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Responses of human sensory characteristics to 532 nm pulse laser stimuli

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Abstract.
BACKGROUND: Lasers are advantageous in some applications to stimulate a small target area and is used in various fields such as optogenetic, photoimmunological and neurophysiological studies.
OBJECTIVE: This study aims to implement a non-contact sense of touch without damaging biological tissues using laser.
METHODS: Various laser parameters were utilized in safety range to induce a sense of touch and investigate the human responses. With heat distribution simulation, the amount of changes in the temperature and the tendency in laser parameters of sensory stimulation were analyzed.
RESULTS: The results showed the identified tactile responses in safety range with various laser parameters and temperature distribution for the laser stimulus was obtained through the simulation.
CONCLUSIONS: This study can be applied to the areas of sensory receptor stimulation, neurophysiology and clinical medicine.

Keywords: Laser stimuli, pulse laser, perception, skin temperature simulation

1. Introduction

Recently, optogenetic, photoimmunological and optoelectronical studies using the laser have actively been in progress. In particular, using laser has a merit that it can minimize side effects that may occur when other nerve cells are stimulated. With high focusing capability, laser can stimulate single nerve cell or single nerve axon locally. Thanks to this merit and specificity of this optic nerve stimulation, various *in vitro/in vivo* studies are in progress, and the fields of the studies can be divided broadly into 1) a study to find a protein as effective as possible, which can stimulate the optic nerve with better properties and verify this; 2) a study to selectively express an ion channel protein that can stimulate the optic nerve in charge of a specific function or causing a lesion; and 3) an *in vitro/in vivo* study for effective optic nerve stimulation [1,2]. Previously, laser has been used in the medical field, such as diagnostic equipment like optical coherence tomography (OCT), ophthalmic surgery and skin treatment, but research related to the sense of touch is very rare. If laser with a very short pulse width is irradiated to an absorption substance,

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the medium is heated locally by momentary laser absorption. With laser beam incidence into the skin, the optical energy distribution in the skin becomes different by optical coefficients. Laser serves as an energy source, and the energy that entered into the skin tissue is converted to thermal energy by heat transfer coefficient, which increases the temperature in the body and transmits the heat to the surrounding tissue. As the heat is accumulated and increased in body, biological transformation takes place [3–5]. The effect of heat when laser is irradiated to a biological tissue has been studied. Using this phenomenon, it is used for diagnosis and treatment in the medical field [6–8]. The existing technique of implementing the non-contact sense of touch using ultrasound needs several actuators to cause stimulation with the limit of spatial resolution, limit of location or distance control and a single focus [9,10]. This study aims to implement a non-contact sense of touch without damaging biological tissues using laser. Thus, within laser safety range such as maximum permissible exposure (MPE), an experiment was conducted using laser with a short irradiation time in the pulse form. And the laser parameters was set up considering MPE as the laser safety standards, and the experiment was carried out in the range without the damage of the organization like the coagulation or ablation, and the temperature-rise and its trend was analyzed through the light distribution simulation on skin [11–15]. It is expected that the result of this study will contribute to the studies on laser stimulation, clinical engineering and neurophysiology.

2. Material and methods

2.1. Laser stimulation

Figure 1 shows the procedure of experiment for stimulating a sense of touch by laser. Diode pumping Q-switch laser (Centurion+, Quantel, USA) with 532 nm wavelength, pulse width of 8 ns, the maximum output energy of 25 mJ, and the pulse repetition rate of 1 to 100 Hz range was used. The beam generated from laser was made to pass through an optical filter and lens to the index finger of the subject. The lens and 3-axis stage were used for controlling of spot size and target position. The laser energy was controlled by the combination of the various optical filters. The laser energy and beam diameter was measured by using pyroelectric energy detector (818E-05-12-L, Newport, Irvine, CA, USA) and an energy meter (1918-R, Newport, Irvine, CA, USA) and the beam profiler (SP620U, Ophir-Spiricon LLC., N. Logan, UT, USA) in the hand position for the laser can be irradiated.

During the progress of the experiment, a fake stimulus was given between laser stimuli, and whether the sense of touch would be differentiated by each subject was checked. The experiment was composed with the total 20 (10 males, 10 females) subjects. This experiment was approved by the Institutional Review Board at Konkuk University (7001355-201408-HR-032).

Table 1 showed the experiment variables for the single shot and repetitive pulse. The experiment used the variable as following table to examine the effect of beam diameter by energy in the laser scope of safety standards. The energy can be changed depending on the change of repetition rate due to the MPE limit (see Section 2.3). The laser irradiation time of repetition rate experiment was fixed as 1 s.

2.2. Simulation for heat and temperature distribution on skin surface

When laser energy is irradiated in very short time, the instantaneous heating of tissue due to the energy absorption by pulsed-laser radiation can induce rapid thermal expansion of the heated volume in tissue. The thermoelastic waves can appear and cause mechanical stress which may induce the stimulation of human mechano-receptors. In this study, the laser absorption distribution in the skin was calculated

Table 1
Laser parameters used in the experiment

Experiment variable	Experiment range	
	Single shot	Repetitive pulse
Energy	1, 1.28, 1.6, 1.9 mJ (4 steps)	0.6, 0.72, 1.28 mJ (3 steps)
Beam diameter	0.22, 0.8, 1, 1.5 mm (1/e)	0.22, 0.48, 1 mm (1/e)
Frequency		5, 50, 100 Hz
Episode time	8 ns	1 s (Stop experimentation if a pain occurs)
Subjects	A total 20 persons (10 males + 10 females)	

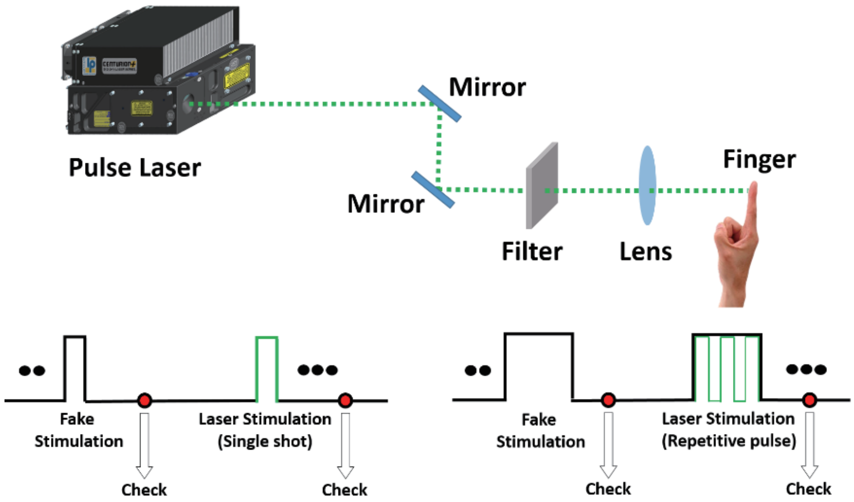


Fig. 1. Schematic of laser stimulation.

considering the scattering and absorption in the reflection of skin surface by simulation about the light distribution of laser using TracePro of Lambda Research Corporation (USA). In addition, the value of the thermal diffusion equation was calculated by using the ANSYS CFD of ANSYS, Inc. (USA) and the simulation about the heat and temperature distribution in the skin was carried out. The thermal diffusion equation which was used in this study is as follows.

$$\rho C = \frac{\partial T}{\partial t} = k\Delta^2 T + W_b C_b (T_a - T) + Q \quad (1)$$

Where, ρ, T, k, W_t, C_t, T_a and Q, respectively, refer to skin density, specific heat on the skin, temperature, heat conductivity of the skin, perfusion rate of blood, specific heat of blood, blood temperature and heat generated by laser absorption per unit time.

2.3. MPE

MPE refers to the abbreviation of Maximum Permissible Exposure, and the laser radiant level that the person is exposed without the adverse effects in the normal state [11]. MPE level shows the maximum level of the eyes or skin that can be exposed without damage immediately after exposure or long time, and it is related to the size on the retina by the radiation wavelength, pulse duration period, dangerous organization, visible and near infrared radiation in 400–1400 mm range. MPE means the applicable energy to 1/10 of dose value with 50% of skin damage, and it means the laser radiation level of the

Table 2
Laser parameters for single shot

Energy [mJ]	Beam diameter [mm]			
	0.22	0.48	1	1.5
1	5%	0%	0%	0%
1.28	10%	0%	0%	0%
1.6	20%	5%	0%	0%
1.9	75%	15%	0%	0%

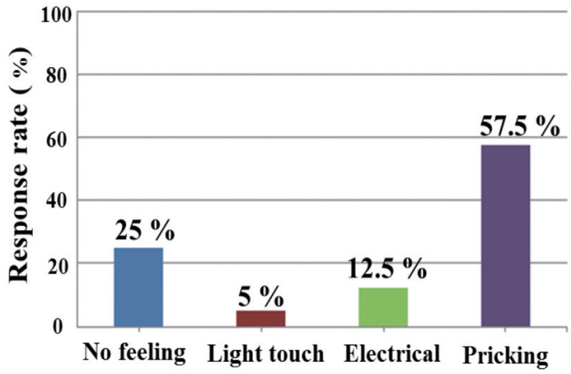


Fig. 2. Results of behavioral responses.

human skin by the irradiation of laser without damage in the normal condition. MPE value cannot be applied to the exposure of the patient about the laser radiation as the purpose of treatment. MPE depends on the laser wavelength and irradiation time. For $\lambda = 532$ nm, which is used in this study MPE can be calculated as the Eq. (2).

$$\mathrm{MPE}_{skin} = \frac{\Phi_o(1 - e^{-(D_f/a)^2})}{\pi(D_f/2)^2} \tag{2}$$

Where, Φ_0 means laser energy [J]; D_f, limiting aperture diameter at skin [cm]; and a, spot diameter (1/e) [cm].

3. Results and discussion

3.1. Single shot stimulation

Table 2 shows the result of response rate of experiment about the various parameters by changing the energy, beam diameter for single shot. When the beam diameter was 0.22 mm, it was found that the touch response rate increased as energy increased. In addition, when energy was 1.9 mJ, it was found that the touch response rate increased as the beam diameter decreased. The laser parameter with the highest response rate within the touch laser safety range was when the beam diameter was 0.22 mm in a condition with energy, 1.9 mJ. In other words, the stimulus of 532 nm laser was judged as the optimal condition without pain in the safety range. Most subjects responded that they felt a sense of touch rather than pain at this time.

Figure 2 is the result of confirmation of the superior sense in a detailed classification and analysis of the sense of touch in the parameter with the highest response rate (energy: 1.9 mJ; beam diameter: 0.22 mm). In the result of analysis of the detailed classification of sense of touching, most of the subjects responded that they felt the mechanical stimulation including pricking and light touch. The subjects responded that the pricking sense they felt was not pain. In addition, the subjects who did not feel the sense were 25%, and the subjects who felt sense weakly were 5%. In addition, the subjects who felt the electrical sting sense were also 12.5%.

Table 3
Laser parameters for repetitive pulse

Energy [mJ]	Repetition rate [Hz]	Beam diameter [mm] 0.22	0.48	1
1.28	5	16%	4%	0%
0.72	50	12%	10%	5%
0.6	100	71%	15%	11%

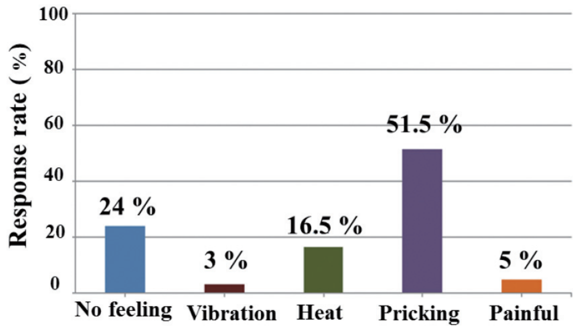


Fig. 3. Results of behavioral responses (repetition rate).

3.2. Repetitive pulse stimulation

Table 3 is the result of a study of the sense of touch according to the changes of the beam diameter and repetition rate in a repetitive pulse. The repetition rate experiment can be conducted by calculating MPE for 5, 50, 100 Hz, so the energy was changed by the change of repetition rate [11]. It can be seen that the response rate increases by decrease of beam diameter when the repetition rate is 100 Hz. In other words, it was found that the response rate increased as the energy density increased. The laser parameters at which the subjects felt a sense of touch rather than pain were when repetition rate was 100 Hz and the beam diameter was 0.22 mm in a condition with energy of 0.6 mJ. About 71% of the subjects responded that they felt a sense of touch.

Figure 3 is the result of an analysis of the superior sense by a detailed classification of senses of touch with the highest response rate for repetitive pulse experiment. After laser stimulation, the participants were asked what they felt. The subjective description was recorded and expressed into no feeling, vibration, heat, pricking, and pain. Some subject felt dual perception for a single stimulation and it was counted 0.5 for each perception (e.g. heat = 0.5, pricking = 0.5). The laser stimulation was repeated 5 times for each subject. Their responses were counted and normalized for perception analysis. In the result of the detailed classification, it can be seen that the mechanical stimulation including vibration and pricking was abundant. In addition, the subjects who felt about 16.5% of sense of heat increased compared to the single shot of the laser stimulus. It is judged that the subjects who felt the sense of heat of the stimulus increased in the repetitive pulse method by the accumulated absorption energy of laser pulse periodically.

3.3. Simulation results for single shot

Figure 4 shows the result of simulation of changes in temperature rise in the skin surface (location: incidence center of the laser beam) according to time. Immediately after the incidence of the laser pulse, the skin temperature tends to increase rapidly and then decreases slowly by the causes, such as temperature diffusion and convection. It is observed that decay time constant which decreases to 1/e size of the maximum temperature is determined by the beam diameter, regardless of the energy of the laser pulse. It was observed that the decay time constant with the beam diameter of 0.22 mm was about 0.09 s, and the decay time constant with the beam diameter of 0.48 mm was 0.16 s. In addition, in the result of simulation of a single shot condition, the maximum temperature rise increased as the laser pulse energy increased when the beam diameter was the same.

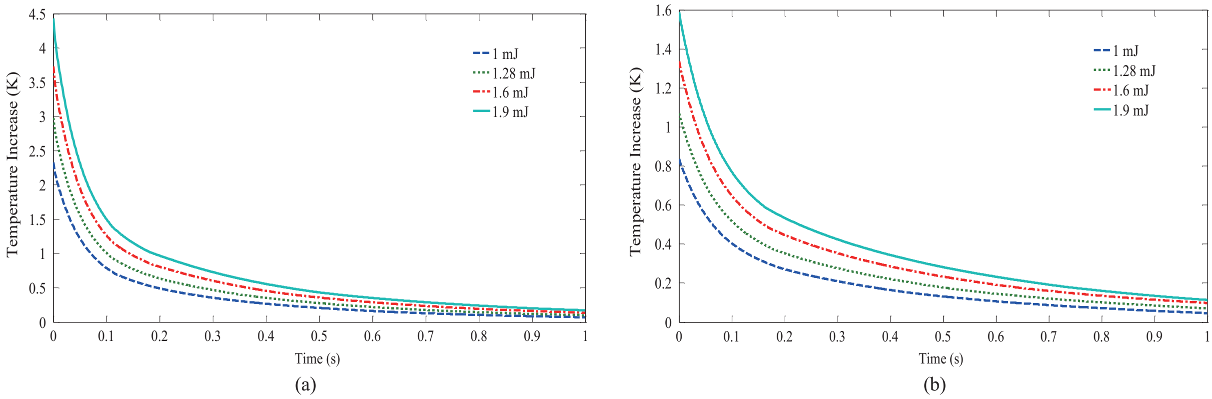


Fig. 4. Results of simulation of change in temperature rise of skin surface according to time (Location: Incidence center of laser beam). (a) Beam diameter 0.22 mm, (b) Beam diameter 0.48 mm.

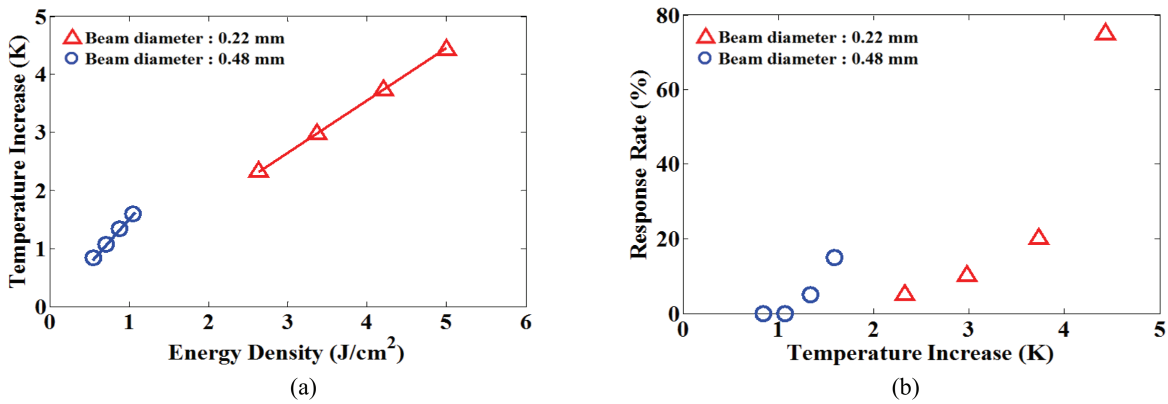


Fig. 5. (a) Change in maximum temperature rise according to energy density when beam diameter is 0.22 mm and 0.48 mm; and (b) Result of simulation of maximum temperature rise and touch perception response rate when beam diameter is 0.22 mm and 0.48 mm.

Figure 5(a) shows the tendency of change in the maximum temperature rise according to energy density in the domain in which the subjects responded that they felt a sense of touch in a single shot condition (beam diameter: 0.22 mm and 0.48 mm). If the beam diameter was the same, the temperature rise was in linear proportion to the energy density. In addition, when the beam diameter was 0.22 mm, it was observed that there was a greater temperature rise than when the beam diameter was 0.48 mm. As a result of simulation, it is judged that the smaller beam diameter caused higher temperature rise due to the increased energy density. Figure 5(b) shows the result of simulation of the maximum temperature rise and a comparison of touch perception response rate when the beam diameter was 0.22 mm and 0.48 mm. When the beam diameter is the same, as the maximum temperature rise increases, touch perception response rate tends to increase. It is judged that the smaller beam diameter induced the higher temperature rise resulting in the increased perception response rate.

3.4. *Simulation results for repetitive pulse*

Figure 6 shows the results of simulation of change in temperature according to changes in the beam diameter and repetition rate by pulse stimulation. As in a single shot, immediately after the incidence of

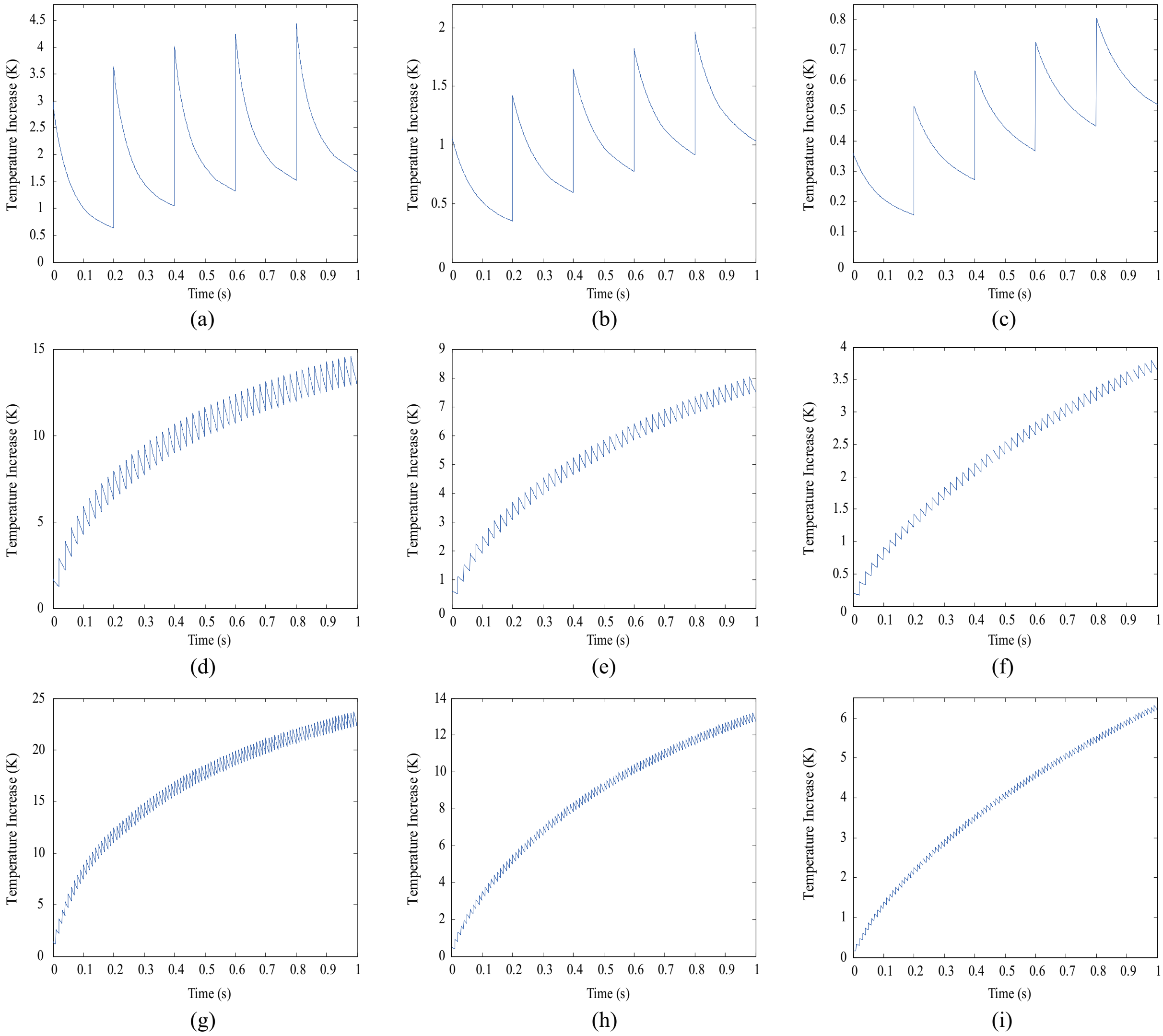
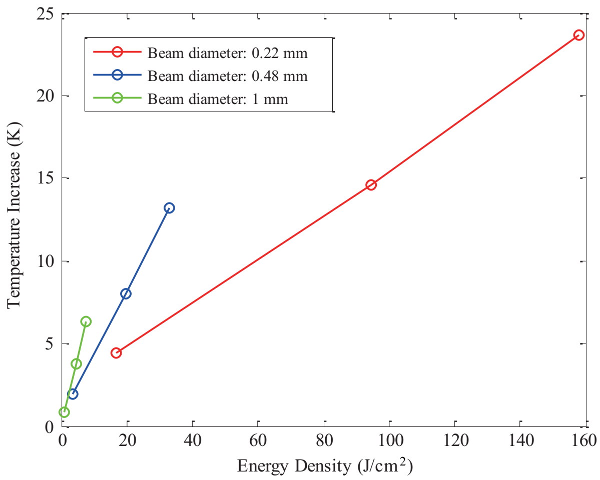


Fig. 6. Result of simulation of change in temperature rise of skin surface according to time (Location: Incidence center of laser beam). (a) Energy 1.28 mJ, Repetition rate 5 Hz, Beam diameter 0.22 mm, (b) Energy 1.28 mJ, Repetition rate 5 Hz, Beam diameter 0.48 mm, (c) Energy 1.28 mJ, Repetition rate 5 Hz, Beam diameter 1 mm, (d) Energy 0.72 mJ, Repetition rate 50 Hz, Beam diameter 0.22 mm, (e) Energy 0.72 mJ, Repetition rate 50 Hz, Beam diameter 0.48 mm, (f) Energy 0.72 mJ, Repetition rate 50 Hz, Beam diameter 1 mm, (g) Energy 0.6 mJ, Repetition rate 100 Hz, Beam diameter 0.22 mm, (h) Energy 0.6 mJ, Repetition rate 100 Hz, Beam diameter 0.48 mm, (i) Energy 0.6 mJ, Repetition rate 100 Hz, Beam diameter 1 mm.

the first laser pulse, it is observed that the skin temperature tends to increase rapidly and then decrease gradually, and with the incidence of the next laser pulse, there is a rapid temperature rise again. It is observed that, before returning to the temperature prior to the incidence of laser, as a temperature rise occurs by the next laser pulse absorption, which accumulates the temperature rise, and as time passes, the temperature tends to increase slowly. The temperature rise gradient tended to decrease as time passed. As in a single shot, as the beam diameter increased, the decay time constant increased (In Figs 6(a), (d) and (g), beam diameter was 0.22 mm; in Figs 6(b), (e) and (h), beam diameter was 0.48 mm; and in Figs 6(c), (f) and (i), beam diameter was 1 mm). With the same energy and repetition rate, as the beam



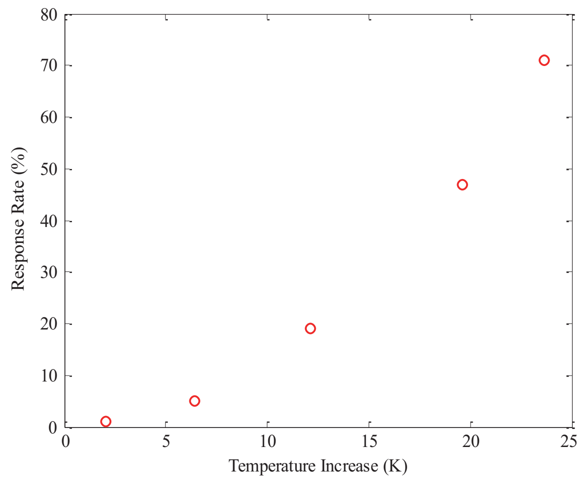


Fig. 7. (a) Change in maximum temperature rise according to total energy density when beam diameter is 0.22 mm, 0.49 mm and 1 mm for repetitive pulses; and (b) Result of simulation of maximum temperature rise according to repetition rate and touch perception response rate.

diameter increased, the maximum temperature rise tended to decrease (see Figs 6(a), (b), (c)), and it is judged that for a small beam diameter, since the temperature reduction rate becomes relatively greater till the incidence of the next laser pulse, the temperature rise gradient as time passes becomes smaller than with a greater beam diameter.

Figure 7(a) shows the maximum temperature rise by the energy density for the repetitive pulse. The total energy density was calculated for examining the relationship between the maximum temperature rise and total energy density (absorbed total energy/beam area for 1 s). In the case of same beam diameters, it can be seen that the temperature rise was shown in the energy density linearly. The bigger the beam diameter was, the larger temperature-rise gradient was shown. When beam diameter was 0.22 mm, 0.48 mm, and 1 mm, the temperature-rise gradient was 0.14 K/(J/cm^2), 0.38 K/(J/cm^2), and 0.81 K/(J/cm^2), respectively. When the beam diameter was 0.22 mm and 0.48 mm, as compared to a single shot, the temperature rise gradient in both cases became smaller, and it is judged that this was caused by the decrease of the temperature by temperature diffusion and convection. In addition, Fig. 7(b) shows the result of simulation of the maximum temperature rise according to repetition rate and a comparison of touch perception response rate. With the increase of the maximum temperature rise, touch perception response rate tended to increase, and it is found that it is consistent with the result of the single shot.

4. Conclusion

In this study, the subjects were stimulated by using the various laser parameters in the laser safety range, and the cognitive characteristics were researched. The temperature-rise data for the laser stimulus was obtained through the simulation, and it was compared with the experimental recognition data. In the result of the experiment, it can be seen that the subjects showed the different cognitive characteristics by the laser energy, beam diameter (energy density), and the repetition rate. In addition, in the same laser energy condition, it was observed that cognitive characteristics differed depending on the beam diameter and repetition rate. Especially, when the laser stimulus was added with the repetitive pulse periodically, the absorption energy of the laser pulse was accumulated and more subjects felt a sense of heat, and at this time, it was observed that the maximum temperature rise increased. As a result of simulation, in the temperature rise and touch perception, it was found that the beam diameter would be a very important laser parameter, and for a single shot and repetitive pulse. To sum up the results of the study, considering various parameters of laser, the strength of various stimuli of laser could be controlled, which means that laser could present senses other than pain. This study found that using laser has a merit that it could transmit energy in a desired size and shape to the exact location without any direct contact. It is expected that the results of this study can be used helpfully for the activation of an ion channel through cell stimulation and for the stimulation of nerves instead of electrical stimulation, treatment using bio-stimulation effect and studies of non-contact tactile technologies and pre-pain.

Acknowledgements

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