Title

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Permalink
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Journal
Journal of Investigative Surgery, 4(4)

ISSN
0894-1939

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Publication Date
1991

DOI
10.3109/08941939109141177

Journal of Investigative Surgery

ISSN: 0894-1939 (Print) 1521-0553 (Online) Journal homepage: http://www.tandfonline.com/loi/iivs20

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To cite this article: Bernard W. Chang, Marc E. Pollock, John Eugene, Michael W. Berns & G. Robert Mason (1991) Experimental Cholelitholysis with the Pulsed Tunable Dye Laser, Journal of Investigative Surgery, 4:4, 467-476, DOI: 10.3109/08941939109141177

To link to this article: http://dx.doi.org/10.3109/08941939109141177

Journal of Investigative Surgery, Volume 4, pp. 467–476
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0894-1939/91 $3.00 + .00

Experimental Cholelitholysis with the Pulsed Tunable Dye Laser

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Abstract *This study evaluates the pulsed tunable dye laser with wavelength 504 nm, frequency 10 Hz, and pulse width 1.2 μs for cholelitholysis. Power of 10–40 kW was directed through a 250-μm quartz fiber optic to ablate 55 gallstones (removed from 14 patients). The fiber was positioned in direct contact with the stones under saline. Power delivery was begun at 10 kW and increased in 10-kW increments until litholysis began. The range of power and energy necessary to fragment the gallstones was evaluated on four common bile ducts (fresh autopsy specimens). Following fragmentation, all stones were analyzed. There were 35 cholesterol stones (3 calcified) and 20 bilirubin stones (4 calcified). Size ranged from 0.012 to 7.56 cm^3 (mean 0.96 ± 1.41 cm^3). Energy necessary for fragmentation ranged from 0.4 to 11.2 J (exposure time 1.0–28 s). Power necessary for fragmentation was 20 kW for 2/55 stones and 40 kW for 53/55 stones. At 40 kW (40 mJ/pulse), common bile duct perforation occurred within 1.1 ± 0.1 s (0.44 ± 0.04 J). The pulsed tunable dye laser can fragment gallstones of all compositions. The threshold for fragmentation is 40 kW, but common bile duct perforation occurs at this power. We conclude that laser radiation sufficient to fragment gallstones can injure the common bile duct.*

Keywords Laser, cholelitholysis, pulsed dye laser.

Introduction

Fragmentation of common bile duct stones by a nonoperative or limited operative approach may be possible by directing a fiber optic into the common duct and delivering laser radiation. This technique has been studied with the continuous wave neodymium-YAG laser (1064 nm),[1] pulsed neodymium-YAG laser (1064 nm),[2] pulsed dye laser (450–700 nm),[3] free electron laser (2.5–3.5 μm),[4] copper vapor laser

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Presented at the Sixth Annual Scientific Session of the Academy of Surgical Research, Long Beach, CA, September 27–29, 1990.

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Table 1
Laser Fragmentation of Cholesterol Calculi Gallstones

Patient	Volume (cm^3)	Energy Delivery (mJ/pulse)	Total Energy (J)	Time to Fragmentation (s)	Cholesterol (%)	Bilirubin (%)	$CaCO_3$ (%)
1	2.72	40	4.8	12	70	30	0
	0.29	40	0.8	2	70	30	0
	0.24	40	1.2	3	70	30	0
	0.29	40	1.6	4	70	30	0
	0.10	40	0.8	2	70	30	0
	0.25	40	1.2	3	70	30	0
	0.29	40	0.8	2	70	30	0
	0.24	40	0.8	2	70	30	0
2	0.125	40	0.8	2	95	5	0
	0.012	40	0.4	1	95	5	0
	0.008	40	0.4	1	95	5	0
	0.012	40	0.4	1	95	5	0
	0.080	40	0.4	1	95	5	0
5	0.24	40	6.0	15	85	15	0
	0.10	40	2.0	5	85	15	0
	0.072	40	2.0	5	85	15	0
	0.045	40	0.8	2	85	15	0
	0.048	40	1.6	4	85	15	0
	0.096	40	0.4	1	85	15	0
6	1.20	40	4.8	12	75	10	15
	1.10	40	0.4	1	75	10	15
	1.20	40	0.8	2	75	10	15
7	1.82	40	11.2	28	90	10	0
	0.28	40	0.8	2	90	10	0
8	0.064	40	0.4	1	90	10	0
	0.048	40	0.4	1	90	10	0
	0.064	40	0.4	1	90	10	0
11	0.28	40	0.8	2	90	10	0
	0.14	40	0.4	1	90	10	0
12	4.33	40	10.4	26	95	5	0
	3.60	40	7.6	19	95	5	0
	2.55	40	6.0	15	95	5	0
	1.30	40	1.2	3	95	5	0
	2.52	40	2.8	7	95	5	0
	2.70	40	10.0	25	95	5	0

Table 2
Laser Fragmentation of Bilirubin Calculi Gallstones

Patient	Volume (cm^3)	Energy Delivery (mJ/pulse)	Total Energy (J)	Time to Fragmentation (s)	Cholesterol (%)	Bilirubin (%)	$CaCO_3$ (%)
3	2.0	20	2.4	12	5	95	0
4	0.90	20	3.0	15	30	70	0
	0.5	40	2.0	5	30	70	0
	0.14	40	0.4	1	30	70	0
	0.24	40	0.8	2	30	70	0
9	3.46	40	3.2	8	10	90	0
	7.56	40	2.8	7	10	90	0
	1.54	40	1.2	3	10	90	0
10	0.9	40	0.8	2	30	70	0
	0.89	40	1.2	3	30	70	0
13	0.048	40	0.4	1	0	60	40
	0.10	40	0.4	1	0	60	40
	0.027	40	0.4	1	0	60	40
	0.018	40	0.4	1	0	60	40
14	2.94	40	7.2	18	20	80	0
	0.88	40	1.6	4	20	80	0
	2.84	40	0.8	2	20	80	0
	0.25	40	0.8	2	20	80	0
	0.75	40	0.8	2	20	80	0
	0.4	40	1.2	3	20	80	0

(510 nm),[5] and excimer laser (308 nm).[6] The neodymium-YAG laser can ablate only bilirubin stones. The other lasers can fragment both cholesterol and bilirubin stones. The pulsed dye laser has been used clinically for the lysis of ureteral stones and may be suitable for use in the biliary system.[7] This report evaluates the range of power and energy necessary for stone fragmentation as well as the effect of laser intensity on the common bile duct.

Materials and Methods

All experiments were performed with a pulsed tunable dye laser (Model MDL-1P Candela Corporation, Natick, MA) with wave length 504 nm, pulse width 1.2 μs, frequency 10 Hz, and power 10–60 kW delivered through a 250-μm quartz fiber. The fiber was freshly cut and polished for each experiment. Power output was measured from the laser head and from the output end of the fiber at the beginning and conclusion of each experiment with a power meter (Model 362, Scientech Corporation,

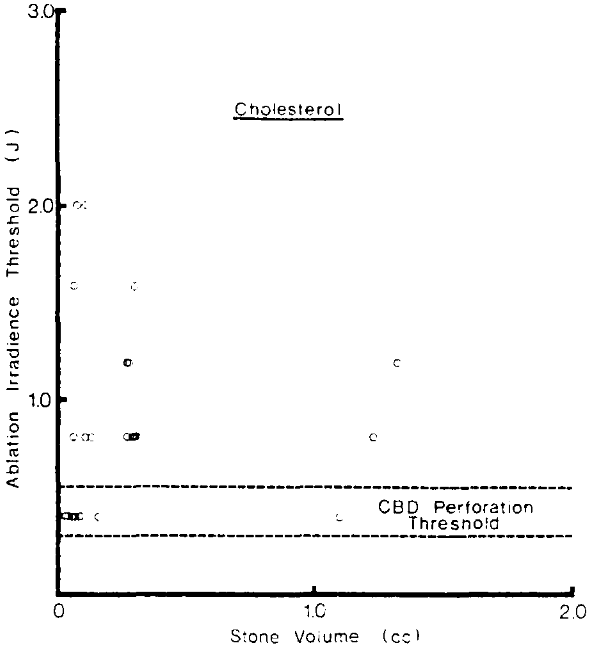


Figure 1. Graphic representation of cholesterol calculi size and laser energy necessary for fragmentation. The ablation threshold for calculi is greater than the perforation threshold for the common bile duct.

Boulder, CO). Human biliary calculi (n = 55) were obtained from 14 patients undergoing cholecystectomy. Human common bile ducts (n = 4) were obtained from four fresh necropsies (less than 24 h) of patients with known gallstone disease.

Each gallstone was placed in saline solution and the quartz fiber was positioned in direct contact with the stone. Energy delivery was begun at 10 mJ/pulse. Energy delivery was increased in increments of 10 mJ/pulse until litholysis began. Each energy level was held constant for 60 s before advancing. Laser radiation was kept constant once fragmentation was begun and laser delivery was continued until the stone was fragmented. The fragments of each stone were collected and crystallographic analysis was performed.

Once the energy threshold for calculus fragmentation was determined, this energy was directed at the common bile ducts. The ducts were suspended in saline. The quartz fibers were positioned at right angles to the mucosal surfaces. Laser radiation at threshold energy levels was delivered 1.0 cm from the mucosal surface and also in contact with the mucosal surface. Laser exposures were performed at multiple sites in each duct for 1.0 s. Following laser irradiation of the common bile ducts, the ducts were examined under a dissecting microscope. They were pinned flat on Teflon blocks, fixed in 3% gluteraldehyde in phosphate buffer at 4 °C for 24 h, and rinsed in phosphate buffer. They were dehydrated through an alcohol series, removed from Teflon, and embedded in paraffin. The specimens were serially sectioned at 6-μm intervals and stained with hematoxylin and eosin. All specimens were examined microscopically to determine the severity of common bile duct injury.

Results

There were 35 cholesterol stones (3 were calcified) and 20 bilirubin stones (4 were calcified). The stones were 0.012–7.56 cm^3 in volume (0.47 ± 0.19 cm^3, mean ± standard error of mean). Fragmentation occurred at 20 mJ/pulse in 2/55 stones. Fragmentation occurred at 40 mJ/pulse in 53/55 stones. Total energy necessary for stone ablation ranged from 0.4 to 11.2 J (exposure time 1.0–28 s). Cholesterol stones required more total energy for fragmentation, 2.45 ± 0.52 J, than bilirubin stones, 1.59 ± 0.35 J, $P < .05$ (Student's t test), even though bilirubin stones were larger than cholesterol stones (Tables 1, 2; Figs 1, 2).

When laser radiation was delivered in contact with cadaver common bile ducts, perforation occurred at every energy delivery level from 10 to 40 mJ/pulse. At 10 mJ/pulse, perforation occurred within 6.7 ± 1.8 s. At 40 mJ/pulse, perforation occurred at 1.1 ± 0.1 s (Fig 3). When laser radiation was delivered at a distance of 1.0 cm from the mucosa, perforation did not occur, but mucosal injury was seen (Fig 4). The energy necessary to perforate the common bile duct when the fiber was in contact with the mucosa was 0.55 ± 0.04 J, whether it was delivered at 10 mJ/pulse for 5.5 s or at 40 mJ/pulse for 1.1 s (Table 3). The irradiance threshold for both cholesterol and bilirubin gallstone ablation was determined to be 40 mJ/pulse. At this threshold, ductal perforation would occur before gallstone fragmentation if the fiber were to contact the common duct (Fig 5).

Discussion

The present study shows that the pulsed tunable dye laser at 504 nm is capable of ablating gallstones of all compositions and sizes. The energy necessary to fragment these stones, however, is within the range of energy capable of perforating the common bile duct if the optical fiber is misplaced and allowed to contact the mucosa. In

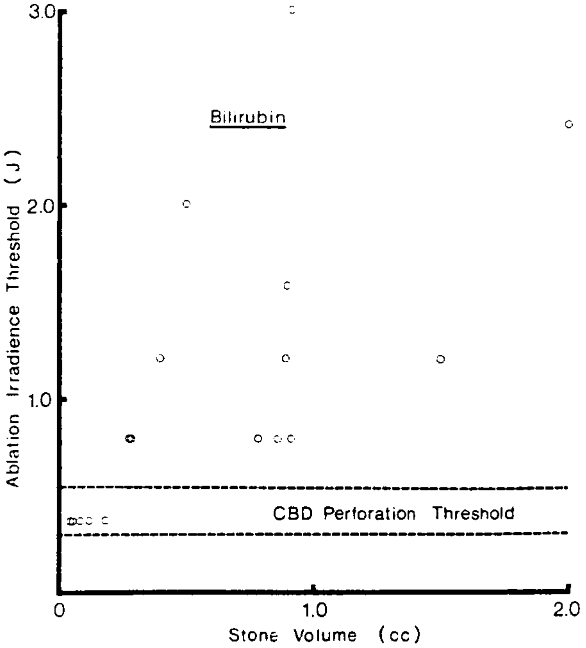
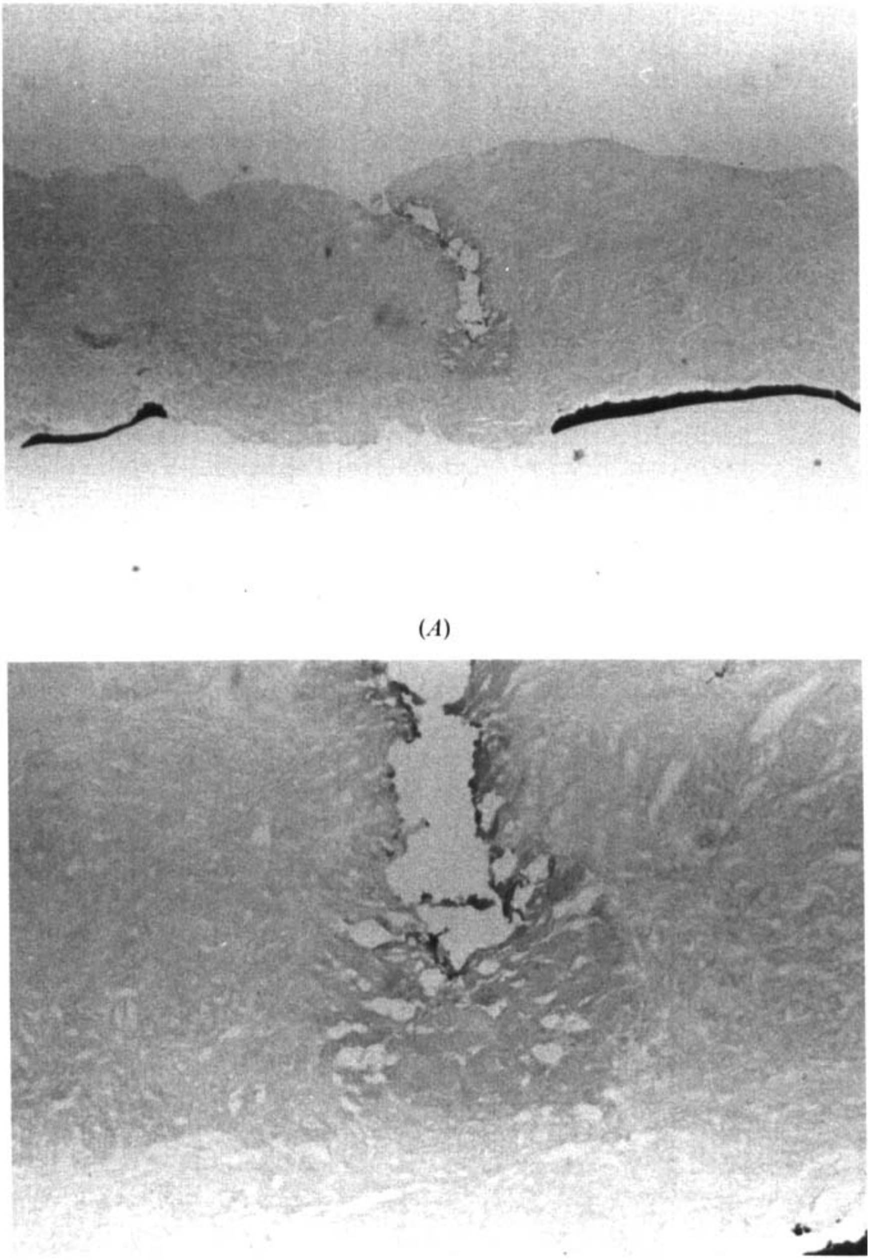


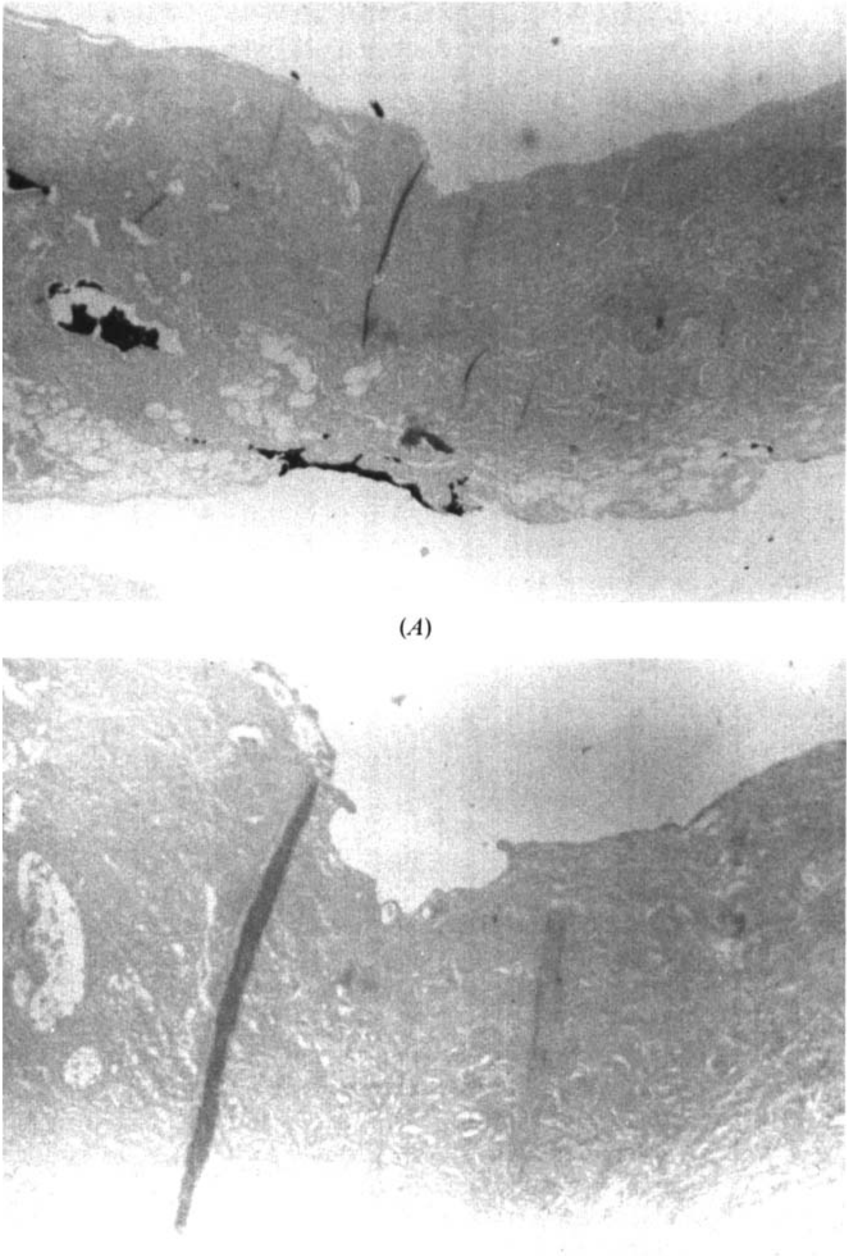
Figure 2. Graphic representation of bilirubin calculi size and laser energy necessary for fragmentation. The ablation threshold for calculi is greater than the perforation threshold for the common bile duct.



(*A*)

(*B*)

Figure 3. Longitudinal section of a common bile duct following contact laser radiation with a 504-nm pulsed dye laser at 40 mJ/pulse, 10 Hz, for 1.0 s. (*A*) Low-power magnification (16×) shows a full thickness injury beginning at the mucosa and extending to the serosa. (*B*) High-power magnification (40×) shows tissue destruction and surrounding coagulation necrosis from the laser injury (Hematoxylin and eosin).



(*A*)

(*B*)

Figure 4. Longitudinal section of a common bile duct following noncontact laser radiation with a 504-nm pulsed dye laser at 40 mJ/pulse, 10 Hz, for 1.0 s. (*A*) Low-power magnification (16×) shows no full thickness injury. (*B*) High-power magnification (40×) demonstrates mucosal irregularity but no injury to deeper layers from the laser exposure (Hematoxylin and eosin).

Table 3
Pulsed Dye Laser (504 nm) Radiation of Common Bile Duct

Specimen Number	Power (kW)	Energy Delivery (mJ/pulse)	Time to Perforation (s)	Total Energy (J)
1	10	10	12.6	1.26
1	20	20	3.6	0.72
1	30	30	2.0	0.60
1	40	40	1.4	0.56
2	10	10	4.1	0.41
2	20	20	2.5	0.50
2	30	30	1.9	0.57
2	40	40	1.0	0.40
3	10	10	3.4	0.34
3	20	20	2.3	0.46
3	30	30	1.5	0.45
3	40	40	1.0	0.40
4	10	10	6.8	0.68
4	20	20	2.9	0.58
4	30	30	2.3	0.46
4	40	40	1.0	0.40

clinical use, the fiber tip must be placed in direct contact with the stone to guard against common bile duct injury.

The possibility of common bile duct injury from laser lithotripsy has also been evaluated by Dayton et al.[5] They used a copper vapor laser to fragment gallstones in vitro and measured heat transmission in a model common bile duct during fragmentation. The elevation in temperature associated with fragmentation suggested common bile duct thermal injury. Ell and associates[2] also reported temperature elevation associated with stone fragmentation and they identified transmural necrosis when delivering laser radiation blindly in the common duct. Yet Nishioka and associates[8] used the pulsed tunable dye laser (504 nm) to fragment human gallstones placed in pig common bile ducts and did not see any short- or long-term laser-induced injury in the common bile ducts. When they applied laser radiation in direct contact with the mucosal surface, however, perforation occurred. These studies imply that common duct injury may occur from lasers even during technically correct ablation, while ductal injury will definitely occur with pulsed lasers only if the fiber is malpositioned. In the clinical setting, perforation may not be of consequence because perforations are microscopic (Fig 1) and approximate the size of the fiber tip (250 μm). An isolated injury this size may seal over quickly and not lead to fistula or abscess formation. Multiple injuries, however, may lead to ductal disruption.

The pulsed dye laser (504 nm) appears to offer several advantages over the continuous-wave neodymium-YAG laser for gallstone lithotripsy. The dye laser can ablate cholesterol and bilirubin stones (even when calcified) and it does not have a thermal effect on surrounding tissues. Orii et al[1] have described laser cholelitholysis by passing a laser fiber through a choledochoscope that had been positioned in the common duct through a T-tube tract. They also passed a laser fiber through a choledochoscope into the hepatic ducts via a percutaneous transhepatic cholangiodrainage tract. With the popularity of laparoscopic laser cholecystectomy[9] it may also be possible to pass a laser fiber through a choledochoscope laparoscopically into the common duct for gallstone lithotripsy. No matter what technique is used to position the laser fiber, the fiber must be kept in direct contact with the gallstone because laser intensity strong enough to fragment gallstones can injure the common duct.

Acknowledgments

The authors thank Jeffrey J. Andrews and L. H. Liaw for technical assistance. Heidi Snincsak prepared the manuscript. This work was supported by NIH Grant RRO-1192.

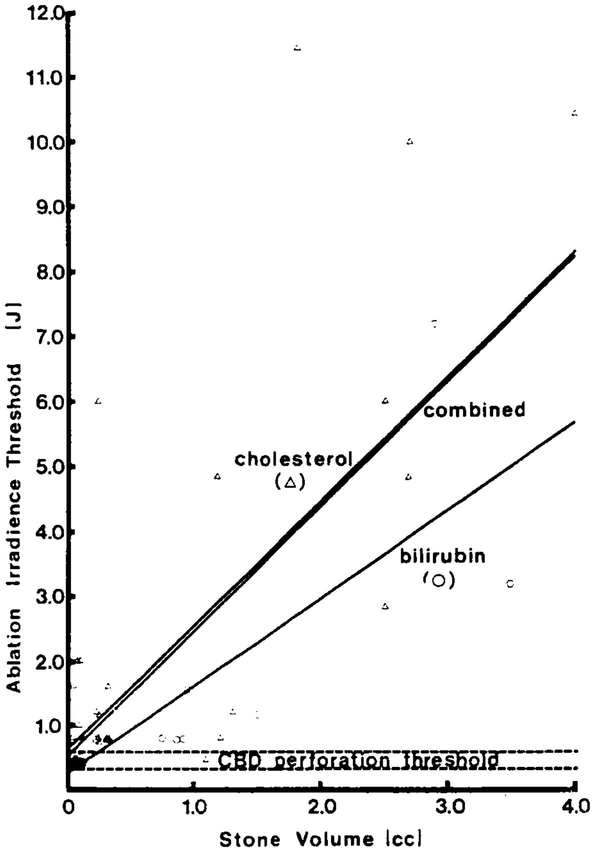


Figure 5. Graphic representation of gallstone size and laser energy necessary for fragmentation. The cholesterol gallstones required greater energy for fragmentation than bilirubin gallstones. The smaller gallstones required less energy for fragmentation than the larger gallstones. The ablation threshold for any of the gallstones is greater than the perforation threshold of the common duct.

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