



Bioactive Ceramic Porcelain/Glass for Dental Application

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Abstract

The development of dental materials with the ability to heal and regenerate the natural architecture of lost or damaged dental or periodontal tissues is an area of ongoing research. In this concept, the term bioactivity has started to emerge as an important property for the dental materials. Several bioactive calcium-based or

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calcium-containing materials, including dental cements, composites, and glass-ceramics that develop a surface layer of an apatite-like phase in the presence of an inorganic phosphate solution, have been proposed in various dental applications. The induction of bioactive properties in conventional dental ceramics used in restorative dentistry could lead to materials able to support tissue attachment, extending their applications beyond the current limitations of restoring only the morphological and esthetics characteristics of the destroyed tooth structures. Among the different fabrication techniques, the application of the low-temperature sol-gel (solution-gelation) process in the fabrication of dental bioactive glasses and glass-ceramics is an advanced well-established approach, as this process allows the tailoring of the structural (specific surface area and porosity) and chemical characteristics, in order to develop optimized bioactive surfaces, with enhanced bioactivity over a wide range of silica concentrations. This chapter reviews some of the key approaches for the induction of bioactivity in commercial bioinert dental composites and mostly highlights the advantages of sol-gel technology in the synthesis of new glass-ceramics and composites for dental restorations which combine bioactive properties and antimicrobial activity with optimum textural characteristics and biological and mechanical properties.

Introduction

The general concept of bioactive restorative dental materials has been applied for several decades. Thinking of the general property of adhesion to tooth structure and the release of fluoride as an adjunct to the prevention of secondary or recurrent caries, dental technology stressed its efforts in developing “bioactive” restorative materials in the form of fluoride- or other element-releasing materials. The term “bioactive material” can be assigned to a material that forms a surface layer of an apatite-like material in the presence of an inorganic phosphate solution (Kokubo et al. 1990). Considering the potential rationales for the use or incorporation of bioactive materials in reconstructive and restorative dentistry, it becomes clear that the need for “bioactive” dental restorative materials is not a new endeavor. In particular, there is a wide range of calcium-based or calcium-containing materials that demonstrate bioactivity and have been used in dentistry. These materials include but may not be limited to crystalline calcium phosphate materials including various apatites and hydroxyapatites, various glasses under the generic terms “bioactive glasses,” various glass-ceramics such as apatite-wollastonite materials, calcium silicate-based cements, and calcium aluminate-based cements. The last two groups (calcium silicates and calcium aluminates) have had significant impact in the area of restorative and endodontic dental materials.

Interestingly, although the huge number of the currently available dental materials and the new technologies applied in dentistry in order to improve dental restoration performance, challenges and issues still remain. Due to the limited potential of self-repair, when dental tissues are damaged, the only treatment option that could potentially repair the damage is the use of biocompatible synthetic

materials (Ratner 2001). Most of the synthetic dental materials are subjected to the hostile microenvironment of the oral cavity and thus have a limited lifespan and functionality. These evidences encourage the consideration of new chemistries and compositions in restorative dentistry. There is a need to develop bio-functional materials that not only aid in dental restoration but can also mimic some of the native tissue functionally.

Recent advances in nanomaterials provide a wider range of dental restorative materials with enhanced properties, such as greater abrasion resistance, high mechanical properties, improved esthetics, and better controlled cellular environment (Piva et al. 2014; Mendonça et al. 2008). Bioactive nanomaterials include hydroxyapatite, tricalcium phosphate, and bioglass nanomaterials. Hydroxyapatite (HAp) is a major component of dentin. Due to its biocompatibility and osteointegration with bone tissue, hydroxyapatite has been widely used as a coating material for various dental implants and grafts. Moreover, HAp is used in various forms, such as powder (Fathi and Hanifi 2007), coating (Sung et al. 2004), and composite (Sung and Kim 2003) for dental restorations. Despite of the various advantages, HAp has poor mechanical properties (highly brittle) and hence cannot be used for load-bearing applications (Cao and Hench 1996). A wide range of techniques have been developed to improve the mechanical properties of HAp (Brostow et al. 2008), such as the hybrid nanocomposites that can be used as bioactive coatings on dental implants, as well as injectable matrix for periodontal regeneration and bone regrowth. Overall, HAp-reinforced dental materials can exhibit improved mechanical and biological properties, meeting significant applications in dentistry.

Another important bioactive glass with extensive use in the field of dental repair is the well-known Bioglass 45S5, due to its unique properties (Kudo et al. 1990). When bioactive glasses are subjected to an aqueous environment, a hydroxycarbonate apatite/hydroxyapatite layer is formed on the surface (Nganga et al. 2012). Thanks to the precipitated apatite layer, these materials can provide a very strong chemical bond with both hard and soft tissues. These materials have been proposed for several kinds of applications in dentistry, being both in bulk and in coating form. Among other materials that are used in the repair and reconstruction of diseased or damaged hard tissues (bones and teeth), bioactive glasses attract special interest (Rizkalla et al. 1996; Verné et al. 2000), because they fulfill the standards for restorative dental applications, like compatibility with the oral environment. Additionally, their surface properties, such as shade translucency, toughness, and wear, correspond to those of natural teeth (Höland 1997). Despite these advantages, bioactive glasses are brittle, and thus they cannot be used for load-bearing applications. A range of different protocols and techniques has been proposed to improve the mechanical properties of the bioactive glasses used in dentistry.

An interesting approach, which is discussed in more detail in part 2.1, was the use of bioactive glass in combination with dental ceramics (Kontonasaki et al. 2003). Briefly, dental ceramics were modified by incorporating Bioglass 45S5 in powder form and in different concentrations. The bioactive properties of the modified ceramics were observed by the formation of apatite layer of the surface of the dental

ceramics after certain time of immersion in simulated body fluid (SBF). These modified ceramics could significantly support the attachment, spreading, and proliferation of periodontal ligament fibroblasts at higher extent compared to unmodified dental ceramics (Kontonasaki et al. 2007). However, the surface reactivity of these modified ceramics has been decreased due to the high reaction temperature of the melting process, resulting in nonporous materials with high heterogeneity, whereas their surface area is depended only on the particle size (Sepulveda et al. 2002).

On the other hand, the application of low-temperature sol-gel (solution-gelation) process in the fabrication of bioactive glasses and glass-ceramics allowed the tailoring of the structural (specific surface area and porosity) and chemical characteristics, in order to develop optimized bioactive surfaces (Arcos et al. 2002), with enhanced bioactivity over a wide range of silica concentration (Zhong and Greenspan 2000; Zhong et al. 2002; Salinas et al. 2002). Sol-gel is an effective method to synthesize a variety of materials with versatile properties. It has been applied for the synthesis of many dental materials such as light-curing dental composites, various glasses, and glass-ceramics, as well as bioactive glasses in a wide range of compositions for bone or periodontal tissue regeneration. This method provides high homogeneity and purity of the synthesized glass and can be applied for the synthesis of glasses that cannot be synthesized by the conventional melt-quenching method.

The idea of applying sol-gel technology for the fabrication of dental ceramics/bioactive glass composites arose from the fact that although conventional dental ceramics used in fixed prosthodontics are considered biocompatible, they cannot restore the structural relationship with the surrounding periodontal tissues. The induction of bioactive properties in this kind of ceramics could lead to materials able to support tissue attachment, extending their applications beyond the restoration of morphology and esthetics of destroyed tooth structures. This could offer a natural seal-up of the micro-gap that exists between the artificial tooth and dentin in conventional fixed prosthetic restorations, which has been implicated as the main reason for secondary carries and micro-penetration. This chapter aims to review the application of sol-gel technology in the synthesis of bioactive dental glass-ceramics applied in dental restorations and to reveal its unique ability to allow the synthesis of bioactive materials in compositions non-bioactive with other ways of fabrication.

Bioactive Glass Modified Dental Porcelain (Conventional Mixing and Sintering)

Composites with Commercial Dental Ceramics and 45S5 Bioactive Glass

The first attempt to introduce bioactive properties on commercial dental porcelain was in 2003, when Kontonasaki et al. (2003) used bioactive glass powder (Perioglas[®], Bioglass[®] Synthetic Bone Graft Particulate, US Biomaterials, FL, USA) mixed with porcelain powder in different weight ratios to produce composites sintered at high temperatures. Perioglas[®] had the nominal composition of SiO₂ 45 wt%, P₂O₅ 6 wt%,

CaO 24.5 wt%, and Na₂O 24.5 wt%, while the commercial dental ceramic was a feldspathic glass consisting of SiO₂ 59.5–65.5 wt%, K₂O 10–14 wt%, Al₂O₃ 13–18 wt%, and Na₂O 4–8 wt% and various oxides below 3.5 wt% and pigments <2 wt%. These composite materials developed a Ca-P layer on their surface after immersion in SBF for 16–25 days, directly proportional to the amount of bioactive glass, its higher amount being 67%. The delay of apatite formation on the composites with the higher amount of porcelain was correlated to the presence of non-bridging oxygen atoms (Chatzistavrou et al. 2006). As the ion Al³⁺ has an ionic radius very similar to that of the Si⁴⁺ ion, it can replace the silicon ion and take part in the structure of the silicate network. However, the replacement of silicon by aluminum ions is associated with a reduction of the number of bridging oxygen ions, since aluminum atoms are in part sixfold coordinated, AlO³⁻_{6/2} units, and aluminum acts as network modifier producing non-bridging oxygen atoms (Aronne et al. 1997; Demirkesen and Maytalan 2001; Tulyaganov et al. 2002); their number is increased by the increased amount of porcelain in the mixture. The formation of AlO bonds was also responsible for the shifting of the melting temperature to lower temperatures with the increase of bioactive glass concentration in the composites.

Almost all modified ceramic composites supported periodontal ligament fibroblasts (PDLFs) attachment and proliferation at higher extent than the control porcelain, as recorded through MTT assays (Kontonasaki et al. 2007). However, although they attained apatite-forming ability and promoted cell proliferation, the onset of apatite formation was delayed for days (Kontonasaki et al. 2007; Kontonasaki et al. 2008), so these materials would be highly impossible to induce soft tissue attachment in clinical applications.

Bioactive Glass/Dental Porcelain Composites by the Sol-Gel Route

Composites with Commercial Dental Ceramics and 58S Bioactive Glass

As the conventional mixing and sintering of the dental porcelain/45S5 bioactive glass composites presented a delayed apatite-forming ability, Goudouri et al. (2009) suggested the synthesis of similar composites by the sol-gel route, as sol-gel technique enables the production of glasses with enhanced bioactivity compared to their melt-derived counterparts. In this way, they used IPS-d-Sign Dentine (Ivoclar, Schaan, Liechtenstein), a needle-like fluorapatite containing dental ceramic in the SiO₂-Al₂O₃-K₂O-Na₂O-CaO-P₂O₅ system, in combination with the sol-gel-derived bioactive glass 58S (SiO₂ 60 wt%, CaO 36 wt% and P₂O₅ 4 wt%). The initial solution formation included the hydrolysis and polycondensation of tetraethoxysilane (TEOS), tri-ethyl-phosphate (TEP), and calcium nitrate tetrahydrate (Ca(NO₃)₂·4H₂O), which are the precursors of 58S bioactive glass. During the gelation stage, various wt% ratios of dental porcelain (10, 20, 30, 40, and 50%) were added in the mixture. The resulting mixtures were sieved to powder of 20–40 μm (Goudouri et al. 2009, 2011a). The powders were mixed with dental

Table 1 Textural characteristics of sol-gel-derived 58S bioactive glass–dental porcelain composites

Sample	Specific surface area (m ² /g)	Total pore volume (cm ³ /g)	Average pore diameter (nm)
DP	0.55	0.005	–
DP50	2.473	0.010	–
DP80	0.83	0.006	–
58S	9.044	0.031	6.96

porcelain modeling liquid using the same liquid-to-powder ratio (0.335), transferred into polysiloxane molds and condensed using a vibrator, to accomplish water removal. The disks were removed by gentle hand pressure and sintered at 870 °C with a rate of 60 °C/min in vacuum. The sol-gel-derived bioactive glass/dental porcelain composites consisted of leucite, calcium silicates, wollastonite, and fluorapatite. The *in vitro* bioactivity of all composites up to 40% of dental porcelain followed an inversely linear relationship with the amount of dental porcelain, while the composite with 50% of dental porcelain was proven non-bioactive. By the sol-gel route, the onset of apatite formation on the surface of the composite containing 20% dental porcelain was recorded after only 2 days immersion in SBF, while on the composite with the higher amount of dental porcelain, apatite aggregates were formed after 12 days in SBF. These findings proved the significant influence of the employed method of fabrication on the composites' bioactive behavior.

Even better results were recorded by using different commercial dental porcelain (DP) by Goudouri et al. (2011b, c, 2014) and Manda et al. (2012). They synthesized sol-gel-derived 58S bioactive glass/dental porcelain composites up to 80% dental porcelain (IPS Inline-Margin Ceramic System, Ivoclar, Schaan, Liechtenstein), and they reported onset of apatite formation after 3 days (50% DP), 6 days (60% DP), 9 days (70% DP), and 21 days (80% DP). The 50% DP and the 80% DP composite textural characteristics are presented in Table 1.

The DP50 specimens correspond to III type (IUPAC classification), which is indicative of non-nano-porous or mesoporous materials, while the adsorption isotherms of DP80 specimens are of type II (IUPAC classification), typical of nonporous or macroporous materials. The above data indicate that the commercial-sintered samples are highly dense and nonporous, in terms of micro- or mesoporosity, while the sol-gel-derived sintered samples exhibit some mesoporosity, still very limited compared to classic sol-gel or ordered template mesoporous silica. Although bioactivity is exerted by nano- or mesoporous materials with surface area larger than 40–80 m²/g, surfaces of high-dissolution rate may alter their textural properties and consequently both porosity and surface area thus becoming able to present bioactive behavior, as in the case of these composites. Goudouri et al. (2016) reported that although the number of blind pores caused by processing of the glass-ceramic was greater than that of the commercial one, the flexural strength was of the same order. Abbasi et al. (2016) reported early apatite formation (6 days) on 58S bioactive glass/dental porcelain (IPSe.max-dentin, Ivoclar, Schaan, Liechtenstein)

composite powders. They further reported that although the characteristic strength (σ) and Young's modulus of sintered composites were lower compared to the commercial dental porcelain, they presented higher Weibull modulus suggesting an homogenous structure with less flaws distributed in the bulk of the specimens. Feldspathic dental ceramics with typical textural characteristics and adequate mechanical properties can be synthesized through the sol-gel method. This method does not compromise their mechanical integrity, while enhances the expression of a bioactive behavior.

Sol-Gel-Derived Dental Bioactive and Antibacterial Glass-Ceramics

The fabrication of a new sol-gel-derived bioactive glass-ceramic for dental applications (COMP) has been presented. The fabricated glass-ceramic was in the system (SiO_2 58.6 – CaO 24.9 – P_2O_5 7.2 – Al_2O_3 4.2 – Na_2O 2.1 – K_2O 3 wt.%), and the potential use in dentistry was demonstrated. The structural and thermal properties as well as the bioactive behavior of the new material were determined. The microstructural characteristics were compared to those of a commercial leucite-based fluorapatite dental glass-ceramic and found to be similar enough, while COMP is expected to exhibit better control of composition, microstructure, and properties, in comparison to current melt-derived counterparts, due to the intrinsic high homogeneity provided by the sol-gel method. The bioactive behavior of the new COMP material was confirmed based on the rapid formation of a robust crystalline HCAP layer upon 3 days of immersion in SBF (Fig. 1a–c). The feasibility of the COMP to be applied as coating and to create bioactive microporous surfaces on inert dental ceramic substrates was also shown (Fig. 1d, e) (Chatzistavrou et al. 2010).

The cell attachment and proliferation of periodontal ligament (PDL) and gingival fibroblast (GF) cells on the surface of the novel sol-gel-derived dental bioactive glass-ceramic has been studied. It has been found that COMP induces cell attachment, spreading, cell migration, and proliferation of PDL cells, processes that are all involved in cell differentiation, maturation, and tissue formation. GF cells, however, demonstrated a quite different behavior on the material. A slower proliferation rate of GF on the surface of the COMP compared to the PDL cells was observed. In particular, after 7 days of cell culture, the surface of the COMP specimens was covered fully by PDL cells, which appeared confluent, creating a cell layer, while GF cells appeared to completely cover the surface of the materials only after 14 days of culture (Fig. 2) (Chatzistavrou et al. 2012a).

The area of application in dentistry demands the use of materials able to challenge the oral bacteria which are present and to enhance the healthy attachment of the surrounding tissue, leading finally to the success of the restoration. Moreover, the increasing clinical need to design novel dental materials that combine regenerative and antibacterial properties led to the development of a new sol-gel-derived Ag-doped bioactive dental glass-ceramic with antibacterial behavior, optimizing the properties of the newly fabricated COMP glass-ceramic. The composition of the COMP has been modified by doping the structure with Ag_2O . The novel sol-gel-derived bioactive and

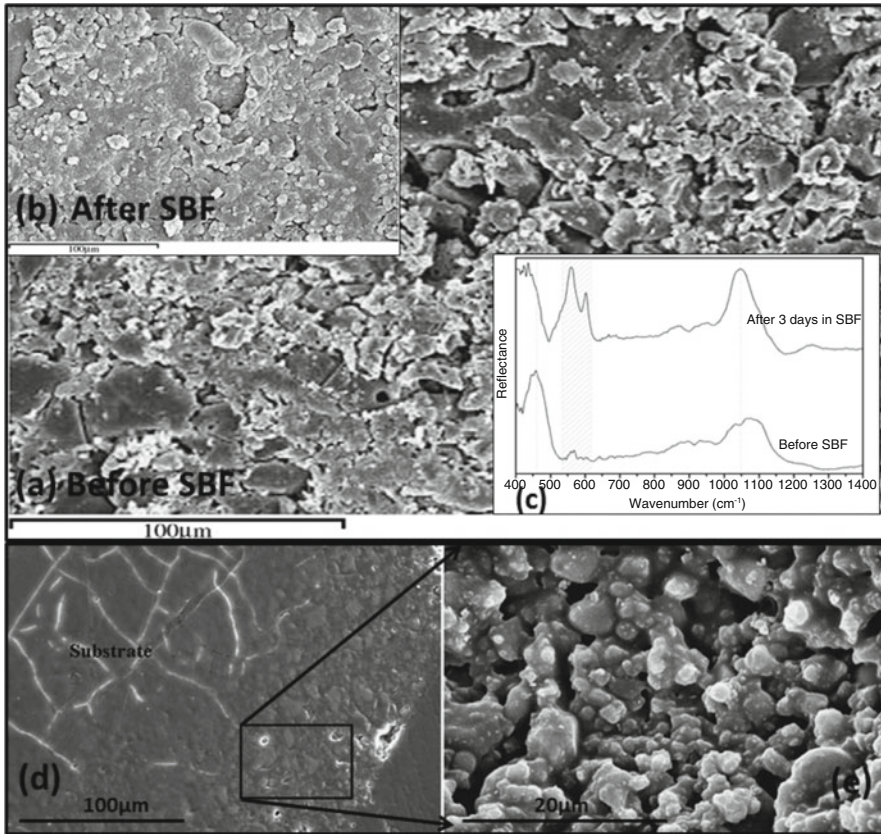


Fig. 1 SEM images of COMP surface before (a) and after (b) immersion in SBF. Apatite formation is also observed by FTIR spectra (c). Cross-section SEM image of COMP applied as coating on dental porcelain substrate (d) and higher magnification image showing the microstructure morphology of the coating (e) (With permission to reproduce, Chatzistavrou et al. 2010)

antibacterial glass-ceramic (Ag-BG) was in the system SiO_2 58.6–CaO 24.9– P_2O_5 7.2– Al_2O_3 4.2– Na_2O 1.5– K_2O 1.5– Ag_2O 2.1 wt% (Chatzistavrou et al. 2012b). The microstructural characteristics of the developed system were characterized by different techniques and compared to those of commercially available dental glass-ceramics. The antibacterial properties of the Ag-BG were tested against the bacterial colony *Staphylococcus aureus* (*S. aureus*) which is very characteristic oral bacteria and against *Enterococcus faecalis* (*E. faecalis*), a bacterium commonly implicated in the pathogenesis of dental pulp infections. The cell–material interaction was monitored in a primary culture of human gingival fibroblasts (HGFs) as well as in dental pulp cells (DPs). It has been observed that silver ions have been successfully incorporated in the glass-ceramic structure and the newly prepared sol-gel-derived Ag-doped material (Ag-BG) presents cell-proliferation-inductive as well as antibacterial properties

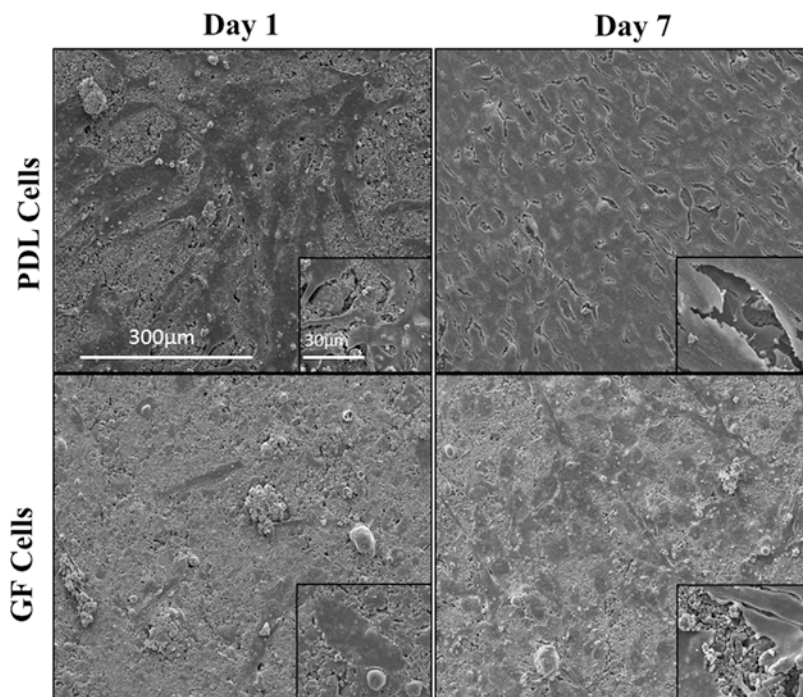


Fig. 2 SEM images of the surface of COMP specimens after 1 and 7 days of cell culture, showing the attachment and proliferation of PDL and GF cells (all images at same magnification and scale bars represent 300 µm and 30 µm (*inset*), respectively). (With permission to reproduce, Chatzistavrou et al. 2012a)

indicating the potential application in dental tissue restoration strategies (Chatzistavrou et al. 2014).

Laser-Assisted Induction of Apatite Formation on Dental Ceramic/Bioactive Glass Composites

Hydroxy-carbonate apatite (HCAp) precipitation on the surface of bioactive ceramics during immersion in simulated body fluids is based on a sequence of interfacial reactions that lead to the dissolution of the silica network and the formation of a hydrated silica-rich layer, which promotes heterogeneous nucleation of HCAp (Ohtsuki et al. 1992). The onset of HCAp nucleation depends on factors related to both bioceramic and simulated body fluid solution. The degree of crystallinity of the ceramic and the remaining amount of residual glassy phase have been reported to influence the time that HCAp starts to precipitate, by altering the activation energy for its nucleation (Li et al. 1992; Peitl Filho et al. 1996).

Concerning the solution, factors such as supersaturation/undersaturation, pH, ionic strength, and the ratio of calcium to phosphate can influence the thermodynamics and kinetics of HCAp nucleation and growth (Wang and Nancollas 2009). Using an approach that mimics the process of biological apatite formation, a novel method has been proposed that utilizes laser energy to enhance the Ca-P deposition (Pecheva et al. 2008). This laser-assisted biomimetic (LAB) method is based on the laser irradiation of a solid substrate while immersed in supersaturated SBF solution at ambient temperature and pressure. The process is based on the concept that laser energy can activate several chemical and physical processes in the solid–liquid interface, accelerating the initial CaP nucleation on the surface of the material. Consequently, the time needed for HCAp precipitation on the surface of Class B biomaterials may be reduced significantly by the increased energy delivered in the system.

This novel method has been recently applied to dental ceramic/bioactive glass composites to significantly accelerate HCAp deposition. Bioactive glass–dental ceramic composites, containing 33.3 wt% of 58S bioactive glass and 66.7 wt% of dental ceramic (IPS Inline-Margin, Ivoclar), were synthesized by the sol-gel method, as previously described (Manda et al. 2012; Goudouri et al. 2014) and sintered at 930 °C with a rate of 60 °C/min under vacuum. A Q-switched Nd:YAG laser (Quantel YG980) was used, and the laser beam was directed to the center of each specimen, while it was immersed in 15 ml of $1.5\times$ SBF precursor liquid. Specimens were irradiated at laser fluence 1.52 J/cm^2 for 30 min, 1 h or 3 h. Immediately after laser treatment, specimens were re-immersed in $1.5\times$ SBF and incubated at 60 °C for up to 7 days. The solution was renewed every 6 h, 24 h, and then 2 days, and the solid-to-liquid ratio was preserved at 1 mg/1 ml. An HCAp layer was precipitated on the specimens irradiated for 3 h (Fig. 3), while exposure for 30 min or 1 h was not efficient in inducing HA precipitation. The application of laser irradiation resulted in three times faster HCAp formation compared to the conventional biomimetic method (Beketova et al. 2016).

Dental Composites Incorporating Bioactive and Antibacterial Glass-Ceramics

There is also much merit in the studies examining how current dental materials can be modified to maintain long-lasting bioactive and antibacterial properties (Graham et al. 2006; Tomson et al. 2007). Many of these studies provide evidence for the potential beneficial use of bioactive glasses (BGs) as additives to dental materials to enhance their biological effect. Bioactive glasses have been reported to induce mineralization of dentin disk surfaces (Forsback et al. 2004). These results suggest that dental materials with incorporated BGs could be instrumental in the remineralization of affected human dental tissues (Yli-Urpo et al. 2005).

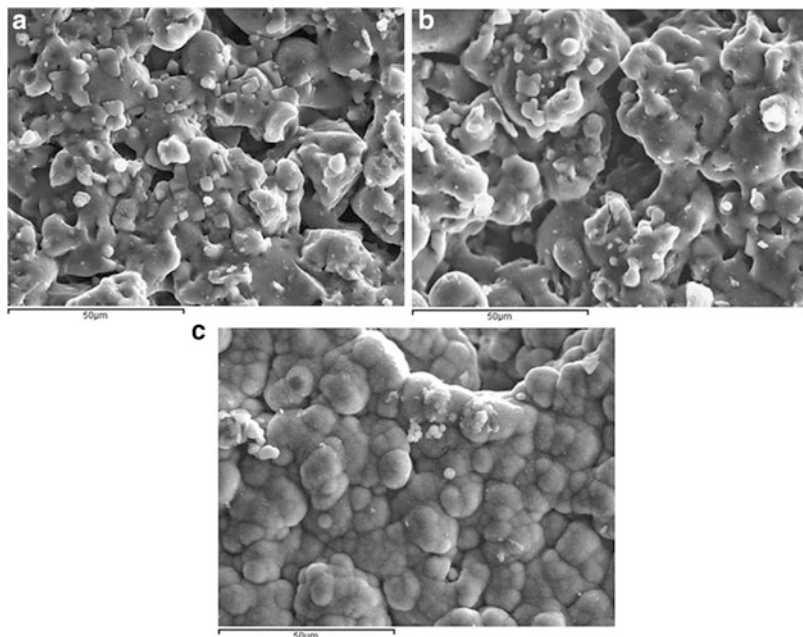


Fig. 3 SEM microphotographs of sol-gel-derived bioactive glass–dental ceramic composites: starting material (a), after laser irradiation (b), and after exposure to $\times 1.5$ SBF (c)

Indeed, new materials that can remineralize the dental hard tissues (Sauro et al. 2012a) will find multiple applications in the minimal invasive dentistry field. The principals of minimal therapeutic restoration may be enhanced by using bioactive materials capable of releasing specific ions within the bonding interface, to evoke a positive response from the biological environment and to induce protection and/or remineralization of the mineral-depleted dental tissues (Sauro et al. 2012b). Targeting this need, the physical, mechanical, bioactive, and antibacterial properties of a flowable resin composite incorporating the sol-gel-derived silver-doped bioactive dental glass-ceramic (Ag–BGCOMP) have been studied. The newly developed modified resin composite Ag–BGCOMP presented slightly decreased volumetric polymerization shrinkage and surface micro-hardness compared to non-modified resin composite, while the total bond strength was not significantly affected (Fig. 4a–c) (Kattan et al. 2015; Chatzistavrou et al. 2015). Moreover, the antibacterial properties against *Streptococcus mutans* (*S. mutans*) were found significantly higher (Fig. 4d), and the capability of the Ag–BGCOMP to exhibit bioactivity by forming on the surface an apatite-like phase was also presented (Fig. 4e, f).

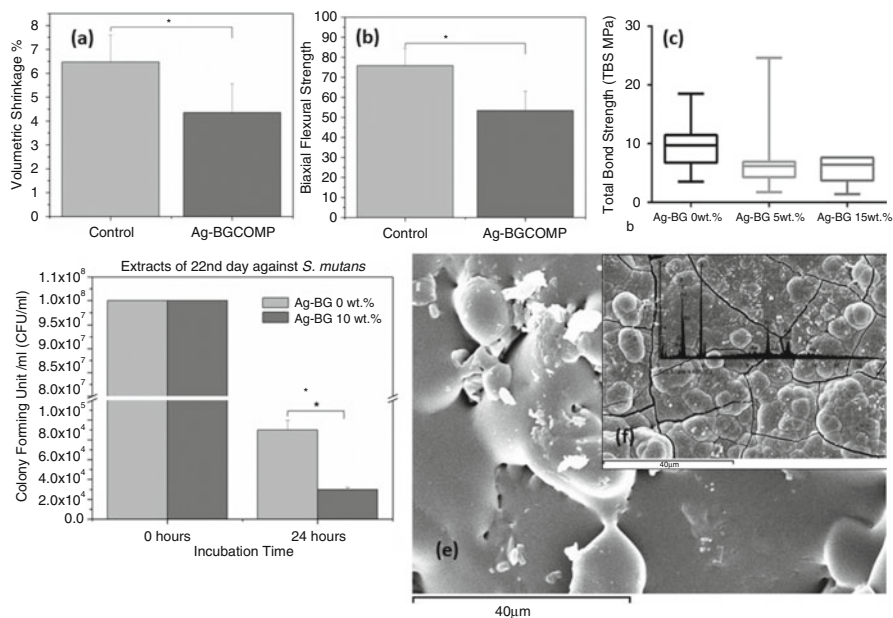


Fig. 4 Characteristic properties of Ag-BGCOMP compared to non-modified resin composite. (a) Volumetric polymerization shrinkage, (b) surface micro-hardness, (c) total bond strength, (d) antibacterial activity against *Streptococcus mutans* (*S. mutans*) and bioactive properties before, (e) and after (f) immersion in SBF (With permission to reproduce, Kattan et al. 2015; Chatzistavrou et al. 2015)

Conclusions and Future Trends

There is a huge need for developing bioactive and antimicrobial dental materials, capable of healing and regenerating the diseased, damaged, or lost dental tissues via tissue engineering approaches. There are still many aspects to be discovered and barriers to be overcome before new multifunctional dental materials become a routine procedure in dentistry. However, extended interdisciplinary research and effective collaboration between basic scientists and clinicians could eventually lead this field to the ultimate goal of developing advanced dental regenerative materials for a routinely use in the dental clinic practice.

References

- Abbasi Z, Bahrololoum ME, Bagheri R, Shariat MH. Characterization of the bioactive and mechanical behavior of dental ceramic/sol-gel derived bioactive glass mixtures. *J Mech Behav Biomed Mater*. 2016;54:115–22. <https://doi.org/10.1016/j.jmbbm.2015.09.025>.

- Arcos D, Greenspan DC, Vallet-Regi M. Influence of the stabilization temperature on textural and structural features and ion release in $\text{SiO}_2\text{-CaO-P}_2\text{O}_5$ sol-gel glasses. *Chem Mater.* 2002;14:1515-22.
- Aronne A, Esposito S, Pernice P. FTIR and DTA study of lanthanum aluminosilicate glasses. *Mater Chem Phys.* 1997;51:163-8.
- Beketova A, Poulakis N, Bakopoulou A, Zorba T, Papadopoulou L, Christofilos D, Kantiranis N, Zachariadis GA, Kontonasaki E, Kourouklis GA, Paraskevopoulos KM, Koidis P. Inducing bioactivity of dental ceramic/bioactive glass composites by Nd:YAG laser. Accepted for publication in *Dent Mater* September 2016.
- Brostow W, Estevez M, Lobland HEH, Hoang L, Rodriguez JR, Vargar S. Porous hydroxyapatite based obturation materials for dentistry. *J Mater Res.* 2008;23:1587-96.
- Cao W, Hench LL. Bioactive materials. *Ceram Int.* 1996;22:493-507.
- Chatzistavrou X, Chrissafis K, Polychroniadis E, Kontonasaki E, Koidis P, Paraskevopoulos KM. Inducing bioactivity in dental porcelain through Bioglass[®] Changes in thermal behaviour. *J Therm Anal Calor.* 2006;86:255-9.
- Chatzistavrou X, Esteve D, Hatzistavrou E, Kontonasaki E, Paraskevopoulos KM, Boccaccini AR. Sol-gel based fabrication of novel glass-ceramics and composites for dental applications. *Mater Sci Eng C.* 2010;30:730-9.
- Chatzistavrou X, Tsigkou O, Amin HD, Paraskevopoulos KM, Salih V, Boccaccini AR. Sol-gel based fabrication and characterization of new bioactive glass-ceramic composites for dental applications. *J Eur Ceram Soc.* 2012a;32:3051-61.
- Chatzistavrou X, Kontonasaki E, Bakopoulou A, Theocharidou A, Sivropoulou A, Paraskevopoulos KM, Koidis P, Boccaccini AR, Kasuga T. Development of new sol-gel derived Ag-doped biomaterials for dental applications. In *MRS Proceedings*. vol. 1417. Cambridge University Press; 2012b. p. mrsf11-1417.
- Chatzistavrou X, Fenno JC, Faulk D, Badylak S, Kasuga T, Boccaccini AR, Papagerakis P. Fabrication and characterization of bioactive and antibacterial composites for dental applications. *Acta Biomater.* 2014;10:3723-32.
- Chatzistavrou X, Velamakanni S, DiRenzo K, Lefkelidou A, Fenno JC, Kasuga T, Boccaccini AR, Papagerakis P. Designing dental composites with bioactive and bactericidal properties. *Mater Sci Eng C.* 2015;52:267-72.
- Demirkesen E, Maytalman E. Effect of Al_2O_3 additions on the crystallization behaviour and bending strength of a $\text{Li}_2\text{O-ZnO-SiO}_2$ glass-ceramic. *Ceram Int.* 2001;27:99-104.
- Fathi MH, Hanifi A. Evaluation and characterization of nanostructure hydroxyapatite powder prepared by simple sol-gel method. *Mater Lett.* 2007;61:3978-83.
- Forsback AP, Areva S, Salonen J. Mineralization of dentin induced by treatment with bioactive glass S53P4 in vitro. *Acta Odontol Scand.* 2004;62:14-20.
- Goudouri OM, Kontonasaki E, Kantiranis N, Chatzistavrou X, Papadopoulou L, Koidis P, Paraskevopoulos KM. A bioactive glass/dental porcelain system by the sol gel route: fabrication and characterization. *Key Eng Mater.* 2009;396-398:95-9.
- Goudouri O-M, Kontonasaki E, Theocharidou A, Papadopoulou L, Kantiranis N, Chatzistavrou X, Koidis P, Paraskevopoulos KM. Modifying a dental ceramic by bioactive glass via the sol-gel route: characterization and bioactivity investigation. *Mater Chem Phys.* 2011a;125:309-13.
- Goudouri OM, Kontonasaki E, Papadopoulou L, Chatzistavrou X, Koidis P, Paraskevopoulos KM. In vitro bioactivity studies of sol-gel derived dental ceramics/bioactive glass composites in periodically renewed biomimetic solution. *Bioceram Develop Appl.* 2011b;1: Article ID D110257. <https://doi.org/10.4303/bda/D110250>.
- Goudouri OM, Kontonasaki E, Theocharidou A, Kantiranis N, Chatzistavrou X, Koidis P, Paraskevopoulos KM. Dental ceramics/bioactive glass composites: characterization and mechanical properties investigation. *Bioceram Dev Appl.* 2011c; 1. <https://doi.org/10.4303/bda/D110257>.
- Goudouri O-M, Kontonasaki E, Papadopoulou L, Kantiranis N, Lazaridis NK, Chrissafis K, Chatzistavrou X, Koidis P, Paraskevopoulos KM. Towards the synthesis of an experimental

- bioactive dental ceramic. Part I: crystallinity characterization and bioactive behavior evaluation. *Mater Chem Phys*. 2014;145:125–34.
- Goudouri O-M, Kontonasaki E, Papadopoulou L, Manda M, Triantafyllidis KS, Stefanidou M, Koidis P, Paraskevopoulos KM. An experimental bioactive dental ceramic for metal-ceramic restorations. Part II: textural characteristics and mechanical properties investigation. Submitted to the *Journal of the Mechanical Behavior of Biomedical Materials* August 2016.
- Graham L, Cooper PR, Cassidy N, Nor JE, Sloan AJ, Smith AJ. The effect of calcium hydroxide on solubilisation of bio-active dentine matrix components. *Biomaterials*. 2006;27:2865–73.
- Höland W. Biocompatible and bioactive glass-ceramics – state of the art and new directions. *J Non-Cryst Solids*. 1997;219:192–7.
- Kattan H, Chatzistavrou X, Boynton J, Dennison J, Yaman P, Papagerakis P. Physical properties of an Ag-doped bioactive flowable composite resin. *Materials*. 2015;8:4668–78.
- Kokubo T, Kushitani H, Sakka S, et al. Solutions able to reproduce in vivo surface-structure changes in bioactive glass-ceramic A-W. *J Biomed Mater Res*. 1990;24:721–34.
- Kontonasaki E, Papadopoulou L, Zorba T, Pavlidou E, Paraskevopoulos K, Koidis P. Apatite formation on dental ceramics modified by a bioactive glass. *J Oral Rehabil*. 2003;30:893–902.
- Kontonasaki E, Sivropoulou A, Papadopoulou L, Garefis P, Paraskevopoulos K, Koidis P. Attachment and proliferation of periodontal ligament fibroblasts on bioactive glass modified ceramics. *J Oral Rehabil*. 2007;34:57–67.
- Kontonasaki E, Kantiranis N, Chatzistavrou X, Papadopoulou L, Paraskevopoulos KM, Koidis P. Studying dental ceramic-bioactive glass composites. *Key Eng Mater*. 2008;361–363:881–4.
- Kudo K, Miyasawa M, Fujioka Y, Kamegai T, Nakano H, Seino Y, et al. Clinical application of dental implant with root of coated bioglass: short-term results. *Oral Surg Oral Med Oral Pathol*. 1990;70:18–23.
- Li P, Yang Q, Zhang F, Kokubo T. The effect of residual glassy phase in a bioactive glass-ceramic on the formation of its surface apatite layer in vitro. *J Biomed Mater Res*. 1992;3:452–6.
- Manda M, Goudouri O-M, Papadopoulou L, Kantiranis N, Christofilos D, Triantafyllidis K, Paraskevopoulos KM, Koidis P. Material characterization and bioactivity evaluation of dental porcelain modified by bioactive glass. *Ceram Int*. 2012;38:5585–96.
- Mendonça G, Mendonca D, Aragao FJL, Cooper LF. Advancing dental implant surface technology— from micron- to nanotopography. *Biomaterials*. 2008;29:3822–35.
- Nganga S, Zhang D, Moritz N, Vallittu PK, Hupa L. Multi-layer porous fiber-reinforced composites for implants: in vitro calcium phosphate formation in the presence of bioactive glass. *Dent Mater*. 2012;28:1134–45.
- Ohtsuki C, Kokubo T, Yamamuro T. Mechanism of apatite formation on CaO-SiO₂-P₂O₅ glasses in a simulated body fluid. *J Non-Cryst Solids*. 1992;143:84–92.
- Pecheva E, Petrov T, Lungu C, Montgomery P, Pramatarova L. Stimulated in vitro bone-like apatite formation by a novel laser processing technique. *Chem Eng J*. 2008;137:144–53.
- Peitl Filho O, LaTorre GP, Hench LL. Effect of crystallization on apatite-layer formation of bioactive glass 45S5. *J Biomed Mater Res*. 1996;30:509–14.
- Piva E, Silva AF, Nor JE. Functionalized scaffolds to control dental pulp stem cell fate. *J Endod*. 2014;40 Suppl 4:S33–40.
- Ratner BD. Replacing and renewing: synthetic materials, biomimetics, and tissue engineering in implant dentistry. *J Dent Educ*. 2001;65:1340–7.
- Rizkalla AS, Jones DW, Clarke DB, Hall GC. Crystallization of experimental bioactive glass compositions. *J Biomed Mater Res*. 1996;32:119–24.
- Salinas AJ, Martin AI, Vallet-Regi M. Bioactivity of three CaO-P₂O₅-SiO₂ sol-gel glasses. *J Biomed Mater Res*. 2002;61:524–32.
- Sauro S, Watson TF, Thompson I, Toledano M, Nucci C, Banerjee A. Influence of air-abrasion executed with polyacrylic acid-Bioglass 45S5 on the bonding performance of a resin-modified glass ionomer cement. *Eur J Oral Sci*. 2012a;120:168–77.

- Sauro S, Osorio R, Watson TF, Toledano M. Therapeutic effects of novel resin bonding systems containing bioactive glasses on mineral-depleted areas within the bonded-dentine interface. *J Mater Sci Mater Med.* 2012b;23:1521–32.
- Sepulveda P, Jones JR, Hench LL. In vitro dissolution of melt-derived 45S5 and sol-gel derived 58S bioactive glasses. *J Biomed Mater Res.* 2002;61:301–11.
- Sung Y-M, Kim D-H. Crystallization characteristics of yttria-stabilized zirconia/hydroxyapatite composite nanopowder. *J Cryst Growth.* 2003;254:411–7.
- Sung Y-M, Lee J-C, Yang J-W. Crystallization and sintering characteristics of chemically precipitated hydroxyapatite nanopowder. *J Cryst Growth.* 2004;262(1):467–72.
- Tomson PL, Grover LM, Lumley PJ, Sloan AJ, Smith AJ, Cooper PR. Dissolution of bio-active dentine matrix components by mineral trioxide aggregate. *J Dent.* 2007;35:636–42.
- Tulyaganov DU, Ribeiro MJ, Labrincha JA. Development of glass-ceramics by sintering and crystallization of fine powders of calcium-magnesium-aluminosilicate glass. *Ceram Int.* 2002;28:515–20.
- Verné E, Brovarone CV, Milanese D. Glass-matrix biocomposites. *J Biomed Mater Res.* 2000;53:408–13.
- Wang L, Nancollas GH. Pathways to biomineralization and biodemineralization of calcium phosphates: the thermodynamic and kinetic controls. *Dalton Trans.* 2009;15:2665–72. <https://doi.org/10.1039/b815887h>.
- Yli-Urpo H, Närhi M, Närhi T. Compound changes and tooth mineralization effects of glass ionomer cements containing bioactive glass (S53P4), an in vivo study. *Biomaterials.* 2005;26:5934–41.
- Zhong J, Greenspan DC. Processing and properties of sol–gel bioactive glasses. *J Biomed Mater Res.* 2000;53:694–701.
- Zhong JP, Greenspan DC, Feng JW. A microstructural examination of apatite induced by Bioglass in vitro. *J Mater Sci Mater Med.* 2002;13:321–6.