Development of Minimally Invasive Mid-infrared Lipolysis Laser System for Effective Fat Reduction

Ji-Young Lee
Han Young Ryu
Young-Seok Seo

R&D Center, Wontech Co., Ltd., Daejeon, Korea

Background and Objectives

Due to changes in diet and lifestyle, the number of obese people worldwide is steadily increasing. Obesity has an adverse effect on a healthy life, so it needs treatment and improvement. Research related to this is continuously being conducted.

Materials and Methods

The laser system to compact designed using 808 nm laser diode and Neodymium Yttrium orthovanadate generates a 1064 nm wavelength, the periodically polarized nonlinear crystal pumping laser beam. The pulsed 1064 nm wavelength beam passing through the AO Q-switch is used as the pumping light of the nonlinear optical crystal and is irradiated to the periodic polarized nonlinear optical crystal with a quasi-phase matching period. Nonlinear optical crystals use an oven to control the temperature to generate the desired 1980 nm and 2300 nm wavelengths.

Results

The 1980 nm and 2300 nm wavelengths generated by temperature control of nonlinear optical crystals are effective for lipolysis. A fiber catheter was used so that the laser could be directly irradiated to the fat cells. In particular, the new wavelength (1980 nm, 2300 nm) can increase the fat reduction effect with low energy (1.3 W). When a laser with a combination wavelength of 1980 nm and 2300 nm was used, an average lipolysis effect of 20% was obtained.

Conclusion

A mid-infrared lipolysis laser system with excellent absorption of fat and water has been developed. We conducted a preclinical study to confirm the efficacy and safety of the lipolysis laser system, and obtained good results for lipolysis with low energy.

Key words

Mid-infrared; Lipolysis laser; Nonlinear crystal; Preclinical

Received March 8, 2021
Accepted March 31, 2021

Correspondence

Ji-Young Lee
R&D Center Wontech Co., Ltd., 64 techno 8-ro,
Yuseong-gu, Daejeon 34028, Korea
Tel.: +82-70-7841-6526
Fax: +82-70-7863-3350
E-mail: yw106707@wtlaser.com

© Korean Society for Laser Medicine and Surgery

© This is an open access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/4.0/>) which permits unrestricted non-commercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

INTRODUCTION

Due to the development of medicine and science, the aging population is increasing as human life span. Due to aging, a lot of time and economic investment led to a healthy life without disease. One of the health-threatening causes is obesity. Obesity is the simple weight of the past means that much of the current obesity is a lot of body fat accumulated in the body, which means a state piled up. Due to changes in eating habits and lifestyles, the number of obese people worldwide is steadily increasing.¹ Obesity affects health and self-esteem in social activities and medical techniques and devices developed. Laser lipolysis reduces fat and shortens recovery time and works to prevent bleeding by coagulating blood vessels and effective skin tightening by inducing collagen production.²⁻⁵ This study has developed the world's first minimally invasive lipolysis laser system with 1,980-nm and 2,300-nm wavelengths. The fat reduction by the laser depends on the wavelength and energy of the laser.⁶ Each wavelength used by lipolysis laser has its own characteristics. It has a high hemostatic function, which is a unique role of the 1,064-nm wavelength, and has a high absorption rate of water, so that it also acts as a tightening function. The 1,320-nm wavelength has higher water absorption than 1,064 nm, and has a fat-dissolving effect. The 1,444-nm wavelength is currently the highest fat solubility wavelength used in laser-assisted liposuction (LAL) equipment, which is 40 times higher than 1,064 nm.⁷ As shown in Fig. 1, as the wavelength increases, the absorption of fat and water increase. In general, the subcutaneous fat layer does not contain only fat, but water and fat are mixed together. When the absorption rate for water and fat increases, the solubility of fat is high, increasing the

Fig. 1. Comparison of laser absorption rate for fat and water.

therapeutic effect. The reason why the 2,000-nm band, which has a higher fat absorption rate at present, is not used because it is technically difficult to generate the desired wavelength and the high absorption of water poses a risk of burns. In this study, 1,980-nm and 2,300-nm laser were developed that are effective for lipolysis. In addition, since it used a lower power (1.3 W) than other wavelength lasers (1,444 nm/12 W), the risk of burns is reduced.

MATERIALS AND METHODS

Laser system development

Generally, neodymium (Nd):yttrium aluminium garnet crystal (YAG) and Nd:Yttrium orthovanadate crystal (YVO₄) are used to generate a laser with a wavelength of 1,064-nm. Nd:YAG diode pumped solid state (DPSS) laser,⁸ the use of a side-pumping DPSS laser and a Faraday Rotator for polarization control through a polarization element limits the laser head size reduction. To overcome the limitation of size, we designed a modified laser head with a structure using Nd:YVO₄ and 808-nm laser diode (LD).⁹⁻¹¹ A high power fiber-coupled diode laser pumped the Nd:YVO₄ crystal at 808 nm with a maximum power of 100 W. Nd:YVO₄ has an absorption rate of 808 nm that is 5 times better than that of Nd:YAG and has the same power at a low output than Nd:YAG diode output, thus doubling the lifetime of the diode. It also has the advantage of generating a linear polarized beam of 1,064-nm wavelength. The lens was designed using CodeV to focus the beam diverging from the 808-nm LD onto Nd:YVO₄. Since Nd:YVO₄ has the characteristic of birefringence, only the beam having the polarization in the direction corresponding to the axial direction can pass. These characteristics affect the output power. As well know, we used a-cut Nd:YVO₄ (4 × 4 × 20 mm, 0.2 % doping) because it has a maximum output power 7 times higher than c-cut.¹² To keep the Nd:YVO₄ temperature constant, an amount including a cooling system was designed. An acousto optical (AO) Q-switch was used to make a pulse beam. AO Q-switch was intended to have a pulse repetition rate of several kHz using crystal quartz.¹³ A pulsed 1,064-nm wavelength beam is used as a pumping beam for the optica parametric oscillators (OPO) cavity. The OPO cavity consists of a periodically polarized nonlinear optical crystal with a quasi phasematching (QPM) period and a back mirror, and an out mirror. To obtain a wavelength of 2 μm suitable for lipolysis, periodically poled stoichiometric lithium tantalate (PPSLT) crystal (3 × 3 × 20 mm, 32.19 μm grating period) was selected as shown in Fig. 2. by calculating the wavelength change with the temperature of the nonlinear opti-

cal crystal.¹⁴⁻¹⁷

We used the depend on temperature Sellmeier equation for the extraordinary refractive index of stoichiometric lithium tantalate crystal (SLT) proposed by Bruner.^{18,19} All of the OPO cavity mirrors were flat mirrors. The back

Fig. 2. Wavelengths variation of nonlinear optical crystal with temperature. PPSLT, periodically poled stoichiometric lithium tantalate.

mirror is highly transmitting ($T > 95\%$) for the pump beam and highly reflective ($R > 97\%$) for the $2\ \mu\text{m}$ wavelengths. Our mirror is highly reflective ($R > 99\%$) for the pump beam and partial transmitting ($T > 50\%$) for the $2\ \mu\text{m}$ wavelengths. To control nonlinear optical crystal temperature to obtain a stable wavelength with heater oven using real-time temperature sensor was made. When the pumping beam of $1,064\ \text{nm}$ is incident on the nonlinear optical crystal, the second harmonic of $532\ \text{nm}$ wavelength is generated.²⁰ It generated the crystal temperature changes, mid-infrared of $1,980\text{-nm}$ and $2,300\text{-nm}$ wavelengths. The result of the wavelength change calculation according to the nonlinear optical crystal temperature was 110°C . We designed and fabricated an oven to control nonlinear optical crystal temperature, as shown in Fig. 3.

A beam of $1,064\ \text{nm}$ is pumped into the nonlinear optical crystal, and the second harmonic of 532-nm wavelength is generated. The wavelengths generation from increasing the temperature of the oven were measured. As a result, we have achieved wavelengths of $1,980\ \text{nm}$ and $2,300\ \text{nm}$ at 175°C . We have a set of nonlinear optical crystal temperatures of about 175°C according to the

Fig. 3. Oven for temperature control of nonlinear optical crystal, (A) design, (B) production and application.

Fig. 4. Output wavelength and power measurement results of the lipolysis laser system.

Fig. 5. Design of mid-infrared lipolysis laser in the ex-vivo experiment.

experimental results.

As shown in Fig. 4, 532-nm second harmonic generation beam is reflected by the folding mirror, 1,980 nm and 2,300 nm are passed through the selection filter. We designed a coupling lens to focus at 1,980-nm and 2,300-nm wavelengths on the fiber. We developed a lipolysis laser system with 1,980-nm and 2,300-nm wavelengths included with laser head, temperature controller, power supply, and cooling system.

RESULTS

Lipolysis preclinical experiment results and discussion

We conducted preclinical ex-vivo and in-vivo to confirm the minimally invasive mid-infrared lipolysis laser safety and efficacy.

Ex-vivo experiment

First, ex-vivo experiments were performed to determine the power of wavelengths of 1,980 nm and 2,300 nm.²¹ It was designed and experimented as shown in Fig. 5. using pig bulk tissue. A cannula is used to deliver the laser irradiated from the fiber tip to the adipose tissue. To confirm reducing the fat cells by laser without damage by the cannula and tissue changes in the red line area were

Table 1. Conditions of mid-infrared lipolysis laser irradiation in the ex-vivo experiment

Wavelength	Power	Time
1,980 nm	0.8 W	1 min, 2 min, 4 min
2,300 nm	0.4 W	1 min, 2 min, 4 min
1,980 nm + 2,300 nm	1.2 W	1 min, 2 min, 4 min

observed. Laser irradiation condition, as shown in Table 1.

The guide beam was used to visually check where the laser was irradiated. After laser irradiation, a tissue sample was extracted and histological analysis was performed.

After laser irradiation, hematoxylin & eosin (H&E) staining was used to analyze changes in adipose tissue. As shown in Fig. 6, in the case of irradiation for 4 minutes with a combination of 1,980 nm and 2,300 nm, fat cells decomposed.

In-vivo experiment

Based on the results of the ex-vivo experiment, in vivo animal experiment was performed. IRB approval was obtained for this experiment. In the experiment design, the abdomen of a 12 months old male mini-pig was divided into six parts and irradiated with a laser. Skin color, hair follicles, sweat glands, and subcutaneous fat were

Fig. 6. Hematoxylin & eosin (H&E) staining results after the ex-vivo experiment (original magnification, $\times 100$).

Table 2. Conditions of mid-infrared lipolysis laser irradiation in the in-vivo experiment

Part #	Wavelength	Power	Time
1 ~ 5 (Experimental Group)	1,980 nm + 2,300 nm	1.2 W	5 min
6 (Control)	1,470 nm	1.2 W	5 min

experimented with using mini pigs similar to humans.^{22,23} Pig skin, similar to humans, has relatively few coats, and the subcutaneous tissue is firmly connected. The overall shape of epidermal thickness, cellular composition, and cutaneous blood supply is similar to that of humans, expect that there is no apocrine sweat gland. The laser irradiation conditions are as shown in Table 2.

After laser irradiation, safety was confirmed through blood tests and visual observation of skin and biopsy. To check the efficacy and the change in the thickness of the fat layer was measured using ultrasound. Visual observation of skin was performed before and at 0, 1, 7, 15, 30, 60, 90 days after laser irradiation. As shown in Fig. 7, the abnormal change due to the laser irradiation confirmed could not be.

To confirm physiology safety, H&E staining of the tissue was performed 15, 30, 60, and 90 days after laser irradiation. As a result, it was observed that other cytoplasm,

muscle cells and intracytoplasmic fibrous tissue were formed in the deformed part of the adipose tissue. As a result of observation, as shown in Fig. 8, after 30 days, other cytoplasm, muscle cells and intracytoplasmic fibrous tissue were generated in all areas, but #6 (control) was relatively lower than that of other elements (experimental group).

During 3 days after laser irradiation, a total of 8 blood tests (0, 2, 4, 8, 12, 18, 24, 48, 72 hours) were performed to confirm changes in liver function, kidney function, and lipid levels. As shown in Table 3, the aspartate transaminase (AST) level showed a tendency to increase between 4 and 24 hours of laser irradiation but returned to normal after 48 hours.

To confirm the efficacy and changes in the fat layer's thickness were measured by abdominal ultrasound before and immediately, 1, 7, 15, 30, 60, 90 days after laser irradiation. Fig. 9 shows the ultrasound measured before and 90 days after laser irradiation in #1. The thickness of the fat layer decreased by 33 % from 7.22 mm before laser irradiation to 4.86 mm after 90 days of laser irradiation. As shown in Fig. 10 of measurement results, found that the thickness of the fat layer increased in all areas after 1 day of irradiation. It can see that it increases by more than 40% in #1 and decreases rapidly after 7 days.

Fig. 7. Visual observation for 90 days before and after laser irradiation.

Fig. 8. H&E staining results after laser irradiation (original magnification, $\times 100$).

Table 3. Blood test results after laser irradiation

Item	TP	ALB	GLB	A/G	AST	ALT	BUN	T-BIL	T-CHO	ALP	Ca	P	TG	CREA	HDL-C	LDL-C	NEFA
Unit	g/dL	g/dL	g/dL	Ratio	IU/L	IU/L	mg/dL	mg/dL	mg/dL	IU/L	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mg/dL	mEq/L
D9-15 0H	7.1	4.1	3.0	1.4	47	42	10.4	0.00	88	73	11.1	6.9	23	2.27	40.9	38.9	147
D9-15 2H	6.7	3.9	2.8	1.4	51	39	10.6	0.02	83	75	10.6	6.4	17	2.27	37.9	38.3	113
D9-15 4H	8.1	4.6	3.5	1.3	102	46	14.3	0.05	96	84	11.8	7.4	20	2.54	44.3	43.4	191
D9-15 8H	7.9	4.6	3.3	1.4	160	48	17.8	0.06	90	85	11.4	7.9	19	2.53	41.7	42.1	198
D9-15 12H	7.5	4.4	3.1	1.4	269	48	22.2	0.09	84	86	10.8	8.2	17	2.53	37.1	40.9	198
D9-15 24H	7.3	4.2	3.1	1.4	90	43	19.8	0.02	79	76	10.2	5.4	17	2.22	38.0	35.9	80
D9-15 48H	8.3	4.7	3.6	1.3	57	52	12.4	0.03	101	81	10.9	6.3	21	2.21	48.7	43.7	141
D9-15 72H	7.8	4.5	3.3	1.4	42	52	13.1	0.02	115	86	11.7	5.9	40	2.22	51.1	50.3	36
Mean	7.6	4.4	3.2	1.4	102	46	15.1	0.04	92	81	11.1	6.8	22	2.35	42.5	41.7	138
SD	0.5	0.3	0.3	0.0	78	5	4.4	0.03	12	5	0.6	1.0	8	0.15	5.2	4.4	59
N	8.0	8.0	8.0	8.0	8	8	8.0	8.00	8	8	8.0	8.0	8	8.00	8.0	8.0	8

D, day; H, hour; SD, standard deviation; TP, total protein; ALB, albumin; GLB, globulin; A/G, albumin/globulin ratio; AST, aspartate transaminase; ALT, alanine aminotransferase; BUN, blood urea nitrogen; T-BIL, total bilirubin; T-CHO, total cholesterol; ALP, alkaline phosphatase; TG, triglyceride; CREA, creatinine; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; NEFA, non-esterified fatty acid.

Fig. 9. Ultrasound results measured before and 90 days after laser irradiation in #1.

Fig. 10. Fat layer thickness change graph after laser irradiation.

The fat thickness of all parts decreased by 30 days and increased by 5% at #4, #5, #6 at 60 days. For 90 days after laser irradiation was the thickness, the difference depending on location decreased 5–35% of all parts. When the combination wavelength of 1,980 nm and 2,300 nm was irradiated (#1–#5), there was a tendency to decrease continuously after 60 days. However, when irradiated with a wavelength of 1,470 nm (#6), there is no tendency to fall.

DISCUSSION

We developed a minimally invasive lipolysis laser system that uses the nonlinear optical crystal to produce wavelengths of 1,980 nm and 2,300 nm with good absorption of water and fat. A preclinical study was conducted in mini pig to confirm the minimally invasive lipolysis laser safety and efficacy. When irradiated with a combination of 1,980-nm and 2,300-nm wavelengths has obtained an average of 20 % fat reduction. Blood tests and biopsies have confirmed the minimally invasive mid-infrared lipolysis

laser system to be safe.

Based on the results of animal experiments, the minimally invasive mid-infrared lipolysis laser system was the first clinical trial with the approval of the clinical protocol of The Ministry of Food and Drug Safety (MFDS). Currently, the clinical trial is finished, and statistical processing is in progress.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

FUNDING

It was carried out with support from Establishment of joint research corporation and operation support industry of Korea Innovation Foundation.

REFERENCES

1. Khan A, Choudhury N, Uddin S, Hossain L, Baur LA. Longitudinal trends in global obesity research and collaboration: a review using bibliometric metadata. *Obes Rev* 2016;17:377-85.
2. Lukac M, Vizintin Z, Zabkar J, Pirnat S. QCW pulsed Nd:YAG 1064 nm laser lipolysis. *J Laser Health Acad* 2009;2009:86493.
3. Badin AZ, Moraes LM, Gondek L, Chiaratti MG, Canta L. Laser lipolysis: flaccidity under control. *Aesthetic Plast Surg* 2002;26:335-9.
4. O'Dey Dm, Prescher A, Poprawe R, Gaus S, Stanzel S, Pallua N. Ablative targeting of fatty-tissue using a high-powered diode laser. *Lasers Surg Med* 2008;40:100-5.
5. Nestor MS, Newburger J, Zarraga MB. Body contouring using 635-nm low level laser therapy. *Semin Cutan Med Surg* 2013;32:35-40.

6. Goldman A, Schavelzon DE, Blugerman GS. Laserlipolysis: liposuction using Nd-YAG laser. *Rev Soc Bras Cir Plást* 2002;17:17-21.
7. McBean JC, Katz BE. Laser lipolysis: an update. *J Clin Aesthet Dermatol* 2011;4:25-34.
8. Kim B, Kim DY. Enhanced tissue ablation efficiency with a mid-infrared nonlinear frequency conversion laser system and tissue interaction monitoring using optical coherence tomography. *Sensors (Basel)* 2016;16:598.
9. Délen X, Balembois F, Musset O, Georges P. Characteristics of laser operation at 1064 nm in Nd:YVO₄ under diode pumping at 808 and 914 nm. *J Opt Soc Am B* 2011;28:52-7.
10. Zhuo Z, Li T, Li X, Yang H. Investigation of Nd:YVO₄/YVO₄ composite crystal and its laser performance pumped by a fiber coupled diode laser. *Opt Commun* 2007;274:176-81.
11. Chen YF. cw dual-wavelength operation of a diode-end-pumped Nd:YVO₄ laser. *Appl Phys B* 2000;70:475-8.
12. Chen YF, Lan YP. Comparison between c-cut and a-cut Nd:YVO₄ lasers passively Q-switched with a Cr⁴⁺:YAG saturable absorber. *Appl Phys B* 2002;74:415-8.
13. Choo HT, Kim GU, Park CG, Choi JH, Rhyee KH. Laser-diode-pumped passively Q-switched Nd:YVO₄ self-Raman laser at 1178 nm. *NPSM* 2016;66:647-53.
14. Myers LE, Eckardt RC, Fejer MM, Byer RL, Bosenberg WR, Pierce JW. Quasi-phase-matched optical parametric oscillators in bulk periodically poled LiNbO₃. *J Opt Soc Am B* 1995;12:2102-16.
15. Duan Y, Zhu H, Xu C, Ruan X, Cui G, Zhang Y, et al. Compact self-cascaded KTA-OPO for 2.6 μm laser generation. *Opt Express* 2016;24:26529-35.
16. Kumar SC, Ebrahim-Zadeh M. High-power, fiber-laser-pumped, picosecond optical parametric oscillator based on MgO:sPPLT. *Opt Express* 2011;19:26660-5.
17. Peltola J, Vainio M, Hieta T, Uotila J, Sinisalo S, Metsälä M, et al. High sensitivity trace gas detection by cantilever-enhanced photoacoustic spectroscopy using a mid-infrared continuous-wave optical parametric oscillator. *Opt Express* 2013;21:10240-50.
18. Bruner A, Eger D, Oron MB, Blau P, Katz M, Ruschin S. Temperature-dependent Sellmeier equation for the refractive index of stoichiometric lithium tantalate. *Opt Lett* 2003;28:194-6.
19. Wen-Le W, You-Wen L, Xiao-Qi Z. Temperature-dependent Sellmeier equation for 1.0 mol% Mg-doped stoichiometric lithium tantalate. *Chin Phys Lett* 2008;25:4303-6.
20. Pati B, Wall KF, Moulton PF. High-efficiency 532-nm generation with PPSLT. *Advanced Solid State Photonics*; 2010 Jan 31-Feb 3; San Diego. OSA Publishing; 2010. p. ATuA17.
21. Kim B, Kim DY. Enhanced tissue ablation efficiency with a mid-infrared nonlinear frequency conversion laser system and tissue interaction monitoring using optical coherence tomography. *Sensors (Basel)* 2016;16:598.
22. Yeom SC. Miniature pig as laboratory animal. *J Korean Vet Med Assoc* 2011;47:142-55.
23. Zhang Z, Monteiro-Riviere NA. Comparison of integrins in human skin, pig skin, and perfused skin: an in vitro skin toxicology model. *J Appl Toxicol* 1997;17:247-53.

How to cite this article: Lee JY, Ryu HY, Seo YS. Development of minimally invasive mid-infrared lipolysis laser system for effective fat reduction. *Med Lasers* 2021;10:82-89. <https://doi.org/10.25289/ML.2021.10.2.82>