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A NEW SIMPLIFIED METHOD FOR LASER SINUS NODE MODIFICATION WITHOUT ELECTROPHYSIOLOGICAL TECHNIQUE

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INDEXING WORDS

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SYNOPSIS

As the treatment of inappropriate sinus tachycardia, β-adrenoreceptor blockade therapy is the most common method for pharmacological heart rate control, but it is occasionally limited by side effects of the drugs, especially in patients with cardiac dysfunction. On the other hand, cryoablation or surgical exclusion of the sinus node have not been accepted generally for their necessity of permanent pacemaker implantation. Modification of the sinus node function is a new method of nonpharmacological treatments, although the skillfull and troublesome technique is required. In this study, the efficacy and safety of laser sinus node modification without electrophysiological technique were investigated as a new simplified method. In six mongrel dogs, the laser-tissue interactions by epicardial Nd-YAG laser irradiation were investigated by measuring the diameter and the depth of the irradiated lesions. Laser irradiations were performed from the head to the tail on the sinus node areas directed only by terminal groove for the visual landmark without electrophysiological technique until about 25% decrease in heart rate occurred in other six open-chest dogs.

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Mean heart rate and maximal heart rate could be significantly decreased from 128±4.7 to 101±4.4 bpm and from 187±1.8 to 144±9.3 bpm, respectively. Sinus node recovery time (613±47 versus 861±20 msec), corrected sinus node recovery time (185±20 versus 236±33 msec), P wave duration and voltage (101±3 versus 105±3 msec and 1.4±0.2 versus 1.3±0.2 mV) and PQ interval (101±3 versus 105±3 msec) were not affected. In all dogs, sinus rhythm was maintained without occurrence of any arrhythmias.

This simplified method would be an alternative nonpharmacological treatment for inappropriate sinus tachycardia in patients with cardiac dysfunction

INTRODUCTION

β-adrenoreceptor blockade therapy is the most common pharmacological heart rate control therapy in patients with inappropriate sinus tachycardia (IST) or with coronary artery disease. However, in patients with cardiac dysfunction, heart rate could not be acceptably controlled due to the negative inotropic effect and/or patient's intolerance. As the nonpharmacological treatments of IST, complete destruction of sinus node areas (SNA) with surgical exclusion or cryoablation was performed in the last decade, [8) 20)] but their results were not satisfactory for the necessity of permanent pacemaker implantation. Recently, electrophysiological study, such as a computerized mapping, has greatly advanced and revealed the unique functional anatomy of SNA in humans and dogs. In this area, pacemaker complex has widespread distribution along the terminal groove and the sites of impulse origin shift from the head to the tail in SNA according to the deceleration of the heart rate by changes in the autonomic nervous tone or some pharmacological interventions, [1) 2) 3) 13) 16)] This unique functional anatomy of SNA led us to speculate that the heart rate would be easily and safely controlled by partial destruction of the pacemaker complex in SNA without electrophysiological technique, if we could create the small lesions with sharp demarcation.

The purpose of this study is to evaluate the feasibility of Nd-YAG laser sinus node modification without electrophysiological technique as a new simplified method.

MATERIALS and METHODS

Twelve mongrel dogs of both sexes weighing between 8 - 15 Kg were anesthetized with sodium pentobarbital and ventilated by a constant volume-cycled respirator (model 607, Harvard Apparatus) on room air through the cuffed endotracheal tube. Lactate Ringer's solutions (100 ml / hour) were infused intravenously to maintain the hemodynamics and one surface electrocardiogram (lead II) and arterial blood pressure (ABP) were routinely monitored. The laser beams were generated by MEDILASER-YAG 500 (model MEL-50, Mochida) and transmitted to the round-shaped ceramic tip (2mm in diameter) through a 0.6 mm water-cooled quartz core fiber. Laser irradiation was performed on the epicardium by a contact method while washing out the irradiated surface constantly with normothermic saline for protecting from excessive thermal damage.

All dogs were divided into three groups. In group 1 (N=3), the chest was opened through a median sternotomy and the pericardium was sewn to the chest wall to cradle the heart. Nd-YAG laser irradiations with a contact method were performed on the ventricular epicardium in the normothermic beating hearts with the total laser energy of 10 joules (10 watts x 1 second) , 30 joules (10 w x 3 sec), 60 joules (20 w x 3 sec) , 90 joules (30 w x 3 sec), 120 joules (40 w x 3 sec). The hearts were examined for gross lesion morphology and fixed in formalin and the largest dimensions (diameter and depth) of the lesions were approximately measured with a micrometer to evaluate the laser-tissue interactions. For lesion measurements, myocardial slices were made through the area of visible injury at 1mm intervals.

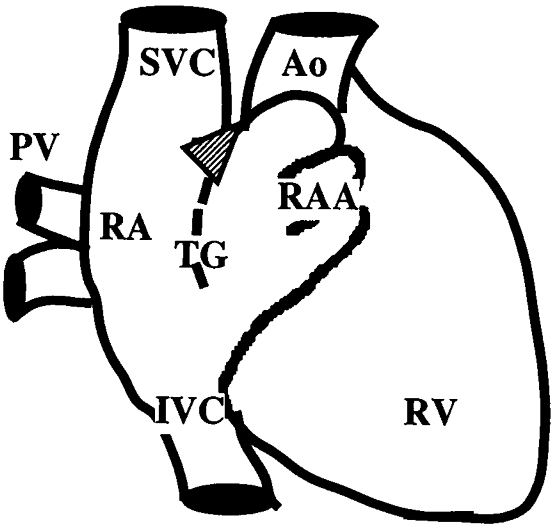
In group 2 (N=3), the cold cardioplegic solution (4 °C St. Thomas Hospital's solution) was infused from the aortic root to achieve the cardiac arrest after clamping of superior vena cava, inferior vena cava and ascending aorta. Laser irradiations were performed with the similar manner maintaining the myocardial temperature at 10 °C. Laser-tissue interactions in this condition were also examined.

In Group 3 (N=6), a right thoracotomy was performed in the fourth intercostal space and the heart was suspended in a pericardial cradle. Reference electrodes were sewn on the anterior abdominal wall and the other five unipolar electrodes were also sewn on the surface of the epicardium in the high right atrium (HRA), the middle right atrium (MRA), the low right atrium (LRA), the right atrial appendage (RAA), and the right ventricular apex (RV) for recording of epicardial electrograms before and after sinus node modification. Another electrode was also sewn on the epicardium in RAA close to SNA to stimulate the atrium.

One surface electrocardiogram (lead II), five unipolar electrograms and ABP were simultaneously displayed on a color-memory scope (model VM-185G, Nihon Koden) and were recorded by thermal-array recorder (model RTA-1200, Nihon Koden) at a paper speed of 100 mm/sec during this procedure. The signals were amplified and band pass filter of 0.15 - 1000 Hz was used. Cardiac stimulator (model BC-03, Fukuda Denshi) was used for measuring sinus node recovery time (SNRT) by overdrive suppression test. [12) 14)] Corrected sinus node recovery time (CSNRT) was calculated as follow : CSNRT = SNRT - basic cycle length (BCL). Nd-YAG laser irradiation (30 joules) was started from the junctional point between superior vena cava and right atrial appendage. Laser irradiation to the pacemaker complex resulted in immediate acceleration of the heart rate followed by deceleration. When the decrease of heart rate was not enough, the irradiation was repeated around the first point and then moved to the caudal site after obtaining the stable heart rate. These procedures were only directed by the terminal groove as the visual landmark and no electrophysiological technique was utilized. The irradiations were repeated within the triangular area, as shown in Figure 1, until about 25% decrease in heart rate occurred. Mean heart rate (HR) and maximal heart rate (Max HR) were calculated by taking the average of 10 consecutive BCL and %change of heart rate (%chang of

HR) was calculated by (Max HR - HR) / HR. SNRT and CSNRT were measured before and two hours after sinus node modification, and P wave configurations recorded from all electrograms and PQ interval were also evaluated before and after sinus node modification.

Figure 1 . The scheme of laser sinus node modification without electrophysiological technique.



SVC : superior vena cava
Ao : ascending aorta
PV : pulmonary vein
RA : right atrium
RAA : right atrial appendage
RV : right ventricle
IVC : inferior vena cava
TG : terminal groove
triangle zone : irradiated area

HR and ABP were measured during isoproterenol (ISP) infusion of several doses (0.05, 0.1, 0.2, 0.5 μg/kg/minutes) to evaluate the function of the pacemaker complex in the remainder of SNA after laser sinus node modification compared with the normal sinus node function. ISP had been infused transvenously for ten minuets and HR was evaluated at each dose of ISP infusion after obtaining stable hemodynamics.

All data were expressed as mean values ± standard error (S.E.). Laser-tissue interactions were calculated with a linear regression analysis and intercepts of normothermic and hypothermic regressions were compared by analysis of variance (ANOVA). The Student's paired t test was used to compare the changes of parameters before and after laser sinus node modification. A p value < 0.05 was considered significant in this study.

All animal experiments were conducted according to the "Guideline for Animal Experimentation at Kobè University School of Medicine".

RESULTS

Laser-tissue interactions : The depth and the diameter of the irradiated lesions were well correlated with total laser energy. When the lasing energy was less than 30 joules, it was obvious that the diameter and the depth of the irradiated lesions were unstable and not enough to obtain the destruction of sinus node area. 30 joules lasing energy showed the stable irradiated diameter (2.8±0.18 mm) and depth (1.3±0.20 mm) in group 1 (Figure 2). With 60 joules, the larger irradiated lesion (4.8±0.34 mm in diameter and 2.4±0.16mm in depth) was obtained. More lasing energy, 90 and 120 joules, could not be irradiate the tissue more than 6mm in diameter, however, the depth was increased (3.4±0.58, 4.8±0.32 mm, respectively), and charring and crater were observed. The effect of Nd-YAG laser irradiation was decreased by the cold temperature. In group 2, the depth was 0.3±0.22 mm with 30 joules lasing energy and 0.5±0.38 mm with 60 joules, which showed significant difference as compared group 1. The diameter of the irradiated lesions of group 2 was also decreased to about 60% of group 1.
Macroscopic findings revealed that the irradiated lesions were well-circumscribed and clearly distinguished from zones of normal myocardium.. Microscopically, the lesions consisted of zones of coagulative necrosis were bordered by layers of contact band necrosis, and zones of normal myocardium were almost intact.

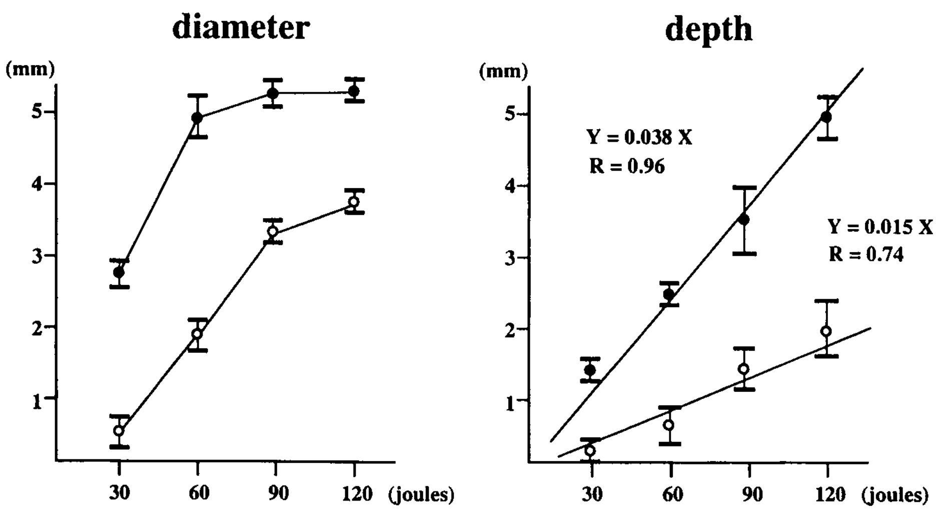


Figure 2 . Laser-tissue interactions with a contact method .
closed circle : Group 1 , open circle : Group 2

Laser sinus node modification : To achieve 25% decrease in heart rate, 750±30 Joules lasing energy was delivered. No change was observed in ABP (80.0±2.8 versus 88.8±3.1) after modification of the sinus node. HR and Max HR were significantly decreased from 128±4.7 bpm to 101±4.4 bpm, and from 187±1.8 bpm to 144±9.3 bpm, respectively, but %change of HR was not changed significantly (46.5±4.6 % versus 42.5±4.4 %). SNRT was prolonged from 613±47 msec to 861±20 msec and CSNRT was also prolonged from 185±20 msec to 236±33 msec, but there was no significant change. In the evaluation of the intra-atrial conduction, no alteration was found after laser sinus node modification, because there was no transformations of P wave configurations which were recorded from any unipolar cardiograms on the atrial epicardium. P wave voltages and durations were also unchanged significantly after laser sinus node modification, and PQ interval was predictably unaffected (Table I).

Table I . Nd-YAG laser sinus node modification .

	#Pre-LSNM	#Post-LSNM	P value
HR	128 ± 4.7	101 ± 4.4	0.023
Max HR	187 ± 1.8	144 ± 9.3	0.019
*%change of HR	46.5 ± 4.6	42.5 ± 4.4	N.S.
SNRT (msec)	613 ± 47	861 ± 20	N.S.
CSNRT (msec)	185 ± 20	236 ± 33	N.S.
PQ interval (msec)	101 ± 3	105 ± 3	N.S.
P voltage (mV)	1.4 ± 0.2	1.3 ± 0.2	N.S.
P duration (msec)	65 ± 12	51 ± 8	N.S.

Data were expresses as mean ± S.E. **# LSNM : laser sinus node modification**

***%change of HR = (Max.HR-HR)/HR**

The dose-response curve of HR to ISP infusion displayed an interested pattern (Figure.3). The slope of postoperative dose-response curve ran a gentle course at relatively low doses of ISP and the whole shape of this curve was depressed compared with the preoperative curve. Although the postoperative response to the relatively low doses of ISP was not sufficient, the adequate infusion of ISP resulted in the satisfactory acceleration in heart rate without any hemodynamic problems.

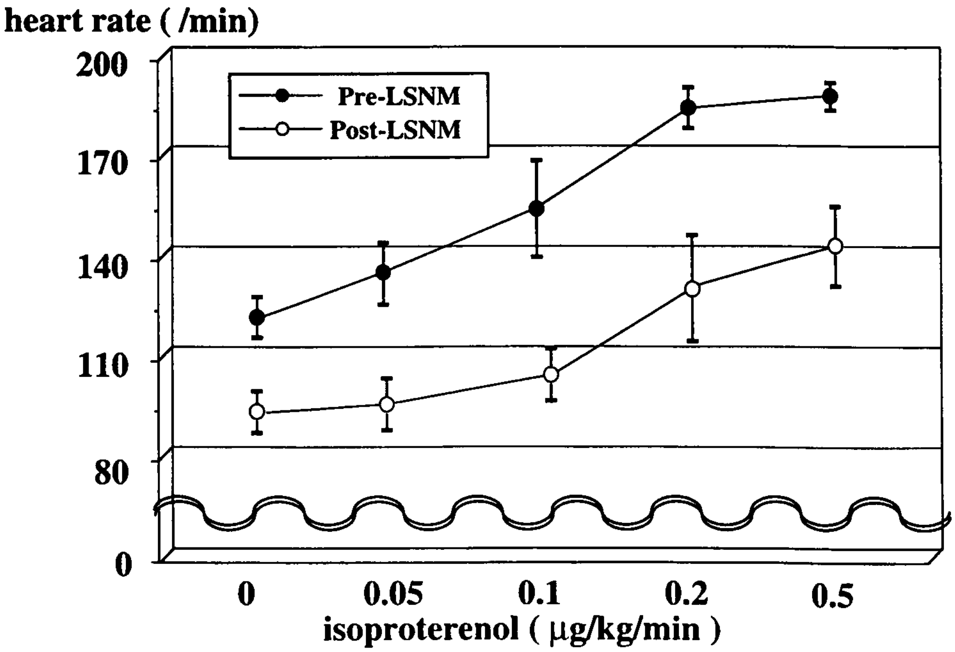


Figure 3 . Response to isoproterenol infusion.

DISCUSSION

Many procedures, such as surgical exclusion, cryoablation and radiofrequency current ablation, are currently used for nonpharmacological treatment of drug-refractory arrhythmias. Laser, an acronym for light amplification by stimulated emission of radiation, is a new technique in arrhythmia surgery. In vitro laser irradiation to pathological endocardium with a CO_2 argon laser was demonstrated in 1984 by Isner .[7] Saksena [15] evaluated and reported its safety and efficacy of intraoperative mapping-guided argon laser irradiation alone or in conjunction with a standard surgical method. In contrast to the carbon dioxide and argon lasers that have been proposed for endocardial resection by tissue vaporization, the Nd-YAG laser has been proposed for photocoagulation of the arrhythmogenic foci without tissue vaporization. The Nd-YAG laser is one of the most useful laser in the optical window (the wavelength region between 600 and 1100 nm) and is available to obtain the enough tissue photocoagulation for ventricular tachycardia safely. Although the efficacy of Nd-YAG laser in the irradiation of ventricular tachycardia has been reported, [10] [17] [18] the applications to electrical modification of other conditions remains unknown. In this study, the feasibility of Nd-YAG laser sinus node modification without electrophysiological technique was tested in dogs for a new simplified nonpharmacological heart rate control without following permanent pacemaker implantation.

Our preliminary results showed that the optimal energy density for Nd-YAG laser sinus node modification in normothermic beating hearts was 30J (10W x 3sec) per emission. Because the atrial wall in sinus node area is thinner than ventricular wall, this energy density is lower as compared with that for ventricular tachycardia. The reduction energy loss by using a contact method would also contribute to the lower energy density. A spot size created by one emission with this manner in normothermic beating hearts was about 1.5mm in depth and 3.0 mm in diameter, and the charring could not be found on the irradiated surface. Therefore, there would be less risk of total destruction of sinus node area or perforation.

The myocardial irradiated lesion size is also affected by the tissue temperature. Svenson and colleagues [19] reported that decreasing myocardial temperatures from 38 to 26 °C resulted in approximately a 20 % decrease in lesion depth using the same power and energy density. In this study, it was also proved that the irradiated lesion size was decreased by 65% in diameter and 30% in depth in hypothermic condition (10°C). From these results, the myocardial temperature at lasing is also important in the application of the Nd-YAG laser to arrhythmia surgery.

In 1910, the rate differentiation in the sinus node area was firstly reported by Lewis, and et al [9] They found that the origin of the impulse changed from the head to the tail of the sinus node area. Later, pacemaker migrations along the terminal groove were observed using in situ mapping or microelectrode studies combined with nerve stimulations.[4] [5] [6] In the last decade, Boineau et al [1] [2] [3] showed separate origin points dominating excitation within specific ranges of heart rate, and also found that spatial distribution of the pacemaker complex exceeded the dimensions of the histologically defined canine sinus node and the same facts were observed in the human heart. Based on these previous investigations, the effects of laser photocoagulation on selected sinus node areas were tested by Littmann and et al [11] using a computerized mapping system. They reported that maximum heart rates were decelerated by graded laser photocoagulation to origin of the sinus impulse (O point) with atrial surface mapping during catecholamine stimulation and its effects were long lasting. Their method could not become popular, because it was very complicated and troublesome. Therefore, we originated a new simplified method of laser sinus node modification that was performed without electrophysiological technique only directed by the terminal groove based on the functional anatomy of the sinus node areas. In this study, proposed decrease of HR could be obtained and Max HR was significantly depressed by our simplified method without any complications. Moreover, some indirect evidence suggested that the sinus node function had not been totally eliminated. Firstly, % change of HR was not changed significantly and the heart rate response to the ISP infusion of the appropriate dosage was also maintained after laser sinus node modification with our simplified method. Secondly, P wave configurations including voltages and durations remained normal, and PQ interval was not also affected by lasing.

It is the benefit of laser sinus node modification that the only negative chronotropic effect is obtained without the negative inotropic effect, which is usually complicated by β-adrenoreceptor blockade therapy. On the other hand, it is disadvantage to need open-chest surgery and electrophysiological technique. Our results suggest that the feasibility of Nd-YAG laser sinus node modification could be performed safely and simply without the special equipment and technique. For an additional procedure at open heart surgery in patients with inappropriate sinus tachycardia in whom high heart rates would require excessive work demands from a compromised heart, this method would be an alternative treatment for nonpharmacological heart rate control.

CONCLUSIONS

1) The optimal laser energy was 30 Joules (10 watts x 3 seconds) with a contact method for sinus node modification in normothermic beating heart.
2) Nd-YAG laser sinus node modification was directed safely by the terminal groove without electrophysiological technique.
3) Nd-YAG laser sinus node modification without electrophysiological technique would become a new nonpharmacological treatment for heart rate control in patients with inappropriate sinus tachycardia or an additional procedure in patients with ischemic heart disease at open heart surgery.

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