High-Throughput Evaluation of Restorative Dental Polymers

Feature

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Polymeric dental composites are widely used in the restoration of anterior lesions and small- to medium-sized defects in the posterior region of the mouth. The composites are comprised of an organic matrix, inorganic fillers, and a sizing agent for improving the interface between the matrix and filler. Upon irradiation with visible light, the organic matrix cross-links to form a rigid polymeric network. For the matrix alone, a large number of material parameters (such as monomer chemical structure, molecular mass, viscosity, and co-monomer composition) and processing parameters (such as light wavelength, intensity, and exposure time) influence the material properties and biological responses.[1]

High-throughput and combinatorial methods have become increasingly popular in material discovery, characterization, and optimization due to faster data acquisition, more thorough examination of experimental variables, equal processing conditions for a given specimen, and lower experimental error.[2] In a typical combinatorial measurement, an array specimen varying in two material parameters (variables) is first fabricated. The material properties as a function of the defined parameters are then characterized and analyzed. Given the vast number of variables in dental research, these approaches are expected to aid in the design of future experiments and facilitate process and application optimization.

In restorative dental materials, the mechanisms by which the monomer structures and composition affects the reaction kinetics, conversion, and a host of material properties are still unclear. In the current study, the relationships between chemical composition, monomer conversion, and polymer
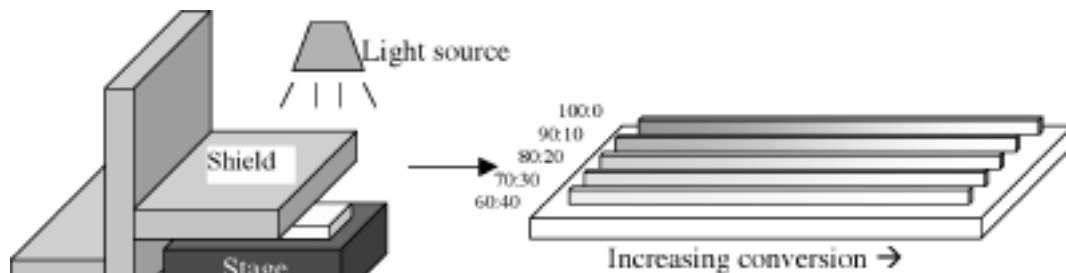

Figure 1. Two-dimensional gradient sample preparation. Each strip corresponds to a discrete dimethacrylate composition, and the degree of conversion is varied orthogonal to the composition gradient.

properties of two-component dimethacrylate networks via combinatorial approaches[3] are assessed. A gradient sample varying in co-monomer composition along one axis in a discrete fashion and continuous conversion gradient in the orthogonal axis was prepared and characterized (Figure 1). The sample was mounted onto a translation stage that was programmed to vary the light exposure time to the sample, thus creating the conversion gradient. As a result of the photopolymerization process, conversion gradients were generated onto a single glass slide (gradient sample shown in Figure 1). Two monomer systems were examined for the current study: 1) BisGMA (2,2-bis[4-(2-hydroxy-3-ethacryloloxypropyl)phenyl]propane) mixed with triethylene glycol dimethacrylate (TEGDMA) and 2) EBPADMA (ethoxylated-BisGMA) mixed with TEGDMA at various compositions. Upon photo-activation and subsequent photopolymerization, three-dimensional cross-linked networks were formed.

All measurements were carried out at least 24 hours after light exposure to ensure that the conversion no longer changed significantly with post-cure time. A notch was made across the composition gradient at the high conversion end and was defined as the zero position for subsequent conversion measurements and mechanical testing. Data were collected and reported over 50 mm at 5 mm intervals beginning at the zero position for each composition. The advantage of keeping the compositions discrete is the absence of ambiguities in the network chemical composition, allowing straightforward data analysis. The current process is also amenable for high-viscosity monomer mixtures and eliminates nonuniform (laminar) flow as typically observed when co-syringing monomer mixtures with a large disparity in viscosity.

The degree of conversion along the exposure gradient was determined using Fourier transform near infrared (NIR) spectroscopy, and the mechanical properties (hardness and modulus) were determined using nanoindentation. The relative uncertainty for all measurements was less than 5 percent. Figure 2 shows the degree of conversion and modulus as a function of the irradiation time for all compositions of the
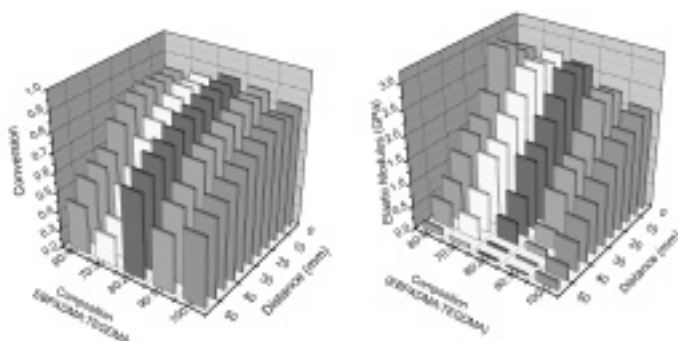

Figure 2. The methacrylate conversion (left) and elastic modulus (right) for EBPADMA:TEGDMA blends of different compositions and photopolymerized by different irradiation times.

High-Throughput Evaluation...

EBPADMA-TEGDMA system. Similar results were observed for the BisGMA-TEGDMA system. The methacrylate conversion was determined by normalizing the area of the methacrylate =C-H absorption band to the aromatic C-H absorption band as compared to the unreacted resin from the NIR measurement. In the current text, the conversion value at the longest exposure time is defined as the ultimate conversion. In general, the gradients exhibited conversions ranging from approximately 40 percent to approximately 85 percent spanning a large cross-linked conversion range. The reaction conversions are nearly identical for distances 0 mm to 10 mm as a result of the fabrication process. Figure 2 clearly illustrates that the ultimate reaction conversion depends on the chemical structure of the co-monomers. For the EBPADMA-TEGDMA system, ultimate conversions for all compositions ranged between 82 percent and 88 percent with the 100:0 composition showing the lowest ultimate conversion and the 80:20 showing the highest ultimate conversion.

The corresponding elastic modulus of the gradient sample was characterized using nanoindentation (Figure 2). The effect of co-monomer composition on the elastic modulus was also evaluated. The 60:40 composition exhibited the highest modulus and the elastic modulus decreased as the TEGDMA content decreased. In BisGMA-TEGDMA networks (data not shown), the flexible lower molecular mass TEGDMA is considered a reactive diluent and thus reduces the modulus. However, co-monomer compositions containing higher TEGDMA contents have a higher number of methacrylates per volume. At comparable reaction conversions, it was concluded that systems containing higher TEGDMA contents had higher cross-link densities. In the EBPADMA-TEGDMA system, the ability of TEGDMA to increase the network cross-link density dominates its diluent effects, as observed by the increased elastic modulus with TEGDMA content increase. Moreover, the 80:20 composition exhibited the highest methacrylate conversion but not the highest modulus. The 60:40 composition exhibited the highest modulus while showing a lower ultimate reaction conversion. This further indicates the complex role of the TEGDMA diluent monomer in affecting the conversion and properties.

The effect of methacrylate conversion on the elastic modulus and hardness for a typical composition (90:10) is plotted in Figure 3. Excellent agreement is observed between the conversion and modulus as an increase in methacrylate conversion corresponds to a dramatic increase in the modulus. The modulus increased over two orders of magnitude as the conversion increased from approximately 50 percent to 86 percent. It is expected that the mechanical properties change rapidly with conversion at the low conversion range. The modulus increased significantly even at the high conversion end, indicating the need to achieve high methacrylate conversion. Equally important is the evolution of the hardness, which increased with increased conversion. This increase was due to changes in the network cross-link density at the high conversion range and clearly illustrates the importance of obtaining high reaction conversion in the dental restorative composites.

For the initial evaluation of cell response to BisGMA-TEGDMA networks, RAW 264.7 macrophages were cultured on samples with a degree of conversion that varied from 43 percent to 62 percent in a continuous fashion. After 24 hours of culture, cell viability was assessed using fluorescent microscopy (Figure 4). In viable cells (green), calcein acetoxymethyl ester diffused through the cell membranes and was hydrolyzed to cell-impermeant fluorescent calcein via intracellular esterases. Compromised/dead cells fluoresced red due to ethidium homodimer-1, which entered via damaged cell membranes and bound to nucleic acids. Cell viability increased
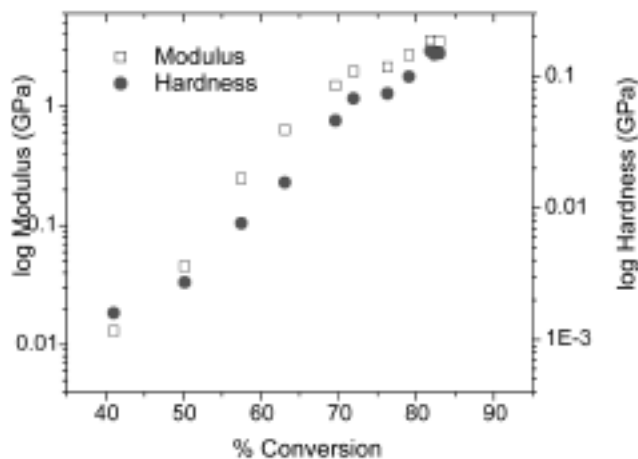

Figure 3. Elastic modulus and hardness measured as function of percent conversion for the 90:10 composition. The standard uncertainty associated with the nanoindentation measurements is smaller than the size of the symbol.
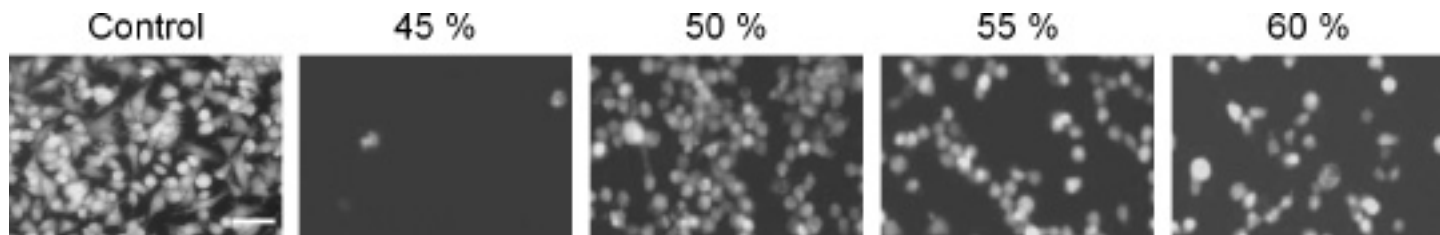

Figure 4. Macrophage viability as a function of methacrylate conversion. Green indicates viable cells and red indicates cells with compromised membranes. Scale bar = 50m.

as the conversion increased, with viability at 60 percent conversion similar to viability on controls (tissue culture polystyrene).

Acknowledgments

References:

1. Sakaguchi, R.L. Clinical Challenges and the Relevance of Materials Testing for Posterior Composite Restorations. Dental Materials 2005, 21, 3.
2. Lin-Gibson, S.; Landis, F.A.; Drzal, P.L. Combinatorial Investigation of the Structure-Properties Characterization of Photopolymerized Dimethacrylate Networks. Biomaterials 2005, in press.
3. Amis EJ. Combinatorial materials science - Reaching beyond discovery. Nature Materials 2004; 3(2):83-5.

Update on the 2006 Annual Meeting

Institute of Mechanical Engineers, the Engineering in Medicine and Biology Society Early Career Achievement Award, Boston University's Metcalf Cup and Prize for Excellence in Teaching, and selection for *Technology Review*'s inaugural TR100 young innovator list. Dr. Collins is a Fellow of the American Physical Society and the Institute of Physics, and of the American Institute for Medical and Biological Engineering. In 2003, he received a MacArthur Foundation "Genius Award," and in 2005, was selected for the Scientific American 50—the top 50 outstanding leaders in science and technology. Dr. Collins is a scientific cofounder and chair of the scientific advisory board of Cellicon Biotechnologies Inc. and Afferent Corp. Dr. Collins' research focuses on developing nonlinear dynamical techniques and devices to characterize, improve and mimic biological function. His specific interests include: systems biology — reverse engineering naturally occurring gene regulatory networks; synthetic biology — modeling, designing and constructing synthetic gene networks; developing noise-based sensory prosthetics.

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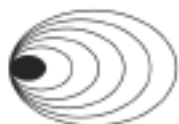
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