ECRONICON OPEN ACCESS

EC DENTAL SCIENCE
Review Article

Metal Particles: A Conundrum in Peri-Implant Tissues

Pooja AjitSankardas* and Sidney H Stein

Department of Periodontology, University of Tennessee Health Science Center, College of Dentistry, Union Avenue, Memphis, TN, USA

***Corresponding Author:** Pooja AjitSankardas, Department of Periodontology, University of Tennessee Health Science Center, College of Dentistry, Union Avenue, Memphis, TN, USA.

Received: February 14, 2025; **Published:** March 31, 2025

Abstract

Dental implants are a popular treatment alternative to replace missing teeth; however, little is known regarding the consequences of dental implant corrosion, wear and metal particle release that occurs over time. Recent research has demonstrated metal particles in tissues surrounding dental implants, but the bioinert nature of these particles remains conflicted. The aim of this narrative review is to shed light on the different ways metal particles can be released into the environment, and their effect on microbial dysbiosis and the inflammatory immune response. In conclusion, this review creates awareness among clinicians regarding the effects of metal particles and their significance in implant dentistry. The importance of understanding the role of these particles is essential in achieving long term success of dental implants and preventing peri-implant diseases.

Keywords: *Dental Implant; Peri Implant Disease; Titanium; Peri Implant Soft Tissue*

Introduction

In the late 1950's the phenomenon of osseointegration revolutionized implant dentistry, making titanium dental implants a popular treatment alternative [1]. Today, titanium and titanium alloys continue to be the most common metal used to manufacture dental implants. However, with increasing number of implants placed, subsequent failure, due to biological, surgical, and prosthetic complications, presents a major concern. Existing literature concluded that 10% to 20% of patients developed peri-implantitis, 5 - 10 years after implant placement [2]. Interestingly, studies on long term effects of orthopedic implants have also projected, that within 15 - 20 years of placement, a revision surgery for these implants seems inevitable [3]. Peri-implant inflammatory diseases and aseptic loosening of implants have been described extensively, but their etiology and pathogenesis remain complex. Amongst the other factors resulting in bone loss around medical implants, clinical studies have suggested implant wear debris to be one of the causes for aseptic loosening of orthopedic implants [4]. Other than physical wear of orthopedic implants, bio corrosion, material fatigue, and inappropriate implant configurations can result in release of metal particles leading to implant failure [5,6]. All these factors remain unexplored for dental implants. Moreover, unlike orthopedic implants that are surgically placed and located in a sterile environment, dental implants are exposed to oral bacteria, which can further potentiate the pathogenic process [7]. Research has also revealed that titanium ions stimulate the release of inflammatory mediators from immune cells that cause bone resorption and ultimately failure of the dental implant [8]. The purpose of this review is to examine the role of metal particles in the development of peri-implantitis.

Different ways of release of metal particles

Numerous theories have been proposed to understand how these particles are released into the surrounding tissues. A study by He., *et al*. demonstrated titanium content in mandibular jaw bones increased as the distance from the implant decreased, suggesting the source of the particles to originate from the dental implant that was placed [9]. One possible mechanism that has been proposed includes detachment of particles during surgical insertion of the dental implant. Frictional forces during implant insertion can lead to dislodgement of metal particles from the implant surface during surgical insertion [10]. Varied surface roughness and chemical composition can also result in different amounts and sizes of particles released into surrounding tissues. Pettersson., *et al*. demonstrated increased amounts of titanium particles around dental implants which had a higher surface roughness [11]. However, in a study by Wennerberg., *et al*. although loose particles were found around commercially available dental implants, they stated that there was no correlation with the implant surface roughness [12]. Along with implant wear another source of metal particles could also be from the implant drill. Re-sterilization of implant drills, wear caused by the increased use of the drill, and lack of sufficient irrigation have all been suggested as different ways particles can be released from the implant drills [13]. Another mechanism that has been proposed to cause release of metal particles is wear, owing to micro-movements between abutment-implant connections. Studies demonstrated that although wear was highest between titanium-zirconia abutment interface, all abutment-implant interfaces lead to release of wear particles on loading the implant [14]. In another study platform switching concept was shown to reduce these tribo-corrosion products [15]. Breakdown of the titanium oxide layer is another mechanism that has been stated in literature to result in the release of metal ions into the environment. The titanium oxide layer formed around dental implants creates a corrosion resistant surface which promotes osseointegration [16]. Alteration of surface characteristics, chemical structure and composition of the implant can create positive changes in this oxide layer promoting osseointegration. Conversely, this oxide layer can also get disrupted due to different reasons, which further results in release of titanium ions into surrounding tissues. Acidic environments created by microbial toxins, comorbid conditions (diabetes; history of periodontitis) and social habits (Smoking, alcohol consumption) can all potentially decrease pH in surrounding tissues and disrupt the oxide layer. Although the latter two conditions remain undetermined, a study by Sridhar., *et al*. demonstrated increased corrosion and surface roughness of acid etched implants immersed in a suspension of *S. mutans* after 2, 22 and 60 days [17]. Low pH and increased lipopolysaccharide seemed to affect the corrosion resistance of titanium implants [18]. It is also interesting to note that apart from microbial toxins even use of therapeutic agents like fluorides in toothpastes and hydrogen peroxide impair corrosion resistance of titanium and simultaneously cause the release of ions [19,20]. Furthermore, after the initial release of metal particles, saliva can act like an electrolyte and potentiate further dissolution of the titanium oxide layer, forming corrosion by-products [21,22]. Finally therapeutic procedures such as ultrasonic scaling, polishing and implantoplasty can also damage the implant surface and result in release of particles [23,24]. When scaling around sandblasted implants as opposed to sand blasted- acid etched implants, particles generated from the sandblasted group, induced a greater inflammatory response [25]. Once again, this study shed light on the importance of long-term effects of surface texture and the effects they have on therapeutic procedures. Use of non-metallic instruments for cleaning implant surfaces have been known to create the lowest damage. In an *in vitro* study by Harrell., *et al*. the highest quantity of metal particles around implants were detected when stainless steel ultrasonic tips were used in comparison to titanium and polyether ether ketone (PEEK) tips [26]. Although the source of the particles could be from the instrument tips during placement or therapeutic procedures, the continuous presence of particles that have been found in surrounding tissues is undisputed (Figure 1).

Distribution of metal particles in healthy and diseased sites

Over the years research has shown that after titanium implants are placed, titanium particles can be found in the tissues surrounding the implant, subsequent spread into the blood stream, and presence in distant organs like the lungs, liver, kidney, and spleen [27]. Although most of these studies were demonstrated in animal models, the presence of titanium ions has also been demonstrated in human studies. A case series conducted by Olmedo., *et al*. was one of the first few studies to reveal macrophage engulfed titanium particles in soft tissue biopsy samples from tissues surrounding failed dental implants [28]. Subsequent studies conducted during Second stage surgery

also revealed titanium particles near the cover screw [29,30]. Flatebo., *et al*. further demonstrated that these particles were not present prior to implant placement, but their presence was detected only after the implants were placed [31]. Analysis of human soft tissue biopsies from sites that developed peri-implantitis also revealed the presence of foreign bodies, predominantly composed of titanium particles [32]. Fretwurst., *et al*. also demonstrated metal particles (titanium and iron) in nine 9 biopsies taken at peri-implantitis sites [33]. Studies demonstrating the same results in clinically healthy implant sites have still yet to be found. In a cytological analysis of oral smears taken from the peri-implant mucosa of 30 patients, Olmedo., *et al*. identified the concentration of titanium particles was higher in the peri-implantitis group compared with the group without peri-implantitis [34]. These findings were similar to another study that demonstrated greater levels of dissolved titanium in sub mucosal plaque around implants with peri-implantitis compared with healthy implants, indicating an association between titanium and peri-implantitis [35]. Although all these studies revealed the presence of metal particles in sites with peri-implantitis, particle sizes and concentrations were highly variable ranging from micro particles to nanoparticles. Furthermore, their role in pathogenesis of periimplantitis still remains unclear.

Metal particles and inflammation

Inflammation is the body's response to harmful stimuli like bacterial toxins, trauma, and heat. Titanium ions/particles released also may have varying impacts on different cells of the periodontium. Studies demonstrated that titanium particles/ions had a size and dose dependent cytotoxic effect on neutrophils and gingival epithelial like cells, respectively [36-38]. A study by Irshad., *et al*. concluded that when human peri implant gingival fibroblasts were exposed to titanium oxide particles ranging from 50 - 100 particles/Peri implant gingival fibroblasts, the cell viability of these cells was reduced [39]. Titanium particles of ≤ 20μm at a concentration of 0.1 mg/ml and 1.0 mg/ml showed medium- and long-term effects on growth rate and proliferation of human gingival fibroblasts and human calvarial osteoblasts. The cells also secreted IL-6 in a dose dependent manner over varying periods of time [40]. Titanium particles were also demonstrated to increase reactive oxygen species production by mesenchymal stem cells and fibroblasts, thereby generating an abnormal increase in neutrophil activity and production of matrix metalloproteinases [41]. In physiological solutions titanium ions activated inflammasomes in macrophages and further lead to the release of IL-1β. M1 macrophages also demonstrated an enhanced response, causing an increased activation of inflammation as opposed to M2 macrophages that promote resolution and repair [42]. Moreover, although both M1 and M2 macrophages have been described in periimplantitis biopsies, M1 polarization was greater in periimplantitis lesions compared to periodontitis samples, indicating the distinct accelerating pattern of tissue destruction in periimplantitis [43]. In an *in vitro* study metal ions were demonstrated to upregulate the expression of IL-6, IL-8, Cyclooxygenase 2 and Receptor activator of nuclear factor Kappa-B Ligand (RANKL) from osteoblastic cells. The exaggerated release of all these inflammatory mediators due to the presence of titanium ions and metal particles can lead to a continuing cycle of events that can finally lead bone resorption and ultimately loss of the dental implant. Another concept that is frequently discussed that results in the loss of dental implants, is the imbalance of foreign body equilibrium. During surgical placement of dental implants an initial inflammatory response is generated which further resolves as the implant undergoes osseointegration. Over a period, however, if the implant is exposed to microbial toxins, like the development of periodontitis around natural teeth, host response can lead to destruction of the tissues surrounding the implant. Interestingly although the etiopathogenesis of the two diseases remain the same, histopathologic analysis shows an increased inflammatory infiltrate around periimplantitis lesions and a faster rate of progression [44]. Several reasons including anatomic differences, like the absence of a periodontal ligament, cementum, and decreased vascularity have been suggested to play a role in the accelerating nature of periimplantitis progression. Studies have demonstrated an increased number of plasma cells and lymphocyte cell infiltrate in peri-implantitis lesions [45]. This increased amount of inflammatory infiltrate also questions the effect of other factors besides bacteria that can induce an immune response. A study by Albrektsson., *et al*. also proposed that peri-implantitis was a result of an immunological foreign body reaction to titanium [46]. According to this hypothesis once the implant undergoes osseointegration, the newly formed bone around the titanium surface shields the dental implant from initiating any inflammatory immune response thus maintaining foreign body equilibrium. However, when the breakdown of osseointegration starts the immune cells like macrophages can initiate the pathway osteoclastic bone resorption resulting in imbalance of foreign body equilibrium thereby initiating a viscous cycle of events [47] (Figure 1).

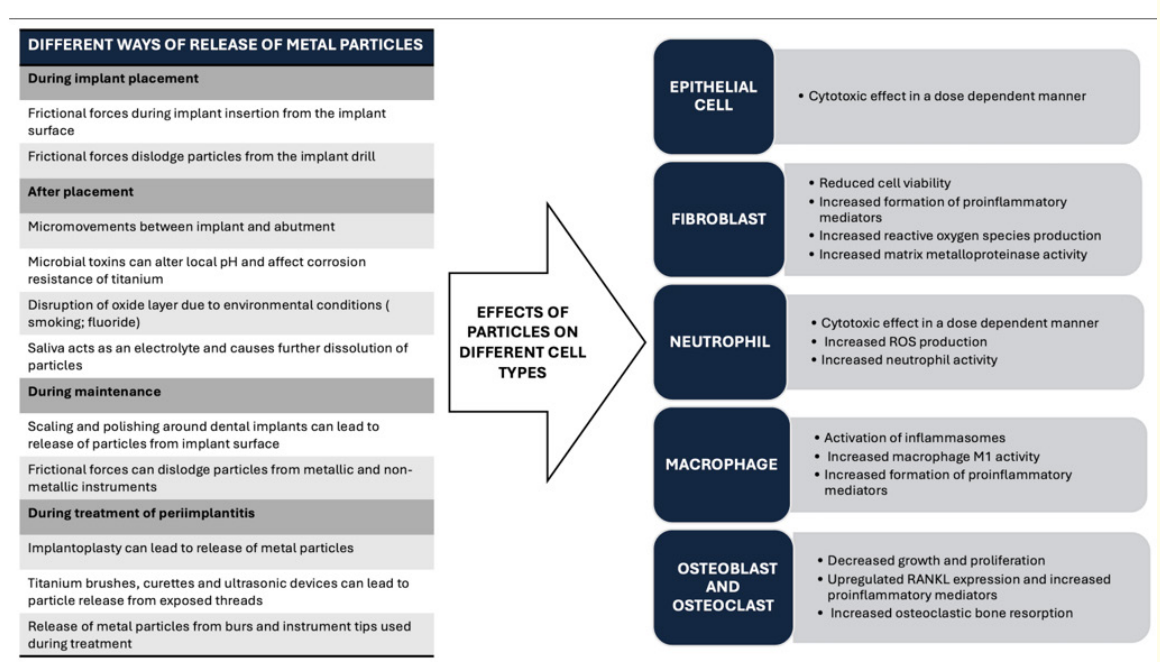

Figure 1: *Different ways metal particles can be released into the oral environment and its impact on different cell types.*

Metal particles and microbial dysbiosis

Breakdown of soft and hard tissues that follow the initial inflammatory can invite secondary invasion of bacteria and production of microbial toxins that can further create a more acidic environment resulting in particle ion corrosion from the dental implant surface [48]. Interestingly studies on corroded titanium discs also showed an increased attachment of *P. gingivalis,* indicating that the corrosive surface favored biofilm formation. Similarly, in a study conducted by Souza., *et al*. when Titanium disks exposed to the oral biofilm when treated with titanium particles and ions, titanium ions seem to upregulate the expression of putative periodontal pathogens from the orange and green complex of species, thereby promoting a dysbiotic environment [49]. As studied in the dysbiosis model for periodontal disease, the latter studies on titanium ions seem to suggest that these particles/ions may be one of the factors that may play a role in converting a symbiotic host environment around implants into peri implant dysbiosis.

Conclusion

There is still a lack of understanding regarding the bioinert nature of titanium particles. However, with the increasing rates of periimplantitis and limited options to manage peri-implant diseases, a deeper understanding of its role in pathogenesis is warranted. Despite different *in-vitro* studies conducted to describe the pathogenic potential of metal particles, there is still limited evidence regarding this hypothesis. Nevertheless, clinicians may want to proactively reduce generating metal particles during implant placement and while performing therapeutic procedures. Furthermore, strategies to reduce titanium particle toxicity and inflammatory cytokine response through alternative approaches can also be considered. Implant surface modifications that enhance or conversely decrease particle release is an-

other area of research that needs to be investigated. Although metal particles may be only one of the causes resulting in aseptic loosening and bone loss around dental implants, decreasing particle release into surrounding tissues should be considered in any clinical setting.

Statement of Originality and Conflict of Interest

As corresponding author, I certify that this manuscript is original, and its publication does not infringe any copyright. There are no conflicts of interests. I declare that the manuscript has not been previously published in whole or in part in any other journal or scientific publishing company.

Bibliography

1. Branemark PI., *et al*. "Osseointegrated implants in the treatment of the edentulous jaw- Experience from a 10-year period". *Scandinavian Journal of Plastic and Reconstructive Surgery. Supplementum* 16 (1977): 1-132.

2. Mombelli A., *et al*. "The epidemiology of peri-implantitis". *Clinical Oral Implants Research* 23.6 (2012): 67-76.

3. Sansone V., *et al*. "The effects on bone cells of metal ions released from orthopaedic implants. A review". *Clinical Cases in Mineral and Bone Metabolism* 10.1 (2013): 34-40.

4. Harris WH., *et al*. "Extensive localized bone resorption in the femur following total hip replacement". *Journal of Bone and Joint Surgery, American Volume* 58.5 (1976): 612-618.

5. Fretwurst T., *et al*. "Is metal particle release associated with peri-implant bone destruction? an emerging concept". *Journal of Dental Research* 97.3 (2018): 259-265.

6. Sundfeldt, M., *et al*. "Aseptic loosening, not only a question of wear: a review of different theories". *Acta Orthopaedica* 77.2 (2006): 177-197.

7. Pettersson M., *et al*. "Titanium ions form particles that activate and execute interleukin-1b release from lipopolysaccharide-primed macrophages". *Journal of Periodontal Research* 52.1 (2017): 21-32.

8. Wachi T., *et al*. "Release of titanium ions from an implant surface and their effect on cytokine production related to alveolar bone resorption". *Toxicology* 327 (2015): 1-9.

9. He X., *et al*. "Analysis of titanium and other metals in human jawbones with dental implants - A case series study". *Dental Materials* 32.8 (2016): 1042-1051.

10. Schliephake H., *et al*. "Metal release from titanium fixtures during placement in the mandible: An experimental study". *International Journal of Oral and Maxillofacial Implants* 8.5 (1993): 502-511.

11. Pettersson M., *et al*. "Release of titanium after insertion of dental implants with different surface characteristics - an *ex vivo* animal study". *Acta Biomaterialia Odontologica Scandinavica* 3.1 (2017): 63-73.

12. Wennerberg A., *et al*. "Titanium release from implants prepared with different surface roughness". *Clinical Oral Implants Research* 15.5 (2004): 505-512.

13. Allsobrook OFL., *et al*. "Descriptive study of the longevity of dental implant surgery drills". *Clinical Implant Dentistry and Related Research* 13.3 (2011): 244-254.

14. Blum K., *et al*. "Fatigue induced changes in conical implant-abutment connections". *Dental Materials* 31.11 (2015): 1415-1426.

15. Alrabeah GO., *et al*. "Reduction of tribocorrosion products when using the platform-switching concept". *Journal of Dental Research* 97.9 (2018): 995-1002.

16. Larsson C., *et al*. "Bone response to surface modified titanium implants studies on electropolished implants with different oxide thicknesses and morphology". *Biomaterials* 15.13 (1994): 1062-1074.

17. Sridhar S., *et al*. "*In vitro* evaluation of titanium exfoliation during simulated surgical insertion of dental implants". *Journal of Oral Implantology* 42.1 (2016): 34-40.

18. Barao VA., *et al*. "The role of lipopolysaccharide on the electrochemical behavior of titanium". *Journal of Dental Research* 90.5 (2011): 613- 618.

19. Noguti J., *et al*. "The role of fluoride on the process of titanium corrosion in oral cavity". *Biometals* 25.5 (2012): 859-862.

20. Peñarrieta-Juanito G., *et al*. "Surface damage of dental implant systems and ions release after exposure to fluoride and hydrogen peroxide". *Journal of Periodontal Research* 54.1 (2019): 46-52.

21. Abey S., *et al*. "Electrochemical behavior of titanium in artificial saliva: influence of pH". *Journal of Oral Implantology* 40.1 (2014): 3-10.

22. Nikolopoulou F. "Saliva and dental implants". *Implant Dentistry* 15.4 (2006): 372-376.

23. Louropoulou A., *et al*. "Titanium surface alterations following the use of different mechanical instruments: A systematic review". *Clinical Oral Implants Research* 23.6 (2012): 643-658.

24. Schwarz F., *et al*. "Surgical therapy of advanced ligature-induced peri-implantitis defects: cone-beam computed tomographic and histological analysis". *Journal of Clinical Periodontology* 38.10 (2011): 939-949.

25. Eger M., *et al*. "Scaling of titanium implants entrains inflammation-induced osteolysis". *Scientific Reports* 7 (2017): 39612.

26. Harrel SK., *et al*. "Titanium particles generated during ultrasonic scaling of implants". *Journal of Periodontology* 90.3 (2019): 241-246.

27. Schliephake H., *et al*. "Metal release from titanium fixtures during placement in the mandible: an experimental study". *International Journal of Oral and Maxillofacial Implants* 8.5 (1993): 502-511.

28. Olmedo D., *et al*. "Macrophages related to dental implant failure". *Implant Dentistry* 12.1 (2003): 75-80.

29. Olmedo DG., *et al*. "Oral mucosa tissue response to titanium cover screws". *Journal of Periodontology* 83.8 (2012): 973-980.

30. Flatebø RS., *et al*. "Host response to titanium dental implant placement evaluated in a human oral model". *Journal of Periodontology* 77.7 (2006): 1201-1210.

31. Flatebø RS., *et al*. "Mapping of titanium particles in peri-implant oral mucosa by laser ablation inductively coupled plasma mass spectrometry and high-resolution optical darkfield microscopy". *Journal of Oral Pathology and Medicine* 40.5 (2011): 412-420.

32. Wilson TG Jr., *et al*. "Foreign bodies associated with peri-implantitis human biopsies". *Journal of Periodontology* 86.1 (2015): 9-15.

33. Fretwurst T., *et al*. "Metal elements in tissue with dental peri-implantitis: a pilot study". *Clinical Oral Implants Research* 27.9 (2016): 1178-1186.

34. Olmedo DG., *et al*. "Exfoliative cytology and titanium dental implants: a pilot study". *Periodontology* 84.1 (2013): 78-83.

35. Safioti LM., *et al*. "Increased levels of dissolved titanium are associated with peri-implantitis. A cross sectional study". *Journal of Periodontology* 88.5 (2017): 436-442.

36. Makihira S., *et al*. "Titanium ion induces necrosis and sensitivity to lipopolysaccharide in gingival epithelial-like cells". *Toxicology in Vitro* 24.7 (2010): 1905-1910.

37. Mine Y., *et al*. "Impact of titanium ions on osteoblast-, osteoclast- and gingival epithelial-like cells". *Journal of Prosthodontic Research* 54.1 (2010): 1-6.

38. Kumazawa R., *et al*. "Effects of Ti ions and particles on neutrophil function and morphology". *Biomaterials* 23.17 (2002): 3757-3764.

39. Irshad M., *et al*. "Influence of titanium on *in vitro* fibroblast-*Porphyromonas gingivalis* interaction in peri-implantitis". *Journal of Clinical Periodontology* 40.9 (2013): 841-849.

40. Happe A., *et al*. "The biologic effect of particulate titanium contaminants of dental implants on human osteoblasts and gingival fibroblasts". *International Journal of Oral and Maxillofacial Implants* 34.3 (2019): 673-680.

41. Bressan E., *et al*. "Metal nanoparticles released from dental implant surfaces: potential contribution to chronic inflammation and peri-implant bone loss". *Materials (Basel)* 12.12 (2019): 2036.

42. Pajarinen J., *et al*. "The response of macrophages to titanium particles is determined by macrophage polarization". *Acta Biomaterialia* 9.11 (2013): 9229-9240.

43. Fretwurst T., *et al*. "Characterization of macrophages infiltrating peri-implantitis lesions". *Clinical Oral Implants Research* 31.3 (2020): 274-281.

44. Schwarz F., *et al*. "Peri-implantitis". *Journal of Clinical Periodontology* 45.20 (2018): S246-S266.

45. Berglundh T and Carcuac O. "Composition of human peri-implantitis and periodontitis lesions". *Journal of Dental Research* 93.11 (2014): 1083-1088.

46. Albrektsson T., *et al*. "Is marginal bone loss around oral implants the result of a provoked foreign body reaction?" *Clinical Implant Dentistry and Related Research* 16.2 (2014): 155-165.

47. Trindade R., *et al*. "Foreign body reaction to biomaterials: on mechanisms for buildup and breakdown of osseointegration". *Clinical Implant Dentistry and Related Research* 18.1 (2016): 192-203.

48. Nakagawa M., *et al*. "Effects of fluoride and dissolved oxygen concentrations on the corrosion behavior of pure titanium and titanium alloys". *Dental Materials Journal* 21.2 (2002): 83-92.

49. Souza JGS., *et al*. "Titanium particles and ions favor dysbiosis in oral biofilms". *Journal of Periodontal Research* 55.2 (2020): 258-266.

Volume 24 Issue 4 April 2025