Opportunities for Fluorochlorozirconate and Other Glass-Ceramic Detectors in Medical Imaging Devices

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Abstract

This article gives an overview of fluorochlorozirconate glass-ceramic scintillators and storage phosphor materials: how they are synthesized, what their properties are, and how they can be used in medical imaging. Such materials can enhance imaging in x-ray radiography, especially mammography and dental imaging, computed tomography, and positron emission tomography. Although focusing on fluorochlorozirconate materials, the reader will find the discussion is relevant to other luminescent glass and glass-ceramic systems.

Keywords

Glass ceramics; Dental imaging; X-ray radiography; Mammography; Positron emission tomography; Computed tomography

Introduction

Glass ceramics are composite materials that share many properties of glass and ceramics. In general, they are fabricated like a glass, but have some of the special properties of ceramics. The synthesis of glass-ceramic materials is usually a 2-step process, in which the constituent powders are melted together for some period of time, followed by rapid cooling. After the glass solidifies and cools, it is heated once more (annealed) and undergoes partial crystallization. The crystallites developed can be in the nanometer range and so exhibit the extraordinary properties of nanomaterials, which are attributed to the large ratio of surface area to volume in the crystallites. The properties of the materials can be tailored by changing the composition of the base glass and the heat-treatment protocol.

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Concerning the use of glass ceramics in medical imaging, transparency and luminescence are important properties; these properties affect the detective quantum efficiency and spatial resolution of the imaging system. Transparency and luminescence are highly dependent on nanoparticle size, which is a direct result of the heat-treatment temperature and duration. Other key properties such as hardness and brittleness affect manufacturability and durability, with the glass ceramic usually performing better than the corresponding unannealed glass. The ability of glass ceramics to be formed near net-shape is also highly advantageous.

Due to their interesting luminescent properties, fluorochlorozirconate (FCZ) glass ceramics doped with rare-earth elements are of special interest to medical imaging. These materials can perform both as scintillators and storage phosphors. Scintillators are materials that spontaneously emit visible light when exposed to ionizing radiation. In contrast, storage phosphors retain the energy in stable electron hole pairs, and although they emit some prompt light, it is usually ignored. The electron hole pairs recombine and emit light when stimulated by a suitable source, such as a laser. The starting point of these detectors is a ZBLAN-based glass matrix with barium chloride partially or fully substituted for the usual barium fluoride [1]. One advantage of this material lies in the amazing versatility of glass synthesis. Small changes in constituents lead to large changes in properties. For example, adding 1–2% FeCl$_3$ vastly changes the crystallization properties [2]. A discussion of the potential of FCZ glass-ceramic scintillators and storage phosphors for use in medical imaging follows, which includes some recent experimental results from the authors. Although focusing on FCZ materials, the reader will find the discussion is relevant to other luminescent glass and glass-ceramic systems. Such materials can enhance imaging in x-ray radiography, especially mammography and dental imaging, computed tomography, and positron emission tomography.

**Glass Ceramics**

**Material Systems**

Glass ceramics can be based upon many different glass systems, including oxides such as phosphates and silicates, fluorides or a mixture such as oxyfluorides. Oxide glass ceramics have been used as implants and in dental applications [3, 4]. Oxyfluoride glass ceramics have no direct use in medical applications as yet, but have been used as a surface modifier in dental materials [5]. Neither oxide nor oxyfluoride medical imaging plates have been developed, so far, but could possibly be in the future. Fluoride glass ceramics have shown great potential as x-ray image plates [6–13]. The development of new glass-ceramic materials is currently a busy field, especially in the sol-gel area due to the room temperature options for synthesis and ability to produce uniform dispersion of nanoparticles.

The glass ceramic found to work best for medical imaging is fluorochlorozirconate-based and a modified form of ZBLAN (zirconium, barium, lanthanum, aluminum and sodium fluoride). In the modified form, some or all of the barium fluoride is replaced by barium chloride. A small amount of indium is added to stabilize the zirconium in the 4+ state and divalent europium is added either in the fluoride or chloride form as an optical activator.
Synthesis Routes

Glass ceramics are typically synthesized by one of two methods. The first and more traditional method, involves creating a glass, then heat treating it to precipitate nanocrystals within the glass matrix to form a glass-ceramic composite material. The second, newer method is the sol-gel process, in which the material begins as a solution then becomes an interconnected network or “gel” after drying; to create a glass ceramic, the resulting material may be heated to induce partial crystallization or alternatively, seeded with crystalline material during synthesis. Example processes for each method are described in the subsequent paragraphs.

In our traditional method, FCZ glass-ceramic samples are generally prepared with a composition in mole percentage of:
51.0ZrF$_4$-20.0BaCl$_2$-20.0NaF-3.0AlF$_3$-3.5LaF$_3$-0.5InF$_3$-2.0EuCl$_2$. The raw materials are weighed in a glovebox (MBRAUN Labmaster SP) with an argon atmosphere to prevent contamination from oxygen or water vapor. Next, the sample materials are heated in a platinum crucible inside a programmable tube furnace (MTI Corporation OTF-1200X) to a temperature of 825 °C. The furnace is connected to the glovebox through a doorway and also contains an argon atmosphere. At the completion of the heating cycle, the molten glass is poured into a brass mold at a temperature of 200 °C. The brass mold is equipped with a cartridge heater connected to a PID controller, allowing for the gradual cooling of the glass to room temperature over a period of four hours.

Samples are typically analyzed by differential scanning calorimetry (DSC) in order to ascertain the glass transition and crystallization temperatures, which in turn determines the heat-treatment protocol for precipitating nanocrystals within the glass matrix. Figure 1 shows a typical DSC curve containing glass transition temperatures and crystallization peaks [14]. In addition to DSC, the structural phase of the nanocrystals, determined by x-ray diffraction, is important as it can change the properties of the material.

The synthesis of glass-ceramic materials by the sol-gel method is, however, very different from the melt-derived methods described above. As an example, we take the preparation of Dy$^{3+}$–Tb$^{3+}$ double-doped YF$_3$-based sol-gel nano-glass-ceramics [15]. Sol-gel processing is a low-temperature synthesis technique, in which the hydrolysis and condensation of the precursors result in the formation of a dispersion of colloidal nanoparticles in a liquid, otherwise known as the sol. The subsequent polymerization and condensation reactions turn the sol into a gel, an interconnected, rigid network with pores of submicron dimensions. The gel is aged, resulting in the coarsening of pores, dried to remove the pore liquid, and then stabilized [16].

Although details vary from sample-to-sample, the general theme is close to what is detailed by Alonso et al. [15]: Tetraethoxysilane (TEOS) Si(OC$_2$H$_5$)$_4$, used as a source of SiO$_2$, is hydrolyzed for one hour at room temperature with a mixed solution of ethanol and H$_2$O, using acetic acid as a catalyst. Y(CH$_3$COO)$_3$·H$_2$O is the source of Y. The required quantities of Y(CH$_3$COO)$_3$·H$_2$O, Tb(CH$_3$COO)$_3$·H$_2$O and Dy(CH$_3$COO)$_3$·H$_2$O are dissolved in a CF$_3$COOH and H$_2$O solution, which is slowly mixed with the initial solution. In order to obtain a homogeneous solution, the resultant solution was stirred vigorously for one hour at

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room temperature. A highly transparent gel is obtained by leaving the resultant homogeneous solution in a sealed container at 35 °C for several days. The gels are then dried by a slow evaporation of residual water and solvent and subsequently heated at 250 °C in order to remove OH-groups. Finally, the sol-gel glasses are heat-treated in air at 675 °C in order to achieve controlled precipitation of nanocrystals, giving rise to transparent nano-glass-ceramics.

The sought-after properties of these materials can be achieved regardless of the synthesis method. The sol-gel method has many advantages over traditional melting techniques [17, 18] like controlled composition, size of nanocrystals, and doping level, together with chemical homogeneity, low cost, lower processing temperature [19–23] and better dispersion than solid state methods, but is not fully developed. Traditional melting techniques, however, hold advantages in that the process is much simpler and greater batch sizes may be created.

**Heat treatments**

Glass ceramics are traditionally cast as glasses and require a subsequent heat treatment process to precipitate crystals within the glass matrix. The heat treatment process is used to control the characteristics of the crystal phases present in a glass ceramic. For example, for FCZ glasses containing barium, at lower temperature heat treatments, hexagonal BaCl$_2$ crystals are precipitated. At higher temperatures, the hexagonal BaCl$_2$ transforms into orthorhombic phase BaCl$_2$ crystals. Unwanted phases may also be produced at elevated heat treatment temperatures. Crystal size is influenced by the heat treatment parameters, with higher temperatures and longer durations leading to larger crystal size. In addition, adequate heat treatment time is required to precipitate the maximum achievable crystallized volume fraction [24, 25].

The heat treatment process is critical because the crystal phases are typically responsible for the optically-active properties of glass ceramics. For FCZ glass ceramics containing BaCl$_2$:Eu$^{2+}$, the orthorhombic phase of BaCl$_2$ is significantly better suited for storage phosphor applications, while the hexagonal phase is generally preferred for scintillator applications [11, 26]. Due to scattering, the transparency of the glass ceramic is dependent upon crystal size: Transparent glass ceramics will have crystallites that are smaller than the wavelengths of incident light, although other factors, such as refractive index matching can play a role in light transmission.

**Overview of Medical Imaging Systems using Scintillators or Storage Phosphors**

**X-ray Radiography**

Exposing the body to x-rays creates radiographic medical images. X-rays are attenuated differently by hard and soft tissue; so various x-ray energies are used depending on the body part being examined. Bones require hard or higher energy x-rays; soft tissue, such as the breast, requires a low energy or softer x-rays. In order to obtain an image, a shadow is created on a fluorescent screen, which can be projected onto a photographic film, or captured by a phosphor and later read out by a laser (computed radiography). Indirect or
direct flat panel detectors (FPDs) can also be used. Indirect detectors, commonly made from amorphous silicon, require a scintillator screen to convert the incoming x-ray radiation into visible light; it is the visible light that is detected, therefore the x-ray radiation is only measured indirectly. Direct detectors do not involve a scintillator and are the most popular choice for mammography; they convert the x-ray directly to an electrical signal; such detectors are generally amorphous selenium. While all these detectors have their pros and cons, all but the direct FPD requires a scintillator or storage phosphor and no commercial systems currently use a glass-ceramic material.

X-ray Computed Tomography

Medical x-ray computed tomography (x-ray CT), also known just as CT, is a technology that uses x-rays to produce radiographic projection data taken around an axis of rotation, see Figure 2. Reconstruction algorithms are then used to generate a number of two-dimensional slices, or a three-dimensional picture of the inside of the body without cutting it open. The use of CT is on the increase; there are about 70 million such scans done per year in the United States. There is no consensus on whether the amount of radiation received from a CT scan could be at the level to be cancer causing, but more sensitive detectors and therefore a lower required dose would certainly be welcome.

Positron Emission Tomography

A typical positron emission tomography (PET) system is shown in Figure 3. PET is a technique that produces a three-dimensional image of functional processes in the body by means of introducing a biologically active molecule or tracer, usually fluorodeoxyglucose (FDG). Regions of metabolic activity then take up the tracer; cancer has a differentially high uptake of glucose-derived molecules in comparison to normal cells. FDG decays by giving off positrons, which then combine with an electron in the body and two $\gamma$-rays are emitted in opposite directions (see Figure 4). The $\gamma$-rays that remain in the plane of the detector ring will hit two of the detectors (opposite to each other) simultaneously. The number of such events indicates how much radioactivity there was on the line of response (LOR) between the detectors and therefore the amount of metabolic activity. Three-dimensional images of tracer concentration within the body are then constructed by computer analysis.

Evaluation of FCZ-based Glass Ceramics with Comparisons against Commercial Imaging Materials

Scintillators

Scintillator-based, indirect conversion is dominant in most clinical radiographic applications with the notable exception of mammography [27]. The most common scintillator for flat panel detectors is thallium-doped cesium iodide (CsI:Tl). The crystal grows in a needle-like fashion, guiding the light forward and therefore increasing efficiency. However, as with most single crystal halides, it is somewhat hygroscopic, crystal growth is complicated and has a large temperature dependence; it is also relatively expensive. CsI:Tl has reasonable density for stopping x-rays and emits at 565 nm where most PMTs have their highest detection efficiency. The decay time constant, however, is rather long at 1 µs.
FCZ-based glass ceramics have demonstrated excellent performance as x-ray and tomographic image plates as shown in Figure 5 [12, 13]. For CT, these glass ceramics could serve as a starting point, but should be tailored to suit the CT application.

CT scanners range from taking a single slice to 720 slices in a single rotation. All CT systems require many detectors arranged in a ring as shown in Figure 6. Pixel sizes in CT are typically 1 mm × 1 mm. Such a large pixel size allows for a discrete build of the detector, spatially matched to the photodiode (Figure 7). The requirement for CT detectors is not only efficiency, as with all detectors, but also a short afterglow time because sampling rates are up to 5 kHz for high-end multi-slice CT scanners, with gantry rotation times as low as 0.3 s. Gadolinium oxysulfide (Gd$_2$O$_2$S aka GSO) or lutetium oxyorthosilicate (LSO) are suitable detector materials for CT.

The use of a CT scan with an effective dose of 1 to 10 mSv may be associated with an increase in the possibility of fatal cancer of approximately 1 chance in 2000, although results are not proved. This is relatively small in comparison to a natural chance of 1 in 5 but within the range of the lowest doses of 5 to 20 mSv received by some of the Japanese survivors of the atomic bombs dropped in World War II (Hiroshima and Nagasaki).

Characteristics of the ideal scintillator for PET are listed in Table 1 of Ref. [28], however, such a material does not exist. Right now we can only use what is available and compromise on certain characteristics. NaI:Tl was the most popular choice at one time, however, it has a low detection of $\gamma$-rays in the required range due to its low density. It is also highly hygroscopic, which means that much time and effort has to be put into packaging the material. BGO emerged later as a better choice due to its higher density; the limitation with this material is the long decay constant that limits coincidence timing resolution [28]. Two materials with much shorter decay constants include CsF and BaF$_2$. CsF has seen limited use due to its low light output and extreme hygroscopicity. BaF$_2$ has been used in several PET scanners but fell out of favor because of its relatively low density. GSO has been used as a PET detector on its own and in conjunction with BGO [29] but GSO is difficult to work with as it cleaves easily. LSO has the best overall properties for PET scintillation: high density, a short decay constant, mechanically rugged, and non-hygroscopic.

Current materials such as GSO and LSO have their limitations, however. GSO has relatively low light output and both GSO and LSO have a large afterglow and a non-linear response over the required energy range, which affects their energy resolution [30]. While the actual performance of modified ZBLAN as a CT scintillator is unknown at this juncture, the potential for development is unbounded. Other fluorides can be added to the glass matrix and alternate nanocrystals can be precipitated, for example SrI$_2$, and there are a plethora of rare-earth elements to be used as dopants, many of which the authors have experience with [31–35]. As well as varying constituent materials, heat treatments play a major role in the properties of the materials. Lower temperatures develop smaller nanocrystals, less light output but higher spatial resolution. Larger nanocrystals are likely to have increased strain, tensile or compressive, changing electronic energy levels, light output mechanism and decays times, all of which can be optimized to produce the desired properties.
As far as PET is concerned, as mentioned above, LSO has the optimum properties at this point. However, it is expensive and while it has high light output, the light output varies over the desired energy range. It also requires crystal growth, which takes longer and is a lot more complicated than casting a glass. One of the most important properties for a PET scintillator is its ability to detect $\gamma$-rays. If a higher number of $\gamma$-rays can be absorbed, scan times can be shortened and tracer activity can be lower, enhancing comfort and safety for the patient. Glass ceramics can be made in any shape or size so can be made thicker for stopping power. Further, a high amount of lead content can be added to provide stopping power for $\gamma$-rays.

The authors have synthesized a sample glass containing lead with the following composition (mole basis): $69.5\text{ZrF}_4-14.5\text{BaF}_2-0.5\text{BaCl}_2-5.0\text{LaF}_3-0.5\text{InF}_3-10.0\text{PbF}_2$, which will be the subject of future studies. In addition to the high quantity of lead for $\gamma$-ray stoppage it has a small quantity of BaCl$_2$, which serves as a luminescent center and host crystal for the rare-earth. The as-poured sample is transparent and appears defect-free on the macroscopic scale, Figure 8. Initial characterization of the glass has shown many beneficial properties. For example, the glass transition temperature for the sample is at a much lower temperature than the bulk crystallization temperature, which is indicative of a stable glass (see Figure 9). Further development of this glass is underway.

**Storage Phosphors**

Storage phosphors have been recognized for their radiographic imaging potential since the middle of the 20th century [36]. However, it was not until the 1980s, that this technology was practically applied to medical imaging in the form of computed radiography (CR) [37, 38]. In CR, after exposure, the radiographic image is stored within the storage phosphor plates in metastable electron-hole pairs. Stimulation with a laser causes recombination of the electron-hole pairs with simultaneous emission of light. The stimulation wavelength is higher than that of the stimulated emission and therefore can be optically filtered out from the image signal. By scanning across the area of a storage phosphor plate and collecting the filtered light output, an image can be assembled via computer, pixel-by-pixel. CR has many advantages over traditional film/screen systems including:

- reusable imaging plates
- increased dynamic range
- less processing (no chemical development required)
- automatic creation of a digital image

CR technology has difficulty matching film in image quality, however, generally having inferior spatial resolution. The primary reason for the relatively poor spatial resolution of CR in comparison to film/screen radiography lies within the construction of the storage phosphor imaging plates. Commercial CR imaging plates use a polycrystalline storage phosphor material held within a polymeric binder. Scattering of the stimulating light at the grain boundaries causes unwanted recombination at adjacent pixels, decreasing image spatial resolution.

Glass ceramics have the potential to surpass commercial storage phosphors in terms of spatial resolution. Both BaCl$_2$ and BaBr$_2$ nanocrystals doped with either Eu$^{2+}$ or Ce$^{3+}$ can
be precipitated within a fluoride glass matrix to create a glass-ceramic storage phosphor [39–41]. Although there is some refractive index mismatch between the crystallites and the glass matrix, there are no large grain boundaries to scatter the stimulating light, as with commercial storage phosphor plates. With crystal sizes significantly smaller than the wavelength of the stimulating laser, scattering is minimized. These plates are particular suited for high spatial resolution applications such as mammography [11, 42]. To take advantage of the high spatial resolution capabilities of glass ceramic storage phosphors, an equally advanced readout system is required [7]. Figure 10 shows a CAD rendering of a large format scanner specifically designed to work with ZBLAN glass ceramics.

However, for glass ceramics to be competitive in medical CR, efficiency must be improved. Although per crystalline volume, glass ceramics compare nicely with polycrystalline materials, they are still far behind in terms of overall conversion efficiency [40]. Because glass-ceramic storage phosphors are sensitive to radiation in the MeV portion of the electromagnetic spectrum [43], these materials may also be suited to portal imaging applications[44–47].

**Conclusion**

In summary, glass ceramics, in particular those based upon FCZ compositions, can be a cost effective, easy to manufacture alternative to scintillators and storage phosphors currently used in medical imaging. The incorporation of nanocrystals into glass yields a single material with the assets of both glass and single crystals. Embedding the optical activator in a glass matrix provides physical and environmental protection, with the potential to enhance performance. Due to the size of the nanocrystals being less than the wavelength of light, this leads to extremely high spatial resolution images, especially useful in such applications as dental radiography and mammography. Such a material offers a robust, cost effective, versatile, easy synthesis solution to a desired application in any shape or size.

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Figure 1.
Plot of the DSC data for an FCZ glass. The heating rate was 10 K/min [14].
Figure 2.
Schematic of computed tomography showing helical rotation [48].
Figure 3.
PET scanner. http://creativecommons.org/licenses/by-sa/3.0/.
Figure 4.
Cartoon of image formation from a PET scanner. http://creativecommons.org/licenses/by-sa/3.0/.
Figure 5.
Tomographic image of a mouse finger joint taken with a ZBLAN glass-ceramic plate [13].
Figure 6.
Detector block and formation of rings for a PET scanner. [http://creativecommons.org/licenses/by-sa/3.0/](http://creativecommons.org/licenses/by-sa/3.0/).
Figure 7.
Coupling of scintillator to photodiode [27].
Figure 8.
ZPBL glass.
Figure 9.
DSC of ZPBL glass.
Figure 10.
CAD rendering of the large format scanner for ZBLAN glass ceramic imaging plates [7].