Silicon Nitride ($\text{Si}_3\text{N}_4$) Implants: The Future of Dental Implantology?

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For decades titanium has been the preferred material for dental implant fabrication, with mechanical and biological performance resulting in high clinical success rates. These have been further enhanced by incremental development of surface modifications aimed at improving speed and degree of osseointegration and resulting in enhanced clinical treatment options and outcomes. However, increasing demand for metal-free dental restorations has also led to the development of ceramic-based dental implants, such as zirconia. In orthopedics, alternative biomaterials, such as polyetheretherketone or silicon nitride, have been used for implant applications. The latter is potentially of particular interest for oral use as it has been shown to have antibacterial properties. In this article we aim to shed light on this particular biomaterial as a future promising candidate for dental implantology applications, addressing basic specifications required for any dental implant material. In view of available preclinical data, silicon nitride seems to have the essential characteristics to be a candidate for dental implants material. This novel ceramic has a surface with potentially antimicrobial properties, and if this is confirmed in future research, it could be of great interest for oral use.

Key Words: silicon nitride, implantology, biomaterials

INTRODUCTION

Since the discovery of osseointegration, dental implantology has been consistently evolving to the point where carefully executed implant treatments deliver very high short- to medium-term success and survival rates. Dental implants have revolutionized oral rehabilitation procedures and allow improved function and enhanced overall quality of life. Until now, the widely accepted ideal material for dental implants has been titanium (Ti) or Ti alloys, with modified microroughened surfaces becoming the norm with passing years.

Nevertheless, with the global boom in dental implant placement, new clinical challenges have arisen. In particular, there has been a large increase in peri-implant inflammatory diseases, particularly peri-implantitis (PI), which is of bacterial etiology and is characterized by mucosal inflammation, breakdown of peri-implant tissues, and bone loss, thus undermining the prognosis of the implant-supported restoration and sometimes necessitating implant removal. Although a number of different management strategies have been advocated for treatment of PI, these all have unpredictable and often unsuccessful outcomes in terms of infection control and prevention of further bone resorption. These clinical issues suggest the potential benefits that might be gained from development of antibacterial implant surfaces or coatings for future dental implants design.

In addition, there has been a renewed search for metal-free implants due to concern about metal corrosion. In fact, there has been concern that Ti corrosion-reaction products could lead to an increased rate of implant failure as well as immunologically mediated surrounding tissue reactions due to metallic particle accumulation. Also, the potential passage of these particles to other parts of the body has also been demonstrated in experimental studies. Furthermore, an increased patient demand for metal-free dental implants rehabilitation has been noticed in everyday practice. All of these reasons have contributed to the introduction of ceramic Zirconia (Zi) dental implants to the market. The latter have shown biocompatibility/mechanical resistance comparable to that of Ti alloy implants. They are also considered to be more biologically inert than Ti. Furthermore, less plaque accumulation has been reported around Zi in comparison to Ti, although this superiority was not consistently reported in all studies. Nevertheless, available data on the clinical performance of Zi and Ti is still scarce, especially when dealing with initial bone resorption and PI prevalence. Hence, it is still unclear if Zi could be a reliable alternative to Ti.

Recent research has investigated a number of new materials for application as orthopaedic surgical implants, such as polyetheretherketone (PEEK) and silicon nitride ($\text{Si}_3\text{N}_4$). In

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fact, Si₃N₄ has high mechanical performance as it was first used in heat engines such as in NASA’s rocket engines.¹⁸ Of potential interest for dental implant application, Si₃N₄ is also reported to possess antibacterial properties and to be better tolerated than any Ti oxide layer particles that may be released in hip periprosthetic tissues, thus possibly reducing the risk of aseptic loosening.¹⁹ Even though, in theory, aseptic failure is less likely to occur in or around the oral cavity, which is septic by nature, multiple studies have pointed out that foreign-body reactions, initiated by Ti oxide wear particles (implant/abutment connection) could be one reason for the initial bone resorption/remodeling associated with implant loading.¹⁹,²⁰ In certain cases, this reaction might favor the development of bacterial-mediated PI. Although the dental community has not fully embraced the concept of foreign-body initiated peri-implant bone resorption, it should be considered when exploring new materials for dental implants use.

Furthermore, the reported antibacterial properties of Si₃N₄ may offer a crucial advantage in comparison to available Ti or Zi dental implants, as these properties might help to tackle the constant rise of PI prevalence and to control its increasing public health burden. The aim of this article is to review the properties of the novel ceramic material Si₃N₄ and discuss its possible application for use as a dental implant material. This was done by reviewing available scientific data on Si₃N₄ orthopedic/facial appliances as well as general mechanical and antibacterial properties were reviewed to assess if a possible analogy with dental implant materials could be drawn. All article types (in vitro, in vivo, human trials) except case reports and editorials were included as the objective of this article was not to conduct a systematic review. In fact, as no dental studies have been published on this material, our aim was to examine the available literature to confirm the possibility of using Si₃N₄ as a dental implant material.

Materials and Methods

Data Collection

An initial search was done on the Medline database advanced search tool. Limiting the search to titles/abstracts, the following Mesh Keywords combinations were used: “osseointegration” OR “bone” OR “bacterial” OR “mechanical” OR “implant” AND “silicon nitride.” Articles concerning silicon nitride use in bone as well as general mechanical and antibacterial properties were reviewed to assess if a possible analogy with dental implant materials could be drawn. All article types (in vitro, in vivo, human trials) except case reports and editorials were included as the objective of this article was not to conduct a systematic review. In fact, as no dental studies have been published on this material, our aim was to examine the available literature to confirm the possibility of using Si₃N₄ as a dental implant material.

Results

Antibacterial Activity

Gorth et al²¹ first examined in vitro bacterial proliferation on Si₃N₄, Ti, and PEEK over a 72-hour time frame. Their study revealed lower bacterial counts and reduced biofilm development on the tested material in comparison to the control Ti and PEEK material. An interesting finding was that this tendency was also present for Gram-negative bacterial strains.

Pezzotti et al²² cultured Porphyromonas gingivalis strains on Si₃N₄ disks up to 6 days. They found that chemical interactions between disk surfaces (especially sintered surfaces) and bacterial metabolic components led to P gingivalis lysis and bacterial metabolism downfall. The formation of peroxynitrite, a specific cytotoxic anion, is thought by the authors to initiate the bacterial membrane lysis. Another recent in vitro study tested the bacterial proliferation of Staphylococcus epidermidis or Escherichia coli on PEEK, Ti, and Si₃N₄ disks.²³ In the study by Webster et al,²⁴ authors performed in vivo inoculation of S epidermidis around implanted Si₃N₄, Ti, and PEEK implants in rat calvariae. At 3 months after surgery, percentages of newly formed bone on implant surfaces were 5%, 9%, and 23% for PEEK, Ti, and Si₃N₄, respectively. Interestingly, at the same endpoint, histologic bacterial count percentages at implant surfaces were 88%, 21%, and 0% for PEEK, Ti, and Si₃N₄, respectively.

Overall, the results of these studies all suggest significant antibacterial activity of Si₃N₄; however, the clinical significance of this potentially important property remains to be demonstrated.

Biocompatibility

After initial doubt about Si₃N₄ biocompatibility, several in vitro reports have confirmed the absence of cytotoxicity of Si₃N₄ in various cell culture models, especially when using sintered Si₃N₄ discs. Kue et al²⁵ and Sohrabi et al²⁶ used an osteoblast-like cell line (MG 63) and found that cell proliferation was not altered on Si₃N₄ disks. Also, osteoblastic cell metabolism was
confirmed by osteocalcin production; inflammatory cytokine production (interleukin 1 beta, tumor necrosis factor alpha) was not increased in cultured cells. This was in accordance with results found in a rabbit marrow stromal cell model in vitro. Seeded cells achieved proper surface attachment on Si3N4. Another in vitro study compared fibroblast (L929 subcutaneous cell line) behavior on Si3N4 or alumina (Al2O3), the latter being a medically used inert ceramic. Cell counts, morphology, and vitality were similar in both groups.

Biocompatibility of Si3N4 has also been shown in vivo: Si3N4 implants placed into intramedullary cavities of rabbit femurs did not initiate any inflammatory reaction, and woven formation, followed by mature bone formation (after 3 months), was observed histologically around placed implants. Interestingly, another animal study comparing Si3N4 and Ti implants placed in rabbit tibias showed no adverse effects and similar bone healing and remodeling in both groups 8 weeks after surgery.

Consistent evidence of Si3N4 biocompatibility has been published, and this was followed by the development of clinical trials to compare performance in different orthopedic indications, such as the SNAP study, which will compare Si3N4 and PEEK cages in lumbar fusion cases.

**Osseointegration**

Animal studies exploring biocompatibility of Si3N4 in bone have found that in a mini-pig model, frontal bone osteosynthesis plates and screws fabricated from Si3N4 were associated with satisfactory bone healing, and histologic/radiographic assessments showed new bone to implant contact at the screw surface. No adverse reactions were noted, and the authors concluded that Si3N4 was suitable for facial bone surgery as a bioinert material.

In the study by Guedes e Silva et al., bone to implant contact was achieved in 8 weeks in a rabbit model. The authors calculated that the corresponding human healing period would be 12 weeks to achieve osseointegration. The same team assessed bony formation around Si3N4 implants using scanning electron microscopy. This showed new bone formation at the implant surface, and development of vascular foramens could be seen in the newly formed bone, thus indicating the quality of bone healing.

Webster et al. compared Si3N4 with Ti and PEEK implants in a calvarial rat model. Three months after surgery, histologic sections showed superior new bone formation around tested implants compared with Ti and PEEK (69%, 24%, and 36% for Si3N4, PEEK, and Ti, respectively).

**Mechanical resistance**

Favorable mechanical properties of Si3N4 have been demonstrated in many different mechanical stress tests. Thus, Si3N4 has been introduced into industrial processes because of its high mechanical strength, high fracture/wear resistance, low elasticity, and thermal shock/abrasion resistance. Many fabrication procedural enhancements (e.g., sintering) have been introduced to further develop the material’s mechanical properties. Hence, toughened Si3N4, by incorporation of yttrium oxide (Y2O3) and Al2O3 additives, has shown superior strength and toughness in comparison to Al2O3 ceramic.

Recently, in a Raman-assisted surface toughness assay, biomedical grade Si3N4 showed higher resistance to microfracture compared with Zi-toughened alumina. On the other hand, in mechanical testing, non-oxide ceramics like Si3N4 have shown superior compressive and tensile strengths compared with Ti alloys, though the latter is still the most resistant to fractures compared with Si3N4 or Al2O3.

**Modifiable surface**

To obtain polished or roughened surfaces, Si3N4 surfaces can be modified. Porous Si3N4 surfaces have been developed to achieve sufficient osseointegration, comparable to that of actually used clinical materials. Bone growth into porous Si3N4 has been observed in animal studies. In an experimental sheep model study, cancellous-structured ceramic Si3N4 implants (with porosity and interconnectivity of the surface similar to that of successfully used metal alloys) were implanted in femoral condyles. At 3 and 6 months after implantation, bone growth into the porous surface was observed using scanning electron microscopy. The results were comparable to previously published findings on bone ingrowth onto Ti porous implants. Other fabrication procedures could increase hydrophilicity or negative surface charge, hence potentially enhancing osseointegration and antibacterial activity.

**Radiodensity**

One quality of Si3N4 is that it is partially radiopaque. This is an important feature of any dental implant candidate material. Thus, during radiographic postoperative examinations the practitioner can clearly visualize radiographic implant integration in surrounding tissues. Hence, this seems to eliminate the radiologic artifacts usually observed around Ti implants in 3-dimensional radiographic reconstruction. This was observed in the study by Neumann et al., where Si3N4 ceramic implants showed radiographic density comparable to that of enamel (computed tomography scanning) and no artifacts; thus, surrounding tissue could be distinctively evaluated, especially bone to implant contact continuity.

**Foreign-body reaction**

Although foreign-body reaction to dental implants is not a universally accepted phenomenon, the question of its occurrence has been raised in the dental literature. Thus, wear at the Ti implant/Ti or Zt abutment is thought to possibly generate particles that could trigger a foreign body reaction. The latter could impair local bone turnover and initiate the initial peri-implant bone resorption, as seen in aseptic loosening around hip prosthesis. This could create an ideal environment for a bacteria-mediated inflammatory burst that leads to PI.

On this issue, Si3N4 has been found to show low wear coefficients when in contact with similar material components. Also, Si3N4 wear particles have been found to be potentially soluble in biological fluids.
No data have been found in the literature comparing fabrication costs of Si₃N₄ to that of other currently used materials. Nevertheless, as orthopedic components are already commercialized and ongoing clinical studies have been initiated, we logically hypothesize that fabrication costs need not be a restraining issue for Si₃N₄ implants in comparison to Ti or Zr.

**DISCUSSION**

In summary, Si₃N₄ has shown satisfactory performance for all prerequisites for a dental implant material. Thus, this ceramic, which was first used in industrial applications owing to its high mechanical/high resistance performance, has attracted attention as a candidate for use as a skeletal prosthetic biomaterial. In order to confirm that, extensive research in vitro and in vivo has shown the biocompatibility of this ceramic when used in medical applications. Furthermore, successful osseointegration and intimate bone to implant contact have been demonstrated with Si₃N₄ surfaces, similar to that of the widely used Ti. Also, Si₃N₄ surfaces have the ability to be modified during fabrication procedures in order to enhance mechanical properties and osseointegration: this is specifically interesting for dental implants as Si₃N₄ implants could have a roughened surface with interconnected microporosity. For patients’ growing demand for metal-free dental implant rehabilitation, Si₃N₄ could be an alternative treatment option.

In addition, there is growing concern over the high prevalence of peri-implant inflammatory diseases and the difficulty of managing them; it has become obvious that an antibacterial dental implant might offer significant advantages over conventional materials and might be a valuable aid to control the financial and health burdens of peri-implant diseases. Hence, studies have aimed to achieve this goal, for example, by incorporating Ti surface antibacterial coatings, such as silver nanoparticles or chemical antibacterials (eg, chlorhexidine or antibiotics). Even though this path could be promising, we should ask questions about the wear of metallic nanoparticles and their evacuation in the body as well as availability and timings of any chemical released. Hence, the potential Si₃N₄ surface antibacterial effect seems very promising, as it is intrinsic to the surface chemical composition. Preliminary data are encouraging as they show that bacterial biofilms have difficulty adhering and developing on a specific Si₃N₄ surface in comparison to PEEK or Ti. Also, one study detected a chemical bactericidal effect in vitro on P gingivalis. If this is confirmed in animal and human trials, this characteristic represents a significant advantage for Si₃N₄ implants as this bacterium is highly virulent and implicated in periodontal and peri-implant diseases. Further research should investigate if the same effect occurs on other oral bacterial strains. This could improve implant survival and success rates, thus enhancing dental implant prognosis and patient quality of life.

Finally, even though foreign-body reaction to implant/abutment wear is still not proven, Si₃N₄ is highly resistant to wear. Preliminary data suggest that Si₃N₄ wear particles seem to have low potential to initiate adverse host tissue reactions.

In summary, Si₃N₄ is a promising biomaterial for application in orthopedic and craniofacial surgical procedures in view of its intrinsic mechanical characteristics and modifiable biocompatible surface. The latter has been extensively enhanced in order to achieve the best biological performance when used in bone surgical applications. The main advantage for dental use would be antibacterial surface activity, but this still has to be confirmed in future preclinical and human trials. In addition, the possibility of fabricating prosthetic elements for implant rehabilitation (screws, abutments) should be confirmed if any commercial fabrication would be considered.


