

# Development of Novel Tunable Light Scattering Coating Materials for Fiber Optic Diffusers in Photodynamic Cancer Therapy

L. Kris Kostanski,<sup>1</sup> Michael A. Pope,<sup>1</sup> Andrew N. Hrymak,<sup>1</sup> Mark Gallant,<sup>1</sup> William L. Whittington,<sup>2</sup> Leonid Vesselov<sup>2</sup>

<sup>1</sup>Department of Chemical Engineering, McMaster University Hamilton, Ontario, Canada L8S 4L7

<sup>2</sup>Walsh Medical Devices Inc., Oakville, Ontario, Canada L6L 5T7

Received 7 April 2008; accepted 17 November 2008

DOI 10.1002/app.29713

Published online 5 February 2009 in Wiley InterScience (www.interscience.wiley.com).

**ABSTRACT:** To homogenize light emitted from fiber optic diffusers for photodynamic therapy (PDT), novel coating materials with tunable properties were designed. A class VI medical grade UV-curable acrylic resin for biomedical applications was used for the polymer matrix, and titanium dioxide (TiO<sub>2</sub>) was added to the resin as a scattering agent. UV-curability of coatings containing TiO<sub>2</sub> was significantly influenced by the grade and surface treatment of the TiO<sub>2</sub> studied. Despite using a free-radical system without inert gas protection, all samples demonstrated considerable thermal postcuring. A novel TiO<sub>2</sub> surface treatment methodology was developed based on unsaturated alkoxyorganosilanes combined with unsaturated carboxylic acids for compatibilizing TiO<sub>2</sub> for use in the resin material studied. By adjusting the concentration

of the surface-modifying agent, the scattering efficiency and UV curability can be controlled by decreasing the effective particle size and enhancing the dispersibility of the powder filler within the resin. This modification will enable fine-tuning of the effective size of TiO<sub>2</sub> particles to the wavelength of laser light to be scattered to maximize scattering efficiency in photodynamic cancer therapy and possibly also in other forms of cancer treatment (interstitial laser hyperthermia or interstitial laser photocoagulation). © 2009 Wiley Periodicals, Inc. *J Appl Polym Sci* 112: 1516–1523, 2009

**Key words:** coatings; photopolymerization; radical polymerization; photodynamic cancer therapy; fiber optic diffusers

## INTRODUCTION

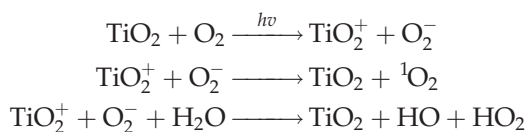
Photodynamic therapy (PDT) is a type of cancer treatment that uses laser light and a photosensitizing drug to cause selective damage to a tumor mass. For endoscopic or interstitial applications laser light is delivered using a probe that illuminates the target tissue, activating the drug locally. A novel thin cylindrical diffuser technology has been developed that enables primary scattering centers to be produced within the optical fiber through controlled disruptions of the glass structure similar to long period gratings.<sup>1,2</sup> These scattering centers allow laser light traveling in multiple modes within the fiber core to be scattered sideways into the cladding and beyond along the length of fiber diffuser. Using this technology, small diameter (100–500 μm), flexible diffusers can be created that minimize tissue damage caused by insertion and are amenable to use with an endo-

scope. However, the scattered light is only quasi-uniform. The uniformity of light emitted from these diffusers can be improved (“homogenized”) by adding a second scattering layer in the form of a pigment/filler containing coating surrounding the optical fiber.<sup>2</sup> The scattering layer needs only be applied to the diffusing tip of the fiber optic requiring a batch coating process making a UV curing coating an attractive option.

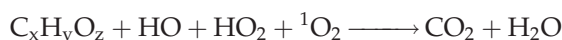
The addition of pigment/filler particles in a UV curing system typically and drastically reduces both the rate of polymerization and final conversion. Recently, the photopolymerization gradient was investigated when titanium dioxide (TiO<sub>2</sub>) particles were added to thick paint films. Decay of UV light throughout thicker coatings was shown to cause a heterogeneous reaction and sometimes no reaction at all<sup>3</sup> in a system that was previously shown to be highly UV curable.<sup>4,5</sup> The rate of polymerization and final conversion are governed by the UV radiation intensity and its decay, by absorption and scattering, throughout the coating. The final conversion of filled systems can be improved by further thermal postcuring of UV-cured samples in all likelihood by freeing active centers trapped in the glassy matrix.<sup>6</sup>

Correspondence to: L. K. Kostanski (kostans@mcmaster.ca).

On the other hand, TiO<sub>2</sub> is also known to adversely affect the polymer matrix as it exhibits a chemically active surface upon UV absorption.<sup>7</sup> The following reactions summarize the UV-degradation mechanism.



Polymers (for simplicity denoted below as C<sub>x</sub>H<sub>y</sub>O<sub>z</sub>) can then be degraded by a combined attack of hydroxyl and hydroperoxyl radicals and also singlet oxygen.



There are two general types of surface modification used in commercial titanium dioxide (also called titania) fillers that help to prevent or reduce polymer degradation. Most typical is modification with glassy insulators, usually silica (SiO<sub>2</sub>), alumina (Al<sub>2</sub>O<sub>3</sub>), or a combination of both—to prevent escape of very active species (electrons, excitons, and radicals) into an organic matrix. However, complete coverage of TiO<sub>2</sub> surface is difficult to achieve.<sup>8</sup> The other type of surface treatment uses organic compounds such as polyols, which can also improve compatibility with the organic matrix. However, it can be expected that if the organic compounds cannot be permanently incorporated into the polymer network while still being attached to the TiO<sub>2</sub> surface, the compounds can migrate into the organic resin causing plasticization. The organic compounds will possibly also phase separate after curing and thus have an effect on adhesion of the coating to the substrate. All this will limit the mechanical protection offered by the polymer coating on the otherwise fragile light diffuser.

The present study focuses on the development of the light scattering composition to be used to coat thin fiber optic diffusers. After investigating the

effects of commercially available TiO<sub>2</sub> grades on UV curability and red laser light scattering, a novel surface-modification methodology is developed that enables the control of TiO<sub>2</sub> agglomerate size and dispersibility within the organic matrix. The effective particle size and loading are investigated with respect to rate of polymerization, final conversion, light scattering, and the extent of thermal-post curing.

## EXPERIMENTAL

### Polymer matrix

A class VI medical grade UV curing acrylic resin (1186-MT, Dymax Corp.) was investigated for use as a matrix in the coating material. The resin cures via photoinitiated free-radical crosslinking polymerization.

### TiO<sub>2</sub> grades

Several different titanium dioxide grades were investigated in this study. Each grade had a different surface treatment. Table I lists some available details about the TiO<sub>2</sub> grades investigated. A TiO<sub>2</sub> type that has the highest level of silica modification (6.5 wt %) but no pre-existing organic treatment (Dupont TiPure R-960) has been selected as a model filler to be additionally modified to develop coating materials containing a designed type and level of additional surface alteration.

### Surface modification of TiO<sub>2</sub>

The additional surface modification of Dupont TiPure R-960 was accomplished by using solutions of 3-(trimethoxysilyl) propyl methacrylate, H<sub>2</sub>C=C(CH<sub>3</sub>)CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub>Si(OCH<sub>3</sub>)<sub>3</sub>, in two different solvents containing also acrylic acid (AA) in the amount enough to achieve an apparent pH 3. Since alkoxy silanes are insoluble in water, 1% by weight solutions of the silane coupling agent were prepared in both acetone ("dry" method) and a 1 : 4 (vol.) mixture of acetone and water ("wet" method).

Thus, first suspensions of TiO<sub>2</sub> in varying amounts of the solutions were prepared. The solution

TABLE I  
Details on TiO<sub>2</sub> Grades Used in this Study

TiO <sub>2</sub> grade	Supplier	Median particle size (μm)	Surface treatment
R102	DuPont	0.23	Organic treatment; alumina surface treatment
RCA	Kalamazoo paper chemicals	1.0	Surface treated <sup>a</sup>
R960	DuPont	0.35	No organic treatment; dense silica surface treatment
Kronos1014	Kronos Worldwide	0.22	Polysiloxane treatment
R105	Dupont	0.31	Organic treatment; silica surface treatment

<sup>a</sup> Type of surface treatment undisclosed.

amounts were such as to contain 0.3, 0.5, 1, and 2 wt parts of the organosilane per 100 wt parts of TiO<sub>2</sub>. Suspensions were then mixed until dry and the rest of volatiles removed at temperature gradually increased up to 120°C under nitrogen gas. No additional rinsing of the modified filler after the final drying was performed.

### UV reactivity

The UV-reactivity of the different filled resin systems was analyzed using real-time Fourier transform infrared (FTIR) spectroscopy. The polymerization kinetic studies were performed directly on the ATR diamond probe of the FTIR instrument (ReactIR 1000; ASI Applied Systems). This permitted a rapid acquisition of FTIR spectra (at the rate of 3 spectra per second) at bottom of the sample (the substrate level) that was illuminated with the UV light from the top.

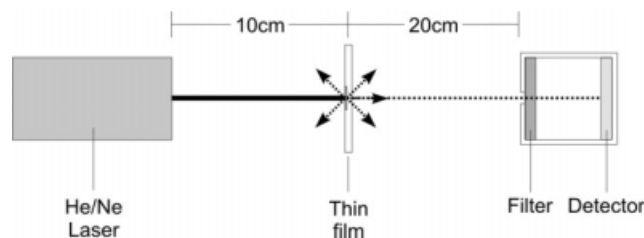
Thus, a 15 W "black light" source (General Electric) emitting low intensity UVA light (4.8 mW cm<sup>-2</sup>, the emission maximum at 365 nm) was used to cure each sample from top to bottom on the FTIR probe. Samples were placed directly on the 5-mm diameter diamond surface filling the divot on the probe surface. Excess sample was carefully scraped off using a clean glass slide to ensure a coating of reproducible thickness be deposited on the probe each run. The UV lamp was clamped 1 cm from the top surface of the sample. The reaction at the bottom of the sample was used to monitor the cure of the resin at the critical substrate level over time. The 810 cm<sup>-1</sup> wavenumber was used to monitor conversion of double bonds (C=C) of acrylate groups within the resin. A reference peak at 1715 cm<sup>-1</sup> corresponding to carbonyl groups was used to calculate the percent conversion at the bottom of the sample according to eq. 1.

$$X_c(\%) = 100 \left( \frac{\frac{A_{0,810}}{A_{0,1715}} - \frac{A_{t,810}}{A_{t,1715}}}{\frac{A_{0,810}}{A_{0,1715}}} \right) \quad (1)$$

### Laser light scattering

A 5 mW He/Ne laser emitting a monochromatic beam of 632.8 nm red laser light was used to pass light through a film (200–300 μm thick) of the cured, filled resin. The voltage drop through the detector was used to estimate the change in light intensity upon light scattering. Figure 1 indicates the experimental set-up. A light filter (OD 1.5-Oriel Instruments) was used when samples with low scattering coefficients were analyzed.

For thin layers and low concentration of the scattering particles (when multiple scattering inside the



**Figure 1** Representation of light scattering apparatus for measuring the relative scattering efficiency of different TiO<sub>2</sub> grades within the polymer matrix.

layer is negligible), one can use a simple relationship (eq. 2), which was employed to estimate the scattering coefficients of films of the filled resin based on the sample thickness ( $\Delta x$ ) and the change in light flux ( $\Phi$ ) estimated by the voltage drop in the detector.

$$\sigma = -\frac{1}{\Delta x} \ln \left( \frac{\Phi_{\text{transmitted}}}{\Phi_{\text{incident}}} \right) \quad (2)$$

Equation 2 is strictly valid for films 5–30 μm thick containing only a small amount of scattering centers. Thus, the effective scattering coefficient ( $\sigma$ ) measured was used as a comparative measure of the relative scattering abilities as larger film thicknesses were used in this study. This also applied when the material is used as a scattering buffer on a diffuser where multiple scattering events are required to attain a Lambertian emitting behavior.

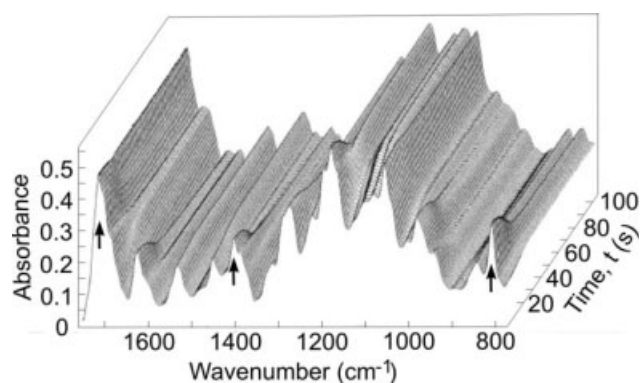
### Thermal post-curing tests

A 100 μm thick layer of the filled resin was spread onto a 1 mm thick strip of woven glass fiber (TA Instruments) cut to 1 cm × 4 cm. The resin was photopolymerized under the UVA light for 20 h. Samples were then placed in a 983 Dynamic Mechanical Analyzer (DMA-Dupont Instruments) and the sample was oscillated at 0.5 Hz. The temperature was ramped from 25 to 100°C at 5°C min<sup>-1</sup> and the loss and storage moduli were recorded. The maximum value of tan( $\delta$ ), the ratio of loss modulus to storage modulus, was used to estimate the glass transition temperature ( $T_g$ ) of the material. Several cycles were performed on each sample until no further change in glass transition temperature ( $\Delta T_g$ ) was observed.

## RESULTS AND DISCUSSION

### Validation of the photopolymerization testing method

As described in detail in the previous section, we attempted a simple and safe method to follow photopolymerization kinetics by directly UVA irradiating the sample from top using a low intensity "black



**Figure 2** Real-time FTIR determination of UV-reactivity of acrylic resin used as a matrix arrows indicate peaks used as reference ( $1715\text{ cm}^{-1}$ ) and to follow reaction conversion ( $1407\text{ cm}^{-1}$  and  $810\text{ cm}^{-1}$ ).

light" source, while collecting FTIR spectra in real time at the critical substrate level. To verify if this methodology is able to capture diminishing concentration of C=C double bonds due to polymerization, we attempted to cure the neat resin first. The selected acrylic resin (Dymax 1186-MT) is FDA approved for use in medical devices and offers a low refractive index complementing the high refractive index of rutile  $\text{TiO}_2$ . The FTIR spectra were acquired in the absorbance mode. Because the absorbance is directly related to concentration, diminishing absorbance values at infrared regions associated with C=C double bond deformations are an indication of the progress of polymerization, i.e., the conversion of reactive groups (C=C bonds).

Figure 2 shows a 3-D graph (wavenumber-absorbance-time) for photopolymerization of the resin. The C=C conversion can be inferred from the bands where the absorbance is clearly being reduced over time:  $\sim 1407\text{ cm}^{-1}$  (H-C=C bending), and  $\sim 810\text{ cm}^{-1}$  (C=C twisting). A band at  $\sim 1715\text{ cm}^{-1}$  (C=O stretching) can be used as reference.

The observed changes in FTIR spectra confirm that—despite using low energy UVA light of low intensity—polymerization was proceeding rapidly and the simple set-up was adequate to capture the progressing C=C conversion.

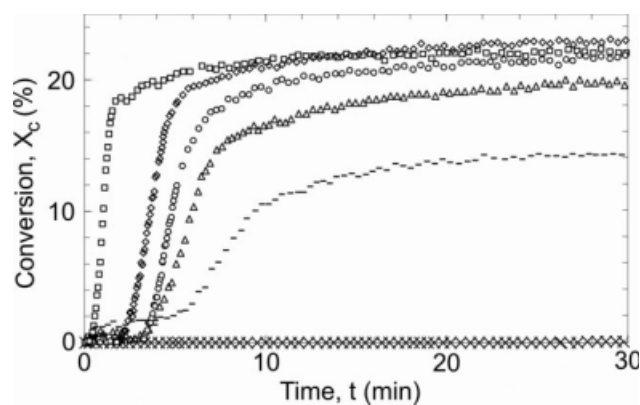
### Effect of $\text{TiO}_2$ filler

To investigate the effects of  $\text{TiO}_2$  on the UV curability of the acrylic resin, several commercially available  $\text{TiO}_2$  grades were obtained from manufacturers. Figure 3 shows the UV curing results for 5 wt % loadings of the different  $\text{TiO}_2$  dispersions.

As expected, the addition of  $\text{TiO}_2$  to the resin lowered the reaction rate and conversion. Nevertheless, it can be noticed in Figure 3 that in general the reaction for the studied coating materials after a brief

induction period proceeds rapidly. This shows the general viability of UV-polymerization for  $\text{TiO}_2$ -containing acrylic resin-based materials even without applying an inert gas blanket that is typically required for free-radical polymerizations. After a fast reaction, vitrification of the polymerization mixture occurs, which stalls the reaction. This vitrification ("solidification") phenomenon happens when—due to the progress of polymerization—the glass transition temperature ( $T_g$ ) of the system becomes equal to the temperature of reaction. The mobility of the reacting groups is then severely hindered, which typically leads to a limited conversion.<sup>9–11</sup> Sometimes vitrification can be moved to higher conversions at a given polymerization temperature by increasing the rate of initiation reaction.<sup>11</sup>

Interestingly, the type of  $\text{TiO}_2$  added to the system had an observable effect on the curing behavior. Accordingly, at the same loading level (5 wt %) different  $\text{TiO}_2$  grades (with different but largely unspecified treatment) cured at various rates and to a different extent over the reaction time as shown by relevant C=C conversion curves in Figure 3. Such large differences in photopolymerization rates for different  $\text{TiO}_2$  grades at the same loading level were unanticipated. In view of the fact that detailed information about the surface treatment was unavailable, various explanations for these observations could be offered. On one hand, the observed differences might be attributed to incomplete coverage of  $\text{TiO}_2$  by components of the surface treatment, which would make possible photocatalytic degradation of the resin. On the other hand, some unknown constituents of the surface treatments themselves might heterolytically decompose the photoinitiator and hence decrease the probability of initiating the polymerization for the same irradiation dose. Still one more possibility is that in some cases undisclosed components of the surface treatment might have



**Figure 3** Effect of  $\text{TiO}_2$  grade on UV-reactivity and conversion of 1186-MT.  $\text{TiO}_2$  was loaded at 5 wt %;  $\square$  = neat resin,  $\diamond$  = RCA,  $\circ$  = R960,  $\Delta$  = R102, - - = Kronos1014,  $\times$  = R105.

**TABLE II**  
Difference in Glass Transition Temperature,  $\Delta T_g$ ,  
Between Thermal Cycles

Filler type	$\Delta T_{g,1}$	$\Delta T_{g,2}$
R102	20	3.2
RCA	13	0.3
R960	15	0.3
Kronos1014	11	2.2
R105 <sup>a</sup>	–	–

One cycle: Temp. ramp 25°C to 100°C at 5°C min<sup>-1</sup>.

$\Delta T_{g,1}$ ,  $T_g$  increase after one cycle;  $\Delta T_{g,2}$ , additional increase after second cycle.

<sup>a</sup> Did not cure enough during 24-hour-period.

the ability to terminate the kinetic chain of polymerization.

Because titanium dioxide R-960 enables achieving relatively high reactivity and has the highest known coverage with silica but has no pre-existing organic treatment; this gave us the opportunity to use it as a model filler and carry out a chemical modification of this titanium dioxide filler in a controlled manner using well-understood silane chemistry.

On the other hand, as can be seen in Table II, all TiO<sub>2</sub> grades investigated showed significant thermal postcuring. This was demonstrated by measuring the effect of subjecting the samples to temperature cycles (linear temperature change at the rate of 5°C min<sup>-1</sup> between 25°C and 100°C) on the resulting increase in glass transition temperature, i.e.,  $\Delta T_g$ . Thus,  $\Delta T_{g,1}$  denotes an increase in  $T_g$  after subjecting the sample to the first thermal cycle, and  $\Delta T_{g,2}$  the additional increase in  $T_g$  after the second thermal cycle. The polymer matrix did not reach a stable  $T_g$  until at least one thermal cycle had been traversed. As discussed above, this is due to the fact that reactive centers (radicals in this case) are becoming trapped inside the glassy matrix as polymerization proceeds. When the thermal cycle elevates the temperature past the initial  $T_g$ , this is releasing the radicals and further increasing the reaction conversion.

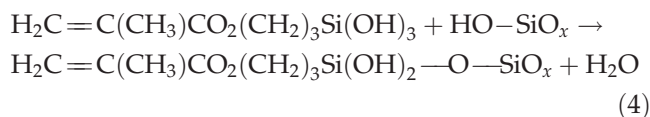
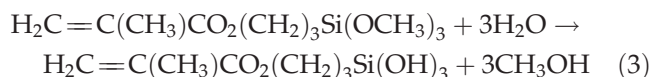
No significant change in  $T_g$  was found between Cycle 2 and 3 for all materials tested indicating complete polymerization after only one thermal cycle.

### Surface modification

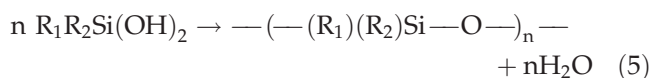
Details of modification for commercially available titanium dioxide are usually treated as trade secrets and few details are revealed. Thus, as is it discussed above, it is challenging to try and explain different conversion rates for different rutile TiO<sub>2</sub> grades at the same loading and in most cases a similar particle size. Consequently, it would be beneficial to conduct a modification of titanium dioxide in a precisely controlled manner using well-understood chemistry to

be able to design coating materials with planned and desired properties.

One of the best-known interfacial chemistries is the reaction between hydroxyl groups present on the silica surface (represented below for simplicity as HO—SiO<sub>x</sub>) and trihydroxyorganosilanes.<sup>12</sup> The hydroxyorganosilanes are typically formed first by hydrolysis of alkoxyorganosilanes, e.g., 3-(trimethoxysilyl) propyl methacrylate.



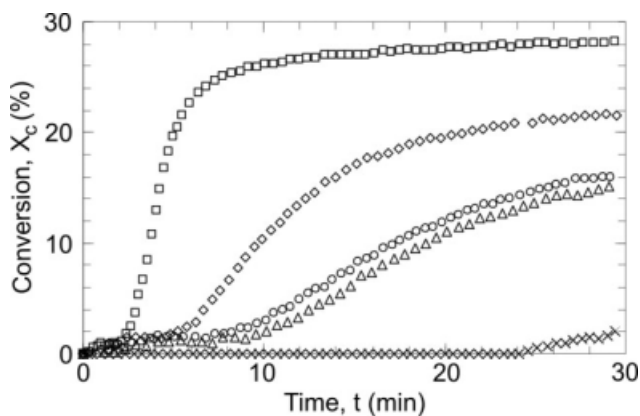
This is accompanied by polycondensation of the hydroxyorganosilane groupings.



where R<sub>1</sub> is H<sub>2</sub>C=C(CH<sub>3</sub>)CO<sub>2</sub>(CH<sub>2</sub>)<sub>3</sub> and R<sub>2</sub> is —O—SiO<sub>x</sub>.

From the information available, it can be inferred that one of the available titanium dioxide grades (Ti-Pure R-960, DuPont) has the highest known coverage with silica (6.5% by weight) and has no pre-existing organic treatment. This enabled “supermodification” of this already silica-modified titanium dioxide by utilizing the described reactivity of silica surface towards the hydroxysilanes. This made possible grafting by employing hydroxyl groups of glassy silica added onto the TiO<sub>2</sub> surface with simultaneous polycondensation of the hydroxyorganosilanes. This resulted in permanent attachment of the coupling agent, which enabled: (1) facilitated dispersion of the particle in the resin by creation of hydrophobic shields on the silica-coated titania particles, and then (2) creation of permanent bridges between the two incompatible (inorganic and organic) phases by incorporating the silane unsaturated groups (H<sub>2</sub>C=C(CH<sub>3</sub>)CO<sub>2</sub>—) into a growing network.

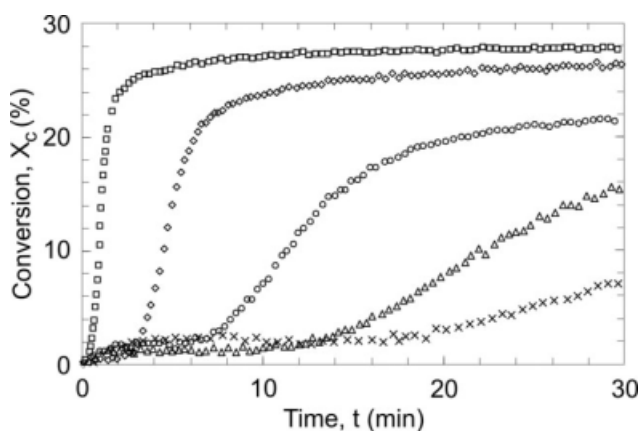
On the other hand, as mentioned before, because a complete coverage of TiO<sub>2</sub> surface is not easy to achieve<sup>8</sup> there is probably a fraction of the TiO<sub>2</sub> particle surface that is not covered. However, it is known<sup>13</sup> that low molecular weight carboxylic acids can strongly attach to bare TiO<sub>2</sub> surface in such a way that the carboxylate group stays at the surface while the rest of the molecule is “sticking out.” In our approach, we propose to make use of polymerization-reactive AA. Because AA has a very strong adsorption tendency towards the TiO<sub>2</sub> surface, as a result the acid can “patch” free surface sites on the



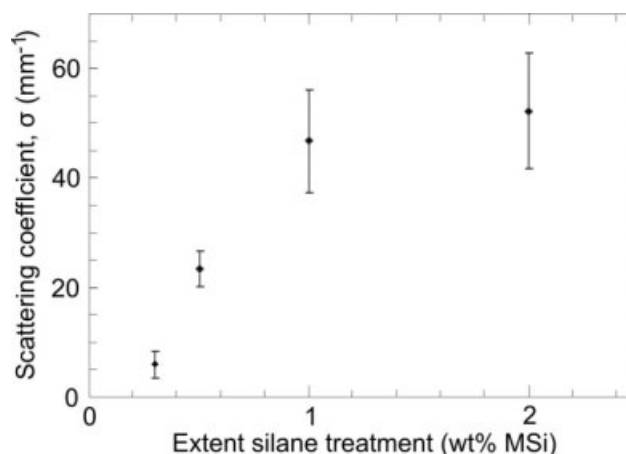
**Figure 4** Effect of treatment level on UV-reactivity and conversion for 2 wt % TiO<sub>2</sub> loading; □ = 0% (pure R960 TiO<sub>2</sub>), ◇ = 0.5%, ○ = 1% (wet), Δ = 1% (dry), × = 2%.

TiO<sub>2</sub>. Moreover, AA addition prevents the adsorption of AA that is already present in the resin, which is important to preserve the adhesion characteristics of the cured coating to the fiber optics. The addition of AA should also accelerate organosilane hydrolysis towards formation of trihydroxymethacryloxypropylsilane. Thus, a novel combination of organosilanes with AA might be called synergistic.

The reactivity of the system filled with surface modified TiO<sub>2</sub> was measured at the bottom layer of the samples and was found to apparently decrease with increasing wt % silane treatment as shown in Figure 4. The treatment method, dry or wet (corresponding to the type of solvent used during treatment), was not found to significantly alter reactivity as could be seen for the 1 wt % treatment level. This at first glance is surprising as the organosilane treatment was expected at least to shield the resin from the adverse effects of titanium dioxide. So, the UV-reactivity results initially seemed discouraging since the treatment apparently reduced the UV curability



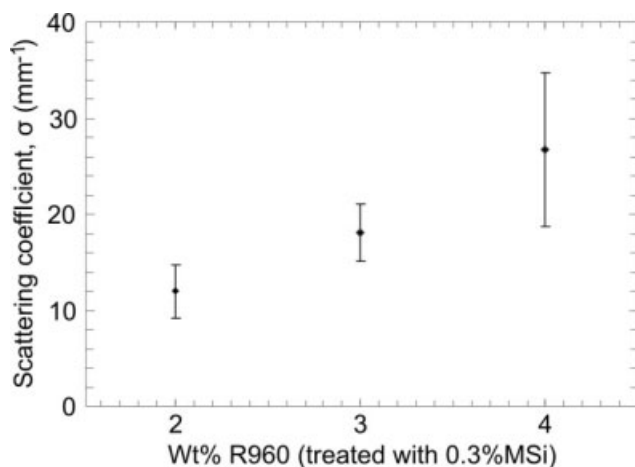
**Figure 5** Effect of TiO<sub>2</sub> loading on UV-reactivity and conversion at 0.3% surface treatment; □ = 0 wt %, ◇ = 2 wt %, ○ = 3 wt %, Δ = 4 wt %, × = 5 wt %.



**Figure 6** Effect of treatment level on the scattering of red laser light.

to a large extent. However, these data should be considered in conjunction with the described below results for scattering the light going through the coating. Hence, it should be realized again that the FTIR measurements for the coating materials were conducted at the substrate level (bottom of the sample). Thus, the photopolymerization initiation rate at the bottom of the sample is directly related to the number of photons of UV light reaching this layer. Tentatively it was explained that our surface treatment might be breaking up the TiO<sub>2</sub> agglomerates to a smaller size, increasing their number in the sample while obviously keeping the volume fraction the same. This would increase the number of scattering centers resulting in a more significant crowding effect and thus reduce the amount of UV radiation that is reaching bottom of the sample. However, the results shown in Figure 4 were obtained for a low level of TiO<sub>2</sub> loading (2 wt %, which with the density of the filler being almost four times higher than the matrix denotes the volume fraction of only ca. 0.5 vol %). Thus, more probable is increased light scattering due to a diffraction effect because it is related to the ratio of the particle size to the wavelength of light.

Moreover, lower cure rate at the bottom of the coating does not necessarily mean a detrimental effect of the filler to the resin. This is because the used TiO<sub>2</sub>, thanks to a combination of silica cladding and our silane exterior treatment, should be prevented from adversely affecting chemistry of the resin. Furthermore, since for curing we used low energy “black light” of low intensity that is commonly used and considered safe to organic matter, the direct photodegradation of resin degradation should not be significant. The recorded cure rates are acceptable but if desired the rates could be easily increased for a given treatment level by reducing the filler concentration. What is the most significant is



**Figure 7** Effect of TiO<sub>2</sub> loading on the scattering of red laser light.

the fact that by changing the level of the surface treatment we can attune the coating scattering properties to the wavelength of light to be scattered because the light scattering due to a diffraction effect is a function of the ratio of the light wavelength to the scattering center size. As discussed in the last section of the article, this has significant practical implications especially for photodynamic light scattering.

On the other hand, as shown in Figure 5, the increased loading of titanium dioxide also has a significant negative effect on the conversion and initial rate of photoinitiated polymerization, which might be expected. However, increasing the level of surface treatment seems to have a more potent effect on the photopolymerization.

### Light scattering measurements

Subsequent measurements indicated a significant increase in scattering efficiency of red (632.8 nm) laser light with the increasing level of silane treatment (i.e., increased weight parts silane per 100 parts TiO<sub>2</sub>). Figure 6 shows the scattering coefficient of the resin filled with 4% (by weight) of R960 treated with varying levels of the used methacryloyloxypropyl silane (MSi). The scattering efficiency increased significantly with the increasing extent of silane treatment.

To determine the effect of the amount of filler (measured in weight percent) on scattering efficiency, TiO<sub>2</sub> treated with 0.3 wt % MSi was used to fill the resin at 2, 3, and 4 wt % levels. Figure 7 shows the increase in scattering efficiency with increased filler concentration. The samples with 2 and 3 wt % filler levels scattered such a small amount of light that no observable change in light intensity was detectable. An attenuating (neutral)

light filter (OD 1.5) was used to increase the sensitivity of the detector for these experiments. Thus, Figure 6 and Figure 7 cannot be directly compared. For example, the data point for the 4 wt % level on Figure 7 is of a higher scattering coefficient than the corresponding data point in Figure 6. The light filter reduced the intensity of light hitting the detector increasing the apparent scattering coefficient.

These results showed that surface treating the TiO<sub>2</sub> with 3-(trimethoxysilyl) propyl methacrylate had a greater effect on scattering efficiency than increasing weight percent of the filler, i.e., improved dispersion of a lesser amount of TiO<sub>2</sub> was superior to increasing the weight loading. This will allow the coating process to use less filler to achieve the desired light scattering properties.

### Stability of the uncured coating material

Silane treatment, even at the lowest level, was observed to significantly increase the dispersion stability of the filler in the resin. Without filler treatment, the dispersion starts settling after 10 min and settles after several hours, but with our treatment the filled resin did not settle to any visible extent.

This, in combination with both UV curing and light scattering results indicates that the proposed treatment of TiO<sub>2</sub> enables preparation of stable coating materials well suited for fiberoptic probes. Moreover, the materials can have light scattering properties predesigned to suit different laser light wavelengths.

### Practical implications

Cylindrical diffusers are useful in interstitial cancer phototherapies; however, a limitation often encountered with interstitial phototherapies using the existing diffusers is unintentional charring at the surface of the diffusers. This unintentional charring is mostly related to the hot spots in the diffuser emission. Reported in this study translucent light scattering coatings enable homogenization of the light emitted by diffusers and hence the removal of "hot spots."

Moreover, it should be emphasized that the developed tunable materials enable the preparation of coatings that can have light scattering properties predesigned to match different laser light wavelengths. This is essential from the point of view of photodynamic cancer therapy, which uses specific laser light wavelengths to activate otherwise inert photosensitizers (photosensitizing drugs). Reactive oxygen species generated by photosensitizers are effective remedy for tumor eradication and the use of photosensitizers allows avoiding general toxicity that is a typical feature of chemotherapy and X-ray treatment. Nonetheless, different photosensitizers

require different wavelengths of light for activation and the current trend for advanced photodynamic cancer therapy is to employ photosensitizers at longer wavelengths to increase the treatment volume. For example, photosensitizers absorbing above 700 nm—where the absorption by the living tissue itself is low (tissue transparency window is at 780–830 nm)—are undergoing *in vitro* studies. Consequently, tunable coatings that not only allow homogenization of the light emitted by the diffusers but also allow adjusting their scattering properties to the light wavelengths required by different photosensitizers are of vital importance.

### CONCLUSIONS

The following are the main highlights of the reported study.

- Novel light scattering coating materials with tunable properties for fiber optic diffusers to be used in photodynamic cancer therapy were developed.
- The coating materials are designed to homogenize laser light decoupled from the fiberoptic diffuser.
- A class VI medical grade UV-curable acrylic resin was used for the polymer matrix and titanium dioxide (TiO<sub>2</sub>) was added to the resin to serve as a scattering agent.
- It was demonstrated that the UV curability of coatings containing TiO<sub>2</sub> was significantly influenced by the grade and surface treatment of the TiO<sub>2</sub> studied.
- All samples showed significant thermal postcuring as indicated by a shift in glass transition temperature by 10–20°C upon thermal treatment.
- A novel TiO<sub>2</sub> surface treatment methodology was developed based on unsaturated alkoxyorganosilanes combined with unsaturated carboxylic acids for compatibilizing TiO<sub>2</sub> to be used in the resin material studied.

- By adjusting the concentration of the modifying agent, the scattering efficiency and UV curability could be controlled by decreasing the effective particle size and enhancing the dispersibility of the powder filler within the resin.
- This modification will enable adjusting the effective size of TiO<sub>2</sub> particles to the wavelength of laser light to be scattered to maximize scattering efficiency in photodynamic cancer therapy and possibly also in other related forms of cancer treatment (interstitial laser photocoagulation or interstitial laser hyperthermia).

Financial support of the Ontario Centres of Excellence is gratefully acknowledged.

### References

1. Lilge, L.; Vesselov, L. M.; Whittington, W. L. *Lasers Surg Med* 2004, 34, 348.
2. Vesselov, L. M.; Whittington, W. L.; Lilge, L. *Appl Optics* 2005, 44, 2754.
3. Azan, V.; Lecamp, L.; Lebaudy, P.; Bunel, C. *Prog Org Coat* 2007, 58, 70.
4. Kim, Y. M.; Kostanski, L. K.; MacGregor, J. F. *Polymer* 2003, 44, 5103.
5. Kim, Y. M.; Kostanski, L. K.; MacGregor, J. F.; Hamielec, A. E. *J Therm Anal Cal* 2004, 78, 153.
6. Cho, J. D.; Kim, H. K.; Kim, Y. S.; Hong, J. W. *Polymer Testing* 2003, 22, 633.
7. Buxbaum, G. *Industrial Inorganic Pigments*; VCH: Weinheim, 1993.
8. Holzen, D.; Dibold, M.; Niedenzu, P. *TiO<sub>2</sub> Photochemistry and Color Applications*; E.I. DuPont de Nemours and Co, 2002.
9. Lange, J.; Altmann, N.; Kelly, C. T.; Halley, P. J. *Polymer* 2000, 41, 5949.
10. Kim, Y. M.; Kostanski, L. K.; MacGregor, J. F. *Polym Eng Sci* 2005 45, 1546.
11. Kostanski, L. K.; Kim, Y. M.; MacGregor, J. F.; Hamielec, A. E. *Designed Monom Polym* 2007, 10, 327.
12. Plueddemann, E. P. *Silane Coupling Agents*; Plenum: NY, 1991.
13. Dibold, U. *Surf Sci Rep* 2005, 48, 53.