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# A Phantom With Tissue-Like Optical Properties in the Visible and Near Infrared for Use in Photomedicine

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**Background and Objective:** Modeling of light transport in tissue requires development of theoretical models and experimental procedures, as well as tissue-simulating phantoms. Our purpose was to develop a phantom that matches the optical characteristics of human skin in the visible and near infrared spectral range.

**Study Design/Materials and Methods:** The phantom consists of a transparent silicone rubber in which  $\text{Al}_2\text{O}_3$  particles and a cosmetic powder are embedded. Layers with thickness as thin as 0.1 mm can be made. The optical properties of  $\text{Al}_2\text{O}_3$  particles and cosmetic powder, i.e., total attenuation, absorption and scattering coefficients, and phase function, have been determined in the visible and near infrared spectral range, by using direct and indirect techniques.

**Results:** By varying the concentration of scattering and absorbing particles, tissue-like layers can be produced with predictable optical properties. In particular, mixing at suitable concentration  $\text{Al}_2\text{O}_3$  particles and cosmetic powder with the silicone rubber, the optical properties of human skin have been simulated over a range of wavelengths from 400 to 1,000 nm. The comparison between the phantom diffuse reflectance spectrum and that of human skin, averaged over a sample of 260 patients, showed a good agreement.

**Conclusion:** The proposed technique allows to produce a stable and reproducible phantom, with accurately predictable optical properties, easy to make and to handle. This phantom is a useful tool for numerous applications involving light interaction with biologic tissue. *Lasers Surg. Med.* 28:237–243, 2001. © 2001 Wiley-Liss, Inc.

**Key words:**  $\text{Al}_2\text{O}_3$  particles; cosmetic powder; optical coefficients; polystyrene microspheres; tissue optics

## INTRODUCTION

In diagnostic and therapeutic applications of light in medicine, it is important to evaluate optical properties of biologic tissues, including total attenuation ( $\mu_t$ ), absorption ( $\mu_a$ ) and scattering coefficients ( $\mu_s$ ), and phase function. Direct and indirect methods, each with their own advantages and limitations, have been proposed to measure optical properties of turbid samples [1]. In direct techniques, optical coefficients are evaluated by measuring the fraction of light absorbed or scattered by optically thin (single scattering) tissue sections. In contrast, indirect

methods involve suitable measurements on thick samples (for example the total diffuse reflectance and transmittance) from which the optical coefficients are derived by solving the so-called inverse problem [2]. Briefly, the estimated optical properties are used as input data of a light propagation model and adjusted until the computed values of reflectance and transmittance match the measured values with the desired accuracy. To establish reliability of experimental techniques as well as of theoretical models of photon transport in biologic tissues, stable and reproducible phantoms are required with optical properties amenable to theoretical calculations. Many tissue-equivalent substances have been used to this purpose, including wax, agarose, and resin as basic materials and homogenized milk, Intralipid, blood and yeast suspension, ink, and polystyrene microspheres as absorbers and diffusers [3–7]. Currently, special phantoms are being developed to be used in the red (630 nm) or near-infrared portion of the spectrum, wavelengths relevant to photodynamic therapy and tissue transillumination studies. Unfortunately, most phantoms may mimic tissue optical properties at selected wavelengths only, are not stable in time, or cannot be used to simulate stratified tissues whose layers can have different optical properties. Our aim was to develop a stable and reproducible phantom whose optical properties can be predetermined and match, at selected wavelengths, those of any tissue and, in particular, of human skin over a spectral range between 400 and 1,000 nm.

## MATERIALS AND METHODS

### Preparation and Characteristics of the Phantom

The basic medium consists of a high-strength two-component room temperature-curing silicone (Elastosil RT 604, Wacker, Germany). The main component and the catalyst were mixed at a ratio of 9:1 by weight and were cured for at least 24 hours at room temperature before handling. Higher temperature can be used but shrinkage could result. The refractive index of the main component (1.404) is similar to that of soft tissue ( $n = 1.33–1.50$ ) [8]. Different absorption, fluorescence, and scattering proper-

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ties could be attained by adding chromophores, fluorophores, and scattering particles to the mixture.

To mimic the optical properties of human skin over a broad range of wavelengths, a cosmetic powder was used (Cream Powder, Deep Beige, Max Factor, UK). Among the available cosmetic powders, all characterized by different color and granulometry, we chose the product that better mixed with silicone. The composition of the used powder is only partially known: talc (>50%), titanium dioxide (<10%), zinc stearate and calcium carbonate (<10%), methylparaben and propylparaben (<0.5%), paraffinum liquidum, parfum, sorbitan sesquioleate, lanolin, polysorbate 60, BHA, CI 77499 (<1%), CI 77491 and CI 77492 (<5%). The diameter of the particles forming the powder was estimated by using an optical microscope (200 $\times$ ) and resulted in less than 100  $\mu\text{m}$ . As additional scatterers,  $\text{Al}_2\text{O}_3$  particles were also used (Sigma Aldrich Chemical Co., Italy). These particles are irregularly shaped with an average diameter of approximately 10  $\mu\text{m}$  and have a refractive index of 1.65 in the visible [Beck et al., personal communication]. Easy to mix with the silicone,  $\text{Al}_2\text{O}_3$  particles resulted homogeneously distributed after the curing process.

Suitable amounts of  $\text{Al}_2\text{O}_3$  particles and cosmetic powder were filtered through 400- and 140-mesh sieve, respectively, and then were mixed with the silicone. After mixing until homogeneous, the catalyst was added. The resulting mixture was stirred and cast into a mold composed of microscope slides, which were suitably spaced depending on the desired phantom thickness. Because the curing process is slow, any air bubbles entrapped during this procedure will migrate toward the free surface of the specimen, provided the layer is thin enough. The solid block was removed from the mold only after 24 hours and left at room temperature for at least 10 days, for the curing to be complete, before starting optical measurements.

## Optical Measurements

**Attenuation coefficient.** The total attenuation coefficient  $\mu_t$  of both  $\text{Al}_2\text{O}_3$  and cosmetic powder embedded in the solid silicone rubber was measured by using the set-up previously described by Marchesini et al. [9]. Measurements were performed at wavelengths of 488, 514, 590, 633, 645, 790, 825 nm by using an Argon or Argon-pumped dye laser. The light beam, collimated by a 2-mm-diameter pinhole, was split to continuously monitor the power of the incident beam. A photodiode, with 1  $\text{cm}^2$  active area, was used to detect the transmitted light, being scattered light rejected by a 2-mm-diameter pinhole placed immediately in front of the detector. The solid angle subtended by this aperture was  $5 \times 10^{-5}$  sr. The correctness of Beer's law was assumed for optically thin samples of material. Several 1-mm-thick samples with different concentration of either  $\text{Al}_2\text{O}_3$  and cosmetic powder were made. Each sample was measured in five different locations.

Accuracy of the attenuation coefficient measurements was checked by using an aqueous suspension of polystyrene microspheres (Polybead Polystyrene Microspheres, Polysciences, Trimital, Italy) of known uniform size and

refractive index. Experimental data were compared with that predicted from Mie theory, whose description is extensively reported in the literature [10,11]. Briefly, this theory gives a rigorous solution for the scattering of a plane monochromatic wave by a homogeneous sphere of any radius and of any composition situated in a homogeneous medium, provided that the concentration of the spheres is low enough to neglect multiple scattering. The microspheres used were either  $0.954 \pm 0.028$  or  $1.914 \pm 0.073$   $\mu\text{m}$  in diameter, with a refractive index of 1.59 at 589 nm (manufacturer's data). To minimize multiple scattering effects, 1-mm-thick samples with concentrations of 0.005%, 0.01%, 0.015%, and 0.02% were used. To avoid changes in optical properties due to aggregation, the microsphere suspensions were made fresh before each use.

**Scattering angular distribution.** The experimental arrangement for measuring the angular dependence  $P(\cos \theta)$  of light scattered by the samples has been previously described [9]. Briefly, the sample was placed at the center of a 15-cm-diameter cylindrical tank of distilled water and irradiated by a laser beam. A photodiode, with 1  $\text{cm}^2$  active area, was mounted on a rotary stage, which was manually rotated around the sample in the plane of the laser beam. A 2-mm-diameter pinhole restrained the measured scattered light within  $2 \times 10^{-4}$  sr. The measurements were performed at angles between 5 and 45 degrees and from 135 to 150 degrees with the sample fixed at 90 degrees with respect to the laser beam. For intermediate angles, the sample was rotated at 45 degrees. No azimuthal angle dependence of scattering was assumed. To minimize multiple scattering effects, 1-mm-thick samples with concentrations of 0.05% and 0.03% for  $\text{Al}_2\text{O}_3$  particles and cosmetic powder, respectively, were used. To describe  $P(\cos \theta)$  by an analytical expression, experimental results were fitted with the Henyey-Greenstein (HG) function at each of the selected wavelengths. Although this function may not exactly represent the actual phase function of biologic tissues, it has been shown experimentally to be a good approximation [2].

To check accuracy of the measurements of the scattering angular distribution,  $P(\cos \theta)$  was also measured for the polystyrene microspheres at a 488-nm wavelength and the results were compared with Mie theory. As predicted by the theory and retrospectively from the measurements of  $\mu_t$ , the mean free path for a microsphere concentration of 0.003% (by weight) was  $\cong 10$  mm. This figure is an order of magnitude greater than the sample thickness, so that multiple scattering may reasonably be neglected.

**Absorption and scattering coefficients.** To determine absorption and scattering coefficients of  $\text{Al}_2\text{O}_3$  and cosmetic powder, 1-mm-thick sections with different concentrations were prepared and the transmitted and reflected intensity under collimated illumination was measured by using a two-channel integrating sphere coupled to a spectrophotometer (Lamba 5, Perkin Elmer, Germany). A schematic diagram of the experimental arrangement is plotted in Figure 1. The light source used to illuminate the sample was a broadband tungsten lamp. Before each

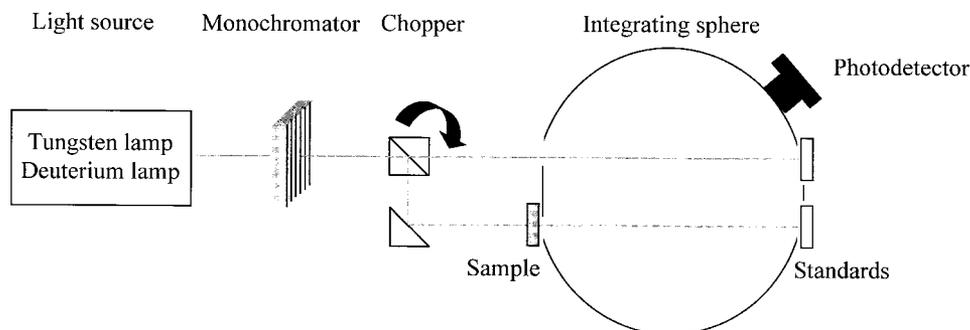


Fig. 1. Schematic diagram of the two-channel integrating sphere spectrophotometer. The setup shows position of sample and standards for transmittance measurement.

set of experiments, the spectrophotometer was calibrated in wavelength by using a deuterium lamp as a reference light source. The integrating sphere, with a diameter of 76 mm and coated with  $\text{BaSO}_4$ , was used to collect the light diffused either from the sample or from the standard. An end window photomultiplier was used as detector. This method, used to evaluate the diffuse reflectance and transmittance of a sample by comparison with a reflectance standard, does not require any a priori knowledge about the geometry of the sphere [12,13]. The reference standards, made of  $\text{BaSO}_4$ , and the sample were positioned in an appropriate location, depending on the optical properties being determined. For transmittance measurements, the sample was located in front of the entrance port and both rear ports covered with the reference standard (Fig. 1). For reflectance measurements, sample and standard were located behind the correspondent rear port.

The phantom optical parameters were determined by using the one-dimensional diffusion-approximation solution of the transport equation [14]. The calculation was carried out by using the algorithm by Jacques and Prahl [15]. Briefly, knowing the anisotropy factor  $g$  as a function of wavelength, an initial estimate of  $\mu_a$  and  $\mu_s$  was made and the expected diffuse transmittance  $T$  and reflectance  $R$  were calculated. Comparison with the measured  $T$  and  $R$  allowed a re-evaluation of  $\mu_a$  and  $\mu_s$ . Eventually, the algorithm converged to a unique set of absorption and scattering coefficients.

## RESULTS

### Cosmetic Powder and $\text{Al}_2\text{O}_3$ Particles Optical Properties

Figure 2 shows the total attenuation coefficient, as a function of concentration, of the 0.954- $\mu\text{m}$ -diameter microspheres, compared with that predicted by Mie theory. Measurements were performed at 633 nm. The best fit to the data gives a measured value of  $\mu_t = 0.365 \pm 0.018 \text{ mm}^{-1}$  for 0.01% concentration (by weight); this result is in excellent agreement with Mie theory of  $0.366 \pm 0.004 \text{ mm}^{-1}$ .

The total attenuation data for cosmetic powder and  $\text{Al}_2\text{O}_3$  are shown in Figure 3A,B, respectively. Each point of these plots resulted from a least-square fit of the

measurements at the corresponding wavelength. The total attenuation coefficients have been normalized to a 1% concentration (by weight) of the components.

With regard to scattering phase functions, Figure 4 shows experimental values of  $P(\cos \theta)$  versus  $\theta$  for the 0.954- $\mu\text{m}$ -diameter polystyrene microspheres. Measurements were performed at 488 nm. A linear combination of two Henyey-Greenstein functions was used to fit experimental data. The result of the fitting (solid line) indicated that scattering may be well described by a superimposition of two HG( $g$ ) functions, one characterized by a forward-directed scattering component and the other by a backward-directed component, with the main contribution due to the former [9]. The average cosine of scattering resulted in  $0.90 \pm 0.02$ . A FORTRAN version of the program given by Bohren and Huffmann [10] was used to calculate the average cosine of scattering for the microspheres accord-

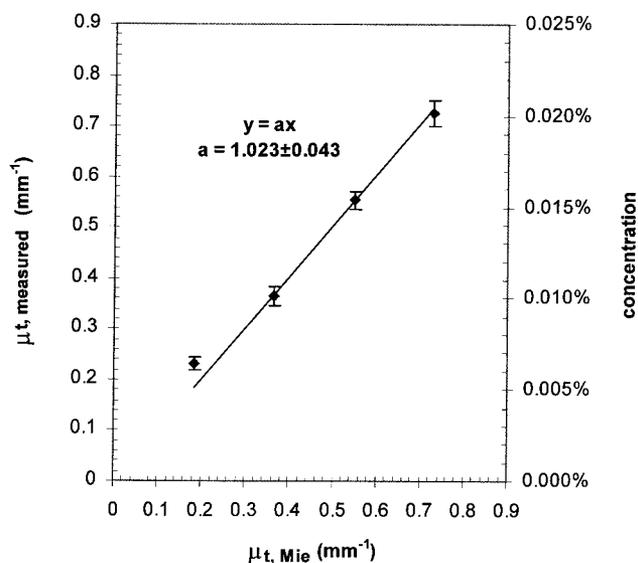


Fig. 2. Total attenuation coefficient, as a function of concentration, of 0.954- $\mu\text{m}$ -diameter microspheres. Comparison between experimental mean results and Mie theory.

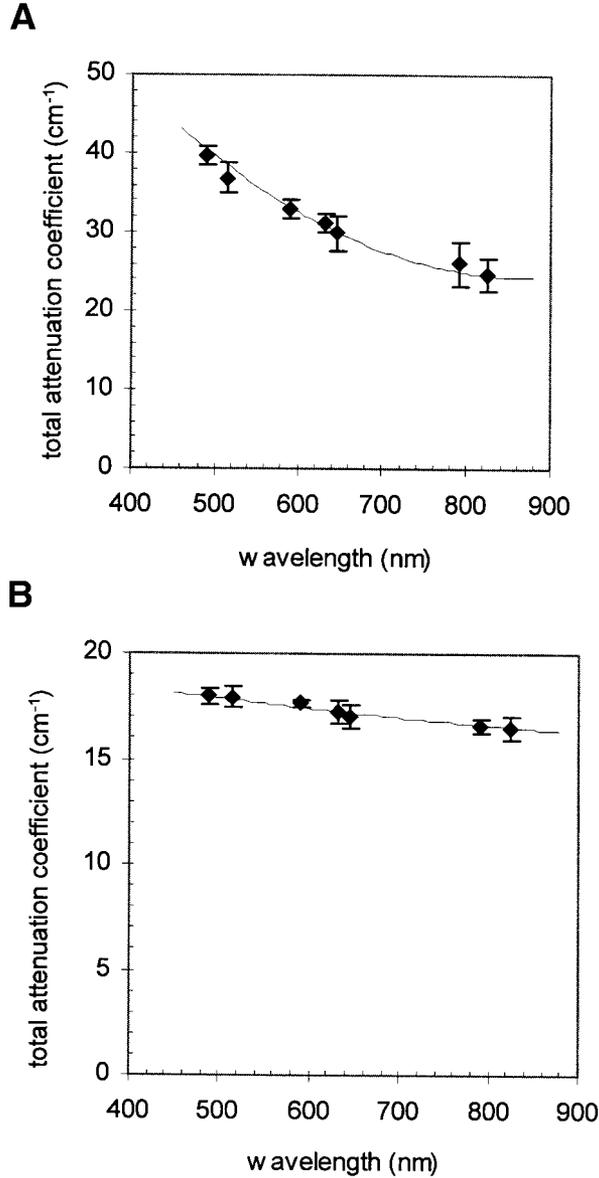


Fig. 3. Total attenuation coefficients of cosmetic powder (A), and  $\text{Al}_2\text{O}_3$  (B) as a function of wavelength.

ing to the Mie theory. The resulting value of 0.93 is in a good agreement with the experimental result. To measure the angular distribution of light scattered from cosmetic powder and  $\text{Al}_2\text{O}_3$  particles, three thin samples characterised by a low scattering coefficient were prepared. The average cosine of scattering was found fitting  $P(\cos\theta)$  data with a linear combination of two Henyey-Greenstein functions. The wavelength dependence of  $g$  is shown in Figure 5.

The calculated absorption coefficients of cosmetic powder and  $\text{Al}_2\text{O}_3$ , normalized to 1% concentration (by weight) of the components, are shown in Figure 6A,B, respectively.

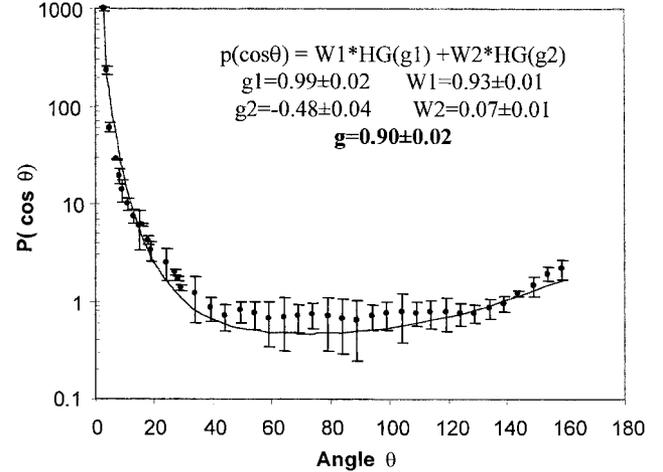


Fig. 4. Scattering phase function of 0.954- $\mu\text{m}$ -diameter polystyrene microspheres ( $n = 1.59$ ) at 488 nm. Three samples with the same concentration have been prepared and submitted to measurements. Experimental points have been fitted by using a linear combination of two Henyey-Greenstein functions (solid line).

The absorption coefficient of the cosmetic powder is 2 orders of magnitude greater than that of  $\text{Al}_2\text{O}_3$ .

#### Human Skin Optical Properties Simulation

Knowing the optical coefficients of both  $\text{Al}_2\text{O}_3$  particles and cosmetic powder, by varying their concentration phantoms with predictable optical properties can be produced. In particular, we were interested in the simulation of the optical properties of human skin. To evaluate the suitable concentration of the two components, we assumed that the following additivity law holds:

$$\mu_t^{\text{CP+A}} \equiv \mu_a^{\text{CP+A}} + \mu_s^{\text{CP+A}} = \mu_a^{\text{CP}} + \mu_a^{\text{A}} + \mu_s^{\text{CP}} + \mu_s^{\text{A}} \quad (1)$$

where  $\mu_{t,a,s}^{\text{CP+A}}$  represent total attenuation, absorption and scattering coefficients, respectively, of a phantom containing cosmetic powder ( $^{\text{CP}}$ ) and  $\text{Al}_2\text{O}_3$  ( $^{\text{A}}$ ). From equation (1) it follows:

$$\mu_a^{\text{CP+A}} \cong \mu_a^{\text{CP}} = \mu_a^{\text{CP}\%} \cdot c^{\text{CP}} \quad (2)$$

$$\mu_s^{\text{CP+A}} = \mu_s^{\text{CP}} + \mu_s^{\text{A}} = \mu_s^{\text{CP}\%} \cdot c^{\text{CP}} + \mu_s^{\text{A}\%} \cdot c^{\text{A}} \quad (3)$$

where  $\mu_{a,s}^{\text{CP,A}\%}$  represents the absorption and scattering coefficient of a single component normalized to 1% concentration (by weight), and  $c^{\text{CP,A}}$  represents the correspondent concentration in silicone. The absorption coefficient of  $\text{Al}_2\text{O}_3$  particles has not been considered in equation (2) being 2 orders of magnitude smaller than that of cosmetic powder. By imposing  $\mu_a^{\text{CP+A}}$  and  $\mu_s^{\text{CP+A}}$ , the mean values of human skin optical properties reported in the literature [16], i.e.,  $\mu_a = 2.1 \pm 0.5 \text{ cm}^{-1}$  and  $\mu_s = 224.1 \pm 32.1 \text{ cm}^{-1}$  at 633 nm,  $c^{\text{CP}}$  and  $c^{\text{A}}$  were obtained.

The samples so realized have been optically characterized by using the same technique as previously reported for the single components. The total attenuation and

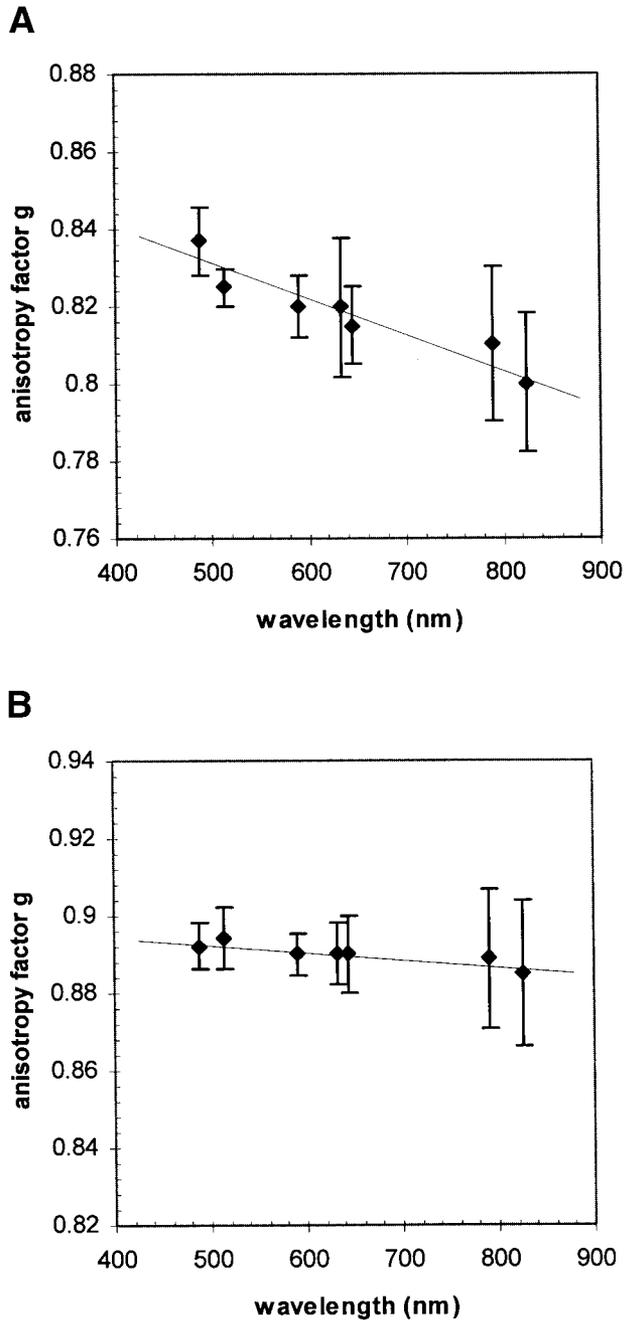


Fig. 5. Anisotropy factor  $g$ , as a function of wavelength, of cosmetic powder (A) and  $\text{Al}_2\text{O}_3$  (B).

absorption coefficients as a function of wavelength are shown in Figure 7. In particular,  $\mu_t$  and  $\mu_a$  at 633 nm resulted in  $227.4 \pm 6.8 \text{ cm}^{-1}$  and  $1.9 \pm 0.1 \text{ cm}^{-1}$ , respectively, in a good agreement with the expected values. The average value of the asymmetry factor  $g$ , in the wavelength range of interest, resulted in  $0.88 \pm 0.03$ , similar to the values reported for most biologic tissues [9,16].

The reflectance spectrum of the realized tissue-like phantom was compared with that of in vivo human skin of

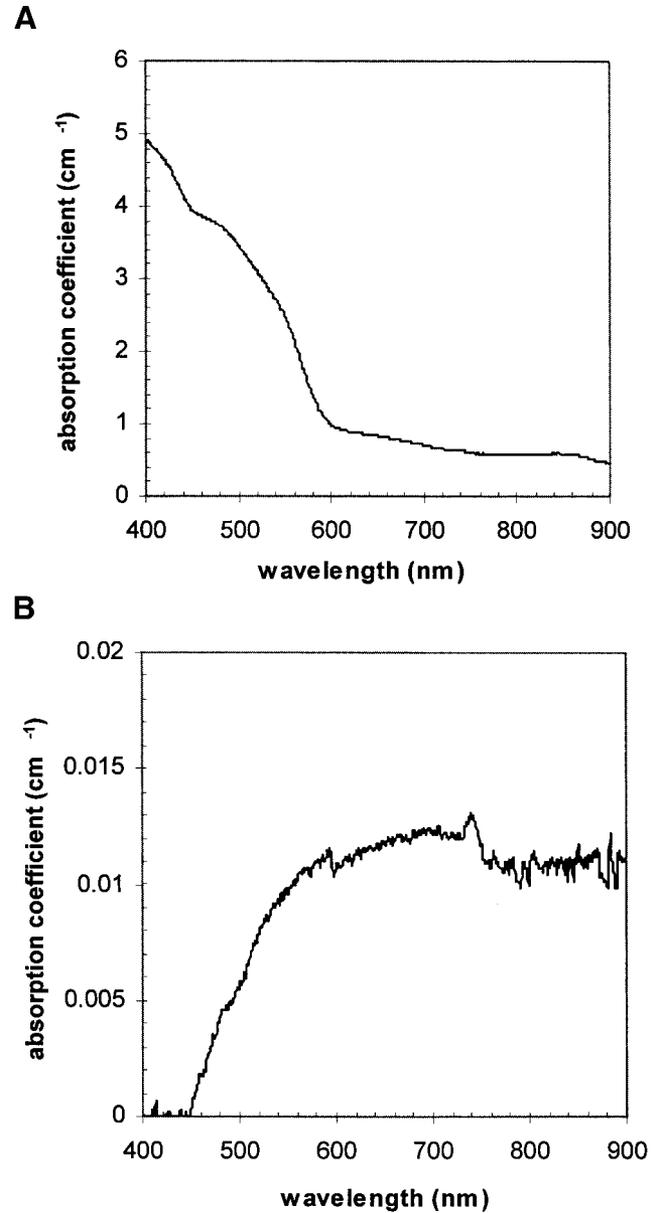


Fig. 6. Absorption coefficient of cosmetic powder (A) and  $\text{Al}_2\text{O}_3$  (B) as a function of wavelength.

260 patients, who were recruited for a special project on melanoma detection [17]. Figure 8 reports the mean value ( $\pm$ SD) of the human skin reflectance as well as the measured reflectance of the phantom.

## DISCUSSION

Differently composed phantoms to simulate human tissue have been described in the literature. One of the most popular phantoms is an aqueous solution of a scattering fatty medium, i.e., Intralipid [5], and a water-soluble dye, i.e., India ink [18]. This kind of phantom can be realized in proper dilution to reproduce the optical proper-

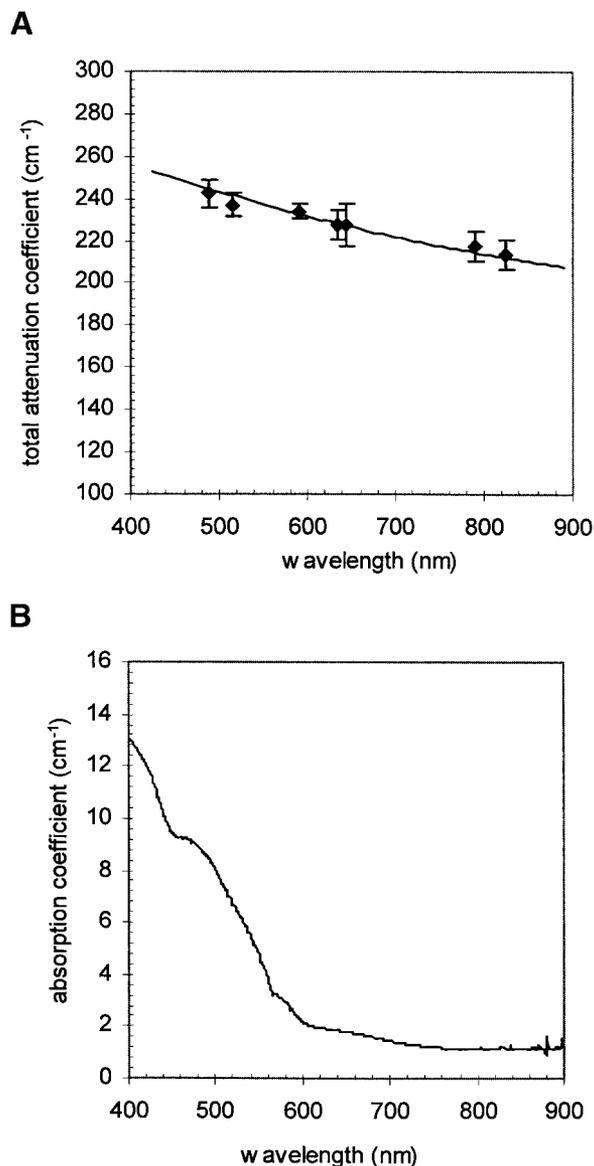


Fig. 7. Total attenuation (A) and absorption (B) coefficients, as functions of wavelength, of the tissue-like phantom. Concentration of cosmetic powder and  $\text{Al}_2\text{O}_3$  were 2.4% and 8.8%, respectively.

ties of biologic tissues, in terms of absorption and scattering coefficients. An important limitation of this liquid phantom is the difficulty in reproducing layered structures [19]. Other phantoms can be made up of Agar [6,20] or alimentary gelatin [21,22], in which absorbing and scattering substances are embedded. These phantoms are easy to make and to handle, and multilayered structures are feasible. The main limitation is that they are not stable over long periods of time, usually no more than 2 months [6,20]. In principle, optical properties of the previously reported phantoms could match those of biologic tissues over a broad range of wavelengths. However, to our know-

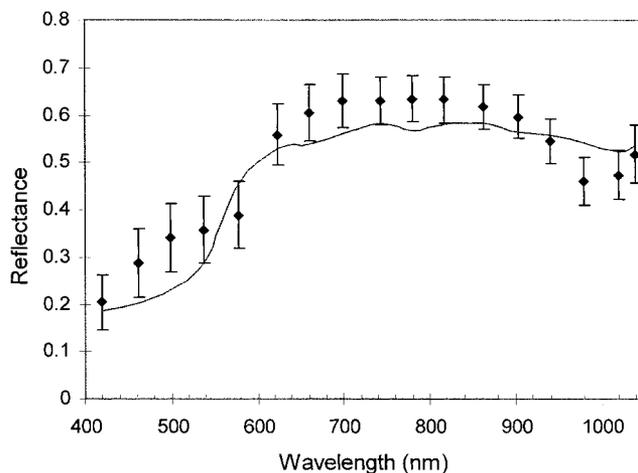


Fig. 8. Comparison between phantom diffuse reflectance spectrum (solid line) and mean value ( $\pm$  SD) of human skin reflectance of 260 patients (symbols).

ledge, phantoms suitable to be simultaneously used at different wavelengths have not yet been developed.

This work describes the preparation of a silicon-based phantom that may accurately mimic the optical properties of biologic tissues in the visible and near infrared spectral range, with the further advantage that it can be cast into arbitrary shapes. Furthermore, by means of sequential castings, layered phantoms with different optical properties can be produced, thus making feasible the manufacturing of anatomically realistic phantoms. Different absorption and scattering properties can be attained by adding to the silicone matrix cosmetic powder and  $\text{Al}_2\text{O}_3$  particles. Preliminary attempts to simulate optical properties of human skin by mixing blood to silicone resulted in a phantom not stable over the time. On the contrary, the optical properties of the used compounds did not show significant changes over a period of 1 year.

The optical properties of the phantom are reproducible, provided that the scattering and absorbing substances are thoroughly dispersed in the silicone rubber. The macroscopic homogeneity of the phantom was checked, by measuring transmittance at several locations of thin samples, and was greater than 95%.

The optical properties of the single components have been calculated by using direct and indirect techniques. Measurements of  $\mu_t$  and  $g$  of the polystyrene microspheres showed a good agreement between experimental results and the Mie theory, thus providing confirmation of the validity of the method used. The absorption and scattering coefficients were calculated on the basis of the diffusion approximation which, according to the theory, gives the best results when tissue is highly scattering (i.e., albedo  $\frac{\mu_s}{\mu_t}$  approaches unity). However, it has been reported [23] that diffusion approximation still holds, with reasonable accuracy, when albedo is greater than 0.6. This finding made us confident in the reliability of our results, because, over the range of wavelengths and concentrations used, albedo

approaches unity and is greater than 0.9 (worst case, at 488 nm) in the case of  $\text{Al}_2\text{O}_3$  and cosmetic powder, respectively.

After characterization of the optical properties of the single components, by varying their concentration and assuming the correctness of the additivity law of the optical coefficients, a tissue-like phantom with predictable optical properties can be produced. The validity of the additivity law has been tested by comparing the predicted optical coefficients with those experimentally determined. The resulting differences were less than 5%.

The method we propose enables the manufacture of a phantom easy to make, to handle, and to mold in different shapes, which may be very useful in photomedicine studies, for instance, simulating a desired *in vivo* condition, as well as to compare light-transport theoretical models with experimental measurements.

As an example of simulation of an *in vivo* circumstance, a phantom with features similar to that of human skin has been modeled. The availability of this kind of phantom, able to mimic the optical properties of the skin over a broad range of wavelengths, will help us in the basic research of a project, currently under development at the Istituto Nazionale Tumori of Milan, whose aim is to optimize a computerized multispectral image analysis for the diagnosis of cutaneous pigmented lesions [17]. An optically heterogeneous phantom, characterized by a multilayer structure, has already been built to simulate the geometry of human skin, and the possibility of simulating heterogeneities with melanin (i.e., to mimic pigmented lesions) is currently under study.

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