In Vitro Fragmentation of Biliary Calculi with a 308 nm Excimer Laser

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ABSTRACT

We report the use of a 308 nm XeCl excimer laser for biliary stone fragmentation. The 130 nsec laser pulses are delivered through UV grade fused silica fibers to the target stones immersed in normal saline solution and placed in direct contact with the fiber. Sixty biliary calculi, 20 cholesterol and 40 pigment, were fragmented in vitro. The effect of laser repetition rate, energy fluence, and fiber core size on stone fragmentation was studied. Fragmentation thresholds for biliary calculi of different compositions were measured. It was found that higher fragmentation efficiency was obtained with larger fluence, lower repetition rate and fiber of larger core. Our study suggests that the long pulse 308 nm excimer laser may be an effective device for laser lithotripsy with low threshold and good efficiency for biliary stone fragmentation.

1. INTRODUCTION

Stone fragmentation with lasers has been achieved with several sources such as the flashlamp pumped dye[1] and Q-switched Nd:YAG lasers[2]. However, the effect of excimer lasers on fragmentation of human calculi has not been well studied, although they have shown promise for such procedures as angioplasty[3], ophthalmology[4] and bone surgery[5]. It is therefore the purpose of this work to investigate the efficacy and efficiency of excimer lasers for biliary stone destruction. In this study, the influence of different experimental parameters including energy fluence, repetition rate and fiber core size on biliary stone fragmentation was examined. The fragmentation thresholds of biliary stones of various compositions were measured.

2. MATERIALS AND METHODS

2.1. Laser and delivery system

We used a long-pulse (130 nsec) xenon chloride (XeCl) excimer laser operating at 308 nm. The laser energy was delivered to the target stone via UV grade fused silica step-index fibers. A 10 cm focal length lens (UV grade) was used to couple the laser beam into the fiber. The laser energy was adjusted with a circular aperture placed after the laser output coupler and measured with a Rj-7200 energy ratiometer (Laser Precision Corp.).

2.2. Stone samples

The biliary stones used in this study were collected at surgery and were stored in normal saline solution at room temperature until use. These stones were grouped into two categories, pigment and cholesterol, according to their surface colors. The stones that were black or dark brown were classified into pigment stones and those that were white or light yellow into cholesterol stones.

A total of sixty biliary calculi (40 pigment and 20 cholesterol) were used for the fragmentation study. The mass of these stones ranged between 0.112 and 0.316 grams with a mean of 0.164 grams. Three biliary stones with predetermined compositions were utilized for surface fragmentation threshold measurements. They were composed of 100% calcium bilirubinate, 40% calcium bilirubinate and 60% cholesterol, and 100% cholesterol, respectively. Stone composition was determined by means of infrared spectroscopy and crystallography. The above mentioned compositions represent those of the surfaces of the stones.

2.3. Fragmentation experiments

During fragmentation, the stone was secured in a wire basket and the fiber was hand held against the stone surface as shown in Figure 1. Stone fragmentation was performed in normal saline solution. Different experimental parameters were employed, including laser repetition rate (5 and 20 Hz), energy fluence (80 and 110 mJ/mm^2) and fiber core size (300 and 600 um). A group of ten stones were

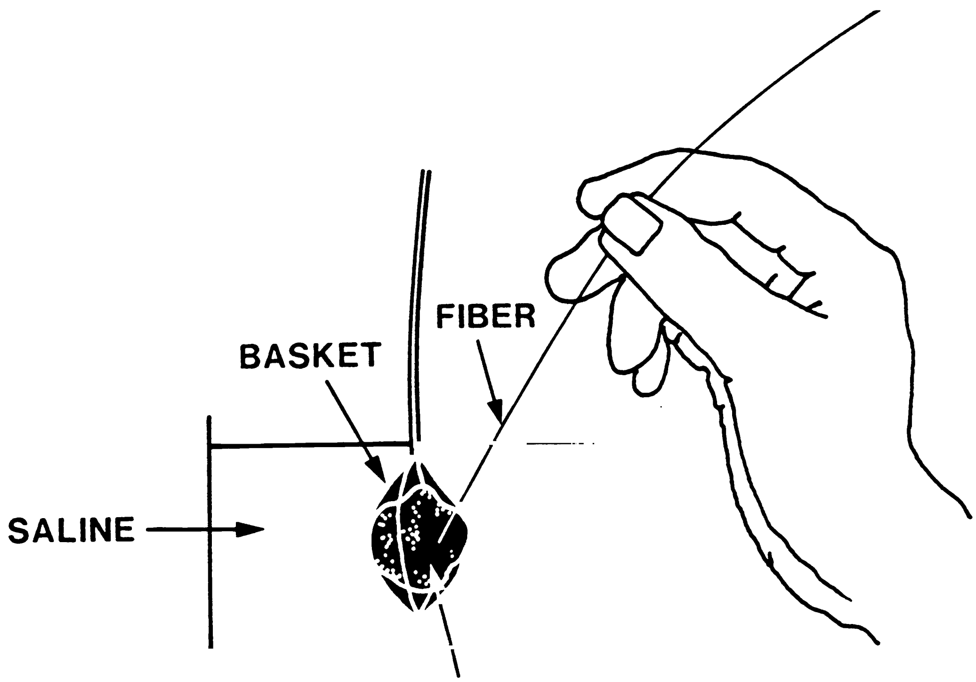

Fig. 1. Schematic of experimental setup.

fragmented with different combinations of these parameters. Only one parameter was varied at a time so that its effect could be evaluated individually. The energy delivered per unit mass of the stone was kept constant at 50 mJ/mg prior to fragmentation for all the parameter combinations used in the study. The total laser energy in mJ delivered to each stone was then calculated by multiplying 50 mJ/mg by its mass in mg. The total energy thereby determined assured no overdose of energy even with the set of parameters leading to the most efficient stone fragmentation. Consequently, the results obtained with various combinations of parameters could be properly compared.

After the designated total energy was delivered, the resulting fragments were collected and their sizes were measured with sieves of different hole diameters. stone fragments were divided into three groups according to their sizes: $d \leq 1.2$ mm, 1.2 mm $< d \leq 2.4$ mm, and 2.4 mm $< d \leq 4.0$ mm. The fragmentation efficiency obtained at different parameters was evaluated by comparing the percentage weight of the fragments with $d \leq 1.2$ mm. The percentage weight was obtained by taking the ratio of the fragments' weight of the size group being examined to the total weight of the stone.

2.4. Fragmentation threshold measurements
The stone under study was held in a wire basket and was placed under direct vision of a microscope. Measurement was conducted with the stone immersed in normal saline and in direct contact with the fiber. Fragmentation threshold was found by slowly increasing the laser energy until some physical change on the stone surface was visible through the microscope. Fibers of different core sizes (300, 600 and 1000 um) were used in the threshold measurements to reveal the effect of irradiation area on the fragmentation threshold of biliary stones. Fifteen data points were taken over the surface of each stone used. The mean therefore represents an average over the inhomogeneous composition distribution over the stone surface.

3. RESULTS AND DISCUSSION

The fragmentation efficiency, defined in our study as the mass in microgram of fragments removed per millijoule of the delivered laser energy (ug/mJ) that are less than 1.2 mm in size, were derived from the fragmentation experiments. This was done for each stone sample by dividing the weight of the fragments ($d \leq 1.2$ mm) by the total laser energy delivered. The fragmentation efficiency thereby obtained permit an estimate of the total energy needed for fragmenting a given stone into fragments smaller than 1.2 mm. The fragmentation efficiency for biliary stones under different conditions are presented in Table 1.

This study demonstrates that biliary stones can be effectively fragmented using 308 nm excimer laser energy delivered via UV grade fibers. The size distribution of the pigment and cholesterol stone fragments obtained at a fluence of 110 mJ/mm^2 at 5 Hz and delivered via a 600 um core diameter fiber is shown in Fig. 2. While both pigment and cholesterol stones were found to be susceptible to excimer laser fragmentation, greater fragmentation efficiency is observed for pigment stones (9.3±2.8 ug/mJ) than for cholesterol stones (5.4±1.7 ug/mJ). This result is consistent with the measured fragmentation thresholds (see Table 2) and is probably due to higher absorption of the pigment stones at 308 nm than the cholesterol stones.

Table 1. Fragmentation Efficiency of Biliary Calculi at 308 nm

Stones	Fluence (mJ/mm^2)	Rep. Rate (Hz)	Fiber Size (um)	Frag. Efficiency (ug/mJ)
Pigment	110	5	600	9.3±2.8
	80	5	600	5.4±1.8
	110	5	600	9.3±2.8
	110	20	600	8.2±0.8
	110	5	600	9.3±2.8
	110	5	300	5.5±1.4
Cholesterol	110	5	600	5.4±1.7
	110	20	600	3.7±1.2

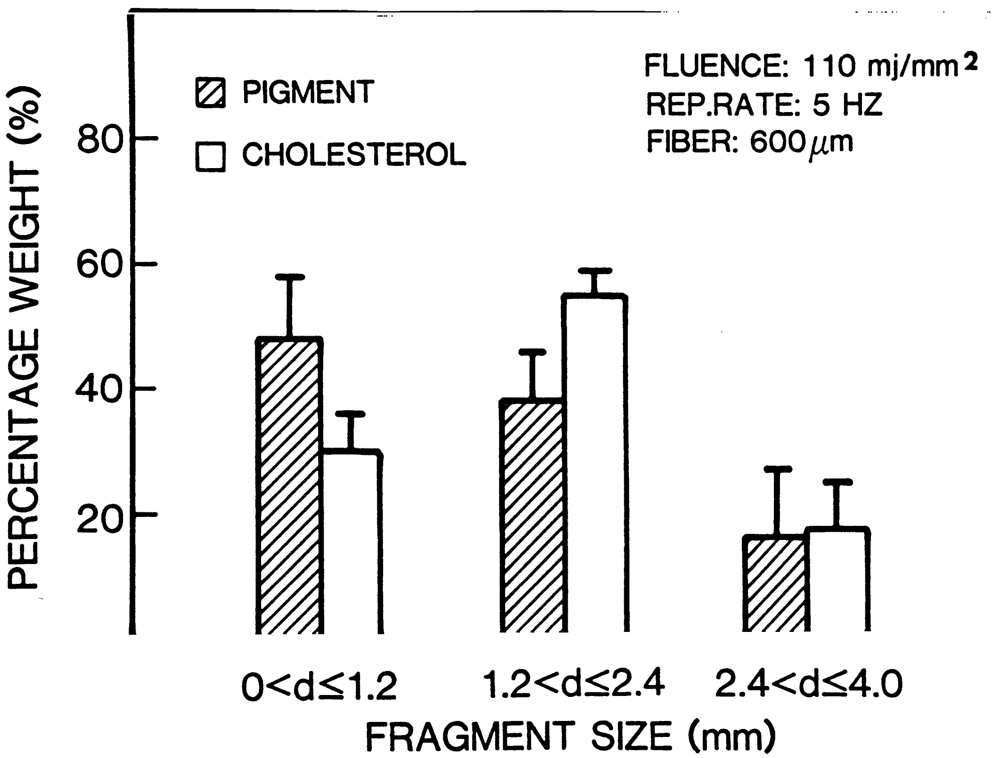

Fig. 2 Size distribution of pigment and cholesterol stone fragments.

The influence of laser repetition rate on stone fragmentation was studied at 5 and 20 Hz. For Pigment stones, the fragmentation efficiency was found to be not significantly affected by the change in repetition rate. On the other hand, higher fragmentation efficiency was observed at 5 Hz (5.4 ± 1.7 ug/mJ) than at 20 Hz (3.7 ± 1.2 ug/mJ). Similar repetition rate dependence of the cholesterol stones was also obtained in our earlier study of biliary stone fragmentation using a flash lamp pumped dye laser[6]. As far as the effect of laser fluence and fiber size on the fragmentation is concerned, it can be seen from Table 1 that the use of 80 mJ/mm^2 energy fluence delivered via a 600 um fiber resulted in a fragmentation efficiency similar to that obtained when the 110 mJ/mm^2 fluence was applied with a 300 um fiber, which is about 40% lower than that obtained at 110 mJ/mm^2 delivered via the 600 um fiber. This suggests that the decrease in laser energy fluence and the reduction in irradiation area generate a similar effect on degrading the fragmentation efficiency for biliary stones.

In order to reveal the effect of the medium in which stone fragmentation took place on the fragmentation process, five cholesterol stones were fragmented in air with a fluence of 110 mJ/mm^2 at 5 Hz delivered through a 600 um core diameter fiber. It was found that laser energy did not shatter the stone as it did in saline. Each laser pulse simply removed a tiny piece of stone of less than 1.2 mm in size. After the total energy of 50 mJ/mg multiplied by the stone mass was delivered, about 25% of the stone was fragmented into sand-like particles while the residual stone was left in bulky form. The fragmentation efficiency, however, was found to be the same as that obtained when stone fragmentation occurred in saline (5.0 ± 1.6 ug/mJ in air versus 5.4 ± 1.7 ug/mJ in saline). These observations suggest that the 308 nm laser energy is able to ablate the stone due to its high absorption by the stone materials as well as to generate a shock wave at the irradiated site. If the stone is immersed in liquid, the shock wave is efficiently coupled into the stone and results in shattering the stone[7]. On the other hand, if stone ablation takes place in air, the shock wave is not well confined by the compressible medium (air) and consequently makes little contribution to crashing the stone.

The fragmentation threshold measurements were conducted at the surface of the stones of known composition. Fibers of three different core sizes (300, 600, and 1000 um) were utilized. The results of the measurements are summarized in Table 2. As shown in Table 2, there is a consistent decrease in threshold fluence with increasing amount of calcium bilirubinate content in biliary stones. The study of optical absorption of biliary stones has been performed earlier by Long et al[8]. However, their study was limited in a spectral range between 350 and 1060 nm. Our results indicate that calcium bilirubinate may absorb stronger at 308 nm than cholesterol. Data in Table 2 also show that within experimental error the threshold fluence of biliary stones at 308 nm is not significantly affected by the irradiation area. The energy fluence, rather than the energy per pulse, determines the initiation of stone fragmentation.

Table 2. Fragmentation Thresholds of Biliary Calculi at 308 nm

Stones	Threshold Fluence (mJ/mm^2) d* = 300 um	600 um	1000 um
100% calcium bilirubinate	3.0	2.7	3.5
60% cholesterol 40% cal. biliru	16.8	13.7	12.7
100% cholesterol	24.7	17.4	17.5

* d is the core diameter of the fibers used for threshold measurements.

4. CONCLUSION

Biliary calculi have been successfully broken into small fragments using 308 nm excimer laser energy delivered via UV grade fused silica fibers. All experiments conducted so far have been in vitro. The results obtained indicate that the 308 nm excimer laser might be effective as a laser lithotriptor with low threshold and satisfactory efficiency for biliary stone fragmentation. Further work is necessary to address the issue of excimer laser safety as well as the delivery system design in order to assess its potential of clinical applications.

5. REFERENCES

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