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ORIGINAL ARTICLE

Selective photothermolysis in acne treatment: The impact of laser power

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Abstract

Background: Selective photothermolysis (SPT) using a 1726 nm laser has emerged as a safe and effective treatment option for acne vulgaris by targeting sebaceous glands (SG). Power output plays a crucial role in determining treatment selectivity and efficacy.

Aims: This work highlights the advantages of a higher-power laser source and outlines the limitations of lower-power laser sources and the subsequent impact on treatment.

Methods: Light transport and bioheat transfer simulations were performed to demonstrate photothermal impact on the SG and the surrounding dermis when irradiated by a high- or lower-power laser source.

Results: The simulations showed that a single higher-power-shorter-pulse (HPSP) selectively increases SG temperature well beyond bulk temperatures, which is desirable for SPT. Selectivity decreases linearly with power for the single lower-power-longer-pulses (LPLP) exposure. A multiple-LPLP approach elevates bulk temperatures significantly more than a single-pulse strategy, compromising selectivity.

Conclusion: The goal of SPT is to damage SG safely and effectively by creating an intense temperature rise localized to the SG while moderately increasing the dermis temperature. This goal is mostly achieved with higher-power lasers that deliver a single HPSP. Lower-power lasers, longer pulse widths, and multi-pulse strategies result in higher bulk temperatures and lower SG selectivity, making such treatment challenging to execute while adding a higher risk of discomfort and downtime.

KEYWORDS
1726-nm laser, acne vulgaris, dermatology, energy-based treatments, sebaceous glands

1 | INTRODUCTION

Energy-based treatments are effective options for acne vulgaris. In recent decades, lasers, intense pulsed light (IPL), and radiofrequency (RF) devices have emerged as effective treatment options for acne vulgaris. These treatments work through three main mechanisms: targeting *C. acnes* and inflammation or sebaceous glands (SG).

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C. acnes, or *Cutibacterium acnes*, is a type of bacteria that commonly proliferates in sebaceous glands and is a known cause of acne vulgaris.[1] One of the earliest known methods of treating acne with energy-based treatment involves natural ultraviolet (UV) exposure, a form of photodynamic therapy (PDT).[2] The UV exposure can kill the *C. acnes* bacteria naturally occurring in the sebaceous glands; however, excessive UV exposure can increase the risk of skin aging and skin lesions. Visible-light lasers and IPL devices can also target *C. acnes*, alone or in combination with PDT.[3] This method has varying results, with a reduction in lesion counts ranging from 40% to 80%.[4,5] However, the effects are often short-lived as *C. acnes* can reproduce in the hyperactive sebaceous glands. PDT using red light at higher doses and longer incubation periods (≥3 h) can inhibit the function of sebaceous glands by destroying sebocytes but can lead to undesirable side effects such as intense pain, long-lasting erythema, oozing, and crusting from epidermal damage.[6]

Alternatively, infrared lasers and RF devices can heat the water in the skin surrounding the sebaceous glands, leading to thermal diffusion and destruction of the glands. Infrared lasers and RF microneedling devices have been shown to reduce lesion counts in the 70%–90% range after 3–5 treatments, with the reductions in some reports persisting for more than 2 years after the final treatment.[7] Histology has shown a reduction in the size of sebaceous glands in treated skin,[7] like that following oral isotretinoin treatment. Infrared lasers that emit wavelengths between 1064 and 1550 nm, excluding 1210 nm, primarily target water, the most abundant chromophore in the epidermis and the dermis. As a result, these devices indiscriminately heat the skin tissues and sebaceous glands (SGs), which can cause adverse effects such as blistering, scarring, and discoloration.[8]

The principles of selective photothermolysis have been employed to develop a cutting-edge laser device that emits energy at $\lambda = 1726$ nm, making it safe and effective in treating acne vulgaris by selectively targeting the sebaceous glands—the host target for *C. acnes*.[9] This state-of-the-art approach is made possible by utilizing sebum as a potential endogenous chromophore that strongly absorbs light at $\lambda = 1726$ nm, compared to water.[10–13]

Selectively targeting the sebaceous glands reduces sebum, decreases the proliferation of *C. acnes*, and preserves the surrounding dermis and epidermis. This mechanism reduces the risk of inflammation and minimizes harm to healthy skin tissue. According to the theory of selective photothermolysis,[14] three parameters are essential for effective therapy: choosing a precise wavelength (in nm), a sufficient fluence (energy per unit area in J cm^{-2}), and pulse duration (in ms) based on the thermal relaxation time (TRT), which is the time needed for 50% of accumulated heat to dissipate after energy delivery. The average TRT for human facial sebaceous glands is 60 ms.[11]

In addition to the TRT, the denaturation temperature is a critical factor affecting selectivity in laser therapy. If sustained for enough time, denaturation temperature (T_{Dn}) causes denaturation of the targeted tissue and impacts clinical outcomes. T_{Dn} and the time required to cause necrosis (t_{Dn}) are both important factors in determining the final clinical outcomes of laser therapy. Based on the Arrhenius equation, calculations have estimated a range of T_{Dn} and t_{Dn} values, with t_{Dn} decreasing as T_{Dn} increases. For example, T_{Dn} values between 60 and 100°C for skin bulk correspond to t_{Dn} values ranging from 1000 to <0.01 ms, respectively.[15] Keeping this concept in mind can assist in selecting the ideal laser pulse widths to achieve selective photothermolysis while maintaining a safe treatment. Achieving selective photothermolysis is crucial because it enables the delivery of energy while preserving the microanatomy of the skin, which is essential for skin safety and homeostasis.[14]

Laser systems must be designed carefully to achieve a rapid and significant temperature increase inside sebaceous glands while meeting precise spectral and spatial boundary conditions. Several conditions must be met to ensure selectivity. Firstly, the laser's optical bandwidth should be narrow and centered at 1726 nm to match the selectivity peak of sebum. Second, the beam diameter should be adjusted to provide a sufficient fluence and penetration depth proportional to the beam diameter. Finally, the pulse width should be designed to achieve denaturation temperatures (T_{Dn}) that last long enough (t_{Dn}) to cause sebocyte necrosis.[15]

To ensure the patient's safety during a procedure, avoiding adverse events such as skin burns, blistering, and scarring that require medical intervention is important. Clinical observations have indicated that keeping the dermal–epidermal junction (D–E Junction) below 50°C can prevent these side effects.

In this study, we compare treatment protocols that use higher-power versus lower-power lasers to achieve both efficacy and safety when targeting the sebaceous glands. Additionally, we examine the impact of different pulsing strategies of a 1726 nm laser on the patterns of heat distribution in sebaceous glands using light transport and bioheat transfer simulations. The degree of thermal damage on the sebaceous glands resulting from different laser powers is inferred from Arrhenius calculations reported in the literature.[15]

2 | METHODS

A 1726 nm laser, coupled with a contact cooling system, is modeled in the work. The laser source generates a 3-mm wide circular beam with adjustable pulse width, while the cooling system consists of a sapphire window with active cooling at 2°C. The target skin volume is cooled for 1 s before laser emission, and the cooling system remains active during and after the laser exposure for the duration of the simulation.

2.1 | Numerical modeling

Numerical light transport and heat transfer models were implemented to characterize the heat distribution in the superficial skin layers and sebaceous glands under different laser parameters. The effect of different power levels and pulsing strategies (pulse width and number) on selective heating of the sebaceous gland with respect to the surrounding dermis is analyzed. The results are intended to provide a good understanding and comparison of the thermal distribution in the target tissue for different laser parameters. Numerical

light transport and heat transfer models were implemented to characterize the heat distribution in the superficial skin layers and sebaceous glands under different laser parameters. The effect of different power levels and pulsing strategies (pulse width and number) on selective heating of the sebaceous gland with respect to the surrounding dermis is analyzed. Although the models make certain assumptions to reduce computational costs, they provide a comprehensive understanding and comparison of thermal distribution in the target tissue for various laser parameters. Readers interested in a more detailed look at the numerical calculations used for the model can refer to our previous publication by Scopelliti et al.[16]

2.2 | Light transport

In the light transport model, the interaction between the laser and the target tissue is characterized using an open-source light transport simulator (Monte Carlo eXtreme v2020). The simulation domain is set up as a 10 mm × 10 mm × 5 mm homogeneous skin volume with a voxel size of 10 μm × 10 μm × 10 μm. A sebaceous gland is modeled as a sphere with a diameter of 0.24 mm and placed at different depths within the simulation domain.

The gland is initially fixed at depth $z = 0.8$ mm and aligned with the center of the laser beam incident on the skin surface, which is modeled with a uniform top-hat profile. The tissue's refractive index (n) and anisotropy factor (g) at 1726 nm were set to $n = 1.363$ and $g = 0.9$, respectively. The absorption coefficients μ_a and scattering coefficients μ_s for skin and human fat are used to approximate the optical properties of sebum and are listed in Table 1.

2.3 | Bioheat transfer

Fluence data from the Monte Carlo simulations are used as input for a finite element (FE) model implemented in COMSOL Multiphysics 6.0. The model utilizes a two-layer representation of the skin with epidermal and dermal layers. A single laser pulse is emitted from the center of the sapphire window, traveling through the skin layers and the sebaceous gland, modeled as a sphere of human fat at a depth of 0.8 mm. In some simulations, the gland depth is swept between 0.5 and 1.5 mm with a step of 0.2 mm. The spatiotemporal temperature distribution within the simulation domain is calculated by numerical solution of the Pennes' bioheat transfer equation, using thermal parameters reported in Table 2.

TABLE 1 Optical parameters used for the Monte Carlo light transport.

Component	Absorption coefficient μ_a (mm^{-1})	Scattering coefficient μ_s (mm^{-1})	Anisotropy factor g	Refractive index n
Skin	0.59	8.5	0.9	1.363
Sebaceous gland (fat)	1.062	8.0	0.9	1.363

Source: Adapted from Scopelliti et al.[16]

3 | RESULTS

3.1 | Single-pulse approach: High power versus low power (at identical incident energy)

This study used light transport and heat transfer modeling to analyze the impact of laser power and pulse width on the sebaceous gland. The goal was to compare the effect of a single higher-power-shorter-pulse (HPSP) to a single lower-power-longer-pulse (LPLP) on the maximum temperatures within the gland while keeping the fluence and laser spot size constant. Maximum gland temperature was compared at a fixed position within the skin (z) and with fluence set to 17 J cm^{-2} for all HPSP and LPLP scenarios. Results showed that the maximum temperature inside the sebaceous gland is directly proportional to the laser power.

The findings, depicted in Figure 1A, reveal that a single laser pulse can affect the maximum gland temperature depending on the operating power of the laser. For example, the heat transfer model indicates that a single HPSP (power = 80 W, pulse width = 15 ms) can result in a maximum temperature of 89.7°C. In comparison, a single LPLP (power = 10 W, pulse width = 120 ms) results in a maximum temperature of 61.6°C.

Figure 1B shows that the modeled temperatures as a function of skin depth demonstrate the thermal selectivity of the laser, with changes occurring only in the sebaceous gland. The epidermis and dermis remain mostly below 50°C with no values exceeding 52°C. The inset of Figure 1B demonstrates a linear relationship between ΔT_{DG} (the temperature difference between the two maxima of the gland and the surrounding dermis) and the peak power. The temperature difference increases from $\Delta T_{DG} = 8$°C (power = 10 W) to 29.6°C (power = 80 W).

These findings emphasize the importance of higher laser power in achieving selective photothermolysis. However, the question arises as to whether multiple pulses with lower powers can still effectively target the sebaceous gland while adhering to the principles of selective photothermolysis. Further simulations are conducted to determine the maximum possible ΔT_{DG} values using the multi-pulse approach and to quantify bulk temperature.

TABLE 2 Thermal parameters used for the bioheat transfer numerical simulations.

Component	Thermal conductivity κ ($W\,m^{-1}\,K^{-1}$)	Density ρ ($kg\,m^{-3}$)	Specific heat C_p ($J\,kg^{-1}\,K^{-1}$)
Sapphire	23.1	3980	761
Epidermis	0.5	1200	3600
Dermis	0.53	1200	3800
Fat (Sebum)	0.21	911	2348

Source: Adapted from Scopelliti et al.[16]

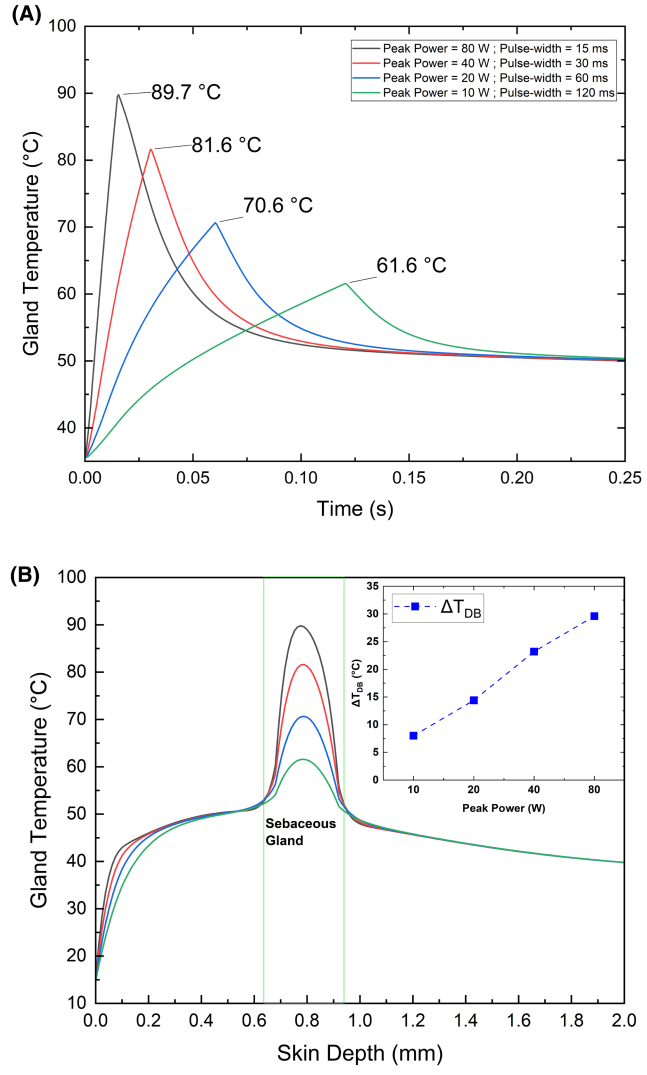

FIGURE 1 (A) Maximum temperature of the sebaceous gland over time as a function of peak power and pulse width. (B) Maximum skin temperature versus skin depth for each set of laser parameters; the inset shows the selectivity ΔT_{DG} as a function of peak power. The legend constructed for (A) applies to (B).

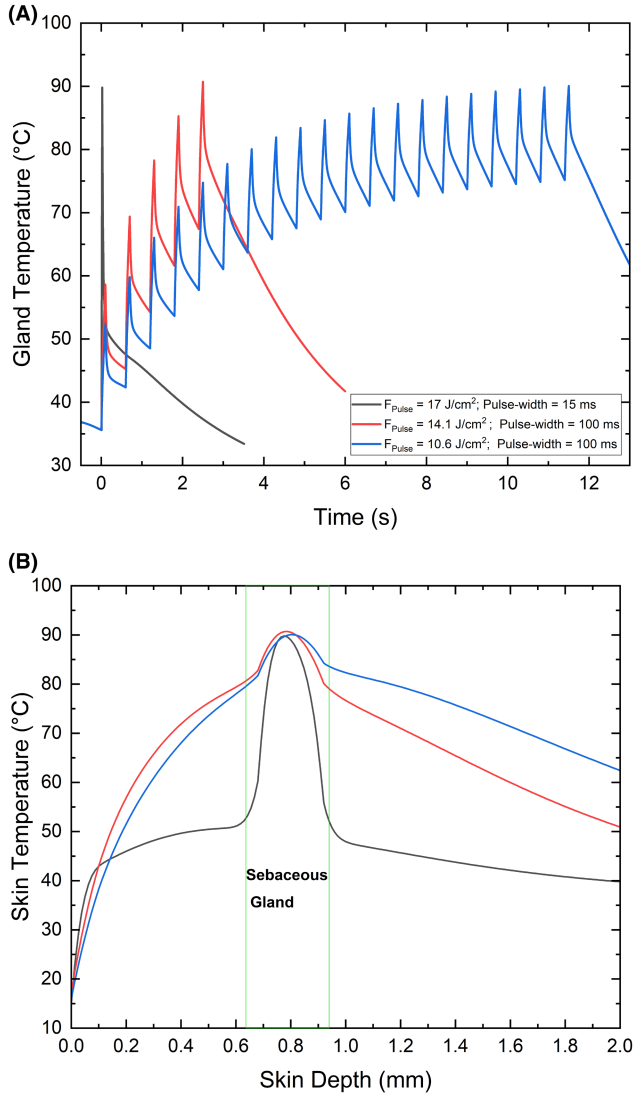

FIGURE 2 (A) Maximum gland temperature for a single HPSP versus 5-LPLP and 20-LPLP. (B) Maximum skin temperature as a function of skin depth for the single HPSP versus 5-LPLP and 20-LPLP. The legend constructed for (A) applies to (B).

3.2 | Single-HSPS versus multi-LPLP approach (for identical gland temperature)

To compare the efficacy of the single-HPSP approach with a multi-LPLP approach, we investigate the number of pulses required to reach a target temperature of 90°C. Figure 2A compares the two approaches, with the gray line representing the single-HPSP approach and the red and blue lines representing two multi-LPLP settings. The aim is to compare the temperature difference between the two maxima of the gland and the surrounding dermis (ΔT_{DG}) in both approaches.

Our results show that lower-power laser requires significantly longer times and more pulses to reach the targeted temperature. The number of pulses needed to reach the target temperature of 90°C using the multi-LPLP approach with 100 ms pulses was 2, 3, 5, and 20 pulses for laser powers of 15.5, 12.5, 10, and 7.5 W, respectively. Multiple pulses with the LPLP approach, as depicted in Figure 2B, lead to an increase in dermal temperatures (T_D) beyond 50°C.

Treatment parameters dictate the maximum targeted temperatures. We normalized the absolute temperatures to the maximum gland temperature to account for these parameters and generalize the results. The differences between dermal and gland temperatures are understood by comparing the maximum dermal temperature to the maximum temperature within the sebaceous gland. We use unitless normalization values ranging from 0 to 1, where 1 indicates no selectivity.

For instance, Figure 3A shows that with low operating power and more pulses, the normalized T_D value (orange bars) approaches 1, which is the normalized value of the maximum gland temperature (T_G^{max}); as a result, there is less gland selectivity. Figure 3B shows

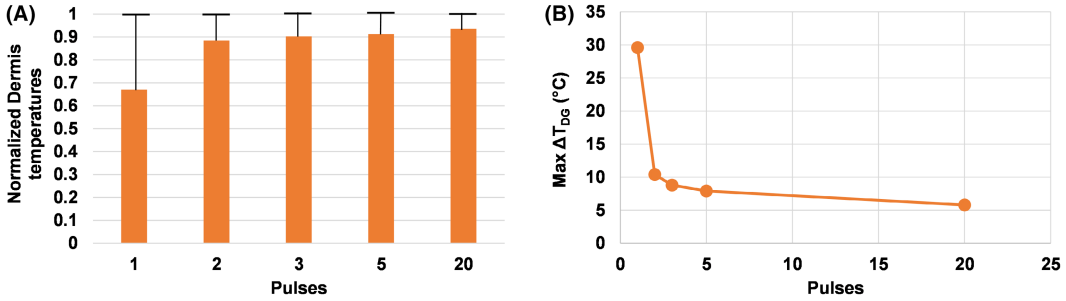

FIGURE 3 (A) Normalized dermis temperatures (T_D/T_G^{max}) orange bars compared to 1—normalized T_G^{max}—as a function of the number of pulses. (B) The Max ΔT_{DG} quantifies the photothermal selectivity as a function of the number of pulses.

that this multi-LPLP approach significantly reduces the maximum difference in dermis-gland temperatures ΔT_{DG}, compromising the selective aspect of SPT and yielding ΔT_{DG} values three to six times lower than a single-HPSP.

The simulations thus far demonstrate that delivering laser energy with a single HPSP provides the most selective photothermal treatment. It is worth noting that these results only consider a fixed location of the sebaceous gland in the skin ($z = 0.8$ mm). However, the depth of glands within the skin can vary greatly between patients.

3.3 | Single-HSPS versus multi-LPLP (at different gland depths)

Figure 4 provides a spatial representation of the skin to better understand the effect of gland position on the photothermal selectivity of different laser treatments. The single-HPSP resulted in the highest normalized temperature in sebaceous glands closest to the epidermis, with a fluence of 17 J cm^{-2} (Figure 4A). The normalized gland temperature decreases linearly with depth, reaching up to 43% lower at $z = 1.5$ mm compared to 0.5 mm.

The multiple-LPLP approach is modeled using five laser pulses (5-LPLP) and compared to the Single-HPHP approach. The 5-LPLP approach (Figure 4B) had fluence = 14.1 J cm^{-2} per pulse, totaling 70.5 J cm^{-2}. The safety of the 5-LPLP approach is evaluated by comparing it to an HPSP single pulse with a higher power, higher fluence, and the same exposure time (dashed orange curve). The position of both temperature profiles relative to the safe temperature of 50°C (green line) and the overall energy delivery time determine the safety of the two approaches.

The 5-LPLP approach results in a smaller decrease in the maximum temperature of the SG with depth, only by 25% at $z = 1.5$ mm (Figure 4B). However, the normalized dermis temperature exceeds safe levels over 93% of the skin depth, reaching a peak at 0.7 mm and compromising photothermal selectivity and, more importantly, the treatment's safety. To better compare the two strategies, a single HPSP at higher fluence (30 J cm^{-2}) is modeled on a gland at $z = 1.5$ mm (dashed orange line). The single HPSP increases the gland temperature compared to 5-LPLP with lower dermis temperature, enhancing photothermal selectivity and safety of the procedure. The short

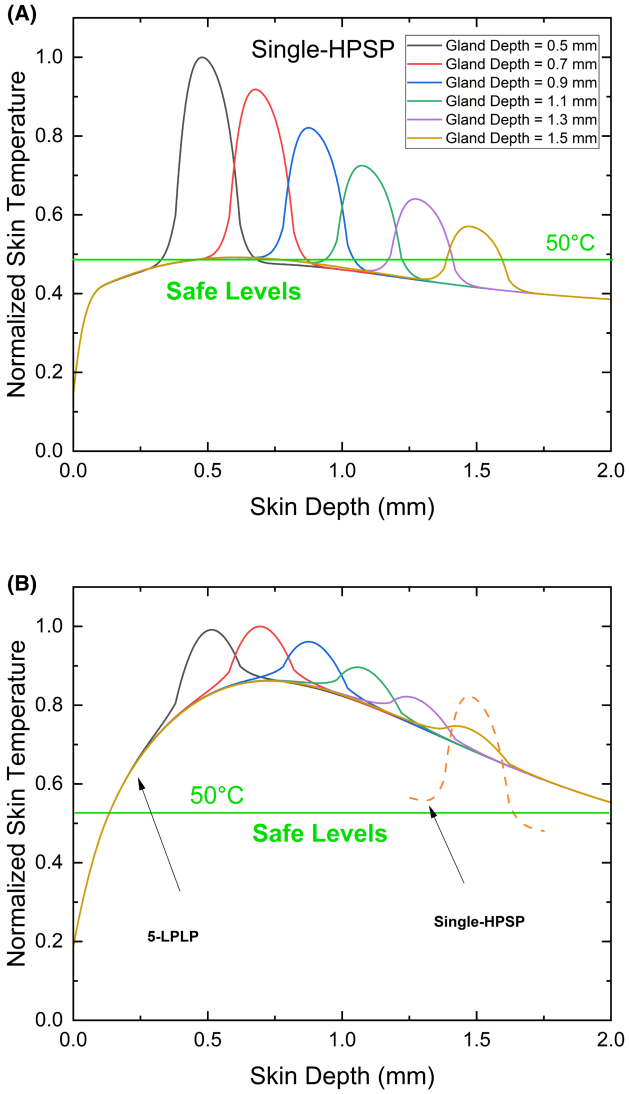

FIGURE 4 The normalized skin temperatures with (A) a single-HPSP approach with fluence = 17 J cm^{-2} and (B) a 5-LPLP targeting SGs at different skin depths with a fluence = 14.1 J cm^{-2} per pulse; the dashed orange curve represents the temperature profile of a SG located at 1.5 mm into the skin receiving a single-HPSP with fluence = 30 J cm^{-2}. The green line represents the safe levels of the skin at 50°C—note that the difference in the green line's position with respect to the normalization scale is due to the difference in maximum gland temperatures achieved for both approaches.

pulse width of the higher fluence single-HPSP (Fluence = 30 J cm^{-2} and t = 15 ms) is much lower than the times necessary to cause necrosis of the dermis (t_{Dn}) at 50°C. Therefore, dermis temperatures exceeding 50°C are more detrimental with a multi-LPLP approach because of their longer exposure times.

Visualizing ΔT_{DG} as a function of gland depth allows us to understand the extent of photothermal selectivity at different z-planes for both pulsing strategies. Figure 5 shows that when a single HPSP is deployed, ΔT_{DG} decreases from 40.9°C (z = 0.5 mm) to 7.6°C (z = 1.5 mm), always favorable to the SG selectivity. In contrast, ΔT_{DG} decreases from 9.2°C (z = 0.5 mm) to −10.5°C (z = 1.5 mm) when adopting a 5-LPLP approach. A negative ΔT_{DG} value at deeper gland locations indicates inverse selectivity in that the dermis temperature exceeds gland temperature. In other words, targeting glands located deeper into the skin causes the already weak photothermal selectivity of the multi-LPLP to shift from the gland to the dermis. Therefore, a multi-LPLP approach may result in dermal damage when targeting SGs scattered deeply into the skin matrix.

4 | DISCUSSION

The comparison between a single HPSP and a single LPLP delivered with contact cooling showed that regardless of the delivered power, the dermis temperatures remained mostly constant throughout the bulk except for the sebaceous gland. The maximum temperature of the gland was observed with higher powers, despite using the same fluence values. The temperature of the SG was a function of the absorption of light energy by the sebum, the preferential chromophore of the 1726 nm radiation, while the temperature of the epidermis and dermis is a function of light energy absorbed by intracellular water molecules and thermal conduction from neighboring SGs.

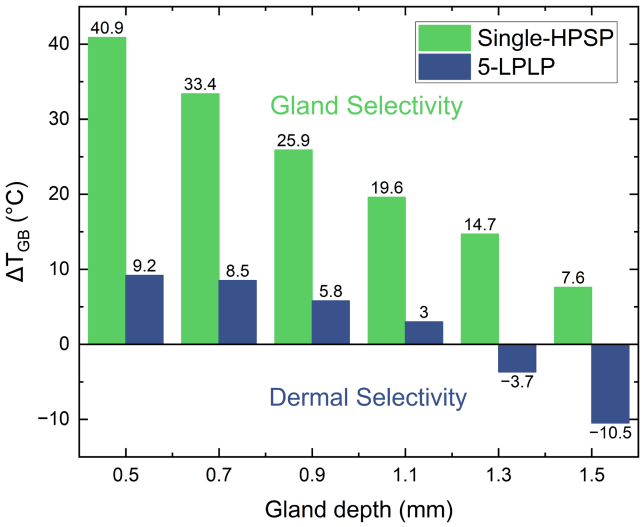

FIGURE 5 The photothermal selectivity of the sebaceous gland as a function of the gland's depth when treated with a single HPSP laser (green color) and 5-LPLP (navy color). For $\Delta T_{DG} > 0$, the gland's temperature is larger than the bulk/dermal temperatures, illustrating a gland selectivity mode. In contrast, for $\Delta T_{DG} < 0$, bulk temperatures are higher than gland temperatures resulting in negative selectivity or a "dermal selectivity" phenomenon.

The laser radiation should deliver energy rapidly to raise SGs temperatures before heat sinks into the dermis; according to the theory of selective photothermolysis, the pulse width should be less than the TRTs. Consequently, to meet the requirements of selective photothermolysis, practitioners must choose a precise, pulsing strategy that can quickly elevate sebaceous glands' temperatures inside the gland without overheating the surrounding tissues to avoid collateral skin damage, which is majorly achieved by using a Single-HPHP approach.

When the laser system is power-limited, a multiple-pulse approach can be adopted to increase the temperature of the sebaceous glands, but this approach lacks the selectivity component, which is imperative to achieve SPT and hence differs in the mechanism of action as a single HPSP. Additionally, decreasing the spot size can increase selectivity by limiting the amount of surrounding tissue being heated. However, this is only of limited possibility because the scattering of light in the skin can attenuate the energy being delivered to the sebaceous gland.[16]

Also, as demonstrated in the results, multi-LPLP increases bulk temperature, minimizing the safety profile of the treatment procedure. The multi-LPLP strategy is further complicated when considering sebaceous glands deeper into the skin. To target those glands with a multi-LPLP approach, the practitioner should raise and sustain the glands' temperature, which cannot be achieved without collaterally inducing damage to the dermis due to lack of selectivity.

Contrarily, a single high-powered short-pulsed (HPSP) approach is specifically designed to selectively heat the sebaceous glands while preserving the surrounding tissue.

5 | CONCLUSIONS

This study used numerical simulations to model the thermal effects of a 1726 nm laser on the sebaceous glands, dermis, and epidermis. The simulations showed that optimal sebaceous gland selective photothermolysis could be achieved using a higher-power laser capable of generating single higher-power-shorter-pulse irradiation. Higher-power laser irradiation ensures an optimal temperature differential between the sebaceous gland and dermis. When combined with contact cooling, these lasers effectively target the sebaceous glands while minimizing adverse events, discomfort, and downtime. Contrarily, the multi-LPLP strategy with a 1726 nm lower-power laser had weaker selectivity for the sebaceous glands and a similar mechanism of action to other infrared lasers. Thus, it may be less effective in achieving optimal results, especially at deeper locations where elevated bulk temperatures may exceed the gland's temperature. These findings highlight the importance of considering the depth of the glands when selecting the laser and exposure parameters.

The results demonstrate that a higher-power laser is essential for optimal targeting of the sebaceous glands, utilizing the principles

of selective photothermolysis. In contrast, a lower-power laser may have compromised selectivity and match the mechanism of action of other infrared devices that achieve results by bulk heating the entire treated area. These findings can help practitioners understand the critical role of laser power in achieving successful therapy with minimum treatment-related discomfort, adverse events, and downtime while ensuring requisite efficacy.

AUTHOR CONTRIBUTIONS

A.K., M.K., S.M., M.S., and A.H-S were involved in the conceptualization and design of the study. M.S executed the numerical modeling and Monte Carlo simulations. A.H-S. was responsible for data analysis, writing, reviewing, and editing the manuscript. All co-authors were involved in the final review and approval of the manuscript. A.H-S and M.S have contributed equally to this work.

CONFLICT OF INTEREST STATEMENT

Amer Hamidi-Sakr, Matteo Giuseppe Scopelliti, Amogh Kothare, Michael Karavitis, and Sönke Möller, Ph.D., are employees of Cutera, Inc., USA.

DATA AVAILABILITY STATEMENT

Data sharing not applicable to this article as no datasets were generated or analysed during the current study.

ETHICS STATEMENT

This was a modeling and simulation study; no animal or human subjects were involved.

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