Ceramic biomaterials in dentistry: chemical structure and biosafety – a review and a bibliometric visual mapping on Scopus database

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Abstract. – OBJECTIVE: A biomaterial is any non-pharmaceutical substance or a mixture of synthetic or natural substances used independently or as part of a system for any amount of time with the aim of mending, supporting the growth, or replacing tissues, organs, or functions of the body. It is a non-renewable material that interacts with biological systems. The purpose of this study was to assess the advances in ceramic biomaterials and perform a bibliometric mapping of the literature on the subject.

MATERIALS AND METHODS: The Scopus database was used for manuscript screening (Elsevier, Amsterdam, The Netherlands). The effect of the scientific production has been assessed using scientometric citational metrics.

RESULTS: A total of 2,554 pieces of literature, including 2,234 papers, 170 conference proceedings, 109 reviews, 35 book chapters, 3 editorial letters, and 3 short surveys, were retrieved. Based on the research conducted, it is noted that ceramic materials are high-performing by being porous or glassy and can, therefore, serve as fillers, covering materials, and scaffolds in medicine and biotechnology.

They are frequently employed not only in orthopedic and maxillofacial surgery but also in dentistry for dental prostheses.

CONCLUSIONS: Materials monitoring methods enable us to track the three-dimensional evolution of ceramics' volume, as well as flaws or micro-cracks.

Key Words:
   Biomaterials, Ceramics, Dental materials, Infection, Periimplantitis, SARS-CoV-2.

Introduction

Thanks to advances in the understanding of materials and the discovery of new analytical methods, control devices, and materials, it is now possible to develop new ways of selecting raw materials. These materials are then used to create advanced materials with specific physical and chemical properties that are desired. Therefore, there is a growing need to choose and create materials with high standards that are able to withstand complex conditions, especially in a biological environment such as that of the oral cavity[1-4]. Therefore, a search for advanced additives or biomaterials is required, which, in addition to the-

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se specific physicochemical properties, should mimic biological materials (such as teeth) once replaced (biocompatible)[4]. Biomaterials come in contact with biological systems, such as human tissues and fluids, but they are not pharmaceutical materials[5,6]. For this reason, they must be biocompatible, bioabsorbable, inserts or surgical materials made from metals, alloys, polymers, glasses (bio-glass), carbon fiber, composites, and biological materials. The biomaterials are modeled to the shape and size of the organic part to be replaced, and their surface can be suitably shaped or have a porous surface to perfectly adhere to the tissues, skeleton, etc. So, with these requirements, biomaterials are not simple inert materials but are directly related to the biological environment. They can react with the tissues and body fluids, but the resulting products should not be toxic to the organism like a xenobiotic substance[2,7]. There is a need for interdisciplinary definitions, such as biocompatibility, bioabsorbency, and toxicity, along with bioethics, for the various materials to be used in the medical field[8]. It has been found[9] that for the normal functioning of the biochemistry of the organism, the electrolytes (inorganic part) must interface in harmony with organic molecules (such as proteins, cells, membranes, DNA, etc.). Generally, ceramics comprise inorganic materials consisting of metallic and non-metallic components chemically bonded together. It can be both crystalline and non-crystalline, and very common is the structure in which a crystalline phase is dispersed in a non-crystalline one. Their main feature is their high resistance to high temperatures, low weight, hardness, wear, and corrosion, as well as the usual insulating behavior[5,10]. Regarding the wide range of ceramics, carbides, nitrides and/or oxides, they find various applications, especially in the field of high temperatures and electronic requirements. The techniques for the production of ceramic powders and finished products are constantly evolving in order to reduce some intrinsic disadvantages of ceramics, such as their fragility. Classification of bioceramics (such as dental ones) is based on their microstructure. The factors that can influence the microstructure of a dental ceramic are many and include matrix, grain size, crystalline content (low or high), porosity (zero, low or high), crystalline phases (single or multiple), and crystal arrangement (random or aligned). In fact, ceramics can be classified into four basic categories and subclasses based on their microstructure.

The first are glass-based materials (mainly silicon), and the second are those based on glass (mainly silicon) with crystalline fillers. The third category has polycrystalline (mainly alumina) with glass fillers and four polycrystalline ones with alumina and zirconia[11,12]. Categories one and two can be divided into three subclasses of ceramics: i) feldspathic vitreous with low to moderate leucite content, ii) glass-ceramics with high leucite content (approximately 50%), and iii) glass-ceramics based on lithium disilicate. Another alternative classification divides ceramic materials for dental use into six categories according to the ceramic material: i) high-glass content ceramic, ii) low-glass content, iii) glassless polycrystalline, iv) hybrid vitreous, v) low-glass content and bimodal filler, and vi) nanostructured polycrystalline. They serve in processes where high temperatures with low electricity and thermal conductivity are required. Hence, they have good mechanical properties and electrical behavior, and a common ingredient is clay, which is argyle. The class of ceramic materials also includes refractory ceramic materials. Refractory ceramics are composite materials (mixtures of aluminum oxides, magnesium, silicon, and dissolved metal elements) that are highly resistant to heat variations and designed to be resistant to extreme temperatures[13]. Thus, the degree of refractory property is determined by the ratio of fusible oxides to the material being used. Finally, ceramic materials allow the activation of the piezoelectric effect and can convert sound into electricity, a property considered in the transmission design of the electrical signal, where it is most needed.

Ceramic materials with a high glass content are characterized by high aesthetics due to the presence of a high glass content. The main component of glass ceramics is silicon dioxide. Most ceramic veneering materials fall into this category. Feldspar ceramics also fall into this category. This material consists of potassium feldspar, quartz, and kaolin. The additional components, present in variable percentages, include sodium, potassium, calcium, aluminum, and magnesium oxides (necessary for the control of the thermal expansion coefficient) and elements such as zinc, copper, tin, manganese, and cobalt (such as pigments)[14-16]. In this class of materials, fillers (usually crystalline or high melting point glasses) are added to the glass matrix to improve the mechanical properties. Leucite crystals are one of the most used reinforcing materials.

These crystals are usually present in a variable percentage between 40 and 55% by weight. The main function of these crystals is to slow down or deflect crack propagation[17]. The percentage of reinforcing crystals of these materials varies between 35 and 45% in volume, and the diameter of the crystals is between 1 and 5 μm. The flexural strength of leucite-reinforced glass ceramics is approximately 160 MPa[18,19]. Low glass-ceramic materials (glass ceramics) are ceramic materials with a strengthening phase based on the SiO_2-Li_2O system. Before the crystallization process, the reinforcing phase, which represents more than 40% by volume of the material, is made up of lithium metasilicate crystals with a variable size between 0.2 μm and 1.0 μm. The ceramic materials based on lithium disilicate can be used with the hot-pressing technique to create both monolithic and stratified restorations. The high content of reinforcing crystals has led to an improvement in the biaxial flexural strength up to over 400 MPa and a toughness (KIc) higher than 2.75 MPa·m1/2[20,21].

The In-Ceram Alumina system consists of a porous structure of slip-cast alumina, which is infiltrated with lanthanum glass to reduce porosity, improve mechanical properties, and reduce the defects from which cracks can develop. The average size of the grains is between 2 and 5 μm, and the production process ends with applying a ceramic coating. The flexural strength of the In-Ceram Alumina system is approximately 600 MPa[20,21]. The In-Ceram Spinell system contains Magnesium Oxide and Aluminum Oxide ($MgAl_2O_4$) and has a flexural strength of approximately 380 MPa. A further variant of this material category is represented by the In-Ceram Zirconia system, which consists of 67% Al_2O_3 and 33% ZrO_2. The zirconia used is of the type partially stabilized with cerium oxide (12% mol)[22]. This system was designed to combine zirconia's toughness and alumina's translucency. The size of the zirconia grains is greater than one μm. In-Ceram Alumina and In-Ceram Zirconia can be used with the slip-casting technique and as pre-sintered blocks. The biaxial flexural strength is 620 MPa for the In-Ceram Zirconia system. The toughness of the In-Ceram Alumina system varies between 3.1 and 4.61 MPa·m1/2, while that of the In-Ceram Zirconia system is approximately 4.9 MPa·m1/2[20]. Alumina and zirconia represent examples of polycrystalline ceramic materials that lack a glass phase, distinguishing them as glassless materials in the polycrystalline ceramic category. Polycrystalline ceramics represent the main alternative to metal-ceramic restorations since they can resist masticatory forces, which, in patients affected by parafunctions, can reach 1,000 N[23,24]. Zirconia is a polymorphic ceramic material that exists in three allotropic forms: monoclinic, tetragonal, and cubic. This material can transform from one crystalline phase to another during sintering. Pure zirconia is in the monoclinic state (m) at room temperature, and this phase is stable up to 1,170°C. Above this temperature, it transforms into the tetragonal phase (t). The transformation into the cubic phase (c) occurs at 2,370°C while the melting point is at 2,680°C. Magnesium oxide is added to pure zirconia to stabilize it and to obtain a material commonly known as partially stabilized zirconia (Mg-PSZ). It is a biphasic ceramic material characterized by the presence of crystals in the tetragonal phase within a cubic matrix. The limited diffusion in the biomedical field is due to several factors[25]. The increased porosity of the material is attributed to its precise features, including a high particle size (up to 30-40 μm) and impurities[26]. The sintering temperature is between 1,680°C and 1,800°C. An improvement to the properties of zirconia is given by the addition of a 3% mol of yttrium oxide (Y_2O_3) to stabilize the material in the tetragonal phase, even at room temperature. Then, the Y-TZP (Yttria-Tetragonal, Zirconia, Polycrystalline), which is used in the dental field, is at room temperature. The phase transition of zirconia can be induced by low-temperature aging (LTD - Low Thermal Degradation) or by procedures such as milling, finishing, and sandblasting. Hybrid glass-ceramic materials are varied. They can consist of a porous ceramic matrix filled with a polymeric material. The ceramic component of this hybrid material, which is 86% by weight, consists of a network of aluminum oxide and finely-structured feldspar ceramics. The organic polymeric component, which is 14% by weight, comprises urethane dimethacrylate (UDMA) and triethylene glycol dimethacrylate (TEG-DMA). The mechanical properties are intermediate between those of glass-ceramic materials and those of composite resins. The rationale based on which this choice was made is that the toughness of a ceramic material can be increased by adding an organic polymer. The reported values of modulus of elasticity, hardness, and fracture toughness (KIc) are respectively 30 Gpa, 2.6 GPa, and 1.7 MPa·m1/2 while the flexural strength is

about 160 MPa[27,28]. The Vickers hardness tests performed on the hybrid ceramics showed that the resinous component can cause greater crack deflection than glass-based ceramic materials. Finally, there is a resinous nano-ceramic made up of 79% by weight of nanostructured particles of silica and zirconia immersed in a crosslinked resinous matrix. This material does not require a firing process, and the manufacturer reports a flexural strength of 204 MPa[29,30]. Ceramic materials with low glass content and bimodal filler can have the matrix constituted by lithium silicate and the reinforcement by 10% by zirconia weight. The size of the lithium silicate crystals varies between 500 nm and 700 nm, and their shape is flat and elongated. This material, endowed with high translucency, must be subjected to a firing to obtain the crystallization of the material once milled with computer-aided design (CAD)/computer-aided manufacturing (CAM) systems. Before the crystallization of the lithium silicate, the material is easy to mill. Final crystallization requires thermal cycling conducted at 840°C for 8 minutes. The fracture toughness (KIc) is approximately 2 MPa·m1/2, and the three-point flexural strength is 420 MPa.58 According to the manufacturer, the modulus of elasticity is about 70 GPa, and the coefficient of thermal expansion is 12.3 10-6 K-1[31,32]. The aim of the present investigation was to investigate the current ceramic biomaterials for dentistry through a literature review and a bibliometric network assessment.

Materials and Methods

Search Process

The manuscript screening has been conducted on Scopus (Elsevier, Amsterdam, The Netherlands). The Boolean search has been conducted according to the following strategy: TITLE-ABS-KEY ((hydroxyapatite OR phosphate OR particulate OR calcium AND sulphate OR tricalcium AND phosphate OR allograft OR ceramic) AND bone AND scaffold). Two expert reviewers (AS, FL) conducted the screening and data analysis on January 12th, 2023.

Data Elaboration

The article's full texts have been collected and categorized according to the author's list, title, journal, subject area, document type, institute, country, affiliations, citation counts, and h-index. The study data have been elaborated on using a specially designed calculation database and an Excel software package (Microsoft Corp., Redmond, WA, USA).

Bibliometric Measurements

The citational impact of the selected articles was calculated by analyzing contributions, authors and their affiliations, and scientific journals. The authors' self-citations were excluded from the data evaluation. The journal impact factor (JIF) and mean JIF percentile were assessed by the Journal Citation Reports (JCR) (Clarivate, London, UK). The authors' "Publication % Ratio" and "Citation % Ratio" were calculated using a previously described method[33]. The visual bibliometric mapping was provided by the VOS viewer software (Universitet of Leiden, Netherlands)[34].

Statistical Analysis

The mean and standard deviation have been considered for the descriptive statistics. The data analysis has been conducted through a specially designed electronic form made with the GraphPad 9 (Prism, San Diego, CA, USA).

Results

General Parameters

The screening revealed a total of 2,554 publications that were as follows: 2,234 original articles, 170 conference papers, and reviews, 109 literature reviews, 35 book chapters, 3 editorials, and 3 short surveys. A total of 7,450 authors have been evaluated, considering the total citations (Ctot), h-index (Htot), and papers (Ptot) separately. The citations (C_{topic}), H-index (H_{topic}) and papers (P_{topic}) were also calculated considering the on-topic articles selected (Table I). The P_{tot} and P_{topic} were respectively 281.79 ± 265.71 and 14.37 ± 5.90 [$P_{\%Ratio}$: 0.09 ± 0.07; $Cit_{\%Ratio}$: 0.19 ± 0.44]. The C_{tot} and C_{topic} were, respectively, 11,346.08 ± 13,014.16 and 691.56 ± 593.21. The H_{tot} and H_{topic} calculated were 48.15 ± 24.71; H_{topic}: 10.06 ± 4.44.

The visual bibliometrical mapping has been calculated through a computational model of the co-authorship. The model adopted is considered a fractional counting computing method. Articles with more than 10 authors have been designated as an exclusion criterion for visual bibliometric mapping. The minimum number of documents an author needed was 10.

Figures 1, 2, 3, and 4 presented the network visualization, the overlay visualization, and the

Table I. Descriptive statistics of citations, H-index and papers calculated in the bibliometric analysis.

	P_{tot}	H_{tot}	C_{tot}	P_{topic}	H_{topic}	C_{topic}	$P_{\%Ratio}$	$Cit_{\%Ratio}$
Minimum	30	9.0	343	5.9	3.0	97	0.070	0.19
25% Percentile	128	28	3,113	10	7.0	246	4.2	4.4
Median	227	46	7,994	12	9.0	581	6.2	7.5
75% Percentile	352	58	13,905	16	12	804	9.3	11
Maximum	1,566	113	64,267	33	26	2,612	37	240
Range	1,536	104	63,924	27	23	2,515	37	240
Mean	281	48	11,377	14	10	690	8.4	18
Std. Deviation	261	24	12,768	5.9	4.4	582	7.4	44
Std. Error	35	3.3	1,738	0.80	0.60	79	1.0	5.9
Lower 95% CI	210	41	7,892	13	8.7	531	6.4	6.1
Upper 95% CI	353	54	14,862	16	11	849	10	30

C_{tot}: total citations, H_{tot}: total H-index; P_{tot}: total papers; C_{topic}: citations calculated by on-topic articles selected, H_{topic}: H-index calculated by on-topic articles selected; P_{topic}: on-topic articles selected.

density visualization, respectively. The network visualization showed the total link strength of the selected author, while the overlay described the average publication per year, and the density overlay adopted a kernel density estimation method.

Discussions

In the present investigation and characterization of the most cited papers, Chang J. of the University of Chinese Academy of Sciences and Hutmacher, D.W. of the Queensland University of Technology in Brisbane showed the most intense mono-institutional publication activity on in-sili-

co, *in vitro,* and *in vivo* investigation of ceramic scaffold for bone regeneration procedure. Moreover, the tracking of the literature spread on this topic and data showed intense activity from the University of China, which represents 30.2% of the worldwide scientific production. The visual bibliometric mapping showed a complex network between several nuclei of the different research teams.

Chemical Properties of the Dental Ceramics

Ceramic materials in the form of hard powder are very resistant, and when heated to high temperatures, they become glassy. Hence, they are
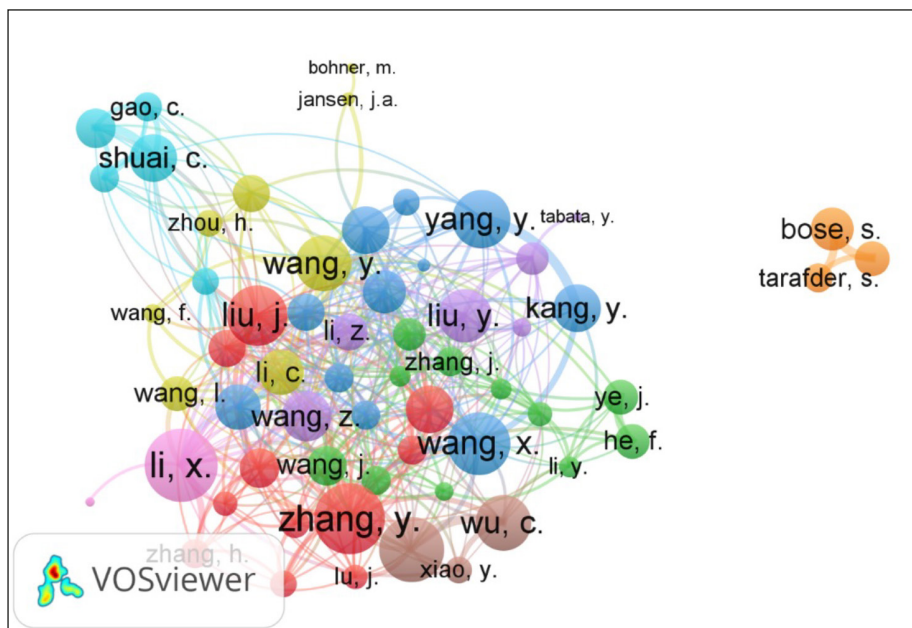
Figure 1. Visual bibliometric mapping through network visualization of the total link strength.

used as non-metallic inorganic materials and are widely used mainly in dental but also orthopedic materials. From alumina ceramics, the most representative are kaolin [$Al_2Si_2O_5(OH)_4$], montmorillonite [$(Na,Ca)_{0.33}(Al,Mg)_2Si_4O_{10}(OH)_2·nH_2O$] and illite ($K,H_{30})(Al,Mg,Fe)_2(Si,Al)_4O_{10}[(OH)_2·(H_2O)$]. Based on the surface type in contact with tissues, there are four categories: (a) none (inert), (b) low, (c) medium, and (d) bioabsorbable. Porous bioceramics are aggregates of higher mechanical strength, referred to as scaffolding or structural bone engineering bridges, as they help the bone grow through their porous network (Figure 5).

It is possible to develop coral-like microstructure materials, which have a controlled pore size[35-37]. To create porous ceramics with uniform porosity and adequate interconnection, the initial necessary condition is the determination of the shape/morphology of the material on a microscopic scale. In fact, the hard corals family of *Porites* (pore size 140-160 μm), and *Goniopora* (pore size 200-1,000 μm), are a model of imitation for the synthesis and thus the production of porous materials such as α-alumina, calcium phosphate, titanium, polyurethane silicone, polimetilmetacrilato (PMMA), and Co-Cr alloys[38,39].

Furthermore, porous ceramic surfaces can be synthesized by mixing soluble metal or salt particles on a surface, where the pore size and their porosity microstructure are proportional to the size and shape of the impurity particles, which are then removed from the surface using a suitable corrosive agent. The porous layer produced with this technique is an integral part of the dense ceramic phase of the material[40]. Another method for creating porous materials such as alumina is the foaming technique, whereby a foaming agent creates gas by heating. For the production of porous alumina and calcium clays, powdered calcium carbonate is mixed with fine alumina powder, having a pore size and volume fraction proportional to the particle size and concentration of the original calcium carbonate[41]. Therefore, in any case of porous ceramic composition, the initial conditions and the materials of the products are interconnected, making it necessary to control the production process, and the choice of materials is a prerequisite for obtaining an adequate porous network.

However, porous materials have a lower resistance than compact ones, because porosity and mechanical resistance are quantities inversely proportional to the Ryshkewitch equation $\sigma = \sigma 0 e - b \varepsilon$ (ε is tablet porosity, σ is tensile strength, σ 0 and b are constants that characterize the tableting properties of a powder)[41,42].

Inert bioceramics (Al_2O_3) alumina belongs to this category) do not show an interfacial connection with the tissue, are resistant to low pH for thousands of hours, and have high inertia, which requires a long period until a stable connection is developed implant to tissue. Once implanted, they are surrounded by a capsule of fibrous connective tissue of varying thickness, which holds the implant site and, at the same time, isolates them from adjacent tissues. Therefore, although they show high biocompatibility and mechanical strength, they are intended for permanent use[43]. The low surface activity, where some protein binding sites such as Na_2O-CaF_2-P_2O_5-SiO_2 are provided. The materials of medium surface activity. The contribution of osteocalcin-mimetic peptide enhances the osteogenic activity and extracellular matrix mineralization of human osteoblast-like cells (they are those of low activity), in addition to binding to certain proteins, also release ions that promote the nucleation of hydroxyapatitis (HA)[44].

Composite materials are heterogeneous and made up of two or more materials without a chemical bond developing between them. In addition to biocompatibility, composite ceramic materials used in clinical applications must exhibit adequate mechanical strength. However, their mechanical behavior is a problem area under conditions of intense stress[45]. They are fragile materials because they present cracks and/or cyclic fatigue phenomena that must be reduced. The use of bio-ceramic coatings and the development of composite ceramics are appropriate approaches to address the above limitations.

The type of ceramic to be used, as inert, absorbable, or bioactive, varies according to the desired reaction required by each application. In most cases, it is necessary to increase the flexural strength, reduce the extent of elasticity, and avoid material failure. Composites are a combination of inorganic and organic materials, e.g., bio-ceramic or bioglass, with proteins or DNA to acquire different physicochemical properties. The architecture of the nanocomposite material, once created, should allow the tissues to self-organize within the organism[46].

Mechanical Behavior of Ceramic Dental Materials

The mechanical properties of the ceramics are (a) a high hardness and high degree of elasticity due to the strong bonds that the motion of distur-

bances in their mass can be planned, (b) a low resistance to tensile loads, and (c) bad behavior and consequent low fracture toughness. Therefore, their main disadvantage is their susceptibility to brittle fracture, with very little energy absorption (there is an area where brittle fracture occurs). Instead, metal alloys have a ductile behavior[47]. At room temperature, both in crystalline and non-crystalline ceramics, when undergoing tensile stresses, fractures are observed before any plasticity deformation occurs. The brittleness process consists of the formation and propagation of cracks with a direction perpendicular to the applied load. In crystalline ceramics, cracks develop both trans granularly or through granules and along certain crystallographic levels with high atomic density. These cracks occur because ceramics exhibit a diverse range of imperfections, varying in sizes and geometry, such as internal pores, micro-cracks, grain angles, impurities, microscopic notches, etc[47]. These defects are usually formed in the process of their preparation from heat treatments (micro-cracks), surface scraping, or corrosion, where it is not possible to eliminate or control them. Therefore, a material containing defects of a certain minor dimension and geometry can be accepted without creating micro-cracks. So, since the ceramics have various imperfections, it is important to know what the maximum tension is. The ability of a material to resist the destructive propagation of a crack

Table II. Mechanical characteristics of the dental ceramics.

Mechanical characteristics of the dental ceramics	
Compression resistance	~300 MPa
Tensile resistance	~35 MPa
Transverse resistance	~50-90 MPa
Shear	~100 MPa
Hardness	460 KHN

is called fracture toughness. The measure of the fragility of a material is the low KIc coefficient (ceramics values lower than 10 MPa·m^{-2}, usually MPa·m^{-2}) compared to metals. For ceramics, then, it is important to know that fracture toughness depends not only on its dimensional tensile stress but also on the duration of its application (Table II)[48,49]. On the other hand, the chipping phenomenon also represents a very common failure model of ceramic materials that some studies[50,51] supply with novel high-strength core materials. Another failure model hypothesis could be correlated to the oxidation process of the ceramic materials and the black core micro-formation[52,53].

In several samples of ceramic material, when the toughness is measured very frequently, a differentiation and distribution of its pieces is observed. This is the case because fracture toughness depends on the likelihood of having a defect capable of triggering a crack. The occurrence of this possibility varies among samples produced
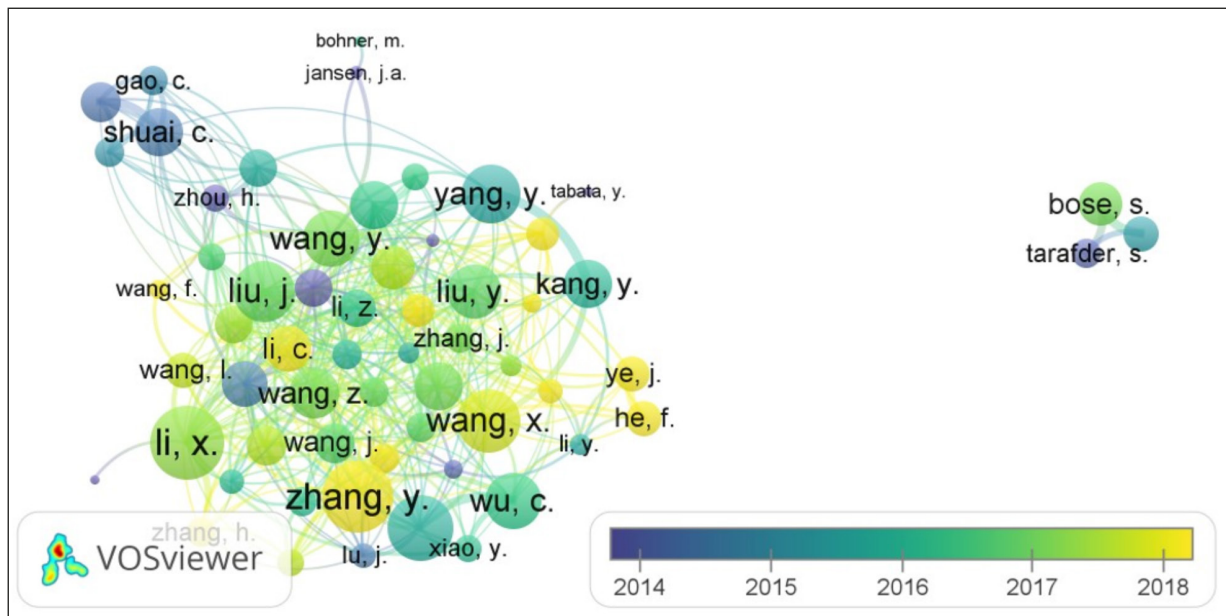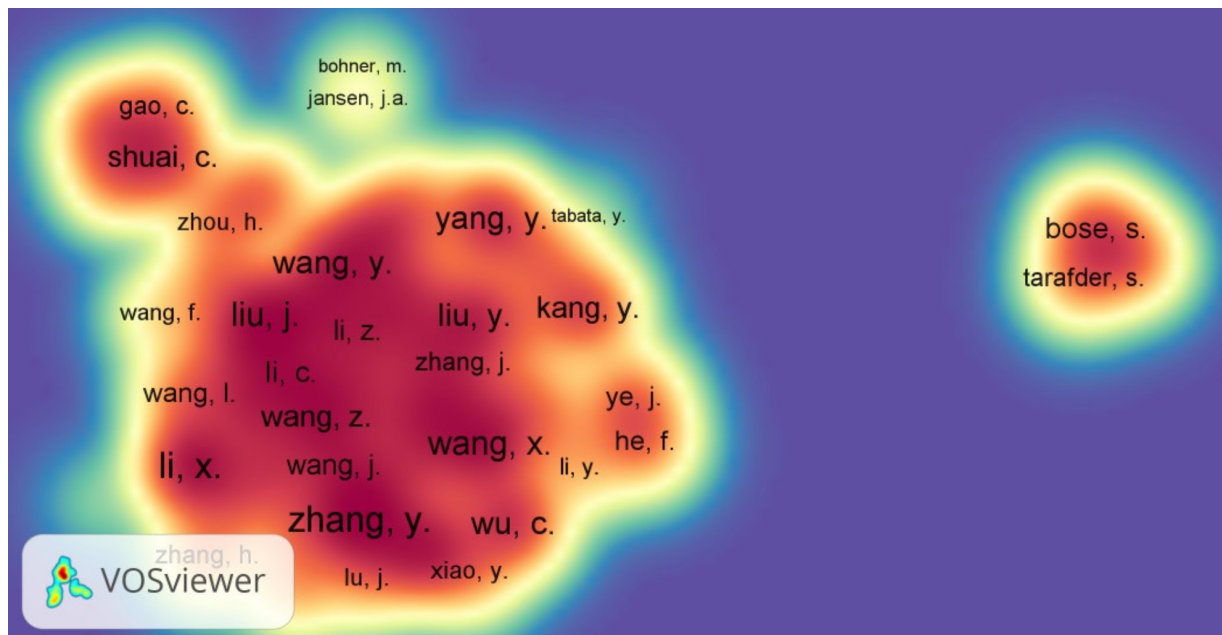

Figure 2. Visual bibliometric mapping through overlay visualization of the average publication per year.

Table III. Summary of the authors with the most articles on the study topic (>10 documents in line with the topic).

Authors	Affiliations	Country	P_{tot}	H_{tot}	C_{tot}	P_{topic}	H_{topic}	C_{topic}	$P_{\%Ratio}$	$Cit_{\%Ratio}$
Chang, J.	University of Chinese Academy of Sciences	China	502	97	30,028	33	26	2,486	6.57%	8.28%
Hutmacher, D.W.	Queensland University of Technology, Brisbane	Australia	536	105	46,733	33	23	2,095	6.16%	4.48%
Bose, S.	Washington State University Pullman	USA	321	75	21,073	31	17	2,612	9.66%	12.40%
Teoh, S.H.	Nanyang Technological University	Singapore	290	58	14,409	23	18	1,537	7.93%	10.67%
Kang, Y.	Florida Atlantic University	USA	105	33	3,484	23	15	423	21.90%	240.34%
Wu, C.	University of Chinese Academy of Sciences	China	313	83	19,167	22	18	1,923	7.03%	10.03%
Tabata, Y.	Kyoto University	Japan	1,042	101	43,304	22	13	745	2.11%	1.72%
Lu, J.	Shanghai Bio-lu Biomaterials Co.	China	69	9	3,186	20	14	950	28.99%	29.82%
Bohner, M.	RMS Foundation, Bettlach	Switzerland	389	57	11,498	19	13	1,429	4.88%	12.43%
Ishikawa, K.	Kyushu University	Japan	363	45	7,648	19	11	406	5.23%	5.31%
Ginebra, M.P.	Universitat Politècnica de Catalunya	Spain	303	58	11,693	18	11	858	5.94%	7.34%
Shuai, C.	Jiangxi University of Science and Technology	China	376	54	10,172	17	12	670	4.52%	6.59%
Jansen, J.A.	Radboud Institute for Molecular Life Sciences	Netherlands	826	103	40,312	17	13	568	2.06%	1.41%
Bandyopadhyay, A.	Washington State University Pullman	USA	364	56	21,655	16	13	1,432	4.40%	6.61%
Zreiqat, H.	The University of Sydney	Australia	187	53	8,575	15	13	742	8.02%	8.65%
Xiong, Z.	Tsinghua University	China	80	32	3,168	15	8	626	18.75%	19.76%
Lee, B.T.	Soonchunhyang University	South Korea	242	39	5,404	15	12	323	6.20%	5.98%
Khojasteh, A.	Shahid Beheshti University of Medical Sciences	Iran	153	29	343	14	10	769	9.15%	224.20%
Shim, J.H.	Tech University of Korea	South Korea	78	35	5,254	14	9	441	17.95%	8.39%
Peng, S	Central South University	China	227	50	8,867	14	12	435	6.17%	4.91%
Li, X	Shanghai Jiao Tong University	China	112	27	2,029	14	9	336	12.50%	16.56%
Qin, L.	Chinese University of Hong Kong	Hong Kong	445	69	17,466	13	11	741	2.92%	4.24%
Ye, J.	ChinaSouth China University of Technology	China	179	26	2,219	13	6	105	7.26%	4.73%
Gbureck, U	Universitätsklinikum Würzburg	Germany	260	64	10,544	12	10	894	4.62%	8.48%
Wang, Z.	Medical School of Nanjing University	China	225	28	3,446	12	6	246	5.33%	7.14%
Wang, C.	Dongguan University of Technology	China	48	18	1,015	12	6	205	25.00%	20.20%
Fischer, H.	Uniklinik RWTH Aachen	Germany	131	33	4,644	12	9	192	9.16%	4.13%
He, F.	Guangdong University of Technology	China	75	18	994	12	6	97	16.00%	9.76%
Rai, B.	A-Star, Institute of Medical Biology	Singapore	30	20	1,833	11	10	891	36.67%	48.61%
Miranda, P	Universidad de Extremadura	Spain	69	28	2,686	11	7	835	15.94%	31.09%
Layrolle, P.	Inserm	France	203	65	13,737	11	10	740	5.42%	5.39%
Li, D.	Xi'an Jiaotong University	China	567	47	10,624	11	8	336	1.94%	3.16%
Gellrich, N.C.	Medizinische Hochschule Hannover (MHH)	Germany	346	45	7,028	11	7	312	3.18%	4.44%
Wang, Y	South China University of Technology	China	478	53	10,508	11	6	242	2.30%	2.30%
Reis, R.L	Universidade do Minho	Portugal	1,566	113	64,267	11	7	199	0.70%	0.31%
Tarafder, S.	Columbia University Irving Medical Center	USA	46	28	3,269	10	9	1,518	21.74%	46.44%
Lin, K.	Shanghai Jiao Tong University	China	161	54	8,339	10	10	794	6.21%	9.52%
Cancedda, R.	Università degli Studi di Genova	Italy	346	48	23,878	10	9	784	2.89%	3.28%
Xiao, Y.	Queensland University of Technology	Australia	348	67	15,236	10	8	766	2.87%	5.03%
Cho, D.W.	Pohang University of Science and Technology	South Korea	382	67	17,107	10	8	686	2.62%	4.01%
Yang, Y.	Stanford University	USA	96	46	6,771	10	10	650	10.42%	9.60%
Jiang, X.	Shanghai JiaoTong University	China	232	55	9,334	10	9	488	4.31%	5.23%
Feng, P.	Central South University	China	133	34	4,552	10	8	451	7.52%	9.91%
Gao, C.	Central South University	China	137	35	4,396	10	8	375	7.30%	8.53%
Henrich, D	Universitätsklinikum Frankfurt	Germany	131	31	2,947	10	7	328	7.63%	11.13%
Matsuya, S.	Fukuoka Dental College	Japan	131	31	2,872	10	6	244	7.63%	8.50%
Hashimoto, Y	Osaka Dental University	Japan	99	20	1,196	10	7	233	10.10%	19.48%
Shinomiya, K	Tokyo Medical and Dental University	Japan	250	56	11,445	10	6	208	4.00%	1.82%
Pei, G.X.	Xijing Hospital, Xi'an	China	227	27	2,675	10	3	204	4.41%	7.63%
Hu, Y.Y.	Xijing Hospital, Xi'an	China	179	24	2,036	10	5	180	5.59%	8.84%
Witek, L.	NYU Tandon School of Engineering	USA	128	23	1,533	10	6	113	7.81%	7.37%
De Aza, P.N.	Universidad Miguel Hernández de Elche	Spain	127	32	3,397	10	5	98	7.87%	2.88%

Figure 3. Visual bibliometric mapping through density visualization.

through the same manufacturing procedure, influenced by construction techniques, subsequent processing, and the associated volume, each exerting a significant impact. The base glass mixture is usually crystallized with powder or crystals of alumina, zirconia, spinel of magnesium (MgAl$_2$O$_4$)[54] etc. By applying controlled heat treatment, collectively called ramification or devitrification, the final result is obtained. When crystals are used, composite materials, known as interacting composites, are formed.

Ceramic-Based Substitutes for Hard Tissues Repair

Bioabsorbable ceramics are designed to persist until the regeneration process is fully accomplished, resulting in the formation of new autologous tissue[41]. This category includes calcium orthophosphates such as HA, calcium phosphate, Ca$_3$(PO$_4$)$_2$, tricalcium phosphate (TCP) etc. Over time, efforts have been made to enhance composite ceramic materials, aiming to give ultra-specialized properties as nanosystems with a crystalline structure and intermediate behavior to the material. Calcium phosphate bioceramics have a number of applications. Some of these can be for dental implants, percutaneous devices, periodontal therapy, alveolar augmentation, orthopedics, maxillofacial surgery, complex implant surgery, and spinal cord surgery (Figure 6)[55-58]. Each application requires the use of bioactive

or bioabsorbable calcium phosphate, which corresponds to a specific phase of the ceramic (Figure 7). The stable phases of calcium phosphate ceramic depend significantly on the temperature and the presence of water, both during treatment and in the environment of use. At body temperature, only two calcium phosphates are stable in contact with aqueous media (body fluids). Therefore, when they are found in a pH<4.2, the constant phase is calcium phosphate or C$_2$P brushite (CaHPO$_4 \cdot$2H$_2$O), while at pH≥4.2 the stable phase is HA [Ca$_{10}$(PO$_4$)$_6$(OH)$_2$] (Figure 7). On the other hand, when the temperature is higher, the preferred phases are tricalcium β-phosphate C$_3$P or TCP [Ca$_3$ (PO$_4$)$_2$] and tetra calcium phosphate [Ca$_4$(PO$_4$)$_2$O][59]. The non-hydrated phases of calcium phosphate in high-temperature environments interact with water or body fluids at 37°C to form hydroxyapatite. The HA forms on the exposed surfaces of the β-phosphate tricalcium[60,61].

Ceramic-Based Dental Restorative Materials

Alumina (Al$_2$O$_3$) has very good wear resistance, good mechanical properties, and much good biocompatibility (bioinert). It also has a very low coefficient of friction with other surfaces and is used in coatings of implants as well as in dental implants. Today, it is one of the most popular ceramic biomaterials. The ceramic materials are interpenetrating phase composites (IPN) in which
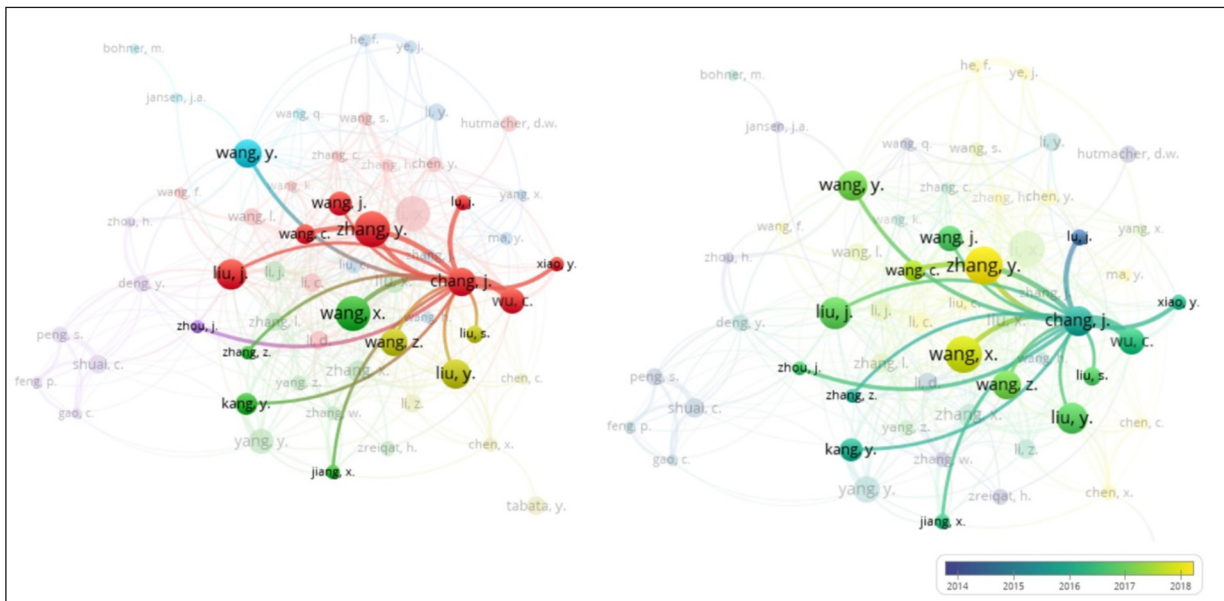
Figure 4. Visual bibliometric mapping of the author with the highest number of publications on the study topic and the citation parameters.

the two parts (glass crystals) are interconnected and constantly expand, one inside the other, without forming a chemical bond. The production of these takes place in two steps. First, this ceramic material is sintered to create a porous nucleus made by spinel of magnesium ($MgAl_2O_4$), crystals of alumina, or by a composite formed by 70% alumina with 30% zirconia[62]. Subsequently, the molten glass is filtered through a network of pores and fissures, filling them and creating a high-strength material. From this, a particular dental porcelain is used as an aesthetic veneer. Instead, the realization of glass ceramics takes place by adding oxide-based powders (the reinforcing particles are mainly lithium disilicate crystals)[63,64]. Zirconia (ZrO_2) is bioinert and biocompatible; it has a smaller modulus elasticity, low coefficient of friction, greater strength, and is less brittle than alumina. It generally has similar applications in dentistry. The yttria (Y_2O_3) is usually added to stabilize the structure, and the resulting biomaterial is called Yttria-Stabilized Zirconia (YSZ) (zirconia stabilized with yttria). New alternative materials are employed for substituting alumina and zirconia in biomedical applications, exemplified by the utilization of alumina-zirconia composite biomaterials[65,66]. Bioactive glasses (bioglasses) can form a strong union with bones and find applications in orthopedics and dentistry. Porcelain is a clay-based ceramic material used in dental applications. The ceramics sector is involved in producing prostheses or devices mainly intended for hard tissue due to its mechanical characteristics. Dental porcelain is a particular type of ceramic material used to manufacture prosthetic products: artificial teeth, jacket crowns, inlays, etc. It is supplied in the form of a powder, which is mixed with a liquid, generally distilled water, to obtain a paste with which the prosthetic product is modeled. Thus, it consists of a vitreous silicate material netting with mineral salts and small quantities of metal oxides. They are used to simulate the desired natural color of the teeth and have a low melting temperature and a high coefficient of thermal expansion[67-70]. This biomaterial is subjected to a thermal cycle (firing) through which sintering is obtained (union of the particles using the connection of their contact surfaces by the action of pressure and heat) of the particles constituting the porcelain. Furthermore, the porcelain material for aesthetic construction can be used to cover the metal surfaces of immovable structures such as dental rims and bridges. Indeed, these metallic biomaterials coated with porcelain are utilized for their biocompatibility in the fabrication of fixed prosthetic structures, including bridges and frames. This applies not only to constructions made entirely from ceramics, such as zirconia and alumina (Table I). Hydroxyapatite is a bioactive calcium phosphate and is a basic natural component of bones and teeth. It is mainly used for bone prosthetics and artificial joint coatings. The body recognizes the hydroxyapatite coatings as familiar and not as a

foreign body, and thus, the adhesion of these new biomaterials is accelerated and improved. Consequently, implant integration with the bones is improved[71]. Pyrolytic carbon (pyrolytic carbon - PyC) is a form of carbon that is quite like graphite. The atoms are organized into levels and are placed in the hexagonal grid, although the planes exhibit variations and irregularities rather than being perfectly parallel and organized[72]. For this reason, new pyrolytic carbon and carbon-coated metallic dental implants can be created. PyC is not found in nature but is man-made with pyrolysis of hydrocarbons such as propane, propylene, acetylene, and methane in the absence of oxygen. Without oxygen, instead of the typical breakdown of hydrocarbons into carbon dioxide and water, a more complex decomposition process is observed, eventually leading to a variety of macromolecular complexes of carbon atoms, creating thin films of pyrolytic carbon[73]. This is a more resistant and durable material (more than graphite) with excellent wear and fatigue resistance, but it is generally more delicate in handling. Silicon is often added in small amounts to improve mechanical properties. It is also a biocompatible material and one of the most hemocompatible materials (does not cause blood clotting easily)[74]. Other forms of amorphous carbon (such as DLC – Diamond-Like Carbon) show good mechanical properties and biocompatibility. However, their use is still in the experimental stage[75]. In addition to their mechanical properties, ceramics can easily obtain the desired shape and color; thus, they find their extensive use in dentistry. Dental porcelain consists of a vitreous silicate matrix in which crystalline mineral salts are dispersed. In its composition, the ceramic contains small quantities of metal oxides, which are used both as dyes to simulate the color of natural teeth and to obtain a reduction in the melting temperature and an increase in the coefficient of thermal expansion (RT)[67-70]. Dental porcelain is used for veneering metal, immobile frames such as metal-ceramic rims and bridges, for constructing indirect aesthetic restorations, e.g., facades and inlays/overlays, and for constructing artificial teeth. In recent years, the technology of all-ceramic systems has been developed to prevent the construction of fixed prosthetic works (bridges and circles) without a metal frame, e.g., entirely from ceramic biomaterials, such as zirconia, alumina, etc. (Table I)[76].

During this time, one of the most important issues raised is related to the prevention of infective complications, both local and systemic, especially in dental implants (Table III)[77-80]. For this reason, several studies[81-84] have been conducted to evaluate the risk and the possible prevention of prosthetic infection, both selecting biomimetic materials to minimize it or adding anti-infective molecules or drugs on their surfaces.
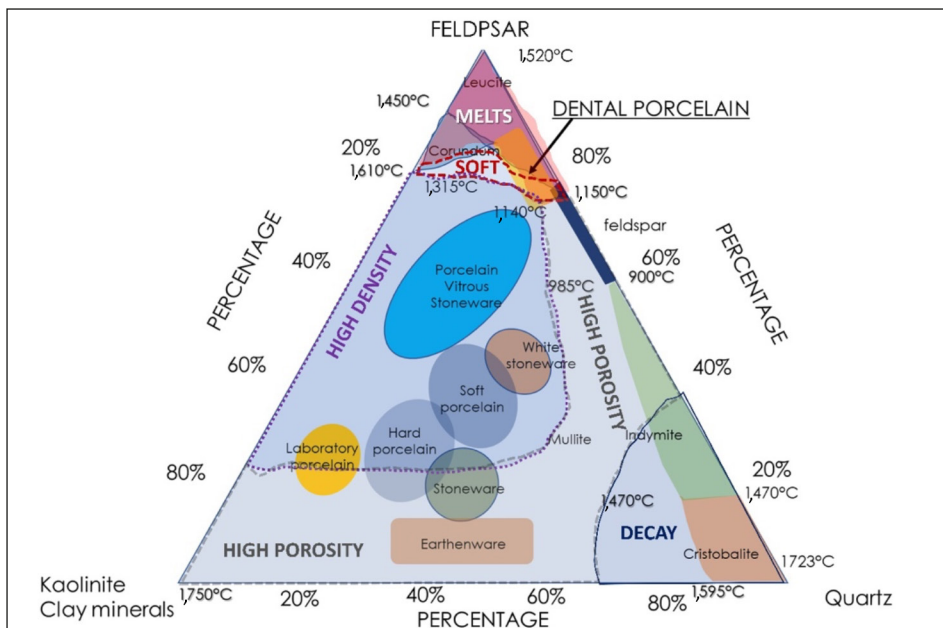

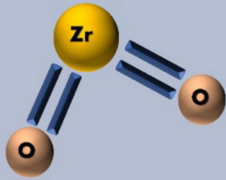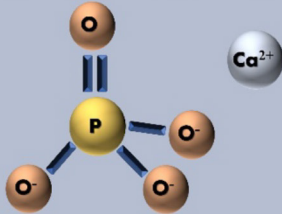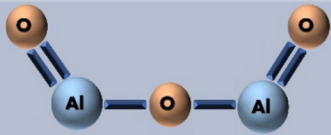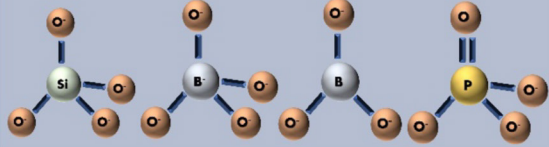**Figure 5.** Composition and main characteristics of the ceramic's materials.

Figure 6. Ceramic bone substitutes and hard tissue scaffold characteristics.
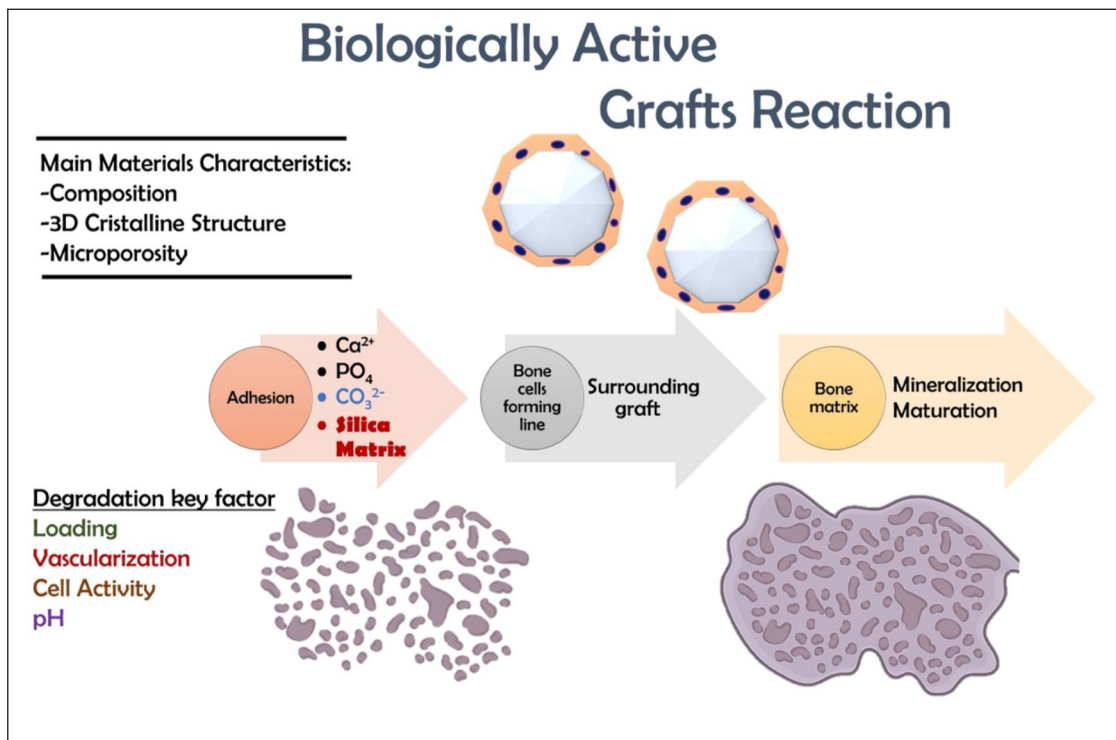

Figure 7. Description of the biologically active graft tissue responses and new bone formation induction.

All the currently available dental materials are effective against microorganisms that are commonly involved in prosthetic infections (i.e., *S. aureus*, *C. albicans*, etc.) and have silver ions in their composition (Table III)[81-87]. However, endodontic materials have recently been improved to face contamination by *E. faecalis,* a causative agent of severe local and systemic infections[88-90]. Noteworthy, such materials have recently been reported as useful for overcoming antimicrobic resistance in certain bacterial strains and as effective against SARS-CoV-2[91-96].

Conclusions

The systems created with the full-ceramic technique have significantly expanded the range of their applications in dentistry, making them increasingly popular and progressively replacing conventional metal-ceramic restorations. They combine high aesthetic performance and biocompatibility. High-strength glass-ceramics have the ability to improve their aesthetic performance, as they bio-mimic the optical properties of hard dental tissues (enamel, dentin) in the best way possible. However, due to their low breaking strength, they are used almost exclusively as cladding materials for high-strength ceramic frames. The bibliometric evidence showed a consistent increase in the literature production both in the Western countries and the Asian community in line with the market interest and the current application for dental restoration materials and bone grafts.

Conflicts of Interest
The authors declare no conflict of interest.

Authors' Contributions
Conceptualization: I.A.C., L.R., A.P.C., A.M.I., G.D., A.S., M.C., F.L., F.I. and G.M.; methodology, A.P., A.D.I., A.M.I, , I.A.C., I.R.B., F.L.,F.I. , and A.S., I.A.C.; software, I.R.B., G.M., I.A.C., A.S., L.R., A.D.I., F.I. and G.D.; validation, F.I., F.L., A.S. , G.D., A.D.I A.P., and A.S.; formal analysis, A.M.I., F.L., A.M.I., M.S.D., M.C., R.G.C., A.P., D.H., F.I. and G.M.; investigation, L.R., G.D., A.D.I., F.L., A.M.I., F.L., I.R.B., A.S., D.H. and F.I. ; resources, A.M.I., A.P.C., I.A.C., R.G.C., G.D., A.D.I., F.I., I.R.B., and G.M.; data curation, G.D., F.I., F.L., M.G., I.A.C A.S., L.R., A.D.I., A.M.I., G.D., and G.M.; writing-original draft preparation, A.D.I.,A.P., A.M.I., G.D., I.A.C. A.S., F.L. and F.I.; writing review and editing, F.I., F.L., I.A.C., A.P., A.S., and G.D.; visualiza-

tion, F.L., A.S., and I.R.B.; supervision, A.M.I., F.I., A.D.I., G.D. and F.L.; project administration, F.I., G.D., G.M., A.S., A.P.C., R.G.C., M.C., L.R. and F.L. All authors have read and agreed to the published version of the manuscript.

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Not applicable.

Informed Consent
Not applicable.

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