up to week 12) due to implant mobility (ISQ lower then 55)
CENTRE 9	Patients 1-7: missed at least one appointment for different reasons unrelated to the study (e.g., forgetting the appointment, general health status, quarantine) Patients 5 and 6: received splinted implant-supported restorations instead of single crowns
CENTRE 10	Patient 2: measurements at both implants were suspended for 2 weeks at week 4 due to Covid-19 quarantine Patient 4: measurements at both implants were stopped at week 6 due to Covid-19 lockdown. Prosthesis delivery occurred 9 months from implant placement

implant continued to be monitored, while the patient from Centre 10 withdrew from the study at week 8. No prosthesis failed in either group up to one year after crown fitting (P = 1). Overall, five complications were experienced, three in the SA group and two in the SOI group. The difference was not statistically significant (P = 1). At Centres 1, 7 and 8, slight horizontal

mobility was perceived manually in four implants (two in each group), but no implant rotation. Those implants were submerged and successfully osseointegrated and loaded at week 12, in line with the study protocol. The last complication was a screw loosening at one implant-supported crown in the SA group (centre 3), which occurred eight weeks after it was fitted. No other complications were observed one year after loading.

The baseline mean ISQ values were 76.57±7.54 (95% CI 74.69 to 78.44) in the SA group and 75.92±7.69 (95% CI 73.89 to 77.73) in the SOI group. The mean ISQ values at 12 weeks were 79.17±7.83 (95% CI 77.03 to 81.29) and 78.82±8.80 (95% CI 76.42 to 81.21) in the SA and SOI groups, respectively. Mixed-effects modelling revealed a statistically significant difference between groups (P = 0.011) over time, with slightly lower ISQ values for the SOI group (-0.65; 95% CI -1.14 to -0.15); this data is presented in detail in a previous publication[19].

Paired t-tests revealed no statistically significant differences in marginal bone level (**TABLE 3**) between SA and SOI groups at either implant placement (MBL IP), prostheses delivery (MBL PD), or one year after loading (MBL 1Y). Neither were between-group differences between MBL IP and MPL PD or MBL 1Y and MBL IP. At the one-year follow-up, no statistically significant differences were found between implants for either bleeding on probing or plaque index (**TABLE 4**).

DISCUSSION

This randomized controlled trial was designed to provide additional data to that published in a previous preliminary report[19] on the clinical performance of Osstem TSIII implants with SA surface modified with pH buffering agent used for the rehabilitation of single implant-supported crowns, as compared to the conventional SA surface. Thus far, few human trials have been conducted, and the majority of the literature is based on animal research. Since histological analysis on people is very difficult because of ethical guidelines, it is not possible to compare the outcomes of animal research with those in humans. However, some hold the opinion that a degree of surface modification can facilitate early osseointegration[20]. One of the best documented implant surfaces in dentistry, involving a combination of physical and chemical procedures, specifically grit blasting with alumina and acid etching, has had long-term success[20-23]. However, modification techniques are in continuous development with a view to improving surface roughness and establishing an environment favourable for osseointegration.

The efficacy of pH-buffered SA surface modification at enhancing osseointegration has been tested in a few in vitro studies[24-26]. Among those, Pae et al. assessed platelet adhesion and osteoblastic affinity between SOI and SA surfaces, demonstrating significantly higher osteoblast migration, platelet adhesion and activation on SOI implants[26].

While the present trial did not reveal any clinically significant differences between SA and SOI groups, there was a statistically significant difference in terms of implant stability (ISQ) favouring the SA surface. ISQ measurement may be affected by a number of factors, including but not limited to bone quality and quantity, even if the same implant and drilling techniques are employed. This creates doubt as to the clinical utility of ISQ measurements for evaluating implant stability, as pointed out in a study[19].

Nonetheless, analysis of the data collected in the present study showed some bone remodelling, and no implant failures in the SOI group one year after loading. Despite a lack of statistical significance, this indicates that SOI implants can be successfully osseointegrated. Our results are in line with those by both Chambrone[27] and Buser[23], neither of whom found statistically significant differences between standard and modified implant surfaces.

The main limitations of the present study are the discontinuation in measurements due to

TABLE 3 MEAN MARGINAL BONE LEVELS (MBL) AND DIFFERENCES BETWEEN AND WITHIN GROUPS

	SA group (n = 24 patients)	SOI group (n = 25 patients)	Difference	P-value
Mean MBL at implant placement (MBL IP)	0.02±0.04 (95% CI 0.01 to 0.03)	0.03±0.13 (95% CI 0.00 to 0.07)	0.01±0.12 (95% CI -0.02 to 0.04)	0.411
Mean MBL at prostheses delivery (MBL PD)	0.15±0.32 (95% CI 0.06 to 0.24)	0.15±0.24 (95% CI 0.08 to 0.21)	0.00± 0.26 (95% CI -0.07 to 0.07)	0.917
Mean MBL at 1 year after loading (MBL 1Y)	0.24±0.37 (95% CI 0.14 to 0.35)	0.21±0.29 (95% CI 0.13 to 0.29)	0.02 ±0.22 (95% CI -0.08 to 0.04)	0.617
Mean difference between MBL IP and MBL PD	0.13±0.32 (95% CI 0.05 to 0.22)	0.11±0.17 (95% CI 0.06 to 0.16)	0.02±0.2 (95% CI -0.07 to 0.03)	0.664
Mean difference between MBL IP and MBL 1Y	0.22±0.35 (95% CI 0.12 to 0.32)	0.17±0.25 (95% CI 0.10 to 0.24)	0.05±0.23 (95% (-0.11 to 0.01)	0.414

TABLE 4. MEAN BOP AND PI VALUES RECORDED AT ONE YEAR AFTER LOADING

	SA group (n = 24 patients)	SOI group (n = 25 patients)	Difference	P-value
Mean BoP 1 year after loading	0.11±0.19 (95% CI 0.05 to 0.16)	0.12±0.20 (95% CI 0.06 to 0.18)	0.01±0.15 (95% CI -0.03 to 0.05)	0.787
Mean PI 1 year after loading	0.13±0.19 (95% CI 0.08 to 0.19)	0.12±0.18 (95% CI 0.06 to 0.17)	0.01±0.11 (-0.04 to 0.02)	0.638

Covid-19-related disruption, and the short follow-up. Nevertheless, both groups were affected in equal measure due to the split-mouth design of the study. Furthermore, both implant surfaces were evaluated under real clinical conditions, and the results should therefore be generalisable to a wider population with similar characteristics. However, further studies are needed to assess the possible benefits of this new surface in more complex cases (e.g., guided bone regeneration, immediate implants, compromised patients, poor bone quality).

CONCLUSIONS

The results of this trial suggest that implants with a surface modified with pH buffering agent (SOI) can be safely used for supporting single crowns. Further studies are needed to evaluate the performance of this novel implant surface in complex cases.

REFERENCES

1. Chrcanovic BR, Kisch J, Albrektsson T, Wennerberg A. A retrospective study on clinical and radiological outcomes of oral implants in patients followed up for a minimum of 20 years. Clin Implant Dent Relat Res 2018 Apr;20(2):199-207.
2. Tallarico M, Meloni SM. Retrospective analysis on survival rate, template-related complications, and prevalence of peri-implantitis of 694 anodized implants placed using computer-guided surgery: results between 1 and 10 years of follow-up. Int J Oral Maxillofac Implants 2017;32(5):1162-71.
3. Atieh MA, Ibrahim HM, Atieh AH. Platform switching for marginal bone preservation around dental implants: a systematic review and meta-analysis. J Periodontol 2010;81(10):1350-66.
4. Chen J, Cai M, Yang J, Aldhohrah T, Wang Y. Immediate *versus* early or conventional loading dental implants with fixed prostheses: a systematic review and meta-analysis of randomized controlled clinical trials. J Prosthet Dent 2019;122(6):516-36.
5. Bateli M, Att W, Strub JR. Implant neck configurations for preservation of marginal bone level: a systematic review. Int J Oral Maxillofac Implants 2011;26(2):290-303.
6. Schwarz F, Hegewald A, Becker J. Impact of implant-abutment connection and positioning of the machined collar/microgap on crestal bone level changes: a systematic review. Clin Oral Implants Res 2014;25(4):417-25.
7. Le Guehennec L, Lopez-Heredia MA, Enkel B, Weiss P, Amouriq Y, Layrolle P. Osteoblastic cell behaviour on different titanium implant surfaces. Acta Biomater 2008;4(3):535-43.
8. Velasco-Ortega E, Alfonso-Rodríguez CA, Monsalve-Guil L, España-López A, Jiménez-Guerra A et al. Relevant aspects in the surface properties in titanium dental implants for the cellular viability. Mater Sci Eng C Mater Biol Appl 2016;64:1-10.
9. Braceras I, De Maeztu MA, Alava JI, Gay-Escoda C. *In vivo* low-density bone apposition on different implant surface materials. Int J Oral Maxillofac Surgery 2009;38:274-8.
10. Cervino G, Fiorillo L, Iannello G, Santonocito D, Risitano G, Cicciù M. Sandblasted and acid etched titanium dental implant surfaces systematic review and confocal microscopy evaluation. Materials (Basel) 2019;12(11):1763.
11. Le Guéhennec L, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. Dent Mater 2007;23(7):844-54.
12. American Academy of Implant Dentistry. Glossary of implant terms. J Oral Implantol 1986;12:284-94.
13. Schwartz Z, Martin JY, Dean DD, Simpson J, Cochran DL, Boyan BD. Effect of titanium surface roughness on chondrocyte proliferation, matrix production, and differentiation depends on the state of cell maturation. J Biomed Mater Res 1996;30(2):145-55.
14. Junker R, Dimakis A, Thoneick M, Jansen JA. Effects of implant surface coatings and composition on bone integration: a systematic review. Clin Oral Implants Res 2009;20(4):185-206.
15. Le Guehennec L, Goyenvalle E, Lopez-Heredia MA, Weiss P, Amouriq Y, Layrolle P. Histomorphometric analysis of the osseointegration of four different implant surfaces in the femoral epiphyses of rabbits. Clin Oral Implants Res 2008;19(11):1103-10.
16. Biesbrock AR, Edgerton M. Evaluation of the clinical predictability of hydroxyapatite-coated endosseous dental implants: a review of the literature. Int J Oral Maxillofac Implants 1995;10(6):712-20.
17. Park C-J, Lim JH, Tallarico M, Hwang K-G, Choi H et al. Coating of a sand-blasted and acid-etched implant surface with a pH-buffering agent after vacuum-UV photofunctionalization. Coatings 2020;10:1040.
18. Kang JH, Kim S-K, Pae HC, Park JY, Cha J-K, Choi S-H. Influence of implant surface coated with pH buffering agent on early osseointegration. J Korean Dental Sci 2018;11:5-13.
19. Zadrożny L, Xhanari E, Gheorghita M, De Waal A, Widmer N et al. Comparison between single early-loaded implants with sandblasted acid-etched (SA) surface *versus* SA surface modified with ph buffering agent (SOI): four-month data from a split-mouth, multicentre randomized controlled trial. Clinical Trials in Dentistry 2021;3(4)33-46.
20. Nicolau P, Guerra F, Reis R, Krafft T, Benz K, Jackowski J. 10-year outcomes with immediate and early loaded implants with a chemically modified SLA surface. Quintessence Int 2019 25;50(2):114-24.
21. Schätzle M, Männchen R, Balbach U, Hämmerle CH, Toutenburg H, Jung RE. Stability change of chemically modified sandblasted/acid-etched titanium palatal implants. A randomized-controlled clinical trial. Clin Oral Implants Res 2009;20:489-95.
22. French D, Ofec R, Levin L. Long term clinical performance of 10871 dental implants with up to 22 years of follow-up: a cohort study in 4247 patients. Clin Implant Dent Relat Res 2021;23:289-97.
23. Buser D, Janner SF, Wittneben JG, Brägger U, Ramseier CA, Salvi GE. 10-year survival and success rates of 511 titanium implants with a sandblasted and acid-etched surface: a retrospective study in 303 partially edentulous patients. Clinical Implant Dent Relat Res 2012;14:839-51.
24. Ting M, Jefferies SR, Xia W, Engqvist H, Suzuki JB. Classification and effects of implant surface modification on the bone: human cell–based *in vitro* studies.J Oral Implantol 2017;43(1):58-83.
25. Conserva E, Lanuti A, Menini M. Cell behavior related to implant surfaces with different microstructure and chemical composition: an *in vitro* analysis. Int J Oral Maxillofac Implants 2010;25(6):1099-107.
26. Pae HC, Kim SK, Park JY, Song YW, Cha JK et al. Bioactive characteristics of an implant surface coated with a pH buffering agent: an *in vitro* study. J Periodont Implant Sci 2019;49(6):366-81.
27. Chambrone L, Shibli JA, Mercurio CE, Cardoso B, Preshaw PM. Efficacy of standard (SLA) and modified sandblasted and acid-etched (SLA active) dental implants in promoting immediate and/or early occlusal loading protocols: a