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Hand-held pulsed photothermal radiometry system to estimate epidermal temperature rise during laser therapy

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Background/purpose: During laser therapy of port wine stain (PWS) birthmarks in human skin, measurement of the epidermal temperature rise (ΔT_{epi}) is important to determine the maximal permissible light dose. In order to measure ΔT_{epi} on a specific PWS skin site, we developed an AC-coupled hand-held pulsed photothermal radiometry (PPTR) system, which overcomes the *in vivo* measurement limitations of bench-top systems.

Methods: The developed hand-held PPTR system consists of an infrared (IR) lens, AC-coupled thermoelectrically cooled IR detector, laser hand-piece holder, and positioning aperture. The raw AC-coupled signal was integrated to obtain a higher signal-to-noise ratio (SNR). The experimental temperature difference (ΔT) calibration was compared with theoretical computations. *In vitro* and *in vivo* measurements of ΔT were performed with a tissue phantom as a function of radiant exposure and human subject as a function of melanin concentration, respectively.

Results: The integrated AC-coupled signal provided higher SNR as compared with the raw AC-coupled signal. The experimental ΔT calibration resulted in good agreements with the theoretical results. The *in vitro* and *in vivo* results also presented good agreements with theory.

Conclusions: A fiber-free, hand-held AC-coupled PPTR system is capable of accurate epidermis temperature rise (ΔT_{epi}) measurements of human skin during pulsed laser exposure.

Key words: AC-coupled detection – skin color – pulsed photothermal radiometry – thermography – IR temperature – chromameter

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To treat hypervascular dermatologic conditions such as port wine stain (PWS) birthmarks, laser therapy is commonly performed. The goal of such a therapeutic procedure is to selectively heat a subsurface target (e.g., abnormal blood vessels). As epidermal melanin also absorbs at laser wavelengths typically used for these procedures (e.g., 585–600 nm), a maximum safe radiant exposure (H_{max}) can be defined, above which epidermal thermal damage would occur. For laser pulse durations on the order of milliseconds, a threshold epidermal temperature (T_{thresh}) of 70 °C has been assumed (1).

A measure of epidermal heating would provide clinicians with an objective means to determine H_{max}. Pulsed photothermal radiometry (PPTR) (2–5) can provide accurate measurements of epidermal heating. In PPTR, time-resolved blackbody emission from a sample is measured with a mid-infrared (IR) detection system after pulsed laser exposure. Algorithms have been developed to convert the acquired IR signal to a depth profile of the initial temperature distribution immediately after pulsed laser exposure (2, 4); this profile provides information on the depth and degree of heating of targeted chromophores (e.g., epidermal melanin and hemoglobin molecules in blood). PPTR can be used to estimate the epidermal heating and the temperature rise (ΔT_{epi}) at a given subtherapeutic radiant exposure H_o. If ambient skin temperature is assumed to be 30 °C, H_{max} is approximately equal to $(40\,^{\circ}\mathrm{C}) \times (H_o/\Delta T_{epi})$, where 40 °C is the difference between the assumed T_{thresh} for epidermal damage (70 °C) and ambient skin temperature (30 °C).

A key component of typical PPTR systems is a relatively bulky liquid nitrogen cooled detector or focal plane array. Katzir and colleagues (6–8) have investigated the use of IR fibers to deliver blackbody emission to a benchtop detector, but these fibers tend to be expensive. To provide the clinician with a user friendly PPTR system that can be used to estimate H_{max} at selected skin sites, we designed a small, fiber-free, hand-held system. Inasmuch as currently available thermoelectrically cooled detectors are AC coupled, the goal of this study was to determine the feasibility and accuracy of an AC-coupled PPTR system for ΔT_{epi} measurements. We characterized AC-coupled PPTR system performance, and then compared measurements of ΔT_{epi} with quantitative skin melanin content measurements to assess system accuracy.

Materials and Methods

AC-coupled PPTR system

Figure 1 shows a photograph of the small, fiber-free, hand-held PPTR system developed in this study. The key component of the system was a customized thermoelectrically cooled HgCdZnTe IR detector (Oriel, Stratford, CT, USA) operating in photovoltaic mode. Specifications of the detector include a $2 \times 2\,\text{mm}^2$ active area, detectivity D* of 1.2×10^{10} at 6 μm, and spectral sensitivity of 2–6 μm. A built-in preamplifier with a bandwidth of 0.01–140 kHz was used to amplify the detected signal. An integrated power supply/controller box regulated the detector temperature.

A holder was designed to position in a repeatable fashion the handpiece of a clinically used pulsed dye laser (PDL) (Candela Corp., Wayland, MA, USA). The holder was positioned to direct PDL light through on open area in a fixed positioning aperture. Time-resolved blackbody emission from a $2 \times 2\,\text{mm}^2$ area on a sample placed at the positioning aperture was collected with a biconvex CaF_2 IR lens ($f = 25.4$ mm, $F/\# = 1$). To operate in a wavelength band over which the blackbody emission attenuation coefficient is uniform, the spectral sensitivity of measured IR radiation was restricted to 4.5–5 μm by placing an optical filter in front of the detector window (5).

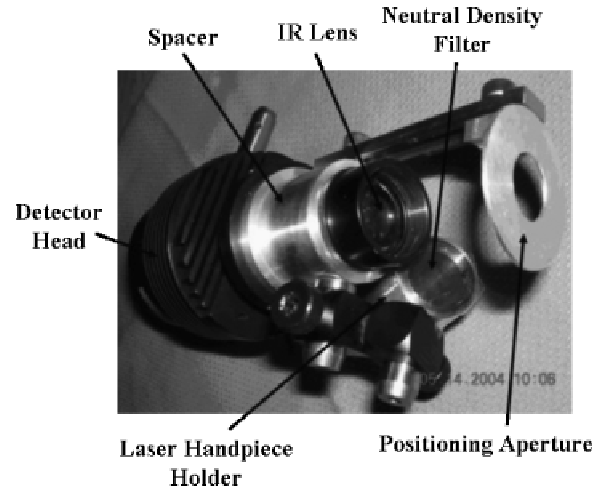

Fig. 1. Photograph of the small, fiber-free, hand-held pulsed photothermal radiometry (PPTR) system.

As the detector preamplifier was designed for AC-coupled signal detection, a reference background temperature measurement was required for calibrated ΔT_{epi} measurements. A shutter system was constructed to provide a variable reference background temperature. The shutter system consisted in part of a thin, thermoelectrically cooled copper plate. To simulate blackbody emission from human skin, one side of the plate was coated with a uniform layer of high-thermal emissivity black paint. A custom-built temperature controller was used to maintain the shutter temperature at a user-specified level.

PPTR system calibration

Temperature calibration of the PPTR system was performed with a blackbody calibration source (Omega, Stamford, CT, USA). The blackbody source was placed at the positioning aperture of the system and the temperature was initially adjusted to the user-specified shutter temperature (i.e., 22 or 33 °C in this experiment) to obtain a temperature difference (ΔT) of zero between the shutter and the source. The ΔT range used in this study was 0– 70 °C, in 2 °C increments.

At each blackbody temperature setting, the shutter was closed and opened and a raw AC-coupled IR signal (ΔS_{raw}) was acquired by a digital oscilloscope (Tektronix, Beaverton, OR, USA) at a sampling rate of 1 kHz. A representative example is shown in Fig. 2a, for ΔT of 35 °C. At $t < 0$, the shutter was closed. At $t = 0$, the shutter was opened to allow measurement of the blackbody emission. ΔS_{raw} was integrated over time to arrive at a signal ΔS similar to that shown in Fig. 2b. The resultant maximum value of ΔS (e.g., $\Delta S_{max} = 2.8$ V in Fig. 2b) then represented the specified value of ΔT. This procedure was repeated for each ΔT value to generate a calibration curve.

The experimentally derived calibration curve was compared with a theoretical simulation using Planck's law (9):

$$W_b(\lambda, T) = \varepsilon_b(\lambda) K_1 \lambda^{-5} / (\exp(K_2/\lambda T) - 1) \quad (\text{W/cm}^2\ \text{mm}) \qquad (1)$$

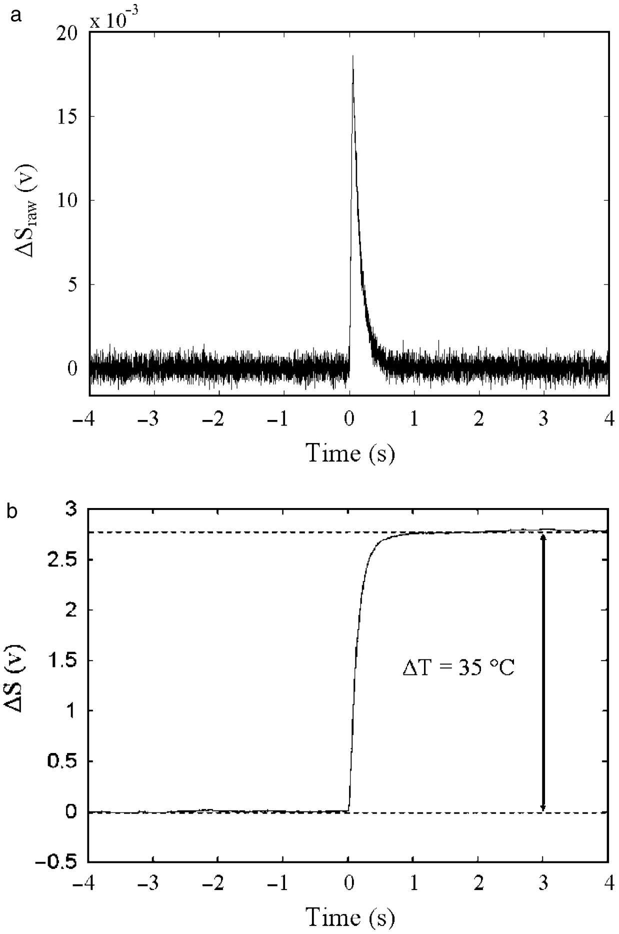

Fig. 2. Signal processing of the AC-coupled pulsed photothermal radiometry (PPTR) signal. The temperature difference (ΔT) between the blackbody (57°C) and the shutter (22°C) temperature was 35°C: (a) AC-coupled PPTR signal (ΔS_{raw}) before ($t < 0$) and after ($t > 0$) the shutter was opened and (b) integrated ΔS_{raw} signal (ΔS). In (b), the maximum value of ΔS (ΔS_{max}) corresponded with ΔT of 35°C.

where $W_b(\lambda, T)$ is the spectral emissive power, $\varepsilon_b(\lambda)$ is the emissivity of the object, $K_1 = 3.743 \times 10^4\,(\mathrm{W} \cdot (\mu\mathrm{m})^4/\mathrm{cm}^2)$, and $K_2 = 1.4387 \times 10^4\,(\mu\mathrm{m} \cdot \mathrm{K})$.

For a Lambertian emitter, the spectral emission power is given by (10)

$$W_{b\theta}(\lambda, T) = W_b \cos(\theta)/\pi(\mathrm{W/cm^2\,sr}\,\mu m) \qquad (2)$$

where θ is the viewing angle relative to the normal surface. In a simulation, blackbody temperatures of 295–365 and 306–376 K were used with shutter temperatures of 295 and 306 K, respectively. Other parameters included $\varepsilon_b = 1$, spectral range of 4.5–5 μm, and $\theta = 26°$. The total emissive power in the selected spectral range was computed at each blackbody temperature. The total emissive power of the shutter was subtracted from each blackbody emissive power value to generate a theoretical ΔT calibration curve.

In vitro and in vivo experiments to evaluate PPTR system accuracy

The relationship between PDL radiant exposure and ΔT was studied using an *in vitro* skin simulating gel model. An agar gel stained with Direct Red 81 (Sigma, St Louis, MO, USA) to absorb incident 585 nm PDL light was prepared. The gel was irradiated with progressively higher radiant exposures, from 8 to 20 J/cm^2, in 1 J/cm^2 increments. The reference temperature (22 °C) of the gel before PDL irradiation was monitored with a patch-type Omega thermocouple during the experiment and ΔT calibration was performed with a shutter temperature of 22 °C.

As a preliminary test of PPTR system accuracy, an *in vivo* human skin temperature measurement was acquired from the dorsal side of a subject's hand. For reference temperature measurements, patch-type Omega thermocouples were placed on the dorsal side of the subject's hand (33 °C) and the shutter (22 °C) surface.

As a first demonstration of the feasibility of our PPTR system to estimate H_{max}, we correlated measurements of ΔT_{epi} with epidermal melanin content based on skin color measurements. Initial skin surface temperature (33 °C) was measured with a patch-type thermocouple and ΔT calibration was performed with a shutter temperature of 33 °C. Epidermal melanin content was indirectly evaluated with a CR-200 chromameter (Minolta, Osaka, Japan), in which b^* values (i.e., of the $L^*a^*b^*$ color space) were utilized as an index (11). Experiments in our laboratory suggest that b^* is a more accurate melanin index than L^*, another popular metric for melanin content (unpublished data). Higher b^* values indicate higher melanin content. Finally, 10 matched pairs of ΔT_{epi} and b^* were acquired from the forearms of five normal subjects. The relationship between ΔT_{epi} and b^* was investigated using regression analysis.

All *in vivo* human skin measurements were acquired under a protocol approved by the Institutional Review Board at University of California, Irvine.

Results and Discussion

Sensitivity of IR radiometry system

Calculation of ΔS resulted in a higher sensitivity, as compared with ΔS_{raw} in the measurement of ΔT (Fig. 3). The signal at $t > 0$ in Fig. 3a represents the ΔS_{raw} (dotted lines) that resulted with a 1 °C temperature rise of blackbody radiation (23 °C)

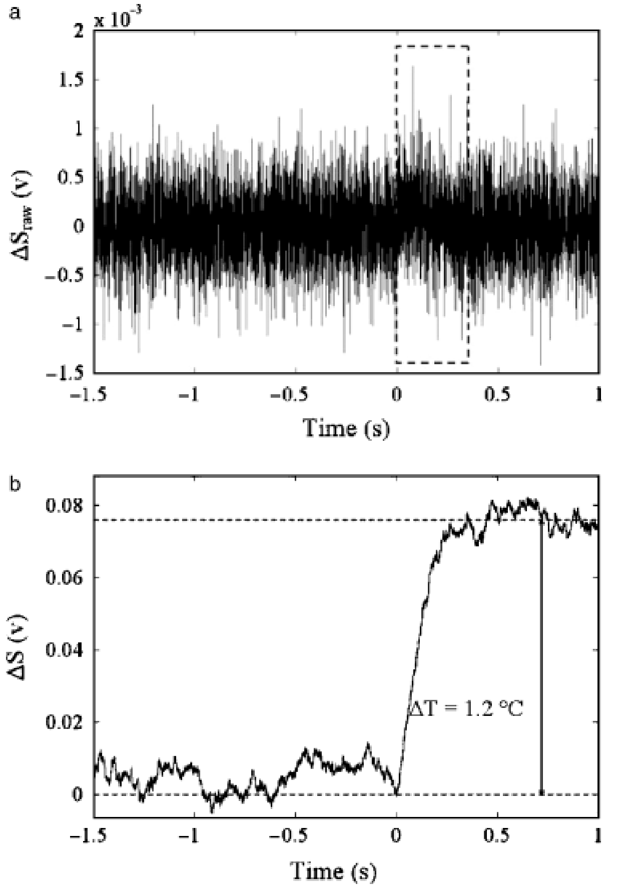

Fig. 3. Of pulsed photothermal radiometry (PPTR) system sensitivity between (a) ΔS_{raw} and (b) ΔS. Sensitivity was improved with integration of the ΔS_{raw} signal (dotted lines) shown in (a). The expected ΔT (1°C) is easily discernible in (b) because of the higher SNR.

over the shutter temperature (22 °C). In Fig. 3a, it is difficult to identify the difference between blackbody and shutter temperatures. However with integration of ΔS_{raw} (ΔS), the SNR was improved (Fig. 3b) and a 1 °C temperature difference can be discerned after integration of ΔS_{raw}, with 0.2 °C error.

The signals at $t < 0$ in Figs. 2b and 3b are ΔS of the shutter. The peak-to-peak value of average ΔS of the shutter was ± 0.015 V across the blackbody temperatures for a ΔT calibration data set. By using the ΔT calibration curve, the corresponding ΔT was determined to be ± 0.5 °C, suggesting that the IR radiometric system can resolve a ΔT of ± 0.5 °C between the reference and sample temperatures.

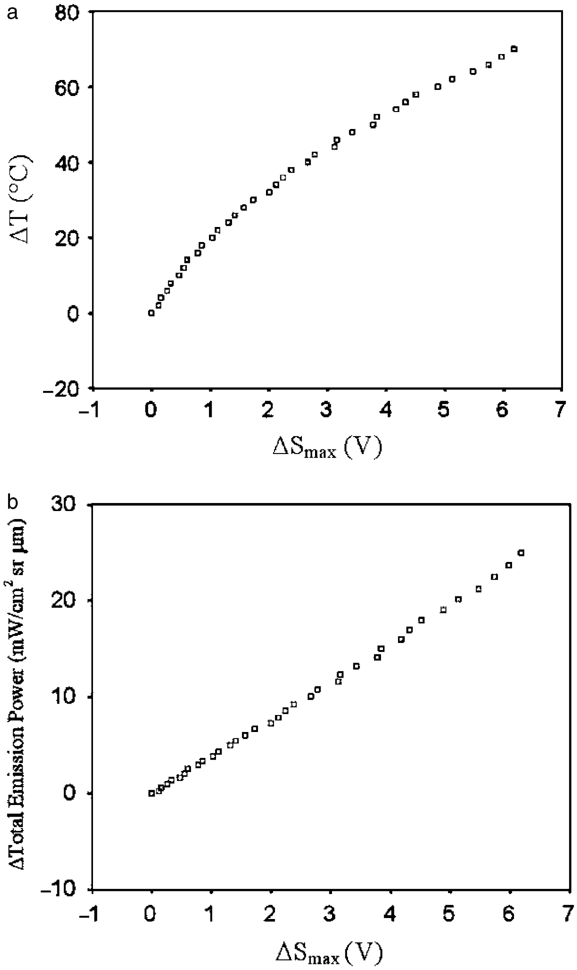

Fig. 4. (a) Experimental ΔT calibration curve as a function of ΔS_{max} and (b) the correlation between experimental and theoretical calibration curves.

PPTR system calibration

Experimental and theoretical calibration curves were similar to one another. As an example, Fig. 4a shows a ΔT calibration curve as a function of ΔS_{max} for a shutter temperature of 33 °C, to which a cubic regression resulted in the best fit ($R^2 = 0.99$) to the measurements. The experimental result in Fig. 4a was compared with theoretical simulation results of Planck's law (Eqs.1 and 2). The experimental and theoretical results showed a strong linear correlation ($R^2 = 0.99$) as shown in Fig. 4b.

In vitro and in vivo experiments to evaluate PPTR system accuracy

In theory, the laser pulse duration (1.5 ms in this study) is shorter than the epidermal thermal relaxation time (~ 20 ms) and thus we expected ΔT_{epi} generated by laser exposure to be directly proportional to the incident radiant exposure (9). In agreement with this hypothesis, a high-positive correlation does exist between ΔT_{epi} and the incident radiant exposure (Fig. 5).

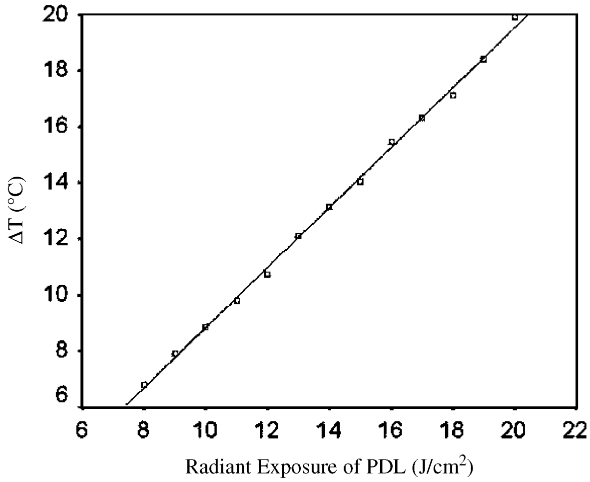

Fig. 5. ΔT as a function of pulsed dye laser (PDL) radiant exposure. An agar gel phantom stained with red dye was used as the sample, with a reference temperature of 22°C.

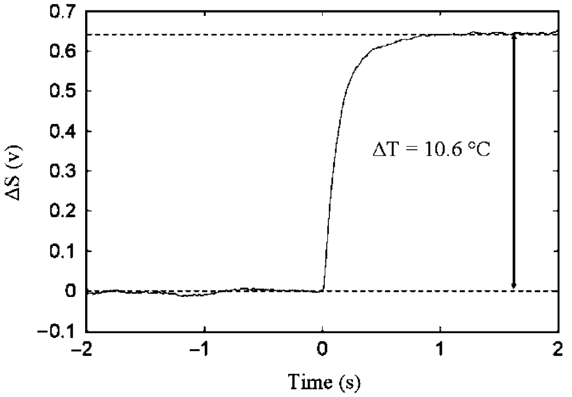

Fig. 6. Measurement of absolute skin surface temperature using ΔT calibration data between the shutter (22°C) and dorsal side of a subject's hand (33°C).

Figure 6 shows a measurement of a ΔT value (10.6 °C) between the dorsal side of the subject's (33 °C) hand and the shutter (22 °C). Thus, the measured absolute skin temperature was 32.6 °C, with the following equation:

$$T_{\text{sample}}(^{\circ}\text{C}) = T_{\text{shutter}} + \Delta T \qquad (3)$$

where T_{sample} and T_{shutter} represent the temperatures of the subject's hand and shutter, respectively. There was a temperature discrepancy of 0.4 °C between the actual (33 °C) and measured temperatures (32.6 °C), demonstrating the accuracy of the AC-coupled PPTR system.

Figure 7 shows the regression analysis between ΔT_{epi} and b^* in which ΔT_{epi} linearly increases with melanin content ($R^2 = 0.99$). This result agrees with the theoretical modeling study by Gabay et al. (12), in which skin surface temperature rise linearly increased as a function of epidermal absorption coefficient (i.e., melanin content).

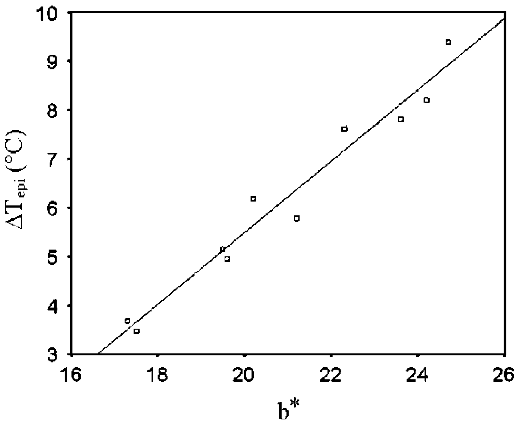

Fig. 7. Measurement of ΔT_{epi} as a function of melanin content (i.e., b). Higher melanin content (i.e., higher b*) resulted in higher ΔT_{epi}, with a strong positive correlation ($R^2 = 0.99$).*

Use of an integrated AC-coupled PPTR signal (ΔS) resulted in higher SNR as compared with a raw AC-coupled PPTR signal (ΔS_{raw}) because of a reduction in the high-frequency noise (Fig. 2). To the best of our knowledge, this technique has not been applied to AC-coupled IR signals. Sade et al. (10) relied on ΔS_{raw} alone in characterization of their AC-coupled PPTR system. Moreover, when using ΔS_{raw}, the shutter speed must be constant during both the temperature calibration process and the sample temperature measurement because the time-resolved intensity of the AC-coupled PPTR signal depends on shutter speed. This dependency can be a limitation in PPTR measurements that involve variable laser pulse durations. Even if the ΔT calibration is performed with a constant shutter speed, the PPTR measurement of ΔT may have additional error if the laser pulse duration, which essentially serves as a shutter, is not identical to the shutter speed used for ΔT calibration. We addressed this issue by using an integrated AC-coupled signal (ΔS), which is not sensitive to shutter speed.

The developed fiber-free, hand-held AC-coupled PPTR system is compact and easy-to-use. By using a positioning aperture, the measurement distance is held constant. In addition, the PPTR system uses a thermoelectrically cooled IR detector that requires infrequent ΔT calibration. We next plan to apply this system to *in vivo* measurement of epidermal damage to investigate further relationship between ΔT_{epi} and $H_{\max}$.

Conclusions

The fiber-free, hand-held AC-coupled PPTR system is capable of accurate ΔT_{epi} measurements. The system has a measured minimum resolvable ΔT of $\pm 0.5\,^{\circ}\mathrm{C}$. The experimental and theoretical calibration curves showed a strong linear correlation. The temperature measurement accuracy was demonstrated with *in vivo* skin measurements on the dorsal side of a subject's hand, with a temperature error of $0.4\,^{\circ}\mathrm{C}$. In a PPTR experiment with a gel phantom, ΔT showed a strong positive correlation with incident radiant exposure, in agreement with our prediction. Finally, measurements of *in vivo* ΔT_{epi} as a function of melanin content showed the potential of the AC-coupled PPTR system for accurate ΔT_{epi} measurements.

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