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In vitro comparative study on the mechanical behavior of Zirconia and Polyetheretherketone in applied dental sciences

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Abstract. – OBJECTIVE: Recently, Zirconia and polyaryletherketone (PEEK) have attracted increasing interest as reliable and safe materials in dental applications, mainly because of their good biomechanical characteristics. The aim of this study was to investigate the response to different loads by prosthetic frameworks for supported fixed partial dentures (FPDs), thus simulating osseointegrated implants.

MATERIALS AND METHODS: The specimens were divided into two groups (n= 5 each). Group A: FDPs in zirconia-ceramic; Group B: FDPs in PEEK-composite. These 2 groups were subjected to vertical loads so to evaluate structural deformation; then, they have been analyzed by scanning electron microscopy (SEM) at different magnifications.

RESULTS: In tested samples, different types of mechanical failures have been observed. In Zirconia-specimens, chipping is the main failure noticed in this study, mostly in distal margins of the structure. Also, peek-specimens show failure and fracture.

CONCLUSIONS: Zirconia and PEEK could be considered both good materials, but several investigations are needed to use these materials as an alternative to metals for fixed partial dentures.

Key Words:
Implants, Materials, Fracture, SEM, Zirconia, PEEK.

Introduction

Dental implants are among the most effective technique for replacing missing teeth, and nowadays implantology has become a predictable treatment with high success rates[1-2]. In the last years, the use of several biomaterials has been investigated in regenerative procedures, also using stem cells of oral origin and growth factors; recently, the scaffold-free techniques have become an attracting topic in regenerative dentistry[3-4]. Moreover, both cell-free and scaffold-free approaches could enhance tissue regeneration, thus replacing the lost function and anatomy[5-7]. Implantology is a dental technique continuously improving itself: dental implants ensure a good rehabilitation when a successful osseointegration occurs; nonetheless, also the performance of the prosthetic components of a replaced tooth have a critical role, and the materials used in dental implantology are a strategic pivot not to under evaluate. Different materials and components have been proposed for implants over time, mostly used to produce supported fixed partial dentures (FPD). Titanium, zirconium, PEEK are the main frameworks used in implantology[8]. Recently, also other allotropic materials have been investigated in medical applications, such as graphene and borophene[9-10].

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The abutments have an important role in masticatory cycles; specifically, prosthetic premolars and molars are subjected to high loads. Traditionally, in such rehabilitations, titanium is the material used, due to its mechanical properties[7-8]. Titanium dental implants have been demonstrated to be highly resistant to different types of forces; moreover, the scientific literature has reported a number of studies describing excellent survival rates of prosthetic rehabilitation supported by titanium implants and related abutments[6-12]. Following all these premises, we can consider Titanium as the "gold standard" for dental implants, and for all such techniques aimed to ensure bone reconstruction in all the maxillary regions[11]. Nevertheless, Titanium may also show issues; for example, some cases of allergies to titanium have been reported[12]: in such patients, Titanium could contribute to implant failure due to inflammatory reactions involving bone tissue[13-14]. Furthermore, the recent demand for metal-free dental implants is constantly growing, there-fore, new materials to replace titanium are requested; among these, PEEK (polyether ether ketone) and Zirconia implants have been successfully used in dental implantology[18-20].

PEEK: Properties and Implications

PEEK is a synthetic, tooth biomimetic material, used as a reconstructive biomaterial in orthopedic field for many decades[15-17]. It belongs to the family of polyarylether-ketone and has an aromatic structure. The monomer unit of etheretherketone (- C6H4—O-C6H4—O-C6H4—O-) polymerizes via a step-growth dialkylation reaction involving bis-phenolates that form the polyetheretherketone. A common synthesis method to obtain PEEK is based on the reaction between 4.40-difluorobenzophenone and the disodium salt of hydroquinone in a polar solvent, such as diphenyl-sulphone at 300 °C. It is a semicrystalline, high-temperature friendly, thermoplastic material, with a melting point around 335°C. PEEK has good resistance to chemical erosion, good mechanical strength, and high inertness to other chemicals[8]. It has Young's (elastic) modulus value more like to human bone, compared to other materials (3-4GPa). PEEK is isoelastic with bone, and this could allow a negligible stress shielding effect, and a homogeneous distribution of loads thus avoid a harmful concentration of stress and forces in the same part of the structure[8]. PEEK dental implants are greatly suitable, and indicated, in those patients suffering of allergies; in fact, the low allergenicity of PEEK ensures a safe use also with different alloys, other material, and their micro/nanoparticles released in the surgical site[18]. PEEK can be easily modified by the incorporation of other materials into its structure; for example, the incorporation of carbon fibers can increase its elastic modulus up to 18GPa[19]. In recent years, this polymer has also been modified at the nanoscale level, to improve its bioactivity and, in particular, its osteoconductive properties[20]. Conventionally, PEEK is used after a passive coating with bioactive compounds, such as calcium hydroxyapatite (HAp), by means of plasma-spraying technique[21-22]. Primary applications of PEEK in dentistry are dental implants, implant abutments, fixed crowns, fixed bridges, removable dentures, and other prosthetic components[20-26]. PEEK materials can be projected and produced by means of CAD-CAM technology[20]. CAD-CAM is a performing technique to manufacture dental restorations, allowing to produce peek-based dental prostheses chair-side[23]. In the last decades, CAD-CAM designed composites and polymethylmethacrylate (PMMA) fixed dentures have been demonstrated to hold superior mechanical properties, compared to conventional fixed dentures[24-25]. PEEK is a safe and suitable material, alternative to PMMA. Three-units fixed-partial-dentures manufactured *via* CAD-CAM have been suggested to have a high fracture resistance[26]. The fracture resistance showed by CAD-CAM milled PEEK fixed dentures is much higher than those made of lithium disilicate glass-ceramic (950N), alumina (851N)[27], and zirconia (981-1331N)[28]. Considering the excellent abrasion resistance showed by PEEK material, the overall mechanical properties, and the adequate bonding to teeth and composites, a PEEK fixed partial denture can be considered an effective rehabilitative solution, and it is likely to have a satisfactory survival rate.

Zirconia: Properties and Implications

Zirconia is, chemically, Zirconium dioxide (ZrO_2). It can exhibit three different crystallographic thermolabile structures: 1. monoclinic (up to 1,170°C), 2. tetragonal crystal (between 1,170 and 2,370°C), and 3. cubic (from 2,370 °C to melting point)[29-30]. There are many stabilizing oxides to obtain suitable alloys from pure zirconia; these alloys are able to ensure the conservation of tetragonal form at room temperature[31]. As an example, Yttria (Y2O3) is the most common stabilizer used for

Zirconia in dental applications. Yttrium-stabilized Zirconia polycrystals (Y-TZP) have been applied since the 1990s in dentistry to synthesize frameworks of dental-fixed prostheses by slip-casting or CAD-CAM techniques. Y-TZP reveals a higher mechanical strength than the other feldspar-based porcelains[32-36]. The application of zirconia in dental implants and dental abutments has been introduced due to its superior fracture resistance, respect to other dental ceramics[37-38].

Zirconia is a dental ceramic with high mechanical strength, and good chemical properties; furthermore, it has a Young's modulus (210GPa) close to stainless steel alloy (193GPa)[35-40]. *In vitro* studies on ZrO2 have revealed a fracture toughness of 9 to 10 MPa/m, and a flexural strength ranging from 900 up to 1,200MPa[39-40]. Retrospective *in vivo* studies have revealed no fracture of Y-TZP frameworks over short or medium[35,41] periods of evaluation. However, failures in dental porcelain-to-zirconia assemblies due to fractures along the porcelain-to-zirconia interface have been reported in previous studies[38-41]. Some studies[42-43] have revealed failures in 8% of dental porcelain-to-zirconia interfaces over a period of 36 months, compared with 13% over 38 months. Another study has revealed failures in 15% of the dental porcelain-to-zirconia interfaces over a period of 24 months, and 25% over 31 months. On the other hand, a low failure rate (2.7-5.5%) has been highlighted in metal-ceramic systems over periods of 10 and 15 years[44-45]. In the modern dentistry, patients have increased their demand for a better aesthetics in dental prostheses. Recently, a new type of zirconia, highly aesthetic, has been introduced: Yttria-stabilized tetragonal zirconia polycrystalline (3Y-TZP)[39]. These ceramics are promising materials in the production of dental crowns and fixed dental prostheses (FDP), because of their superior biocompatibility[46], excellent mechanical properties, and improved aesthetics[47-49]. To predict the clinical performance of ceramic and polymer-based dental prostheses (Zirconia and PEEK, respectively), in this study the mechanical behavior of these materials has been investigated. Essentially, we have reproduced a biomechanical system to investigate all the potential relationships between biomechanical properties of 2 different materials, and their mechanical failures, including crack formation, chipping, bond failure and bulk fracture. Other types of failures, such as secondary fractures, marginal discrepancies, and surface roughening are of secondary interest in this study.

Materials and Methods

Twenty titanium fixtures have been embedded in 10 resin mandible section simulators to mimic osseointegrated implants placed in the first premolar and molar areas. The embedded implants were then divided into two groups:

- Group A: five Fixed Partial Dentures (FPDs) in zirconia–ceramic connected to titanium abutments,
- Group B: five FPDs in PEEK-composite connected to titanium abutments.

The specimens allocated into the 2 groups were loaded in a dynamometric testing machine (Instron 5,566, UK), adopting the three-point bending tests configuration. The cyclic load applied to the structures ranged from a minimum of 0N to a maximum of 860N. This load was not applied randomly, but it was consequent to those known parameters characterizing the load on a molar during the chewing cycle (75-89 Kg). A vertical load of 860N was also applied on each sample. Samples showing macroscopic failure were analyzed by scanning electron microscopy (SEM) and compared.

SEM Analysis

The microscopy analysis was performed on those sections close to the fractures. The in-depth analysis at different magnifications aims to understand the differences between zirconia/titanium and peek/titanium fractures, and their potential impact on clinical failure. Surfaces fragments (Figure 1a, b, c) were obtained after 3-points bending mechanical tests: these specimens were characterized by scanning electron microscopy (SEM, Zeiss Supra 120). Briefly, samples were glued on SEM tabs, and have been covered by 12 nm thin Au layer, so to avoid bias in the images because of secondary electrons' emission.

Results

The group A showed a significatively higher number of superficial fractures per each specimen: to explain the fracture pattern, SEM analysis was performed. After careful evaluation of the SEM analysis, it can be affirmed that the initial crack is typically developed on the ceramic surface, then extended to the core of the specimen. At the same time, the design of ceramic crack has been well described: it develops on the core surface, and then it seems to prefer to in-

Figure 1. Samples characterized by scanning electron microscopy (SEM).

volve the veneering ceramic, leading to the failure of whole samples (Figure 2). Chipping has been the first failure analyzed in the tested samples. Microscopic analyses (Figure 3, Figure 4 a, b) show that all the specimens retain a perfect adhesion at the interface level, even if the locations tested are very close to the loading zone. Specimens were classified under their failure mode as adhesive, cohesive or mixed: (1) adhesive, if no remnants of porcelain were found in the metal or zirconia surface; (2) cohesive, if fractures occurred within the porcelain side; (3) mixed, if remnants of porcelain were found in the metal/zirconia surface. Structural defects vary in size between 1 micron and 450 nm, which can be detected only at high magnification and identified in the structure of zirconia. However, has been supposed that such "defects" are a direct result of ceramic porosity. In PEEK composite group an adhesive failure between PEEK and framework was assumed, while a cohesive failure characterizes the detached specimens obtained. It's interesting to notice that near the inner margin of fracture, we have structural defects, spherical air bubble of composite (Figure 5, Figure 6). The failure was obtained for an adhesive breakdown between bonding and PEEK.

Discussion

As emphasized in previous studies[50], zirconia is a brittle and vulnerable ceramic material, and this may become critical when dental implants are immediately exposed to huge masticatory forces. Chipping has been widely investigated as it represents the first failure in zirconia specimens subject to experimental *in-vitro* testing.

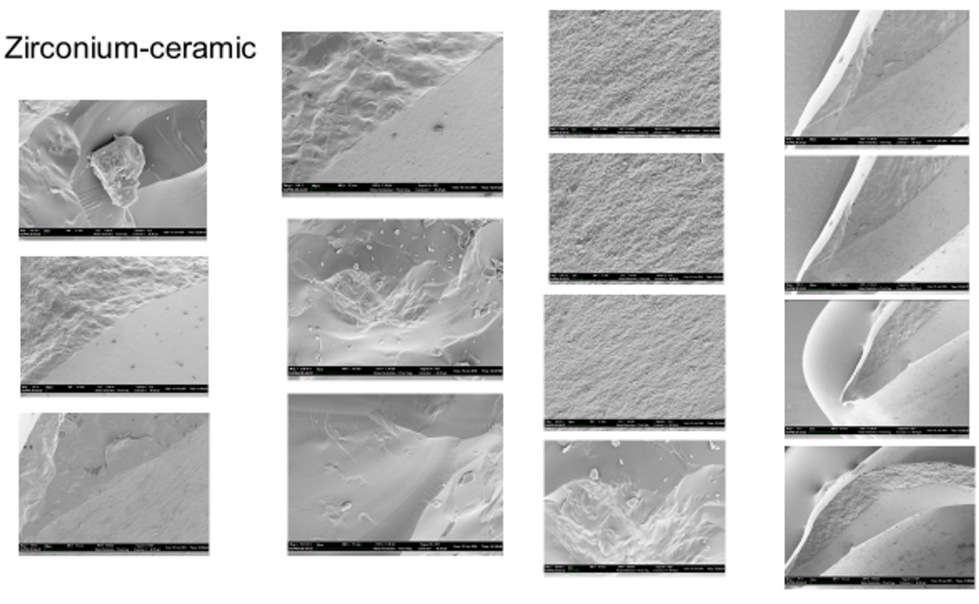

Figure 2. SEM images of zirconia specimens.

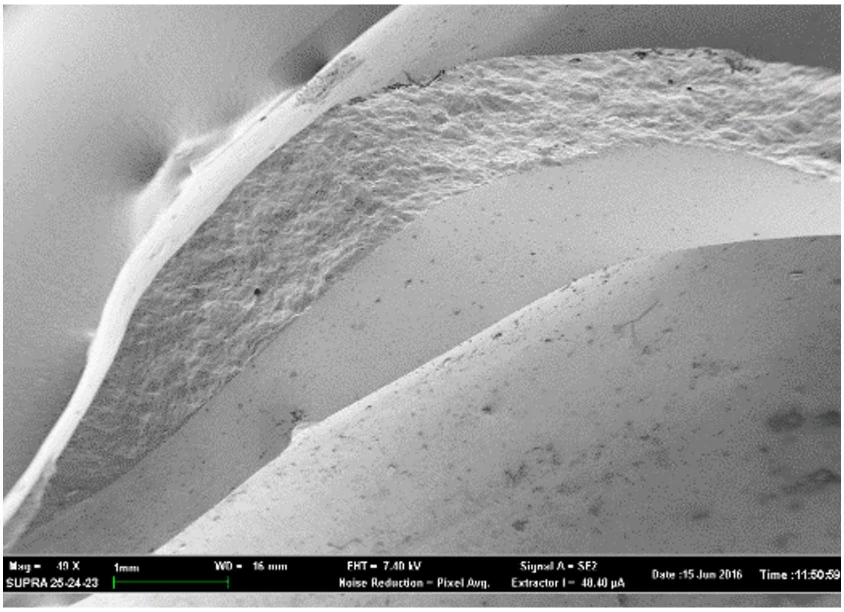

Figure 3. SEM analysis of pontic fragment.

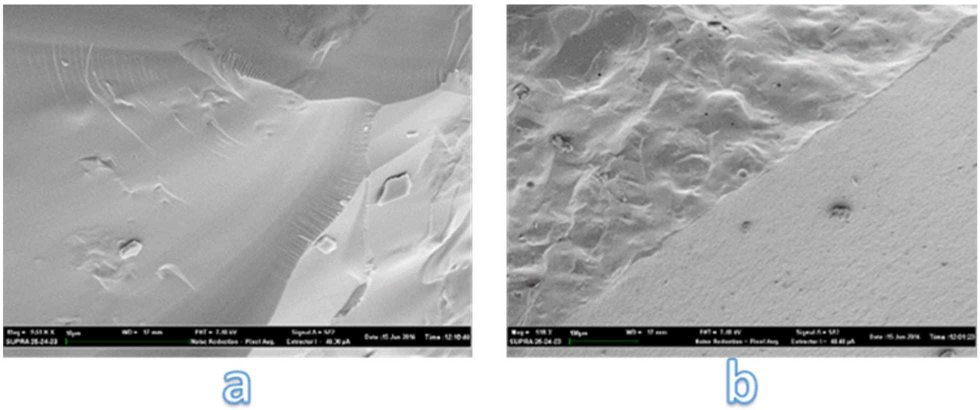

Figure 4. Zirconia ceramic bonding at high magnification **(a)**, small magnification **(b)**.

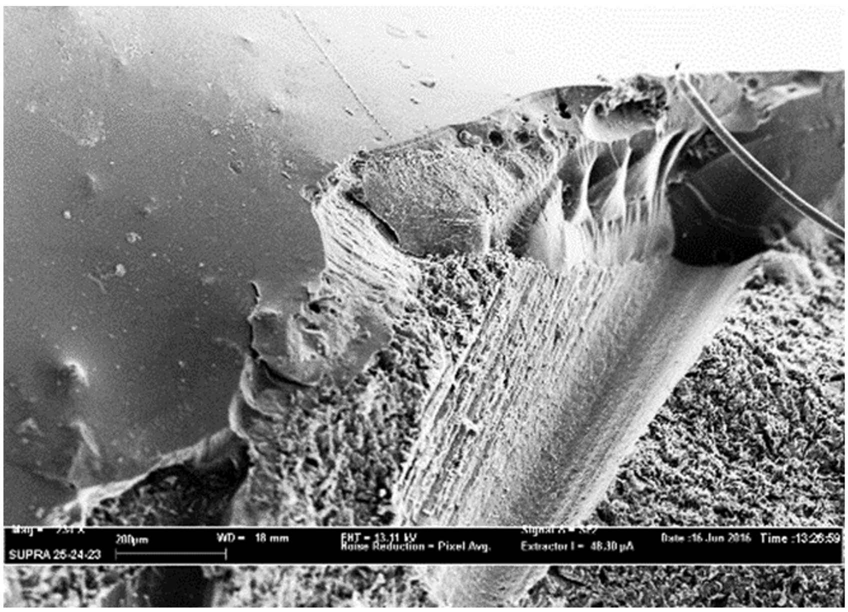

Figure 5. SEM images of PEEK composite samples.

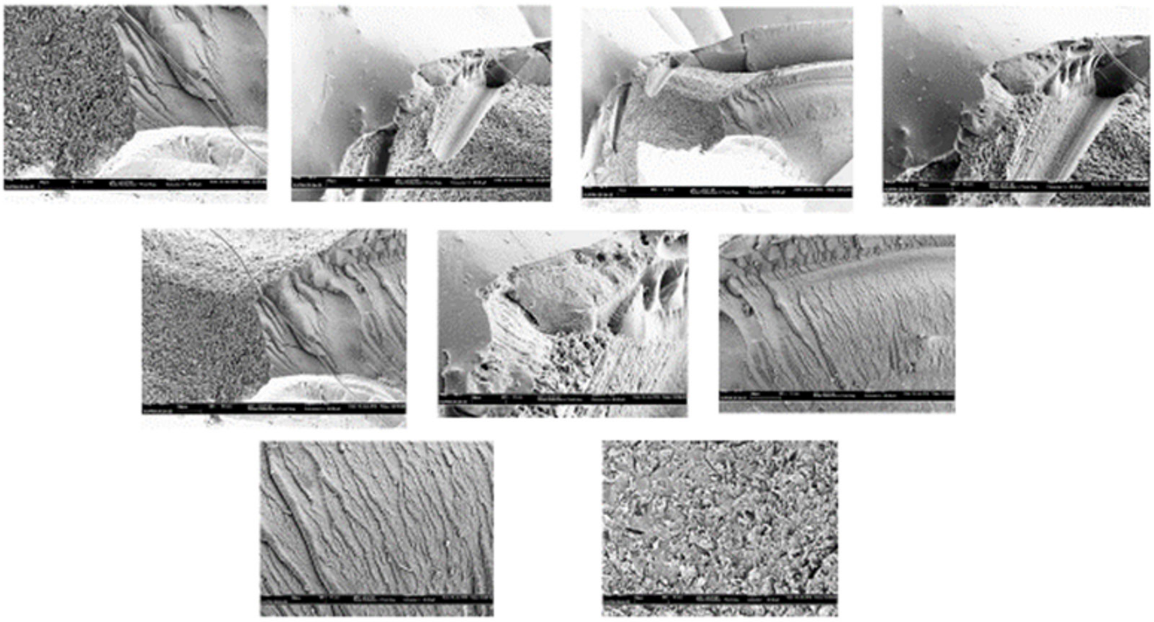

Figure 6. SEM analysis of PEEK specimens near the fracture area.

The failure rate related to chipping reported in our study is 15.2% over than the values reported in the literature[51]. Possible reasons for such higher chipping are both the insufficient bond strength, excessive tensile stress. This situation in especially noticed when a considerable thermal gradient develops through the layers' system upon rapid cooling. The visual analysis of failed samples together with the SEM analysis suggested that the chipping phenomenon is observed in the FDP where it is connected to the abutments. This result could be due to the loss of integrity of zirconia in this area. Evaluating SEM failures obtained with this ceramic, it can be assumed that it is a cohesive failure. Although the chipping occurring, the FDP maintained his elasticity and rigidity. Therefore, a good connection can be supported and the adhesion between these two materials (metal and ceramic) has certainly excellent values.

SEM analysis of peek specimens show that completely failure modes incur when the bond strength exceeds the cohesive strength of bonding resin, agreeing with literature. The PEEK composite groups show a compressive strain state higher than the zirconia ceramic. This data can be easily explained by the differences in elastic moduli of FDP constitutive materials[19]. The rigidity of the zirconia ceramic FDP is significantly higher respect to the PEEK composite. Furthermore, in the peek composite, the higher rigidity contribution is ensured by the composite veneer. By analyzing the study of Taufall et al[52] it is possible to affirm that failure and fracture type is related to the veneering method, showing the same fracture type for digital and conventional veneer: crack starts in the veneering in the pontic region of the connector area. This observation agrees with failure types of this study. The fractographic analysis of fractured samples namely zirconia ceramic and PEEK composites showed a brittle failure pattern for the zirconia samples, with a dump and ripples fractured surfaces. PEEK's surface is a rough surface with an isotropic orientation of fiber. Analyzing its structure, we can consider two different types of failure or fracture: inter-fiber fracture (matrix cracking) and fiber fracture. Experimental evidence has shown that the failure in a laminated composite is often progressive, occurring by a process of damage accumulation. Therefore, the progressive loss of lamina stiffness must be considered as a function of the type of damage predicted.

Delamination is one of the predominant forms of failure in laminated composites due to the lack of reinforcement in the thickness direction. Delamination because of impact or a manufacturing defect can cause significant reductions in the compressive load-carrying capacity and bending stiffness of a structure. The stress gradients that occur near geometric discontinuities promote delamination initiation, trigger intralaminar damage mechanisms, may cause a significant loss of structural integrity. Examples of these stress gradient are ply drop-offs, stiffener terminations and flanges, bonded and bolted joints, and access holes. Clinical applications on such and other disease mode[53,54] can be used as a comparation, to increase the reliability and strongness of this study. Similar clinical *in vivo* applications[55-58] have been also considered to set up this study; the challenge is to use these preliminary results to translate them into clinical applications.

Conclusions

Two different materials with different properties and widely adopted like prosthetic solutions have been compared in this study with the aim to evaluate the clinical performance of these implants. In Zirconia composites chipping phenomenon has been observed. Chipping is usually found in distal margins of the structure, as a direct result of the fragility of ceramics which opposes the slightest, elastic recoil of the structure subjected to bending. The realization of prosthesis in zirconia can offer a high aesthetic satisfaction but a good design and a good evaluation of occlusal loading should be considered to have a good clinical performance. PEEK composite is a new material and its characteristics (high chemical and mechanical resistance against wear, high tensile, fatigue and flexural strengths) make this polymer attractive for industrial usage. In this study PEEK could be considered a "good material", with a great elastic deformation and a high value of vertical displacement. PEEK material can be used for different prosthetic solutions; this is scientific acknowledge. However, several long-term investigations and comparative study will have to verify that PEEK worth being used as the material of choice for definitive reconstructions in the future or that chewing cycle could be a real limit for its long life. Nowadays there is an increasing tendency to use polymer or "metal free" materials. PEEK and Zirconia could satisfy the aesthetic and metal-free demands of the patient. However, analyzing literature and this study, can be confirmed that metal ceramic re-mains a gold standard for dental arches rehabilitation of mandible.

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Data Availability Statement
Data supporting reported results can be found in the private repositories of the authors.

Conflicts of Interest
The authors declare no conflict of interest.

References

1) Jung RE, Pjetursson BE, Glauser R, Zembic A, Zwahlen M, Lang NP. A systematic review of the 5-year survival and complication rates of implant-supported single crowns. Clin Oral Implants Res 2008; 19: 119-130.
2) Pjetursson BE, Thoma D, Jung R, Zwahlen M, Zembic A. A systematic review of the survival and complication rates of implant-supported fixed dental prostheses (FDP s) after a mean observation period of at least 5 years. Clin Oral Implants Res 2012; 23: 22-38.
3) Tatullo M, Codispoti B, Paduano F, Nuzzolese M, Makeeva I. Strategic Tools in Regenerative and Translational Dentistry. Int J Mol Sci 2019; 20: 1879.
4) Tatullo M. About stem cell research in dentistry: Many doubts and too many pitfalls still affect the regenerative dentistry. Int J Med Sci 2018; 15: 1616–1618.
5) Tatullo M, Gandolfi MG. Cells: Are They (Still) Essential for Dental Regeneration? Cells 2021; 10: 498.
6) Codispoti B, Marrelli M, Paduano F, Tatullo M. NANOmetric BIO-Banked MSC-Derived Exosome (NANOBIOME) as a Novel Approach to Regenerative Medicine. J Clin Med 2018; 7: 357.
7) Tatullo M, Marrelli B, Zullo MJ, Codispoti B, Paduano F, Benincasa C, Fortunato F, Scacco S, Zavan B, Cocco T. Exosomes from Human Periapical Cyst-MSCs: Theranostic Application in Parkinson's Disease. Int J Med Sci 2020; 17: 657-663.
8) Verma A. Novel innovations in dental implant biomaterials science: Zirconia and PEEK polymers. Int J Appl Dent Sci 2018; 4: 25-29.
9) Tatullo M, Zavan B, Genovese F, Codispoti B, Makeeva I, Rengo S, Spagnuolo G. Borophene is a promising 2D allo-tropic material for biomedical devices. Appl Sci 2019; 17: 3446.
10) Tatullo M, Genovese F, Aiello E, Amantea M, Makeeva I, Zavan B, Rengo S, Fortunato L. Phosphorene Is the New Graphene in Biomedical Applications. Mater 2019; 12: 2301.

11) Ottria L, Lauritano D, Andreasi Bassi M, Palmieri A, Candotto V, Tagliabue A, Tettamanti L. Mechanical, chemical and biological aspects of titanium and titanium alloys in implant dentistry. J Biol Regul Homeost Agents 2018; 32: 81-90.
12) Thomas P, Bandl WD, Maier S, Summer B, Przybilla B. Hypersensitivity to titanium osteosynthesis with impaired fracture healing, eczema, and T-cell hyperresponsiveness in vitro: case report and review of the literature. Contact Derm 2006; 55: 199-202.
13) Siddiqi A, Payne AG, De Silva RK, Duncan WJ. Titanium allergy: could it affect dental implant integration? Clin Oral Implants Res 2011; 22: 673-680.
14) Fusco A, Dicuonzo G, Dell'Atti V, Tatullo M. Blockchain in Healthcare: Insights on COVID-19. Int J Environ Res Public Health 2020; 17: 7167.
15) Toth JM, Wang M, Estes BT, Scifert JL, Seim III HB, Turner AS. Polyetheretherketone as a biomaterial for spinal applications. Biomaterials 2006; 27: 324-334.
16) Kurtz SM, Devine JN. PEEK biomaterials in trauma, orthopedic, and spinal implants. Biomaterials 2007; 28: 4845–4869.
17) Pokorný D, Fulin P, Slouf M, Jahoda D, Landor I., Sosna, A. Polyetheretherketone (PEEK). Part II: Application in clini-cal practice. Acta Chir Orth Traumatol Cech 2010; 77: 470-478.
18) Brindicci G, Picciarelli C, Fumarola L, Carbonara S, Stano F, Ciracì E, Gramiccia M, Sannella AR, Milella M, De Vito D, Monno R, Monno L. Amoebic hepatic abscesses in an HIV-positive patient. AIDS Patient Care STDS 2006; 20: 606-611.
19) Skinner HB. Composite technology for total hip arthroplasty. Clin Orthop Relat Res 1988; 235: 224-236.
20) Canullo L, Signorini L, Pistilli R, Patini R, Pistilli V, Pesce P. A prospective case series on surgical treatment of cir-cumferential and semi-circumferential defects due to peri-implantitis. Braz Oral Res 2019; 33: 072.
21) Suska F, Omar O, Emanuelsson L, Taylor M, Gruner P, Kinbrum A, Hunt D, Hunt T, Taylor A, Palmquist A. En-hancement of CRF-PEEK osseointegration by plasma-sprayed hydroxyapatite: a rabbit model. J Biomater Appl 2014; 29: 234-242.
22) De Vito D, Monno R, Nuccio F, Legretto M, Oliva M, Coscia MF, Dionisi AM, Calia C, Capolongo C, Pazzani C. Diffusion and persistence of multidrug resistant Salmonella Typhimurium strains phage type DT120 in southern Italy. Biomed Res Int. 2015; 2015: 265042.
23) Signorini L, Faustini F, Samarani R, Grandi T. Immediate fixed rehabilitation supported by pterygoid implants for par-ticipants with severe maxillary atrophy: 1-Year postloading results from a prospective cohort study. J Prosthet Dent 2021; 126: 67–75.
24) Alt V, Hannig M, Wöstmann B, Balkenhol M. Fracture strength of temporary fixed partial dentures: CAD/CAM versus directly fabricated restorations. Dent Mater 2011; 27: 339-347.
25) Stawarczyk B, Ender A, Trottmann A, Özcan M, Fischer J, Hämmerle CH. Load-bearing capacity of CAD/CAM milled polymeric three-unit fixed dental prostheses: effect of aging regimens. Clin Oral Investig 2012; 16: 1669-1677.
26) Cascardi E, Cazzato G, Daniele A, Silvestris E, Cormio G, Di Vagno G, Malvasi A, Loizzi V, Scacco S, Pinto V, Cicinelli E, Maiorano E, Ingravallo G, Resta L, Minoia C, Dellino M. Association between Cervical Microbiota and HPV: Could This Be the Key to Complete Cervical Cancer Eradication? Bi-ology 2022; 11; 1114.
27) Limongelli L, Cascardi E, Capodiferro S, Favia G, Corsalini M, Tempesta A, Maiorano E. Multifocal Amelanotic Me-lanoma of the Hard Palate: A Challenging Case. Diagnostics 2020; 10: 424.
28) Kolbeck C, Behr M, Rosentritt M, Handel G. Fracture force of tooth–tooth-and implant–tooth-supported all-ceramic fixed partial dentures using titanium vs. customised zirconia implant abutments. Clin. Oral Implants Res 2008; 19: 1049-1053.
29) Subbarao EC. Zirconia-an overview. Adv Ceram 1981; 1: 1-24.
30) Kisi EH, Howard CJ. Crystal structures of zirconia phases and their inter-relation. In Key Eng Mater 1998; 153: 1-36.
31) Osman RB, Swain MV. A critical review of dental implant materials with an emphasis on titanium versus zirconia. Mater 2015; 8: 932-958.
32) Zarone F, Russo S, Sorrentino R. From porcelain-fused-to-metal to zirconia: clinical and experimental considerations. Dent Mater 2011; 27: 83-96.
33) Spagnuolo G, Ametrano G, D'Antò V, Formisano A, Simeone M, Riccitiello F, Amato M, Rengo S. Microcomputed tomography analysis of mesiobuccal orifices and major apical foramen in first maxillary molars. Open Dent J 2012; 6: 118-125.
34) Parrotta EI, Scalise S, Scaramuzzino L, Cuda G. Stem Cells: The Game Changers of Human Cardiac Disease Modelling and Regenerative Medicine. Int J Mol Sci 2019; 20: 5760.
35) Tamma R, Limongelli L, Maiorano E, Pastore D, Cascardi E, Tempesta A, Carluccio P, Mastropasqua MG, Capodi-ferro S, Covelli C, Pentenero M, Annese T, Favia G, Specchia G, Ribatti D. Vascular density and inflammatory infiltrate in primary oral squamous cell carcinoma and after allogeneic hematopoietic stem cell transplantation. Ann Hematol 2019; 98: 979–986.
36) Tinschert J, Zwez D, Marx R, Anusavice KJ. Structural reliability of alumina-, feldspar-, leucite-, mica-and zirconia-based ceramics. J Dent 2000; 28: 529-535.
37) Garvie RC, Hannink RH, Pascoe RT. Ceramic steel? Nature 1975; 258: 703-704.
38) Riccitiello F, De Luise A., Conte R, D'Aniello S, Vittoria V, Di Salle A, Calarco A, Peluso, G. Effect of resveratrol re-lease kinetic from electrospun nanofibers on osteoblast and osteoclast differentiation. Eur Polym J 2018; 99: 289-297.

39) Piconi C, Maccauro G. Zirconia as a ceramic biomaterial. Biomaterials 1999; 20: 1-25.
40) Christel P, Meunier A, Heller M, Torre JP, Peille CN. Mechanical properties and short-term in vivo evaluation of yttrium-oxide-partially-stabilized zirconia. J Biomed Mater Res 1989; 23: 45-61.
41) Raigrodski AJ, Chiche GJ, Potiket N, Hochstedler JL, Mohamed SE, Billiot S, Mercante DE. The efficacy of pos-terior three-unit zirconium-oxide–based ceramic fixed partial dental prostheses: A prospective clinical pilot study. J Prosthet Dent 2006; 96: 237-244.
42) Sailer I, Feher A, Filser F, Lüthy H, Gauckler LJ, Schärer P, Hämmerle CHF. Prospective clinical study of zirconia posterior fixed partial dentures: 3-year follow-up. Quintessence Int 2006; 37: 685-693
43) Swain MV. Unstable cracking (chipping) of veneering porcelain on all-ceramic dental crowns and fixed partial den-tures. Acta Biomater 2009; 5: 1668-1677.
44) Walter M, Reppel PD, Böning K, Freesmeyer WB. Six-year follow-up of titanium and high-gold porcelain-fused-to-metal fixed partial dentures. J Oral Rehabil 1999; 26: 91-96.
45) Coornaert J, Adriaens P, De Boever J. Long-term clinical study of porcelain-fused-to-gold restorations. J Prosthet Dent 1984; 51: 338-342.
46) Manicone P F, Iommetti PR, Raffaelli L. An overview of zirconia ceramics: basic properties and clinical applications. J Dent 2007; 35: 819-826.
47) Miyazaki T, Nakamura T, Matsumura H, Ban S, Kobayashi T. Current status of zirconia restoration. J Prosthodont Res 2013; 57: 236-261.
48) Zhang Y. Making yttria-stabilized tetragonal zirconia translucent. Dent Mater 2014; 30: 1195–1203.
49) Vichi A, Carrabba M, Paravina R, Ferrari M. Translucency of ceramic materials for CEREC CAD/CAM system. J Esthetic Restor Dent 2014; 26: 224-231.
50) Payer M, Arnetzl V, Kirmeier R, Koller M, Arnetzl G, Jakse N. Immediate provisional restoration of single-piece zir-conia implants: a prospective case series–results after 24 months of clinical function. Clin Oral Implants Res 2013; 24: 569-575.
51) Sailer I, Fehér A, Filser F, Gauckler LJ, Lüthy H, Hämmerle CHF. Five-year clinical results of zirconia frameworks for posterior fixed partial dentures. Intern J Prosthodont 2007; 4: 20.
52) Taufall S, Eichberger M, Schmidlin PR, Stawarczyk B. Fracture load and failure types of different veneered polyether-etherketone fixed dental prostheses. Clin Oral Investig 2016; 20: 2493-2500.
53) De Angelis MT, Santamaria G, Parrotta EI, Scalise S, Lo Conte M, Gasparini S, Ferlazzo E, Aguglia U, Ciampi C, Sgura A, Cuda G. Establishment and characterization of induced pluripotent stem cells (iPSCs) from central nervous system lupus erythematosus. J Cell Mol Med 2019; 23: 7382-7394.
54) Cicinelli E, Ballini A, Marinaccio M, Poliseno A, Cosci MF, Monno R, De Vito D. Microbiological findings in en-dometrial specimen: our experience. Arch Gynecol Obstet 2012; 285: 1325-1329.
55) Giancotti A, Garino F, Mampieri G. Lower incisor extraction treatment with the invisalign® technique: Three case re-ports. J Orthod 2015; 42: 33-44.
56) Condò R, Mampieri, G, Giancotti A, Cerroni L, Pasquantonio G, Divizia A, Convertino A, Mecheri B, Maiolo L. SEM characterization and ageing analysis on two generation of invisible aligners. BMC Oral Health 2021; 21: 316.
57) Condò R, Mampieri G, Pasquantonio G, Giancotti A, Pirelli P, Cataldi ME, La Rocca S, Leggeri AA, Notargiacomo A, Maiolo L, De Filippis P, Cerroni L. In vitro evaluation of structural factors favouring bacterial adhesion on orthodon-tic adhesive resins. Materials 2021; 14: 2485.
58) Huang ZL, Shi JY, Zhang X, Gu YX, Lai HC. The influence of the shock-absorbing restorative materials on the stress distributions of short dental implant rehabilitations. Eur Rev Med Pharmacol Sci 2021; 25: 24-34.