Bioactive Ceramics for Pediatric Dentistry

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11.1 Bioceramics

Our world is comprised of substances that are organic, metallic, ceramic, or combinations thereof, as depicted in Fig. 11.1. Organic materials have carbon-hydrogen bonds (C-H), which include monomers, polymers, and many other organic compounds; metals are often shiny and good conductors of heat and electricity. Ceramic materials are those materials that are neither metallic nor organic and are often, but not exclusively, oxide compounds. Many ceramic materials are crystalline compounds, but glasses, which are amorphous (non-crystalline), are also ceramics and are often combined with ceramic crystals. Most glasses are based on silica (silicon dioxide, SiO_2), which is distinct from silicone, an organic substance.

Biomaterials are subset of materials (Fig. 11.1) that are used in vivo. Metal, ceramic, and organic compounds may be biomaterials, which are sometimes combined. For instance, composite resin combines organic resins and ceramic filler particles. All dental restorative and prosthodontic materials are biomaterials, and many of them are bioceramics.

Bioceramics may be bioinert, radiopaque, or bioactive (Fig. 11.2) but are best known for being bioinert. Bioinert materials do not elicit a response from the host and do no harm. Alumina and zirconia are examples of inert bioceramics used for prosthodontics, implants, polishing media, and orthodontic brackets. Some bioceramic powders are radiopaque (white on X-ray images), including barium sulfate, bismuth oxide, calcium tungstate, and tantalum oxide. All glass formulas are bioceramics; some glasses are inert, others are inert and radiopaque, and other formulas are bioactive. Bioactive ceramics, the subject of this chapter, do elicit a response in vivo.

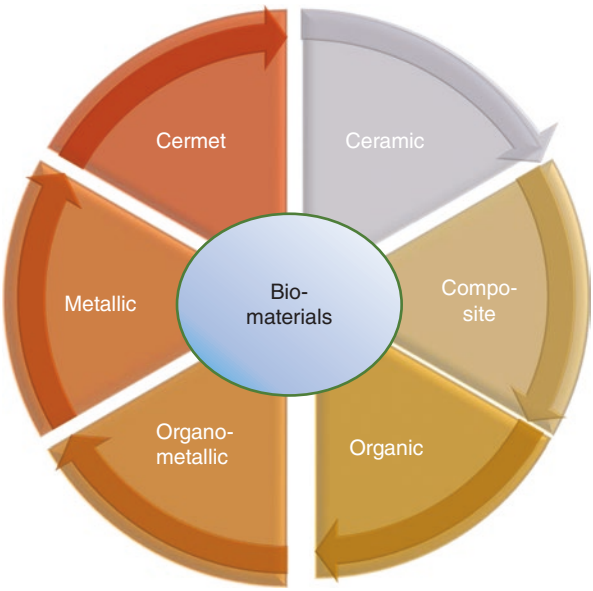

Fig. 11.1 Categories of materials showing the main categories and the subset of biomaterials

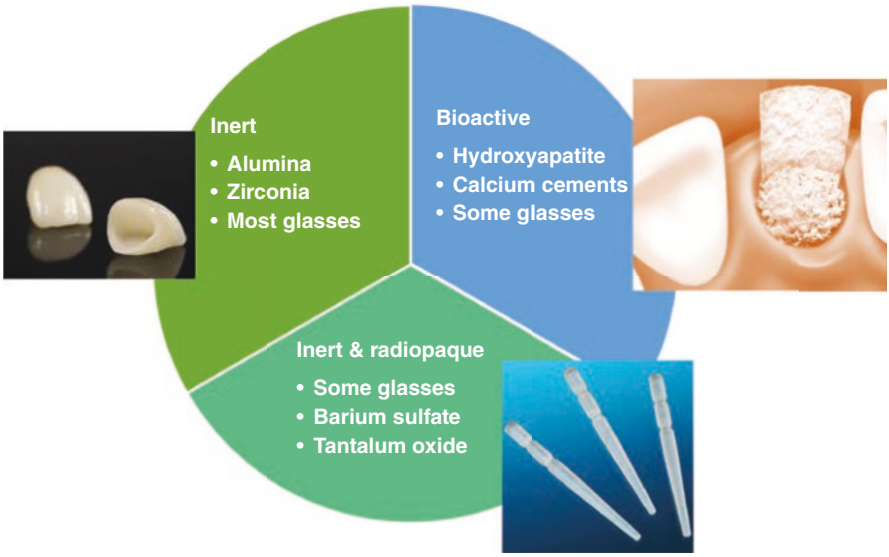

Fig. 11.2 Three categories of bioceramics with examples of crowns, glass fiber posts, and bone grafting material

11.2 Bioactive Ceramics and Biomineralization

Bioactive ceramics provide benefits for healing [1], such as beneficial ion release to stimulate new bone or dentin formation. In this chapter, a more narrow definition of bioactivity is followed as defined by an international standard for surgical materials, ISO 23317:2014: the in vivo formation of a calcium phosphate layer, similar to hydroxyapatite, on the surface of the biomaterial. This international standard has an *in vitro* test for bioactivity using phosphate-buffered saline. This bioactivity has also been denoted as biomineralization. Bioactivity is not limited to biomineralization, which is also the cellular process by which living organisms secrete inorganic minerals [2], but for simplicity, biomineralization is synonymous with bioactivity. Bioactive ceramics, in this context, have two key characteristics: they create a high pH by releasing hydroxide ions, and they release calcium ions in vivo into the body fluids. Body fluids, being supersaturated in phosphate ions, react near the surface of the ceramic where the pH is high, and precipitate a hydroxyapatite-type ($Ca_{10}(PO_4)_6(OH)_2$) layer on the surface of the ceramic, as expressed in Eq. 11.1.

$$10Ca^{+2} + 6PO_4^{-4} + 2OH^- \rightarrow Ca_{10}\left(PO_4\right)_6\left(OH\right)_2 \tag{11.1}$$

[calcium ions + phosphate ions + hydroxide ions] in solution → hydroxyapatite precipitate [crystals].

This precipitation reaction occurs acellularly when bioactive ceramics are placed in simulated body fluid, *in vitro* [3] and in vivo [4]. The precipitated layer may begin as an amorphous calcium phosphate and transform over time to poorly crystalline,

β-type carbonated apatite crystals. The ratio of calcium to phosphate may be lower than 1.67, the ratio in bone. The layer is self-limiting, because when the hydroxyapatite (HA) layer thickens, ion diffusion from the bioactive ceramic is inhibited. When the hydroxyapatite precipitate is formed, the surface of the bioceramic is hidden from the body's immune system and reduces the "foreign body" reaction by which the body identifies, attacks, and attempts to destroy (resorb) the ceramic. The formation of the HA layer precedes a cascade of healing reactions [5, 6] of the pulp or alveolar bone, which are not described in this chapter.

Only a small subset of bioceramics are bioactive, including certain silicate glasses (often denoted as bioglasses), calcium hydroxide, hydroxyapatite, other calcium phosphates, calcium silicate cement, and calcium aluminate cement. The focus of this chapter is on calcium silicate and calcium aluminate cements. These unique cement powders react with water to harden and cause this bioactive reaction in Eq. 11.1.

"Bioactive glasses" were first invented by Hench [7, 8] and contained silica, calcium, and phosphorous oxide but now include similar glasses with magnesium oxide [9] and boron oxide [10] as components. Some bioactive glasses are a component of alveolar bone grafting materials [11] where a coarse (~100 μm) glass powder is implanted, such as in an extraction socket [12]. Bioactive glass and other bone graft materials release ions into the tissue fluids and are slowly replaced by advancing bone tissue. Bone grafting materials rely on micro-, meso- or macroporosity, and their coarse particles serve as bone cell scaffolds [13] for gradual dissolution and resorption of the glass. Both crystalline hydroxyapatite grafting materials and bioactive glass particles are resorbable.

Calcium hydroxide has long been used in dentistry as an antimicrobial [14] medicament that is biomineralizing and stimulates reparative dentin [15]. However, calcium hydroxide is not the best material for pulpotomies for primary teeth, because the histological response has been formation of a deficient, porous reparative dentin [16, 17]. Calcium hydroxide particles gradually form calcium carbonate, which is a bioinert ceramic. Calcium hydroxide is not a cement (it doesn't set nor form a hard layer), unless combined with other substances, such as the resins in Dycal.

Calcium phosphate cements were invented by Chow [18] and are self-setting, bioactive ceramics. Calcium phosphate compounds react to form HA. That is, tetracalcium phosphate, dicalcium phosphate, and dicalcium phosphate dihydrate can gradually dissolve under neutral pH conditions and precipitate HA, amorphous calcium phosphate, or brushite, via self-setting reactions to form a hard mass. The magnesium phosphate cements [19] are similar and are also biomineralizing/bioactive. These cements form HA but are generally slow to set and are considered weak.

The calcium silicate and calcium aluminate cements differ from the bioactive glasses, hydroxyapatite, calcium hydroxide, and calcium phosphate cements. These

calcium cements form a solid mass (set) by reaction with water; that is, they are hydraulic, like calcium phosphate cements. Calcium silicate and calcium aluminate cements are not currently designed to have pores for osseous ingrowth or resorption, unlike the bioactive glasses or calcium phosphate cements; therefore, these solidified cements are usually not resorbable or dissolvable. The cements set within minutes to hours and are bioactive. (See Fig. 11.3 for an ex vivo example showing a hydroxyapatite (HA) layer formed on a calcium silicate cement that had been placed in a root-end filling, soaked in phosphate-buffered saline, and then sagittally sectioned.) The calcium silicate/aluminate cements begin to biomineralize (form HA) acellularly within 30 min. The clinical and histological responses to the calcium silicate/aluminate cements are equal to, or superior to calcium hydroxide [17, 20, 21], perhaps because the cements set and form a matrix and reservoir of hydroxide and calcium ions. This is different from a non-setting paste of calcium hydroxide, a resin cement containing calcium hydroxide, or so-called bioactive resin-modified glass ionomers.

In the last three decades, bioactive calcium silicate and calcium aluminate cements have achieved prominence in pediatric dentistry and endodontics for vital pulp and periapical tissue therapy. This chapter introduces the reader to the unique and beneficial characteristics of bioactive calcium silicate and calcium aluminate cements, explaining the setting reactions, and comparing the dental materials available for pediatric dentistry. From this information, pediatric dentists may make more informed choices for their benefit and the oral health of their patients.

Fig. 11.3 Biomineralization layer (white) on gray calcium silicate cement used in root-end filling. This tooth was filled, soaked in phosphate-buffered saline, and then sectioned

11.3 Bioactive Ceramic Cements

Dental cements include materials to coronally affix prosthodontic or orthodontic devices, either adhesively or via luting (non-adhesive). Dental cements are also used to line a cavity or create an insulating base under a restorative material. The term dental cement is also used for materials that seal root canals with gutta percha. Many compositions of "cements" are used, including the traditional zinc oxide-based cements (phosphate, carboxylate, and eugenolate), glass ionomer, and composite resins. Such cements usually rely on acid-base reactions, and they do contain bioceramic powders but are not bioactive. In this chapter, we focus on the bioactive calcium silicate and aluminate cements that require water for setting and are used in endodontic therapy.

The word "hydraulic" has two meanings: exertion of a uniform pressure by a liquid and materials that set (harden) with water. Hydraulic cements refer to the water-setting ceramics, especially calcium silicate and calcium aluminate compositions. Many non-scientific terms have been used to describe these hydraulic bioactive ceramic cements including mineral trioxide aggregate (MTA), MTA-type materials, tri-/dicalcium silicate-based material/cement, ordinary hydraulic silicate cements, HSC, Portland cement, OPC, PC, calcium silicate cement (CSC), hydraulic cements, hydraulic calcium silicate cement (HCSC), biosilicate, calcium silicate, calcium aluminate, bioceramic cement, BC, and bioactive cement/sealer. Dental product trade names for these bioactive bioceramics often include "MTA," of which ProRoot MTA was the first. Other prominent trade names in this category include Biodentine®, EndoSequence® BC, iRoot®, NeoPUTTY®, MTA Plus®, ProRoot® MTA, and TotalFill® BC.

The earliest publication on calcium silicate cement in dentistry dates from 1878 when Dr. Witte of Germany filled root canals with a locally made, pulverized Portland cement [22]. Portland cement was a new invention at this time. He mixed the cement powder with water and carbolic acid or creosote and filled 25 teeth, with no failures after 1 year. No other mention of using Portland cement in dentistry is known until the twentieth century. Professor Torabinejad at Loma Linda University in California disclosed using Portland cement for dentistry in 1993, based on a specific construction-grade Portland cement that he blended with bismuth oxide powder. Dr. Torabinejad used his calcium silicate cement mixture for endodontic surgery [23] and perforations [24], which were two indications which had been especially problematic for healing. He dubbed his mixture "mineral trioxide aggregate" (MTA) [25] and received a patent with his co-inventor patient, who was an expert in construction-grade Portland cement. The cement of their invention included about 5% iron oxide, which gave the cement a very dark color. His dark-gray, patented composition was commercialized by Dentsply Sirona (USA) in 1997, who manufactured it as ProRoot® MTA. The commercial dental version was a purer, finer powder than the original prototype material from Dr. Torabinejad, having been manufactured by following ISO 13485 and FDA good manufacturing practices. That is, ProRoot MTA did not have the impurities inherent in most construction-grade cements, commonly arsenic, which is restricted (<2 ppm soluble As) in

dentistry. Portland cement is the term used to describe construction-grade, calcium silicate cement and is inappropriate for dental materials, and is not used in this chapter to describe the dental materials. After the gray ProRoot MTA, product, a white version was commercialized and is often denoted as "white" or "tooth-colored" ProRoot MTA in the dental literature. The key to the white ProRoot MTA was reduction of the iron oxide content in the cement. Both ProRoot products were calcium silicate cements blended with bismuth oxide. The ProRoot MTA products were quickly adopted by endodontists, based on the remarkable histological results published for the original material [23, 26]. For instance, cementum and periodontal ligament tissues regenerated over the calcium silicate cement root-end fillings in animals. This healing had not been so pronounced with other root-end filling materials and was greatly appreciated, though at first of unknown mechanism.

Many similar formulas have now been marketed containing calcium silicate cement, many having MTA in their name and other products with new trade names; however, the early imitators of ProRoot MTA all contained calcium silicate cement. In general, the products contain calcium silicate cements of similar but not identical formulas to the cement in ProRoot MTA and a radiopaque powder. Other radiopaque powders are often used, rather than bismuth oxide. Such bioactive ceramic cements are indicated for any pulp, dentin, or alveolar bone-contacting procedure and have become the standard of care for vital pulp therapy [27]. Pediatric dentists use bioactive ceramic cements for pulp capping, lining or base of a cavity, pulpotomy, apexification, resorption, or revascularization. (See the collage of suitable indications in Fig. 11.4, although the indications vary with the products.) Notably, the indications are all within the dentin, not exposed to the oral cavity. This

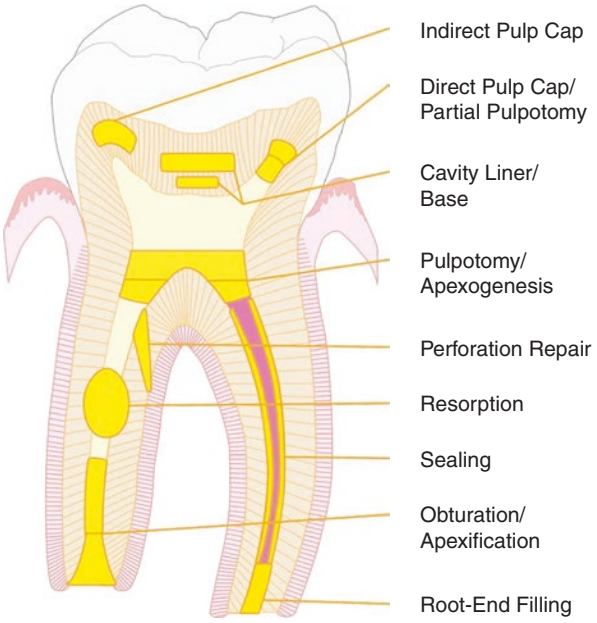

Fig. 11.4 A collage of indications for use of the bioactive ceramic cements, especially for vital pulp therapy. Cement is shown in yellow

limitation is imposed because calcium silicate cement is vulnerable to acids. The calcium silicate cements can be disintegrated by strong acids. Therefore, this cement is unsuitable as a restorative material, where materials are constantly exposed to our acidic diets, unlike the pH-neutral tissue fluids [28]. Obturation after a pulpectomy may be suitable for immature permanent teeth or primary teeth when a successor is absent. However, the current bioactive ceramic cement products are considered non-resorbable and not suitable for primary tooth obturation for fear of disrupting the eruption of the permanent teeth. Despite the versatility in Fig. 11.4 for vital pulp therapy, high-priced bioactive cement products have prevented their universal adoption in pediatric dentistry.

The calcium silicate and calcium aluminate cement powders possess properties not found in most other dental materials. The cement powders set with water, are dimensionally stable, release calcium ions, and form alkaline hydroxides within an amorphous, hydrated cement matrix. Requiring moisture to set is a tremendous benefit for dental applications. Lack of contraction or expansion helps seal the area of the tooth anatomy filled with the cement, unlike other dental materials that often shrink when they set. Most importantly, calcium silicate and calcium aluminate cements release calcium and hydroxide ions from the surfaces of their powders, on contact with moist tissues. These ions create bioactivity and impart antimicrobial action on planktonic bacteria and yeast [29], although insufficient to destroy tenacious biofilms [30]. Calcium aluminate cements have been used in dental restorative materials and crown cements [31, 32]. Calcium aluminate cements have greater acid resistance than calcium silicate cements, a beneficial characteristic for their oral use in acidic and bacterial environments [33]. The pH of the calcium aluminate cements is not quite as high as the calcium silicate cements, but is sufficiently alkaline to produce biomineralization and osteogenic effects [34, 35]. Calcium silicate cement also release silicate ions, which are known to benefit osteogenesis [36], a key phenomenon for healing pulpal or periapical tissue.

11.4 Bioactive Cement Compounds

Phase diagrams are used by materials scientists to understand what compounds (phases) can be manufactured from a particular combination of components. The compositional ranges for the calcium silicate and the calcium aluminate cements are outlined in the partial ternary (3-component) phase diagram shown in Fig. 11.5. A small range of composition is suitable to manufacture the calcium silicate or the calcium aluminate cement phases. The phase diagram shows that some silica may be dissolved in the calcium aluminate cement and some alumina can be dissolved in the calcium silicate cement. Calcium aluminate cement compounds are chemically separate and distinct from the calcium silicate cement region and do not overlap as shown in Fig. 11.5; therefore, the two calcium cements (silicate and aluminate) must be fabricated separately, but may be combined.

Calcium silicate and calcium aluminate bioactive ceramic cements are not naturally occurring; high temperature manufacturing is required. To make these cements,

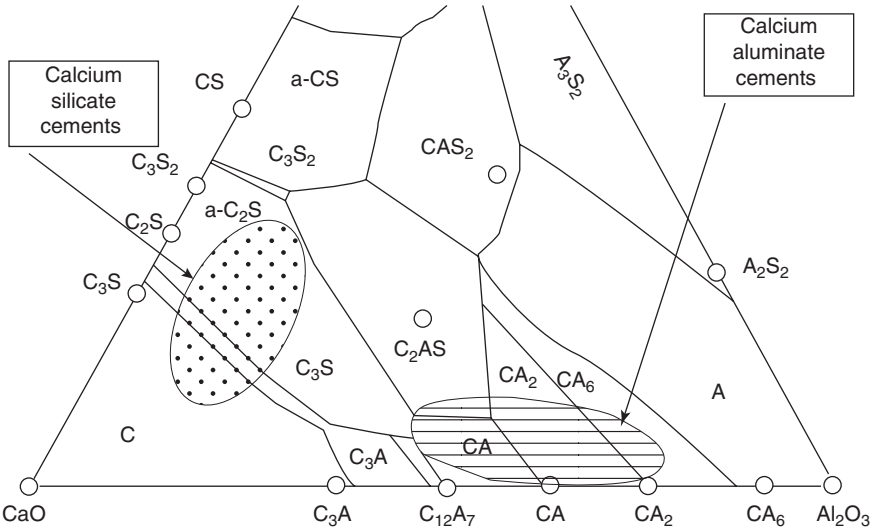

Fig. 11.5 Ternary phase diagram for calcia (CaO, C), silica (SiO_2, S), and alumina (Al_2O_3, A), showing the compositional range for the calcium silicate (area 1) and calcium aluminate cements (area 2)

raw materials are blended, which are ceramic powders, usually containing calcium carbonate, silica, and alumina powders (from varied sources). The blended powders are heated to a peak temperature of about 1500 °C in a kiln. At this high temperature, the raw materials can quickly react to form the cement compounds. The nodules of cement are expelled from the high temperature kiln for quick air cooling, which ensures that the most water reactive phases of cement are maintained. The nodules of cement are called clinker. Minor oxides, such as iron oxide, may be used to control the cement phases and lower the firing temperature. Solution-gelation techniques are an alternative method to manufacture the cement, generally a more expensive route. The fired ceramic cement is ground into a fine powder and sieved via various means. The fine cement powder is placed in a sanitary blender to disperse the cement, radiopaque powder, and any other additive powders evenly. The blended powders may be packaged, or the powder may be mixed with an organic liquid into a paste for placement in syringes. Researchers have speculated on the sources and techniques used for manufacturing the dental cements; however, the compositions and methods are proprietary trade secrets that cannot be easily discerned.

Calcium silicate and calcium aluminate cements discussed above appear to be just two compounds. Chemically, these cements represent six hydraulic ceramic compounds (phases). Calcium silicate cement powders for dentistry are primarily composed of two ceramic compounds: tricalcium silicate (Ca_3SiO_5) and dicalcium silicate (Ca_2SiO_4). These two silicates are known as alite and belite in the commercial Portland cement vernacular, and haturite and larnite in the mineralogical literature, although neither are naturally occurring minerals.

Tetracalcium aluminoferrite ($4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$, ferrite) was present in the original ProRoot MTA, which lowers the firing temperature needed to make calcium silicate cement. Unfortunately, tetracalcium aluminoferrite crystals are black, which darkened teeth immediately where the overlying tissue was thin. The ferrite phase is not considered a necessary component for these bioactive dental cements, so it has been avoided for esthetic reasons. For instance, White ProRoot MTA has low iron content (<1%); consequently, very little of the black ferrite phase is present.

A minor amount of alumina is often intentionally combined with silica and calcia raw materials for making calcium silicate cement to reduce the firing temperature, which is an economic benefit for manufacturing. When alumina is present in larger amounts, tricalcium aluminate ($Ca_3Al_2O_6$ or $3CaO.Al_2O_3$) crystals are formed during firing, concomitant with tri/dicalcium silicate crystals. Tricalcium aluminate is a bioactive cement phase and is present in many of the calcium silicate dental products [37]. Researchers have found the aluminate phase beneficial because of its very rapid hydration, which will accelerate cement setting. The tricalcium aluminate cement compound can be manufactured as a separate powder for addition to calcium silicate cement.

Calcium aluminate cement depicted in Fig. 11.5 is primarily composed of two phases, calcium monoaluminate ($CaO.Al_2O_3$, calcium aluminate) and monocalcium dialuminate ($CaO.2Al_2O_3$, calcium dialuminate), with very little silica. Tricalcium aluminate is usually not included. These two calcium aluminate cement phases react with water to form a hard matrix while releasing Ca^{+2}, $Al(OH)^{-4}$, and OH^- ions at the surface into the tissue fluids, to achieve the same biomineralization (HA precipitation) reaction as the calcium silicate cements. Calcium aluminate cement must be fired separately from the calcium silicate cement formulas, as depicted in Fig. 11.5, showing separate compositional ranges.

11.5 Cement Hydration Reactions

The hydration setting reactions for the bioactive ceramic cement phases are unlike the polymerization reactions used for many dental restoratives. The reactions occur with water and are not catalyzed or activated, unlike light-curing, chemical-curing, or dual-curing dental cements. The hydration reactions show how bioactivity originates. Of the cement phases, tricalcium aluminate sets the fastest, which reacts as in Eq. 11.2.

$$3CaO.Al_2O_3 + 6H_2O \rightarrow 3CaO{\cdot}Al_2O_3{\cdot}6H_2O \tag{11.2}$$

Tricalcium aluminate + water → amorphous hydrated tricalcium aluminate.

The reaction product of Eq. 11.2 is a hydrated gel of calcium aluminate. The rapid hydration of tricalcium aluminate phase speeds setting of calcium silicate cements; therefore, some researchers have intentionally added more tricalcium aluminate powder [38]. Tricalcium aluminate releases heat as it hydrates. In a tooth, the heat is easily mitigated, and enough tissue fluid is available to continue hydration.

However, calcium sulfate is sometimes used to modulate the setting of the tricalcium aluminate crystals. Calcium sulfate reacts with water and the tricalcium aluminate to form the intermediate product of ettringite ($Ca_3Al_2O_6.3CaSO_4.32H_2O$) or monosulfate ($Ca_3Al_2O_6.CaSO_4.12H_2O$), evolving less heat. This mitigation of rapid hardening is similar to the use of calcium sulfate dihydrate in alginate to slow its setting time.

The ferrite cement phase also undergoes rapid hydration, as noted in Eq. 11.3. The reaction products include a hydrated cement of calcia and alumina and release alkaline iron hydroxide.

$$4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3 + 19H_2O \rightarrow 2\left[2CaO{\cdot}Al_2O_3.8H_2O\right] + 2Fe\left(OH\right)_3 \quad (11.3)$$

Tetracalcium aluminoferrite + water → amorphous hydrated ferrite + iron oxide hydrate.

Calcium sulfate and calcium oxide are also used to mitigate overly fast setting of the ferrite, similar to tricalcium aluminate. Ferrite may also form complex calcium-alumino-ferric-sulfate hydrates, such as $3CaO{\cdot}(0.5Al_2O_3{\cdot}0.5Fe_2O_3){\cdot}3CaSO_4{\cdot}32H_2O$, $Ca_2(Al,Fe)_2O_5$, or $4CaO{\cdot}Al_2O_3{\cdot}Fe_2O_3$ [39].

The main hydration setting reactions for calcium silicate cement phases are shown in Eqs. 11.4 and 11.5.

$$2\left[Ca_3SiO_5\right] + 7H_2O \rightarrow 3CaO{\cdot}2SiO_2{\cdot}4H_2O + 3Ca\left(OH\right)_2 \quad (11.4)$$

Tricalcium silicate (alite) + water → amorphous calcium silicate hydrate + calcium hydroxide.

$$2\left[Ca_2SiO_4\right] + 5H_2O \rightarrow 3CaO{\cdot}2SiO_2{\cdot}4H_2O + Ca\left(OH\right)_2 \quad (11.5)$$

Dicalcium silicate (belite) + water → amorphous calcium silicate hydrate + calcium hydroxide.

After a brief induction period, the tricalcium silicate phase hydrates, faster than the dicalcium silicate phase. Both calcium silicate phases react to form an amorphous hydrated calcium silicate ($3CaO{\cdot}2SiO_2{\cdot}4H_2O$) concurrently releasing calcium hydroxide, known as portlandite in cement literature and occasionally in dental literature [40]. Dicalcium silicate crystals gradually hydrate, which decreases the porosity of the setting cement. Setting may take minutes to hours, depending on the composition and proportions of the phases. The compressive strength increases over about 4 weeks; however, most of the strength is developed in less than a week.

The calcium aluminate cement phases, calcium aluminate ($CaO.Al_2O_3$) and monocalcium dialuminate ($CaO.2Al_2O_3$, calcium dialuminate), have interesting hydration reactions that vary with temperature from 0 to 100 °C [41]. Fortunately, the body maintains a constant temperature for the hydration reactions, which are expressed in Eqs. 11.6 and 11.7 for the calcium aluminate ($CaO.Al_2O_3$) and calcium dialuminate ($CaO.2Al_2O_3$) cement phases.

$$3\left[CaO.Al_2O_3\right] + 12H_2O \rightarrow 3\left(CaO\right){\cdot}Al_2O_3{\cdot}6\left(H_2O\right) + 2\left[Al_2O_3.3H_2O\right] \quad (11.6)$$

Calcium aluminate + water → amorphous calcium aluminate hydrate + aluminum hydroxide.

$$3\left[\mathrm{CaO}\left(\mathrm{Al_2O_3}\right)_2\right]+21\mathrm{H_2O}\rightarrow 3\left(\mathrm{CaO}\right)\cdot\mathrm{Al_2O_3}\cdot 6\left(\mathrm{H_2O}\right)+5\left[\mathrm{Al_2O_3}.3\mathrm{H_2O}\right] \quad (11.7)$$

Calcium dialuminate hydration + water → amorphous calcium aluminate hydrate + aluminum hydroxide.

Calcium aluminate cements, like the calcium silicate cement phases, create a high pH environment and release calcium ions, which are the prerequisites for biomineralization (bioactivity/apatite formation). Some investigators have combined these calcium aluminate phases with calcium silicate compounds to combine the benefits of the silicate ion release for osteogenesis and the acid resistance of calcium aluminate cement for dentistry.

Pozzolanic cement, Roman cement, is based on the reaction of silica with calcium hydroxide or calcia (CaO). With water, the ceramics react as in Eq. 11.8, where the proportions of the hydrated calcium silicate are indefinite (m, x, and n) and depend on the composition. The silica and calcium hydroxide react with water, forming a hard hydrated calcium silicate phase cement that differs from the tri-/dicalcium silicates.

$$\mathrm{SiO_2}+\mathrm{Ca}\left(\mathrm{OH}\right)_2+\mathrm{mH_2O}\rightarrow\left(\mathrm{CaO}\right)_x\,\mathrm{SiO_2}.\mathrm{nH_2O} \quad (11.8)$$

[silica + calcium hydroxide + water → hydrated calcium silicate].

For construction, calcium silicate cement (Portland cement) supplanted pozzolanic cement in the 1800s, because Roman cement doesn't have the strength of the calcium silicate cements. Two dental products have been advertised as "fast-setting, mineral trioxide aggregate–derived pozzolan cements," but the components are not known; they may include fine, amorphous silica and calcium hydroxide. The pozzolanic hydration reaction may cause shrinkage [42], an undesirable effect for dental cements. No clinical or physical benefits have been published for the pozzolanic dental cements [43].

The calcium aluminate, calcium silicate, and pozzolanic cements react with water by surface hydration of the powder particles, which release calcium and hydroxide ions into the tissue fluids. These ions enable the formation of HA on the cement surface in vivo, which is herein denoted as bioactivity.

11.6 Pediatric Bioactive Ceramic Dental Cements

Many bioactive cement products are available for pediatric use, and some are listed in Table 11.1. Various salient properties should be considered for choosing a bioactive cement product including the ones discussed below: indications, composition, format, packaging, and product characteristics.

Table 11.1 Bioactive ceramic cement dental products

Product name (alphabetical order)	Manufacturer or distributor	Format	Unit/ multi-dose?	Radiopaque component	% Cement in powder	$CaSO_4$, $Ca(OH)_2$, or $CaCO_3$	SiO_2	Other
Original MTA	Courtesy of Dr. M. Torabinejad	Powder/water	Multi	Bi_2O_3	70	3.7	1.7	2.2
BC Root Repair Putty	Innovative Bioceramix, distributed by Brasseler, FKG Dentaire, and EdgeEndo	Single paste	Multi	ZrO_2, Ta_2O_5	63	3.2		
BC Fast-Set Putty		Single paste	Multi	ZrO_2, Ta_2O_5	55	7.7		
BC Root Repair-jar		Single paste	Multi	ZrO_2, Ta_2O_5	59	8.0		
BioAggregate	Innovative Bioceramix	Powder/water	Unit	Ta_2O_5	88	5.4		
Biodentine	Septodont	Powder/liquid	Unit	ZrO_2	83	13.7		
Bio-C Repair	Angelus	Single paste	Multi	ZrO_2	37			
BIOfactor MTA	Imicryl	Powder/liquid	Multi	Yb_2O_3	Unknown			
BioMTA	Diadent	Powder/liquid	Unit	ZrO_2, Yb_2O_3, $CaTiO_3$	40	9.1		
BIO MTA+	Cerkamed	Powder/liquid	Multi	ZrO_2	Unknown			
CEM	Bionique	Powder/water	Multi	$BaSO_4$, ZrO_2, ZnO	83	4.3		
Channels MTA	Angelus/Schein	Powder/liquid	Multi	Bi_2O_3	Unknown			
CPM Endo	Egeo	Powder/liquid	Multi	Bi_2O_3, $BaSO_4$	78	14.8		
e-MTA	Kids-e-dental	Powder/water and gel	Multi	Undisclosed	Unknown			
EndoBinder	Binderware	Powder/liquid	Multi	$CaZrO_3$, ZrO_2	80			
EndoCem MTA	Maruchi	Powder	Unit	Bi_2O_3	36	42.0		
EndoCem Zr	Maruchi	Powder/water	Unit	ZrO_2	36	45.4	2	1.1

(continued)

Table 11.1 (continued)

Product name (alphabetical order)	Manufacturer or distributor	Format	Unit/ multi-dose?	Radiopaque component	% Cement in powder	$CaSO_4$, $Ca(OH)_2$, or $CaCO_3$	SiO_2	Other
Endo-PASS	DEI Italia	Powder/water	Unit	$BaSO_4$	73			
Harvard MTA	Harvard	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Master-Dent MTA	Dentonics	Powder/gel	Multi	Bi_2O_3	77	1.8		
Medcem	Medcem	Powder	Unit	None, or ZrO_2	70	6.7		
MM-MTA	MicroMega	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
MTA Caps	Acteon	Dual-compartment capsules	Unit	$CaWO_4$	48	18.3	0.4	
MTAFlow	Ultradent	Powder/gel	Multi	Bi_2O_3	73	2.0		
MTAFlow (White)	Ultradent	Powder/gel	Multi	Ta_2O_5	72	2.2		
MTA gray or white	Angelus	Powder/liquid	Multi	Bi_2O_3 or $CaWO_4$	83	5.6		6.7
MTA HP	Angelus	Powder/liquid	Unit	$CaWO_4$	81			
MTA Plus	Prevest Denpro	Powder/gel	Multi	Bi_2O_3	77	1.8		1.7
MTA+	Cerkamed	Powder/water	Multi	Bi_2O_3, ZrO2	67	2.0	14	
MTA White	Angelus	Powder/water	Multi	$CaWO_4$	92			
NeoLINER LC[a]	NuSmile	Single-paste resin	Multi	Undisclosed	Unknown			
NeoMTA 2	NuSmile, Avalon Biomed	Powder/gel	Multi	Ta_2O_5	63	0.6	1.2	
NeoMTA Plus	NuSmile	Powder/gel	Multi	Ta_2O_5	72	1.3	1.6	
NeoPUTTY	NuSmile, Avalon Biomed	Single paste	Multi	Ta_2O_5	47	1.0		

OliMTA	Olident	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Orbis MTA	Orbis	Dual-compartment capsules	Unit	Bi_2O_3	Unknown			
Ortho MTA	bioMTA	Powder/water	Unit	Bi_2O_3	Unknown			
PD MTA	Produit Dentaire	Powder/water	Unit	Bi_2O_3, $BaSO_4$	50	36.4		4.7
Oxford MTA	Oxford scientific	Powder/liquid or dual-compartment capsules	Multi or unit	Undisclosed	Unknown			
ProRoot MTA (gray)	Dentsply Sirona	Powder/water	Unit	Bi_2O_3	76	3.6		
ProRoot MTA (white)	Dentsply Sirona	Powder/water	Unit	Bi_2O_3	80			
ReMTA	Dental Solutions Israel	Powder/water; single paste, and dual paste	Unit and multi-dose	Bi_2O_3	Unknown			
RetroMTA	bioMTA	Powder/water	Unit	ZrO_2, $CaZrO_3$	66			
Smart MTA	Sprig	Powder/water	Unit	ZrO_2	73			
TheraCal LC[a]	Bisco	Single-paste resin	Multi	$BaZrO_3$	78	5.5		
TheraCal PT[a]	Bisco	Dual-paste resin	Multi	$BaZrO_3$, YbF_3	20	33.8		
Trioxident	Vladmiva	Powder/water	Unit	ZrO_2	79			
Vivid Root MTA	Pearson dental	Dual-compartment capsules	Unit	Undisclosed	Unknown			
Well-Root PT	Vericom	Single paste	Multi	ZrO_2	57	1.9		

[a]Resin-based
Blanks indicate the compound is not present

11.6.1 Indications

All the products in Table 11.1 are suitable for pulpotomies and other vital pulp procedures except the resin-containing cements: TheraCal® LC is only indicated for pulp capping, NeoLINER™ LC is indicated for lining a cavity preparation (not pulp capping), and TheraCal PT is limited to pulpotomies. EndoCem Zr is not indicated for use as a base. Biodentine is the only material that is used as a temporary restorative for up to 6 months. No product is specifically indicated for revascularization.

The resin-based materials contain monomers with dispersed bioactive cement powders; however, they have not been as clinically successful as bioactive cements without resin [44, 45], although they are reasonably priced. Resin-containing products are more suitable for indirect pulp capping [46]. TheraCal PT may be more biocompatible than TheraCal LC, but not as biocompatible as MTA Angelus [47], a non-resin containing bioactive cement. The clinical performance of TheraCal PT in clinical tests of pulpotomies has not been tested, although a trial is underway (NCT04167943).

No clinical superiority has been established for any other of the bioactive ceramic cement products. The amounts of the cement vary in the products, as discussed below, but a lower limit for cement content has not been established. Nor has an "optimum cement composition" been determined, based on the individual cement phases discussed above. In fact, commercial, construction-grade, Portland cement has been considered as clinically effective as the dental bioactive bioceramic, despite the construction-grade cement being coarse radiolucent, tending to wash out and setting slower. However, using non-dental cement is ill-advised at best. Other than bismuth oxide (discussed below), no superiority has been established for any radiopaque additive, nor for any minor additive.

11.6.2 Composition

The composition of the bioactive ceramic products has been confusing for dentists because of the various advertising claims and non-sensical, non-chemical product names that are used, as mentioned previously. Furthermore, the cement compounds were misidentified in the first publication of MTA's [37] composition. Clinicians can identify some components of the bioactive ceramic products by examining the Safety Data Sheets (SDS) for a product, and reading the dental literature. The SDSs should reveal any hazardous components but are often non-specific and incomplete as to the composition.

Dental publications about the composition of these bioactive ceramic cement products have often been based on scanning electron microscopy (SEM), including atomic analysis using energy-dispersive spectroscopy (EDS), a.k.a. energy-dispersive X-ray spectroscopy (EDX or XEDS) [48]. The SEM/EDS technique can image the product, before or after setting, and can identify the major atoms present. For instance, calcium and silicon can be identified by SEM/EDS, but whether the phases were dicalcium silicate or tricalcium silicate must be inferred because SEM/

EDS equipment cannot identify the ceramic phases (compounds). Another problem with the EDS technique is that the spectra represent a sample deeper and wider than the electron beam, which makes EDX quantitative analysis imprecise, particularly if a material is being examined inside a tooth. Porosity also interferes with EDS spectra; therefore, the spectra may not represent the composition where the electron beam is "pinpointed." Energy dispersive spectra is a "rougher" material science tool for chemical analysis compared to other methods, such as wavelength dispersive X-ray spectroscopy (WDS), performed with an electron microprobe, but less commonly used by researchers. X-ray fluorescence (XRF) is also used to analyze the elements present in materials and can measure trace elements present in parts per million, a much more precise elemental analysis than EDS. XRF atomic results are converted to oxides using software, but XRF requires the destructive analysis of a larger, non-microscopic sample and does not reveal the compounds present. X-ray diffraction is used by materials scientists to determine the crystalline phases (compounds), such as the cement phases discussed before. X-ray diffraction may be performed with powders or pastes, but does not identify trace metals, organic compounds, amorphous materials, or crystalline phases present at less than about 1%. No one analysis technique is a comprehensive tool, but a combination of analyses is useful for understanding materials and their behavior for its presentation in the dental literature.

X-ray diffraction was used by this author to compare the bioactive bioceramics powder, paste, and resin products suitable for pediatric dentistry. The results in Table 11.1 also include some data from the dental literature, the gray literature, and the companies' safety data sheet (SDS) for products that were not available for analysis. The total amount of the cement phases varied from 36 to 92% by weight, and the cement phases were mostly tricalcium silicate and dicalcium silicate. Most products contained more tri- than dicalcium silicate; however, EndoCem MTA and EndoCem Zr contained only dicalcium silicate. Aluminate cement phases were identified in Angelus MTA HP, CPM Endo, EndoBinder, BioMTA, MTA +, MTA Caps, NeoPUTTY, PD MTA, ProRoot MTA, Sprig SmartMTA, RetroMTA, TheraCal PT, and Trioxident. Two products contained the calcium aluminate cement phases ($CaO.Al_2O_3$ or $CaO.2Al_2O_3$): NeoPUTTY and EndoBinder.

Some products contained significant amounts of calcium oxide, hydroxide, or calcium carbonate. The calcium compounds are not cement phases and do not add radiopacity. Calcium sulfate was present in some products, perhaps for setting control or calcium release. Other minor components were identified by XRD: magnesia, silica, calcium hypophosphite, and calcium chloride. Amorphous or low-crystallinity components may be present in the powders or pastes including fumed silica, chitosan, cellulose, and various clays; these compounds cannot be discerned by X-ray diffraction, as they would only appear as broad humps, not sharp peaks in the X-ray diffraction spectra. However, these additives have been mentioned in patents for such materials, used to thicken and stabilize pastes for better handling. These non-cement components may be included to augment calcium ion release, speed up setting, increase strength, or reduce the firing temperature required for manufacturing the cement (e.g., MgO).

11.6.3 Radiopacity

Diverse ceramic powders have been blended into the bioactive ceramic cements for radiopacity (Table 11.1), which are, in order of increasing molecular weight, zinc oxide (81 g/mol), zirconia (123 g/mol), calcium zirconate (179 g/mol), ytterbium fluoride (230 g/mol), barium sulfate (233 g/mol), barium zirconate (277 g/mol), calcium tungstate (288 g/mol), ytterbium oxide (394 g/mol), tantalum oxide (442 g/mol), and bismuth oxide (465 g/mol). Newer bioactive cement tend to contain more radiopaque powder than the 20 weight percent bismuth oxide in the ProRoot MTA patent. The radiopacities of the bioactive ceramic cements vary from about 1 to 8 mm of equivalent aluminum for pediatric bioactive cements, when tested per the standard method of ISO 13116. For reference, dentin has a radiopacity equivalent to about 1 mm of aluminum. Resin-containing products, such as TheraCal LC and PT, have the lowest radiopacity (~1 mm equivalent Al) [49].

Antibiotics or injury may discolor teeth, but the gray and white ProRoot MTA products also discolored teeth. Discoloration can be immediate from using a gray-colored powder such as the original, dark gray, ProRoot MTA, containing the ferrite cement phase. Surprisingly, the white ProRoot MTA also caused gradual, delayed discoloration, especially in the thinner, primary teeth [50]. The primary cause of discoloration has been traced to the inclusion of the bismuth oxide powder used for radiopacity. When exposed to light and certain chemicals, Bismuth oxide forms darker-colored bismuth compounds, such as bismuth subcarbonate, $Bi_2O_2(CO_3)$, sodium bismuthate, or reddish Bi_2O_{4-x} [51], when exposed to light and certain chemicals. The color change is caused by bismuth ions that transform under oxidation or exposure to light from trivalent (Bi^{+3}) to pentavalent (Bi^{+5}). The darkening of the bismuth oxide in the bioactive cements was not esthetic, but does not compromise the dental cements' safety or efficacy [50]. Although the original ProRoot MTA products continue to contain bismuth oxide, most newer products do not contain this radiopaque component. Notably, many products in Table 11.1 have "MTA" in their trade name, but do *not* contain bismuth oxide. Therefore, not all "MTA" products discolor, despite some generalizations made in the literature. The only common characteristic of the so-called MTA products is the presence of calcium silicate cement.

11.6.4 Pastes and Resins

Another tool of materials scientists is thermogravimetric analysis (TGA). Using this technique, a small sample is gradually heated to about 1000 °C, while its weight change is monitored. TGA was used to measure the amount of organic liquid or resin present in some of the single- and dual-paste products (Table 11.2). About 15 to 30% organic liquid, such as glycols of various molecular weights, are used in some cement pastes that set in vivo. The EndoCem paste is known to contain another liquid, dimethyl sulfoxide (DMSO). For all these paste products, the organic liquid diffuses from the cement paste *in vivo*, while water from tissue fluids migrates into the cement pastes to cause setting. Resin-containing pastes are different because

Table 11.2 Bioactive ceramic cement dental paste products for pediatric dentistry

Product name (alphabetical order)	Manufacturer or distributor	Format	% Organic liquid	% Resin
BC Root Repair Putty	Innovative Bioceramix, distributed by Brasseler, FKG Dentaire, and EdgeEndo	Single paste	16	
BC Fast-Set Putty		Single paste	15	
BC Root Repair-jar		Single paste	19	
Bio-C Repair	Angelus	Single paste		
NeoLINER LC[a]	NuSmile	Resin		Unknown
NeoPUTTY	NuSmile, Avalon Biomed	Single paste	20	
TheraCal LC[a]	Bisco	Resin		33
TheraCal PT[a]	Bisco	Dual-paste resin		37
Well-Root PT	Vericom	Single paste	21	

[a]Resin-based

resins remain in place after setting. Polymerized resins control the release of the cement ions that are embedded in the resins. As a result, bioactivity (ion release) is lower in these resin products. Resin products contain about 35% monomer.

11.6.5 Format

The formats of the bioactive ceramic cement products vary widely, with some more convenient and others more affordable [27]. The products contain bioactive cement powder formatted as (1) powder and liquid that the clinician mixes into a viscous paste, (2) single pastes, or (3) resin-based materials (that contain some bioactive cement particles). Powder/liquids products set because the water in the liquid starts the setting; these products may be single or multi-dose in format. Pastes set because tissue fluids provide water for setting. Well-Root PT is a single-dose, single paste in a compule-type dispenser, but usually pastes are sold in multi-dose syringes. Resin materials set because the matrix is cured, but the cement is not set except on the surface where it is exposed to tissue fluids. The formats of these bioactive ceramic cement products are important to clinicians for convenience, speed of treatment, and cost. Table 11.1 lists many bioactive ceramic cement products for pediatric dentistry, designating the format as single or multi-dose.

The first bioactive bioceramic cement kit, ProRoot MTA, contained foil sachets of powder and ampoules of water for clinicians to mix as individual doses. The sachets contain 0.5 g, much more than needed for a pediatric dose (<0.1 g), and resealing the sachets is not possible. This foil sachet format has been copied for products such as RetroMTA, PD MTA, Trioxident, and reMTA (Fig. 11.6a) and the original BioAggregate product.

Unique capsules of powder have been offered as unit doses by Septodont, Medcem, and Angelus, companies containing 0.7, 0.35, and 0.19 g (Fig. 11.6b). Biodentine (Septodont) and Angelus capsules are plastic, whereas Medcem MTA and Endo-PASS MTA are sold in gelatin capsules. Septodont Biodentine® and Angelus MTA HP kits include ampoules of water-based liquid containing a salt and polymer (calcium chloride and an unidentified carboxylate polymer) to impart faster setting and higher strength [52]. The dentist adds the Biodentine liquid dropwise to the powder in the capsule; then the capsule must be triturated to mix. 0.7 g of powder per capsule of Biodentine is large for one tooth but useful when many

Fig. 11.6 (**a**) Unit-dose packaging of bioactive ceramic cement powders in foil sachets. (**b**) Unit-dose packaging of bioactive ceramic cements in capsule or vials, used for powder or liquid or both. Some products include foil pouches; others use plastic packages. The centrifuge for mixing OrthoMTA is shown in the lower right-hand corner. (**c**) Dual-compartment capsule products for powder and liquid. (**d**) Multi-dose kits of bioactive ceramic powder and liquid. (**e**) Paste forms of bioactive cements that self-set. (**f**) Resin-based materials that set by light curing or dual curing

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

Fig. 11.6 (continued)

teeth need treatment, such as pediatric pulpotomies [27], or as a temporary restorative. MTA HP powder and liquid are hand-mixed on a glass or impermeable pad. The Medcem MTA and Endo-PASS MTA gelatin capsules tend to be brittle and messy when opened; they must be mixed with a clinician-supplied liquid. Other unit-dose packaging options for the bioactive cement powders have included plastic "centrifuge" vials, often with a 0.3 g dose as shown in Fig. 11.6b. For the OrthoMTA product, the dentist mixes with water in the vial and then uses a battery-operated centrifuge for mixing. These unit-dose powder and liquid capsules and vials are often, but not exclusively, sold in protective foil pouches to prevent the ingress of water. Some of the vials of water-based liquid are also packaged in foil pouches, some resealable, others not.

Dual-compartment capsules for trituration of a unit-dose are shown in Fig. 11.6c. These capsules are similar to amalgam or glass-ionomer unit-dose capsules and usually provided in foil pouches. The capsules have two compartments: one for the cement powder and one for water or a water-based liquid separated by a membrane of foil. The capsules are "activated" by the dentists compressing a plunger and then triturating the capsule. The wet cement mixture is dispensed by opening the capsule or using a capsule product that has a dispensing tip. Dual-compartment capsules for trituration usually contain 0.3 g of powder and water and have been sold by Acteon, Harvard, Micro-Mega, Orbis, Oxford, and Pearson. Usually, two capsules are packaged in a foil pouch. From the similarity of the capsule products, one may surmise that some are private labeled. In 2022, Biodentine introduced their unique design of a single-dose, dual-compartment capsule and a special mixer. The cost of dual-compartment capsules is higher per dose or per gram, compared to hand-mixed and multi-dose products.

Multi-dose powder/liquid kits of bioactive cements (Fig. 11.6d) began with the first Angelus MTA products, gray and white, which included a bottle of cement and a dropper bottle of water. The advantage of multi-dose bottles is the clinical control, i.e., one has to dispense only what is needed. Mixing a powder and liquid requires a bit of skill and familiarity but allows a clinician to customize the viscosity and handling. Variations in the powder-to-liquid ratio have been explored; a weight ratio of 3 to 1 is most common and often used in research tests, but ratios have been evaluated from 2:1 to 4:1 [53]. Higher powder-to-liquid ratios increase the viscosity of the mixed cement, shorten the setting time, and lead to a higher strength cement. Hand, ultrasonic, and trituration mixing have been evaluated for their effects on mixed MTA Angelus, but only small differences were observed. The relatively high cost of the calcium silicate cement products has made mixing an issue, because of the potential for waste of mixed, unused cement paste, but savvy assistants can avoid waste with a little practice. Water-based gel is included in some of the multi-dose kits shown in Fig. 11.6d for products including MTA Plus®, NeoMTA Plus®, NeoMTA®2, Masterdent® MTA, MTAFlow® (white and gray), and e-MTA products. Water-based gels are higher in viscosity (thicker) than water, from which one surmises the gels contain water-soluble polymers or organic liquids. The gels improve the handling, ease of placement, and washout resistance of the mixed cements [54]. Some multi-dose products include water (CEM) or a salt solution (BioMTA +).

Paste products (Fig. 11.6e) that set in vivo are the latest format of the bioactive ceramic cements. Such single-paste products may be denoted as premixed pastes or putty and have a high viscosity that is a thick, putty-like, consistency similar to IRM® and quite suitable for pediatric dental procedures. These pastes are available either in syringes or a small "pot." The syringes have had superior shelf life compared to one, expensive brand sold in a small jar [55]. Only Well-Root PT paste is sold in compules for individual doses. For these pastes, the cement powder has been blended into a water-free, organic liquid. Being water-free, the cement doesn't set in the syringe or compule. However, when the paste is placed in vivo, water from the body tissues diffuses into the paste and causes setting of the cement, while the organic liquid diffuses into the body tissues; no light activation and no catalyst are needed. These pastes are very washout resistant and provide a very fast convenient dispensing option. These putty-like pastes set over a few hours because the body has to supply the water for setting. These paste products of bioactive cements are convenient and economical for dispensing, with little waste; however, the pastes cost more per gram than the powder-liquid systems.

11.6.6 Packaging Materials

Clinicians should be aware that all packaging materials are imperfect barriers and usually control the shelf life of products. Water can permeate all barriers to powder packaging, including foil and plastics, although multi-layered foil/polymer resealable pouches are superior. Even glass bottles may allow water to enter through the plastic cap and its seal. Some of these bioactive cement powders are packaged in foil sachets (small pouches) for powder; other products package the cement powder in glass or plastic bottles, capsules, or vials as noted before. Desiccants in the bottles of powder are used for NeoMTA2 powder, MTAFlow, and the MasterDent products to prolong the powders' shelf life. When water permeates the bioactive ceramic cement powder packaging, the setting time is lengthened; handling is degraded by partial hydration, making it granular (crumbly); and the set cement is weaker. This problem is worse for the foil sachets which cannot be resealed, such as the one used for ProRoot MTA.

Evaporation from the unit-dose containers of water-based liquid is also important. Over the shelf life of the product, usually 2 to 3 years, evaporation of water will occur from the unit-dose liquid containers, which increases the powder-to-liquid ratio of unit-dose products. Also, it is difficult to precisely package weights of powder in vials, ampoules, or pouches. Liquid dose packaging can be more accurate than powders, but the evaporation through the packaging can reduce the amount of liquid over time. These minor variations can be detectable to clinicians. Slightly thicker mixtures may be detected when mixing unit-doses of powder and liquid that are nearing their expiration date. Also, select dental materials are sold as sterile, which must be marked as sterile. Most dental restoratives or cements are not sterile. Some authors have believed that the bioactive cement products are sterile or have sterile liquid components; however, sterile products are always marked as sterile.

Combining all these factors, these bioactive ceramic cement products have a shelf life of 2–3 years, as do most dental products.

11.7 Cement Product Characteristics

The first calcium silicate cement products (ProRoot MTA and MTA Angelus) were clinically effective, but tended to wash out, had a long setting time (>2 h), caused tooth darkening, and had high cost (~$50/g). The products were maligned as "just expensive Portland cement." Newer and modified products have moderated these issues. The current hydraulic, bioactive ceramic cements have easier handling and faster setting time, do not darken teeth, and have lower cost while maintaining excellent clinical performance. These product improvements have been made possible by manufacturers making finer particles sizes of powders, modifying the liquids for mixing, adding some other ceramic powders, inventing paste forms, and incorporation of non-bismuth oxide radiopaque ceramic powders, all amid international competition. The current properties of various bioactive cements for pediatric dentistry are discussed below.

11.7.1 Handling

The original MTA prototype and ProRoot MTA was considered "sandy" in consistency, that is, the powder was coarser than powder products to which dentists are accustomed. Manufacturers have improved the powders, making them very fine, eliminating the coarse powders. Newer, more radiopaque powders are also very fine, with some powder particles in the nanoparticle range (<0.1 μm, <100 nm). Finer particles contribute to easier handling, better cohesion when mixed with liquids, and faster setting/hydration. The newer, water-based solutions and water-based gels create benefits of washout resistance, easy handling and placement, a more desirable "plastic" consistency, and faster setting of the bioactive cements. Many of the bioactive bioceramic cements can be mixed to a dough-like consistency that can be picked up with a small instrument like amalgam carriers, or the small "MTA" carriers. (See Fig. 11.7.) These improvements eliminate the need for special "MTA" instruments for clinical placement. The paste products streamline the application with no need for mixing; however, the viscosity is not usually adjustable, unless extra liquid or powder is supplied.

Practice is often needed to economically mix the bioactive, powder-liquid, multidose, cement products. Impermeable pads are a necessity; otherwise, the pad absorbs the liquid and creates problems; glass palettes are especially suitable. A medium-stiffness metal spatula is best to ensure the powder and liquid are well mixed; plastic spatulas are not well designed for mixing these very fine powders. Problems with mixing proportions can arise because scoops and drops vary among users. When too much powder is added to the liquid, the mixture is dry and crumbly; however, more liquid should be added in small increments, usually less than a

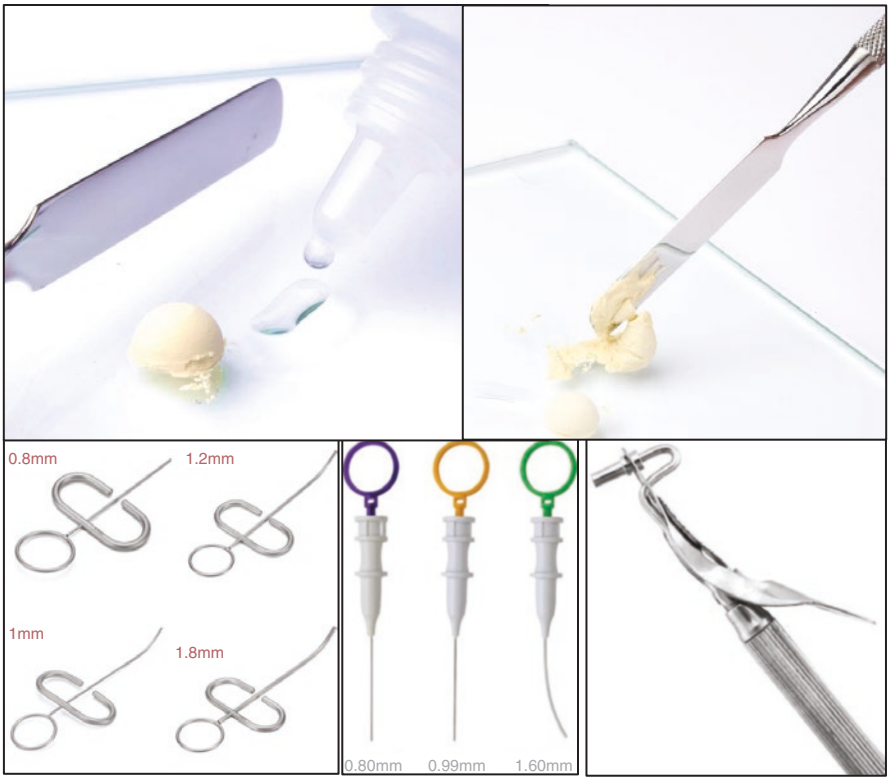

Fig. 11.7 Instruments for mixing and placing bioactive bioceramics having a putty-like consistency

drop. When too much liquid is added to the powder, the mixture is unmanageable, thin, and slow to set. When the mixture is thin, the tendency is to add more powder. If time permits, the thin mixtures can be spread out to allow the water-based liquid to evaporate and thicken the cement. Very little bioactive cement is needed clinically, so any increment of powder added to a thin paste should be very small, less than the scoop provided by a manufacturer. Adding powder can create a lump of cement that is much more than needed – a costly mistake!

11.7.2 Setting Time

Dentists thrive on fast-setting products, but the original ProRoot MTA powders mixed with water required more than 2 h to set [37]. Newer bioactive ceramic cement products have shorter initial setting times, often about 15 min [56]. The final (effective) setting time for the non-resin products is longer, usually several hours. Various means have been used to reduce the setting time, including the use of finer particles and the inclusion of calcium chloride, reduced calcium sulfate content, and

water-soluble polymers in water-based solutions for mixing with powders. Higher temperature and humidity and smaller and thinner samples speed the setting of the bioactive ceramic cements.

Setting time for these cements has been measured with the Gilmore indentation apparatus. The Gilmore apparatus has two indenters: one indenter has a larger diameter and a lighter weight to judge the initial set time, and the other indenter is heavier, which has a smaller diameter indenter for the "effective" (final) set. Unset materials allow an indentation on the sample surface. Notably, the current initial and effective (final) setting times for the bioactive ceramic cements are longer than required for base or liner materials (less than 10 min) in ISO 9917-1 or ISO 3107 standards for water-setting cements and zinc-oxide eugenol materials.

A few bioactive ceramic cement products have compensated for longer setting times than "conventional" dental materials by being washout resistant. Completion of setting of the bioactive cement is not required for many indications, such as pulpotomies and crown placement. Some bioactive cement products easily remain within the pulp chamber; while a crown is seated, setting is completed after the procedure. Products with gels for mixing with the powder and the single cement pastes create excellent washout resistance. Bioactive cement powders that are mixed with plain water or anesthetic solution are not washout resistant. When a crown preparation is required after the pulpotomy, a thin layer of glass ionomer cement, compomer, resin-modified glass ionomer, or flowable composite can be used to stabilize the bioactive ceramics in the pulp chamber; these restorative materials enable easier rinsing after crown preparation is complete and stabilize the bioactive cement. Despite the perceived goal for fast-curing, the newer, washout-resistant products, including the slower-setting single pastes, are popular and convenient.

The products discussed above all rely on the hydration of the cement to set. Dentists are very familiar with fast-setting, light-curing, single-paste composites for restoratives, which start to set when exposed to blue light. Dual-paste products are also common in dentistry, where the components are mixed to start the setting reaction. Some two-component, resin-based materials are dual-cured, that is, light and chemical curing occurs. Resin-based products containing bioactive cements available from BISCO or NuSmile contain the calcium silicate cements but rely on the setting of their polymer (resin) matrix (Fig. 11.6e). TheraCal LC paste contains a light-curable resin as does NeoLiner LC. TheraCal PT is a two-paste, dual-cured, resin product for pulpotomies. Resin-based materials are also washout resistant, but not as clinically effective as non-resin-based cements because the resin matrix controls the release of ions from the bioactive powder.

11.7.3 Solubility

Bioactive calcium silicate/aluminate cements are classified as a permanently implanted material according to ISO 7405, a standard for biocompatibility of dental materials this is an indication where the material should be insoluble and, usually, non-porous. Researchers have reported some cement products have less than 10%

porosity, with one-half being closed pores, and solubility less than 3% after 72 h [57]. Others have reported high solubility (~20%), water sorption (~12%), and porosity (40%) for other products [58]. These solubility measurements are a point of confusion because high porosity or solubility would allow bacterial migration and dissolution, which is contrary to the excellent clinical performance of bioactive ceramic cement materials.

Calcium silicate and calcium aluminate bioactive cements inherently release calcium and hydroxide ions into the tissue and create a high pH (>10) environment, which continue to be released over 4 weeks in diminishing amounts. The chief benefit of the persistent alkalinity has been the formation of the biomineralization layer on the surface, but it also contributes to local antibacterial [59] and antifungal effects [60]. The solubility test method of the ISO 6876 standard tests requires that samples with a high surface-to-volume ratio be soaked in water then the material eluted into the solution is measured. This method emphasizes the weight loss from the dissolution of calcium hydroxide from the surface, but calcium hydroxide is essential for bioactive bioceramics. The test method currently does not measure the insolubility of the cement matrix. The test method is inappropriate for these cement materials and doesn't illustrate the stability of the calcium silicate and calcium aluminate cements. As a practical point, if calcium silicate cements were soluble, concrete structures would dissolve and collapse!

11.7.4 Dimensional Stability

Dental materials may shrink or expand during setting. Shrinkage can allow bacterial infiltration (microleakage), and expansion can cause tooth fracture. Microleakage avoidance is important in preventing bacteria in the oral cavity from migrating into the tooth or reaching the alveolar bone. Many test techniques have been used to assess leakage: dye penetration, dye sorption, bacterial or endotoxin infiltration, and fluid filtration. The lower microleakage of the bioactive ceramic cement products is well established, particularly compared to amalgam or zinc oxide-eugenol cement. Lower microleakage may be attributed to the dimensional stability [61, 62] of the bioactive ceramic cements. Linear changes as small as 0.5 to 1.0% [61] after 30 days have been measured, with some dependence on the powder-to-water ratio used for mixing. Volumetric changes have also been reported from computerized microtomography (μCT) tests; however, the results are less than ±1% [63]. This dimensional stability is another advantage of using these calcium cements.

11.7.5 Bonding

Bonding is essential for restorative materials, and shear bond strengths to tooth structure are expected to be high. The bioactive ceramic cements are placed under restorative materials, and they function to stop bacterial migration and induce pulpal or periapical tissue healing; they are not used for their adhesive qualities. Pushout

strength tests have been used to test calcium silicate materials' bonding to teeth. Such tests have also served as a surrogate for assessing microleakage, shear bond strength, and dentinal tubule penetration. The pushout bond-strength values vary widely, and the techniques have been criticized [64] for the experimental designs. Generally, any bonding values have been low compared to restorative materials.

Etching is a common procedural step for bonding in dentistry, but etching is of no benefit in placing restoratives over bioactive cements. Acids will soften, not roughen, the hydrated matrix of the calcium cements; neither chemical nor mechanical adhesion occurs via etching the bioactive ceramic cements. Nor have polymer adhesives over the calcium silicate/aluminate cements have improved bonding [65]. A high bond strength of these materials to restoratives or teeth is not essential, and high bond strengths have not been measured. The likelihood of displacement or "debonding" of the bioactive cements is very low because they are used intracoronally. No case reports of dislodgement of the calcium silicate cements have been published. Bonding restorative materials over the bioactive ceramic cement should focus on bonding the restorative to the surrounding tooth structure, without expecting any added benefit of bonding to the underlying bioactive cement.

11.7.6 Strength

Ceramic materials perform best in compression and are weak in tension. Luckily, for pediatric dental indications, the bioactive cements undergo compressive forces under a restorative material. Compressive strengths have varied widely for bioactive cements. Some materials meet the ISO 9917-1 standard's requirement (>50 MPa), with the caveat of testing after a few days of setting, not after the 24-h time period given in the test method [37]. However, in the ISO 3107 standard for zinc oxide eugenol used as a base, the requirement is only 5 MPa; therefore, bioactive ceramic cements can be used as a base, e.g., indirect pulp capping. An interesting aspect of the calcium silicate cements is that strengthening (hydration) continues after setting, for about 4 weeks [66], unlike other dental materials.

11.7.7 Costs

The cost of the original MTA products has been a sore point between manufacturers and dentists [16]. Costs are now lower than the original materials [27], although still significant on a per dose basis, compared to other dental materials. Competition among manufacturers is expected (hopefully!) to continue to lower the price per dose to levels competitive with other dental products. Today, multi-dose, powder-liquid systems are very economical per dose. The single-paste materials have minimal waste and may be affordable if judiciously dispensed.

11.7.8 Other "Bioactive" Materials

The bioactive ceramic cements have prompted a trend in dentistry for companies to advertise materials as "bioactive." Some nominally "bioactive" materials release ions, but do not create the surficial hydroxyapatite layer created by the calcium silicate and calcium aluminate cements. Clinical benefits of bioactivity may be absent or erroneously advertised in materials such as resin-modified glass ionomers that release ions; sometimes, the SEM/EDS spectra in teeth have been misinterpreted. Glass-ionomer cements are well known in dentistry for their fluoride ion release, which does exchange at body temperature into the apatite of enamel or dentin, to harden (remineralize) the tissue. However, fluoride ion release alone does not create biomineralization/bioactivity, that is, formation of HA. "Giomer" glass releases six ions that may be beneficial, but not form a HA layer: fluoride, sodium, strontium, aluminum, silicate, and borate. The pH created by glass ionomer cements is less than 7, which is unable to cause the biomineralization reaction of Eq. 11.1. The term "biointeractive" is more appropriate for such products, rather than bioactive or biomineralizing. No well-documented clinical and histological evidence bioactive ability has been published for biointeractive materials, and some analyses are spurious using SEM/EDS analysis.

11.8 Summary

Bioactive calcium silicate and calcium aluminate ceramic cements are wonderful materials for pediatric dentistry, general dentistry, and endodontics. Contemporary calcium silicate or calcium aluminate cement products are known by many names; chief among them is MTA, which is a trade name that indicates products containing the calcium silicate cement powder. The key to these bioactive calcium cements' performance is the bioactivity/biomineralization that occurs because of their high pH and calcium ion release when the cements react with water. The ion release continues over a few weeks, providing local antimicrobial effects. The products containing the bioactive bioceramic cements form a layer of hydroxyapatite in contact with tissue fluids. This layer assists with healing, unlike alternative treatments such as formocresol or ferric sulfate.

Bioactive bioceramic products have been improved over the past 25 years since their introduction. Newer products have finer powders and convenient liquids or gels that make handling and placement easier with stability when placed (washout resistance). Various additives have reduced the setting times of the powder/liquid products although the cement products set more slowly than composite materials. Powder-liquid products usually set in about 15 min, but do not delay a procedure; completion of setting is not required before a restorative is placed. Novel pastes have made the bioactive cements more convenient for pediatric dentists; they can be the most cost-effective and convenient and set in vivo over a few hours.

Discoloration has been eliminated, even for some products with the trade name "MTA," by choosing products without bismuth oxide. These bioactive cements have only limited ability to bond, but their high dimensional stability and insolubility is suitable for preventing microleakage. Packaging innovations have included unit-dose and multi-dose products, for convenience and economy. Products with resins for light-curing or dual-curing exist, but don't have the same bioactivity or versatility as the powder/liquid or self-setting paste products.

Bioactive cements eliminate the need for formocresol and its potential health risks. Furthermore, bioactive cements do not cause the internal resorption that has characterized ferric sulfate-treated pulpotomies. No significant differences have been confirmed among the non-resin products for histological performance; however, clinicians may choose a product based on convenience or cost. Resin-containing products remain confined to limited indications with fewer benefits than the other products.

With the continuing clinical success of such products, pediatric dentists should embrace these bioactive ceramic cements for their "everyday" dental procedures to offer the highest level of care. Bioactive cement products will continue to evolve for new indications, such as primary tooth pulpectomies, cervical resorption, and socket grafts. When all their physical properties are considered, calcium silicate and calcium aluminate cements are well suited as pediatric dental materials for procedures contacting pulp and periapical tissues. The clinical results, discussed in other chapters, confirm that the bioactive bioceramic cements are the new gold standard for minimally invasive, conservative pediatric dentistry procedures.

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