European Journal of Musculoskeletal Diseases
ISSN 2038-4106/2023

Review

THE BONE-IMPLANT CONTACT AND OSSEOINTEGRATION OF DIFFERENT IMPLANT SURFACE TREATMENT: THE FINDINGS FROM A SYSTEMATIC REVIEW OF LITERATURE

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ABSTRACT

The dental implant is associated with high long-term predictability for fixed rehabilitation in edentulous patients. The aim of the present review was to evaluate the state-of-art of dental implant surface treatment and their effect on osseointegration. The Pubmed/Medline, EMBASE, Cochrane Library databases has been screened to identify the histologic studies regarding the dental implant surfaces *in vivo*. The screening process revealed a total of 3173 papers with a total of 24 articles obtained by the manual search. A total of 482 duplicates have been removed and 2691 papers were assessed for the full-text evaluation. A total of 2527 articles were removed after the eligibility process and 149 articles were evaluated for the descriptive analysis. The implant osseointegration process is a complex combination of events that is oriented to an intimate interface between the dental implant surface and the host peri-implant tissues that oriented to produce a functional ankylotic relationship between the components under the masticatory loading.

KEYWORDS: *implant, fixture, surface, osseointegration, bone*

INTRODUCTION

The dental implant osseointegration represents the turning point for edentulous ridge rehabilitations due to the more

Received: 02 August 2023
Accepted: 09 September 2023

ISSN: 2038-4106
Disclosure: All authors report no conflicts of interest relevant to this article.

recent advances in titanium biocompatibility, enhanced surface treatment and novel high hydrophilic/bioactive materials (1), with a long-term implant success rates over 90% (2). The osteoconduction process is involved with the recruitment and migration of osteogenic cells to the implant surface determines the early events correlated to the dental implant osseointegration. This phase produces a mineralised osteoid matrix deposition representings the main non-functionalised new bone formation at the level of the bone-implant interface. These events are strictly correlated with several factors including the dental implant microtopography (3). Other key factors are represented by the implant material, macro design, surface chemistry, bone density, surgical technique, and implant loading protocol (4). In literature, the bone-implant contact (BIC) percentage represent one of the most reliable parameter for dental implant osseointegration, while values >50% are considered optimal for a long term stability findings (5). On the contrary, the main disadvantage of this parameter is dynamic and could potentially vary over time. In addition, the BIC% is a bidimensional parameter that could be determined only with retrieved biopsies and is not replicable.

Also, the torque removal force has been suggested as an additional technique to assess the implant anchorage for research purposes evaluating the biomechanical behaviour of osseointegration (6). In this way, the roughness of a surface is one of the major factors contributing to implant stability, based on the assessment of the surface peaks and valleys. For this purpose, the arithmetic mean height deviation from a mean bi-dimensional plane (Ra); the Sa is considered in the case of a three-dimensional evaluation (7). The “osseointegration” concept was introduced by Branemark et al. (1) as the direct contact between living bone and a functionally loaded implant surface without interposed soft tissue at the light microscope level (8).

Today, titanium is the most common material for dental implants due to its low weight, high strength/weight ratio, low elasticity modulus, corrosion and wearing resistance, and biocompatibility (9). The most frequent titanium alloy (Ti6Al4V) is composed of 6% of aluminium and 4% vanadium (10). Lincks et al. (11) reported that the osteoblasts-like cells responded differently to cpTi and Ti6Al4V materials due to the alloy mosaicism and the surface chemistry. A passive surface oxide film around the titanium core (12) determines the interface generation between the titanium surface and the surrounding hard tissue. The oxide layer produces hydroxyl functional groups when exposed to the air environment (13). The hydroxyl functional groups dissociate when exposed to body fluid to generate an electric charge that is correlated to the pH of the fluids (13). In this way, the point of zero charge of rutile is 5.3, while the anatase point of zero charge is 6.2 (14, 15). The TiO2 shows reported a neutral property. The hydroxyl concentration of TiO2 is relatively large, representing an advantage for the proteins and cytokines adsorption promotion (12). The machined surfaces of the implant device are provided only by decontamination after the turning procedure.

Various treatments were proposed to improve the surface properties, taking advantage of rough interfaces with high implant stability and the surface contact area (6, 16, 17). In addition, rough surfaces seem to be effective in improving the osteogenic cell’s behaviour (18, 19), proliferation and differentiation (20, 21) due to the release of signal mediators, transforming growth factor beta, and prostaglandin E2 (PGE2) (21-24). The optimal roughness for dental implant surfaces range is approximately 1.5 µm (25). Several methods have been suggested, such as modified surfaces, additive coating protocols, and subtractive methods, while today, the optimal surface type has not been defined. The present systematic reviews aimed to investigate the recent updates of bone-implant contact (BIC) effectiveness of different implant surface treatments.

MATERIALS AND METHODS

Article search methodology

The screening phase was conducted according to the Standards for Reporting Qualitative Research principles (SRQR) and the PRISMA guidelines (26). The selection was based on a keyword strategy synthetised in Table I.

Table I. *Boolean search and keyword strategy.*

	Search Strategies
Keywords	Advanced keywords search: ((dental AND (implant OR implants OR implantation OR implantology) AND (surface OR surfaces OR surface topography) AND (Histo*))
Databases	Pubmed/Medline, EMBASE, Cochrane Library

The papers' title and abstracts were assessed for an initial screening, and the manuscripts were limited to histological studies with bone-to-implant contact (BIC) outcomes. The full texts were finally collected and evaluated to assess the eligibility for the descriptive analysis.

Inclusion and exclusion criteria

The inclusion criteria for the eligibility synthesis were limited to histological studies that assessed bone-to-implant contact (BIC) outcomes from 1995 to today. The exclusion criteria were systematic and literature reviews, letters to the editor, *in vitro* and laboratory simulation, pilot studies, preliminary reports, no loading outcomes and early follow-up. The articles written in non-English language were excluded from the review.

RESULTS

Screening process

The electronic database identification process revealed a total of 3173 and 24 articles screened trough a manual search. A total of 482 duplicates have been removed from the articles list, and 2691 articles have been submitted for the full-text screening process. A total of 2527 papers were excluded for the following reasons: 1302 for the wrong outcome, 668 for the wrong device, 259 for wrong study design, 147 for wrong publication type, 101 written in a foreign language, 34 for wrong study duration and 16 for the wrong study population.

Sandblasted surfaces

The sandblasting procedure was proposed by sandblasting the metal surface with gritting agents. The number and rotations speed, the flux pressure, and the granulometry of the agent particles (10, 27) determine the treatment. The sandblasting procedure increases the surface irregularity and the implant biomechanical characteristics. The most common sandblasting agents are aluminium oxide/alumina (Al2O3) and titanium oxide (TiO2). The primary studies concerning the sandblasted surfaces are summarised in Table II. The procedure can influence the adhesion, proliferation, and differentiation of osteoblasts (20, 28).

Moreover, the fibroblasts result in a more difficult adhesion to the implant surface and a lower soft tissue proliferation around the implant in favour of the new bone formation (27, 29). Using surfaces blasted with Al2O3 particles was investigated compared to turned titanium surfaces. In the literature, the sandblasted implants showed higher BIC than the machined (30). In another study, the machined implants with Sa of 0.96 µm were compared to different blasting sizes, and after 12 weeks, all blasted surfaces demonstrated higher BIC compared with machined surfaces.

The blasting procedure leaves residual particles over the implant's surface, which can modify the bone healing process. Some authors support that the presence of remaining particles may benefit osseointegration, catalysing this process (31); others support that aluminium ions are suspected to impair bone formation by a possible competitive action to calcium (32-35). TiO2 particle blasting was proposed to promote bone contact (27). Dental implants with TiO2 surface were compared to machined implants with a statistically significant higher removal torque compared to machined implants. No differences in BIC were detected (25). A combination of TiO2 blasted surface with fluoride ions has been proposed to improve the early osseointegration of dental implants (36). This method reported a bone-to-implant contact mean of >48% after 2 months of healing, which was higher than the blasting procedure alone (36).

At the same time, the precise nature of multinucleated giant cells is not thoroughly investigated, while a histological study suggested a priming effect on osteoblast activity similar to the hypothetic role of osteoclasts (37). Additional studies focus on sandblasted implants (38-40).

Plasma sprayed and plasma-chemical vapour surface

The plasma-sprayed treatments were studied in orthopaedics (41) and dental implants with no histological evidence of connective tissue infiltration at the interface level (42). Plasma-sprayed implants are obtained by spraying heat molten metal on the implant core, producing irregularly sized and shaped rounded particles and splats with valleys, pores and crevices (43). This treatment improves implant stability, bone growth (44), and higher surface contact area (10).

This treatment has been successfully investigated in rabbits (45), monkeys (46, 47), and humans (48-51), in different functional loading conditions (52). *In vivo,* no significant differences were detected between plasma-spray vs. machined implant, with a BIC percentage ranging between 55.9% and 56.2% (53). An alkali modification of the plasma-spraying

Table II. *Comparative studies which used sandblasted implants.*

Author	Implant surface	Results	Findings	Experimental design
Piattelli et al. (1998) [30]	**(1) Al_2O_3 blasted** **(2) Turned**	**BIC values** (1) 60%±1.4% (2) 51%±1.9%	The blasted sites presented BIC values statistically higher in comparison to turned.	Implants inserted in the femoral articulation of rabbits. Healing period: 8 weeks
Piattelli et al. (1996)[37]	**(1) Al_2O_3 blasted** **(2) Turned** **(3) Plasma-spray**	**ACP, ALP activity** **(1), (2) and (3)**	No MGS activity was reported for (1) and (2). At 2 weeks, Plasma spray revealed MGS activity.	Healing period: 2, 4 and weeks
Wennerberg et al. (1998)[38]	**(1) Al_2O_3 blasted** (25µm, 75µm, and 250µm particles) **(2) Turned**	**BIC values** (1) Ranging from 31 to 47% (2) Ranging from 18 to 23%.	Blasted surfaces demonstrated more bone in contact to implant surface compared to turned surface.	Implants inserted in the tibia of rabbits. Healing period: 12 weeks
Wennerberg et al. (1996)[31]	**(1) Al_2O_3 blasted** (25 µm particles) **(2) TiO_2 blasted** (25 µm particles)	**BIC values** (1) 49.2 % (2) 47.6 % **Removal torque** (1) 26.5 Ncm (2) 24.9 Ncm	No statistically different values concerning torque removal BIC values between the surfaces blasted with the same size of particles.	Implants inserted in the tibia of rabbits. Healing period: 12 weeks
Wennerberg et al. (1995)[25]	**(1) TiO_2 blasted** (25 µm particles) **(2) Turned**	**BIC values** (1) 40.9 % (2) 34.5 % **Removal torque** (1) 35.4 Ncm (2) 29.2 Ncm	BIC values were not significantly different between the implants. However, TiO_2 blasted implants demanded a statistically significant greater removal torque force than turned implants.	Implants inserted in the tibia of rabbits. Healing period: 12 weeks
Gotfredsen et al. (1992)[39]	**(1) TiO_2 blasted** (10-53 µm particles) **(2) Turned**	**Removal torque** (1) 150 Ncm (2) 60 Ncm	BIC not significantly difference (data not shown), but, blasted implants presented higher removal torque values in comparison to turned sites.	Implants were immediately placed, in dogs. No prosthetic rehabilitation was performed. Healing period: 12 weeks
Ivanoff et al. (2001)[40]	**(1) TiO_2 blasted** (25 µm particles) **(2) Turned**	**BIC values** (1) 37 % (2) 9 %	The analysis of the results revealed a significantly higher BIC for the blasted implants than turned groups.	Microimplants were inserted in the ridge of 27 patients. Mean healing period ranging from 3.9 to 6.3 months.
Rocci et al. (2008)[36]	**(1) TiO_2 blasted** (25 µm particles) **(2) TiO_2 blasted with fluoride ions**	**BIC values** (1) 24.8 % (2) 48.3 %	The implant surfaces grit-blasted seems to produce a positive effect on osseointegration, the adding of fluoride ions could produce a sensible bioactive effect on the integration process.	A total of 7 implants positioned in human mandible. Mean healing period 8 weeks.

technique by sodium hydroxide solutions at 40^{o}C for 24 h can determine an oxide layer Ra = 17.6 μm) and 20 nm thickness (44). The main reported disadvantage of plasma-spray is the detachment of titanium after implant insertion. Franchi et al. (54) reported the particle detachment of plasma spray, sandblasted and acid-etched, and machined implants in sheep. The authors reported that the titanium particles were detected only in plasma-sprayed implants. This phenomenon can be related to the friction between the implant surface and host bone cavity during implant placement, but its implications are unclear. Recent non-thermal and argon-based plasma applications have been proposed for dental implants, reporting no significant changes in new bone formation compared to sandblasted dental implant (55-58).

On the contrary, a significant increase in argon-based plasma-spray implant-bone contact was reported by Qiao et al. compared to sandblasted and acid-etched fixtures (59). Several studies increased the new bone formation of hybrid titanium-zirconia dental implants obtained through a novel plasma spray technique (60, 61). The microwave plasma-chemical-vapour deposition (MWP-CVD) of diamond-coated Ti-Al6-V4 dental implants compared to Ti-Al6-V4 implants have been investigated (62, 63). No differences in BICs, delamination, or particle-dissociation due to shearing forces have been detected (62).

Acid-etched surfaces

The acid-etch implant was proposed to avoid the residues released from sandblasting, a non-uniform surface modification of the implant body (10). For this purpose, different acid-etching solutions have been proposed, such as chloridic (HCl), sulfuric (H2SO4), hydrofluoric (HF), and nitric (HNO3), in different combinations. The acid-etching process effectiveness is by the baseline roughness, acid composition, temperature, and etching time. The histologic assessment results have been evaluated in Tables III and IV. A study compared two different etching of solution HCl and H2SO4, reporting that the surfaces presented a homogeneous distribution of small 1-2 μm peaks and valleys and a removal torque 4 times higher for acid etched (6). The dual acid-etched procedure was proposed to obtain a macro- and micro-texture of the titanium surfaces (6) and higher platelet and osteogenic molecular signals (64, 65). Degidi et al. (66) reported histologically a mean BIC percentage of 61.3%, with no gaps or fibrous tissues present at the interface. Similar BIC results were reported after four months of healing on non-loaded implants (67).

In immediate loading protocols, the mean BIC levels ranged between 78% and 85% in vivo in humans (68). In the posterior maxilla after 6 months of healing, the BIC values of dual acid-etched sites were statistically higher than in turned sites (~70%) (69). Different acid concentrations were evaluated by Cho et al. (70), reporting a removal torque for dual acid-etched implants statically higher compared to the machined surface. The removal torque of 2mm diameters triple-etched micro-implants has been investigated by Pontes et al. (71), who reported an increase of the strength resistance >6Ncm after 8 weeks of healing. In a sheep study, Jinno et al. (72) reported that the dual-acid etch technique produces similar BIC findings to dual etching-sandblasting surfaces. Some authors associated the main findings for bone response to the dental implant macro-geometry (72-74). Halldin et al. reported that nano- and microtopography indicted by dual etching can potentiate the initial biomechanical behaviour, while for a more extended osseointegration period, the surface interlocking capacity seems more effective (75). On the contrary, several studies reported that the roughness scale seems to be effective for new bone formation (76, 77).

A similar outcome was reported by Yoo et al. that highlighted higher BICs and removal torque resistance of dual-acid etched implants compared to grit blasted/acid etch with low bone remodelling rates (78). Also, others obtained similar results (79).

Sandblasted and acid-etched surfaces

The combination of sandblasting and acid-etching technique has been suggested to produce uniform scattered gaps and hole distribution and slightly less rough than the plasma-sprayed surface, which is characterised by profoundly irregular micro-texture and less favourable substrate for cell proliferation (80). The histological studies have been summarised in Tables V and VI. Higher torque removal values of sandblasted/acid-etch surfaces have been reported (+75%-125%) compared to acid-etched implants (81). Abrahamsson et al. (82) reported that the BIC values in dogs were significantly higher in sandblasted/acid-etched implants compared to machined surfaces. Similar results were observed in the comparative evaluation of sandblasted/acid-etched compared in plasma-sprayed implants(83). Sandblasted and acid-

Table III. *Comparative studies which used acid etched and plasma-sprayed implants.*

Author	Surface treatment	Results	Findings	Experimental design
Klokkevold et al. (1997)[6]	**(1) Acid-etched** (HCl / H_2SO_4) **(2) Turned**	**Removal torque** (1) 20.50 Ncm (2) 4.95 Ncm	The resistance to torque removal was 4 times greater for acid etched implants in comparison to the turned surfaces.	Implants were inserted in the femur of rabbits. Healing period: 2 months
Cho et al. (2003)[70]	**(1) Acid-etched** (HF and HCl / H_2SO_4) **(2) Turned**	**Removal torque** (1) 34.7 Ncm* (2) 15.2 Ncm	Dual acid etched implants required a higher removal torque average force than the turned surface implants.	Implants were inserted in the tibia of rabbits. Healing period: 12 weeks
Weng et al. 2003[67]	**(1) Acid-etched** (Osseotite®) **(2) Turned** **(ICE®)**	**BIC values** (1) 62.5 % (2) 39.5 %	BIC values were significantly higher in dual acid-etched sites in comparison to turned sites.	Implants were inserted in areas with poor bone quality in the mandible of dogs. Healing period: 4 months
Klokkevold et al. (2001)[79]	**(1) Acid-etched** (HCl / H_2SO_4) **(2) Plasma-spray** **(3) Turned**	**Removal torque** (1) 27.40 Ncm (2) 59.23 Ncm (3) 6.73 Ncm	Statistically significant differences were observed between acid-etched and turned implants, and between plasma-sprayed and turned implants. However, differences between acid etched and plasma-sprayed were not statistically different.	Implants were inserted in the femur of rabbits. Healing period: 3 months**
Pontes et al (2015) [71]	**(1) Triple Acid-etched**	**Removal torque** (1) 3.3 ± 1.7 Ncm (2) 2.2 ± 1.3 Ncm (3) 6.7 ± 1.4 Ncm	The triple acid etching can create a promising and efficient surface for the process of osseointegration.	Healing period: 8 weeks Implants were inserted in rats.
Rezende de Jesus et al. (2017) [73]	**(1) Acid-etched** **(2) Sandblasted and Acid-etched**	**BIC values** 2 weeks (1) 19.57±13.57% (2) 20.33±7.99% 4 weeks (1) 40.25 ± 9.45% (2) 42.80± 4.48%	Bone-to-implant contact and BD increased with time in both surface treatments implants	Implants were inserted in dogs Healing period: 2 and 4 weeks.
Carr et al. (2000)[53]	**(1) Plasma-spray** **(2) Turned**	**BIC values** (1) 55.9 % (2) 56.2 %	No significant differences could be observed between groups concerning the BIC percentage.	Implants were inserted in the mandible of baboons. No prosthetic rehabilitation was performed. Healing period: 6 months.

etched surfaces reported increased osteoconductive cell proliferation characteristics compared to plasma-spray implants (80, 84, 85). The histological findings of sandblasted/acid-etched reported after six months of healing in humans a mean BIC of 76.6 % (86). After 40 months, a 75.4 % BIC mean was observed on retrieved human implants (87).

Some studies reported sufficient bone volume and density that sandblasted/acid-etched surfaces can present a success rate of 99 % after two years (88). The combination of acid-etching and ZrO2 particles sandblasting produces an increased bone deposition compared to plasma-sprayed and machined implants (54). Several authors reported that the depth and distribution of irregularities, the cavity morphology, and contaminating elements derived from the treatment procedures

Table IV. *Histologic studies in which acid etched implants were retrieved from humans.*

Author	***Surface treatment***	***Results***	***Findings***	***Experimental design***
Testori et al. (2001)[68]	**Acid etched** (Osseotite®)	**BIC values** ranging from 78% to 85%	Implants were successfully used in immediately loaded protocol.	Histologic analysis of two retrieved immediately loaded implants. Healing period: 4 months.
Degidi et al. (2003)[66]	**Acid etched** (HCl and H_2SO_4)	**Mean BIC value** 61.3%	No gaps or fibrous tissues were observed at the interface.	Histologic analysis of two retrieved implants. No prosthetic rehabilitation was performed. Healing period: 6 months.
Trisi et al. (2002)[69]	**(1) Acid etched** (Osseotite®) **(2) Turned**	**BIC values** (1) 72.35 % (2) 35.32 %	BIC values in dual acid-etched sites were statistically higher than in turned sites.	Histologic analysis of implants inserted in the posterior maxilla of 11 patients. Healing period: 6 months.

play an important role in cell behaviour (89). In different animal study models, the sandblasted and acid-etched surfaces seem to produce in animals very similar BICs (~60%) compared to RBM, acid treatments and micro-arc procedures with no significant differences (90-96). At the same time, Marinho et al. reported a significantly higher new bone contact compared to the comparison of machined implant surfaces (97). Similar results were obtained by Buser et al. (98).

Nodized surfaces and micro-arc treatment

The oxidation technique has been proposed to modify the oxide layer properties and the surface biocompatibility (99), avoiding the deposit of grit particles (100). The anodised surfaces are obtained by a voltage application on the titanium surface in an electrolyte bath. The treated surface appeared with micro-pores of variable diameters without cytotoxicity (101). The removal torque of different thicknesses of anodised surfaces was investigated, which was significantly higher than that of smooth surfaces (99).

In the rabbit model, anodised, anodised and hydrothermally treated, and machined implants were investigated, reporting BIC values ranging between 40% and 50% and removal torque differences between the study groups (102). Authors reported that differentiation and calcification occurred on rough and smooth surfaces, indicating that the porous microstructure could enhance cell proliferation (43). In literature, it was demonstrated that the voltage for the anodising technique could produce a sensible influence on osseointegration properties, while the optimal value seems to be at ~550 V (103). In this way, the micro-roughness generated by anodic oxidation seems to significantly ameliorate BICs compared to sandblasted surfaces (104, 105) and machined implants (106). Moreover, using a super-hydrophilic surface of anodic oxidation implants has been proposed to potentiate this histological finding (107), while using biologically-derived triterpenoids adjuvant coating seems to produce no significant effect on this parameter 108).

In addition, the electrochemical anion sulphuric acid and phosphoric acid incorporation significantly affect BICs with an increase of ~200% histological bone contact (109). The micro-arc surface oxidation treatment has been proposed to improve the titanium dental implant. The biocompatibility of micro-arc oxidation has been tested by several authors, producing an acceleration and enhancement of the fixture's osseointegration (90, 110–113). Dundar et al. (90) reported similar BIC means (~60%) comparing different surfaces RBM, SLA, micro-arc, and sandblasted-micro-arc treatment with no significant difference.

Hydroxyapatite-coated surfaces and ceramic-coating implants

Hydroxyapatite implants have been studied to improve bone-implant fixation due to an increased osteoblast activity to this contact and adhesion, proliferation, and differentiation (114). Histological findings of hydroxyapatite implant

Table V. *Comparative studies that used sandblasted and acid-etched implants.*

Author	*Surface treatment*	*Results*	*Findings*	*Experimental design*
Abrahamsson et al. (2004)[82]	**(1) Sand-blasted and acid-etched** **(2) Turned**	-	BIC values (data not shown) were significantly greater in sandblasted and acid-etched sites than in turned surfaces	Implants were inserted in the mandible of dogs. No prosthetic rehabilitation was performed. Healing period: 1, 2, 4, 6, 8 and 12 weeks.
Marinho et al. (2003)[97]	**(1) Sand-blasted and acid-etched** **(2) Turned**	-	The SLA surfaces revealed a higher bone response vs. machined surfaces.	Implants were inserted in rats. Healing period: 5, 15, 30, and 60 days
Coelho et al (2011) [57]	**(1) alumina-blasting** **(2) biologic blasting** **(3) plasma** **(4) microblasted RBM** **(5) Sand-blasted and acid-etched (AB/AE)**	**BIC values** (1) 40.13± 2.54% (2) 37.23 ± 2.14% (3) 38.56 ± 2.49 % (4) 39.65± 2.27% (5) 38.72± 1.44%	No significant differences of BIC were detected at 4 weeks. An higher reoval torque was detected for RBM implants.	Implants were inserted in dogs. Healing period: 4, weeks.
Cochran et al. (1998)[83]	**(1) Sand-blasted and acid-etched** (250-500μm corundum particles, and etched with HCl / H_2SO_4) **(2) Plasma-sprayed**	**BIC values** (1) 71.68 % (2) 58.88 %	The sandblasted and acid etched implants had a significantly greater BIC percentage than did the plasma-sprayed. However, no qualitative differences in bone tissue were observed between groups.	Implants were inserted in the mandible of dogs. Loading period: 12 months Healing period: 15 months
Buser et al. (1999)[98]	**(1) Sandblasted and acid-etched** (0.25–0.50 μm particles, etched with HCl / H_2SO_4) **(2) Plasma-sprayed** **(3) Turned**	**Removal torque** (1) 1.43 Ncm (2) 1.54 Ncm (3) 0.26 Ncm	Statistically significant differences were observed between sandblasted and acid-etched and turned implants, and between plasma-sprayed and turned implants. However, differences between sandblasted and acid etched and plasma-sprayed were not statistically different.	Implants were inserted in the maxilla of miniature pigs. No prosthetic rehabilitation was performed. Healing period: 12 weeks*

**Data from the 1st and 2nd healing periods were not included in this table.*

Table VI. *Histologic studies in which sandblasted and acid-etched implants were retrieved from humans.*

Author	**Surface treatment**	**Results**	**Findings**	**Experimental design**
Hayakawa et al. (2002)[86]	**Sandblasted and acid-etched** (Straumann®)	**BIC value** 76.6 %	Bone surrounding the implant was uniformly and maturely structured.	Histologic analysis of one retrieved implant that was inserted in the palatal bone of the maxilla of a patient as anchorage for orthodontic treatment. Healing period: 6 months
Sakakura et al. (2005)[87]	**Sandblasted and acid-etched**	**BIC value** 75.4 %	The surrounding bone healed in a well-organized pattern and could not be differentiated from the original alveolus.	Histologic analysis of one retrieved implant of a patient. Loading period: 40 months

indicated a BIC range between 87.5%-97.4% (115). This coating technique reported high survival rates at medium- and long-term follow-ups (2, 116, 117). After 12 years of loading, the survival rate of hydroxyapatite implants was 93.2%, statistically increasing compared to titanium implants (2). After 10 years of loading, the hydroxyapatite implants reported a BIC range between 70.74%-86.23% (118).

Piattelli et al. (119) reported a localised chronic suppurative bone infection associated with peri-implantitis in a hydroxyapatite-coated implant, where the coating appeared detached from the titanium surface. Different methods can be used for hydroxyapatite coating, such as coating/sintering, electrophoretic deposition, immersion coating, hot isostatic pressing, solution deposition, sputter coating, and thermal spraying techniques (120). Hydroxyapatite plasma-spraying was indicated to combine the hydroxyapatite characteristics and the bone-implant mechanical interlock associated with the plasma-spraying procedure. Higher BIC values were reported for hydroxyapatite implants than titanium plasma-spray implants and machined fixtures (121). The Resorbable Blast Material (122) also known as the technique of ion-beam-assisted deposition (IBAD) (123, 124) has been proposed to improve the coating quality properties.

In vivo, the BIC values were significantly higher in IBAD surfaces compared to blasted and machined implants. The authors suggested that the advantages of the HA-coated implants in the early healing period could be apparent, while the separation or fracture of the coating layer could be prevented. However, the resorption needs to be further investigated123. Svanborg et al. (125) investigated different hydroxyapatite (HA) nanocoating thicknesses on titanium grade Ti-6A1-4V implants of 15 mm in length and 3.85 mm in diameter in rabbits.

The single layer-HA coating reported a mean Sa 0.91 (0.20) μmm while the double layer-HA coating showed a mean Sa 0.77 (0.19) μmm125. After 9 weeks of healing, the single layer-HA coating reported higher values of removal torque ($p<0.05$) and at 2 weeks reported an increase of almost 5% of new bone formation compared with the control and the double layer-HA coating. After 9 weeks, the BIC for both groups was similar (~60%) (125). The advantage of ceramic-coating implants has been described due to the high osteoconductivity of the surfaces, while these techniques can produce a surface biofunctionalisation that can increase the implant osseointegration (126-167).

The surface functionalisation seems to maintain the implant roughness, while Jimbo et al. reported no significant differences between the smooth bioceramic surface and the rough bioceramic coated implants (142). In addition, other studies investigated different ceramic coatings such as calcium carbonate, ceramic brushite, glass fibres, phosphate-containing polymers, magnesium-containing polymers, and calcium-phosphate (126-167). Granato et al. investigated the coating thickness and demonstrated that the optimal Ca- and P-derived bioceramic coating layer ranged between 300-500

Table VII. *Comparative studies which used anodized implants.*

Author	Surface treatment	Results	Findings	Experimental design
Sul et al. (2002)[99]	**(1) Anodized** (oxide thickness approximately 200, 600, 800 or 1000 nm) **(2) Turned** (oxide thickness: 17.4 nm)	**Removal torque** (1) Ranging from 0.113 to 0.129 Nm (2) 0.075 Nm	The preliminary results of this study suggest that the oxide thickness influence the bone tissue formation.	Implants were inserted in the tibia of rabbits. Healing period: 6 weeks
Son et al. (2003)*[102].	**(1) Anodized** **(2) Turned**	**Removal torque** (1) 51.35 Ncm (2) 35.28 Ncm	Difference between groups was not statistically significant concerning removal torque and BIC values (data not shown).	Implants were inserted in the tibia of rabbits. Healing period: 12 weeks
Ivanoff et al (2003)[113]	**(1) Anodized** **(2) Turned**	**BIC values** (1) 34 % (2) 13 %	BIC values were statistically higher in oxidized than in turned sites.	Histologic analysis of implants inserted in the ridge of 20 patients. Mean healing period: 6.6 months

** Data from the 1st healing period, and an experimental group were not included in this table.*

nm (150). Moreover, the fluorapatite and heated-hydroxyapatite coatings present a decreased respiration rate compared to hydroxyapatite implant surfaces (167).

Thermal oxidation and heat surface treatment

The investigation of innovative procedures able to contrast surface wearing and successful bioactivity and osseointegration represents the current breakthrough in implantology. Thermal oxidation aims to create a highly crystalline oxide coating able to potentiate the interaction between the titanium surface and the host surrounding bone (168, 169). A 700°C exposure for 1 hour by a controlled furnace of Ti6Al4V alloy can induce the formation of a rutile oxide layer that could improve the osteoblast attachment on the implant surface in vitro (170). In addition, the heat treatment at 800°C in the air for 1 minute also seems to increase the BICs in vivo of acid significantly etch Ti6Al4V implants (171). The Al obtained similar results (2) (3) abrasive particle blasting with thermochemical treatment in minipigs compared to SLA (shot blasting surface) (172).

Quameya et al. reported that adding a supplemental fluoridic acid etch to the thermally oxidised surface did not significantly affect osseointegration compared to standard SLA surface implant (173). The heat-derived oxide layer has been studied by Kim et al. (174), which compared different oxide layer thicknesses of 20nm to 80nm and the additional treatment of CaP coating. The same authors detected no significant differences in BICs and ISQ at 5 weeks on dogs (174).

Zirconia implants and acrylic materials

Zirconia (zirconium oxide, ZrO2) is a ceramic material purposed as dental implant material due to its biocompatibility, esthetic properties, and mechanical behaviour, which are better than alumina (60, 61, 175-188). Zirconia is reported to present a bone contact similar to titanium implants189,190. The interface is composed of a proteoglycan layer that is thicker than titanium (191, 192). Zirconia implants are biocompatible, bioinert, and radiopaque, with high corrosion and wearing resistance, flexion and fracture (193-197).

In rabbits, the BIC value of zirconia implants was 68.4% after 4 weeks with no foreign bone reaction and fibrous tissue infiltration at the level of the interfaces (198). Loaded zirconia implants were evaluated in monkeys, with BIC values ranging between 66%-81% (199). Zirconia implants submitted to Al2O3 sandblasting were compared to titanium (Al2O3 sandblasting followed by H2O2 and HF etching reporting BIC values of 67.4% for zirconia, and 72.9% for titanium surfaces with no statistically significant differences (190). Various types of zirconia implants have been investigated in the literature, while the most investigated are yttria-stabilised tetragonal zirconia polycrystalline (3Y-TZP) and ceria-stabilised zirconia-alumina nanocomposite (NanoZr) (176).

Mijhatovic et al. investigated three different roughnesses of zirconia implants compared to sandblasted large grit and acid-etched titanium implants, showing no significant differences in total BICs after 10 weeks on dogs. The hybrid hydrophilic titanium-zirconium alloy (TiZr1317) revealed a lower removal torque at 2 weeks compared to standard titanium implants, while no differences were detected at 4 and 12 weeks. At 4 weeks, hybrid hydrophilic titanium-zirconium alloy (TiZr1317) showed significantly higher BICs in the marrow area of 19.25% (179). Very few studies investigated in vivo the properties of plastic and acrylic resin implants (200). Okamatsu et al. (200) studied the hybrid titanium-plastic implants and evaluated a homogeneous 150- to 250-nm acrylic layer coating. The authors reported new bone formation in the test and control groups, with no direct bone contact with the plastic implant.

UV and biologically functionalised surfaces

In literature, photodynamically functionalised implant surfaces have been investigated (201-204). Mehl et al. (201) reported no significant differences between BICs and ISQ in a split-mouth study model using a high-energy UV-irradiation in epicrestally titanium implants. On the contrary, a significant increase in removal torque and BICs was reported by Shen et al. (203). The authors evaluated a different combination of SLA-surfaces treated by UV-bactericidal irradiation at 15-20W, 0.1mW/Cm2 and 0.2mW/Cm2 (203). The UV photo-functionalisation seems effective, especially in the early phases of osseointegration (202), with a significant increase in bone contact and dental implant stability. This treatment seems to take a significant advantage when combined with biologically functionalised treatment with fibronectin and osteopontin (204, 205) due to a significant increase in the hydrophilicity of the surface.

DISCUSSION

Several authors investigated the biological properties of dental implant surfaces under *in vitro* conditions. At the same time, this kind of research is consistent in investigating the specific cell response, the clinical relevance of these results is discussible, and the development of long-term clinical evaluations is fundamental. Different implant topographies seem to influence the outcome of dental implants, but the magnitude and clinical relevance of this influence are still being investigated.

On the other hand, many studies are being published to investigate the viability of modified surfaces. Regarding the titanium alloy, a study performed in rabbits reported that the removal torque was statistically different after 6 months and 12 months, where the cpTi implants were significantly more stable. The BIC means presented no significant differences between the materials (206). In another investigation, cpTi and Ti6Al4V dental implants were positioned in baboons, reporting that BIC means were significantly higher in cpTi and Ti6Al4V implants, but differences after six months were not significantly different (207).

Even if the use of the alloy represents a mechanical advance compared to cpTi, biomechanical tests revealed that cpTi presented an increased stability. Moreover, the titanium implants, after the air exposure, can form an oxide layer all over the surface of 2–5 nm thickness. The oxide layer (208, 209) plays a key role in corrosion resistance, biocompatibility and implant osseointegration (210-212). The layer is mainly formed by TiO2 (213), and the crystalline structure, the thickness and stability of this layer varies according to the surfaces of the implant (99, 214, 215).

Promising findings for dental implants concerning nitride titanium (TiN), nanostructured texture, laser-treated surfaces, and ceramic materials have been recently reported (188, 216). The nanostructured surfaces (1-100nm) could improve the early interface and bone-implant contact (217, 218). Authors reported that dogs presented a higher percentage of newly formed bone in contact with nanostructured implants than plasma-spray and machined implants (219, 220), and BIC values ranged between 55 and 96% in humans (221).

Nitride titanium (TiN) was proposed to produce a surface less susceptible to the ions release. For this purpose, the physical vapour deposition technique can produce a thin TiN layer (~1µ) for an osseointegration quality similar to standard titanium implants. This layer increases corrosion resistance, lower bacterial adhesion, and a golden aspect of the implant surface (222-227). The laser ablation is a reproducible procedure for a controlled, micron-sized surface with topographical features on the flanks of the threads. Lasered implants demonstrated significantly higher BIC and removal torque peaks than machined implants (228, 229). Calcium phosphate and ceramic coating are correlated to a high chemical bonding property, similar to hydroxyapatite (86). Biphasic calcium phosphate (162, 230, 231) or tricalcium phosphates have been investigated as implant coating (232, 233).

In conclusion, proper long-term studies have been published for TiO2 surfaces, but other surfaces are documented with a medium-term follow-up period (234). While clinicians should consider that several new treatment surfaces are constantly purposed and currently available in the market, long-term findings are necessary to comprehend their long-term biological response.

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