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IMAGING OF PORT WINE STAIN LESIONS USING A MULTI-SENSOR PHOTOACOUSTIC PROBE

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ABSTRACT

Successful treatment of port wine stain (PWS) birthmarks in human skin utilizes cryogen spray cooling (CSC) in conjunction with laser treatment. CSC pre-cools the epidermis to protect it from subsequent laser irradiation which raises the temperature of both the epidermis and the deeper PWS. As the epidermal temperature is depressed by cryogen, damage to the skin surface is minimized while the PWS reaches temperatures sufficient to permanently damage the lesion. In order to optimize cooling and laser heating dosages and to properly guide laser therapy, the spatial relationship of epidermal melanin and PWS must be known.

Photoacoustic depth profiling of human skin uses low energy, nanosecond pulses of laser light to induce acoustic waves in optically absorbing media, such as blood and melanin. We used a 532 nm Nd:YAG laser to measure total epidermal melanin content in human skin, comparing the results with visible reflectance spectroscopy. Furthermore, we performed numerical simulations of photoacoustic generation in skin, showing that a hemisperical acoustic sensor array could be used to reconstruct the rete pattern of epidermal melanin in the basal layer. Finally, we built a hemispherical probe for use in future experiments for imaging of human skin.

INTRODUCTION

Epidermal melanin content has been measured noninvasively by Kollias, *et al*. [1, 2] and Svaasand *et al*. [3], among others, using visible reflectance spectroscopy (VRS). As most laser dermatologic procedures result in absorption of laser light by melanin, intended or not, the total content and distribution of melanin are required to optimize a laser procedure, such as laser therapy of port wine stain (PWS) skin [4, 5]. In this procedure, laser energy is used to thermally coagulate the blood vessels in a PWS lesion. Cryogen spray is used to pre-cool the epidermis, to prevent scarring due to absorption of high energy laser light. In order to optimize the laser and cryogen parameters, the spatial relationship of epidermal melanin and the PWS vessels must be known.

We propose to use photoacoustic generation and analysis in human skin to determine total epidermal melanin content and for possible depth profiling and imaging of melanin. Photoacoustic methods have been used for probing subsurface structures in tissue and tissue phantoms [6–9]. We previously performed depth profiling of PWS skin [10] and measured epidermal melanin content in human skin [11]. We continue those studies to measure photoacoustically the total melanin content in human skin and construct a multi-sensor photoacoustic probe for imaging of melanin in human skin.

In this paper we measure epidermal melanin content in human subjects using a single sensor photoacoustic probe. We then simulate photoacoustic generation and detection in human skin for various geometries of melanin expected in human skin and show backprojection reconstructions using a multi-sensor hemispherical photoacoustic probe. Finally we construct a multi-sensor photoacoustic probe for use in future studies for image reconstruction of skin structure.

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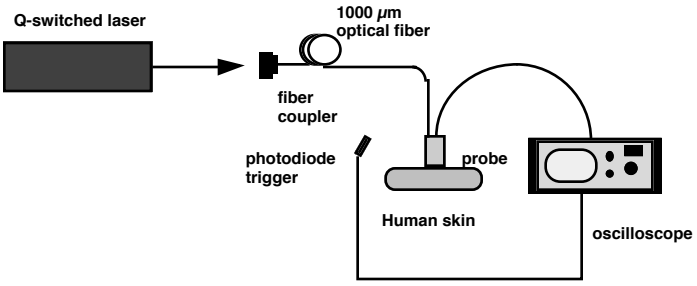

Figure 1. THE PHOTOACOUSTIC APPARATUS USED FOR MEASUREMENT OF EPIDERMAL MELANIN IN HUMAN SKIN.

MATERIALS AND METHODS

Photoacoustic Apparatus

The apparatus used for measuring photoacoustic melanin is shown in Figure 1. The laser was a Q-switched, frequency doubled Nd:YAG (Quantel Brilliant, Big Sky Laser, Bozeman, MT) operating at 532 nm. The pulse duration was 4 ns. The laser output was coupled into a 1000 μm diameter quartz optical fiber which terminated in a small, cylindrical acrylic handpiece, measuring 16 mm in diameter and 22 mm in length. The optical fiber was directed to a 1.5 mm spot at the bottom of the probe, which was placed onto the skin surface for measurements. Laser energy ranged from 3–6 mJ per pulse in all experiments, though pulse energy was determined to 5% accuracy for each measurement. Radiant exposures were approximately 0.15–0.35 J/ cm^2. A piezoelectric element made from polyvinylidene fluoride (PVDF) was recessed 3 mm into the probe housing detected any photoacoustic waves generated by laser light and created an acoustic delay of approximately 2 μs. Water was used to couple the sensor and skin surface acoustically. The piezoelectric element was attached to a rigid coaxial cable which was connected to an instrumentation amplifier with a gain of 125 (SR445, Stanford Research Systems, Sunnyvale, CA). The amplified signal was sent to an oscilloscope (TDS 3014, Tektronix, Wilsonville, OR) with a bandwidth of 100 MHz sampled at 1.25 gigasamples per second and was triggered by a photodiode (DET-210, Thorlabs, Inc., Newton, NJ) which monitored laser output. The waveforms were averages of 32 pulses.

Measurement of Total Melanin Content

We measured the epidermal melanin of ten human subjects on their hands, inner forearms, and foreheads using photoacoustic and VRS means. The skintypes varied from I–VI, covering very light skin caucasians to dark skinned africans. Care was taken to avoid hair, an obvious optical absorber, so that all readings reflected the actual content of epidermal melanin. Photoacoustic measurement of melanin content was derived from the total energy absorbed, which was represented by the area under the initial pressure curve of the photoacoustic waveforms. Melanin was assumed to be within the first 150 μm, so only the initial waveform was used for this measurment. Subsequent waveforms were assumed to be diffractive or deeper absorbing structures and were ignored.

$$\mathrm{E_t} \propto \int_0^\infty \mathrm{p_0(z)dz} \tag{1}$$

where $\mathrm{E_t}$ is total absorbed energy and $p_0(z)$ is the initial pressure as a function of depth, z. The integral gives a quantity that is expressed in terms of J/ cm^2, so total energy detected is related to this quantity by the detector active area. Thus, this integral is proportional to epidermal melanin content and, after normalizing by total pulse energy, can be defined as a preliminary photoacoustic melanin index (pPAMI). This index is still dependent on acoustic detector active area, so scaling by active area gives a device independent PAMI. Scaling of the active area was achieved by taking the ratio of active area to laser spot size, hence, PAMI is dimensionless.

$$\mathrm{PAMI} = \frac{\mathrm{A_t}}{\mathrm{A_s}} \frac{\int_0^\infty \mathrm{p_0(z)dz}}{\mathrm{E_t}} \tag{2}$$

We compare photoacoustic measurements with VRS measurements, a well established method. The apparatus for performing VRS measurements consisted of a spectrometer, white light source, integrating sphere, and computer The spectrometer (HP 8452A, Hewlett Packard, Palo Alto, CA) was used to measure 500–820 nm. The light source was a tungsten halogen lamp within the integrating sphere (RSA-HP-84, Labsphere, North Sutton, NH) and was coupled to the spectrometer. The skin surface of human subjects was positioned at the 25.4 mm diameter port of the integrating sphere and sampled with an integration time of 500 ms. UV-Visible ChemStation software (Hewlett Packard, Palo Alto, CA) was used as an interface to the spectrometer. A 99% diffuse reflectance standard (WS-1, Ocean Optics, Dunedin, FL) was used to calibrate the spectrometer. Analysis of the reflectance consisted of fitting the spectra using optical diffusion theory and deriving the melanin content iteratively. VRS melanin index was defined as the absorption coefficient of melanin at 690 nm.

Photoacoustic Simulations

Photoacoustic waveforms were simulated using C code. The time integral of the acoustic pressure is the velocity potential, which is better suited for use in image reconstruction as it is non-negative and represents the optical energy deposition in tissue.

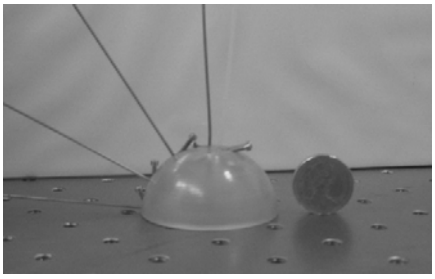

Figure 2. THE NEW MULTI-SENSOR PROBE CONSTRUCTED FOR IMAGING OF MELANIN DISTRIBUTION IN HUMAN SKIN.

Velocity potential can be expressed as

$$\phi(r,t) = \frac{-\beta}{4\pi\rho C_p} \int \frac{W(r')}{(r-r')} \delta(t - \frac{(r-r')}{c_s}) d^3r' \qquad (3)$$

where β is the thermal expansivity, ρ is density, C_p is the specific heat, W(r') is the energy deposition, and δ is the Dirac delta. For computation, velocity potential can be described as

$$\phi(k) = \frac{-\beta}{4\pi\rho C_p} \frac{1}{\Delta t} \sum_i \frac{W(i)}{r(i)} V(i) \qquad (4)$$

where Δt is the time step, V(i) is the local subvolume, and k = round($\frac{r_i}{c_s \Delta t}$) is the time index. Using this equation, time resolved velocity potentials can be simulated due to laser irradiation of absorbing tissue.

We simulated photoacoustic waves generated in flat, planar layers of melanin, assuming a bulk absorption coefficient of 60 cm^{-1}. We also showed photoacoustic waves generated in a sinusoidally varying epidermal melanin sheet, with a period of 50 μm and an amplitude of 50 μm. We compared the photoacoustic waveforms arising from these geometries and showed backprojection reconstruction of them. We also compared a flat sheet of melanin to a flat sheet with a 20 μm melanin invasion, simulating a melanocytic invasion into the dermis.

Multi-sensor Probe

The multi-sensor photoacoustic probe is shown in Figure 2. It was made from a hemispherical acrylic housing with a 1000 μm optical fiber for laser light delivery and four acoustic sensors positioned at 0, 30, 60, and 90^o. The probe will be used with the same apparatus shown above, but may allow for accurate reconstruction of melanin distribution in human skin.

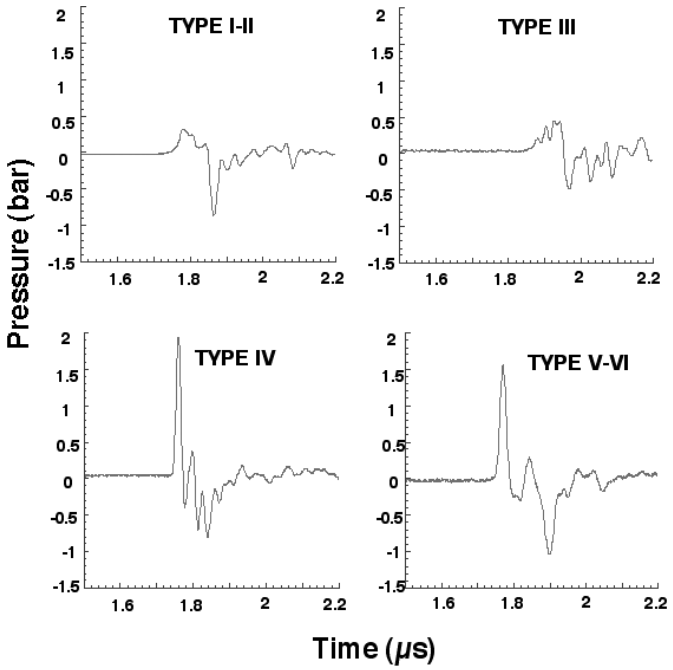

Figure 3. PHOTOACOUSTIC WAVEFORMS FROM EPIDERMAL MELANIN FOR VARIOUS SKIN TYPES. THE AREA UNDER THE FIRST PRESSURE PEAK INDICATES TOTAL LASER ENERGY ABSORBED AND HENCE TOTAL MELANIN CONTENT.

RESULTS

Photoacoustic Measurement of Epidermal Melanin

Four photoacoustic waveforms are shown in Figure 3. Total melanin content can be derived from the area under the first pressure peak. Later signal content is primarily diffraction and deeper optical absorbers beneath the epidermis. A comparison of photoacoustic and VRS measurements of total melanin content is shown in Figure 4.

Photoacoustic Waveforms

A simulation of waveforms for the 0^o and 90^o acoustic sensors is shown in Figure 5 for a planar melanin sheet and a sinusoidally varying epidermal sheet.

Backprojection Imaging

A simulation of a backprojection image of planar sheet of melanin and sinusoidal undulating sheet of melanin are shown in Figure 6. These sheets represent a simplified epidermis that is composed of a homogeneous material with melanin as an optical absorber.

A simulation of a backprojection image of a 100 μm planar melanin sheet and such a sheet and a 20 μm melanin invasion into the dermis is shown in Figure 7. The the left image indicates a

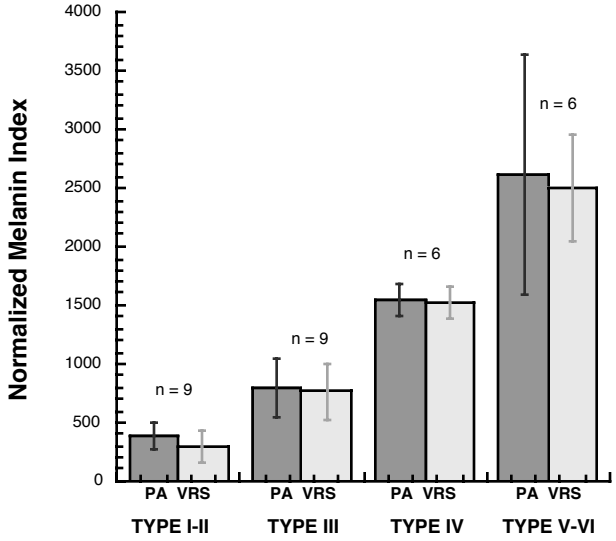

Figure 4. COMPARISON OF PHOTOACOUSTIC AND VRS MEASUREMENTS OF EPIDERMAL MELANIN SHOW EXCELLENT CORRELATION FOR ALL SKIN TYPES EXCEPT THE DARKEST, TYPE VI.

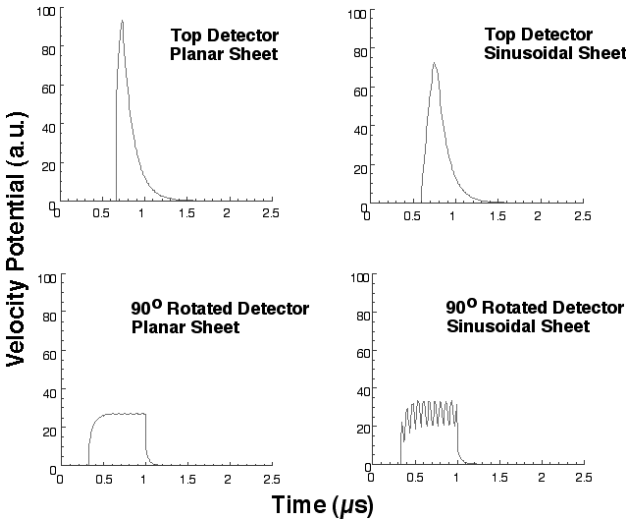

Figure 5. PHOTOACOUSTIC WAVEFORMS FROM PLANAR AND SINUSOIDAL MELANIN SHEETS AS DETECTED BY ACOUSTIC SENSORS AT THE 0^O AND 90^O POSITIONS.

planar sheet of approximately 100 μm thickness, while the image on the right indicates a small invasion, evident from the false color extending underneath the main mass of the sheet.

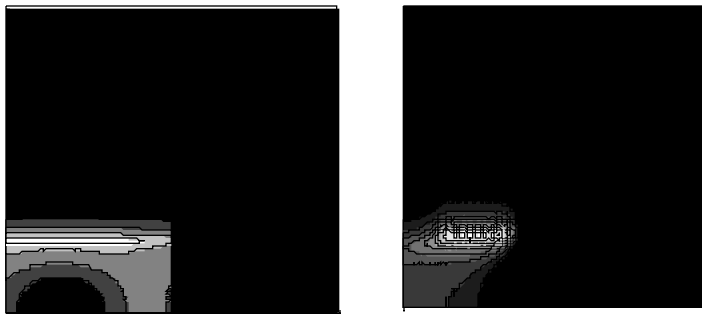

Figure 6. PHOTOACOUSTIC BACKPROJECTION RECONSTRUCTION OF PLANAR AND SINUSOIDALLY VARYING MELANIN SHEETS.

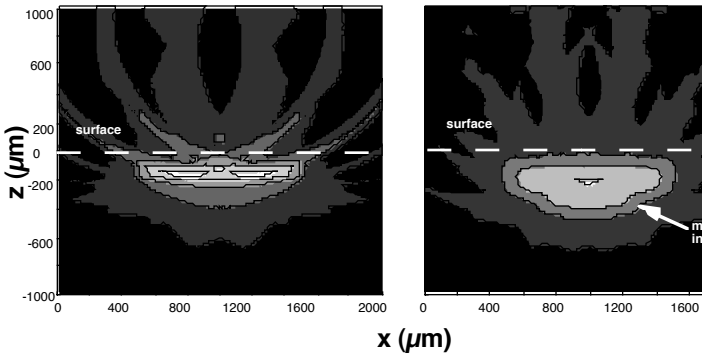

Figure 7. PHOTOACOUSTIC BACKPROJECTION RECONSTRUCTION OF A 100 MICRON THICK PLANAR SHEET AND A PLANAR SHEET WITH A 20 MICRON MELANIN INVASION INTO THE DERMIS

DISCUSSION

Epidermal melanin measurement is important, not only for laser dermatologic procedures, but also for monitoring and detection of melanocytic nevi and melanoma in human skin. If a photoacoustic method can be implemented to image melanin in human skin, it may be possible to provide clinically relevent information for clinicians involved in treatment of such conditions. We have shown that not only is it possible to measure total melanin content in skin using photoacoustics, but that it may be possible to image melanin in skin, showing the distribution of melanin in the epidermis and possible invasion of melanin or melanotic lesions into the dermis.

Photoacoustic Measurement of Epidermal Melanin

Photoacoustic measurements of epidermal melanin showed excellent correlation with VRS. However, the deviation in measurement of the darkest skin type was great, indicating difficulty in making absolute measurement in skin with high levels of melanin. Future work may involve varying laser wavelength to

choose spectral regions of lesser absorption in order to improve measurements. Otherwise, total epidermal melanin content can be quantified well using the photoacoustic method.

Backprojection Imaging

Back projection reconstruction simulations using the hemispherical multi-sensor probe showed that a single element detector, such as the one used in the measurement of total epidermal melanin, is incapable of imaging melanin distribution in a complicated geometry. Figure 5 showed that using only the top detector (0o detector), a planar sheet is indistinguisable from a sinusoidal sheet. It is only when the 90o rotated detector is used that the sinusoidal pattern is seen. Such a pattern is also seen to lesser extents at intermediate angles. These intermediate angles would be important for imaging more irregular geometries, such as those seen in the normal rete pattern of the epidermis. Using such a multi-sensor probe was used to show the capability for imaging planar and sinusoidal melanin distributions (Figure 6) and also for detecting melanin invasion into the dermis (Figure 7), such as would be seen in pathological conditions such as melanoma. We propose to use the multi-sensor probe in future work to measure and image skin structure, to include normal melanin distribution, PWS skin, and melanotic lesions.

ACKNOWLEDGMENTS

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