EXPERIMENTAL STUDY

Experimental Study with Regard to the Effects of Energy Titration of the Laserballoon on the Lesion Creation Using Porcine Myocardium

Kaoru Okishige,1 MD, Takatoshi Shigeta,1 MD, Rena A. Nakamura,1 MD, Tatsuhiko Hirao,1 MD, Hiroshi Yoshida,1 MD, Atsuhito Oda,1 MD, Yasuteru Yamauchi,1 MD, Tetsuo Sasano,2 MD and Kenzo Hirao,2 MD

Summary

Laserballoon-based pulmonary vein isolation has proven to be safe and effective. However, the influence of the laser energy titration on the lesion formation has never been fully investigated. The aim of this study was to determine the relationship between the delivered laser energy and lesion size, as well as the incidence of steam pop.

The whole porcine heart was excised, and the left ventricular myocardium was separated into four specimens. Myocardial specimens were embedded in a warm mattress to keep the myocardial temperature around 37°C. The laserballoon was located so that the surface of the laserballoon was attached to the myocardium. The laser energy was irradiated against the surface of myocardium at 5.5, 8.5, 10.0, and 12.0 W for 3, 5, 10, and 20 seconds. The depth, surface area, and lesion volume were measured using a digital vernier caliper.

At constant laser energy and time, the lesion size increased significantly with the increasing energy ($P < 0.001$) and application duration ($P < 0.001$). The steam pop was provoked when a 12.0 W laser energy was applied for longer than 16 seconds, and it occurred in 2 out of 8 lesions.

The laserballoon demonstrated the ability to create a lesion formation in a dose- and time-dependent manner. Steam pop could be provoked with high-energy irradiation.

Key words: Catheter ablation

Pulmonary vein isolation (PVI) is a well-established rhythm control treatment strategy for paroxysmal atrial fibrillation. Ablation catheters have been developed to measure the real-time catheter-tissue contact force (CF) during catheter mapping and ablation, and it has been suggested that increasing the CF improves radiofrequency lesion formation.1-5 The PVI procedure has been simplified by balloon catheter-based ablation systems such as the cryoballoon and laserballoon.6-8 The laserballoon ablation system is a balloon-based technology using endoscopic visualization of the target region to navigate the laser energy delivery to achieve ostial PVI. Although energy titration is unnecessary for the cryoballoon usage, it is one of the crucial factors for a successful and safe PVI using the laserballoon.9-11 The purpose of this study was to determine (1) the relationship between the laser energy and lesion size, as well as the incidence of steam pop and (2) the accuracy of predicting the lesion size created by the laserballoon application using adult porcine whole heart preparations according to the delivered energy and its duration.

Methods

Experimental preparation: The experimental protocol was approved by the Japan Red Cross Yokohama City Bay Hospital Committee on the Use and Care of Animals. This experiment was undertaken in a shade cage (Figure 1), which can prevent injurious effects from the diode laser to the human eye. Myocardial specimens had to be adhered to the surface of the laserballoon (HeartLight, Cardio-Focus) for the sake of a successful lesion formation. The diode laser uses a semiconductor technology that produces a coherent projection of light in the visible to infrared range. In addition, the diode laser uses the principle of selective photothermolysis to target specific chromophores in the cardiac tissue, resulting in damaging them by selective heating while leaving the surrounding tissue unharmed. This mechanism of damage by the diode laser is closely associated with conductive heating. Therefore, the myocardial temperature provides significant effects on the lesion formation with the diode laser applica-
The myocardium was soaked in hot water at 37°C for at least 30 minutes in order to raise the myocardial temperature to around 37°C and was placed on a warming mattress to maintain the myocardial temperature at 37°C.

**Ablation protocol:** The laser energy applications were performed at separate sites on the left ventricular surface while avoiding the location of the coronary arteries and veins. The laser energy was delivered with four different levels and four different durations of 5.5, 8.5, 10.0, and 12.0 W and 3, 5, 10, and 20 seconds, respectively. All lesions were separated at least 1 cm apart from each other for accurate measurement of the lesion size. In one specimen, we kept the laser energy power and application duration identical to avoid any incorrect recognition of the created lesions. When an average of 6 lesions was created on the surface of the myocardial specimen, a new myocardial specimen was used for further lesion creations. In the event of a steam pop, which was confirmed by a macroscopic image or histology with a small cavitation or crater formation, the laser application was continued to allow a comparison of the lesion size.

**Measurements:** All lesions were visible, and we were able to macroscopically distinguish between lesions and non-damaged areas (Figure 1). Immediately after accomplishing lesion creation on each myocardial specimen, a measurement of the lesion size was undertaken. At first, the maximum transverse and vertical diameters of the surface lesions were measured with a digital vernier caliper (DN-100, Niigata Seiki Inc., Niigata city, Japan). After completing the measurement of the lesion surface, an incision was created at the center portion of each lesion to measure the maximum lesion depth using the same caliper.

**Statistical analysis:** All data were expressed as the average ± standard deviation (95% confidence interval [CI]). Pearson’s linear regression analysis was conducted to identify the correlation between the two variables. All statistics were computed using JMP10 software (SAS Institute Inc. Cary, NC, USA).

**Results**

**Relationship between the laser power and lesion size:** A total of 50 lesions were created by the laser application against the porcine ventricular myocardium. In the case of a laser application with 5.5 W for 3 seconds, no visible lesion was recognized and was excluded from the measurements. A laser application with 5.5 W for a longer duration than 3 seconds could create a visible lesion, and a higher power laser application than 5.5 W was also able to provide recognizable lesions. Regarding the lesion area, a significant increase in the lesion area (95% CI = 3.247-4.043 for 10 seconds, 95% CI = 1.8235-8.69 for 20 seconds, and 95% CI = 2.0108-13.324 for 30 seconds, respectively), depth (95% CI = 1.6263-2.1803 for 10 seconds, 95% CI = 2.8115-4.4752 for 20 seconds, and 95% CI = 2.0452-4.7415 for 30 seconds, respectively) and volume (95% CI = 6.14-7.716 for 10 seconds, 95% CI = 10.01-27.686 for 20 seconds, and 95% CI = 10.06-57.243 for 30 seconds, respectively) were observed along with the laser application duration (Figure 2). Similar findings were obtained when the laser power was delivered at 8.5, 10.0, and 12.0 W. All measurements, including the lesion area (8.5 W; 95% CI = 0.2196-2.764 for 3 seconds, 95% CI = 1.7935-5.823 for 5 seconds, 95% CI = 1.35-11.429 for 10 seconds, 95% CI = 4.2109-16.909 for 20 seconds, 10.0 W; 95% CI = 2.3938-3.268 for 3 seconds, 95% CI = 4.6068-4.631 for 5 seconds, 95% CI = 3.717-6.169 for 10 seconds, 95% CI = 8.1499-8.359 for 20 seconds, 12.0 W; 95% CI = 3.2292-4.621 for 3 seconds, 95% CI = 4.1168-5.525 for 5 seconds, 95% CI = 6.8526-9.423 for 10 seconds, 95% CI = 8.7744-10.933 for 20 seconds), depth (8.5 W; 95% CI = 0.8278-1.9189 for 3 seconds, 95% CI = 2.2193-2.344 for 5 seconds, 95% CI = 2.2254-2.3013 for 10 seconds, 95% CI = 3.0806-5.9061 for 20 seconds, 10.0 W; 95% CI = 0.6786-1.5481 for 3 seconds, 95% CI = 2.2193-2.344 for 5 seconds, 95% CI = 2.2254-2.3013 for 10 seconds, 95% CI = 3.0806-5.9061 for 20 seconds).
Figure 2. Correlation between the duration of the laser energy application and lesion area (A), lesion depth (B), and lesion volume (C), when a laser power of 5.5 W was applied.

Figure 3. Correlation between the duration of the laser energy application and lesion area (A), lesion depth (B), and lesion volume (C), when a laser power of 8.5 W was applied.

Figure 4. Correlation between the duration of the laser energy application and lesion area (A), lesion depth (B), and lesion volume (C), when a laser power of 10.0 W was applied.

= 1.3466-2.58 for 5 seconds, 95% CI = 1.7811-3.1589 for 10 seconds, 95% CI = 3.4947-5.8053 for 20 seconds, 12.0 W; 95% CI = 1.0407-1.8726 for 3 seconds, 95% CI = 1.4823-2.7444 for 5 seconds, 2.5157-4.3576 for 10 seconds, 95% CI = 3.4191-5.4276 for 20 seconds), and volume (8.5 W; 95% CI = 0.14-3.914 for 3 seconds, 95% CI = 3.94-13.411 for 5 seconds, 95% CI = 20.77-35.081 for 10 seconds, 95% CI = 33.18-53.974 for 20 seconds), correlated well with the laser application duration ($P < 0.05$, Figures 3-5). When we focused on the lesion area, the lesion area exhibited a significant correlation with the laser energy power and application duration ($P < 0.001$, Figure 6). The increase in the lesion depth during the laser application was significantly correlated with the laser energy power and application du-
Figure 5. Correlation between the duration of the laser energy application and lesion area (A), lesion depth (B), and lesion volume (C), when a laser power of 12.0 W was applied.

Figure 6. Influence of the laser power and its duration on the lesion area.

Figure 7. Influence of the laser power and its duration on the lesion depth.

Relationship between the laser power and incidence of steam pop: Steam pops were provoked when the laser energy was delivered at a power of 12.0 W for 20 seconds during 2 out of 12 applications (16.7%), and the pop was audible and was recognized at laser irradiation durations of 18 and 16 seconds. A crater formation was observed on the surface area of the lesion, and the depth was approximately 6.4 and 7.2 mm (Figure 9).
Discussion

In this study, we investigated the effects of the laser power and application duration on the lesion formation and incidence of steam pops. The main findings of this study were as follows: (1) there was a significant correlation between the laser power and the lesion size, (2) there was a significant correlation between the laser application duration and lesion size, and (3) steam pop were provoked when the laser was applied at a power of 12.0 W and for longer than 16 seconds.

The ablation was carried out using a 980 nm diode laser that creates a 30°arc of energy. An aiming beam of green light allows the user to see where the lesion is being placed on the tissue. The energy levels can be selected by the user, depending on the level of the balloon occlusion of the PVs. The user has the option to titrate the dose with six different settings from 5.5 W for 30 seconds to 12 W for 20 seconds.

The balloon catheter was designed as an anatomic ablation device to facilitate the PV access with limited navigation efforts.10 The balloon catheter is prone to having a reduced risk of cardiac perforation due to the easier navigation properties and lower mechanical force per square inch due to its larger surface compared with a catheter with a standard tip.11 As different from the cryoballoon application, such as a single shot manner, the laserballoon ablation system uses a point-by-point application fashion and takes a longer time than that of the cryoballoon application. Endoscope adopted in the laserballoon allows for permanent visual control of the ablation lesion deployment, and the serial PV occlusion angiograms required to ascertain the optimal cryoballoon position is unnecessary for the laserballoon application. However, the energy has to be reduced when ablating near pulsatile blood in order to prevent boiling blood, resulting in a balloon rupture. In addition, no laser energy applications should be performed inside the PV or at sites where stagnant blood overlaps with the PV tissue.12

Bordignon, et al. reported that a high laser power affects the acute and chronic clinical outcomes, allowing for high acute and chronic success rates of the PVI.13 However, Metzner, et al. reported that esophageal thermal lesions were detected in patients treated with a high laser energy power.14 They also suggested that the use of higher laser energy levels does not necessarily correlate with greater intraluminal esophageal temperatures or with the incidence of esophageal thermal injury. The position and anatomical course of the esophagus in relationship to the PVs is a crucial factor in terms of provoking esophageal thermal lesions.15 For example, esophageal ulceration was detected despite a maximal luminal esophageal tem-
perature (LET) of lower than 38°C, and no esophageal lesions were found in spite of a high LET, exceeding 40°C. Therefore, esophageal temperature monitoring might be fairly sensitive with a rather poor sensitivity in identifying patients with thermal lesions on subsequent laserballoon applications for the PVI.\(^9\) A relatively lower laser energy application coupled with a shorter irradiation duration could be preferable in order to avoid esophageal lesions in patients with close anatomical proximity between the esophageal location and sites of the laser application, according to the present results.

In the present study, we found that there was a significant correlation between the laser energy, its application duration, and the thermal lesion size sparing the surface area from thermal injury. Even though this experiment was carried out under a non-clinical setting (without blood flow of body temperature), we considered that we might be able to expect a comparable lesion formation, depending on the laser energy power and duration. At present, the laser energy level is titrated according to the degree of tissue exposure between 5.5 and 12 W, and the laser energy is applied for 20 to 30 seconds.\(^9\) High-power and short radiofrequency applications have recently been permeating for the PVI; however, such a procedure seems to connote the risk of provoking steam pops and thromboembolic events.\(^6\) An open-irrigated radiofrequency catheter could provide a larger lesion and fewer complications with higher power settings, and the lesion width rather than the depth contributed to its volume. The characteristics of the laser energy are similar to irrigated radiofrequency energy in this regard.\(^7\) High power and short duration radiofrequency energy applications were investigated, and a shorter duration of the laser application for 5 to 10 seconds combined with relatively higher energy might be able to prevent esophageal thermal injury, as considered from the results of the present study.

An experimental investigation demonstrated that the maximum absorption of the laser energy is reached in the myocardium beyond the endocardial level, reducing the probability of charring and ablation-related thrombogenesis.\(^8\) In contrast, Perrotta, et al. reported that steam pops could infrequently occur with the laserballoon ablation.\(^9\) In the present study, steam pops were provoked in sporadic cases. However, a large series of clinical studies have never reported its incident.\(^9\) The discrepancy between the present study and previous reports might be derived from the circumstance of the present experiment. In the present study, the laser energy application had to be performed without blood flow, which would have enabled the cooling of the myocardial specimens resulting in the avoidance of an excessive elevation of the myocardium temperature because of the laser irradiation.

**Limitations:** The experiment was undertaken under circumstances without blood flow of body temperature. The lesion formation by the laserballoon application was carried out by the effects of conductive heating.\(^9\) Therefore, the results of the present study might not be able to directly applied in clinical cases. In addition, the incidence of the steam pops in the present study might not be applicable to the clinical cases due to the difference in the circumstances between in vivo and clinical settings. A histological examination could not be performed in the present study, and we failed to evaluate the severity of the tissue damage created by the laser application.

**Conclusions**

The laser power and its application duration had a strong correlation to the thermal lesion size. The incidence of steam pops could be negligible under clinical circumstances.

**Disclosure**

**Conflicts of interest:** None.

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