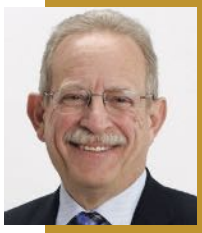
Does The Implants Condition At Manufacturing And Packaging Have An Effect On Peri-Implantitis?



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Introduction:

Dental implants have become standard treatment for replacement of single missing teeth, the fully edentulous arch, and edentulous portions of the arch. Dental implants have maintained a very high level of success for decades. Yet, problems may arise related to the bone to implant contact (BIC) leading to bone loss at the interface (peri-implantitis) and potential loss of the implant.

Peri-implantitis is a pathological process that occurs at the bone surrounding dental implants characterized by inflammation of the soft and hard tissues adjacent to the implant, which leads to progressive bone loss supporting the implant. When not treated early enough, eventual loss of the implant can result. Peri-implantitis may appear early in the life of one or more implants or many years after restoration of the implant(s) and may progress slowly or in an accelerated manner depending on the causative factor and the patient's host immune system.

Increasing focus on peri-implantitis has occurred in recent years, due to an escalation in the reported incidence. This has not been due to growing case numbers based on

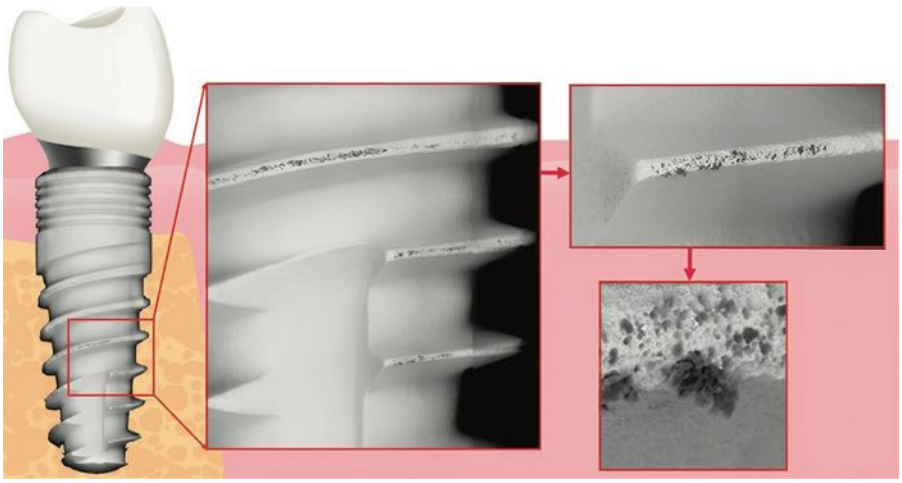

Figure 1: Factory-related impurities and carbonaceous particles can detach from the implant surface during implant insertion.

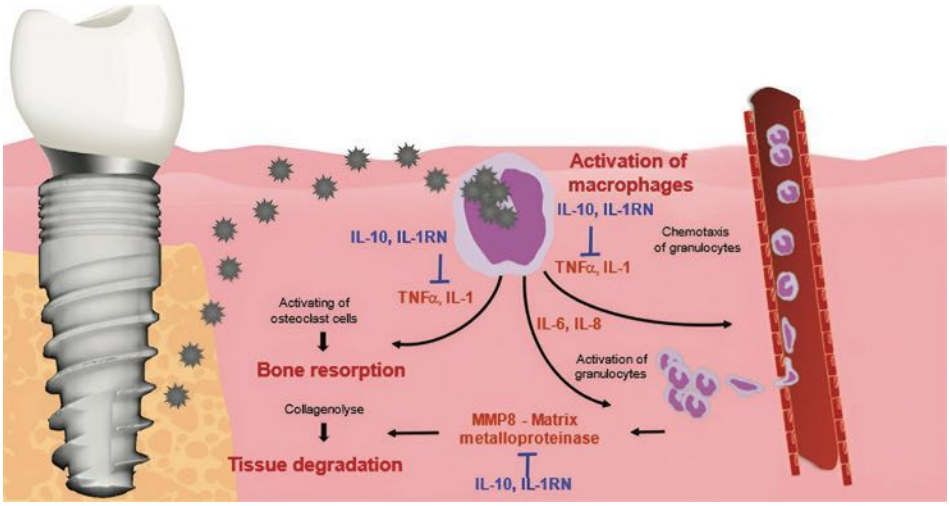

Figure 2: The peri-implantitis follows a foreign body type reaction, triggering the hosts immune response that results in bone loss and soft tissue degradation around the implant.

world-wide acceptance of dental implant over decades, but to more frequent identification of this pathological process as practitioners come to understand the signs and symptoms associated with the disease.[1] Yet, the histological and clinical conditions leading to the conversion from gingival inflammation to peri-implantitis are not completely understood.[2] Clinically at the histologic level, sites that have peri-implantitis often have larger inflammatory lesions than sites around natural teeth that have periodontitis. That evidence suggests that progressive crestal bone loss around implants in the absence of clinical signs of soft-tissue inflammation is rare.[2]

Peri-implant disease is classified into peri-implant mucositis and peri-implantitis. Peri-implant mucositis is classified as inflammation found only around the soft tissues adjacent to the implant, with no evidence of bone loss. Generally, peri-implant mucositis is a precursor to peri-implantitis and may be successfully treated to prevent progression to peri-implantitis when identified and treated early enough. With peri-implantitis, the gingival inflammation has progressed to the underlying bone, leading to deterioration of osseous support of the implant. Treatment of peri-implantitis typically requires surgical intervention to stop progression and repair the lost hard tissues. Thus, timely identification of peri-implant mucositis and early intervention to prevent its progression to the hard tissues supporting the implant is a key to clinical success.

Implants, as with natural teeth require regular homecare to maintain the soft tissue, which acts as a barrier to deeper progression of inflammatory factors. Other risks factors for developing peri-implant disease include previous periodontal disease diagnosis, poor plaque control, smoking, and diabetes. Dental implants need to be routinely monitored as part of a comprehensive periodontal evaluation.[1]

The reported occurrence of peri-implant mucositis and peri-implantitis ranges in studies from 46% to 63% and 19% to 23%.[3-6] Thus, peri-implant diseases affect a significant number of patients who have implants. Therefore, it is necessary to understand diagnosis of these diseases and the risk factors that can be modified to reduce the potential for disease occurrence or progression.

Peri-implant disease contributors:

The acceptance of dental implants as "conventional" dentistry for patients who are missing teeth translates to a growing number of implants placed globally. As described, dental implants are not free of risk or problems after placement. Evidence has been reported that there is an increased risk of the development of peri-implantitis in patients who have a history of chronic periodontitis and poor plaque control skills and who fail to maintain regular maintenance care after implant treatment.

The literature reports that smokers have a high incidence of peri-implantitis (72.7%) compared to non-smokers (27.3%), with higher richness of microbiota identified in patients with peri-implantitis who are smokers.[7,8] Another significant variable is that patients with periodontitis demonstrated a 50% chance of having peri-implantitis.[9,10] Patients who have oral inflammatory changes associated with their remaining natural teeth are at a much greater risk of acquiring peri-implantitis. Additionally, oral biofilm in periodontally involved patients may make them more immunologically sensitive to further insult from particles that are present around or on the implant surface. Recently it has been reported that patients who report an allergy to penicillin have double the failure rate of dental implants, and it may also be related to receiving alternative antibiotic therapy.[11]

Systemic diseases such as arterial hypertension, diabetes mellitus, osteoporosis, and cardiovascular diseases do not show a statistically significant influence on the incidence of peri-implantitis. Management of those risk factors, include improving homecare, treating periodontal issues, and addressing systemic health issues (ie. diabetes), can aid in decreasing the incidence of peri-implantitis and its severity.[5]

Sterile but contaminated implants:

An important and understated risk factor that needs to be better understood has increasingly become a focus in the dental implant industry. The manufacturing process, handling during quality control, and even the sterile packaging of dental implants are largely unknown and underestimated factors that can affect the short- and long-term condition of the implant. How a dental implant is manufactured and packaged can significantly influence how surrounding bone in close contact to the dental implant interacts with the implant's surface at time of placement and in early stages of osseointegration. The manufacturing process needs to be meticulous in all phases to ensure that the end-product is not only just sterile but also free of surface contaminants that are technically avoidable. Although the implant is sterile when removed from the package from the manufacturer, thin-film contaminants, organic and/or non-organic particles on the

implant's surface that are directly related to the complex and elaborate manufacturing process may be present.[11]

Particles of material, be it metals, and carbonaceous organics left on the implants surface during manufacturing or plastics resulting from the packaging can initiate an immune reaction in the patient via a foreign body reaction. (Figure 1) During that foreign body response, tumor necrosis factor alpha (TNF-α) promotes osteoclastic activity that leads to bone loss at the osseous interface with the implant.[12] (Figure 2)

Quality assessment studies on dental implants conducted by the CleanImplant Foundation in collaboration with Charité University Medicine in Berlin and the Sahlgrenska Academy in Gothenburg, Sweden, utilized scanning electron microscopy (SEM) to identify impurities on new and sterile-packaged dental implants. Findings of particulate contamination were reported for both titanium and zirconia (ceramic) implants specific to the process used during the manufacture and packaging of those implants.[11,13] Reported data demonstrated that one out of three implant systems analyzed contained significant amounts of factory-related impurities. Those contaminants included organic particles from the manufacturing process, metallic particles containing inter alia iron-chromium compounds, nickel, tungsten, copper, and tin from the milling or surface treatment process, and plastic from handling and packaging.

SEM images of implants showed not only isolated spots of impurity, but also larger areas of the implant surface that were either insufficiently cleaned in the production process chain or contaminated without being noticed during packaging of the implants. Under high magnification in the BSE mode of SEM imaging, organic carbonaceous particles appeared as black spots. The SEM images in low (500x) and high magnification (2,500x) revealed thermoplastic materials, synthetic polymers, and polysiloxanes on sterile implant surfaces. This has been identified in both titanium implants (Figures 3 and 4) and zirconia implants (Figure 5) from various manufacturers. Some ceramic implants demonstrated significant organic debris related to the packaging material, analyzed in the SEM following removal from the manufacturer's packaging.[13]

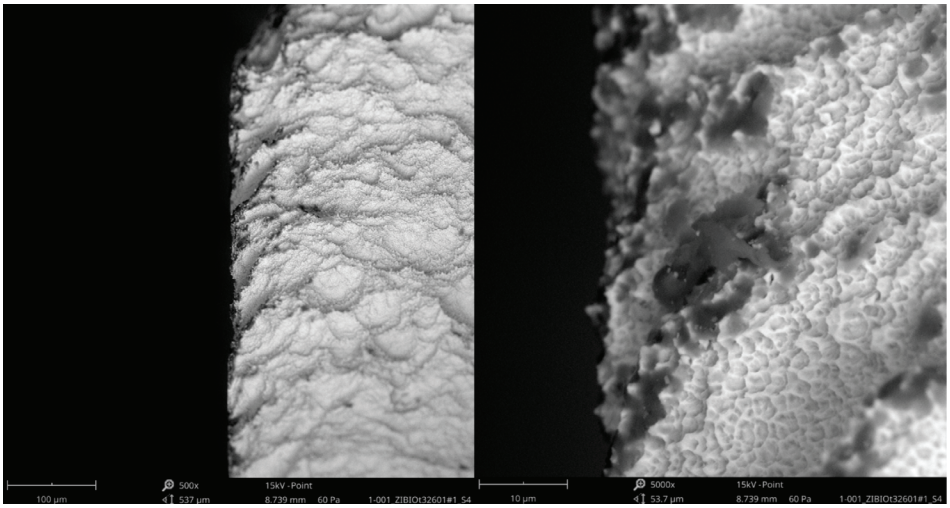

Figure 3: SEM of a titanium implants surface at the apical region directly out of the manufacturers packaging demonstrating numerous carbonaceous organic particles (synthetic polymers) that can induce an immune response leading to bone loss at 500x (left) and at 2,500x (right).

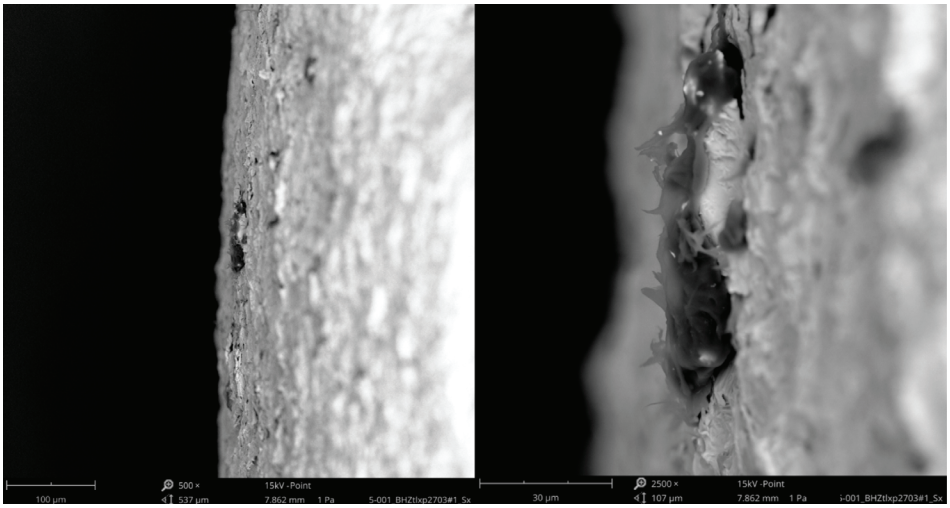

Figure 4: SEM images of another titanium implant at 500x (left) and at 2,500x (right) directly after unboxing of the sterile packaged sample. The apical region shows plastic residuals of the packaging material that will be inserted into the implant site.

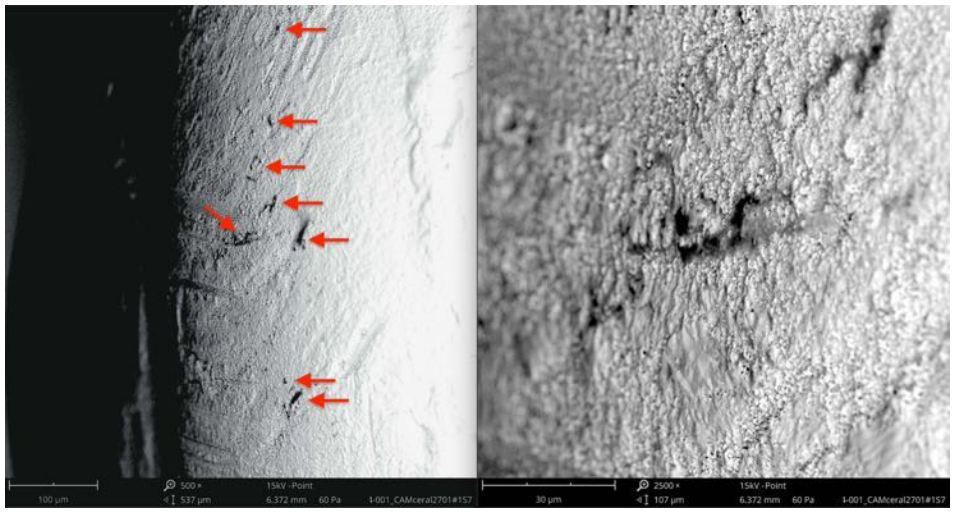

Figure 5: SEM images of significant organic contamination (foreign material 5 to 50 µm in diameter) at the apical region of a new and sterile-packaged zirconia implant 500x (left) and at 2,500x (right).

Organic carbonaceous particles in particular have been associated with peri-implant bone loss and peri-implantitis.[14] Osseous exposure to those foreign particles activates macrophages to secrete pro-inflammatory cytokines, such as TNF-α, interleukin (IL)-1b, IL-6. This in turn stimulates the differentiation of osteoclast precursors into mature osteoclasts. The increased osteoclast activity associated with a foreign-body reaction may result in peri-implant bone resorption.[15] Foreign materials 0.2 µm to 7.2 µm in size are especially classified as highly pro-inflammatory.[16-18] If those particles detach from the implant surface during the implant insertion process, macrophages take up the particles by phagocytosis and subsequently release pro-inflammatory cytokines as described above. In addition, this leads to the expression of matrix metalloproteinase (MMP-8) with an expanding zone of soft-tissue damage and inflammation.[13]

The exposure of implant threads to the oral environment with subsequent bacterial colonialization is often described as the "beginning of a bad ending". One might expect to see mainly bone loss in the crestal area and translucencies in the corresponding radiographs. However, significant carbonaceous contaminants at the apical region of implants may well lead to bone resorption that look in radiographs like a periapical lesion of an implant. (Figures 10 and 11))

An even greater threat to the healing of an implant is posed by thin-layered residues of highly aggressive cell-toxic cleaning agents (e.g. DBSA) or quaternary ammonium compounds (biocides), as identified by Time-of-Flight Secondary Ion-Mass Spectrometry (ToF-SIMS) on the surface of some brand-new implants. Even in low concentrations, these chemicals are directly toxic to cells and do not promote implant healing at all.

All of the implants with reported significant impurities carried the CE mark or had US Food and Drug Administration or Health Canada's HPFB clearance. Ultimately, contaminated medical devices, even in sterile packaging, can be harmful to patients and lead to implant failure related to peri-implantitis stemming from inflammatory reactions to those impurities.

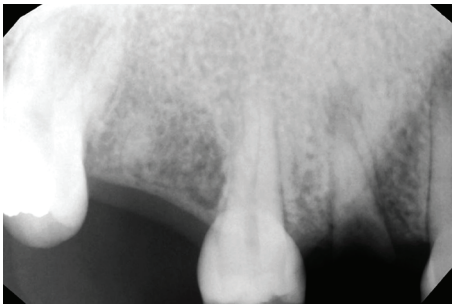

Figure 6: Preoperative of the right maxillary quadrant demonstrating a residual root at the planned implant site.

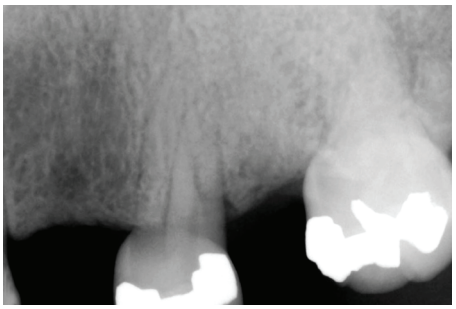

Figure 7: Preoperative of the left maxillary quadrant demonstrating a healed site at the planned implant site.

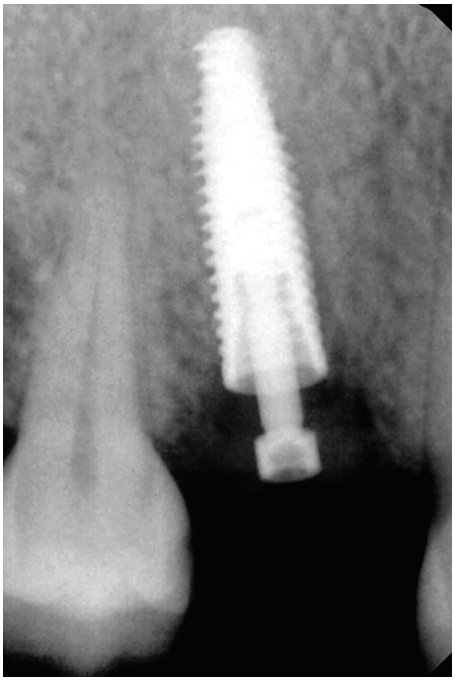

Figure 8: Post placement radiograph of an implant placed into a healed site at the maxillary right 1st premolar.

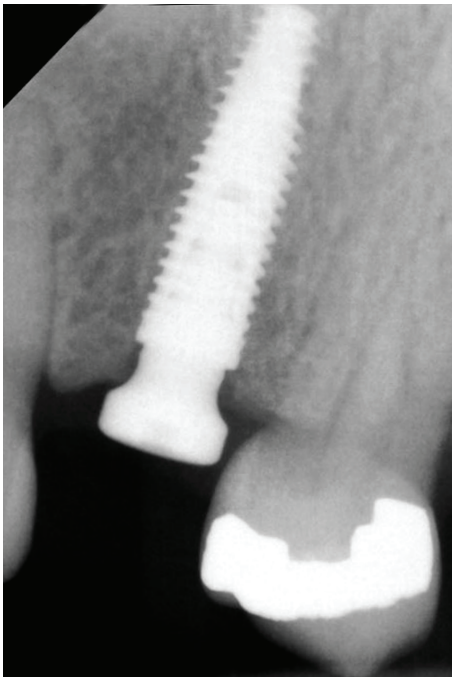

Figure 9: Post placement radiograph of an implant placed into a healed site at the maxillary left 1st premolar.

Case examples:

As an illustrative example, implants placed into healed sites do not have the potential bacterial issues as those placed into immediate sites. Additionally, when bone loss is noted during the integration period on a non-loaded implant that is not observed in the crestal portion of the implant, but confined to the apical area overloading and residual issues related to the condition of the tooth just extracted are removed from the equation.

A 32-year-old female patient with no significant medical history and no none allergies presented for replacement of missing maxillary right and left 1st premolars. The right side site revealed a retained root tip which exhibited a small periapical lesion, (Figure 6) the left side site was well-healed and did not not exhibit any pathology as pathology was noted on the initial radiograph (Figure 7) The right-side root tip was carefully elevated and removed with periotomes and elvatomes (TBS Instruments) and the socket debrided and rinsed with chlorhexidine gluconate 0.12% followed by a saline flush. After conventional osteotomy preparation a 3.75 x 13 mm implant was placed with good stability and excellent ISQ measurements (74-77) sufficient for a one-stage protocol (IDx Osstell Sweden) with a transmucosal healing abutment. The tissue was then closed around the abutment with 4-0 Vicryl sutures (Ethicon). The left site followed a similar protocol in a healed site of natural bone with a one-stage healing collar based on ISQ values were 77/77. Post insertion radiographs were taken to document implant positioning relative to the anatomy. (Figures 8 and 9) The patient was seen at two weeks for suture removal and healing check.

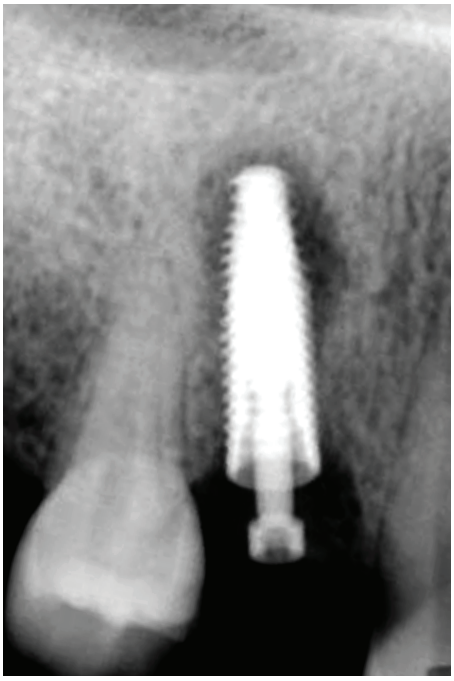

Figure 10: Radiograph of the implant in the posterior maxillary premolar site at 8 months post placement and unloaded demonstrating peri-implantitis at the apical half of the implant with no noted bone loss at the crestal half of the implant.

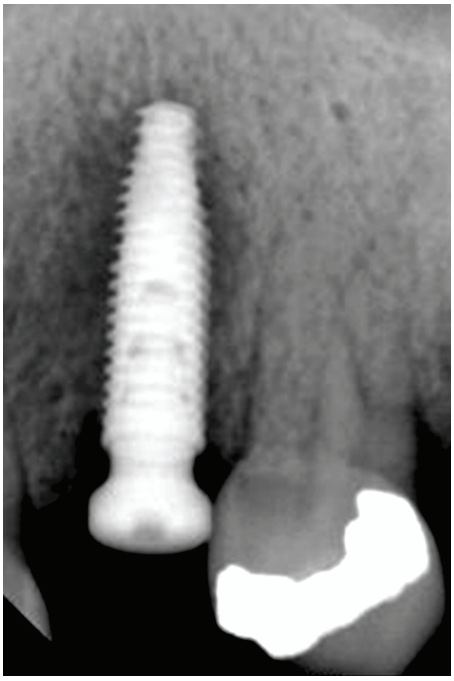

Figure 11: Radiograph of the implant in the posterior left maxillary premolar site at 8 months post placement and unloaded demonstrating peri-implantitis at the apical half of the implant with no noted bone loss at the crestal half of the implant.

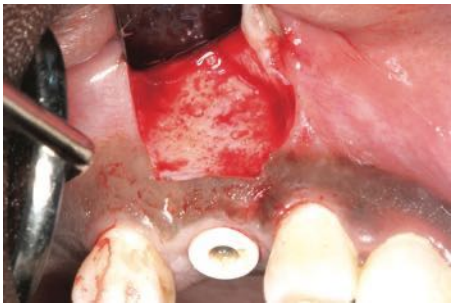

Figure 12: Clinical appearance of the buccal plate overlaying the implant in the upper left maxillary premolar area following elevation of a full thickness flap.

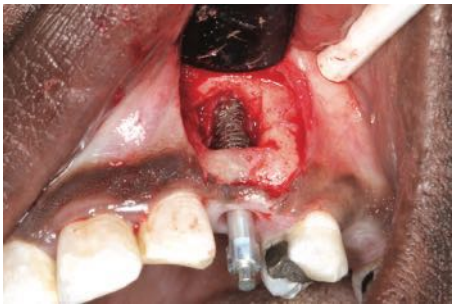

Figure 13: The buccal plate was carefully removed utilizing Piezosurgery exposing the apical portion of each implant.

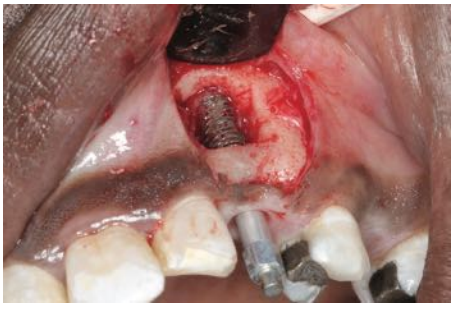

Figure 14: ISQ was tested with a SmartPeg demonstrating a value of 77 indicating implant stability despite the apical defect, so osseous repair could be performed verses explantation.

At 8 weeks post implant placement the patient returned to monitor the progress of soft and hard tissue healing. A periapical radiograph was utilized to evaluate any changes in the implant's appearance in relationship to the surrounding bone. The radiograph's for both implants revealed a radiolucent "halo" at the apical 1/3 – 1/2 of the implant while the coronal aspect of the bone remained stable. (Figures 10 and 11) The patient was informed about the unusual clinical presentation and was prescribed Amoxicillin to reduce the bacterial count although there was no exudate or fistula present. The proposed intervention procedures were reviewed with the patient. Two potential etiologies were discussed: (1) the implants may be failing; and (2) there may be a specific issue occurring only at the apex of each implant. The patient was then re-scheduled for a surgical intervention the following week while the antibiotics were present in her system. The healing collars were removed and objective ISQ measurements were recorded for both maxillary implants and both registered a stable 75 - 77. Based on the stable ISQ values, it was determined that both implants were integrated enough for loading, but due to the radiolucent presentation it was explained to the patient that a surgical flap procedure could be accomplished to assess the radiolucent areas, clean out and potential pathogens, place bone grafts if applicable, and with time the areas should fully heal. Patient consented to treatment.

The surgical intervention was similar for both right and left implant receptor sites. Local infiltration with 2% Lidocaine with 1:100,000 epinephrine in the vestibule over the implant sites. Right and left semi-lunar full thickness flaps approximately 5 mm below the gingival crest revealed intact buccal plates without apparent fenestration. (Figure 12) The buccal plate was carefully removed utilizing Piezosurgery (Mectron Columbus, Ohio) exposing the apical portion of each implant. (Figure 13) The SmartPeg (silver post) secured to the implant recorded the ISQ values demonstrating a value of 77 indicating stability of the implant and repair of the apical defect could be performed versus explantation. (Figure 14) The thickness of the buccal cortical plate can be visualized in Figures 16 and 17. The areas were then mechanically debrided, rinsed with chlorhexidine gluconate 0.12% followed by thorough flushing with sterile saline. 0.5 cc's of mineralized cortico-cancellous bone (Maxxeus Kettering, OH) was packed within each defect and then covered with dehydrated human deepithelialized amnion-chorion membranes (BioXclude Snoasis Medical Golden CO). Soft tissue was repositioned, and primary closure achieved with 5-0 Glycolon sutures (RESORBA Medical GmbH, Germany). The patient was then advised to rinse with H2O / salt water 3-4 times per day for ten days.

Conclusion:

As dental implant use continues to increase globally, patients receiving those devices need to be carefully monitored during the lifetime of the restoration. Early identification of peri-implant mucositis and intervention

is key to preserving the bone surrounding the implant, preventing progression to peri-implantitis, and improving long-term clinical results. Peri-implantitis is more prevalent than previously accepted as dental practitioners gain more understanding of the signs and symptoms of this inflammatory disease. Factors that contribute to peri-implant disease include smoking, certain systemic health issues such as uncontrolled diabetes, and lack of follow-up.

Implant surface quality may play a role in peri-implant disease. Whether the implants are made of titanium or ceramic, the implant's surface must be free of foreign particles after removal from the sterile packaging. Those particles are not visible to the naked eye or with magnification (loupes or microscope). While in most cases of peri-implantitis or implant loss clinicians assume the problem lies with the patient, the analysis results of sterile-packaged implants as cited earlier suggest that the medical device in use should also be considered as a possible cause for an inflammatory reaction and potential trigger of peri-implantitis upon insertion. Clinicians can be assured they are using a sterile and clean implant after a thorough SEM analysis has proven cleanliness across different batches of the implant product and sufficient clinical documentation stating so is made available.[19-21]

The case presentation represented two implants placed in the same patient. One implant was placed in an immediate root extraction site which exhibited periapical pathology (right side), while the left side implant was placed in a ling healed site of native bone. Drilling protocols were identical, implant manufacturer and sizes were identical, manufacturer's LOT numbers were confirmed to be different, insertion torques were similar, and initial stability was objectively measured with resonance frequency analysis (ISQ) and found to be suitable for a one-stage protocol with healing collars. Since it was possible to objectively measure implant stability over time, the ISQ values indicated that there was no change in stability of both implants over the initial 10 weeks of healing although surrounding apical bone was compromised without fenestration of the buccal plates. While it could be argued that the right-side implant may have been compromised by the cystic non-purulent root lesion, the left side implant was placed in native healed bone without any pathology present. Apical bone loss around an implant is not a usual presentation post placement. Those cases where the implant has not been restoratively loaded and apical bone loss is noted prior to restoration, after osseointegration in prior healed sites, it is postulated that the resulting peri-implantitis may be a result of surface contamination during implant manufacturing and/or subsequent sterile packaging. ■

Disclosure:

Dr. Ganz is a member of the CleanImplant Foundation scientific advisory board. Dr. Duddeck is Managing Director of the CleanImplant Foundation. Dr. Kurtzman had no disclosures to report. Dr. Serota is the North American representative of the CleanImplant Foundation.

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