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Urological Research

Laser lithotripsy of ureteral calculi

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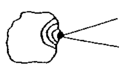
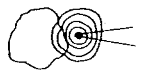
Physical basis of laser-induced shock-wave lithotripsy

Depending on the laser type, three mechanisms for stone disintegration are possible: (1) continuous-wave lasers (CW lasers) induce thermal stress on the stone by heating the surface; (2) flashlamp-pulsed lasers (e.g. dye lasers) act by an optoacoustically released mechanical stress. Absorption at the stone causes a plasma with optoacoustic effects. (3) Q-switched lasers (e.g. Nd:YAG lasers) cause a laser-induced breakdown (LIB) in the liquid around the stone. The stone composition is decisive only with the dye laser, for which a given wavelength is selected for absorption in the stone (Table 1).

With a Nd:YAG laser, the liquid around the calculus acts as an energy converter, propagating the laser-induced shock wave to the stone, whereas the stone itself is used for energy transformation with the dye laser. With a Q-switched Nd:YAG laser, shock waves with a high pressure amplitude (1,000–10,000 bar, highly focused) can be generated by a LIB.

Table 1. Mechanism of stone disintegration according to the laser type and mode of action

			
Laser type	Continuous wave (e.g. Nd:YAG)	Flashlamp-pulsed (e.g. dye laser)	Q-switched (e.g. Nd:YAG)
Mechanism	Heating by absorption at the stone surface	Absorption at the stone causes optocoustic effects	Laser-induced breakdown in a liquid around the stone produces shock waves
Pulse duration	s	1 μs	8 ns
Energy	20–80 W	50–100 mJ	30–80 mJ
Wavelength	1,064 nm	504 nm	1,064 nm
Intensity	17.6 kW/cm^2	0.3 GW/cm^2	1.2 GW/cm^2
Fiber-core diameter	0.6 mm	0.2 and 0.32 mm	0.32, 0.4 and 0.6 mm

Laser-induced breakdown

By focusing the pulses of a Nd:YAG laser, large photon-flux densities can be reached, which can produce free electrons by means of multiphoton ionization in matter. Inverse bremsstrahlung accelerates the electrons until they can ionize matter by themselves. This results in an electron avalanche that converts matter into the plasma state. After emission of the shock wave, the plasma expansion ceases and a cool, gas-filled void is left, which collapses under the liquid pressure and leads to cavitation and the emission of further shock waves.

Laser-induced shock waves

Using a Q-switched Nd:YAG laser (8-ns pulse duration, up to 80-mJ single-pulse energy), a shock wave can be generated with a rise time of about 3 ns and an overall duration of 180 ns. In the surrounding field (approx. 3 mm), the shock wave propagates with supersonic velocity (in water, 2,500 m/s). The pressure amplitude at a distance of 1 mm amounts to 1.5 kbar (pulse energy, 35 mJ) (Fig. 1). In vitro experiments have shown that urinary and biliary calculi of any composition can be fragmented with laser-induced shock waves into particles measuring <1 mm (average, 0.4–0.5 mm).

Using a Nd:YAG laser with a 1,064 nm wavelength, an 8-ns pulse duration, and a single-pulse energy of 20–80 mJ, shock waves can be created with peak pressures of 1,000 bar in <4 ns. Shock waves reaching an area with different sound wave impedance, such as a urinary calculus, are partly reflected. At the front of the calculus, some pressive (and at the rear, tensile) pressure is generated, with consequent disintegration of the calculus. Combination of the extremely short discharge time of the pulse with plasma formation and cavitational effects results in

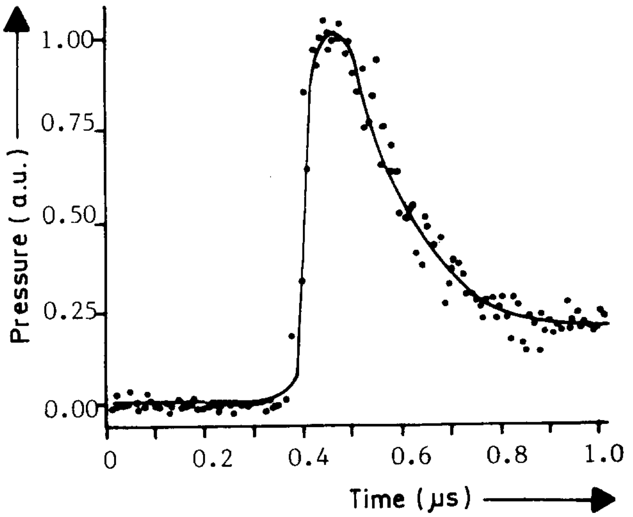


Fig. 1. Laser-induced shock waves: pressure vs time

an undetectable temperature rise around the LIB. The average energy applied is at most a few watts, such that in practice, no thermal effects at all are involved. Moreover, the interval between two short-term pulses is so high (50-Hz pulse-repetition rate means an 8-ns pulse duration) that thermal effects from a series of pulses can be ruled out. The ratio of a nanosecond (8×10^{-9} s) pulse of the 50-Hz repetition rate (50 pulses/s) – as applied in our laser system – would equal, on an enlarged scale, a pulse of 1 s followed by a pause of 28.9 days. This comparison illustrates the laser principle of using an extremely short pulse with a steep, high-intensity shock wave followed by a long pause.

For intracorporeal application of LIB, the laser energy has to be transmitted through a small, preferably highly flexible, fiber. Therefore, the mean energy density must be chosen such that no breakdown can be induced within the light guide, yet it must be high enough to generate breakdown at the exit site of the fiber (energy of about 30–50 mJ). The Q-switched laser energy is coupled into a 600- to 400-μm quartz tube at the planar end of the fiber. Focusing of the laser pulses at the fiber tip in the form of a laser cone was achieved by a specially formed tip. No lens system is attached to the fiber end. Focusing is obtained solely by the shaped fiber end (Fig. 2.)

Optimal stone disintegration is performed within the LIB, seen at the fiber tip as a light cone. Fragmentation can also be heard as a series of slight clicking sounds. Brief contact of the fiber with the stone or the spray of fragments does not damage the fiber, whereas constant laser irradiation with stone contact results in cracks of the fiber surface. The highly flexible quartz fiber can easily be changed during the operation by removing the plug-shaped end from the coupling device in the laser.

Biologic effects of laser irradiation

Experimental setting

Laser light from a Nd:YAG laser (1,064 nm, 8-ns pulse duration) was delivered either as a single pulse or as a pulse series of 20 Hz. Single-pulse energy ranged from 50 to 120 mJ and was up to 4 times higher than that now used in patient treatment (35 mJ). Energy variation was obtained using gray filters in the laser beam. The horizontal laser beam was reflected 90° downward by a 200% reflecting mirror fixed in bars, which made it easily movable in all three dimensions. The exact irradiation site could also be defined by the mirror, which was moved horizontally by means of a precision screw with a scale. This facilitated focusing directly onto the tissue surface or cell culture with a small focusing device. This sterilizable apparatus was built using a biconvex lens in a cylindrical tube and a fixed-up Plexiglas cone. The opening of the cone on the lower side was placed on the tissue surface and, with the help of the red light of the helium-neon pilot laser, the laser beam focused exactly onto the irradiation site. The interior of the device could be filled with sterile solution (such as physiologic saline). Additional experiments were carried out with irradiation focused onto the urothelium directly out of the 600-μm quartz fiber.

The biologic effects of laser irradiation were evaluated by irradiation of cell cultures, whole blood and urothelium of porcine bladder, ureter and kidney parenchyma:

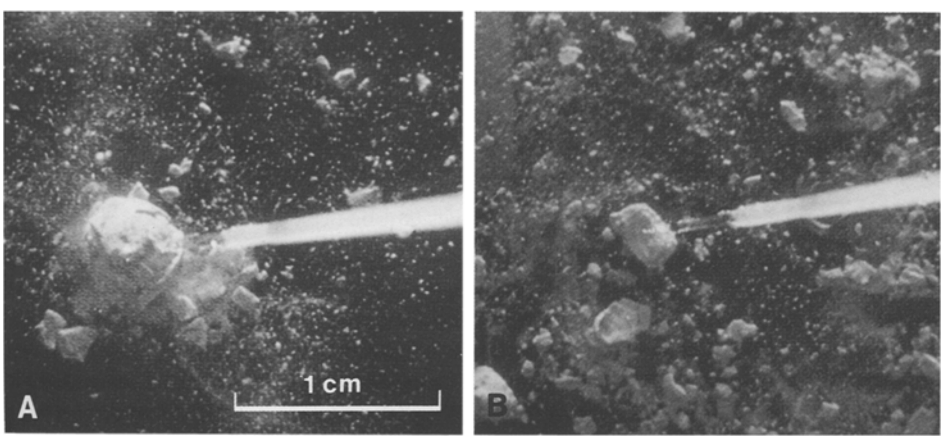


Fig. 2 A, B. Laser-induced shock wave lithotripsy of a calcium oxalate-uric acid calculus. **A** Disintegration after 50 pulses (81 s). **B** Same stone after 2,500 pulses (50 s): note the tiny fragments created

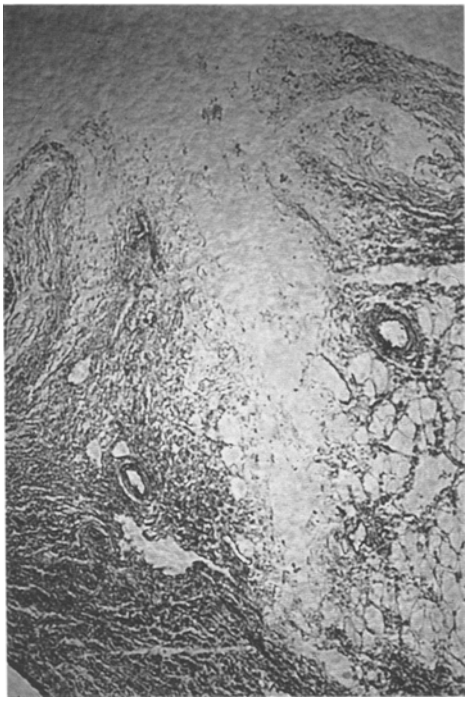


Fig. 3. Ureter after focussed laser irradiation (60 mg, 20 pulses). Maximal depth of the rupture cone, 40 μm

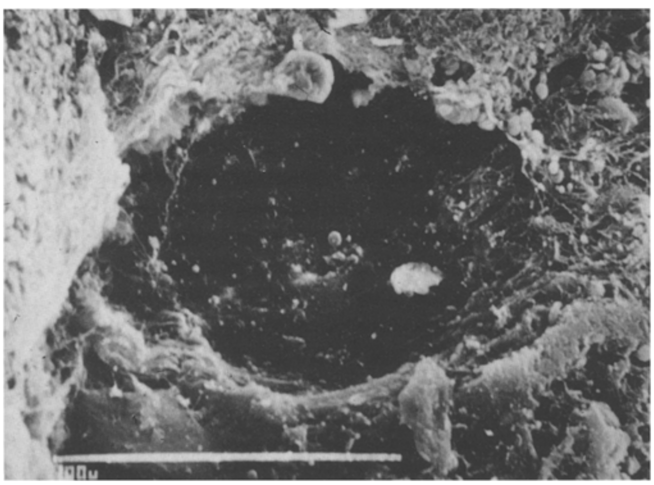


Fig. 4. Electron microscopy of the ureter immediately after focussed laser application (60 mJ, 20 pulses). ×60

1. Irradiation of various tissue cultures was performed (fibroblasts-brief cultures of allogenec renal cancer cells-xenogenec kidney tumor cells). Pulse energy varied from 50 to 84 mJ, with up to 600 pulses. The cell-culture monolayers were stained with methylene blue for vital cells.
2. Irradiation of whole blood was performed by focusing the laser beam into a flask filled with 20 ml blood.
3. Kidneys, ureters and urinary bladder of pigs were exposed transperitoneally. The ureter and the bladder were opened, the lumen was held open with threads and the urothelium was exposed to radiation:

a. Urothelium was irradiated in three pigs to study the immediate effects of radiation. Laser energy varied from 50 to 84 mJ with 20 pulses and, in a second series, to 75 mJ with 1, 10, 20 and 60 pulses for evaluation of the depth of the lesion. These animals were put to sleep immediately following irradiation. The exposed areas were enclosed by non-resorbable threads for easier histologic identification of the lesion.
b. Late effects were studied in another four pigs using laser irradiation of 60 or 80 mJ single-pulse energy for 10 and 30 s and 30 mJ for 10 and 30 s. The exposed tissue was examined 2, 4, 8 and 12 days thereafter. Electron microscopic and histologic evaluation was performed using Elastica-van Gieson and Elastica-Ladewig staining.

Results

Tissue culture irradiation

Only directly hit cells in the focus were destroyed and flushed away, whereas all cells surrounding the focus were vital and continued to grow in the culture.

Irradiation of whole blood

Whole-blood irradiation showed no significant haemolysis after laser exposure for up to 15 min.

Immediate effects of nanosecond laser pulses

Macroscopically, the area of irradiation could some times be found as a tiny point in the urothelium. Of 18 tissue sections, 4 showed a small rupture cone with a maximal depth of 40 μm. The electron microscope revealed a cone-like defect about 40–50 μm deep and 100 μm wide (Figs. 3, 4).

Late effects of nanosecond laser pulses

No macroscopic change could be seen on porcine urothelium 2, 4, 8 or 12 days after laser irradiation. Serial cuts of 5 μm in the exposed area showed no histologic change, especially thermic damage, necrosis or hemorrhage. Electron microscopy also revealed tissue alteration (Fig. 5).

Technical development

For intracorporeal use of the LIB, the laser energy has to be transmitted through small, highly flexible quartz fibers. Therefore, the mean energy has to be chosen such that no breakdown can be induced within the light guide, yet it must be high enough to generate a LIB at the exit side of the fiber. Using a Q-switched laser with 8-ns pulse duration and a wavelength of 1,064 nm, either 200-, 320-,

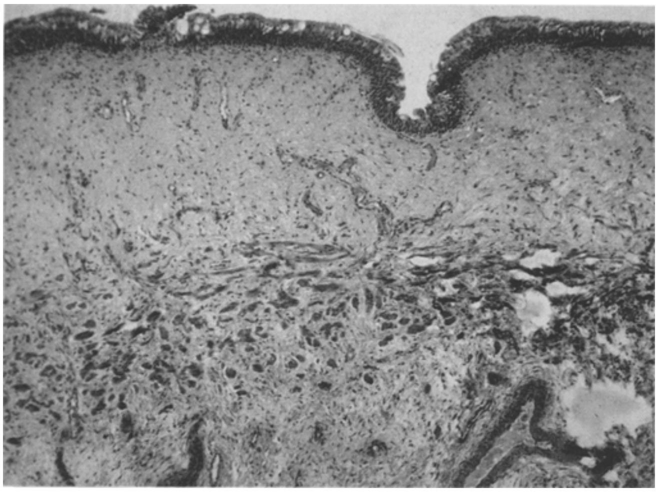


Fig. 5. Ureter 8 days after focussed laser irradiation (-mJ, 30 s, 10 Hz). Collagen stain according to Ladewig. No histologic alterations, especially thermic effects or necrosis, are found

Fig. 6. Nd:YAG laser with three functions: nanosecond pulses for urinary stone disintegration and millisecond pulses for biliary stones and coagulation

400- or 600-μm quartz fibers can be used (up to 80 mJ single-pulse energy), with a repetition rate of up to 50 Hz.

However, the 200-μm fiber proved to be very delicate and is no longer used for patient treatment. Meanwhile, a multifunctional laser with three functions has been developed for clinical use: (1) nanosecond pulses for shock-wave creation (LIB) and disintegration of urinary calculi (20 ns); (2) millisecond pulses for biliary stone fragmentation; and (3) millisecond pulses for thermic effects (coagulation of urothelial tumors or following resection

Table 2. Patients and stone localization in 181 patients with 183 calculi, June 1987 to December 1989

177 ureteric calculi:	
Upper ureter	(n = 29)
Middle ureter	(n = 44)
Lower ureter	(n = 110)
4 kidney calculi:	
Calix	(n = 2)
Pelvis	(n = 2)
Obstructing ureteric calculi with stone size of 3 × 5–15 × 40 mm	(n = 114)
Steinstrasse following ESWL	(n = 5)
Undisintegrated stones following ESWL	(n = 32)

ESWL = Extracorporeal shock-wave lithotripsy

of bladder tumors). The sizes of quartz fibers used include 320 μm (up to 40-mJ single-pulse energy), 400 μm (up to 50 mJ single-pulse energy) and 600 μm (up to 80-mJ single-pulse energy; Fig. 6)

Clinical application

Only stones that did not pass spontaneously out of the ureter after at least 4 weeks of conservative treatment, including obstructive ureteral stones and ureteral and kidney calculi not suitable for extracorporeal shock-wave lithotripsy (ESWL) were selected (Table 2).

Endoscopy

Rigid instruments. A 4-F ureteral catheter is passed through a rigid 9-F or 11.6-F ureteroscope and into the ureteral orifice. With a 180° turn of the instrument in front of the orifice, the catheter is gently advanced into the ureter while the endoscope is returned. Using this technique, no dilatation of the orifice is necessary.

Flexible endoscopes. For LISL, actively steerable, flexible endoscopes (8- and 9-F with a 3.6- or 2.8-F channel or 11.8-F with a 4.3-F channel) and passively steerable, flexible endoscopes (9-F with a 9.1-F channel and 7-F with a 2.4-F channel) are used. Using the 7-, 8- or 9-F endoscope, passage of the ureteral orifice is accomplished either directly, with a rigid cystoscope placed in front of the ureter, or along a 3-F ureteral catheter or a guidewire. Using the 11.8-F ureteroscope, prior dilation of the orifice with coaxial catheters is necessary. The results of LISL are shown in Table 3.

Influence of pulse-energy repetition rate and irrigation solutions on the efficacy of LISL

LISL is applicable in all fluids, with a pressure amplitude in saline of about 300–900 bar, but shock-wave pressure can be augmented in metallic solutions (Fe-KKK-dextran,

Table 3. Results of treatment by LISL

161 calculi	Complete fragmentation	
18 calculi	Reduction of stone size and removal together with the endoscope to pervent migration of the stone in the ureter	
10 calculi	Fragmentation too slow	
Stone analysis:		
Calcium oxalate monohydrate		($n=121$)
Calcium oxalate dehydrate		($n=$ 36)
Apatite		($n=$ 9)
Uric acid		($n=$ 12)
Struvite		($n=$ 5)
Time for disintegration:		
Laser irradiation time	20 s to 25 min	
Total operation time	patients 1–11	36.7 min
	patients 11–180	22,6 min
Postoperative stent following LISL		($n=$ 22)

LISL = Laser-induced shock-wave lithotripsy

Table 4. Complications of treatment with the pulsed-dye laser

Perforation of the ureter with the endoscope[a]		($n=$ 2)
Bleeding (forced diuresis sufficient)		($n=12$)
Laser irradiation of the urothelium (no side effects)		($n=10$)
Stone-flushing to the upper urinary tract:		
before	LISL	($n=15$)
with subsequent	URS	($n=$ 3)
	PCN	($n=$ 4)
	ESWL	($n=$ 8)

[a] Perforations of the ureter were treated by double-J stenting; one case resulted in a ureteral stricture

1 mg/l; MgCl, 50 mmol/l. Metallic solutions probably act by a self-focussing effect of the laser beam. Higher pulse-repetition rates and high laser energy in combination with Fe-III-dextran results in smaller stone fragments. With a 320-μm fiber, LISL solutions are unnecessary, as the focal area of the laser beam is smaller and the results of disintegration are equal to those obtained with the 600 μm fiber.

Advantages of LISL over ultrasound ureteral lithotripsy include the creation of smaller stone particles, one-time insertion of the instrument into the ureter without frequent removal during the operation to remove stone particless or the stone powder, and the active drainage of stone fragments (1 mm; average, 0.4–0.5 mm) even through small, flexible endoscopes during the operation. No harm is done to the urothelium with the Q-switched Nd:YAG laser, even in cases of inadvertent irradiation. The pulse-dye laser, in contrast, can cause considerable hemorrhage or even ureteral perforations due to the high energy necessary for disintegration of harder calcium oxalate monohydrate calculi (Table 4). Moreover, Nd:YAG laser irradiation in the infrared light spectrum does not irritate the vision during endoscopy, whereas the bright light in the visible spectrum of the dye laser impairs laser lithotripsy (Figs. 7–10).

Fig. 7. Calcium oxalate monohydrate stone in an 83-year-old woman. The stone, present for 10 years, resulted in colic and flank pain

Fig. 8. Intravenous pyelogram (IVP) with delayed excretion of contrast material after 50 min

Fig. 9. LISL with 35-min laser time (total operation period, 70 min), 8-ns pulse duration and 60-mJ pulse energy

Fig. 10. IVP at 6 weeks after LISL

Discussion

Q-switched laser pulses from an Nd:YAG laser disintegrate urinary calculi by transformation of laser energy into mechanical energy as shock waves. Due to the extremely short pulse duration (8 ns) and the short rise time of the shock wave, the fragmentation threshold of urinary stones is about 30–35 mJ. Laser energy with nanosecond pulses can be coupled into currently available 200-, 400- or 600-μm quartz fibers with a maximal single-pulse energy of up to 70 mJ per pulse. Laser pulses with a repetition rate of 50 Hz can be safely transmitted from 35 to 60 mJ without damaging the fiber. Extensive animal studies using this type of laser did not reveal any serious tissue damage at an energy level of up to 4 times that currently used in patient treatment (160 mJ). Immediate effects of the focussed laser beam on the urothelium consisted of a crater-like hole with a maximal depth of 40 μm. No late effects, especially thermal side effects or necrosis, have been noted. Unfocused irradiation does not cause any harm to the tissue. Clinical application of the laser did not shown any laser-induced side effects.

Ureteroscopy seems to be the most critical part of ureterolitholapaxy. No dilation of the ureteral orifice was necessary since the instrument could be advanced to the stone by passing the orifice with a slight torsion of the entire ureteroscope.

Laser stone fragmentation proved to be effective in all but four stones. More fragile calculi, such as struvite and calcium oxalate dihydrate, could easily be fragmented within a short interval, whereas less fragile calculi, such as amorphous calcium oxalate monohydrate, needed a longer disintegration and operation period.

Optimal conditions for stone disintegration using the Nd:YAG laser at 1,064-nm wavelength were recorded with 8-ns pulse duration, 35–50 mJ single-pulse energy at the fiber tip and 40–50 Hz repetition rate. Stone powder and particles created by the high-intensity pulsed laser were so tiny that they were washed out of the ureter during the operation. In a few cases larger stone fragments separated, were lying between the instrument and the residual stone, and had to be disintegrated first for protection of the fiber tip. Optimal stone disintegration was performed within the LIB, seen in the instrument as a light cone, and could be heard as a series of slight clicking sounds.

The fiber must be approximately 2–5 mm away from the stone for optimal fragmentation. With some clinical experience and skill, this distance can be maintained during ureteroscopy under visual control. Brief contact of the fiber with the stone or the spray of fragments does not damage the fiber, whereas constant laser application with stone contact results in cracks in the fiber surface. The highly flexible quartz fiber can easily be changed during the operation by removing the plug-formed end from the coupling device.

Recently, photofragmentation with a flash-lamp pumped – dye laser has been introduced. This procedure works by absorption of laser energy directly into the calculus at a 1-μs pulse duration, up to 60-mJ single-pulse energy and 10-Hz repetition rate, whereas nanosecond laser pulses transmitted through quartz fibers (400 or 600 μm) act through cavitation and through shock waves created by the formation of a laser-induced breakdown in the liquid surrounding the calculus. With the Nd:YAG laser, the liquid acts by transforming the laser energy into mechanical energy, whereas the calculus itself is used as an energy converter with the dye laser.

To date, fragmentation has been performed only with rigid ureteroscopes. The flexible quartz fiber, however, enables the miniaturization of these instruments and their use with small, flexible probes. The laser action enables controlled fragmentation of the calculus such that no additional measures, such as removal of stone fragments with forceps or basket, are necessary. Larger stones created at the disintegration site with electrohydraulic or ultrasound probes must be collected from the ureter, resulting in prolonged manipulation or stress to the ureteral orifice. Laser stone disintegration proved to be a one-step procedure in the ureter that did not require removal of the instrument from the orifice.

Effective and secure stone disintegration with small, flexible fibers has proved to be a prerequisite for application with flexible endoscopes, currently used only as diagnostic instruments. Flexible ureterorenoscopy in combination with laser stone disintegration implies the possibility of an atraumatic, one-step procedure for fragmentation of ureteral and kidney calculi without the use of general anesthesia.

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