Bioactive and inert dental glass-ceramics

Maziar Montazerian* and Edgar Dutra Zanotto

Department of Materials Engineering (DEMa), Center for Research, Technology and Education in Vitreous Materials (CeRTEV), Federal University of São Carlos (UFSCar), São Carlos, SP, 13.565-905, Brazil

www.certev.ufscar.br

*Corresponding author: Maziar Montazerian
Telephone: +55-16-33518527 / +55-16-33518556, E-mail: maziar_montaz@yahoo.com

Abstract

The global market for dental materials is predicted to exceed 10 billion dollars by 2020. The main drivers for this growth are easing the workflow of dentists and increasing the comfort of patients. Therefore, remarkable research projects have been conducted and are currently underway to develop improved or new dental materials with enhanced properties or that can be processed using advanced technologies, such as CAD/CAM or 3D printing. Among these materials, zirconia, glass or polymer-infiltrated ceramics, and glass-ceramics (GCs) are of great importance. Dental glass-ceramics are highly attractive because they are easy to process and have outstanding esthetics, translucency, low thermal conductivity, high strength, chemical durability, biocompatibility, wear resistance, and hardness similar to that of natural teeth, and, in certain cases, these materials are bioactive. In this review article, we divide dental GCs into the following two groups: restorative and bioactive. Most restorative dental glass-ceramics (RDGCs) are inert and biocompatible and are used in the restoration and reconstruction of teeth. Bioactive dental glass-ceramics (BDGCs) display bone-bonding ability and stimulate positive biological reactions at the material/tissue interface. BDGCs are suggested for dentin hypersensitivity treatment, implant coating, bone regeneration and periodontal therapy. Throughout this paper, we elaborate on the history, processing, properties and applications of RDGCs and BDGCs. We also report on selected papers that address promising types of dental glass-ceramics. Finally, we include trends and guidance on relevant open issues and research possibilities.

Keywords: Glass-ceramic; dental; mechanical properties; biomedical.
Content

1. Introduction

2. Glass-ceramic processing

3. Structure and properties of teeth

4. Restorative dental glass-ceramics (RDGCs)
   4.1. Manufacturing procedures for RDGCs
   4.2. Mica-based glass-ceramics
   4.3. Leucite-based glass-ceramics
   4.4. Lithium disilicate glass-ceramics
   4.5. Apatite-based glass-ceramics
   4.6. Zr-containing silicate glass-ceramics
   4.7. Miscellaneous RDGCs
      4.7.1. Fluorrichterite glass-ceramics
      4.7.2. Fluorcanasite glass-ceramics
      4.7.3. Apatite-mullite glass-ceramics
   4.8. Commercial RDGCs

5. Bioactive dental glass-ceramics (BDGCs)
   5.1. Coatings on dental implants
   5.2. Hypersensitivity treatment
   5.3. Bone and periodontal healing

6. Conclusions and trends

Acknowledgment

References
1. Introduction

The dental materials market is composed of several segments, including implants, core materials, restorative materials, impression materials, dental cements and bonding agents [1], [2]. The Research & Market group announced that the U.S. market value for dental materials was greater than $1 billion as of 2013 [3]. According to prediction by this group, the market is expected to grow substantially and approach $1.5 billion by 2020 [3]. Another report predicts that the global dental implants and prosthetics market is expected to reach approximately $10.5 billion in 2020 and will continue to grow at an annual rate of 7.2% from 2015 to 2020 [4]. Therefore, persistent competition exists among dozens of companies in research and development, marketing, and product prices, which drives continuous technological progresses in dental materials [3]-[5]. The main objectives behind this endeavor are to ease the workflow of dentists and to increase the comfort of patients [3]-[5]. These factors make dental materials a highly dynamic and exciting field [3]-[5]. Furthermore, market research groups have predicted that the segments of restoratives, dental cements, bonding agents, and core build-up materials will significantly increase in market value in the 2010-2020 decade [3]-[5]. However, certain sub-segments within these categories might decline, including amalgam and resin-based restoratives, which undergoing replacement by more modern and effective materials processed by CAD/CAM, 3D printing and tissue engineering [6]-[14]. Among the most promising materials, zirconia (ZrO₂), hybrids, glass-ceramics and glass-infiltrated ceramics are of great importance [6]-[14]. An analysis of glass-ceramic research and commercialization suggests that dental glass-ceramics is a potential thrust field for advanced technology [13]. Furthermore, research and development in academic communities and companies show increasing trends in the number of published papers and patents in this field, as summarized in Figure 1(a) and (b).
Previous review papers, book chapters [15]-[32] and, more recently, Gracis et al. [33] have classified dental ceramics into the following three groups: (1) glass-matrix ceramics, (2) polycrystalline ceramics, and (3) resin-matrix ceramics. In other words, these materials are classified according to whether a glass-matrix phase is present or absent, or whether the material contains an organic matrix that is highly filled with ceramic particles [15]-[33].

Dental glass-ceramics belong to the family of glass-matrix ceramics, and we have decided to divide them into the two sub-families of bioactive and restorative dental glass-ceramics. Bioactive dental glass-ceramics (BDGCs) are materials that show bone/tooth bonding ability and stimulate a particular biological reaction at the material/tissue interface. These materials have been suggested for use in hypersensitivity treatment, implant coating, bone regeneration and periodontal healing [15]-[33]. In contrast, most restorative dental glass-ceramics (RDGCs) are inert and biocompatible and are considered for use in restoration and reconstruction of teeth [15]-[33].

We recently reviewed the history and trends of bioactive glass-ceramics for use in medicine and demonstrated their enormous potential [34]. We also believe that dental glass-ceramics deserve much more attention due to their attractive properties, ongoing progress and significant market potential. Therefore, throughout this paper, we elaborate on the processing, properties and applications of RDGCs and BDGCs. In this context, we also report on selected valuable papers that have addressed promising types of dental glass-ceramics in recent years. Where deemed appropriate, we include future trends, open issues and guidance from a materials engineering perspective.

This critical review article is structured as follows. A brief introduction to glass-ceramic processing, properties and the structure of teeth is given in Sections 2 and 3. Commercial and promising types of RDGCs are classified and reviewed in Section 4. Potential applications and promising researches on BDGCs are explained in Section 5.
Finally, open relevant issues, trends and future research directions are highlighted in Section 6.

2. Glass-ceramic processing

Glass-ceramics were discovered by D. R. Stookey at Corning Inc., USA in 1953 and are polycrystalline materials produced by controlled heat treatment of certain glasses that contain one or more crystal phases embedded in a residual glass matrix [34], [35]. Figure 2 shows the main stages of the synthesis of glass-ceramics. First, the reactants are weighed, mixed and melted, usually in a platinum crucible. Glass articles are shaped by casting, pressing, blowing or any other traditional glass forming techniques. Finally, monolithic glass-ceramics are obtained after controlled heat treatment of the glass at temperatures above the glass transition temperature \( T_g \) to induce internal nucleation and growth of the desired crystal phase(s) [35].

A second, less frequently used, but interesting method is sintering with concurrent crystallization of a powdered glass (e.g., for preparing a slurry and veneering dental materials). In this method, the melt can be quenched into water or air before grinding and sieving into the desired particle sizes to obtain a “frit”. An advantage of the fritting route is that mixtures of different compositions can be developed. These mixtures are subsequently formed into the desired shapes using molds (with proper binders) and densified by sintering. Sintering usually proceeds concurrently with crystallization in which the free surfaces of the glass frits encourage crystallization. Sinter-crystallization is the process followed in the manufacture of selected glass-ceramics that show poor internal crystallization. Pressure is sometimes applied to increase the density and minimize residual porosity during sintering [34], [35].
Finally, the sol-gel method has been used to make a new generation of bioactive gel-derived glass-ceramics and allows easy tailoring of their composition to match the requirements of specific applications [36]-[38]. The sol-gel approach is a chemically based method for producing glass-ceramics at much lower temperatures than the traditional processing methods described above. Frequently, certain steps shown in Figure 2 are involved in making glasses or glass-ceramics via the sol-gel method. Densification and crystallization of gel-derived glasses finally lead to glass-ceramics [34]-[38]. The fundamentals of glass-ceramic development via melting or sol-gel procedures have been comprehensively described in numerous textbooks [35]-[38]. Glass-ceramics always contain a residual glassy phase and one or more embedded crystal phases. The crystal content varies between 0.5 and 99.5 percent but most frequently lies between 30 and 70 percent, and the remaining content is the residual glass phase. Controlled crystallization yields glass-ceramics with interesting, at times unusual, combinations of properties such as biological, electrical, thermal, mechanical, etc [6]. The types of crystals, crystal volume fraction, distribution in the matrix, and physicochemical properties of both the crystals and the residual glass control the properties of glass-ceramics (including dental GCs), such as translucency, strength, fracture toughness, machinability, and chemical durability [35].

3. Structure and properties of teeth

Teeth have a complex structure that originates from specialized cells known as ameloblasts, odontoblasts and cementoblasts [1], [2]. Figure 3 shows a cross-section of a tooth. The enamel is the hard outer layer that appears as the crown and is formed by ameloblasts. These cells accumulate on the outside layer of the tooth bud. When the tooth erupts, ameloblasts are not able to further proliferate, and thus enamel can no longer be
formed, which means that the body cannot repair the enamel. The dentine is formed by odontoblasts. These cells are located on the inner side of the tooth bud, between the enamel and the pulp. The dentine is considered the main foundation of the tooth and supports the enamel, creates protection for the pulp, and through its covering below the gums, enhances the attachment by ligaments to the surrounding bone. The pulp is the inner portion of a tooth, which consists of living connective tissue and odontoblasts. The functions of the pulp are to form dentin, supply nutrients and perceive pain. Gums surround the teeth and create a seal around them. Bone holds the teeth firmly in place, and nerves and blood vessels keep them alive and healthy [1], [2].

According to the ISO 6872 standards, a dental material must have notably good chemical, mechanical, and optical properties comparable to those of natural teeth. For example, the chemical durability must be higher than that of natural teeth [40].

The mechanical properties of the three hard tissues mentioned above, i.e., enamel, dentine and bone, are of great importance because stresses are applied to teeth as a result of chewing and tooth grinding and during periods of psychological stress [40]. The enamel is relatively hard and brittle, the dentine is much softer and more compliant, and bone is even more compliant. Table 1 summarizes the mechanical properties of enamel, dentin and bone. Therefore, mechanical properties of dental materials such as fracture strength (σ), fracture toughness (KIC), and wear resistance are highly important for avoiding material damage and breakage. In terms of optical properties, these materials must exhibit translucency, color, opalescence, and fluorescence similar to those of natural teeth [41].
Table 1. Mechanical properties of enamel, dentin, and bone [41].

<table>
<thead>
<tr>
<th></th>
<th>Strength (MPa)</th>
<th>Fracture toughness (MPa.m$^{0.5}$)</th>
<th>Young's modulus (GPa)</th>
<th>Vickers Hardness (GPa)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enamel</td>
<td>260-290$^*$</td>
<td>0.5-1.5</td>
<td>70-100</td>
<td>3-5</td>
</tr>
<tr>
<td>Dentin</td>
<td>230-305</td>
<td>3</td>
<td>15-30</td>
<td>0.6</td>
</tr>
<tr>
<td>Cortical bone</td>
<td>50-150</td>
<td>2-12</td>
<td>5-20</td>
<td>-</td>
</tr>
</tbody>
</table>

* If supported by dentin

4. Restorative dental glass-ceramics (RDGCs)

A restorative material that mimics the tooth properties can be used as inlays, onlays, full crowns, partial crowns, bridges, and veneers. Figure 4 shows a selection of these applications.

Ceramics

Historically, Dr. Duchateau, with the aid of dentist Dr. Chemant, developed the first restorative ceramic-based material made from porcelain in 1774 for his tooth [42]. Approximately sixty years later, Stockton Co. was the first industry to manufacture a porcelain tooth in 1837. C. H. Land followed Stockton's invention in 1889 and patented the all-porcelain crown, which was further developed and used until the 1950s. To improve mechanical strength, porcelain restorations in the 1950s were reinforced with a metal substructure on which the porcelain was fused. The new restorations were known as porcelain-fused-to-metal restorations (PFMs). Since then, these constructs have been extensively used for improved esthetics and quality and have demonstrated excellent clinical performance [42], [43]. Although PFMs have certain esthetic disadvantages due to their metal frameworks (anesthetic metal rings at the tooth margin and a grayish appearance of the gums), they are still considered the gold standard in terms of reliability. Extra efforts in this
field led to the development of the first machinable CAD/CAM porcelain Vitablocs® Mark I, made by Vita Zahnfabrik Co., Germany, in 1985. This company also introduced In-Ceram® products in the 1990s, which are porous alumina/zirconia materials infiltrated with an esthetic glass. Later on, Procera®, a pure alumina veneered with esthetic porcelain, was developed by Nobel Biocare, Switzerland, in the mid-1990s. Currently, zirconia (ZrO_2) and composites made of sintered ceramic with pores filled with a polymer material are available in the market [16]-[20], [42]-[44].

Glass-ceramics

The first dental glass-ceramic was a mica-based material known as Dicor® that was introduced by Malament and Grossman [45] in the mid-1980s. This castable glass-ceramic was gradually modified because a high risk of fracture was observed, and the manufacturing procedure used in the dental laboratory was complicated. Later on, in the 1990s, scientists focused on the development of stronger and more reliable glass-ceramics to cover all restorative aspects of teeth [16]-[20], [42]-[44]. Tremendous efforts led to the introduction of various dental glass-ceramics, and, in this section, we explore the history, processing, properties and applications of these materials. First, a short introduction to manufacturing procedures of RDGCs is presented, the RDGCs are classified according to their composition and crystal phases, and finally, selected recent relevant research studies on each type of glass-ceramics are reviewed.

4.1. Manufacturing procedures for RDGCs

In general, dental technicians prepare RDGCs using the following four popular methods: (1) lost-wax casting, (2) heat-pressing, (3) CAD/CAM and (4) pressureless
sintering. Figures 5-7 schematically show the various stages and instruments used in these techniques.

In lost-wax casting, an accurate impression of the prepared tooth is first obtained by a dentist (Figure 5a), and a cast is made from the impression (Figure 5b). Later, a model of the restoration that resembles the shape of the final restoration is shaped on the cast using a particular type of wax (Figure 5c). The model is invested in special refractory materials (Figure 5d). Wax burnout takes place at 900 °C, and the ceramic mold is partially sintered. The material for fabrication of a glass-ceramic is supplied as a glassy ingot, which is located in a furnace specially designed for casting. The glass ingot becomes liquid during heating, and following a short time hold at 1300-1500 °C, the melt is forced into a mold by centrifugal force (Figure 5e). The glass casting is retrieved, excess glass is polished off, and after the final controlled heat treatment and coloring processes, the glass-ceramic restoration is ready for clinical use (Figure 5f) [35], [44], [46]. The mold is cooled to room temperature, and the cast glass dental restoration is removed. The glass is usually transparent, and quality control can be applied to locate possible defects. The glassy dental restoration is placed in an oven for the controlled crystallization process. During heat treatment, the glass is converted into a glass-ceramic. Finally, the dental technician applies a colored frit to the surface of the glass-ceramic to match the color of the patient’s teeth and performs the final heat treatment to melt the glaze [35], [44], [46].

In the heat-pressing method, the dental technician uses as-prepared glass-ceramic ingot to produce the final restoration. First, a mold is produced via the previously described lost-wax procedure. The mold and glass-ceramic ingot are placed in a furnace specially designed for this processing method (Figure 6) [35]. Once the glass-ceramic ingot has become a very viscous liquid of approximately $10^{11}$ Pa.s, it is forced by an Al$_2$O$_3$ plunger (via application of a relatively low force of 200-300 N) into the hollow portion of the mold at approximately
1000-1200 °C. After the cylinder has adequately cooled, the investment material is removed from the glass-ceramic restoration by blasting it with silica sand, aluminum oxide, glass beads, or silicon carbide grit. Generally, heat-pressed glass-ceramics have advantages over castable ones, such as the absence of shrinking during the crystallization process and no need for preparation in the dental lab, a step that results in time-consuming extra work flow, high risk of inhomogeneity, and poor margin fit [35].

In the third method, machinable restorative glass-ceramics are fabricated using a CAD/CAM (computer-aided design and computer-aided manufacturing) system [47], [48]. Typically, CAD/CAM dental restorations are machined from solid blocks of partially crystallized glass-ceramics (containing a machinable crystal phase) that are subjected to further heat treatment to fully develop the glass-ceramic and achieve adequate properties and color that closely match the basic shade of the restored tooth (Figure 7). After the decayed or broken areas of the tooth are corrected by the dentist, an image (scan) is taken of the prepared tooth and the surrounding teeth (Figure 7a). This image, known as a digital impression, is used as data input into a computer. Proprietary software creates a replacement part for the missing areas of the tooth, thus creating a virtual restoration (Figure 7b). The software sends this virtual data to a CAD/CAM machine in which the replacement part is carved out of a solid block of glass-ceramic (Figure 7c). Stains and glazes can be fired onto the surfaces of the machined crown or bridge to correct the chromatic appearance of the restoration (Figure 7d). The restoration is adjusted in the patient’s mouth and cemented or bonded in place [47], [48].

In the fourth method, known as pressureless sintering, a thin layer of glass-ceramic is veneered over restorative materials such as zirconia, metals or glass-ceramics. Veneering is performed to adjust the final shade of the restoration. In general, a slurry containing glass-ceramic fine powders plus coloring agents is brushed over the surface. The artifact is held in
a furnace at an appropriate temperature for the required time to sinter and crystallize the glass-ceramic and fuse it to the restoration [35]. In the following section, we describe the various types of dental glass-ceramics.

### 4.2. Mica-based glass-ceramics

Glass-ceramics containing mica crystals \( (X_2Y_{4+6}Z_8O_{20}(OH,F)_4 \) in which \( X = K, Na, \) or Ca; \( Y = Al, Mg; Z = Si \) or Al) were the first type of glass-ceramics used in the fabrication of dental restorations. Dicor® was the first material in this family and was introduced by Malament and Grossman in the mid-1980s [45] and commercialized by Dentsply International [35].

A typical glass composition contains \( (56-64)SiO_2–(0-2)Al_2O_3–(15-20)MgO–(12-18)K_2O–(4-9)F–(0-5)ZrO_2–0.05CeO_2 \) in wt%. The glass is shaped via lost-wax centrifugal casting after a hold at 1370 °C for ~6 min. The machinable block of Dicor® MGC is also available for CAD/CAM processing [35]. It was demonstrated by Bapna and Mueller [49] that during devitrification of Dicor®, spinodal decomposition of the glass matrix occurs, followed by precipitation of fine round crystals. Further, an isothermal hold for 6 h at 1075 °C transforms the round mica grains into plate-like mica crystals via a dissolution and reprecipitation mechanism [49]. The restoration is further glazed with coloring agents. The final product contains mica crystals embedded in the residual glass [35]. Figure 8 shows the microstructure of a mica glass-ceramic. Mica has a sheet-like and interlocked morphology amenable to machinability and with advantageous mechanical properties [35]. The size and volume fraction of the mica plates are critical parameters for adjusting the wear resistance and the mechanical properties of the respective glass-ceramic [50].
Dicor® is a classical example of a mica-type glass-ceramic because it is translucent, machinable, and has fair mechanical properties. The bending strength, fracture toughness, Vickers hardness and Young's modulus of Dicor® are $\sigma = 150$ MPa, $K_{IC} = 1.4$-$1.5$ MPa.m$^{0.5}$, $HV = 3.5$ GPa and $E = 70$ GPa, respectively, and its thermal expansion coefficient is $7.2 \times 10^{-6}$ K$^{-1}$ (at 25-600 °C). Shading is performed using colorants premixed with a glazing material. The applications of Dicor® glass-ceramic in restorative dentistry are veneers, inlays, onlays and dental crowns. The cast Dicor® glass-ceramic is mostly used to fabricate complete crowns. This glass-ceramic is not recommended for fixed partial dentures, abutments, or dental bridges because its mechanical strength is not sufficient [35].

A relatively low mechanical strength and difficult processing conditions are the main drawbacks of mica-based glass-ceramics, which restrict their application and popularity. Therefore, numerous attempts in 1990s and early 2000s were made to overcome the weakness of this material. Prof. Denry's group at Ohio State University pioneered modifications of the composition of Dicor® and improved its properties. The Denry group replaced potassium with lithium and developed taeniolite, a lithium-containing tetrasilicic fluormica (KLiMg$_2$Si$_4$O$_{10}$F$_2$) with improved thermal and mechanical properties [51]. By changing the glass composition, a new glass-ceramic was developed based on the crystallization of mica (KNaMg$_2$Si$_4$O$_{10}$F$_2$) and K-fluorrichterite (KNaCaMg$_5$Si$_8$O$_{22}$F$_2$) crystals, which were tougher (Section 4.7.1) [52]-[54]. Uno et al. [55] and Qin et al. [56] substituted K$^+$ or Na$^+$ with Ba$^{2+}$ or Ca$^{2+}$ as the interlayer ions of mica crystals, which resulted in the formation of high-strength mica glass-ceramics [55], [56]. Oriented mica glass-ceramics fabricated by hot-pressing or extrusion processes had higher strength and toughness than the conventional castable mica glass-ceramics that contained randomly oriented mica crystals with a house-of-cards structure [57]-[61]. In addition, these materials could be reinforced with ZrO$_2$ crystallized from the bulk glass [62]-[66]. It has been reported that a
calcium mica-based nanocomposite containing nano-size (20-50 nm) tetragonal-ZrO$_2$ particles exhibits notably a high flexural strength (500 MPa) and fracture toughness (3.2 MPa.m$^{1/2}$) [62]. The excellent mechanical performance is related to crack deflection by mica plates and ZrO$_2$ particles [62]. All of these modifications improved the properties of mica-based glass-ceramics, but they still could not compete with alternative materials such as lithium disilicate GC to survive in this competitive market. Dicor® always suffered from relatively low strength, inability to color internally and a difficult manufacturing process. However, in a 20-year clinical study with Dicor® GC, Malament and Socransky [67] reported an estimated success rate of greater than 90%. These materials are still used by dentists and technicians who prefer old materials that they know well and trust. However, these materials are undergoing gradual replacement by new CAD/CAM and heat-pressed GCs.

4.3. Leucite-based glass-ceramics

Leucite (KAlSi$_2$O$_6$) mineral was first added to feldspathic porcelains to raise the coefficient of thermal expansion to match the metals on which they were fused. Leucite-containing glass-ceramics were introduced in the early 1990s and were the first heat-pressed GCs [25]. Leucite glass-ceramics are derived from the SiO$_2$–Al$_2$O$_3$–K$_2$O glass system. The typical glass composition is (59-63)SiO$_2$–(19-23.5)Al$_2$O$_3$–(10-14)K$_2$O–(3.5-6.5)Na$_2$O–(0-1)B$_2$O$_3$–(0-1)CeO$_2$–(0.5-3)CaO–(0-1.5)BaO–(0-0.5)TiO$_2$ in wt%. The glass-ceramic is produced in the form of ingots, and the dental technicians heat-press these ingots at 1150 °C (with a pressure of 0.3 to 0.4 MPa) into a mold made using the lost-wax technique. This temperature is held for 20 minutes in a specially designed automatic heat-pressing furnace (Figure 6) [35]. Leucite crystals precipitate with controlled surface crystallization. To this end, the crystals nucleate and grow from glass particle surfaces that are densified upon firing.
at 950 °C to form a homogeneous glass-ceramic block. A final heat treatment at 1050 °C encourages further crystal growth. This controlled heat treatment yields glass-ceramics with flexural strength, fracture toughness, Vickers hardness and Young's modulus of $\sigma = 160$ MPa, $K_{IC} = 1.3$ MPa.m$^{1/2}$, $HV = 6.2$ GPa and $E = 65$ GPa, respectively. The leucite crystals are responsible for the high linear thermal expansion of the glass-ceramic of $15 \times 10^{-6}$ K$^{-1}$ to $18.25 \times 10^{-6}$ K$^{-1}$ in a temperature range of 100-500 °C [35].

According to Höland and Beall, the leucite crystals strengthen the glass-ceramic by deflecting the propagating crack [35]. Furthermore, Serbena et al. [68] concluded that the main toughening mechanisms in glass-ceramics (without the chance of phase transformation toughening) are caused by crack bowing and trapping (for low crystallized volume fractions), as well as by the greater elastic modulus and fracture toughness of the crystal precipitates. The chemical durability and abrasion properties of this glass-ceramic are acceptable according to the ISO standard. Glass-ceramic blocks for CAD/CAM processing are also available (Table 2). The restorations are placed using the adhesive bonding technique. Leucite glass-ceramics are used as veneers, inlays, onlays, and anterior and posterior crowns, but their strength is insufficient for fixed posterior bridges. For bridges, this type of GC is veneered onto a flexible, tough metallic framework [35].

In the early 2000s, Höland and coworkers at Ivoclar Vivadent AG succeeded in introducing apatite-leucite glass-ceramics as an alternative to their leucite-based product (Table 2) [69]. These researchers reached a stage at which it became possible to produce restorations that contain building blocks in the form of needle-like apatite, similar to those of natural teeth. The needle-like apatite crystals with a hexagonal base (Figure 9) positively influenced the esthetic properties and various mechanical parameters of the material. The composition also contained fluorine, which induced the formation of fluorapatite ($Ca_3(PO_4)_2F$) and enhanced the chemical properties of the material. Therefore, this glass-ceramic...
ceramic was commercialized (Table 2) as a sintered glass-ceramic to replace dentin, reproduce the incisal area and create specific optical effects (e.g., opalescence over a metallic substrate) [69], [70].

Leucite-apatite glass-ceramics are applied on metallic frameworks via pressureless sintering. However, the risk of the glass-ceramic pulling away from the metal surface still exists. Therefore, sintering should be carefully performed within a temperature range of 550-900 °C, and shrinkage must be controlled to prevent tearing. Michel et al. [71] attempted to minimize this risk by developing nano-coatings on leucite-fluorapatite glass-ceramic particles prior to sintering. The coating influences the rheology of the slurry and the properties of the veneer. The following two substances were chosen for the coatings: (a) a combination of inorganic chemicals (ZnCl₂, AlCl₃, or BCl₃) and polyethylene glycol (PEG) and (b) an exclusive polymer. Both groups of materials positively improved the sintering properties of the glass-ceramics and suppressed extensive tearing [71]. A nano-sized leucite glass-ceramic was further developed by Theocharopoulos et al. [72], who sintered nano-sized commercial glass particles (Ceramco® and IPS Empress®) prepared by high-energy milling to trigger surface crystallization of leucite crystals at the nano-scale. As a result, these new glass-ceramics showed an increased leucite crystal number at the nano-scale (median crystal sizes of ~0.05 µm²). These new glass-ceramics had a higher mean bending strength than the competing commercial materials. The mean bending strengths were, e.g., 255 ± 35 MPa for the nano-leucite glass-ceramic, 76 ± 7 MPa for Ceramco® (restorative porcelain) and 166 ± 31 MPa for IPS Empress® (Leucite GC) [72]. More recently, Aurélio et al. [73] observed an increased bending strength and decreased surface roughness for a leucite-based glass-ceramic sintered at a higher sintering temperature after machining. The crystalline structure was not modified. However, increased sintering time and firing below T_g significantly reduced the fracture strength [73].
Leucite-based glass-ceramics are also well suited for the CAD/CAM process developed by Ivoclar Vivadent AG. This product is available in multi-colored CAD/CAM blocks [74]. The block (Figure 10) allows the optical properties of natural teeth to be closely imitated. This glass-ceramic consists of a total of four to eight main and intermediate layers [74].

In 2000-2011, novel low-wear/high-strength leucite-based glass-ceramics were developed at Queen Mary University by Dr. Cattell’s team to prevent fracture and wear of dental ceramic restorations. Dr. Cattell began his research to overcome problems related to the brittle fracture of porcelain restorations and their poor survival rates and intended to develop leucite-based glass-ceramics by heat-extrusion. This novel method led to a homogenous distribution of fine crystals and increased reliability (Weibull modulus, $m = 9.4$ and $\sigma = 159$ MPa) compared with commercial materials ($m = 6.1$ and $\sigma = 120$ MPa, Empress®) [75]. Additionally, controlling the leucite crystal size to $0.15 \pm 0.09 \mu m^2$ was the key to enhancing the properties of Dr. Cattell’s glass-ceramic [76], [77]. The Cattell team also focused on the fundamental aspects of nucleation and crystal growth of leucite glass-ceramics and powder processing to control surface crystallization and produce first fine and later nano-scale leucite glass-ceramics [78]. These studies were critical to reduce the size of the leucite crystals and had enormous benefits in terms of reduced enamel wear, improved esthetics and increased strength. Leucite glass-ceramics were subsequently produced with significantly higher flexural strength ($\sigma > 250$ MPa), reliability ($m = 12$) and lower enamel wear [79], [80]. This material could be processed using heat-extrusion, CAD-CAM and 3D printing and was later commercialized by Den-Mat Holdings as an esthetic restorative material with the name of Lumineers® (Table 2).

Fradeani et al. [81] reported on the survival rate of leucite glass-ceramic crowns. Crowns were studied over periods ranging from 4 to 11 years. The probability of survival of 125 crowns was 95.2% at 11 years (98.9% in the anterior segment and 84.4% in the posterior
segment). Only six crowns had to be replaced. Most of the 119 successful crowns were rated as excellent. Guess et al. [82] investigated the long-term performance of leucite glass-ceramic veneers. Twenty-five patients underwent restorations using 42 overlap veneers (incisal/palatal butt-joint margin) and 24 full veneers (palatal rounded shoulder margin). All restorations were anterior veneers. The 7-year Kaplan-Meier survival rate was 100% for full veneers and 97.6% for overlap veneers [82].

4.4. Lithium disilicate glass-ceramics

In 1998, a third generation of dental glass-ceramic, lithium disilicate (LS2) glass-ceramic was introduced for single- and multiple-unit frameworks. This material re-emerged in 2006 as a heat-pressable ingot and a partially crystallized machining block and was successfully used to produce a crown or bridge framework with mechanical properties that were almost three times higher than those of the leucite-based glass-ceramic. Currently, lithium disilicate glass-ceramic is the most popular restorative glass-ceramic in the field of dental materials [31], [35].

A typical glass composition of this glass-ceramic contains (57-80)SiO$_2$–(11-19)Li$_2$O–(0.0-13)K$_2$O–(0-11)P$_2$O$_5$–(0-8)ZrO$_2$–(0-8)ZnO–(0-5)Al$_2$O$_3$–(0-5)MgO in wt%. Coloring oxides are also included in the glass composition. The glass composition was designed such that it contains at least 65 wt% fine rod-like entangled lithium disilicate crystals (Li$_2$O-2SiO$_2$). The glass is molded via heat-pressing followed by a controlled heat treatment that leads to the final product. The aim of the heat treatment is to induce internal nucleation and crystallization. The initial thermal treatment is performed slightly above $T_g$ to control the number of nuclei (450-550 °C for 5 min to 1 hour). When the temperature is increased to 750-850 °C for approximately 2 hours, lithium disilicate crystallizes. Later on, in the dental
lab, the glass-ceramic ingot is heat-pressed at 920 °C for 5-15 min to flow viscously into a mold made using the lost-wax technique to form the desired restoration. The bending strength and fracture toughness of heat-pressed LS2 glass-ceramics are approximately 350-400 MPa and 2.3-2.8 MPa.m$^{1/2}$, respectively [31], [35]. Chung et al. [83] have reported that repeated heat-pressing can produce a statistically significant increase in the flexural strength of lithium disilicate glass-ceramic (IPS Empress® II).

The interlocked lithium disilicate crystals dispersed within the glassy matrix impart desirable mechanical and optical properties to the product. One of the main toughening mechanisms of brittle materials is the deflection of cracks around the crystals. This effect is illustrated in Figure 11 in which lithium disilicate crystals of 20 µm are precipitated in the glass-ceramic matrix. The material was indented with a pyramidal tip, and the propagating cracks were deviated from their natural path by the crystals. The fracture toughness of oxide glasses is typically between 0.50 and 0.75 MPa.m$^{1/2}$, whereas that of the LS2 glass-ceramic reaches 2.8 MPa.m$^{1/2}$ [84], [85], [86].

A particular type of lithium disilicate glass-ceramic can also be shaped by CAD/CAM. To meet the challenging requirements of the CAD/CAM process, a particular heat treatment is followed, as shown in Figure 12, e.g. for IPS e.max® CAD [86]. First, a monolithic piece of glass is prepared by casting the melt in a mold (Figure 12a). Second, a glass-ceramic containing lithium metasilicate (Li$_2$O-SiO$_2$) is developed by intermediate heat treatment of the glass at 690-710 °C for 10-30 min (Figure 12b). This intermediate material (which is supplied in blue color) has been specially designed to facilitate the machining process in the CAD/CAM technique (Figure 12b). After the machining process (Figure 12c), the material is heated at 850 °C for 20-31 min to form the lithium disilicate glass-ceramic that displays a characteristic tooth color (Figure 12d). The resulting dental restorations can be polished and...
completed with glazing to match the color of the patient’s teeth. The glass-ceramic ingot containing lithium metasilicate crystals, as provided by the material suppliers, has a flexural strength of 130 MPa, but the strength and fracture toughness increases to 360 MPa and 2.3 MPa m$^{\frac{1}{2}}$, respectively, after conversion of the machined glass-ceramic to the final product. The reduced strength and toughness of CAD/CAM materials compared with the heat-pressed material is due to the fact that the latter glass-ceramic contains needle-like and elongated crystals with higher aspect ratio than its CAD/CAM counterpart [31], [35], [86].

An interesting study by Lien et al. [87] revealed that intermediate heat treatments in temperature ranges below 590 °C, between 590 and 780 °C, and above 780 °C can influence the final microstructure and properties of the lithium disilicate glass-ceramic (IPS e.max® CAD). The finely knitted mesh of Li$_2$O-SiO$_2$ predominated below 590 °C; spherical-like phases of Li$_2$O-SiO$_2$, Li$_2$O-2SiO$_2$, and Li$_3$PO$_4$ emerged between 590 and 780 °C; and, irregularly oblate crystals of Li$_2$O-2SiO$_2$ arose above 780 °C. At each of those three evolutionary stages, the glass-ceramic formed through controlled crystallization often yielded a microstructure that possessed interesting and sometimes peculiar combinations of properties. Additionally, the growth of Li$_2$O-2SiO$_2$ crystals within the IPS e.max® CAD blocks was independent of the overall heating time but dependent on a minimum temperature threshold (780 °C). Groups of samples heated above the minimum temperature threshold (780 °C) up to 840 °C exhibited enhanced flexural strength, fracture toughness, and elastic modulus compared with those of groups that were intentionally not heated above 780 °C [87].

Recent research by Al Mansour et al. [88] showed that spark plasma sintering (SPS) can be used to refine the microstructure of lithium disilicate glass-ceramics (IPS e.max® CAD). Densification by SPS results in textured and fine nano-crystalline microstructures. This group believes that SPS generated glass-ceramic might have unique properties and could be useful in the production of CAD/CAM materials for dentistry [88].
Although $P_2O_5$ and ZnO initiate microphase separation, which induces the crystallization pathways and kinetics, it appears that $ZrO_2$ has a more beneficial effect on the crystallization and strengthening of lithium disilicate glass-ceramics [89], [90]. New commercial lithium disilicate glass-ceramics for CAD/CAM are advertised as tougher and more reliable due to the presence of at least 10 wt% $ZrO_2$ dissolved in the residual glass. These glass-ceramics (Table 2) are Celtra Duo® (Dentsply), IPS e.max CAD® (Ivoclar) and Suprinity® (Vita). Zirconia influences the crystallization by hampering crystal growth. With increasing $ZrO_2$ content, the crystals become smaller. By increasing the crystallization temperature, the crystal growth increases, as expected. The translucency of the glass-ceramic can be adjusted by adding $ZrO_2$. A highly translucent glass-ceramic with a contrast ratio of ~0.4 and high three-point bending strength (700-800 MPa) was developed [89].

According to Kaplan-Meier method, the cumulative survival rate of lithium disilicate crowns is 94.8% after 8 years [91], but only 71.4% of three-unit bridges survive after 10 years [92]. Therefore, crowns made of a lithium-disilicate framework can be safely used in the anterior and posterior regions [91], but bridges present a higher risk of fracture than metal-porcelain prostheses or other more recently developed ceramic materials, such as zirconia and alumina [92], [93]. Figure 13 shows the successful use of CAD/CAM lithium disilicate glass-ceramic crown in a posterior restoration [74].

### 4.5. Apatite-based glass-ceramics

To further improve the translucency and shade match and to adjust the wear behavior to that of the natural tooth, lithium disilicate, leucite glass-ceramics, and sintered $ZrO_2$ are veneered with an appropriate apatite-containing glass-ceramic using a pressureless sintering process. For example, Ivoclar Vivadent AG developed the fluorapatite glass-ceramic IPS
e.max® Ceram, which is a low-fusing aluminosilicate glass-ceramic specially designed for veneering lithium disilicate glass-ceramic (IPS e.max® CAD and IPS e.max® Press) or CAD/CAM zirconia. A typical composition of this glass-ceramic is (60-65)SiO$_2$–(8-12)Al$_2$O$_3$–(6-9)Na$_2$O–(6-8)K$_2$O–(2-3)ZnO in wt% with the addition of CaO, P$_2$O$_5$, F (2-6 wt%), other oxides (2-8.5 wt%) and pigments (0.1-1.5 wt%) [21], [31], [35]. This glass-ceramic is offered in powdered form for the slurry layering technique and is available in all classical tooth shades. The material is fired at 750-760 °C and crystallizes in the volume, resulting in different concentrations of nano-fluorapatite crystals with a diameter of 100 nm and a length of less than 300 nm and micro-fluorapatite crystals with a diameter of 300 nm and a length of 2-5 µm. The total adjustable amount of fluorapatite in the glass-ceramic is between 19 and 23 wt%. The fluorapatite crystal (Ca$_5$(PO$_4$)$_3$F) acts as a component that adjusts the optical properties of the restoration to those of natural teeth. For this reason, researchers have attempted to crystallize apatite in the nano-sized dimension. The strength, hardness and thermal expansion coefficient of the final product are $\sigma = 90$ MPa, $HV = 5.4$ GPa and $CTE = 9.5 \times 10^{-6}$ K$^{-1}$, respectively. The leucite-apatite glass-ceramic described in Section 4.3 is another good veneering material [74].

4.6. Zr-containing silicate glass-ceramics

After the development of the ZrO$_2$ root canal post and implant abutment, a restorative material was required that can be placed on ZrO$_2$. To fulfill this need, a lithium zirconium silicate glass-ceramic was developed to adjust the coefficient of linear thermal expansion to that of ZrO$_2$ and achieve a certain degree of opacity. This glass-ceramic is layered on the ZrO$_2$ post via heat-pressing. Consequently, this material offers an esthetic solution for an abutment on which a leucite glass-ceramic crown (as an example) might be positioned. The
The glass composition range is (4-15)P₂O₅–(42-59)SiO₂–(7-15)Li₂O–(15-28)ZrO₂ in wt% with the addition of K₂O, Na₂O, Al₂O₃ and up to 11 wt% F [35], [94]. The glass-ceramic shaped products are produced via viscous flow of as-prepared glass-ceramic ingots in heat-pressing kilns. In a glass-ceramic containing 16 wt% ZrO₂, crystals of Li₂ZrSi₆O₁₅ are crystallized at 900 °C and reach a bending strength of 160 MPa. This material shows notably good optical properties, especially high translucency, and this composition can be used as an anterior prosthesis. The glass-ceramic with 20 wt% ZrO₂ is opaque white, shows minor translucency, and contains rod-shaped Li₃PO₄, ZrO₂ micro-crystals, and ZrO₂ macro-crystals after heat treatment at 950-1050 °C. Figure 14 shows a typical microstructure of this glass-ceramic. The material has a bending strength of 280 MPa and a KIC of 2.0 MPa.m⁰.⁵. The improved mechanical properties of the glass-ceramic containing 20 wt% ZrO₂ makes this material appropriate for use in the posterior region because the esthetics and the opacity of the glass-ceramic play a less important role in this region of the mouth. Finally, the coefficients of linear thermal expansion for both glass-ceramics are somewhat lower than that of the ZrO₂ post. As a result of this adjustment, a crack-free bond between the glass-ceramic and the ZrO₂ abutment is achieved [35], [94]. Although these glass-ceramics were tested under a relatively short period of clinical observation, no signs of failure of conventionally cemented zirconia posts were observed with these materials [95], [96].

4.7. Miscellaneous RDGCs

As described previously, dental glass-ceramics are attractive materials for dental restoration because they display excellent esthetics, low thermal conductivity, relatively high strength, chemical durability, biocompatibility, ease of processing and high wear resistance. However, compared with those of metals and ceramics, the low mechanical strength and fracture toughness of these materials restrict their application for long-term high load-bearing
posterior restorations. Therefore, continuous attempts have been made to develop new glass-ceramics with improved mechanical properties and good clinical performance. Some of these glass-ceramics are fluorrichterite, fluorcanasite, diopside and apatite-mullite glass-ceramics.

### 4.7.1. Fluorrichterite glass-ceramics

The main characteristics of fluorrichterite glass-ceramics are their high fracture toughness ($K_{IC} > 3$ MPa.m$^{1/2}$), optical translucency and high resistance to thermal shock [35]. High-performance laboratory tableware and domestic kitchenware are manufactured from these glass-ceramics [35]. In 1999, Denry and Holloway [52] began to develop fluorrichterite glass-ceramic for use in dentistry and first investigated the role of MgO content in a glass composition of $67.5\text{SiO}_2–2\text{Al}_2\text{O}_3–12\text{MgO–9CaF}_2–4\text{Na}_2\text{O–3.5K}_2\text{O–1Li}_2\text{O–1BaO}$ (wt%). The hypothesis was that increasing the amount of magnesium might promote the crystallization of double-chain silicate (amphibole) crystals. Richterite is a sodium calcium magnesium silicate mineral that belongs to the double-chain silicate group. In K-fluororichterite, potassium replaces sodium and fluorine replaces hydroxyl. This crystal has a monoclinic (2/m) structure. The double chain ($\text{Si}_4\text{O}_{11})^6^-$ backbones parallel to the c-axis and are bonded together by ionic bonds to interstitial cations such as $\text{Na}^+$, $\text{K}^+$ and $\text{Ca}^{2+}$. The basic structures of chain and double-chain silicates are explained in detail in various textbooks, such as Ref. [35]. The high fracture toughness of amphibole-based glass-ceramics is due to the random orientation of the interlocked crystals, which gives rise to crack deflection [35]. Denry and Holloway also found that in a glass containing 18 wt% MgO, both mica and fluorrichterite are crystallized. In this material, the microstructure consists of interlocked acicular crystals of fluorrichterite (5-10 micrometers) and mica, and this structure promoted crack deflection and arrest [52]. Furthermore, this same research group increased the sodium amounts in a base
glass composition of $57.7\text{SiO}_2-23.9\text{MgO}-6\text{CaF}_2-0\text{Na}_2\text{O}-8.5\text{K}_2\text{O}-3\text{Li}_2\text{O}-1\text{BaO}$ (wt%).

Increasing sodium content led to a decrease in all transformation temperatures, including the onset of melting. A decrease in the viscosity of the glass-ceramics was observed for the glass-ceramic composed of fluorrichterite and mica and was retained after heat treatment at 1000 °C for 4 h [53]. The glass-ceramic containing 1.9 wt% sodium had the highest mean fracture toughness of $2.26 \pm 0.15 \text{MPa.m}^{\frac{1}{2}}$, which was not significantly different from that of the control material (OPC®, Pentron) [54]. The microstructure of this glass-ceramic (Figure 15) exhibited prismatic fluorrichterite and interlocked sheet-like mica crystals. Crystallization of fluorrichterite might account for the significant increase in fracture toughness compared with that of mica-based glass-ceramics (as an example) [54]. The effect of crystallization heat treatment on the microstructure and biaxial strength of fluorrichterite glass-ceramics was also reported by the same authors [97], who observed two-fold variation in the biaxial flexural strength of fluorrichterite glass-ceramics depending on the temperature and duration of the crystallization heat treatment. This result was believed to be due to the formation of a low-expansion surface layer composed of roedderite ($K_2\text{Mg}_5\text{Si}_{12}\text{O}_{30}$). The expansion mismatch promoted the development of surface compressive stresses and efficiently increased the flexural strength of the glass-ceramic. Higher heat treatment temperatures or longer durations likely led to an increase in thickness of this layer, thereby reducing the intensity of the surface compressive stresses and causing a decrease in strength. In addition, these conditions caused a coarsening of the microstructure that could also weaken the glass-ceramic by reducing the number of possible crack-crystal interactions [97]. The significance and long-term goal of Denry and Holloway's work was to develop a dental glass-ceramic processed at low temperature, e.g., with heat-pressing, that retained the fluorrichterite microstructure and excellent mechanical properties. Later on, other scientists also attempted to crystallize different chain silicate minerals, such as diopside or wollastonite, in the vicinity of mica.
crystals to benefit from their toughening ability [98]-[100]. Almuhamadi et al. [101] and Sinthuprasirt et al. [102] also prepared diopside and leucite-diopside glass-ceramics, respectively, to produce novel strong and thermally compatible veneers for zirconia restoration to overcome chipping and failure issues. The improvements were significant, but it appears that these materials have not yet been considered for clinical applications.

4.7.2. Fluorcanasite glass-ceramics

Fluorcanasite (Ca$_5$Na$_4$K$_2$Si$_{12}$O$_{30}$F$_4$) is another double-chain silicate mineral which its crystallization in glasses with an acicular interlocked microstructure gives rise to strength and fracture toughness of the resulting glass-ceramics [35]. A number of initial studies were performed by Anusavice's and Noort's team at Florida and Sheffield Universities, respectively, to evaluate potential application of fluorcanasite glass-ceramics in restorative dentistry. In the period 1997-2003, van Noort et al. [103] demonstrated that fluorcanasite glass-ceramics derived from the base glass composition of 60SiO$_2$–10Na$_2$O–5K$_2$O–15CaO–10CaF$_2$ (wt%) show promising properties and can be fabricated using conventional routes [103]-[105]. At the same time, Anusavice and Zhang [106] reported that the chemical durability of fluorcanasite glass-ceramics is not adequate for dental applications, and they were not able to improve either chemical durability or mechanical strength via the addition of Al$_2$O$_3$ up to 15 wt%. It was observed that increased Al$_2$O$_3$ content significantly affected the crystal size, crystal shape, aspect ratio, and crystal aggregation characteristics of the fluorcanasite glass-ceramics [106], [107]. In an attempt to control the solubility of this glass-ceramic, systematic additions of SiO$_2$ and AlPO$_4$ were tested by Bubb et al. [108]. The solubility was reduced from 2359 to 624 µg/cm$^2$ (according to ISO 6872). An initial increase was observed in biaxial flexural strength, i.e., 123-222 MPa with small additions, but larger additions reduced the strength to 147 MPa. These findings were attributed to an increased
volume fraction of residual glassy matrix [108]. Stockes et al. [109] attempted to further reduce the chemical solubility of these glass-ceramics by investigating the mixed alkali effect due to variation in the K and Na contents and found that by changing the alkali ratio of the base glass composition (the above composition) from K/(K+Na) = 0.33 to 0.47, it was possible to significantly reduce the chemical solubility of the glass-ceramic. This glass-ceramic exhibited a minimum chemical solubility of 650 µg/cm$^2$ at a composition of K/Na=7/8. This solubility is acceptable for dental core ceramics, which should have a solubility of less than 2000 µg/cm$^2$, but it is not suitable for direct contact with the mouth environment, which requires a solubility of less than 100 µg/cm$^2$ [40], [109]. Finally, Pollington and van Noort [110] managed to adjust the chemical solubility and mechanical properties of the glass-ceramic with ZrO$_2$ addition, and their optimum composition approximately contained 61SiO$_2$–6Na$_2$O–8K$_2$O–11CaO–12CaF$_2$–2ZrO$_2$ (wt%). The appropriate melting schedule for this composition was found to be one hour of holding and stirring at 1350 °C. The heat treatment schedule of 2 h nucleation and 2 h crystallization produced the greatest amount of the fluorcanasite phase. The glass-ceramic had an acceptable chemical solubility (722 ± 177 µg/cm$^2$) and high biaxial flexural strength (250 ± 26 MPa), fracture toughness (4.2 ± 0.3 MPa.m$^{1/2}$) and hardness (5.2 ± 0.2 GPa) and had the potential for use as a core material for veneered resin-bonded ceramic restorations. Furthermore, this fluorcanasite glass-ceramic was found to be machinable using standard CAD/CAM technology and demonstrated a high degree of translucency [110]. It has also been proved that this glass-ceramic forms a sufficient and durable bond when bonded with a composite resin, without the need for acid etching with HF solution [111]. More recently, Eilaghi et al. [112] have shown that fluorcanasite glass-ceramic can be pressureless sintered at 1000 °C to an appropriate relative density of 91.3 ± 0.1 % and desirable mechanical properties ($\sigma = 137 \pm 7$ MPa and $K_{IC} = 2.6 \pm 0.1$ MPa.m$^{1/2}$) [112].
4.7.3. Apatite-mullite glass-ceramics

In the mid-1990s, Hill et al. [113] introduced apatite-mullite glass-ceramics as potential dental or bioactive glass-ceramics. The optimum glass composition was 33.33SiO$_2$–11.11P$_2$O$_5$–22.22Al$_2$O$_3$–22.22CaO–11.11CaF$_2$ in mol%. This glass-ceramic, which was heat treated at approximately 900 °C, consisted of elongated fluorapatite (Ca$_{10}$(PO$_4$)$_6$F$_2$) and mullite (3Al$_2$O$_3$.2SiO$_2$) crystals. Crystallization occurred by an internal nucleation mechanism that involved prior amorphous phase separation. A fracture toughness value greater than 3 MPa.m$^{1/2}$ was reported [113], [114]. Later, Gorman and Hill [115], [116] attempted to develop a dental restoration material using a similar glass-ceramic via the heat-pressing technique by reducing the Al$_2$O$_3$ content and envisioning that this reduction could adjust the viscosity for heat-pressing [115], [116]. The conclusion of these researchers was that glasses with various Al$_2$O$_3$ contents are easily formed and crystallized to fluorapatite. Mullite and/or anorthite were formed as a second crystal phase. However, crystallization during heat-pressing resulted in a loss of control of the process but was not considered detrimental if the future growth of these crystals could be controlled [115]. A fracture toughness of 2.7 ± 0.4 MPa.m$^{1/2}$ was reported for the glass-ceramic containing 32.6SiO$_2$–10.9P$_2$O$_5$–20.3Al$_2$O$_3$–32.6CaO–3.6CaF$_2$ (mol%) that was heat treated for 8 h at 1150 °C. The highest flexural strength of 194 ± 75 MPa was obtained by heat-pressing the same glass for 1 h at 1150 °C. Increasing the holding time increased the crystal size and the extent of microcracking in this glass-ceramic, thus lowering the flexural strength. Microcracks appeared to increase the fracture toughness of the glass-ceramics, probably by a crack termination mechanism [116]. However, the relatively high solubility of apatite-mullite glass-ceramics was always the main issue [117]. Consequently, Fathi et al. [118] evaluated the effect of varying the CaF$_2$ content on the chemical solubility. They increased the CaF$_2$ in the
initial glass from 4 to 20 mol%. All compositions easily formed glasses and, upon heat treatment, crystallized to form apatite and apatite-mullite. Increasing the CaF$_2$ content led to an increase in bending strength but also increased the solubility. The chemical solubility (150-380 µg/cm$^2$) was still higher than that of the control glass-ceramic (IPS Empress® II, 78 µg/cm$^2$) but was acceptable for a dental core ceramic [118], [119]. A maximum bending strength of 157 ± 15 MPa was reported for a sample containing 20 mol% CaF$_2$ [119]. These same researchers also added TiO$_2$ and ZrO$_2$ to control the mechanical properties and solubility [120], [121], and their studies demonstrated that up to 1 mol% of ZrO$_2$ and TiO$_2$ were effective for controlling the solubility and mechanical properties of these apatite-mullite glass-ceramics [120]. The lowest chemical solubility and highest bending strength were 204 ± 29 µg/cm$^2$ and 174 ± 38 MPa, respectively [120]. However, increasing the TiO$_2$ concentration to greater than 2.5 wt% led to a significant increase in solubility and reduced bending strength [121]. Mollazadeh et al. [122] showed that 3 wt% TiO$_2$ and BaO addition increased the bending strength and fracture toughness of apatite-mullite glass-ceramics. However, 3 wt% ZrO$_2$ and an extra amount of SiO$_2$ had no significant effect [122]. The mechanical properties of the resulting glass-ceramics after temperature changes (5 to 60 °C) in aqueous media remained nearly unchanged for the samples containing TiO$_2$ and ZrO$_2$, whereas a high reduction was observed with the addition of BaO and extra amounts of SiO$_2$. Furthermore, after immersion in hot water, the concentration of Ca$^{2+}$ and F$^-$ ions released from samples with BaO or with excess amounts of SiO$_2$ were higher than those of TiO$_2$- and ZrO$_2$-containing glass-ceramics [123]. It is apparent that these apatite-mullite glass-ceramics are promising restorative materials, but their high chemical solubility still restricts their application for use in the mouth environment. Therefore, these materials must be first considered for core build-up.
4.8. Commercial RDGCs

Several companies around the world already manufacture restorative dental glass-ceramics. Table 2 summarizes the most prominent companies and their glass-ceramic products. These glass-ceramics compete with other types of restorative materials, mainly zirconia and composites.

Table 2. Prominent companies and dental glass-ceramic products.

<table>
<thead>
<tr>
<th>Company / Country</th>
<th>Products</th>
<th>Technology</th>
<th>Type</th>
</tr>
</thead>
<tbody>
<tr>
<td>3M/USA</td>
<td>Paradigm™ C</td>
<td>CAD/CAM</td>
<td>Leucite-based</td>
</tr>
<tr>
<td>Aidite/CHI</td>
<td>Cameo®</td>
<td>CAD/CAM</td>
<td>Lithium disilicate</td>
</tr>
<tr>
<td>Den-Mat/USA</td>
<td>Lumineers®</td>
<td>Heat-extrusion</td>
<td>Leucite-based</td>
</tr>
<tr>
<td>Dentsply/USA</td>
<td>Dicor®</td>
<td>Lost-wax casting</td>
<td>Mica-based</td>
</tr>
<tr>
<td></td>
<td>Dicor MGC®</td>
<td>CAD/CAM</td>
<td>Mica-based</td>
</tr>
<tr>
<td></td>
<td>Ceramo®</td>
<td>Sintering for veneering</td>
<td>Leucite-based</td>
</tr>
<tr>
<td></td>
<td>Cerox Kiss®</td>
<td>Heat-pressing</td>
<td>Leucite-based</td>
</tr>
<tr>
<td></td>
<td>Celtra Duo®</td>
<td>CAD/CAM</td>
<td>ZrO₂-reinforced lithium disilicate GC</td>
</tr>
<tr>
<td>Gildewell/USA</td>
<td>Obsidian®</td>
<td>Heat-pressing on metal and CAD/CAM</td>
<td>Lithium disilicate</td>
</tr>
<tr>
<td>Ivoclar/LIE</td>
<td>IPS Empress®</td>
<td>Heat-pressing</td>
<td>Leucite-based</td>
</tr>
<tr>
<td></td>
<td>IPS Empress® CAD</td>
<td>CAD/CAM</td>
<td>Leucite-based</td>
</tr>
<tr>
<td></td>
<td>IPS d.SIGN®</td>
<td>Sintering on metal frameworks</td>
<td>Leucite and apatite</td>
</tr>
<tr>
<td></td>
<td>IPS Empress II®</td>
<td>Lost-wax casting</td>
<td>Lithium disilicate</td>
</tr>
<tr>
<td></td>
<td>IPS e.max Press®</td>
<td>Heat-pressing</td>
<td>Lithium disilicate</td>
</tr>
<tr>
<td></td>
<td>IPS e.max CAD®</td>
<td>CAD/CAM</td>
<td>Lithium disilicate</td>
</tr>
<tr>
<td></td>
<td>IPS Empress Cosmo®</td>
<td>Heat-pressing on ZrO₂ posts</td>
<td>Lithium zirconium silicate</td>
</tr>
<tr>
<td></td>
<td>IPS Eris®</td>
<td>Sintering on IPS Empress II</td>
<td>Apatite-based</td>
</tr>
<tr>
<td></td>
<td>IPS e.max Ceram®</td>
<td>Sintering on IPS e.max CAD</td>
<td>Apatite-based</td>
</tr>
<tr>
<td></td>
<td>IPS e.max ZirPress®</td>
<td>Sintering on ZrO₂</td>
<td>Apatite-based</td>
</tr>
<tr>
<td></td>
<td>IPS InLine®</td>
<td>Heat-pressing on metal</td>
<td>Composite of leucite GC and ceramic</td>
</tr>
<tr>
<td>Noritake/JPN</td>
<td>EX-3 PRESS®</td>
<td>Heat-pressing on metal</td>
<td>Leucite-based</td>
</tr>
<tr>
<td>Pentron/USA</td>
<td>Optec OPC®</td>
<td>Heat-pressing</td>
<td>Leucite-based</td>
</tr>
<tr>
<td></td>
<td>3G™</td>
<td>Heat-pressing</td>
<td>Lithium disilicate</td>
</tr>
</tbody>
</table>
5. Bioactive dental glass-ceramics (BDGCs)

In the late sixties, Larry L. Hench invented a new generation of materials known as "bioactive glasses" [30] and observed that certain glasses could bond to living bone and even soft tissues by a complex mechanism based on ion leaching, controlled dissolution of glass and precipitation of an apatite layer on their surfaces. Bioactive glasses show both osteoconduction and osteoinduction properties and can be used in a variety of applications in dentistry and medicine, such as bone grafting, scaffolding, drug delivery, coatings and soft tissue engineering. For example, some commercial bioactive glass products (Perioglas®, NovaBone® and NovaMin®) have been used clinically as ossicular reconstruction prostheses, endosseous ridge maintenance implants, bone grafts to restore bone loss from periodontal disease in infrabony defects, bone grafts in tooth extraction sites and alveolar ridge augmentation, orthopedic bone grafting in general, and as particulate in Sensodyne® toothpaste for dentinal hypersensitivity treatment. However, the major disadvantages of these materials are low mechanical strength and fracture toughness. These poor mechanical characteristics restrict their use to only a few applications that do not demand significant loads [34]. To improve their mechanical strength, various types of glasses can be crystallized by controlled heat treatments and are known as "bioactive glass-ceramics". The history,
processing, properties and applications of bioactive glass-ceramics, particularly in medicine, have been reviewed elsewhere [34]. In spite of the fact that crystallization increases the mechanical properties, it retards the rate of biochemical reactivity in general. However, certain highly bioactive glass-ceramics exist that can compete with bioactive glasses in terms of reactivity and offer better mechanical properties [34]. These glass-ceramics are usually synthesized via controlled heat treatment of bioactive glasses and are used to coat dental implants, treat hypersensitivity, heal periodontal diseases, and repair root canal/dentin. In this section, we review promising researches on bioactive glass-ceramics specifically developed for dental applications.

5.1. Coatings on dental implants

It is well known that biologically inert implants such as Ti alloys and zirconia (ZrO₂) do not bond to bone by biochemical interaction but simply via morphological fixation. Their inadequate adhesion to bone leads to interfacial displacements and clinical failure. Moreover, metals may chemically degrade. Therefore, metallic and ceramic implants can be coated with bioactive materials, such as hydroxyapatite, glasses and glass-ceramics, to enhance interfacial bonding and protect them from corrosion. Glass-ceramic coatings for biomedical applications were the subject of many studies and have been comprehensively reviewed by Rawlings [124], Cao and Hench [125], Kasuga [126], Verné [127], and Marghussian [128] and more recently by Xuereb et al. [129] and our group [34]. Almost all commercial bioactive glass-ceramics, e.g., Cerabone®, Biosilicate®, Bioverite®, and Ceravital®, and promising ones such as fluorapatite, apatite-mullite, calcium pyrophosphate and composites have been used to coat Ti or ZrO₂ dental implants [34]. To this end, many methods, such as enameling, plasma spraying, flame spraying, sputtering, laser deposition, electrophoretic deposition, etc., have
been attempted for application of perfect coatings [127]. Indeed, all coatings that are produced as amorphous or glassy layers in the first stage of their fabrication process and are subsequently subjected to a controlled heat treatment to transform them into polycrystalline materials, can be classified as glass-ceramic coatings [128]. The results are promising, but scientists are still working to optimize/improve the coating properties before translation into clinical applications. These properties include homogeneity, ease of application, interface bonding strength and good biological properties. However, degradation over time, which leads to detachment of the coating, is still a noticeable drawback and cannot be predicted. Clinical trials are still required to produce convincing results for long-time successful outcomes [124]-[129]. We do not intend to review, as others did [124]-[129], the entire body of researches that address glass-ceramic coatings on dental implants, but instead, we explain selected promising studies in this work.

Verné et al. [130] prepared double-layer bioactive glass-ceramic coatings on Ti-6Al-4V implants using a simple dip-coating and firing process. A 61.1SiO$_2$–12.6CaO–10.3Na$_2$O–7.2MgO–6.0P$_2$O$_5$–2.8K$_2$O in wt% based glass was used as the first layer in direct contact with the metallic substrate, and a 26.2SiO$_2$–17.9Al$_2$O$_3$–17.5P$_2$O$_5$–10.5K$_2$O–19.6CaO–8.3F in wt% based glass-ceramic was used as the outer bioactive layer. The Verné group designed above low-melting intermediate glass composition that could work below the point of transformation of α-Ti to β-Ti to ensure adhesion of the outer bioactive layer. The intermediate layer was also chosen to match the thermal expansion coefficient of both the metal and the outer glass-ceramic. The process applied for the coating did not affect the bioactivity of the glass-ceramic surface and did not modify either the nature of the crystalline phases (needle-like fluorapatite) or their shape. This method has been recommended for coating of Ti-6Al-4V screws for dental applications [130]. Ferraris et al. [131] reported that glazing could be successfully used to coat zirconia dental implants with bioactive glass-
ceramics. An intermediate layer often forms between the coating and the substrate, e.g., between a glass coating and a zirconia substrate, and a "composite" layer exists made of glassy phase and zirconia particles. During thermal treatment above the liquidus temperature, the glass diffuses within the zirconia substrate, and hence, the zirconia granules are surrounded by a glassy matrix, leading to the formation of a "composite" layer, which assures the continuity of the thermal and mechanical properties of the zirconia substrate to the glass-ceramic coating. The osseointegration of bioactive glass-coated zirconia cylinders has been evaluated in an animal model and compared with that of uncoated cylinders [131]. After 30 days, bone bonding was better than that of the uncoated cylinders, but after 60 days, the difference was equal within the statistical uncertainty [131]. Nano-structured coatings on dental implants have also been developed by Xiao et al. [132], who attempted to coat titanium substrates using the liquid precursor plasma spraying (LPPS) process. Tetraethyl orthosilicate, triethyl phosphate, calcium nitrate and sodium nitrate solutions were mixed together to form a sol after hydrolysis, and this liquid was used as feedstock for plasma spraying of P2O5–Na2O–CaO–SiO2 bioactive glass-ceramic. Bioactive glass-ceramic coatings with nano-structures were successfully synthesized, and the coatings showed quick formation of a nano-structured HCA layer after soaking in SBF. Overall, the results indicate that the LPPS process is an effective and simple method for synthesizing nano-structured bioactive glass-ceramic coatings with good in vitro bioactivity [132].

One type of dental implant failure, known as peri-implantitis, is derived from bacteria. Peri-implantitis is a destructive inflammatory process that affects the soft and hard tissues surrounding dental implants [1]. Peri-implantitis is related to accumulations of periodontal pathogens, and its treatment includes removal of the bacterial biofilm, debridement of the exposed surface, and surgical regeneration of the peri-implant pocket [1]. A bioactive and bactericide coating can minimize this problem. Therefore, researchers are currently seeking
such a coating. For example, Esteban-Tejeda et al. [133] and Diaz et al. [134] have tried to develop a mechanically stable antimicrobial glass-ceramic coating on zirconia (Y-TZP) and Ti-6Al-4V substrates. A soda-lime-based glass was first deposited on implants by dip coating or flame spraying. Glass-ceramic coatings containing nepheline (Na$_3$KAl$_4$Si$_4$O$_{16}$) and Na$_2$Ca$_2$Si$_3$O$_9$ crystalline phases were coated on Y-TZP and Ti-6Al-4V substrates after heating at 750 °C for 1 h. Precipitation of needle-like hydroxyapatite on the coating took place during the artificial saliva solubility test, indicating the bioactive character of this layer. The coatings were proven to be antimicrobial versus Escherichia coli, Staphylococcus aureus and Candida krusei [133], [134].

5.2. Hypersensitivity treatment

Dentin hypersensitivity (DH) is one of the most common clinical problems. DH is a sharp and short pain arising from exposed dentin surfaces in response to thermal, evaporative, tactile, osmotic, chemical or electrical stimuli. DH is caused when fluids within the dentinal tubules are subjected to changes (thermal, mechanical and osmotic), and movement in the fluids stimulates a nerve receptor sensitive to pressure, which leads to transmission of the stimuli. Consequently, dental materials proposed to treat DH seek to interrupt the pulp neural response of pain and/or to block the sensitive mechanisms through closure of the open dentinal tubule [1], [2].

Treatment of hypersensitivity has been clinically attempted using bioactive glasses since 2004, when a very fine Bioglass® 45S5 particulate known as NovaMin® with a particle size of approximately 18 µm was first used in Sensodyne® toothpaste. The common abrasive additive in toothpastes is alumina particles, which can be replaced by Bioglass® 45S5. Clinical studies have shown that the Bioglass® 45S5 particles adhere to the dentine, form a
hydroxyapatite layer and block the tubules, which are near 1 µm in diameter, thus relieving pain for a long duration [135]. Although Bioglass® has shown successful results for hypersensitivity treatment, dentists and patients do not like the idea of using crushed glass in the mouth, which can often cut and irritate the gums.

Certain bioactive glass-ceramics can play a similar role in this application. Highly bioactive Biosilicate® is the most investigated glass-ceramic by our group for this function [136]. Biosilicate® is the designation of the particular composition 23.75Na₂O–23.75CaO–48.5SiO₂–4P₂O₅ (wt%). Under controlled double-stage heat treatments, the microstructure of the material can be engineered to be composed of one or two crystalline phases as follows: a sodium-calcium silicate phase (Na₂CaSi₂O₆) or both Na₂CaSi₂O₆ and sodium-calcium phosphate (NaCaPO₄) [136]. The first study on Biosilicate® for hypersensitivity treatment was reported by Tirapelli et al. in 2010 [137]. The target glass-ceramic consisted of one crystalline phase, Na₂CaSi₂O₆. The authors evaluated the efficiency of powdered Biosilicate® in occlusion of open dentinal tubules using dentin disc models. The results revealed that Biosilicate® requires only 24 h to induce the precipitation of a homogeneous HCA layer covering the entire dentin surface [137]. In a clinical study using Biosilicate®, a total of 142 patients were randomized into four groups that received different desensitizing treatments of Sensodyne®, SensiKill® or Biosilicate® dispersed in a gel suspension or in a solution with distilled water. Over a period of 6 months, a total of 232 teeth were evaluated, and the study was performed using pain assessments. With respect to the global diminution of pain over the course of the study, Biosilicate® mixed with distilled water displayed the greatest effect and was able to diminish the pain in the first periods of the experiment. This study indicated that micron-sized Biosilicate® could offer an immediate, effective and long-lasting treatment alternative for patients who suffer from DH [138]. Another clinical study investigated the in situ influence of Biosilicate® on whitened enamel and dentin surfaces after tooth bleaching.
The results indicated that when combined with whitening gel, this biomaterial improved tooth hardness and morphology, thus preventing demineralization [139]. Another group in China also tested their novel bioactive glass-ceramic for hypersensitivity treatment. Bioactive glass-ceramic toothpaste significantly and immediately lowered dentine permeability. The highest reduction in dentine permeability was observed after 7 days of treatment [140]. Figure 16 shows the formation of apatite-like crystals inside dentine tubules and on its surface after brushing of the dentine with toothpaste containing bioactive glass-ceramic [140]. One interesting advantage presented by glass-ceramics in this application is that because these materials are fully crystalline, they do not present sharp cutting surfaces. In contrast, glasses possess conchoidal fracture surfaces that can lead to gum irritation during brushing [136]-[140]. Therefore, bioactive glass-ceramics deserve much more attention for this application.

5.3. Bone and periodontal healing

Teeth are supported by alveolar bone, the periodontal ligament, and gingival connective tissue. Alveolar bone surrounds and holds teeth firmly in their position. The periodontal ligament maintains the attachment of teeth to the jaws, whereas gingival connective tissue covers the alveolar bone to protect it from the oral environment. These vital tissues might lose their functions due to trauma, disease or congenital abnormalities. Malfunction of teeth in aging populations reduces an individual's quality of life [1], [2]. Therefore, in recent years, extensive researches have been conducted on healing or engineering of dental tissues. Among the large number of materials chosen for these purposes, bioactive glasses and glass-ceramics have also been considered. Our focus in this review is on bioactive glass-ceramics used in dentistry, rather than on glasses, because bioactive glasses have already been widely tested and reviewed [141]-[143]. We believe that special consideration of bioactive glass-ceramics
is of great importance in this field. The reason for this focus and research topics on the use of bioactive glass-ceramics in dentistry are summarized in three fields of interest as follows.

(1) **Tough bioactive glass-ceramics for dental implants.** After the development of the first bioactive glass-ceramic (Ceravital®) by Brömer *et al.* in 1973, a worldwide quest for tougher bioactive glass-ceramics ensued [34]. Such glass-ceramics could be used as bone substitutes or dental implants. However, the fracture toughness of commercial bioactive glass-ceramics and some promising ones (\(K_{IC} < 3 \text{ MPa.m}^{\frac{1}{2}}\)) were below the desired standards, and significant improvement was required to approach the properties of cortical bone (\(K_{IC} = 2-12 \text{ MPa.m}^{\frac{1}{2}}\)). This topic is still of great interest, and an intense search is currently underway for novel compositions and microstructures designed to increase toughness to \(K_{IC} > 3 \text{ MPa.m}^{\frac{1}{2}}\) and also increase bioactivity [34]. For examples, Saadaldin *et al.* [144], [145] suggested two wollastonite and miserite glass-ceramics for dental implants and reported a high fracture toughness of 4.5-5.5 MPa.m\(^{\frac{1}{2}}\). We believe that materials that have an interlocked house-of-cards structure are good candidates, but the method (indentation and crack length measurement) used to measure fracture toughness is not reliable because it usually shows high values and should be revised [144], [145].

(2) **Glass-ceramic scaffolds for engineering bones or restoring supporting dental tissues.** In recent years, bioactive glass-ceramic scaffolds have opened new avenues for treatment of bone defects in orthopedic, dental and maxillofacial situations. Scaffolds contain 3D interconnected pores with diameters of at least 100 \(\mu\)m that can host biofactors, support vascularization, encourage cell growth and thus promote tissue formation. Comprehensive reviews on the state-of-the-art in bioactive glass-ceramic scaffolds have been published by numerous scientists [34], [146]-[149] who believe that glass-ceramics have a combination of better properties, such as high strength and fracture toughness (due to their unique toughening mechanisms), for scaffold development compared with those of glasses [146]-[149].
Therefore, almost all commercial bioactive glass-ceramics and others under development [34] have been the subject of study for scaffold development using various fabrication techniques, including, e.g., foam-replication methods, salt or sugar leaching, thermally induced phase separation, microsphere emulsification sintering, electrospinning to form nano-fibrous structures, freeze casting, additive manufacturing technologies, computer assisted rapid prototyping techniques, etc. [146]-[149]. The results are inspiring, and it appears that in future, biomimetic regeneration of the complex structure of teeth demands 3D porous materials, and bioactive glass-ceramics are promising for this application. Research and development in this area might lead to the first bio-tooth development [7]-[9].

(3) Bioactive and bactericidal glass-ceramics for bone regeneration or attaching fixed restorations to soft periodontal tissue. Gel-derived bioactive glass-ceramics are modern and promising biomaterials for this application. These highly bioactive and mesoporous materials have begun to emerge in various applications in dentistry, including dental tissue and bone regeneration, drug delivery and hybrid materials. As good examples of research for this application, Vallet-Regi's team has demonstrated that controlled heat treatment of mesoporous gel-derived glasses can lead to glass-ceramics with improved mechanical properties without deterioration of their bioactive behavior. A gel-derived bioactive glass-ceramic containing pseudo-wollastonite, wollastonite, tricalcium phosphate and cristobalite was developed by heating a gel-glass (55SiO$_2$–41CaO–4P$_2$O$_5$ in mol%) at 1300 °C. This glass-ceramic shows efficient in vitro bioactive behavior, i.e., an apatite layer covered the sample surface after 3 days of soaking in SBF [150], [151]. To use this material as a substrate for bone tissue engineering, the authors synthesized scaffolds with a network of designed three-dimensional interconnected macropores 400-500 µm in diameter. Further studies revealed that the resulting glass-ceramic is bioactive, cytocompatible and capable of promoting in vitro the differentiation of mesenchymal stem cells into osteoblasts. For that
reason, this material could offer a suitable matrix for bone tissue regeneration. Additionally, in vivo evaluation of $70\text{SiO}_2-30\text{CaO}$, $80\text{SiO}_2-17\text{P}_2\text{O}_5-3\text{CaO}$ and $36\text{SiO}_2-7\text{P}_2\text{O}_5-44\text{CaO}-13\text{MgO}$ (mol%) glasses and glass-ceramics in New Zealand rabbits showed potential for bone substitute and regeneration [150], [151]. Another example is the gel-derived microporous bioactive glass-ceramic developed in Boccaccini’s group in Germany [152]-[154], which has potential application in dental restoration. These glass-ceramics show bioactive behavior around the margins of fixed restorations and create a bioactive surface that can lead to periodontal tissue attachment, thus providing complete sealing of the marginal gap between teeth and fixed prosthesis. The sol-gel route was adapted for the development of $60\text{SiO}_2-3\text{P}_2\text{O}_5-14\text{Al}_2\text{O}_3-6\text{CaO}-7\text{Na}_2\text{O}-10\text{K}_2\text{O}$ (wt%) glass-ceramic and a related composite material that combines this glass-ceramic with a mesoporous $58\text{SiO}_2-33\text{CaO}-9\text{P}_2\text{O}_5$ (wt%) bioactive glass [152], [153]. This method resulted in a homogeneous microporous glass-ceramic composite that can be applied as a coating on commercial dental ceramic substrates [152], [153]. The attachment and proliferation of both the periodontal ligament and gingival fibroblast cells confirmed the bioactive behavior of the new materials and their potential ability for use in dental restorations for soft tissue regeneration and sealing of the marginal gap [153]. Furthermore, an Ag-doped composite showed pulp-cell proliferation and antibacterial properties that could facilitate potential applications in tooth regeneration approaches [154]. Interested readers are encouraged to refer to comprehensive reviews and book chapters such as [8], [9], [34], [142], [151], [155], which address gel-derived glasses and glass-ceramics and their derivative products for dental applications.
6. Conclusions and trends

Restorative dental materials are moving from metal alloy-containing to all-ceramic restorations, and this review demonstrates that glass-ceramics work well as all-ceramic restorations. The following 10 topics warrant further research:

(1) Research and development are underway to further improve the fracture toughness and esthetics of dental glass-ceramics to enable them to compete with their current contenders (e.g., zirconia and hybrids) for posterior restorations. We agree with Höland et al. [156] that comprehensive knowledge of toughening mechanisms is a necessary step to open new directions for development of tough glass-ceramics. Therefore, future research activities should be focused on gaining a better understanding of the mechanisms of toughening, such as transformation toughening, bridging, micro-cracking, and pulling out, that can be stimulated by controlled crystallization of different crystals with a variety of morphologies and microstructures. Additionally, various coloring agents and pigments should be deeply and thoroughly tested to adjust the shades and esthetics of glass-ceramics. On the other hand, the morphology of crystals from the nano- to micro-scale, which can be controlled by precise adjustment of the chemical composition and crystallization process, might strongly influence their optical properties, but the published information on these topics is scarce.

(2) New methods (e.g., meta-analyses) can be used to expand the range of glass-ceramic composition. For instance, it was recently demonstrated that new nano–glass-ceramics with a notably high ZrO₂ content can be synthesized using sol-gel methods [157], [158]. The technology required to achieve this goal could rely on chemistry-based and applied nanotechnology.
(3) New or improved sintering/crystallization processes, such as microwave heating [159], laser crystallization [160], [161], spark-plasma sintering [88], biomimetic assemblage of crystals, textured crystallization, and electron beam crystallization, should be further developed.

(4) Chemical strengthening of RDGCs by ion exchange, as tested by Kawai et al. [162] and Fischer et al. [163]-[165], is a promising route and should be further pursued.

(5) Glass-ionomer composites are widely used in restorative dentistry. We believe that glass-ceramic powders, including bioactive formulations, can also be used as inorganic fillers in these composite restoratives. In at least two research studies, Liu et al. [166] and Mollazadeh et al. [167] used porous mica-fluorapatite and fluorapatite-mullite glass-ceramic fillers to reinforce dental resin-based composites.

(6) New coating technologies and the properties of coatings on dental implants should be improved. For example, degradation over time, which leads to detachment of coating, is a noticeable drawback.

(7) The development of restorative glass-ceramics or composites which in contact with bone and surrounding tissues show a cement-like behavior and facilitate biological surface responses for marginal attachment is another challenging field of research.

(8) Glass-ceramic matrix composites have been rarely investigated for restorative dentistry and demand additional attention.
(9) Dental tissue engineering for construction of tooth organs is a brand new and highly interesting direction. A clear and distinct shift is occurring in regenerative medicine from use of synthetic materials or tissue grafts to a more explicit approach that applies scaffolds for hosting cells and/or biological molecules to create functional replacement tissues in diseased or damaged dental sites.

(10) Finally, (expensive, time-consuming) clinical tests should be encouraged to evaluate dental glass-ceramics in real application cases.

All of these ideas and several others not reported in this work can only be achieved by increasing interactions among materials engineers and scientists, chemists, dentists and biologists.

Acknowledgements

The authors are grateful to the São Paulo Research Foundation (FAPESP, # 2013/07793-6) for financial support of this work and for the post-doctoral fellowship granted to Maziar Montazerian (# 2015/13314-9).
References


[4] Markets and Markets Inc., *Dental implants and prosthetics market by material (Titanium, Zirconium, PFM, All Ceramics), stage (Two Stage, Single Stage), connectors (External hexagonal) & product type (Crowns, Bridges, Dentures, Abutments) - global forecast to 2020*, June 2015, USA.


Synthesis and characterisation of dental composite materials reinforced with 
fluoroapatite-mullite glass-ceramic particles, Advances in Applied Ceramics 112(5) 
(2013) 294-300.
Figure captions

**Figure 1.** (a) Number of scientific publications (articles, conference papers, books, etc.) (Source: www.scopus.com), (b) Number of granted patents related to dental glass-ceramics (Source: www.thomsonreuters.com/derwent). The results were obtained by searching the keywords “dental glass-ceramic*” or “teeth glass-ceramic*” or “tooth glass-ceramic*” in the article or patent title and the title, abstract and keywords.

**Figure 2.** Schematic diagram of the main stages of the synthesis of glass-ceramics. Reproduced from Ref. [34] with permission from Wiley.

**Figure 3.** Cross-section of a tooth [39].

**Figure 4.** Examples of dental restorative glass-ceramics (RDGCs): (a) Dental onlay, (b) inlay, (c) crown, (d) veneer and (e) 3-unit bridge (Images are from www.filippini-gray.com and www.dentopolis.blogspot.com.br).

**Figure 5.** Different steps in lost-wax casting of RDGCs [46].

**Figure 6.** Schematic of the furnace used in heat-pressing [35].

**Figure 7.** Work flow of the CAD/CAM process in dentistry. (a) Scanning, (b) Virtual restoration (modeling), (c) Machining, and (d) Final product (crown and 3-unit bridge) (Images are from www.dental-tribune.com, www.osovnikar.com and www.dentalcompare.com).

**Figure 8.** Typical microstructure of a mica glass-ceramic [Personal image].

**Figure 9.** TEM micrograph of a glass-ceramic containing apatite (A) and leucite (L) crystals [70].

**Figure 10.** Multicolor block of leucite-based glass-ceramic for a CAD/CAM process [74].
Figure 11. Propagating crack deflected by lithium disilicate crystals in the glass-ceramic [84].

Figure 12. Various stages of fabrication of lithium disilicate glass-ceramics by CAD/CAM. IPS e.max® CAD from Ivoclar Vivadent AG was selected as an example.

Figure 13. Application of a lithium disilicate-based glass-ceramic (IPS e.max® CAD). (a) Initial situation, worn gold crown. (b) Preparation of molar for a full contour crown. (c) Try-in of a full contour crown in its lithium metasilicate state. (d) Final clinical situation after the crystallization step (stained and glazed) and adhesive cementation of the crown. Dentist: A. Peschke (Ivoclar Vivadent AG) [74].

Figure 14. Back-scattered scanning electron image from dental glass-ceramic containing 20 wt% ZrO₂ heat-pressed at 1000 °C. Dark holes correspond to the Li₃PO₄ crystals dissolved in etchant solution (3% HF) and ZrO₂ micro-/macro-crystals are brighter and elongated (needle-like) [94].

Figure 15. Scanning electron micrograph of mica-fluorrichterite glass-ceramic. The darker area represents prismatic fluorrichterite crystals dispersed in the brighter area of mica crystals [54].

Figure 16. SEM images show apatite-like deposits inside the dentine tubules (a) and on the dentine surface (b) after 7 days of treatment with toothpaste filled with a bioactive glass-ceramic [140].
Figure 1. (a) Number of scientific publications (articles, conference papers, books, etc.) (Source: www.scopus.com), (b) Number of granted patents related to dental glass-ceramics (Source: www.thomsonreuters.com/derwent). The results were obtained by searching the keywords “dental glass-ceramic*” or “teeth glass-ceramic*” or “tooth glass-ceramic*” in the article or patent title and the title, abstract and keywords.

110x129mm (300 x 300 DPI)
Figure 2. Schematic diagram of the main stages of the synthesis of glass-ceramics. Reproduced from Ref. [34] with permission from Wiley.
Figure 3. Cross-section of a tooth [39].

529x529mm (300 x 300 DPI)
Figure 4. Examples of dental restorative glass-ceramics (RDGCs): (a) Dental onlay, (b) inlay, (c) crown, (d) veneer and (e) 3-unit bridge (Images are from www.filippini-gray.com and www.dentopolis.blogspot.com.br).

27x5mm (300 x 300 DPI)
Figure 5. Different steps in lost-wax casting of RDGCs [46].
Figure 6. Schematic of the furnace used in heat-pressing [35].
Figure 7. Work flow of the CAD/CAM process in dentistry. (a) Scanning, (b) Virtual restoration (modeling), (c) Machining, and (d) Final product (crown and 3-unit bridge) (Images are from www.dental-tribune.com, www.osovnikar.com and www.dentalcompare.com).
Figure 8. Typical microstructure of a mica glass-ceramic [Personal image].

249x169mm (300 x 300 DPI)
Figure 9. TEM micrograph of a glass-ceramic containing apatite (A) and leucite (L) crystals [70].

250x172mm (300 x 300 DPI)
Figure 10. Multicolor block of leucite-based glass-ceramic for a CAD/CAM process [74].
Figure 11. Propagating crack deflected by lithium disilicate crystals in the glass-ceramic [84].

255x190mm (300 x 300 DPI)
Figure 12. Various stages of fabrication of lithium disilicate glass-ceramics by CAD/CAM. IPS e.max® CAD from Ivoclar Vivadent AG was selected as an example.
Figure 13. Application of a lithium disilicate-based glass-ceramic (IPS e.max® CAD). (a) Initial situation, worn gold crown. (b) Preparation of molar for a full contour crown. (c) Try-in of a full contour crown in its lithium metasilicate state. (d) Final clinical situation after the crystallization step (stained and glazed) and adhesive cementation of the crown. Dentist: A. Peschke (Ivoclar Vivadent AG) [74].

48x32mm (300 x 300 DPI)
Figure 14. Back-scattered scanning electron image from dental glass-ceramic containing 20 wt% ZrO2 heat-pressed at 1000 °C. Dark holes correspond to the Li3PO4 crystals dissolved in etchant solution (3% HF) and ZrO2 micro-/macro-crystals are brighter and elongated (needle-like) [94].

371x274mm (300 x 300 DPI)
Figure 15. Scanning electron micrograph of mica-fluorrichterite glass-ceramic. The darker area represents prismatic fluorrichterite crystals dispersed in the brighter area of mica crystals [54].
Figure 16. SEM images show apatite-like deposits inside the dentine tubules (a) and on the dentine surface (b) after 7 days of treatment with toothpaste filled with a bioactive glass-ceramic [140].