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REVIEW ARTICLE

EFFECT OF IMPLANT DESIGN AND SURFACE MODIFICATION ON OSSEOINTEGRATION

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ABSTRACT

Background: Since the introduction of dental implants, they have been accepted as a predictable and reliable modality for both partially and completely edentulous patients. Successful implant placement depends on the osseointegration of the implant into the host bone. Integration of the implant is greatly influenced by the properties of the implant surface and its design.
Objectives: The objective of this review is to determine the effect of implant design and surface modification on implant osseointegration.
Data Sources: A complete online search for articles was made using PubMed and Google Scholar.
Study eligibility criteria: All articles that were published in English or those having detailed summary in English were included. Only those articles that were published between 1st January 1994 and 31st March 2016 were considered. Randomized controlled trials and cohort studies with data on osseointegration of implants with different implant designs and surface modifications done on animals were considered. Articles having histomorphometric and histologic method of analysis with a study period of more than 6 weeks were selected.
Results: The review gives an insight of the various surface modifications and designs that can be successfully applied on dental implants so that a greater level of osseointegration can be achieved.
Limitations: Few articles do not clearly mention the results which makes the interpretation difficult.
Conclusions: Major advancements have been made in order to develop implants with innovative surface topography and design. These modifications have greatly influenced the rate and degree of osseointegration. Hence, such implants have set the stage for the future of successful implantology.

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INTRODUCTION

The dental implants have a very interesting and fascinating journey of transformation through time. They have been used by mankind in one form or another to replace missing teeth. The first known evidence of dental implants was around 600 AD where the Mayan population utilized pieces of shells as implants as a replacement for mandibular teeth. (Ring Malvin, 1985) In 1965, Dr. P. Branemark placed dental implants that were the first implants to be well maintained and well documented. (Abraham, 2014) With his implant, he also came up with the concept of "osseointegration". He defined it as "a direct structural and functional connection between ordered, living bone, and the surface of a load carrying implant". (Osteointegration: Associated Branemark Ossointegration Centers, 2010) Branemark used cylindrical implants but later on tapered implants were introduced and they began to be used. Dr. Schroder and Dr. Straumann of Switzerland are the other ground-breaking persons of modern implantology. They fabricated dental implants by using metals that were used in orthopedic surgery. (Leney, 1993) In the 1980's the endosseous root form implants were introduced. As time progressed various advancements were made in the design as well as surface texture of the implant. The main motive behind these modifications was to enhance osseointegration in a relatively short time. The only part of the dental implant that is in contact with the bio-environment is its surface. Its uniqueness initiates a response and ultimately affects the mechanical strength of the implant-tissue surface. The surface treatment layer that is coated on to the implant increases the functional surface area of the bone-implant interface so that stress can be effectively transferred and at the same time promotes bone apposition. (Eriksson *et al.*, 2001; Wen *et al.*, 1996; Albrektsson and Jacobsson, 1987; Schroeder *et al.*, 1981) The various treatments include mechanical (machining and grit blasting), chemical (acid etching), electrochemical (anodic oxidation), vacuum treatments, thermal treatments, and laser treatments. These surface treatments were found to influence the metabolic action and growth of cultured osteoblasts. Surface roughness has shown to influence cytokine and growth factor production by

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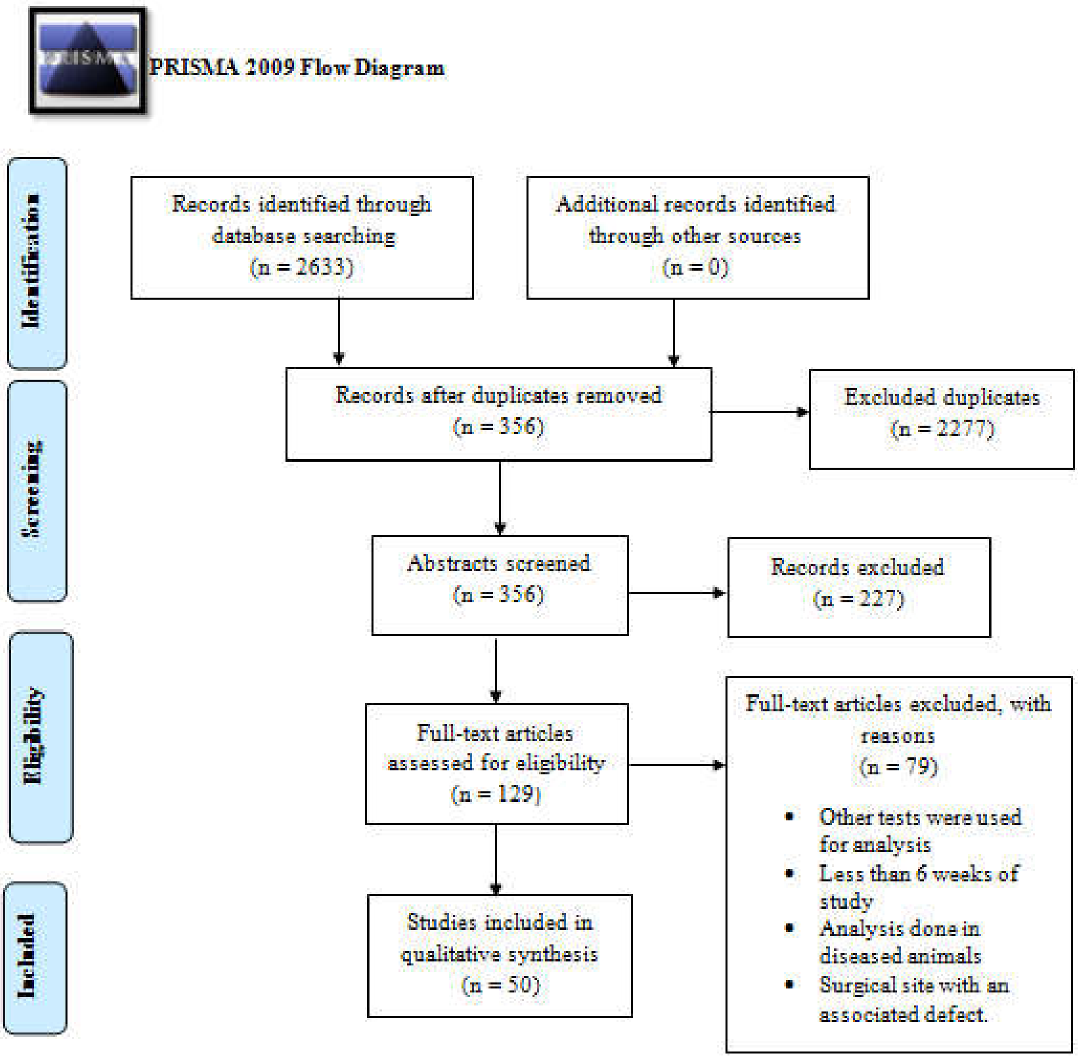
osteoblasts. Increased osteoblast cell propagation was observed due to the increase in surface roughness that resulted in production of transforming growth factor-beta (TGF-β). (Boyan *et al*., 2003) It has been proved that the structure of the implant affects the interaction between that implant metal and bio-environment. The surface roughness of an implant impacts cell movement as well as cell growth. (Boyan *et al*., 2003) This systematic review focuses on the question that in context with dental implant which implant design and surface modification will help achieve a successful osseointegration?

MATERIALS AND METHODS

Component	Description
Participants	Animals
Intervention	Modification of the basic design and surface texture of implant
Comparison	with the conventional implant design with no surface modification
Outcome	Osseointegration
Study Design	Randomized Control Trials and Cohort Studies

RESULTS



Eligibility criteria

Inclusion Criteria

1. Articles in English or those having detailed summary in English
2. Articles published between 1st January 1994 and 31st March 2016
3. Randomized controlled trials and Cohort studies with data on osseointegration of implants with different implant designs and surface modifications done on animals.
4. Animal studies.
5. Articles having histomorphometric and histologic method of analysis with a study period of 6 weeks or more than 6 weeks.

Exclusion Criteria

1. Review, abstracts, letters to editors and editorials.
2. Studies published in languages other than English.
3. Studies done on diseased animals.
4. Studies done for a period less than 6 weeks.

Information sources

Internet sources of evidence were used in the search of appropriate papers satisfying the study purpose: the National Library of Medicine (MEDLINE PubMed), Google Scholar, Google, and manual search using DPU college library resources. All cross reference lists of the selected studies were screened for additional papers that could meet the eligibility criteria of the study. The databases were searched up to and including 31st March 2016 using the search strategy.

Study selection

Preliminary screening consisted total of 2633 articles out of which 356 articles were selected. The duplicates were thereafter removed and finally 129 articles were remaining. At first the papers were screened by title and abstract. As a second step, full text papers were obtained when they fulfilled the criteria of the study aim. For full-text screening, the following criteria were taken into consideration: randomized controlled trials and cohort studies; studies done for a period of 6 weeks or more; studies done on healthy animals; Histomorphometric analysis used as the test to calculate bone-implant osseointegration. Finally a total of 50 articles were included.

Data collection process

A standard pilot form in excel sheet was initially used and then all those headings not applicable for review were removed. Data extraction was done for few articles and this form was reviewed by an expert and finalized. This was followed by data extraction for all the articles. All the articles selected primarily were read thoroughly and the data was analyzed. The data obtained was then segregated and an excel sheet was prepared.

Summary of evidence

Researchers and scientists have been really working very hard to modify the most biocompatible and clinically proven commercially pure titanium surface to accelerate the process of osseointegration so that the patients regain their esthetics and function as early as possible. Some studies have shown significant increase in the osseointegration potential after surface modification while a few studies have shown a positive response only in the initial stages. However, many studies have shown insignificant increase in osseointegration. The following are the in vivo studies done on various animals in search of a better future for implantology.

Implant Surface Modifications

1.Modified Sand blasted/Acid- etched Surface (SLA)

Abdel-Haq *et al.* (2011) conducted a study in Istanbul where 30 implants were placed in 3 female sheeps. The implant surface was prepared by acid etching after large-grit blasting the implant surface. The modSLA implants were additionally rinsed under nitrogen protection and stored in an isotonic NaCl solution. There was no statistically significant difference between modSLA and SLA implants after 6 weeks of healing. It was concluded that higher bone contact and stability was achieved only at earlier time points with modSLA implants.

2.Selective Infiltration Etched Zirconia Implant

Aboushelib *et al.* (2011) compared the osseointegration achieved with selective infiltration etched (SIE) zirconia, as sintered zirconia and titanium implants. Sixty implants were placed in 40 white rabbits. The SIE implants were prepared by coating them with infiltration glass, thermal heating and washing off glass residues. After 4 and 6 weeks BIC for SIE zirconia implant surface remained statistically higher ($P<.05$) than that of as-sintered zirconia and titanium implants. Hence, selective infiltration-etched surface treatment enhanced osseointegration.

3.Plasma Rich in Growth Factors (PRGF)

Anitua (2006) conducted a randomized control trial where non coated titanium implants were compared with implants coated with plasma rich in growth factors (PRGF). A total of 23 implants were placed in the tibiae and radii of goats, 13 implants were coated while 10 were placed uncoated (controls). The protein-rich material was adsorbed by the implant surface. After 8 weeks histomorphometry revealed that the surface coated with PRGF enhanced osseointegration (bone-implant contact: 51.28% +/- 4.7% vs 21.89% +/- 7.36%; $P < .01$).

4.Gold alloy implant

Abrahamson and Cardaropoli (2007) compared implants with the same shape and surface roughness for peri-implant hard and soft tissue integration. The implants were made of commercially pure titanium and gold alloy. 32 implants were placed in four beagle dogs, histomorphometric analysis done after 6 months shows that the titanium implant surface had higher BIC% than gold surfaces. Moreover, the metal did not influence the peri-implant soft tissue dimensions in the 'marginal' zone of the implant.

5.Resorbable Blast Media (RBM) Surface Treatment

Ahn *et al.* (2010) placed 120 implants in the rabbit tibiae (medial side) to compare machined implants; RBM-treated implants; machined implants with a long vertical groove; RBM-treated implants with a vertical groove; RBM-treated implants with a vertical groove on the upper thread; and RBM treated implants with a vertical groove on the lower trunk. The animals were sacrificed at 2, 4 and 8 weeks post implant insertion. Histomorphometric studies revealed that the BIC% and bone area were greater in the RBM group than in the machined group. Hence RBM treatment of small diameter implants enhances osseointegration.

6.Nano-Meter-Scale Hydroxyapatite Surface-Modified Implants

Al-Hamdan *et al.* (2011) compared grit-blasted acid etched implants (SLActive®) with nano-meter-scale hydroxyapatite surface modified implants (NanoTite®). 22 implants of each group were placed in 11 Beagle dogs. Histomorphometric analysis done after 2, 4 and 8 weeks revealed that both the implants induced a similar bone response. The difference observed was not statistically significant.

7.Glass Fiber-Reinforced Composite Implants

Ballo *et al.* (2009) evaluated bioactive fiber-reinforced composite implant (FRC) in vivo for bone implant contact. Threaded sand-blasted FRC implants; threaded FRC implants with bioactive glass (BAG) and normal titanium implants were compared. 18 implants were placed in the tibia of six pigs. After 12 weeks, FRC-BAG implants showed better osseointegration as compared to other implants.

8.Dendrimers of phosphoserine and polylysine

Bengazi *et al.* (2014) compared the osseointegration of ZirTi surface (zirconia sand blasted, acid etched) and ZirTi-modified surface with dendrimers of phosphoserine and polylysine. Thirty implants were placed in 6 beagle dogs. After 3 months histomorphometric analysis showed that the BIC%

for ZirTi® implants was 74% as compared to the dendrimers-coated implants which was 65%. This difference was statistically significant.

9.Chemically Modified SLA Titanium Surface

Buser *et al.* (2004) evaluated and compared bone apposition to a modified sandblasted/acid-etched (modSLA) titanium surface with a standard SLA surface for 2,4 and 8 weeks. 46 implants were placed in 6 adult miniature pigs. The test surface was prepared by submerging the implant in an isotonic NaCl solution after acid etching so that there is no contamination with molecules from the atmosphere. Significantly greater mean percentage of bone implant contact was seen with Test implants as compared with controls at 2 (49.30 *vs.* 29.42%; $p = 0.017$) and 4 weeks (81.91*vs.* 66.57%; $p = 0.011$) of healing. Similar results were observed at 8 weeks. Hence, the modSLA surface promoted bone apposition during early stages of bone regeneration.

10.Hydride Ion Surface Coating on Titanium Implants

Cheng *et al.* (2010) investigated the effect of hydride ion on bone formation and bone bonding strength at the early stage of implantation. The test implants had a coating of hydride ion they were compared with control implants which did not have any surface coating. Sixty implants were placed in 10 rabbit tibias. After 2 and 8 weeks the tibias were subjected to histomorphometric analysis. Results show that the presence of hydride ion in the implant surface may improve bone integration with implant surfaces at the early stage of implantation.

11.Atmospheric Pressure Plasma (APP) Treatment

Danna *et al.* (2015) assessed osseointegrative effects of atmospheric pressure plasma (APP) surface treatment for implants. The control surface were untreated textured titanium (Ti) and calciumphosphate (CaP). Experimental surfaces were their 80- second air-based APP-treated counterparts. 44 implants were placed in 11 beagle dogs. Histomorphometric analysis done at an interval of three and six weeks showed that there was a significant ($P < 0.001$) increase in BIC for APP-treated textured titanium surfaces. It was finally concluded that air-based APP surface treatment may improve osseointegration of textured Ti surfaces but not CaP surfaces.

12.Hydroxyapatite Coating on Implants

Eom *et al.* (2012) evaluated the osseointegration of Hydroxyapatite (HA) coated implant. 72 implants were placed in 12 miniature pigs. They compared the implants by dividing them into the following groups Group A: implants with RBM surface, roughened by blasting hydroxyapatite powder with high biocompatibility on the prepared titanium surface. Group B: Craters formed on implants by alumina blasting and subsequently forming micropits by dual acid etching methods. Group C: implants treated by the hybrid-type coating with HA and RBM, and the HA crystallinity (98%). Two mm of the upper fixture was RBM surface, and the rest was HA surface. After 4, 8 and 12 weeks histomorphometric analysis showed that the BIC ratio of HA was significantly higher than that of resorbable blast medium (RBM) or sand blasted with alumina and acid etched ($P < .05$).

13.Nd:YAG Laser ablation and hydroxyapatite coating

Faeda *et al.* (2012) studied the effects of titanium surface modification by Nd:YAG laser-ablation followed by thin chemical deposition of hydroxyapatite. A total of 72 implants were placed in 48 rabbit tibiae. The implants were divided into 3 groups Group MS: implants as manufactured (pure titanium implants), Group LMS: implants Nd:YAG laser ablated, Group HA: Implants laser ablated and HA coated. The implants were evaluated after 4, 8 and 12 weeks. Results showed that the average BIC in the cortical region was higher ($P < 0.001$) on the laser ablated implants and hydroxyapatite implants for all periods. For the cancellous area, in the initial period the LMS and HA implants showed higher ($P < 0.01$) BIC than the manufactured implants. The LMS and HA showed similar values in the cortical region, but a tendency of higher values for HA in the cancellous region was observed in all periods. Hence, laser treatment followed by hydroxyapatite biomimetic coating induced the contact osteogenesis. It also allowed the formation of a more stable bone–implant interface (even in earlier periods).

14.Calcium Phosphate Coating

Fontana, Rocchietta *et al.* (2011) evaluated the efficacy of calcium phosphate coating in promoting osseointegration. They compared Calcium phosphate surface with titanium porous oxide surface in terms of bone-implant contact. 216 implants were placed in tibiae of 36 rabbits. Histomorphometric analysis at the end of 2,4 and 9 weeks revealed that the oxidized surface inserted in the rabbit tibia revealed higher BIC values than the Ca–P surface but was statistically insignificant. It was concluded that the Calcium phosphate coating had no beneficial effect in improving the bonding strength at the bone–implant interface.

15.Oxidized surface of Titanium implants

Gottlow *et al.* (2012) compared 90 implants with an oxidized surface (OX) and 90 implants with a hydrophilic sand-blasted and acid etched (HSBA) surface. These implants were placed in the distal femur ($n = 1$) and tibia ($n = 2$) of 30 rabbits. Histomorphometry was carried out at 10 days, 3 weeks and 6 weeks. Histomorphometric analysis revealed that the BIC was significantly higher for HSBA implants after 10 days ($p < .01$), similar values were observed after 3 weeks but after 6 weeks significantly higher BIC was seen in OX implants ($p < .001$).

16.Anodized Implants coated with Escherichia coli-derived rhBMP-2 coating

Huh, Kim *et al.* (2012) in a split mouth design, randomly compared eighteen anodized implants coated with ErhBMP-2 (BMP group) and eighteen uncoated implants (control group) in dogs. Histomorphometric analysis at the end of 8 weeks showed that the implants in the BMP group can stimulate bone formation and also significantly increase implant stability on completely healed alveolar ridges. Histological observations revealed that the changes in bucco-lingual alveolar bone levels were higher for the coated implants ($p < 0.05$).

17.Anodized porous titanium implants modified with 0.175 wt% ammonium hydrogen fluoride solution followed by Ultraviolet irradiation

Jimbo *et al.* (2011) conducted a study where they compared anodized porous titanium implants (TiU) and TiU implants modified with 0.175 wt% ammonium hydrogen fluoride solution followed by ultraviolet irradiation done 24 hours before insertion. 30 implants were placed in the rabbit tibial metaphyses and these were analyzed at 2 and 6 weeks post insertion. Histomorphometric analysis showed that during the early stages of osseointegration, the enhanced photo-induced hydrophilicity of the NH_4F-HF_2-modified anodized implants significantly promoted bone apposition.

18.Microplasma Sprayed Calcium phosphate coated Titanium Implants

Junker *et al.* (Junker *et al*., 2010) compared non-coated, acid-etched standard titanium implants with an average roughness of 0.29 mm; conventionally plasma spray-coated implants [HACAM: crystallinity 65%, average roughness; two experimental MPS-coated implants [MPS A: crystallinity 67%, average roughness (Ra) 4.78 mm (SD: 0.24 mm); MPS B: crystallinity 80%, average roughness (Ra) of 4.23 mm (SD: 0.37 mm)]. Histomorphometric analysis done after 6 and 12 weeks showed that conventionally plasma spray coated implants showed significantly higher osseointegration than other implants. The difference between the two experimental implants was not statistically significant. The study revealed that the intervention did not significantly affect the adjacent bone positively.

19.Modified Anodized Titanium Implants

Kim *et al.* (2015) compared 4 types of implants: machined titanium, sand blasted and acid etched implants, anodized implants and modified anodized implants (sand blasted and acid etched implants followed by anodization). 32 implants were placed in beagle dogs and they were subjected to histomorphometric analysis after 8 weeks. Tests revealed that the bone-to-implant contact (BIC) of modified anodized implants (74.20% ± 10.89%) was higher than the machined (33.58% ± 8.63%), SLA (58.47% ± 12.89), or simply anodized implant (59.62% ± 18.30%). The modified anodized implants improve cell adhesion and bone ongrowth as compared with the other category implants. Thus the application of modified anodized surface treatment could improve the osseointegration of dental implant.

20.Calcium Liberating Titanium Oxide Coating over Zirconia Implants

Koch *et al.* (2010) in their study compared an uncoated zirconia implant, a calcium-liberating titanium oxide coating zirconia implant, a titanium implant and an experimental implant made of polyetheretherketone. 48 implants were placed in Mongrel dogs. After 4 months of implantation histomorphometric analysis showed that zirconia implants and titanium implants show similar rates of bone-implant contact with the same surface modification and roughness.

21.Chemically and pharmaceutically modified titanium and zirconia implants

Langhoff *et al.* (2008) tested 6 types of implants for osseointegration, Sand blasted and acid etched implant, calcium phosphate coated implant, Plasma anodized implant, Collagen I plus chondroitan sulphate treated implant, Bisphosphonate treated implant and Zirconia implant. Histomorphometric analysis at the end of 2, 4 and 8 weeks showed that the BIC of zirconia implant (77%) was slightly better as compared to all titanium implants at 2 weeks (57–61%). After 8 weeks, the pharmacologically coated implants (78–79%) and the calcium phosphate coated implants (83%) showed similar results compared with the sand blasted and acid etched implant (80%). Hence, no significant differences were observed.

22.Alumina, BCP and OCP Modified Dental Implants

Le Guehennec *et al.* (2008) studied the osseointegration of 4 types of implants namely alumina-Ti, BCP-Ti, OCP-Ti and SLA implants. The alumina-Ti implants were obtained by blasting titanium implants with alumina powder of 110 mm diameter (Al_2O_3 particles) and then etched with nitric acid at 5%.For the BCP-Ti implants the BCP powder consisted of a mixture of HA and tricalcium phosphate (b-TCP) in an HA/TCP ratio of 60/40 sintered at 1250°C, ground and sieved. The OCP-Ti implants were grit blasted using BCP powder of 200–400 mm diameter, washed in deionized water, heated at 60°C for 24 h in NaOH solution at 5M and rinsed in deionized water. Histomorphometric analysis done at 2 and 8 weeks revealed that there was significantly greater bone-to-implant contact for both the SLA and OCP-Ti surfaces as compared with the grit-blasted surfaces, alumina- and BCP-Ti. Hence, the biomimetic coating on the titanium implants may enhance bone apposition.

23.Nano-Technology Modified, Micro-Structured Zirconia Implant Surfaces

Lee *et al.* (2008) conducted a randomized control trial where they compared test zirconia ceramic implants exhibiting a proprietary porous surface modification in the micrometre scale modified by means of two different nano-technologies, each applying the implants with a CaP nano-layer (test group) and ZiUnite™ implants without the CaP nano-layer and standard micro-structured titanium porous oxide implants (control group). 80 implants were placed in 40 adult white rabbits. Histomorphometric analysis done after 6 weeks shows that the control group implant surfaces have osteoconductive properties. The addition of CaP nano-technology to the ZiUnite™ surface does not further improve the osteoconductivity.

24.Carbon-oxygen (CO) ion modified Titanium Implants

Maeztu *et al.* (2008) compared machine-turned implants subjected to CO ion implantation surface treatment, Machine-turned implants subjected to diamond-like carbon coating; Acid-etched (sulfuric acid–hydrochloric acid) implants, Sandblasted and acid etched (sulfuric acid–hydrochloric acid) implants, TiUnite® Oxidized implants and Machine-turned titanium implants (control implants). Histomorphometric analysis done at 3 and 6 months respectively revealed that the percentage of BIC were significantly higher in implants treated with CO ion implantation compared to the commercially treated implant group ($p = 0.002$ and $p = 0.025$) and the control implants ($p = 0.001$ and $p = 0.032$). The three groups of commercially treated implants did not show significant differences. The larger percentage of BIC of the ion implanted group was observable at an early stage.

25.Acid Etched Titanium Implant Surfaces with Different Biomolecular Coatings

Mueller *et al.* (2011) compared 10 types of acid etched implants coated with collagen I and varying amounts of bone morphogenic protein 2, vascular endothelial growth factor 165, basic fibroblast growth factor 2 or a combination all 3 factors by using the biodot method. Histomorphometry was carried out after 2, 4 and 8 weeks. It showed that there was an increase in the level of collagen I (P = .028) and osteocalcin (P = .037) expression after 2 weeks in the implants coated with collagen I. The levels of osteocalcin (P = .042) and the bone implant contact (P = .049) was increased after 4-weeks compared with pure titanium. The additional cytokine coating had no significant effect as compared with to the collagen I coating. Thus, osseointegration is enhanced by collagen I coating and no further beneficial effects occur with additional growth factor application.

26.Biomedical Ti–Mo Alloys with Surface Machined and Modified by Laser Beam

Oliveira *et al.* (2013) compared machined surface (control) and laser beam irradiated (test implant) Ti-15Mo dental implants. A total of 32 wide cylindrical implants were used. Histomorphometric analysis after 8 weeks showed that the LS implants showed higher Bone-to-implant-contact percentage both in the cortical and marrow regions.

27.Anodized Titanium Implants under Different Current Voltages

Park *et al.* (2007) compared anodized implant surface in potentiostatic mode with a pulse power (660 Hz, 10% duty). The implants were anodized under different voltages of 190, 230 and 270 volts. Histomorphometric analysis after 6 weeks proved that the anodized titanium implants showed more intimate and stronger connections with peri-implant bone during early osseointegration than the turned control titanium implants. The anodized implant exposed to 270 volts showed the maximum bone implant contact at the end of the study.

28.Fusion Sputtered Zirconia Implant

Salem *et al.* (2013) compared the test implant which was prepared by fusion sputtering surface treatment through spraying a suspension of zirconia mixture composed of 5 g ultrafine zirconia powder (1– 5 μm) and 10 ml ethyl alcohol (70%) with control implants which were standard titanium implants. Histomorphometric analysis after 4 and 8 weeks showed that the BIC was significantly for fusion-sputtered zirconia implants compared to the control However, statistically significant difference could not be achieved by 12 weeks.

29.Titanium-Zirconia Alloy Implant

Saulacic *et al.* (2012) compared TiZr implant with a 15 % zirconium content (α-structure) and a sandblasted and acid etched chemically modified, hydrophilic surface (SLActive); Ti implant made of commercially pure titanium (cpTi) (grade 4) with a sandblasted and acid-etched chemically modified, hydrophilic surface (SLActive) and Ti_6Al_4V implant with a sand-blasted and acid-washed surface. According to histomorphometric analysis all materials showed significantly different surface roughness parameters. The amount of new bone within the implant grooves increased over time, without significant differences between materials. However, BIC values were significantly related to the implant material and the healing period. For TiZr and cpTi implants, the BIC increased over time, reaching values of 59.38 % and 76.15 % after 2 weeks, and 74.50 % and 84.67 % after 8 weeks, respectively. In contrast, the BIC for Ti_6Al_4V implants peaked with 42.29 % after 2 weeks followed by a decline to 28.60 % at 8 weeks. Significantly more surface was covered by multinucleated giant cells on Ti_6Al_4V implants after 4 and 8 weeks. In conclusion, TiZr and cpTi implants showed faster osseointegration than Ti_6Al_4V implants.

30.Surface Modified Zirconia Implant

Schliephake *et al.* (2010) compared and studied 3 types of implants (i) a zirconia implant with a sandblasted surface; (ii) a zirconia implants with a sandblasted and etched surface; and (iii) a titanium implant with a sandblasted and acid-etched surface (control). Histomorphometric analysis after 13 weeks showed that the BIC% was significantly higher for titanium implants as compared to the zirconia implants($p<0.05$).

31.Implants Coated with Collagen, Chondroitin Suphate and BMP-4

Stadlinger *et al.* (2008) compared 4 types of implants namely titanium implants, implant with collagen I surface treatment, implant with collagen I + chondroitan sulphate surface treatment, implant with collagen I + Chondroitan sulphate + rhBMP-4 surface treatment.120 implants were placed in minipigs. Histomorphometric analysis was done at the end of 6 months. 39.2% implants were excluded from the study due to specific animal model and strict criteria in placement of implants. Of the successfully gained 73 implants, the highest percentage of BIC was obtained for coll/CS (40%), followed by coll (30%) and coll/CS/rhBMP-4 (27%), P = 0.013. BIC within the recesses was highest for coll/CS (51%), followed by coll (43%) and coll/CS/rhBMP-4 (34%), P = 0.025. The study concluded that the BIC% can be increased by inclusion of CS compared to collagen coated implants. However, the further addition of a low amount rhBMP-4 had a detrimental effect on bone formation compared to coll/CS, $P < 0.05$.

32.Biofunctionalized Porous Anodized Titanium Implant

Shim *et al.* (2014) compared 5 types of implants namely Untreated titanium disc implant; Drug unloaded electrospray (ESP) nanoparticles coated disc with 0.05 mL PLGA solution (0 ng Fibroblast growth factor -2/disc); FGF-2 loaded ESP nanoparticles coated disc with 0.05 mL FGF-2/ poly(lactide-co-glycolide) (PLGA) solution (3.0960.56 ng FGF-2/disc); FGF-2 loaded ESP nanoparticles coated disc with 0.15 mL FGF-2/PLGA solution (10.5863.06 ng FGF-2/disc); FGF- 2 loaded ESP nanoparticles coated disc with 0.30 mL FGF-2/PLGA solution (20.0668.93 ng FGF-2/disc). Histomorphometric analysis done after 12 weeks showed that the mean osseointegration value of FGF-2 releasing implant groups (70.1%) was significantly higher than that of untreated implants (47.1%). Hence, ESP nanoparticle coating enhanced osseointegration.

33.Matrix Based Implant surface Coating

Stadlinger *et al.* (2008) conducted a study to analyze how bone formation around implants is influenced by differently composed collagen matrices and RGD peptide surface coatings compared to a sandblasted titanium surface. Five different types of implant surfaces were compared. Histomorphometric analysis after 6 months concluded that osseointegration was achieved for all implant surfaces. However, a statistically significant increase in BIC could not be demonstrated for the experimental coatings, there was also no discernible detrimental effect of the coatings in comparison to the uncoated titanium surfaces.

34.Type I Collagen Coating

Sverzut *et al.* (2012) compared titanium surface implants that were acid etched (AETi) with collagen Type I coating and those without collagen coating. Histomorphometric analysis was carried out at 3 and 8 weeks post implantation. It was observed that coating AETi with collagen fastens the osseointegration by stimulating bone formation at the cellular and molecular levels, making this combination of morphological and biochemical modification a promising approach to treat Ti surfaces. The Acid etched titanium implant showed a BIC% of 31.78 as compared to Type I Collagen treated AETi which was 45.99. Hence, type I collagen coating positively influences osseointegration.

35.Porous and Ro Titanium Implants

Vasconcellos *et al.* (2008) compared porous cylindrical implants which had a total porosity of 37% and average pores diameter of 480 μm and rough cylindrical implants with Ra = 5.3 μm. Histomorphometric analysis was carried out at 4 and 8 weeks. The results suggested that there is improved osseointegration seen with porous implants.

36.Strontium Containing Hydroxyapatite Coating Produced by Microarc Oxidation

Yan *et al.* (2013) compared implants of four types HA- Ti (Control), 5% Sr-HA-TI, 10% Sr-HA-Ti, 20% Sr-HA-Ti. According to the authors Strontium-containing hydroxyapatites (Sr-HA) combine the desirable bone regenerative properties of hydroxyapatites (HA) with anabolic and anti-catabolic effects of strontium cations. Histomorphometric analysis carried out after 12 weeks shows that the 20% Sr-HA coating promotes early bone formation as well as substantially increases bone–implant integration.

37.Biomimetically and Electrochemically deposited Nano-hydroxyapatite coatings

Yang *et al.* (2009) compared forty two implants divided into 3 groups: roughened group, biomimetically deposited CaP (BDCaP) group, and electrochemically deposited HA (EDHA) group. Histomorphometric analysis was made at 6 and 12 weeks. The EDHA implant revealed significantly greater bone-implant contact and bone area compared with the roughened and BDCaP implants ($P < .05$). Thus, EDHA coating has a better osseointegration potential than the BDCaP coating.

38.Calcium Modified Titanium Implant

Anitua *et al.* (2015) compared titanium control implants, implants coated with calcium ions and implants coated with Caions and autologus plasma rich in growth factors (PRGF). Histomorphometric analysis made at 8 weeks suggested that Ca ion surfaces when compared with controls show significantly higher osseointegration potential. The addition of autologous PRGF to the modified surfaces enhanced the peri implant bone formation. Hence, calcium titanium surfaces are efficient stimulators of implant osseointegration.

39.Surface-modified Zirconia Implants

Gahlert *et al.* (2012) compared the bone tissue response to surface modified zirconia (ZrO_2) and titanium implants (Ti-SLA). Thirty six implants were placed in eighteen female mini pigs. The Ti-SLA implants served as controls. The animals were euthanized at 4, 8 and 12 weeks. Direct osseous integration was observed in both the materials on histomorphometric analysis. The BIC% mean values for ZrO_2 ranged from 67.1% (SD +/- 21.1) to 70% (SD +/- 14.5) and for Ti-SLA from 64.7% (SD +/- 9.4) to 83.7% (SD +/- 10.3). No statistically significant differences were seen at any point of time. Hence, there was no difference in osseointegration between surface modified zirconia implants and titanium implants regarding peri-implant bone density and BIC ratio.

40.Low Pressure Injection Moulded Zirconia With Surface Treatment

Gahlert *et al.* (2009) compared zirconia implants that were prepared using low pressure injection moulding followed by surface treatment by acid etching (test implants) with titanium implants that had the exact shape and were surface treated by sand blasting and acid etching (Controls). Histomorphometric analysis was done after 4, 8 and 12 weeks. It showed that with respect to the bone–implant contact ratio, the mean values for test implants ranged from 27.1% (SD +/- 3.5) to 51.1% (SD +/- 12.4) and for Ti-SLA, it ranged from 23.5% (SD +/- 7.5) to 58.5% (SD+/- 11.4). No statistically significant differences were observed between both types of implants. The study also concluded that due to the limited number of animals per group the results cannot be taken for sure although the data suggests such a trend.

41.Nano-crystalline diamond-coated titanium dental implant

Metzler *et al.* (2013) compared twenty four microwave plasma-chemical-vapour deposition (MWPCVD) diamond-coated $Ti\text{-}Al_6\text{-}V_4$ dental implants with twenty four uncoated dental titanium-alloy implants. After 2 and 5 months histomorphometric analysis was done. Both the implants showed a comparable degree of osseointegration. No significant difference in BIC was observed.

42.Zirconia Implants

Moller *et al.* (2012) compared titanium and zirconia implants. Sixty four implants were placed domestic pigs. Histomorphometric analysis was carried out at 4 and 12 weeks. A slight delay in osseointegration was observed in the zirconium implants with respect to bone–implant contact as measured by histomorphometry (after 4 weeks, zirconium (59.3 +/- 4.6%) versus titanium (64.1 +/- 3.9%); after 12 weeks, zirconium (67.1 +/- 2.3%) versus titanium (73.6 +/- 3.2%). The results did not show statistically significant difference between the two groups. Thus it was concluded that both zirconium and titanium implants show similar biocompatibility and osseointegration.

43.Cp-Ti Implants With Surfaces Modified By Laser With And Without Silica Deposition

Souza *et al.* (2014) compared 4 types of implant surfaces: laser modified (LS); laser modified with sodium silicate deposition (SS); and commercially available surfaces modified by acid etching (AS) and machined surface (MS). Yetterium laser was used for surface treatment. Histomorphometric analysis was done at 4, 8 and 12 weeks post implant insertion. The LS and SS implants showed statistically higher BIC than that of AS and MS in most of the analyzed periods. The study concluded that LS and SS implants provided the highest degree of osseointegration as they accelerated the stages of the bone tissue repair process around the implants.

Implant Design Modifications

1.Microthread Design

Abrahamsson and Berglundh (2006) analyzed bone tissue reactions at implants with and without a microthread configuration. A total of 24 implants, one test and two control implants were placed in 6 beagle dogs. The test implants had a microthread configuration in the marginal portion. Histomorphometric analysis done after 16 months revealed that the degree of bone-implant contact was significantly higher for the test implants (marginal portion) than for the controls. It was thus concluded that the microthread configuration offered improved conditions for osseointegration.

2.RBM Treated Implants with Grooves at Different Locations

Ahn *et al.* (2010) placed 120 implants on the medial side of the rabbit tibia to compare machined implants; RBM-treated implants; machined implants with a long vertical groove; RBM-treated implants with a vertical groove; RBM-treated implants with a vertical groove on the upper thread; and RBM treated implants with a vertical groove on the lower trunk. The animals were sacrificed at 2, 4 and 8 weeks after surgery. Histomorphometric studies revealed that RBM treated implants with a long vertical groove had the highest BIC percentage. Hence the long vertical groove positively enhances osseointegration.

3.Tapered and Cylindrical Screw Type Implants

Aldosari *et al.* (2014) compared thirty two implants of 4 different types, tapered implants, cylindrical implants, HA-coated tapered implants, and HA-coated cylindrical implants. After 8 weeks histomorphometric analysis was made which revealed that the BIC% was higher for HA-coated tapered implants followed by cylindrical non-coated implants. All four types of implants did not show any statistical significance between them. Hence according to the study implant design and surface composition had little effect on the bone-to-implant interface.

4.Implant Diameter

Brink *et al.* (2007) compared 20 standard (3.75 mm) and 20 wide (5mm) implants to know the impact of implant diameter on surrounding bone. Histomorphometric analysis was carried out after 3 months revealed that the BIC% for standard implants was 71% and for wide implants was 73%. The difference was not statistically significant (P> 0.05). Hence, within the limits of this study it was concluded that the implant diameter does not influence osseointegration significantly.

5.Specific Cutting Flute Design

Jimbo *et al.* (2014) compared 24 specific cutting flute design and 24 self-tapping design. Histomorphometric analysis was done at 3 and 6 weeks it revealed that there was no statistically significant difference between the two implants with respect to BIC. The insertion torque was reduced for implants with the modified cutting flute design compared to the self-tapping implants with a traditional cutting thread. Hence, specific cutting flute design showed better peri-implant bone organization.

6.Plateau root form Vs. screw root form implants

Leonard *et al.* (2009) compared the bone healing process around plateau root form (PRF) and screw root form implants (SRF). 32 implants were allotted to each group but for the analysis 16 implants were excluded as they were in contact with the canine. So finally 48 implants were included for Histomorphometric analysis at 3 and 12 weeks post implantation. The BIC results recorded for the SRF implants were higher at four time-points, increasing from 70.9% at 3 weeks to 89.6% at 12 weeks. For the PRF implants, they increased from a low of 57.5% at 3 weeks to a high of 84.4% at 12 weeks. According to the study results no statistically significant differences were seen between the two implants when compared with respect to bone implant contact.

7.Cylindrical Versus Conical Implants

Mueller *et al.* (2013) compared six different types of implants. Histomorphometric analysis was done at 2 and 4 months. There were no significant differences observed between titanium and zirconium were found with respect to bone-implant contact. Cylindric zirconium implants showed a higher BIC than conic zirconium implants after 2 months. Among zirconium implants, those with an intermediate surface roughness value showed a significantly higher BIC compared with low and high surface roughness implants 4 months after surgery. According to the study titanium and zirconium showed equal properties with respect to osseointegration. It was concluded that cylindrical implant design and intermediate surface roughness seemed to enhance osseointegration. Olate *et al.* (2011) analyzed the mineralized tissue formation on the screw threads of conical and cylindrical dental implants. 11 cylindrical and 13 conical implants were placed. At the end of 6 weeks histomorphometric analysis showed that statistically significant differences were not found between the conical and cylindrical implants. The conical implants presented fewer threads, a smaller area, and more bone formation when compared with the cylindrical ones, without significant differences (P = .1226). The highest values concerning bone formation were observed for the cervical area (P = .4005), and the lowest for the apical area (P = .1899); however, no statistically significant difference was observed. In conclusion, no statistically significant difference was observed in thread bone formation between the cylindrical and conical implant designs when placed using the non-submerged technique.

Limitations

Some studies did not give concrete conclusions due to various reasons like limited sample size, exclusion of study samples due to failure of osseointegration or inability to place the implants correctly in the desired position.

Conclusion

There have been several attempts by investigators and researchers to develop an implant system that will promote rapid healing and successful osseointegration of the endosseous implants into the jaw bone. Titanium implants have been the material of choice clinically because of their biocompatibility and superior mechanical properties. Several studies show that there has been a stronger and faster osseointegration when the implant surface is modified. Incorporation of Plasma rich growth factors, calcium ions, carbon-ion oxygen, anodization of the implant surface, strontium containing hydroxyapatite coating produced by microarc oxidation etc. surface modifications have shown a positive impact on osseointegration. Hence it can be said that surface conditions such as surface roughness and surface composition have an important influence on the process of osseointegration. Further studies need to be done to manufacture an implant system that will promote both short term and long term predictable success.

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