Experimental Studies of Laser Photodynamic Therapy (II)

- Intratumor Temperature Rise and Photochemical Reaction -

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Introduction

The origin of the tumor destruction by the laser photodynamic therapy is generally attributed to a photochemical reaction, and not to a hyperthermal effect. However, clinically to destroy the deep tumor cell, high power density irradiation, which might cause a hyperthermal effect, is necessary.

In order to clarify the effect of heat production during a laser treatment, variations of temperatures were measured and the efficiency of the tumor destruction was examined histopathologically.

Materials and Methods

Tumor model is MH-134 transplanted in C3H/He mice. Mice were administered HpD (5mg/kg) i.p. and 24hours post injection, tumors were irradiated by laser light. The measurements of intratumor temperatures were made using a thermistor probe inserted into the tumor at a depth of 3mm below the irradiated surface.

Argon-pumped dye laser (635nm) and Nd:YAG-pumped pulse dye laser (635nm) were used for the photodynamic treatment, and Nd:YAG laser (1.06 μ) was used only for the evaluation of the thermal effect.

Forty-eight hours after the laser treatment, mice were sacrificed, and effects of tumor destruction were examined histopathologically.

Temperatures of agar-agar, which contained HpD and human serum (8.4×10^{-5} M, 4.2×10^{-4} M, 8.4×10^{-4} M) were measured by the same manner as the intratumor measurement.

Results and Discussion

In the case of Nd:YAG-pumped pulse dye laser irradiation, the degree of temperature rise (ΔT) was restricted only from 0.8 to 1.7°C at 50mW/cm² (average power), while in the case of Argon-pumped dye laser irradiation, ΔT was rather high ranging from 3 to 4°C at 50mW/cm², 6°C at 100mW/cm², 10°C at 200mW/cm², from 13 to 14°C at 300mW/cm² and from 18 to 19.5°C at 400mW/cm², respectively. (Fig.1)

In the case of Nd:YAG laser irradiation, ΔT was estimated as 6.5°C at $400\text{mW}/\text{cm}^2$, 14°C at $750\text{mW}/\text{cm}^2$ and 16 to 30°C at $1\text{W}/\text{cm}^2$, respectively. These results indicate that in the case of CW laser treatment, intratumor temperature rises with increasing laser power density.

Table 1 shows the observed histological necrosis as a function of irradiated laser intensity. Noticeably, in the case of Nd:YAG laser irradiation, the histological necrosis was observed at $750\text{mW}/\text{cm}^2$, which produced the same ΔT rise at $300\text{mW}/\text{cm}^2$ in the case of Argon-pumped dye laser irradiation. These results indicate that origins of the tumor destruction by Argon-pumped dye laser at $300\text{mW}/\text{cm}^2$ should be partially attributed to the hyperthermal effect.

Temperature rise of agar-agar was 1.4°C at the concentration of $8.4 \times 10^{-5}\text{M}$, 3°C at the concentration of $4.2 \times 10^{-4}\text{M}$ and 3.7°C at the concentration of $8.4 \times 10^{-4}\text{M}$, respectively.

Conclusion

These results strongly suggest that photodynamic treatment using HpD should be regarded as partially taking an advantage of a hyperthermal effect brought about at high power density after laser irradiation.

Fig. 1 Intratumor temperature rise during the laser irradiation

Laser Source	Power Density	Tumor	Necrosis Necrobiosis
Argon pumped Dye laser (CW)	$35\text{mW}/\text{cm}^2$	±	— +
	$70\text{mW}/\text{cm}^2$	++	— +++
	$95\text{mW}/\text{cm}^2$	+++	
Nd-YAG pumped Dye laser (Pulse)	$35\text{mW}/\text{cm}^2$	±	— +
	$70\text{mW}/\text{cm}^2$	+	— ++
	$95\text{mW}/\text{cm}^2$	++	— +++
Nd-YAG laser (CW)	$400\text{mW}/\text{cm}^2$	±	— +
	$750\text{mW}/\text{cm}^2$	++	
	$1.2\text{W}/\text{cm}^2$	+++	

Table 1 Histological result