Bioactivity in restorative dentistry: A user’s guide

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Introduction

The word “bioactivity” is one of the latest buzzwords in the dentistry. It is highlighted as a feature in many restorative products with different and conflicting claims. This has stirred up confusion and controversy surrounding the concept. This article will attempt to provide clarity for the practising restorative dentist regarding the following: What is bioactivity? What are bioactive products? How can they be used to provide the best dental care?

The term “bioactive material” originated with Dr Larry Hench in 1969. He was looking for an improved graft material for bone reconstruction needed by injured returning soldiers of the Vietnam war. Hench was searching for a material that could form a living bond with tissues in the body. All the available materials at the time were rejected by the body. He developed bioglass (calcium silico-phosphate glass), a completely synthetic material that chemically bonds to bone.1 Hench defined a bioactive material as “one that elicits a specific biological response at the interface of a material which results in the formation of a bond between the tissues and the material”.2

Today, there are many different definitions of bioactivity found in the dental literature, dependent on the research and on the researcher. The definition fits the research, whereas it should fit the concept. In order to achieve clarity of meaning, it is best to go with what can be most easily understood by clinicians and patients alike, the definition found in the dictionary: "bioactivity”, noun: any effect on, interaction with or response from living tissue.

Historically, dental materials were designed to have a “neutral” effect on the tooth.3 Many current dental materials are not neutral. They are "active", not "passive", participants in the restorative process. New materials are being developed to harness this potential behaviour. These are “bioactive” materials.

For simplification and clarity in discussing bioactive restorative materials, it is best to separate them according to their mechanism of action. There are three separate mechanisms that are demonstrated by bioactive restorative materials (Table 1 lists examples of bioactive restorative materials by their mechanism of action). A bioactive restorative material can display one or more of the following actions:

1. remineralises and strengthens tooth structure through fluoride release and/or the release of other minerals;
2. forms an apatite-like material on its surface when immersed in body fluid or simulated body fluid over time;4
3. regenerates live tissue to promote vitality in the tooth.

Materials that remineralise

Dental caries is the cumulative result of consecutive cycles of demineralisation and remineralisation at the interface between biofilm and the tooth surface. Oral bacteria excrete acid after consuming sugar, leading to demineralisation. Hydroxyapatite crystals are dissolved from the subsurface. Remineralisation is the natural repair process for non-cavitated lesions. It relies on calcium and phosphate ions, assisted by fluoride, to rebuild a new surface on the existing crystal remnants in the subsurface.5

Under normal physiological conditions at a pH of 7, saliva is supersaturated with calcium and phosphate ions, making caries progress slow. As the pH is lowered, higher concentrations of calcium and phosphate are required to reach saturation with respect to hydroxyapatite.6 This is called the “critical pH”, the point where equilibrium exists and there is no mineral dissolution and no...
mineral precipitation. The critical pH of hydroxyapatite is around 5.5 and that of fluorapatite is around 4.5. This varies with individual patients. Below critical pH, demineralisation occurs, while above critical pH, remineralisation occurs (Figs. 1 & 2).43

If fluoride is present in the plaque fluid, it will penetrate the enamel, along with the acids at the subsurface, adsorb to the apatite crystal surface and protect the crystals from dissolution.6 This coating makes the crystals similar to fluorapatite (critical pH of 4.5), ensuring that no demineralisation takes place until the pH reaches this point. Fluoride present in solution at low levels among the enamel crystals can markedly decrease demineralisation.7, 8

When the pH returns to 5.5 or above, the saliva, which is supersaturated with calcium and phosphate, forces minerals back into the tooth.8 Fluoride increases remineralisation by bringing calcium and phosphate ions together and is preferentially incorporated into the remineralised surface, which is now more acid-resistant.

The benefits of fluoride are maintained long term through the mechanism of fluoride reservoirs. Fluoride is retained intracorally after fluoride treatments, such as fluoridated toothpaste and fluoride varnish application, and is then released into the saliva over time.8, 9 Fluoride can remain on teeth, mucosa or dental plaque or within bioactive restorative materials. Fluoride retention is clinically beneficial, since it can be released during cariogenic challenges to decrease demineralisation and enhance remineralisation.5

When the enamel and dentine no longer have adequate structure to maintain their mineral framework, cavitation takes place and simple remineralisation is an insufficient treatment. Tooth preparation and restoration are now required.

Bioactive restorative materials replace dental hard tissue and help to remineralise the remaining dental structures. Glass ionomer cements and their derivatives, such as resin-modified glass ionomers, compomers and giomers, fall into this category.
Glass ionomer cements

Glass ionomer cements were developed in the early 1970s. They are particularly valuable for caries control in high caries risk patients and in areas where location or isolation create restorative challenges (Figs. 3a & b). Glass ionomers have a true chemical bond with dental tissue. They encourage remineralisation of the surrounding tooth structure and prevent bacterial microleakage through ion exchange adhesion with both enamel and dentine.11 A new, ion-enriched layer is created at the tooth–glass ionomer interface. This layer contains phosphate and calcium ions from the dental tissue, and calcium (or strontium), phosphate and aluminium from the glass ionomer cement.11 The remineralisation process creates a harder dentine surface (Fig. 4).12, 43 Restoration fracture is usually cohesive, leaving the ion exchange layer firmly attached to the cavity wall. The dentinal tubules are sealed and protected from bacterial penetration.13

In order to eliminate the physical property disadvantages of glass ionomers and harness their remineralising benefits, dental researchers have produced an assortment of glass ionomer derivatives: resin-modified glass ionomers, compomers and giomers. Two product lines in this category are ACTIVA BioACTIVE-RESTORATIVE (Pulpdent; Fig. 5) and the Beautiful giomer family of restorative materials, including Beautiful II and Beautiful Flow Plus (SHOFU; Fig. 6). Studies have shown ACTIVA’s remineralisation potential through fluoride release and recharge and calcium release.14, 15 Giomers are used in restorative dentistry as equivalent to composite resin, in all their applications.

Giomers

Giomers represent the hybridisation of glass ionomer and composite resin properties: the fluoride release and recharge of glass ionomers, and the aesthetics, physical properties and handling of composite resins.16 The giomer concept is based on PRG (Pre-Reacted Glass) technology: a glass core, surrounded by a glass ionomer phase enclosed within a polyacid matrix. Studies show that dentine remineralisation occurs at the preparation surface adjacent to the giomer.17

Giomers, through the creation of fluoride reservoirs, release and recharge fluoride efficiently, significantly better than do compomers18 and composite resins, although not as well as glass ionomers.19 The clinical performance of giomers has been tested against those of hybrid resin composites. Giomers have been found to compare positively for all criteria.20

Materials that deposit hydroxyapatite

Some bioactive materials not only remineralise by adding minerals to tooth structure, but also create an apatite-like material on their surfaces when immersed in body fluid or simulated body fluid over time.4 There are
two chemical classes of these bioactive restorative materials: calcium silicates and calcium aluminates.\textsuperscript{21, 22} These materials are non-resin-based. Both materials set with an acid–base reaction and produce an alkaline pH after setting. High pH levels (7.5 or higher) appear to stimulate more active and complete bioactivity.\textsuperscript{4}

Ceramir (Doxa Dental; Fig. 7) is a calcium aluminate material developed for cementation. An \textit{in vitro} study found that this apatite-forming bioactive cement can occlude artificial marginal gaps. This is beneficial clinically at the margin of the prepared tooth and cemented restoration. It suggests that bioactive dental materials may significantly improve clinical outcomes and longevity of dental restorations.\textsuperscript{23}

Calcium silicates have also been shown to deposit hydroxyapatite.\textsuperscript{23} Even more importantly, they can stimulate the regeneration of live tissue: dentine, pulp, blood vessels and bone.\textsuperscript{24–26}

\section*{Materials that can regenerate live tissue}

Some bioactive materials not only remineralise and form hydroxyapatite, but also regenerate live tissue. This is crucial in many restorative and pulp-related treatments. One major example is vital pulp therapy. The goal of vital pulp therapy (direct pulp capping and pulpotomy) is to treat reversible pulpal injury arising from trauma, caries or restorative dentistry. These injuries destroy the normal tissue architecture at the pulp–dentine interface, but can be healed if the wound is properly protected.\textsuperscript{27}

Treatment must maintain pulp vitality and function and restore dentine continuity below the injury through hard-tissue bridge formation.\textsuperscript{28} Optimal quality of this hard-tissue bridge is essential to the long-term success of vital pulp therapy.\textsuperscript{29, 30} There is a pulp tissue-specific response to the capping material, and this determines the quality of the dentine bridge.\textsuperscript{28}

Calcium hydroxide products have been used in vital pulp therapy for many years. The ability of calcium hydroxide to promote dentine bridge formation and enhance wound healing is well established.\textsuperscript{31} However, calcium hydroxide has inadequate physical properties and produces poorly formed dentinal bridges containing tunnels.\textsuperscript{32} This has directed research to seek out new materials for this therapy.

The first of these materials created for practical clinical use was mineral trioxide aggregate (MTA).\textsuperscript{33} MTA was originally developed as a root end filling material for apicectomy procedures and to repair root perforations.\textsuperscript{34} Indications for its use have expanded broadly within restorative dentistry and paediatric dentistry.\textsuperscript{27}

MTA is a calcium silicate-based material (derived from Portland cement) with high sealing ability and excellent biocompatibility. MTA-based materials stimulate faster formation of dentinal bridges that are of better quality than those of calcium hydroxide.\textsuperscript{35, 36} Since the mid-1990s, MTA has been recognised as the standard in conservative pulp vitality treatment.\textsuperscript{37} MTA-based materials have limitations however:

- long setting time;\textsuperscript{38}
- weak mechanical properties;\textsuperscript{38}
- difficult handling;\textsuperscript{38}
- may produce tooth discoloration;\textsuperscript{39}
- may contain heavy metals.\textsuperscript{40}

Much research has followed to build on the advantages of MTA while eliminating most of the disadvantages. One such material is Biodentine (Septodent; Fig. 8). It was formulated by improving the physical and handling properties of MTA-based endodontic repair cement technology and creating a dentine replacement material with significant reparative qualities.

Biodentine can be used as a complete dentine replacement material to treat damaged dentine in both the crown and the root with clinical indications that exceed those of MTA and other related Portland cement calcium silicate products.\textsuperscript{21} Biodentine can be used as a:

- cavity base/liner in deep carious lesions;
- pulp capping agent in vital pulp therapy (both direct pulp capping and pulpotomy);
- root repair material for perforations, resorptions, apicification and root end filling material in endodontic surgery; and
– restorative material to replace missing or defective dentine.

It cannot be used to replace enamel.

The advantages of Biodentine over MTA and modified MTA materials include:

– ease of handling;
– high viscosity;
– shorter setting time (12 minutes);
– better physical properties;\(^{41}\)
– composition containing raw materials with known degree of purity;\(^{42}\) and
– good colour stability, so there is no discoloration.\(^{43}\)

Biodentine is a tricalcium silicate-based material. Its mechanical properties compare to those of dentine, and it can be used as a dentine substitute in both the crown and the root.\(^{44-46}\) It stimulates deposition of hydroxyapatite when exposed to tissue fluids.\(^{47}\) It is non-toxic as tested on human pulp cells.\(^{48}\) Studies have shown complete dentinal bridge formation after six weeks in human teeth.\(^{49}\)

Biodentine provides a hermetic seal that protects the dental pulp by preventing bacterial infiltration. This creates a protected environment where healing can take place. The seal is created through micromechanical retention by infiltrating the dentine tubules and by stimulating odontoblasts to deposit dentine.\(^{25}\)

It is the calcium-releasing ability of pulp capping materials that induces pulp tissue regeneration. Tricalcium silicate-based materials like Biodentine produce calcium hydroxide as a product of hydration.\(^{50}\)

The calcium silicate setting reaction is as follows:

\[
2(\text{Ca}_3\text{SiO}_5\text{O}_2) + \text{6H}_2\text{O} \rightarrow 3\text{CaO.2SiO}_3.3\text{H}_2\text{O} + 3\text{Ca(OH)}_2
\]

Calcium silicate in the powder interacts with water, leading to the setting and hardening of the cement. This produces hydrated calcium silicate gel and calcium hydroxide. Calcium hydroxide can now stimulate pulp regeneration within a gel-like material that is strong and not porous; this harnesses the regenerative powers of calcium hydroxide without its physical disadvantages.

Biodentine in vital pulp therapy, through the action of calcium hydroxide in this enhanced physical state, boosts the deposition of reparatory dentine by odontoblasts. This creates a dense dentine barrier,\(^{51,52}\) as well as heals damaged pulp fibroblasts.\(^{53}\) Clinical results have confirmed Biodentine’s ability to preserve pulp vitality even in very difficult cases. It has the potential to heal pulps, avoiding what may have been inevitable endodontic involvement in the past.

**Resin-modified calcium silicates**

Studies have shown that the presence of a resin matrix modifies the setting mechanism and calcium leaching of calcium silicates.\(^{54}\) A partial pulpotomy clinical study compared TheraCal (BISCO), a light-cured, resin-modified calcium silicate base/liner designed for direct and indirect pulp capping, with non-resin-containing materials Biodentine and ProRoot MTA (Dentsply Sirona). The results showed that Biodentine achieved complete dentinal bridge formation in all teeth. The rates for bridge formation were 56 % for ProRoot MTA and 11 % for TheraCal.\(^{55}\) Normal pulp organisation was seen in 66.6 % of the teeth in the Biodentine group, 33.3 % of the ProRoot MTA group and 11.1 % of the TheraCal group. The study concluded that the non-resin-based partial pulpotomy materials perform better than the resin-based materials and present potential for the best clinical outcomes.\(^{55}\)

Another recent study compared Biodentine with TheraCal with respect to how they each affect inflammation and regeneration of the pulp in a direct pulp capping in vitro model. TheraCal was shown to increase inflammatory cells and decrease the regenerative processes of the pulp, whereas Biodentine did not increase inflammation and supported the regenerative processes of the pulp.\(^{56}\)

These two studies seem to suggest caution in using resin-based materials for vital pulp therapy. Biodentine has good biocompatibility and bioactivity for use in vital pulp therapy.
Calcium silicates as endodontic sealers

The ability to deposit hydroxyapatite and regenerate live tissue has brought calcium silicate technology into the scope of endodontic sealers. After obturation, there is generally contact between the obturating materials and the periapical tissue. The success of treatment greatly depends on the integrity of the obturated seal to prevent recurrent infection of the periapical space.

The introduction of bioactive endodontic sealers has changed the concept of obturated seal from hermetic sealing with inert materials to biological bonding with bioactivity. The sealer becomes a filler, not only a sealer.

Calcium silicates are well suited to endodontic obturation owing to the following properties:

– high pH (antibacterial);
– hydrophilic (use moisture present in dentinal tubules to initiate set);
– biocompatible;
– do not shrink or resorb;
– excellent seal (bond chemically and mechanically to dentine); and
– ease of use (can be used with many methods of condensation).

Furthermore, they are bioactive:

– remineralise hard tissue;
– deposit hydroxyapatite to improve the seal over time;
– regenerate and heal surrounding periapical tissue.

BioRoot (Septodont; Fig. 9) has been developed to incorporate these bioactive traits. Research has shown:

– Hydroxyapatite formation upon setting reaction: Bio-ceramic sealers bond to dentine through the process of alkaline etching. This is due to the alkalinity of the sealer. A mineral infiltration zone develops between the dentine and the sealer.
– Tissue healing: A study that compared the effects of BioRoot RCS on human periodontal ligament cells with the standard zinc oxide eugenol-based root canal sealer, Pulp Canal Sealer (Kerr Dental), showed BioRoot to have fewer toxic effects on periodontal ligament cells and that it induced greater secretion of angiogenic and osteogenic growth factors. These properties are essential in periapical tissue regeneration. BioRoot also showed excellent biocompatibility when compared with many other contemporary endodontic sealers.

Conclusion

With a bit of simplicity and focus on the essentials of bioactivity in dentistry, it becomes clear that bioactivity is now an essential part of the practice of clinical dentistry. Dentists can now harness the potential to remineralise and generate tooth material and heal biological structures for their ultimate objective: attaining the best possible clinical outcomes for their patients.

Editorial note: A list of references is available from the publisher.

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Dr Fay Goldstep has been an ADA (American Dental Association) Seminar Series Speaker and lectured at the ADA, Yankee, American Academy of Cosmetic Dentistry, Academy of General Dentistry and Big Apple dental conferences. She has lectured nationally and internationally on proactive/minimal intervention dentistry, soft-tissue lasers, electronic caries detection, healing dentistry and innovations in hygiene. Dr Goldstep has served on the teaching faculties of the postgraduate programmes in aesthetic dentistry at the State University of New York at Buffalo, universities of Florida and Minnesota, and University of Missouri–Kansas City in the US. She sits on the editorial boards of the Oral Health Journal (healing/preventative dentistry), Dental Tribune U.S. Edition and Dental Asia. She is a fellow of the American College of Dentists, International Academy for Dental-Facial Esthetics and American Society of Dental Aesthetics. Dr Goldstep has been a contributing author to four textbooks and has published more than 60 articles. She has been listed as one of the leaders in continuing education by Dentistry Today since 2002. Dr Goldstep is a consultant to a number of dental companies and maintains a private practice in Toronto in Canada. She can be contacted at epdol@rogers.com.