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A portable illumination device for photodynamic therapy of the oral cavity

Jiyuan Xiong*, Xu Wang*, Xiaoming Hu*,‡, Ying Han†,§ and Qin Li*
*Key Laboratory of Convergence Medical Engineering System and Healthcare Technology, Ministry of Industry and Information Technology
School of Life Science, Beijing Institute of Technology
Beijing 100081, P. R. China

†Department of Oral Medicine
Peking University School of Stomatology
Beijing 100081 P. R. China
‡bithxm@bit.edu.cn
§13683375487@163.com

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Photodynamic therapy (PDT) is a minimally invasive method for treating oral leukoplakia. In this paper, we propose a portable PDT device consisting of a flexible circuit board with a liquid flow cooling module on the back. The light source size was 17 mm × 11 mm × 4 mm, and the irradiation area of the light source was up to 100 mm^2. The irradiance range of this device was from 10 mW/cm^2 to 100 mW/cm^2. Simulation and experimental results showed that the irradiance coefficient variation for a treatment area of 81 mm^2 was less than 7%. At an irradiance of 100 mW/cm^2, a device surface temperature of lower than 42°C can be achieved to satisfy the safety requirements under the conditions that the temperature of cooling liquid is 10°C and the liquid flow speed is above 12 mL/min.

Keywords: Photodynamic therapy; oral leukoplakia; illumination device; irradiance uniformity.

1. Introduction

Oral leukoplakia is a potentially malignant disease leading to oral squamous cell carcinoma, and it usually occurs months or years earlier than malignant transformation.[1] The incidence rate of oral leukoplakia is 1.49–4.27%,[2] and oral cancer accounts for 2% (377,713) of new cases, with a mortality rate of 1.8% (177,757 deaths) worldwide.[3] Therefore, early diagnosis and treatment of oral leukoplakia can help reduce the incidence of oral cancer, improve the life quality of patients, and save medical costs.

In recent years, photodynamic therapy (PDT) has achieved great progress in basic research and clinical application, and it has become the fourth minimally invasive treatment modality for cancer

‡,§Corresponding authors.

after surgery, radiotherapy, and chemotherapy. The basic principle of PDT is that the photosensitizer is activated by light at a specific wavelength and then interacts with molecular oxygen to generate active substances with cytotoxicity. It can destroy cells, resulting in necrosis, shedding or decomposition, and absorption of local tissues.[4] Therefore, PDT has become the preferred treatment for oral leukoplakia, oral lichen planus, oral verrucous hyperplasia, and oral candidiasis.[5–8] Compared with traditional surgical resection and other treatment methods, PDT has higher efficiency and fewer side effects, and it can be used repeatedly without scar formation.[9,10]

At present, the main light sources for PDT are laser and light emitting diode (LED).[11] Han adopted a laser source in oral photodynamic therapy.[12] A He–Ne laser is transmitted to the patient's oral lesion through an optical fiber, and the treatment irradiance is up to 500 mW/cm^2. During the operation, a doctor holds the light source during the treatment period and adjusts the relative position and angle between the optical fiber and the oral cavity while patients keep their mouths open. To achieve uniform irradiation on the target lesion, the laser beam should be as perpendicular to the surface of the lesion as possible, and the distance between the end of the optical fiber and the lesion should be appropriate to ensure efficacy during laser exposure. Canavesi placed an optical fiber in the radial direction of the cylindrical reflector, and achieved three types with dimensions of 5.5 mm × 7.2 mm × 10 mm, 6.8 mm × 6.8 mm × 50 mm, and 5 mm × 10 mm × 11 mm.[13] Their spatial uniformity is more than 94%, and the average irradiance is 51 mW/cm^2 on an area of 25 mm^2 when the input power is 70 mW. Oguz used the light-emitting fabric woven with optical fibers composed of polymethylmethacrylate as the PDT light source, and obtained a uniform light distribution (12.8 ± 3 mW/cm^2) within a zone of 21.5 cm × 5 cm.[14] Compared with the laser light source, LED light source has advantages in price, illumination area, uniformity, and equipment volume. Siddiqui presented a 1 mm-diameter flexible fiber optic delivery system with fiber tip adaptors and mouth prop for intra-oral light delivery, which achieved an irradiance of 54 mW/cm^2 at the lesion surface and released the operator's hand.[10,15] Chen developed a LED-based illumination system that can serve as an alternative light source for PDT.[16] The light source system consists of a 7 × 10 LEDs array with an interval of 13 mm, and the standard deviation for irradiance is 15% within a zone of 80 mm × 120 mm. Mallidi designed a portable, battery-powered LED lighting device for low-cost application, and the treatment effect is not significantly different from that of the standard laser light source.[17] Masuda designed a flexible light source unit that is composed of 405 nm and 505 nm LED arrays and found that the irradiance can reach 69 mW/cm^2.[18] Hempstead evaluated the working characteristics of a 635 nm LED powered by a battery.[19] The LED temperature is approximately 30°C with a heat sink in ambient lab atmosphere on the condition of 375 mA working current, approximately 5° half angle, and 68 mW/cm^2 irradiance over a circular region of approximately 5.33 mm in diameter when the LED power output is 15 mW.

Inspired by Siddiqui's hands-free device and other above researchers, we proposed a portable LED light source device for oral PDT in accordance with the standards of the Chinese Stomatological Association. The device was small enough to fit into a patient's mouth, the light source uniformity, temperature simulation and experimental measurement of this light source were also evaluated, which verified that this device can satisfy the requirements for oral PDT.[20]

2. Materials and Methods

2.1. *Light source design*

Figure 1 illustrates the treatment diagram and components of our proposed PDT equipment, which was composed of a light source, a power driver module, and a pump. Figure 1(a) shows a schematic of oral photodynamic therapy. Figure 1(b) reveals the detailed structure of the light source, which was composed of a water-cooling groove, a circuit board, and a waterproof coating. The circuit board was composed of copper and epoxy resin as the medium, and it was also flexible with a thickness of 0.13 mm. The surface-mounted LED (632 nm red light, 0.65 mm × 0.35 mm × 0.4 mm, Shenzhen Guangerte Electronics Co., Ltd., China) was adopted as the light source. The maximum forward DC current was 25 mA, the forward voltage was 1.6–2.4 V, and the divergence angle of the LED was 120°. All LEDs were arranged into an array of 10 rows and 10 columns with an interval of 1 mm. A waterproof was coated outside the LED array. Figure 1(c) shows a

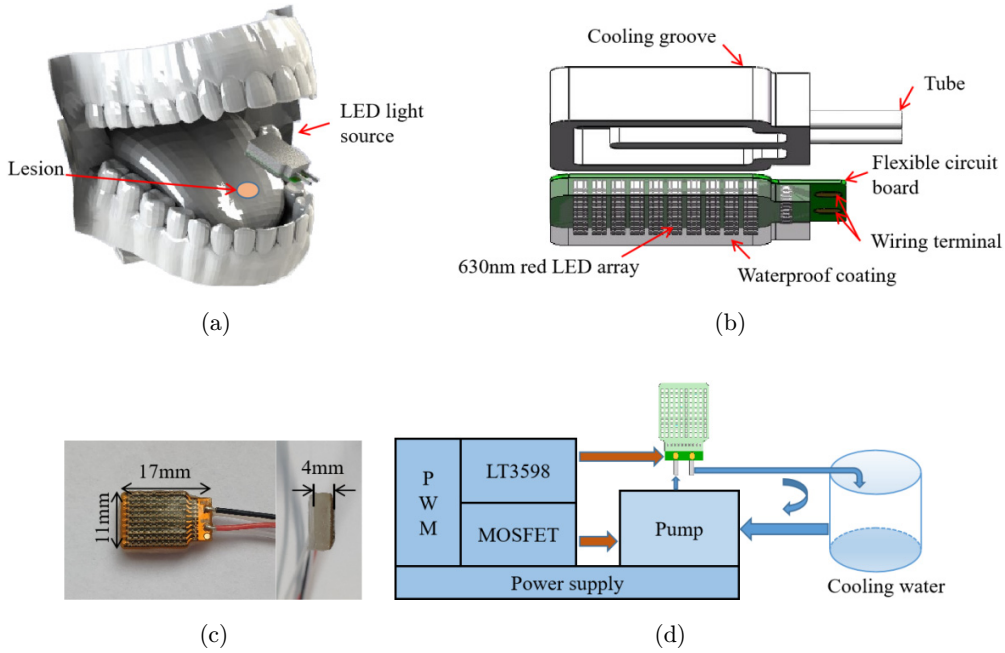

Fig. 1. Application and composition of portable illumination device. (a) Schematic of oral leukoplakia treatment. (b) Schematic of LED light source composition. (c) Physical drawing of LED light source. (d) Working diagram of portable illumination device.

physical view of the light source with dimensions of 17 mm × 11 mm × 4 m. Figure 1(d) demonstrates the circuit module structure, which included a LED driver circuit and a water pump drive circuit. The LED driver circuit consisted of a DC/DC boost mode converter with a maximum output voltage of 44 V (LT3598, ADI Inc, USA). It can connect up to six channels with a maximum output current of 30 mA for each channel. Each channel can be used in parallel to improve its current driving capacity. It can adopt analog or pulse width modulation (PWM) dimming. The PWM dimming ratio was as high as 3000:1, and the LED current matching accuracy was approximately ±1.5%. The pump drive circuit adopted a MOSFET (IRF1404, Infineon Technologies AG, German) to control the speed of the pump motor by PWM. The rated working voltage of the water pump was 12 V DC (MN1A/ZL-S1-12V-280R-3*1, Jihpump Co., Ltd., China), and its maximum flow was 85 mL/min. A PWM circuit had two potentiometers to generate their corresponding PWM signals to control the LT3598 and MOSFET.

2.2. *Uniformity verification on irradiance*

Light source uniformity is an important index for PDT equipment. The illumination uniformity was analyzed using Monte Carlo simulation (TracePro V7.3, Lambda Research Co., USA) to quantify the illumination uniformity accurately. On the basis of the main LED characteristics, a LED luminous model with 100 LEDs arranged in 10 rows and 10 columns was established. A 15 mm × 15 mm plane detector was placed 1.5 mm in front of the light source to evaluate uniformity.

The uniformity was also evaluated by calculating the coefficient variation of the light source on a translucent plastic plate (Oudifu, China) at a distance of 1.5 mm, which is shown in Fig. 2. The uniformity of light source irradiance was evaluated by evaluating the gray value of the image with a mobile phone camera (MIX2S, Xiaomi, China).

2.3. *Thermal simulation*

A cooling groove was attached on the back of the circuit board to cool down the light source by

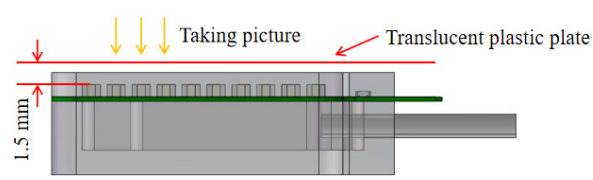

Fig. 2. Evaluation diagram on irradiance uniformity measurement.

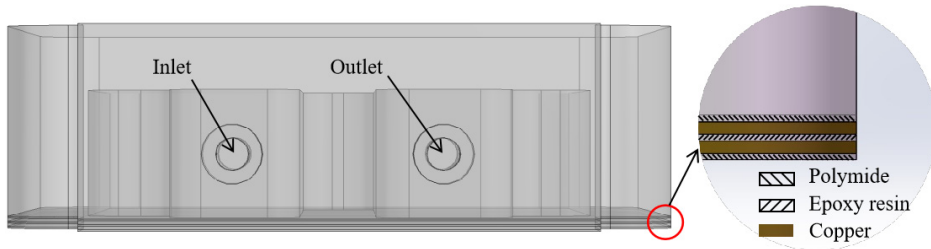

Fig. 3. Thermal simulation model for the light source.

Table 1. Material properties for finite element analysis (20°C).

Material	Density kg/m^3	Specific heat capacity J/(kg·K)	Coefficient of thermal conductivity W/(m·K)	Thickness mil
Water	1000	4187	0.594	79
Copper	8960	385	400	2
Polyimide	1200	752	0.792	1
Epoxy Resin	1673	550	0.425	1

circulating the water through a pump. A thermal model of the LED light source was also established by a finite element analysis software to evaluate the surface temperature distribution (COMSOL 5.6, COMSOL Inc., Sweden). The light source model was abstracted into five layers with three types of material, such as polyimide layer, copper foil layer, and epoxy resin layer, to reduce the complexity of the simulation. The stack setup is shown in Fig. 3. The thermal properties of each layer of the flexible circuit board are shown in Table 1. In this simulation, the heat source was set at the bottom copper foil of the circuit board. The thermal power was set the same as the electrical power when the irradiance of the light source was 100 mW/cm^2 and the ambient temperature was 20°C.

3. Results

3.1. *Uniformity of light source*

The normalized results of Monte Carlo simulation are shown in Fig. 4, the raw data of Fig. 4 were exported to MATLAB, and the coefficient variation of light source irradiance was calculated. The coefficient variation was less than 19% within the zone of 10 mm × 10 mm and dropped below 7% within the zone of 9 mm × 9 mm.

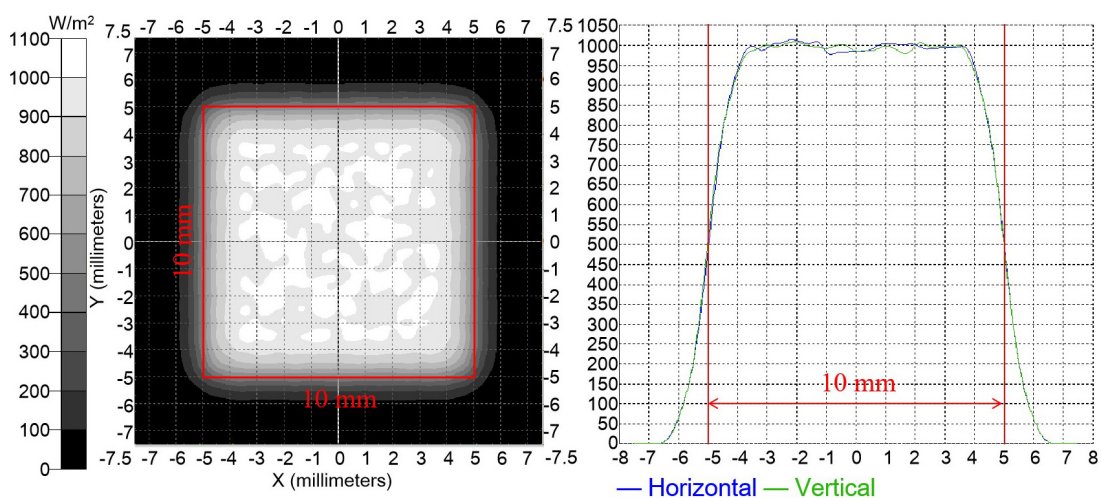

Fig. 4. Monte Carlo simulation for LED light source uniformity.

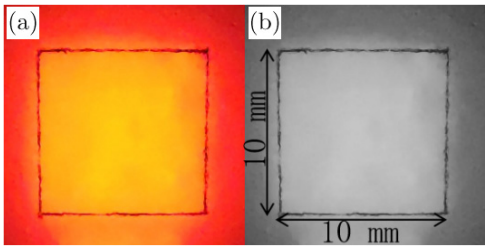

Fig. 5. Irradiance map of LED light source.

The original picture behind the plastic plate with an exposure time of 1 ms is presented in Fig. 5(a), and the grayscale map is shown in Fig. 5(b). The coefficient variation was down to 4.9% within the zone of 10 mm × 10 mm and 3.7% within the zone of 9 mm × 9 mm. Compared with the simulation results, the actual measured coefficient variation is lower. This result may be due to the scattering effect of translucent plastic in Fig. 2, which had the same effect as the human tissue.

3.2. *Irradiance linearity of light source*

A light power meter (S130C, THORLABS, USA) was used to measure the irradiance of the proposed LED light source. The PWM was set uniformly for 10 steps from 10% to 100%, and the irradiance values under different PWM values were recorded in Fig. 6. The maximum irradiance can reach up to 108 mW/cm^2 when the maximum pulse width reached 100%.

A linear regression was first performed for the irradiance less than 60 mW/cm^2 in Fig. 6. The results are shown as Eq. (1) ($R^2 = 0.9997$):

$$y_I = 1.1354 * x_p + 1.1511, \tag{1}$$

where y_I (mW/cm^2) is the irradiance and x_p (%) is the duty cycle of PWM. The irradiance showed a good linear relationship with PWM under low irradiance (< 60 mW/cm^2). Another linear regression was further performed for the irradiance between 60 and 100 mW/cm^2, and the results are shown in Eq. (2) ($R^2 = 0.9988$):

$$y_I = 0.977 * x_p + 10.677. \tag{2}$$

The curve showed a downward bend when the irradiance was greater than 60 mW/cm^2. This effect may be due to the high temperature of LED. The LED data sheet showed that the luminous intensity decreased with increasing temperature. In general, the linear regression equation for the whole scale of 10–100 mW/cm^2 is shown as Eq. (3) with a good linear relationship ($R^2 = 0.9983$).

$$y_I = 1.0689 * x_p + 3.2878. \tag{3}$$

3.3. *Thermal response of the light source*

When the light source was placed on the lesion of a patient's mouth, the patient's oral cavity may be scalded by excessive temperature. To determine the thermal equilibrium time of the light source, the cooling water flow was limited to 7.9 mL/min, and the irradiance was set to 50 and 100 mW/cm^2. As shown in Fig. 7, the surface temperature reached its equilibrium after 2 min.

3.4. *Relation between temperature and liquid flow*

Finite element analysis of the light source temperature distribution is shown in Fig. 8. The highest

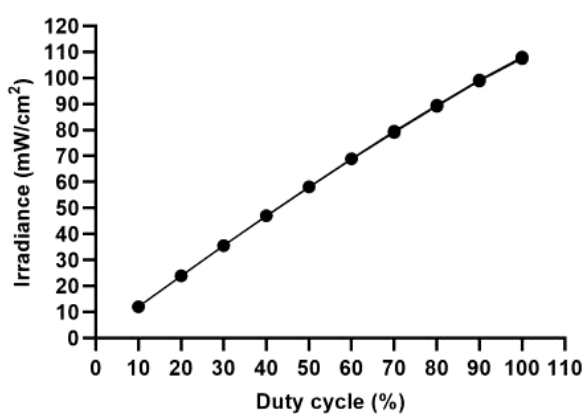

Fig. 6. Relationship between irradiance and PWM values.

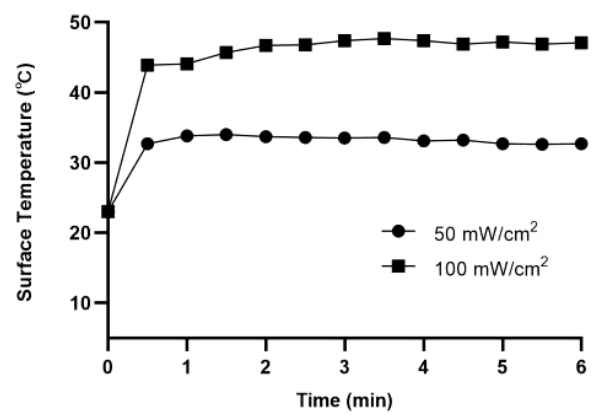

Fig. 7. Surface temperature of LED light source.

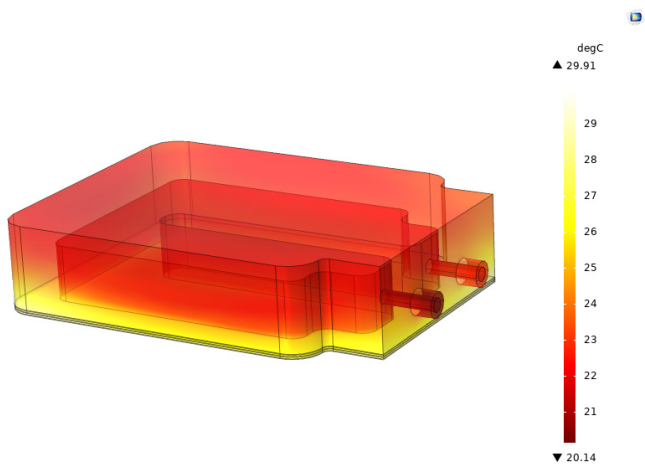

Fig. 8. Temperature distribution map of the light device under a cooling water flow rate of 19.5 mL/min.

temperature was obtained on the side of LED, and the temperature distribution was also uniform on the side of the circuit board.

As the surface temperature is related to the safety of the light source, temperature measurements of the light source were performed at four flow levels of 8.7, 11.1, 13.8, and 19.5 mL/min. After the light source worked for more than 2 min with the irradiance of 100 mW/cm^2, the temperature was recorded three times at each flow rate. As shown in Fig. 9, when the environment temperature was 20°C and the cooling liquid temperature was 10°C, the linear regression equation between the surface temperature and the water flow was estimated using

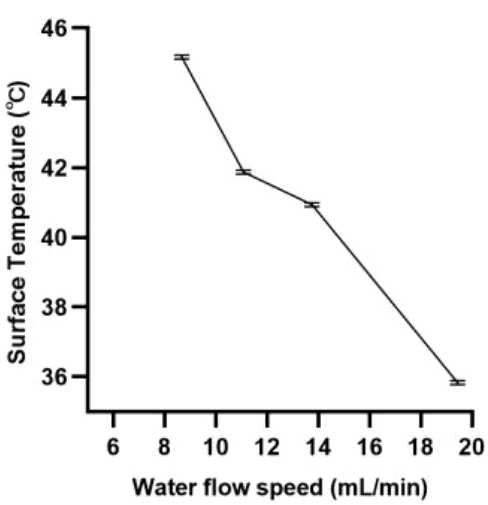

Fig. 9. Relationship between the LED surface temperature and cooling water flow.

Eq. (4) ($R^2 = 0.9757$):

$$y_T = -0.813 * x_w + 51.735, \tag{4}$$

where x_w (mL/min) is the water flow, and y_T (°C) is the surface temperature of the LED light source.

4. Discussion

4.1. *Irradiance linearity of light source*

The efficacy of PDT is strictly related to the optimization of treatment parameters: (i) Intensity and dosage, (ii) fluence rate, (iii) wavelength, (iv) pulsing or continuous mode, and (v) treatment duration. The optimal clinical light intensity or irradiance was considered to be approximately 50–100 mW/cm^2. Good linearity can satisfy the requirements of different levels of PDT irradiance, irradiation times, and other parameters. The linear relationship between irradiance and PWM signal reduces complexity and cost of the illumination device, which may help doctors optimize the treatment parameters.

4.2. *Irradiance and uniformity of light source*

According to the expert consensus on 5-aminolevulinic acid PDT for oral potentially malignant disorder, the preferred area of light source is about 1 cm^2, and the preferred irradiance is 100–150 mW/cm^2.[20] Three other center spacing configurations of 0.8 mm, 1.2 mm and 1.4 mm are also simulated to find the optimal solution, and the total irradiance and their coefficient variation within the zone of 8×8 mm^2 and 10×10 mm^2 are taken as evaluation indicators. The simulation results are shown in Fig. 10, which shows that the spacing between LED should be minimized as small as possible to achieve the greater irradiance, and the configuration of 1 mm has the best uniformity. Figure 10(e) shows that the coefficient variation is affected by the average value over the whole illumination area (10×10 mm^2), and it cannot accurately reflect the variation for the center region (8×8 mm^2). However, due to the limitation of LED package size and processing technology of printed circuit boards, the configuration of 0.8 mm is difficult to manufacture, the proposed configuration is an optimal solution for preferred treatment area and irradiance of oral photodynamic therapy.

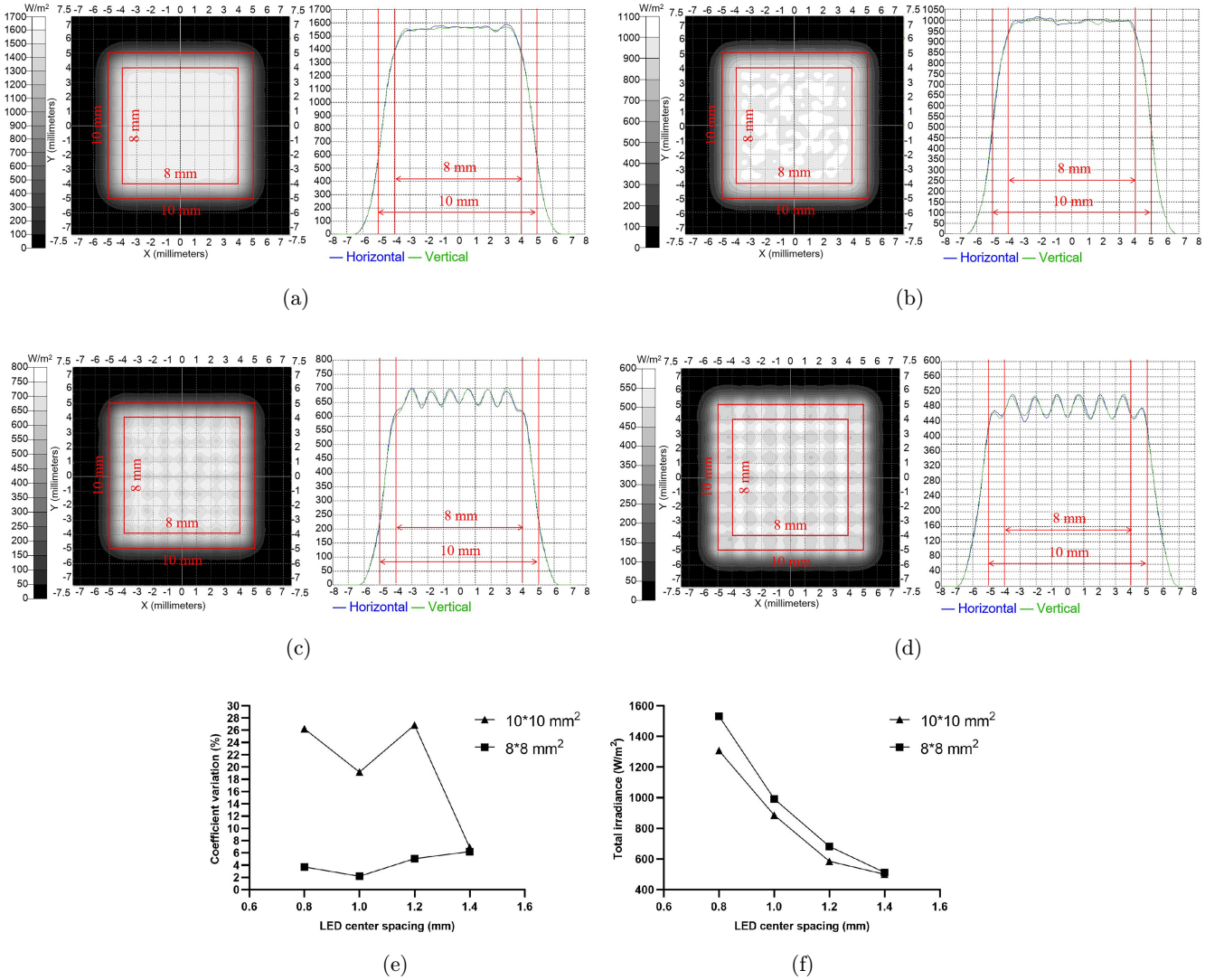

Fig. 10. Irradiance simulation results of four LED configurations. (a) 0.8 mm spacing with 12×12 LED array. (b) 1.0 mm spacing with 10×10 LED array. (c) 1.2 mm spacing with 8×8 LED array. (d) 1.4 mm spacing with 8×8 LED array. (e) coefficient variations, and (f) total irradiance of four LED configurations.

4.3. *Thermal safety*

Thermal is related to biological tissue safety, pain, and oxygen regulation. As discussed in a previous study, pain is significant when the irradiance is at $75\,\mathrm{mW/cm^2}$ but minimal at $60\,\mathrm{mW/cm^2}$ or below.[10] A light source surface temperature lower than 42°C can be achieved when the cooling water flow rate was greater than 12 mL/min, guaranteeing biological tissue safety and reducing the pain caused by excessive temperature of the light source. Meanwhile, a higher temperature can increase the blood flow velocity in the mouth within a specific range, which may increase the supply of oxygen for tissue for photodynamic therapy.[21] The proposed device can regulate the surface temperature by changing the temperature and flow speed of water, which may provide a new regulating parameter for doctors.

5. Conclusion

A portable LED light source for oral PDT is proposed in this paper. The light source has an illumination area of $1\,\mathrm{cm^2}$, which can cover oral lesions well. Doctors can easily adjust the position during treatment, reducing the complexity of PDT procedures. The irradiance can be modulated by the pulse width, and the temperature of the light source can be varied by modulating the flow speed or

temperature of the cooling water. The optical effectiveness and thermal safety of the device can satisfy the expert consensus requirements for oral PDT.

Conflicts of Interest

The authors declare no conflicts of interest relevant to this article.

Acknowledgments

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