Holmium:YAG LASERにおける衝撃エネルギー挙動の特徴と至適治療条件に関する検討

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The Characteristics of the Behavior of Impact Energy and Treatment for Urolithiasis by Holmium:YAG Laser

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要 旨

Ho:YAG laser治療にあたり, 至適照射条件を確認した. 誘起された気泡を高速度ビデオカメラで形成から崩壊までの挙動を観察した. 壁面近傍での誘起気泡挙動と衝撃エネルギーの測定では明らかに対象との至適照射距離を有し, 照射方向による違いがあることが確認された. レーザ照射による有効なエネルギーの獲得は照射方向や照射環境によって異なる特性を有し, 照射スタイルを適応することにより有効なエネルギーの獲得, 周辺組織影響の回避が可能であることが確認された.

キーワード：ホルミウムヤグレーザー, 尿路結石症, TUL, キャビテーション

Abstract

We conducted objective observations and compared the crushing effects of engineered energy caused by laser radiation according to the irradiation distance to the target as well as the irradiation direction. Observations were carried out in a water bath and the behavior from bubble formation to collapse was observed with a high-speed video camera synchronized with the impact at bubble collapse. Observations of the behavior and impact energy of induced bubbles in the vicinity of the wall clearly indicated that there is an optimal irradiation distance from the target and that it differs depending on the irradiation direction. Experiments were carried out with fibers placed parallel or perpendicular to the solid wall surface. We found that the acquisition of effective energy by laser irradiation has different characteristics depending on the irradiation direction and irradiation environment, and that it is possible to acquire effective energy and avoid influencing the peripheral tissues by adapting the irradiation style to various situations.

Key words: Ho:YAG laser, urolithiasis, TUL, cavitation
Introduction

Advancement of the flexible scope over the last ten years has changed the options for treatment for urolithiasis. With the end of the heyday of ESWL treatment, opportunities to select transurethral lithotripsy (TUL) using a small diameter flexible ureteroscope that can approach not only the ureter but also the inferior renal calix have witnessed a rapid increase. More and more surgeons and patients choose this method because advances in flexible ureteroscope devices as well as devices related with calculus treatment such as laser fibers, laser output devices, and appliances for harvesting crushed pieces of a calculus have considerably suppressed treatment invasiveness and enabled not only calculi crushing but also the harvesting (extraction) of crushed pieces thereof.

The use of collapse energy from single bubbles induced by a focused laser has been studied for a long time\(^1\),\(^2\). In recent years, Brujan\(^3\)\(^,\)\(^4\) and Kobayashi et al.\(^5\) investigated the influence on wall elasticity and the bubble behavior under conditions with high flexibility similar to body tissues such as gelatin wall surfaces and the influence on flexible wall surfaces\(^6\), demonstrating many characteristic bubble collapse and related behaviors in the vicinity of the wall surface.

As described above, basic research in the engineering field has been developed in various approaches. However, there have been only a few medical studies covering the impact effect on individual boundaries in laser treatment, compared to the studies on bubbles caused by a focused laser\(^7\),\(^8\). There are no reports indicating clear and optimal conditions for laser treatment in the urinary tract against urolithiasis. The aim of this study is to improve the crushing efficiency of TUL, which has become a common treatment, and to prevent the influence of the treatment on the living body as much as possible. In the present study, we conducted objective measurements and compared the crushing effects of engineered energy caused by laser radiation during treatment for urolithiasis using a Ho:YAG laser, according to the irradiation distance to the target and the irradiation direction. These results revealed the behavior of bubble collapse and optimal irradiation conditions to obtain effective crushing efficiency. Taking into consideration the influence on the ureteropelvic mucosa, which is presumed to be the experimental model wall surface, we created narrow space models to enable safe laser irradiation in vivo, observing the laser collapse behaviors excited by the laser and conducting a study on the characteristics thereof.

Methods

We used the laser research system illustrated in Fig.1 for the observation of bubble behavior excited by the laser and the measurement of impact energy on bubble collapse. An irradiation experiment was carried out using a Ho:YAG laser (wavelength: \(\lambda = 2.06\ \mu\text{m}\), pulse width: \(\tau = 250\ \mu\text{s}\)), with optical fibers (\(d = 365\ \mu\text{m}\)) connected to the laser irradiation apparatus installed (VersaPluse, Holmium:YAG laser 30 W, Luminas, USA) in a transparent water tank made of acrylic resin and filled with water samples at various water temperatures set at constant temperature (\(T_w = 283\ K–322\ K\)) units (Advantee, TBH035AA, JAPAN). In the present laser device, the output has a pulse width of 250 to 300 \(\mu\text{s}\) by changing to 0.5 to 1.5 J/pulse. It is confirmed that the pulse width does not change greatly with respect to the repeat rate.

Bubble behavior excited by laser irradiation was observed by the back light method using a high-speed video camera (Photon SA5, JAPAN). The bubble behaviors are observed by a high-speed video camera (Photon, SA5, Spatial resolution: 0.01 mm/pixel) triggered by an output of hydrophone (B&amp;K, 8103). The bubble is illuminated by a light source (NPI, PCS-MH375RC) with a flat light guide (NPI, PLG-B100X). The shooting speed was \(F_s = 100,000\ \text{fps}\), the laser irradiation time was \(t = 0\ \text{s}\), and the shooting was carried out from \(t = -0.05\ \text{ms}\) (before irradiation) to \(t = 1.50\ \text{ms}\) (after irradiation). The irradiation conditions of the laser in the experiment were as follows: laser output, from \(E = 0.5\ \text{J}\) to \(E = 1.5\ \text{J}\) (every 0.5 \(\text{J}\)); and two fiber diameters, \(d = 420\ \mu\text{m}\) and \(d = 360\ \mu\text{m}\).

The sound pressure at the time of bubble collapse was measured using a hydrophone (B&amp;K, 8103, Frequency response: 0.1 Hz–180 kHz ±3 dB) installed 10 mm above the tip of the fiber, at the same time of video shooting. The impact on the solid wall surface was measured by a self-made sensor of the impact force using PVDF piezoelectric film (Polyvinylidene difluoride) as illustrated in Fig.2. The PVDF film was adhered to an acrylic resin plate and a pressure receiver with a diameter of 4 mm was made of epoxy resin. The pressure receiver was protected by a silicon gasket or a silicon tube to prevent detection of the impact on sites other than the pressure receiver. The sensor was calibrated using the steel-ball dropping method. Fig.3 illustrates examples of waveforms measured by the impact force sensor. Fig.3(a) illustrates the wave form at the time of steel-ball dropping, while Fig.3(b) illustrates the wave form at the time of bubble collapse. As a result, the onset impact caused by cavitation bubble is approximately 5 \(\mu\text{s}\), which was thought to be within an adequate range to capture the collapse impact of bubbles.

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Fig.1 Experimental setup.
in this study. The behavior of laser-excited bubbles and measurement of impact force distribution was observed at various distances between the wall surface with the impact sensor installed and the fiber as illustrated in Fig.4. The tip of the fiber was located on the central axis of the pressure receiver of the sensor. The distance between the impact force sensor and optical fiber in the horizontal and vertical directions varied from \( x = 0 \) mm to 5 mm.

### Results

#### Behavior and effects of bubble collapse in spaces without a wall surface

Fig.5 illustrates the observation results of high-speed video of the behavior of bubbles immediately after laser irradiation. \( t = 0 \) indicates the start of laser irradiation. The formation of bubbles could be observed immediately after laser irradiation \((t = 0.05 \text{ ms})\) under any conditions. After reaching the maximum diameter, primary bubbles collapsed at approximately \( t = 0.50 \text{ ms} \), followed by several rebounds and re-collapse behavior.

Fig.6 illustrates a comparison of the bubble diameters observed in two groups: in one group, the diameter of the fiber was fixed to 420 \( \mu \text{m} \) and the irradiation energy of the laser was set at 1.5 J, 1.0 J, or 0.5 J; while in the other group, the irradiation energy was fixed to 0.5 J, with the fiber diameter set to 420 \( \mu \text{m} \), 360 \( \mu \text{m} \), or 550 \( \mu \text{m} \). We found that increases in the fiber diameter resulted in larger size bubbles even at the same output level of laser irradiation. Moreover, as the laser output was increased, the maximum bubble diameter significantly grew and the time to collapse increased accordingly.

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**Fig.2** Schematic diagram of impulsive force sensor.

**Fig.3** Output of impulsive force sensor.

**Fig.4** Arrangement of laser fiber and impulsive force sensor.

**Fig.5** Bubble formation and collapse behavior.

**Fig.6** Time course of bubble radius.
Behavior and effects of bubble collapse near wall surfaces

The experiment of laser irradiation in the vertical direction (Fig.7) was carried out with the distance between the tip of the fiber and the wall surface set to $x = 0.33$ mm (a), $x = 2.83$ mm (b), and $x = 3.79$ mm (c) to investigate the behavior near the wall surface and the impact force of the laser-excited bubbles. The irradiation conditions here were fixed at laser output $E = 0.5$ J and fiber diameter $d = 420$ μm. In Fig.7(a) and 7 (b), the bubbles formed and grew larger in a hemispherical shape in contact with the sensor surface, reaching the maximum diameter, beginning to contract in contact with the wall surface, and collapsing in the wall surface direction. Afterwards, rebounding occurred as in the observation in the open space (without wall surface). In Fig.7(c), the bubble grew without coming into contact with the wall surface and collapsed near the tip of the fiber at approximately $t = 0.45$ ms after reaching the maximum diameter at $t = 0.25$ ms. Thereafter, bubbles generated during rebounding moved toward the wall surface but could not reach it while repeatedly growing and collapsing ($t = 0.50–1.00$ ms).

We also conducted an analysis in the horizontal direction (Fig.8). Observation was carried out with the distance from the wall surface set to $h = 0.28$ mm (a), $h = 3.11$ mm (b), $h = 4.03$ mm (c) under the same irradiation conditions. The impact energy exhibited the highest value when closest to the wall surface and the energy efficiency decreased as the distance from the wall surface increased.

In addition, based on the waveform of the impact force $F$ under each irradiation condition in the vertical direction and the horizontal direction, the maximum value was recorded at the time when the primary bubble collapsed in each condition. Fig.9 illustrates the relationship between the distance $x$ between the sensor and fiber in the vertical direction and the impact value $F$ at the first collapse. As can be seen from the figure, the maximum impact value $F$ is the highest near the wall surface but slightly away from the wall surface, with the impact force $F$ decreasing as $x$ increases. On the other hand, Fig.10 illustrates the relationship between the distance $h$ between the sensor and fiber in the horizontal direction and the impact value $F$ at the first collapse. As can be seen from the figure, the maximum impact value $F$ is the highest in the vicinity of the wall surface, with the impact force $F$ decreasing as $h$ increases. The above results demonstrated that the appropriate distance to obtain the maximum energy differs depending on the irradiation approach of the laser fiber.

**Discussion**

For ureteral stones, endoscopic surgery has been performed and various devices for calculus crushing and extraction have been developed and used. Electrohydraulic, pneumatic, or
pulsed lasers, etc. are used as crushing methods using a small diameter flexible ureteroscope, which is less invasive and enables efficient stone extraction with the aim of being stone free. The use of flexible ureteroscope as a new device resulted in the reduction of complications compared to treatment using only a conventional rigid ureteroscope; however, it was reported that both treatments resulted in approximately 3% of the incidence of complications in the surrounding tissues.

Because it is a treatment that introduced a new engineering technique, we believe that if surgeons understand the laser crushing principle and take into consideration the crushing efficiency and influence on the surrounding tissues, more effective outcomes can be obtained and the influence on the surrounding tissues can be minimized. In medical applications of laser energy, there are three kinds of interactions occurring when energy reaches the target: photochemical, photomechanical and photothermal. In laser treatment for urolithiasis, thermal energy generated in the photothermal mechanism by emitting laser energy via pulsed output forms microbubbles. The treatment exhibits its efficacy by converting

\[ T_w = 292K, \ E = 0.5J, \ d = 420\mu m, \ \beta = 8.2mg/L \]

\[ T_w = 291K, \ E = 0.5J, \ d = 420\mu m, \ \beta = 8.5mg/L \]

**Fig. 8** Bubble collapse behavior and the resultant impulsive force near a horizontal wall surface.

\[ \gamma = \frac{x}{R_{max}} \]

\[ \gamma = \frac{h}{R_{max}} \]

**Fig. 9** Changes in impulsive force (vertical wall surface).

**Fig. 10** Changes in impulsive force (horizontal wall surface).
the collapsed energy of the bubbles into impact wave energy. On the other hand, in other treatments using the same photothermal mechanism such as HoLEP\(^{2}\) (holmium laser enucleation of the prostate) treatment or laser scalpel, treatment purposes are achieved by directly adding the heat energy generated by the laser to the tissue without conversion. As shown above, there is a big difference in the choice of thermal energy propagation system depending on the intended use/target of lasers\(^{13}\). The characteristic of laser medical care including Ho:YAG is that if practitioners do not recognize the difference between the two, they cannot provide safe and efficient treatment by setting effective irradiation conditions.

As shown in the results of this study, irradiation in the vertical direction from the point approximately 0.2 to 3 mm distant from the target results in efficient impact wave energy, while irradiation in the horizontal direction from the point that is actually in contact with the target obtained the most efficient impact wave energy. In the vertical direction without space in the irradiation direction, bubble formation is insufficient, thus preventing effective energy from being obtained. On the other hand, even in contact with the target, irradiation in the horizontal direction has space in the direction of laser emission, resulting in effective bubble formation and efficient impact energy. Horizontal irradiation can obtain relatively stable energy efficiency and appears to be an approach to be selected as a therapeutic strategy. However, the mucosa of the urinary tract (living body tissues) must be present on the opposite of the target in the horizontal approach in vivo, and there is a risk that excessive energy may act as unnecessary energy that may result in surgical complications such as injury to the urethral mucosa. In addition, it has been reported that the longer the pulse width of the laser, the lower the efficiency of bubble formation and energy conversion to plasma, such that the laser may influence the surrounding tissues as thermal energy\(^{14}\). In order to produce strong and safe impact waves at a set short pulse width, it is important to lower the output as low as possible and set an appropriate irradiation distance. In either case, these phenomena indicate that the space for bubble formation during the energy acquisition process by bubble formation after laser irradiation is a very important factor for laser lithotripsy. This study demonstrated that energy cannot be acquired by collapsing bubbles excited by a laser without sufficient bubble forming space and that bubble behavior and the propagation of impact waves can be observed if there is a small space where bubbles can grow. In addition, the study results on the optimal irradiation distance and irradiation direction may enable the selection of a safe and appropriate laser fiber irradiation style in different living bodies in various environments, avoiding damage to used fibers, maximizing the crushing efficiency with minimal invasiveness, and thus contributing to the improvement of medical efficiency.

In this study, we found that the acquisition of effective energy by laser irradiation has different characteristics depending on the irradiation direction and irradiation environment, and that it is possible to acquire effective energy by adapting the irradiation style to various situations. It is assumed that contact with targets in irradiation in the vertical direction may decrease the energy efficiency as well as the crushing efficiency. We believe that the recognition of bubble collapse behavior and energy propagation efficiency of laser irradiation in the ureter/renal pelvis may be useful in the selection of crushing and extraction methods and the irradiation style as a part of TUL strategies.

We hope this study report may spread the recognition of the principle of calculus crushing of Ho:YAG laser by the surgeon, enable the selection of a strategy with better treatment efficiency based thereon, and avoid circumferential tissue damage.

**Conflict of interest statement**

The authors declare that in no conflict of interest.

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