

Dental Biomaterials: Where Are We and Where Are We Going?

Stephen C. Bayne, M.S., Ph.D., F.A.D.M.

Abstract: This article reviews the current state of the art for restorative biomaterials by examining the roles of 1) truly biological biomaterials, with respect to the “near-future” of five to ten years, 2) traditional synthetic biomaterials, and 3) performance outcomes for biomaterials. Biological biomaterials are discussed in terms of tissue engineering and stem cell research, self-assembling system opportunities, and nanotechniques or technologies. Future developments for major areas of synthetic biomaterials are considered for bonding systems, composites, VLC curing, ceramics, and cements. Performance outcomes are discussed for all biomaterials in terms of safety, efficacy, and longevity of materials.

Dr. Stephen C. Bayne is a Distinguished Professor, Department of Operative Dentistry, University of North Carolina School of Dentistry. Direct correspondence to him at the UNC School of Dentistry, CB#7450, University of North Carolina, Chapel Hill, NC 27599-7450; 919-966-2776 phone; stephen_bayne@dentistry.unc.edu.

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Biomaterials science is in the midst of the largest transition in its history in terms of refocusing and embracing new and exciting technologies. For older academics or clinicians, this change might be viewed as the death of conventional dental materials, but for most others, this is the birth of true biomaterials.

For many years, one of the in-house questions among biomaterials teachers¹ was if or when anyone would move the field of biomaterials from the materials engineering side (materials) more toward the biological engineering side (biology). The earliest dental materials science began in the laboratory of G.V. Black at Northwestern University in 1900 with the first controlled experiments on dental amalgam. The field vaulted forward when the excellent textbooks in the field became available (e.g., EW Skinner, *The Science of Dental Materials*, 1936²). In those earlier times, dental materials were focused exclusively on synthetic restorative dental materials. By the early 1970s, the term “biomaterials” became more prominent with the formation of the Society for Biomaterials, yet even its focus remained primarily on orthopedic applications that utilized existing dental materials for the next thirty years. Despite continual discussions about refocusing the field of biomaterials, the greatest impetus for change did not arrive until the decoding of the human genome at the end of the last century. Suddenly, the real potential for biological engineering of tissues and organ systems was revealed. The question for us today is how to paint the future for biomaterials. Perhaps the correct image is that we are now immersed in a twenty- to twenty-five-year transition of

shifting emphases from traditional synthetic biomaterials toward a time when the routine options involve truly biological materials.

The purpose here is to examine the near-future or the next five-to-ten-year period (see Figure 1 for impacts of this transition). This state-of-the-biomaterials report will be examined in terms of biological materials fabrication (tissue engineering, nanoengineering, self-assembling systems), leading edge synthetic biomaterials utilized in chairside dental applications (bonding, composites, curing, cements, and ceramics), and assessment of the performance outcomes of these strategies (longevity).

It is easy to list the large number of doors now open for biomaterials research, but it is much more complicated to define an accurate timeline for the future. Most of the crucial steps for biological materials success have yet to become well defined. It may be possible now to demonstrate the production of a biologically new tooth using stem cell pathways, but it is very hard to imagine the moment in the future when practical and low-impact methods will exist for placing these entities into full function in patients by general practitioners. In the excitement of the moment, we dream of those possibilities. However, at the moment, a safer guess about translation of biological materials into routine practice is twenty years.

Any impact of truly biological materials depends on a combination of both technology and cost. If replacement teeth were available today from a hypothetical personal tissue bank, would this be a practical option for most restorative circumstances? Would a patient with pit-and-fissure caries be better served with a minimal composite restoration or an

entire tooth replacement? When would one draw the line between discontinuing synthetic biomaterials approaches for restoring teeth and shifting to biological materials approaches? A substantial window remains for developing much better synthetic materials. Most likely there will be a mixture of both strategies in general practice for at least two decades.

New Biomaterials

True biological biomaterials are ones that lead to natural tissue restoration. At the moment, tissue engineering approaches rely on synthetic scaffolds that are generally resorbable as a means of managing tissue development, but that need not always be the case. The paragraphs that follow consider the impacts of tissue-engineered systems seeded with stem cells, biologic and non-biologic self-assembling systems, and nanotechniques and technologies.

Tissue Engineering and Stem Cell Research

An excellent summary of tissue engineering for dentistry and the role of bone morphogenic proteins (BMPs) has been presented by Nakashima and Reddi³ and is summarized in Figure 2. There is significant potential in the orofacial complex for fracture healing, bone augmentation, TMJ cartilage repair or regeneration, pulpal repair, periodontal ligament regeneration,⁴⁻⁵ and osseointegration⁶ for implants.

Regenerative treatments require the three key elements: an extracellular matrix scaffold (which can be synthetic), progenitor/stem cells, and inductive morphogenetic signals. The oral cavity offers special advantages over other parts of the body for tissue engineering because there is ready access and ease of observation. At the present time, the signaling processes that control the development of discrete dental morphologies for incisors, canines, premolars, and molars are not clear. Successful bioengineering of recognizable tooth structures has been reported using cells from dissociated porcine third molar tooth buds seeded on biodegradable polymer scaffolds that were grown in rat hosts for twenty to thirty weeks.⁷ Successful bioengineering has demonstrated that mature tooth structures form single-cell suspensions of four-day postnatal cultured rat tooth bud cells on polylactic acid scaffolds grown as implants in the omenta of adult rat hosts over twelve weeks.⁸ Murine teeth have been produced recently using stem cell-based engineering techniques.⁹

The developmental capacity of embryonic stem cells (ESCs) and the tissue repair potential for adult stem cells (ASCs) make their use truly exciting.¹⁰ At the present time, the politics of collecting ESCs has severely restricted research in this arena.¹¹ However, if ASCs turn out to have potential similar to ESCs, then this political hurdle may be circumvented. For dentistry, the transplantation of dental pulp stem cells may some day be used to repair bone or regenerate teeth. Using a patient's own stem cells avoids issues of histocompatibility. There is strong evidence for

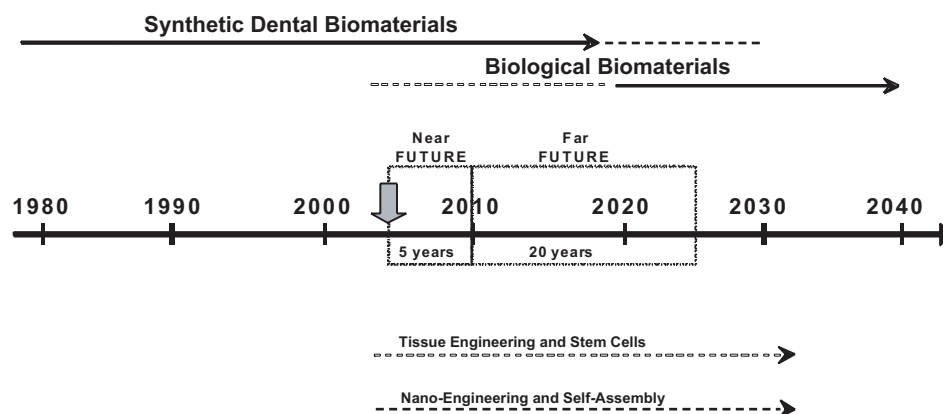


Figure 1. Timeline of the recent past, near future, and far future for the use of synthetic dental biomaterials versus truly biological materials

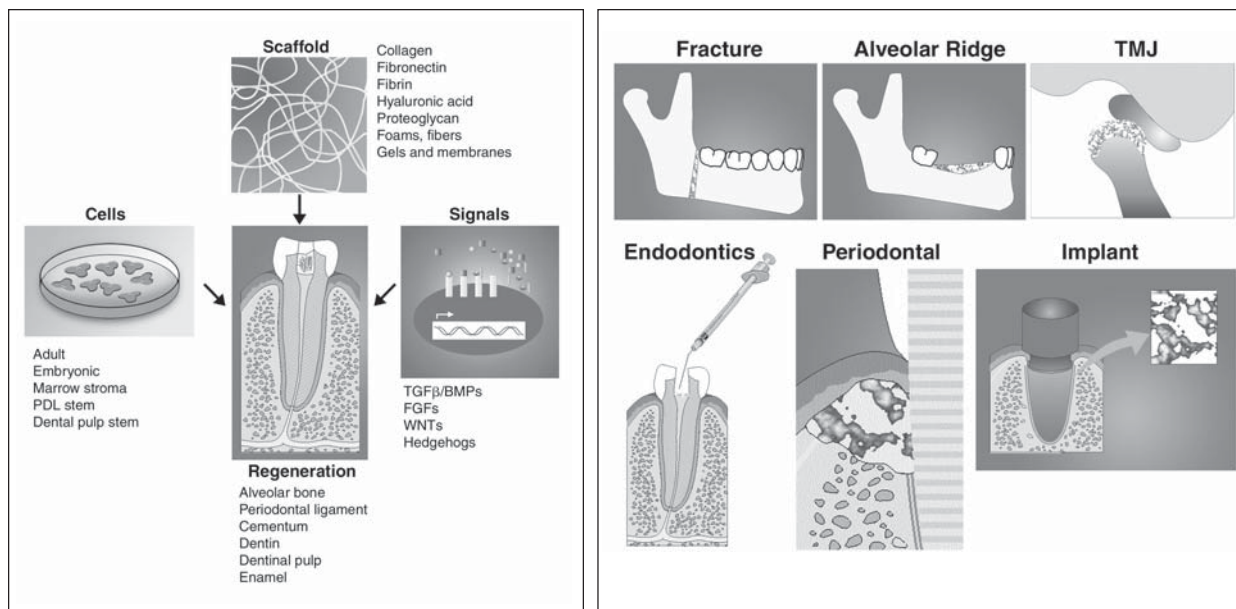


Figure 2. Summary of the opportunities for tissue engineering to develop scaffolds, cells, and signals to create substitute or replacement dental tissues in the future

Potential applications include fracture replacement, alveolar ridge augmentation, TMJ reconstruction, dentin replacement, PDL replacement, and pre-osseointegration of dental implants.

Source: Nakashima M, Reddi H. The application of bone morphogenic proteins to dental tissue engineering. *Nature Biotech* 2003;21:1025-32. Reprinted with permission.

this potential in regeneration experiments conducted in animal models. However, significant technical hurdles still exist.

Scaffolds, cells, and signals have been combined without much elegant control until relatively recently. The same lithography and printing techniques discussed for ceramics are also available to lay down scaffolds, cells, and signals in a well-controlled three-dimensional architecture.¹² Printing is a special tissue engineering tool for the future.

Numerous surfaces of nonbiological materials such as implants could benefit by pre-treatment (pre-integration) with those tissues that would normally result from healing or osseointegration. This has already been evaluated with existing implant systems.⁶ This may make possible a much more biologically and physiologically stable, immediately loaded implant. Eliminating long healing phases is desirable for dental implant acceptance by patients.

Self-Assembling Systems

Self-assembling systems are ones that automatically construct prespecified assemblies. These

can be biological assemblies (e.g., viruses, cells, tissues, organisms) or nonbiological ones (e.g., crystals).¹³ These can produce domains at nano-, micro-, milli-, and macro “scales.” Assemblies can be made from metals, ceramics, polymers, or complex constructions of several materials. However, at the moment, the most intriguing systems are nanoscale objects involving organic or ceramic construction. Production of assemblies occurs in orchestrated stages of initiation, propagation, and termination. Control systems for initiation and/or propagation may be templates (e.g., template polymerization of proteins, patterning for silica templates for electrical circuits), or they might depend simply on natural rules corresponding to energetically favorable physical, chemical, mechanical, and/or biological events (e.g., capillary forces,¹⁴ heterogeneous nucleation of crystallization, surface energy reduction, phase separation, micelle formation, steric probabilities for molecular folding). The intrigue for current engineers is that self-assembling nanoscale objects can become nanoscopic pharmaceuticals, nanosensors, nanodomains, or nanophases with special properties, nanobuilding blocks,¹⁵ nanocontrol systems, nano-

devices,¹⁶ and many other functional entities. The potential is infinite.

At the moment, the challenge is to learn how to take advantage of natural rule systems (e.g., micelle formation, energy minimization, crystallization) and learn to build geometries of interest that will have useful functions. For example, it is possible to construct a nanocage, but not be able to control transport in and out of the cage. It is possible to construct a nanoswitch but have no systems that it can switch on. Perhaps a more sophisticated way of envisioning the potential of self-assembling systems is in terms of multistage constructions with complex functions. One of the great advantages for individuals involved with this emerging field is that the science of biomaterials (or materials) is the same science associated with natural rule systems for self-assembling processes.

Presently, tissue engineering relies heavily on systems outside the body to create scaffolds, provide cells, and create signaling systems. It is certainly

conceivable that the same events could be managed on a nanoscale within the body and with the proper self-assembling nanoscaffolds this process could be highly targeted.

Nanotechniques or Technologies

Not only has the scale of research changed for the design of new biomaterials, but so have the research tools. At UCSF, Dr. Sally Marshall's team has been conducting an in-depth investigation of dentin structure for more than ten years,¹⁷⁻²² utilizing a unique set of nanoscopic tools. They have collected evidence for a nanoscopic view of normal and abnormal dentin. The UCSF team was first to take advantage of unique x-ray scanning tomography (XTM) to profile in three-dimensional micro-architecture of 1x1x1 μ m cube of normal and carious dentin.²³ Their team built the first fully functioning atomic force microscope (AFM) to explore dentin and modified dentin nanostructure (see Figure 3)²⁴ while measur-

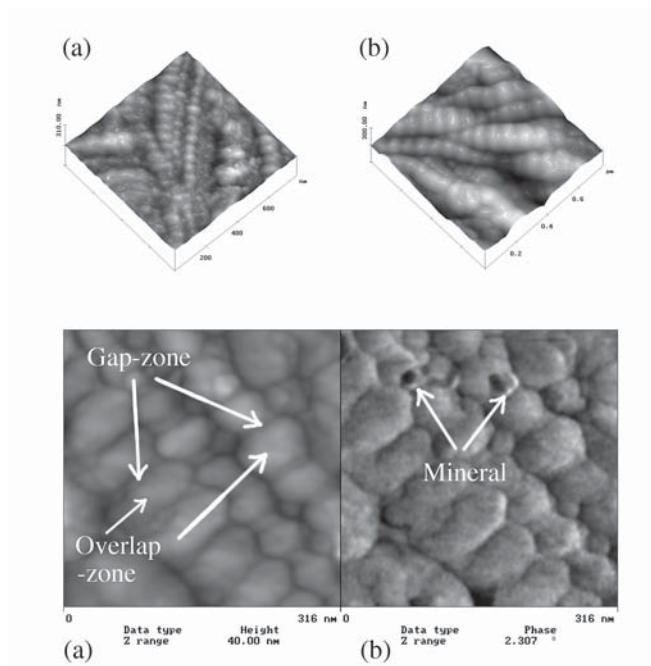


Figure 3. Nano-AFM image of collagen fibrils in dentin after decalcification in preparation for hybrid layer formation

Top: Mixed-mode surface plots of tapping and phase mode AFM images of dentin collagen fibrils, obtained a) in liquid and b) in air. The axial repeat pattern is still present after dehydration.

Bottom: AFM images of dentin collagen fibrils obtained in liquid: a) tapping mode image: gap and overlap zones of adjacent fibrils interlock; b) phase mode image reveals the presence of mineral particles attached to fibrils.

Source: Habelitz S et al. In situ atomic force microscopy of partially demineralized human dentin collagen fibrils. *J Struct Biol* 2002;138:227-36. Reprinted with permission.

ing nanohardness and nanomodulus (modulus mapping)²⁵ information to assess the true mechanical properties of nanodomains of tooth structure. That instrumentation has been further refined to permit pico-measurements of some features.

State of the Art of Key Synthetic Dental Biomaterials

Where are we at this moment in the adoption of newer and better biomaterials? What is the immediate or near future? Despite the protestations of many older practitioners about the serviceability of amalgam restorations, that is not the future. Amalgam will not disappear, but it is not the future for restorative dentistry.²⁶⁻²⁷ Clearly, the major research efforts of the last decade have been heavily focused on bonding systems, composites, ceramics, and esthetics (and bleaching). The following paragraphs consider their status and potential over the next five years.

Bonding Systems

Bonding systems have been in continual development for dentistry for fifty-five years since acid etching was introduced.²⁸ We have cycled through times when there were no bonding systems, enamel-only bonding systems, separate enamel bonding and dentin bonding systems, and now to combined enamel/dentin bonding systems.²⁹ Current bonding systems now are optimized to work well on dentin. For many years, there was a popular classification system that suggested that bonding systems evolved in generations,³⁰ but finally that concept has fallen out of vogue. New bonding systems come in many different flavors. A better approach for classifying bonding systems is in terms of the number of components, their actions, and/or the type of acid being used. All focus on formation of a hybrid layer in dentin.³¹

Kanca³² introduced a simple shorthand years ago that is very instructive in this regard (see Figure 4). Conventional three-component systems can be represented in terms of their etching (E), priming (P), and bonding (B) operations. Etching is required to remove the smear layer and decalcify intertubular zones of dentin or decalcify portions of rods in enamel. Etchants must be relatively strong and effi-

cient to guarantee that decalcification occurs in five to eight seconds. Priming materials are optimized to ensure wetting and flow occur on substrates. They usually are optimized for the surface characteristics of dentin rather than enamel. Primers are hydrophilic and low viscosity. Solvent typically is added to adjust primer viscosity and improve its wetting. Thus, it is crucial that multiple layers of primer be applied to ensure that it simply does not soak into and below the surface of dentin. It must fill up the outer dentin surface and be available for contact with the bonding agent. Since almost all restorative filling materials (e.g., composite) are hydrophobic, a bonding agent must chemically bridge between the more hydrophilic primer and hydrophobic restorative material. If a bonding agent were not present, then the two surfaces would not wet and could not effectively bond together. Thus, a standard or traditional three-component bonding system is represented as E+nP+B. The “n” is used to remind one that multiple applications of primer are required to adequately fill the surface.

In response to concerns by practitioners that bonding procedures were too complicated and seemed time consuming, there was a movement to reduce the number of steps. Two principal approaches arose. Early the 1990s, Japanese scientists began utilizing acidic monomers to combine the etching and priming steps. A few years later, North American scientists were pushing to combine the priming and bonding steps, while retaining the traditional etching process. We will consider these in the opposite order.

If one retains the etching (E) step but combines the priming and bonding steps (nP), then the bonding system is purportedly simpler and faster (E+nP). Normally, this would be described as a two-component total-etch system on the basis that two bottles (phosphoric acid solution and primer-bonding material) are in the commercial kit. The etchant is the traditional phosphoric acid solution or gel (15 percent, 35 percent, or 37 percent H_3PO_4 in water) that works quickly and allows preservation of a hydrated dentin surface. Any system that combines primer-bonding materials generally has a high concentration of solvent to keep the two components miscible. An extreme case is the 90 percent acetone utilized in Prime&Bond (Dentsply, York, PA). Most others are at least 65 percent solvent and might include water/alcohol combinations or acetone.³³ There are different advantages for each choice.

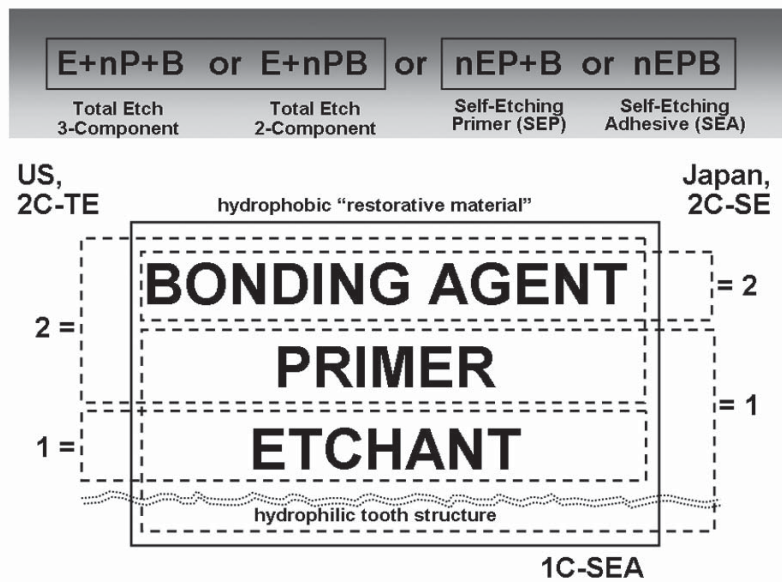


Figure 4. Simple classification scheme for dentin bonding systems using a formula method first proposed by John Kanca (2004) to remind users of the functions and proper use of the components for dentin bonding systems. (E=etching, P=priming, B=bonding)

As one moves away from phosphoric acid toward acidic organic monomers, the challenges increase. No option that has yet been tested is as efficient and as effective as phosphoric acid for etching tooth structure. Phosphoric acid has the advantage of being very acidic (37 percent solutions in water has pH=0.2). Remember that pH is the negative logarithm of the hydrogen ion concentration. So if one defines pH=7 as neutral, values decrease with increasing acidity. pH=6 is ten times more acidic than neutral. pH=1 is 1,000,000 times more acidic than neutral. The scale is continuous and actually goes below zero. Phosphoric acid is only partially dissociated. Therefore, as it reacts on tooth structure, the pH is effectively buffered, and the solution maintains its acid strength for a long time. This is crucial for good etching. Organic acids, however, suffer from the fact that most are not very acidic (pH=1-3) and do not have the extraordinary buffering capacity of phosphoric acid solutions. Therefore, they must work quickly. These solutions become less acidic as the etching proceeds.

Japanese scientists³⁴⁻³⁶ have examined a wide range of self-etching monomers. The two-component systems they have developed involve acidic mono-

mers that must both dissolve the smear layer and decalcify the intertubular dentin while penetrating to embed superficial collagen and produce an effective hybrid layer. Many complicated events must occur in this zone of the intertubular dentin. Etchant-primer (nEP) must dissolve the smear layer or, at least, produce sufficient dissolution to penetrate the smear layer and surround any remaining pieces. Decalcification must occur while this solution penetrates into the dentin. Once the hybrid layer is formed and acidic monomers are polymerized, new polymer must not allow continuing decalcification by its acidic side groups that might deleteriously affect dentin below the smear layer. All of these steps must occur in a uniform and predictable way over the widely ranging microstructure of dentin along the walls of a tooth prepara-

tion. At the same time, similar events must prepare any enamel surfaces for micromechanical bonding. These bonding systems are called “self-etching” primers (SEPs). These systems do not involve “total etching” (TE) typical of phosphoric acid-based systems.

It is possible to go further and combine all three functions into a single package (nEPB), producing one-component systems called self-etching adhesives (SEAs). These have all the challenges discussed for SEPs but additionally must create a surface compatible to hydrophobic restorative materials. SEAs actually are not formulated to work independently as a single bottle. Rather, they use novel packaging methods to allow a critical component for the setting reaction to come into contact with the main portion of the SEA during the procedure. 3M ESPE’s Adper Prompt L-Pop³⁷ uses an intriguing triple pouch (adhesive, initiator, and applicator compartments) to mix two components and load the applicator brush. AQ Bond (Sun Medical, but marketed under the trade name of Touch & Bond in the United States by Parkell, Farmingdale, NY) places the initiator species within the foam applicator tips, so that final mixing occurs at the time of dipping prior to application.

For both SEPs and SEAs, the composition becomes a chemical milieu of competing reactions when so many different things are combined. These systems tend not to be very stable. It is common to recommend cold storage and rapid use since the shelf-life is very short. These systems principally include water as a solvent. While gentle air-drying may be recommended, air-thinning is not. It tends to displace unset materials from tooth surface and prevent future contact with the restorative material. Since one major challenge for SEAs and SEPs is to dissolve the smear layer quickly, agitation with the applicator or brush is recommended to allow mechanical disruption of the smear layer as well. Smear layers can be slightly different in properties depending on the type of rotary instrumentation used. Typically, smear layers produced by diamond burs are more compact and difficult to dissolve. In the case of SEPs and SEAs, some have argued that, for the present time, it may be better to use carbide burs for final tooth preparation to ensure the smear layer will be less resistant to dissolution. In addition, if complex clinical conditions further hamper effective etching, manufacturers recommend total etching in advance. Since these bonding materials are designed to be hydrophilic, they absorb water from the layers below the hybrid layer. They actually wick water toward the tooth preparation side of the bonding agent film. One must anticipate this as a potential problem and work quickly to complete the restorative material placement. Otherwise, the bonded surface may become contaminated with water droplets arriving from below the film.³⁸

Despite our enthusiasm for these newer systems, for many clinicians it is not yet practical to rely on these systems for complex bonding situations. A common conservative stance is to remain with total-etch systems to guarantee predictable bonding behavior. At the same time and despite pleas for caution, there is commercial pressure to carry bonding further down the path to what has been called “no steps.” The presumption here is that the materials in the one-component systems or SEAs can become part of the matrix of the restorative material. During restoration placement, it is assumed that the matrix phase would start etching and priming on its own. During subsequent polymerization, the restoration would be locked onto a hybrid layer mimicking traditional bonding systems. At the moment, it may be practical to make self-etching restoratives or cements, but it is not practical yet to supply them as truly single-

component systems. They require mixing regardless of their curing mechanism.

Since the goal is clearly to move toward simpler and more predictable bonding results, bonding systems for enamel and dentin may someday disappear. Up to this point, we have ignored the fact that bonding is required for other substrates such as amalgam and ceramic. In those cases, traditional designs for dentin do not work as well. Modified bonding systems are required; this will probably continue to be true.

Composites

Despite the rich history associated with development of dental composites (see the chronology presented in Figure 5) and their prominent position in dentistry today, their future is even more promising for a number of reasons. Non-shrink prototypes will reach the market in the short term, solving some of the problems related to premature bonding system stresses. This will also reduce internal porosity that may have contributed to higher than desired water absorption. Silanes, while used for almost the entire history of formulation of composites, have never been optimized or well controlled to produce potentially excellent interphase bonding. More attention is being focused on this problem.³⁹ Filler technologies, which directly affect most composite properties including wear resistance, now include more and more nanofiller use. Nanofillers permit substantially smaller interparticle distances and shelter the resin matrix from wear.⁴⁰ Certain types of nanofillers may allow better coloration and radiopacification systems.

There also is interest in moving away from light-curing methods and toward homogeneous curing options. Despite the dental profession’s enchantment with light-curing methodology, that approach does not allow consistent depth of curing or degree of conversion in cavity locations that are poorly accessible. Therefore, there is a reconsideration of chemical curing strategies and new investigations into other curing strategies.

All potential improvements, taken together, mean that composites may become substantially better in the future. These points, and other important questions, are considered in depth in the following paragraphs.

Shrinkage in composites is fickle. Levels are relatively low but occur quickly and affect many processes during the setting process. The most domi-

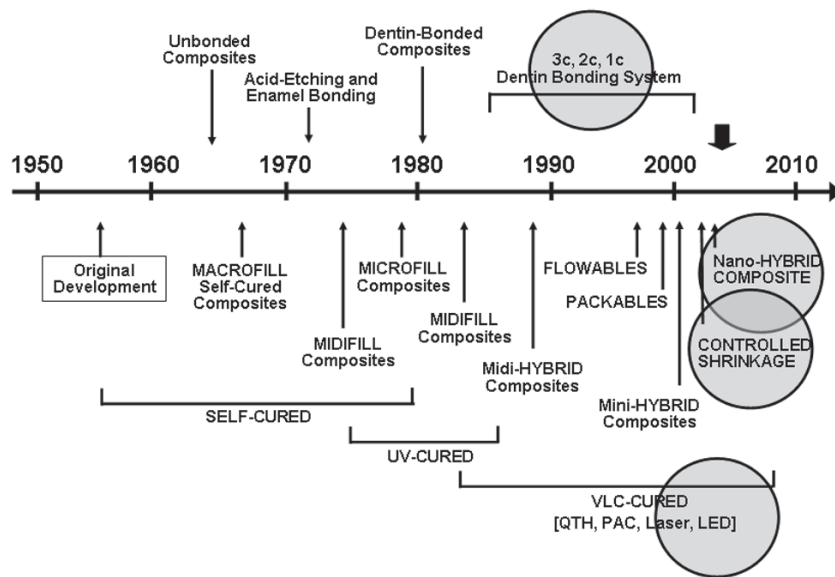


Figure 5. Simple chronology of the development of dental composites based on their filler technologies and textures in comparison to curing systems and available bonding system technologies. Topics of interest reviewed in this article are highlighted.

nant point of view is that, during shrinkage, composite restorations place high levels of stress on relatively immature dentin bonding films. A simple example follows. For a composite formulated with 75 weight percent filler (~50 volume percent filler), half of the restoration is resin undergoing shrinkage. Bisphenol-A-glycidyl dimethacrylate (BIS-GMA) or similar monomers shrink about 10-12 volume percent.⁴¹ Polymerization only produces about 65 percent reaction conversion because steric hindrance limits the extent of reaction of monomers. Actual polymerization shrinkages of about 3-3.5 percent are typical. With adjustments in filler levels or monomer combinations, this level can be controlled downward. During curing, the majority of the reaction (and shrinkage) occurs literally in five to ten seconds. With the emphasis on chairside speed during dental procedures, the push is toward even faster curing procedures. Polymerization stresses occur quickly and unevenly. After a few minutes, stresses relax for a variety of reasons, but they potentially have done some damage. Despite the fact that newer generations of dentin bonding systems produce better hybrid layers, they are not necessarily any stronger at the start and can be dislodged by early stresses. If polymerization of dentin bonding systems is inad-

equate or ineffective, then interfacial failures may occur. At the same time, other key interfaces between the matrix and filler phases may be affected. Incomplete or non-uniform silane bonding to the filler particles prevents appropriate coupling, and local shrinkage may result in either separation or porosity along the filler interfaces. In addition to these porosity effects on fracture resistance, the same sites act as water absorption reservoirs.

Low shrinkage or no shrinkage composites have already been demonstrated⁴²⁻⁴³ as prototypes using varying chemical approaches. The first evidence of these systems was revealed by 3M⁴⁴ and ESPE⁴⁵ during conferences in 2000. In this particular case, prototypes utilized ring-opening reactions typical of epoxy systems to compensate for the double-bond reaction shrinkage.^{43,46} These particular systems are not entirely trouble-free. The reaction chemistry is tainted by contact with other dental materials and requires some accommodation in formulation of other dental materials products. However, this was a valuable demonstration that shrinkage could be managed with existing technologies.

Silane chemistry has been part of the polymer chemistry and composite fields for almost seventy years. These systems work only with Si-O based sub-

strates, and since so much filler use in dentistry is silica, they have been very popular. However, silanation has never been optimized. Theoretically, A174 silane (3-methacryloxy-propyl-trimethoxy silane) acts as a good coupling agent. One end contains three methoxy sites that potentially etherify with hydroxyls on the hydrated surface of silica to produce one to three possible ether bridges and chemically bond to that surface. The opposite end is a double-bond functional methacrylate, which becomes co-polymerized with the resin matrix to complete the chemical coupling. By chemically bridging the matrix and filler phases, interfaces effectively can transfer stresses and also drive future cracks toward the stronger reinforcing filler phase. Yet, there is evidence of several problems in this hypothetical chain of events.³⁹ It is difficult, if not impossible, to produce a monomolecular film of silane on the surface of filler particles. Silane does produce outstanding wetting of the filler and may primarily function in helping matrix monomers to adapt very closely to the filler at a microscopic level. However, silane has a propensity to dimerize or trimerize creating methacrylate moieties that no longer can act as coupling agents. Thus, coupled surfaces might be poor at best. Long term, the coupling reaction, which is a condensation reaction that eliminates water as a by-product, may be reversed by hydrolysis when water penetrates into the resin matrix.⁴⁷ This is particularly true under basic conditions.⁴⁸⁻⁴⁹ Due to the nanoscale of these interactions, it has been impossible to date to measure the extent of actual chemical interaction along filler particles. Finally, when shrinkage does occur, it produces stresses at external interfaces with tooth structure and internal interfaces with filler particles. Shrinkage leads to phase separation or porosity. Porosity in composites is typically at the level of 2-5 percent. While this seems like a low level, it may be concentrated at critical interfaces and have an even greater effect than predicted. If these shortcomings can be managed, there is a strong indication that the mechanical properties of today's composites could be substantially improved.

For many years,⁵⁰ the potential of nanofillers has been touted. Dentistry is one of the latecomers to adopt this technology. Nanofiller is a part of many other commercial composite formulations. Mechanical properties of composites depend critically on the filler levels within the formulations. Generally, increased filler leads to greater stiffness, higher elastic limits, better fracture resistance, and improved wear

characteristics. The last point deserves special attention. Strength alone does not explain the relationship of filler to wear resistance. Intraoral wear occurs via several different mechanisms,⁵¹ but most occlusal wear is caused by ~0.1 m diameter abrasive particles⁵² that exist within food that are suspected to be silica. The matrix phase of a composite is subject to wear, but the much harder filler phase is not. Therefore, sheltering of the matrix is possible by designing the filler particles to be close enough together to protect the matrix phase from contact with abrasive food particles. This process is called "micro-protection"⁷⁴⁰ and had strong support based on evidence from long-term clinical trials.⁵³ The protective capacity was obvious from the excellent wear behavior observed anecdotally for microfill composites. It is particularly obvious in the newer microhybrid and now nanohybrid formulations that are being sold. One might expect that a purely nanocomposite might someday be the ideal composite design.

Nanofillers are not all the same. A variety of nanofillers have already been demonstrated. 3M uses sol-gel technology to produce tiny nanospheres they call nanomers.⁵⁴ These can be agglomerated into nanoclusters, and either the spheres or clusters can become filler particles for composite formulations. 3M ESPE Filtek Supreme⁵⁵ uses primarily nanoclusters in combination with submicron fillers to produce a hybrid. Pentron has had excellent success with Simile utilizing POSS technology borrowed from Hybrid Plastics.⁵⁶ In this case, molecular-sized silicate cages are produced from silane and functionalized for co-reaction with matrix monomers. This technology has great potential that is still being explored. Still others have designed nanoscale fillers using tantalum nanoparticles.^{57,58}

For several years now, the use of the term "nanofiller" has been tainted by everyone wanting to be on the nanotechnology bandwagon. Typically, nanoscale is reserved for things that are on the order of magnitude of 10^{-9} meters. It is standard for scientists to use those units to refer to dimensions that are one to ten units in that size range. Materials with domain sizes of 1-10 nm do have very special properties.

Suddenly, it is in vogue to report even conventional fillers in terms of nanoscale units. Normally, one would not report these sizes as nanoscale entities. 1 mm is actually 1000 nm. Microfiller particles have diameters of 20-40 nm. It would be more accu-

rate to describe these as “near-nanoscale” phases rather than actual nanoscale ones. In a positive light, this means that we still have yet to realize the potential advantages of true nanoscale phases in new composite formulations.

Visible-Light Curing

Light curing of composite formulations arose during the late 1960s with the adoption of ultraviolet (UV) light polymerized systems. In just a few years, it became obvious that visible-light cured (VLC) had many advantages over UV-light cured composites, and practitioners made the shift. Dentistry has been wed to VLC systems ever since. Despite the apparent chairside advantage for command curing, these systems have a significant number of shortcomings. By contrast, chemically cured systems polymerize much more uniformly throughout the entire composite.

VLC systems depend on available access to provide high-intensity visible light. VLC suffers from three major categories of problems.⁵¹ First, VLC lights have technical shortcomings. This was exemplified by quartz-tungsten-halogen lights that have been so popular over the last thirty years. Fluctuations in line voltage, problems with light reflectors, degradation of filters, non-uniform fiberoptic transport properties, and many other effects have led to variable outputs. Second, light intensity depends on several technical operations by the dentist such as close approximation to the material to be cured, use of thin enough increments to ensure sufficient light penetration, proper light angles, and overlapping light exposures, all of which are necessary to ensure proper opportunities for adequate light curing. Third, composite formulations affect the depth of penetration of visible light. Darker shade composites may have as little as .05-1.0 mm effective depth of cure. Certain filler particles are in the visible light spectrum range (e.g., 0.474 μ m filler particle diameters correspond exactly to 474 nm light wavelengths) and can interact with key wavelengths of light. Monomers do not all react equivalently to VLC photoinitiation. Monomers have different copolymerization tendencies. While newer VLC approaches such as light emitting diode (LED) systems have helped to solve some of the first category of problems, they do nothing to manage the other two sets of challenges. It is becoming increasingly obvious that most VLC systems tend to have some portion undercured. If one considers that an effective degree of conversion is

about 65 percent, then many portions may only be cured to 45-55 percent conversion, thereby affecting the resulting properties of the restorative material. Actual degrees of conversion depend on the type of monomers involved. In composites, the monomers are predominantly difunctional ones, and so these values are typical. For many of the newer bonding systems, monofunctional monomers dominate and so undercured systems would be represented as 90 percent conversion.

Best estimates are that, in clinical practice at the moment, ~85 percent of the VLC units are quartz-tungsten-halogen (QTH) types and that LEDs dominate the remaining 15 percent. Clearly, the shift is under way toward LED units. They have many advantages. They often do not require fans, have fewer parts, and are much more lightweight and often portable; most are rechargeable battery-operated; output intensities for second-generation units are excellent; and they have excellent reliability characteristics. Some units include more than one type of LED (e.g., UltraLume 5, Ultradent, Provo, UT) but most are designed to provide light to cure camphorquinone initiators (e.g., Elipar Freelight 2, 3M ESPE, St. Paul, MN; Allegro, LEDemetron, Kerr, Orange, CA; Denmat, Santa Maria, CA; SmartLite iQ, Dentsply, York, PA). Despite early sales at relatively high prices, excellent units are now available for under \$500 (e.g., the CURE, Spring Health Products, Philadelphia, PA). While they do not solve access and depth-of-cure problems, they do represent an improvement in equipment operation and design. Thus, LED curing units are expected to dominate the near-future period.

Ceramics

Ceramics have noteworthy advantages of esthetics, biocompatibility, and mimicry of natural enamel properties. However, most are custom fabricated into dental restorations and contain porosity and/or stress risers that lead to cracks. More robust ceramics are on the way. Until relatively recently, dentistry had not employed ceramic technology at a very sophisticated level. Restorations are still custom made using either all-ceramic or porcelain-fused-to-metal systems without much underlying control or engineering of the microstructures. Dental ceramics have relied primarily on the presence of reinforcing second phases as a crack controlling mechanism. A wide range of all-ceramic materials have been employed (feldspathic porcelains, leucite-reinforced porcelains, alumina-reinforced porcelains, high-den-

sity alumina ceramics, high-density zirconia ceramics, glass-infiltrated ceramics, glass ceramics), but not much elegance has been applied to local control of domain properties within ceramic.

There still is a clear need for more crack-resistant or crack-tolerant designs in dental ceramic engineering. Both pathways are being explored. Crack-resistant materials include zirconia and alumina cores. Both have interesting potential. Yet, these approaches introduce other problems such as alloying esthetic ceramic veneers or creating strong attachment opportunities for dental cements or bonding systems.

There is ever-increasing interest and research on options for crack-tolerant designs. This involves identification of new mechanisms to arrest cracks or slow down their propagation rates. Layered ceramics have potential because different layers can be designed to have different properties (moduli) that produce crack blunting.⁵⁹ Textured ceramics (woven ceramic microstructure motifs) create local variations in properties that discourage crack formation and make growth very difficult. Surface film modifications⁶⁰⁻⁶⁴ or surface retreatments such as sandblasting⁶⁵ also may be used to eliminate fabrication defects that otherwise might generate cracks.

Ceramics are difficult to form into complicated geometries using high-temperature processes in a cost-effective manner in small dental laboratories. Other processes are well suited for custom operations. Hot-isostatic-pressing (HIP) has great advantages for creating standard shapes in a reusable mold, such as preable zirconia abutments for implants. Yet, for custom prostheses (crowns and bridges), it is currently more practical to rely on milling operations or molding operations to form dental shapes.

CAD/CAM ceramic materials provide a unique option to start with almost defect-free materials, but they don't provide flexibility to regionally customize esthetics or other properties for a restoration. That is a large part of the reason that CAD/CAM has not replaced much of traditional ceramic fabrication technology. No alternative yet competes with the esthetic result of dental porcelain being layered by an artistic ceramic technician to fully characterize a restoration. While one can speculate that this is possible, this is not currently an option. When this is true, then CAD/CAM might have much grander appeal.

When CAD/CAM first became commercially available in dentistry in 1989,⁶⁶⁻⁶⁸ one of the initial appeals was the generation of an all-ceramic bondable restoration chairside in just a few minutes. How-

ever, as the complexity, sophistication, and expense of the CAD/CAM design and milling operations expanded, this technology has moved back into the dental laboratory. Despite the fact that the original goal for CAD/CAM generated restorations was to provide a low-cost alternative to dental amalgam, all the research has evolved in quite a different direction.

The key challenges for improved dental ceramic systems seem to be crack-tolerance, low cost, bondability, and excellent esthetic characterization. These goals involve materials design more than fabrication limitations. Major dental laboratories now provide full-service ceramic processing options, so many cost concerns for expensive processing equipment have disappeared when considering the potential for new processing technologies for dental restorations. Novel ceramic textures and microstructural control can be produced by rapid prototyping, stereolithography, and other printing techniques. Their potential has not yet been realized.

Cements

While dental cements do not represent much volume of dental material, they are involved in a crucial step of luting and bonding restorations. The preferences of U.S. clinicians have been slowly shifting away from traditional cements (e.g., zinc phosphate) toward resin-based cements (e.g., resin-modified glass ionomers). In 1990⁶⁹ there was already some evidence of this shift in usage (zinc phosphate=22 percent, polycarboxylate=33 percent, glass ionomer=42 percent, resin=2 percent). It was estimated in 2001⁷⁰ that the shift toward glass ionomer types was dramatic (zinc phosphate=10 percent, polycarboxylate=5 percent, glass ionomer types=75 percent, resin=10 percent). For metal alloy substructures (e.g., gold alloy crowns and bridges, PFMs), resin-modified glass ionomer cements have been far and away the most popular choice. However, resin (i.e., composite) cements are ideal for all-ceramic restorations since they much more effectively transfer stresses.⁷¹ For almost fifteen years, the need for these two types of cements was emphasized. Since 2002, there has been a new class called "universal cements" (e.g., Unicem, 3M ESPE, St. Paul, MN; MaxCem, Kerr, Orange, CA) which are a hybrid of the properties of resin-modified glass ionomers and composites that purport to replace the two types with one. They are designed to be self-etching. In 2004, universal cements seem to be the popular choice for young clinicians.

Performance Outcomes for Synthetic and Biological Biomaterials

Stepping back from the glitter of technologies involved with new biomaterial engineering, fabrication, and investigation, one is still confronted by another important core question. What are the safety and efficacy of these options? Concerns for safety include the procedure, materials, and risks posed by failure. This type of information has been very limited in scientific depth. Efficacy is concerned with the comparative longevity. True long-term estimates of efficacy depend on longitudinal clinical trial information, and that is just starting to be emphasized in biomaterials research.

Biocompatibility of biomaterials has never been investigated from a truly scientific base. Most tests have been crude screening procedures. Even traditional guideposts for screening tests, such as the Ames Test, have been withdrawn by its own author as ineffective.⁷² Practical substitutes have not yet emerged. More times than not, we depend on the clinical record of reported problems to discern the relative biocompatibility of a biomaterial. Yet that record remains incomplete because we refuse to look closely. The Dental Biomaterials Adverse Reaction Unit⁷³ at the University of Bergen in Norway has been studying posttreatment reactions to dental materials for several years and reports a much higher level of patient problems than is routinely acknowledged in the United States. Clinical trials of a biomaterial's performance are short-term and ignore important changes that may occur later and take ten to forty years to surface. There are concerns that the polymer matrix of dental composites may undergo degradation reactions in the presence of esterases commonly found in saliva.⁷⁴⁻⁸⁵ While the effects may seem minor in the near term, should we classify a composite as biologically safe? Do these changes affect restoration properties such as wear? Surface changes can dramatically alter the receptivity toward biofilms. This entire area clearly deserves a much closer look and more careful scientific review.

Longevity, on the other hand, has been studied in terms of cross-sectional and longitudinal clinical trials. Concern for longevity arises from pressures for evidence-based dentistry. For any dental procedure, there are clearly a number of events that could lead to a pronouncement of clinical failure. Some

are more traumatic than others. An esthetic failure might be easy to manage by resurfacing or a repair. A fracture would require replacement of the restoration in most cases. Regardless of the definition or complexity, it is important to know the distribution of values for longevity associated with a procedure. Amalgam is normally chosen as the standard for comparison of all other longevities. In a controlled long-term clinical trial, amalgam longevity was around twenty-four years.⁸⁶

Longevity must be defined in relative and not absolute terms, as is explained by the following. For any procedure, there are many possible variables that influence outcomes, including the clinician and the patient, and many possible failure modes. A minor failure in one mode might not require repair or replacement. Longevity is the average survivability for a pool of restorations taking into account all possible outcomes. For example, consider examining procedures involving Class II composites in maxillary first molars being monitored for several years in terms of a wide range of clinical performance criteria. Overall, the performance for the pool of restorations can be summarized as a success (or failure) curve (see Figure 6). With time, the success level decreases from 100 percent. Over relatively long periods, ten to twenty years, it becomes obvious that the overall curve is shaped like an inverted "S." It may never fall all the way to 0 percent, but is still quite symmetrical in shape. For convenience, the curve can be described by the point at which 50 percent or half of the pool of restorations has failed as a definition of longevity. In other words, the half-life is the number-average longevity for the pool. This has been called the "clinical longevity for 50 percent" or CL_{50} for the pool.⁵¹ In dentistry, the practical goal for the CL_{50} might be ten years. Shifting the entire curve to the right represents a positive situation of improved longevity. Shifting the curve to the left represents a poorer longevity.

Factors influencing the curve are a combination of effects including 1) operator factors, 2) design factors (such as resistance and retention form, cavosurface margin bevels), 3) restoration material factors, 4) intraoral location factors (maxillary versus mandibular, anterior versus posterior, premolar versus molar), and 5) patient factors (fluoride history, diet, dental IQ, genetic predisposition to dental disease).⁸⁷⁻⁸⁸ Risk factors are not equal. Generally, operator factors are suspected to be the most important and may represent >50 percent of the risk. Materials factors may be very minor and could be the

smallest effect. Thus, design of new dental materials is concentrated on eliminating, as much as possible, operator's effects on performance and shifting the focus to the material's effects. In recent years, mixing of dental materials has almost been entirely eliminated from the armamentarium to prevent errors in proportioning and technique.

A CL_{50} of ten years is certainly not ideal. One would like to shift this substantially to the right. However, the practicality of a restorative material lasting a real lifetime is far off. Consider the following two thoughts. First, the current middle-aged population generally has a relatively low caries experience and an ever-increasing longevity. To last a lifetime, a cemented restoration in a woman who is around sixty years old might require survival for up to forty years. Normal mechanical stresses in the oral environment are estimated to provide about 1 million loading cycles per year. Typically, we have designed engineering materials that do not survive beyond ten to twenty million cycles of loading (or ten to twenty dental years). Therefore, newer biomaterials will have to become much more damage-tolerant to provide longer service lifetimes. For this same reason, one might argue that true biological replacements (tissue engineered or cloned teeth) would be a better choice for treatment. However, this argument presupposes that there is sufficient bone, normal healing processes, and good health for the dental patient. These shortfalls are all reasons that synthetic biomaterials still may be employed for a long time to come.

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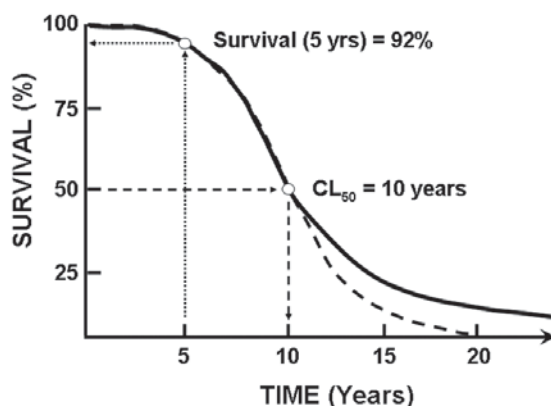


Figure 6. Schematic summary of the key parts of a survival (failure) curve for a restorative dental material

The half-life for a population of restorations is typically reported as the "clinical longevity for 50% of the restorations" or CL_{50} . If only a small portion of the curve has been defined, then it is more convenient to report the survival level at a certain time period. The dashed curve is the hypothetical curve. The solid curve is more typical, where a few restorations appear to survive forever.

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