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How much energy do we need to ablate 1 mm³ of stone during Ho:YAG laser lithotripsy? An in vitro study

Frédéric Panthier^{1,2,3} · Eugenio Ventimiglia^{1,2,4} · Laurent Berthe³ · Catherine Chaussain⁵ · Michel Daudon^{1,6} · Steeve Doizi^{1,2} · Olivier Traxer^{1,2}

Abstract

Introduction Holmium:yttrium–aluminium–garnet (Ho:YAG) is currently the gold standard for lithotripsy for the treatment of all known urinary stone types. Stone composition and volume are major determinants of the lithotripsy. This in vitro study evaluated the required energy to ablate 1 mm³ of various stone types with different laser settings using Ho:YAG.

Methods 272 µm core-diameter laser fibers (Boston Scientific[®]) were connected to a 30 Watt MH1 Ho:YAG generator (Rocamed[®]). An experimental setup consisting of immersed human stones of calcium oxalate monohydrate (COM), uric acid (UA) or cystine (Cys) was used with a single pulse lasing emission (0.6/0.8/1 J), in contact mode. Stones were dried out before three-dimensional scanning to measure ablation volume per pulse (AVP) and required energy to treat 1 mm³ (RE).

Results All settings considered, ablation volumes per pulse (AVP) for COM were significantly lower than those for UA and Cys ($p=0.002$ and $p=0.03$, respectively), whereas AVP for Cys was significantly lower than those for UA ($p=0.03$). The mean REs at 0.6 J pulse energy (PE) for COM, Cys and UA were 34, 8.5 and 3.2 J, respectively. The mean REs at 1 J PE for COM, Cys and UA were 14.7, 6.4 and 2 J, respectively. At 0.6 J PE, RE for COM was more than tenfold and fivefold higher than those for UA and Cys, respectively.

Conclusion This in vitro study shows for the first time a volumetric evaluation of Ho:YAG efficiency by the ablation volume per pulse on human stone samples, according to various pulse energies. The REs for COM, UA and Cys should be considered in clinical practice.

Keywords Holmium YAG · Laser · Lithotripsy · Volume

Introduction

Over the past three decades, holmium:yttrium–aluminium–garnet (Ho:YAG) laser has become the main player among lasers currently used for lithotripsy, due to its effectiveness, versatility, and safety profile [1]. Although Ho:YAG represents an effective alternative for the treatment of all known urinary stone types [2], stone composition itself is still one of the main determinants of lithotripsy

efficacy itself [3]. Despite this, stone composition and stone volume are not taken in consideration in pre-operative planning tools [4–8]. Moreover, international guidelines as well do not include stone composition and volume in the chart of surgical options [4, 5]. Consequently, surgical planning in stone surgery is limited. The main reason for this lack of appraisal is that the actual energy needed to ablate a specific unit of volume of stone, together with its determinants, remains unknown. Moreover, no previous reliable and reproducible methodology has ever been developed to estimate the lithotripsy duration among laser settings and stone volume, despite that available technology would allow to do it [9]. Against this background, we aimed to estimate in a laboratory setting the minimum amount of energy required to ablate 1 mm³ of stone, according to different stone compositions and energy parameters, with the ultimate purpose that these estimates will be useful to improve pre-operative planning strategies and predictive tools.

Frédéric Panthier and Eugenio Ventimiglia Equal contribution

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Methods

Ho:YAG laser generator

A low-power (30 Watts), short-pulse MH1 Ho:YAG generator (Rocamed®) with a 272 μm core-diameter laser fiber (Sureflex, Boston Scientific®) was used in this study. Three different laser pulse energies (PE) were chosen: 0.6, 0.8 and 1 J. The laser generator was modified to deliver a single pulse emission. Pulse duration was verified before our study using an amplified photodetector (InGaAs PDA10D2, Thorlabs®, Newton, USA) with a peak spectral response from 900 to 2600 nm connected to an oscilloscope (InfiniiVision DSO5014A, Agilent Technologies®, Santa Clara, USA).

Kidney stones

We used human stone samples from our institutional stone bank and classified according to the Daudon classification [10]. We selected pure stones composed of calcium oxalate monohydrate (COM), uric acid (UA), and cystine (Cys). For each type, three samples were chosen. We focused on COM, UA, and Cys, since they represent different stone populations and a large panel of patients. Before laser emission, the samples were immersed into a saline solution for 30 min. After experiments, the stones were dried at ambient temperature for 3 days before three-dimensional acquisition.

Experimental setup

Immersed stones were immobilized into a bench model and filled with saline solution (NaCl 0.9%) at ambient temperature. No irrigation was required for our study. The laser fiber was placed vertically in contact with the sample, controlled by a micrometric screw. A specific fiber support was manufactured to assure perfect immobility during laser emission (Fig. 1). The laser machine was modified to deliver a single pulse emission. After each emitted pulse, we cleaved the laser fiber with ceramic scissors. Figure 1 shows the experimental conditions for in vitro tests. All laser pulses were repeated three times per stone sample. After lithotripsy, stones were dried as previously described and scanned (micro-CT Quantum FX, Perkin Elmer®) at the Life Imaging Platform (Paris Descartes University, Montrouge, France) with a visual range of 20 mm and a 10 μm resolution. Ablation volumes per pulse (mm^3) were assessed by 3D segmentation using 3D Slicer (NIH®) (Fig. 2) [11]. The required energy (RE) to ablate 1 mm^3 was then calculated from PE and ablation volumes.

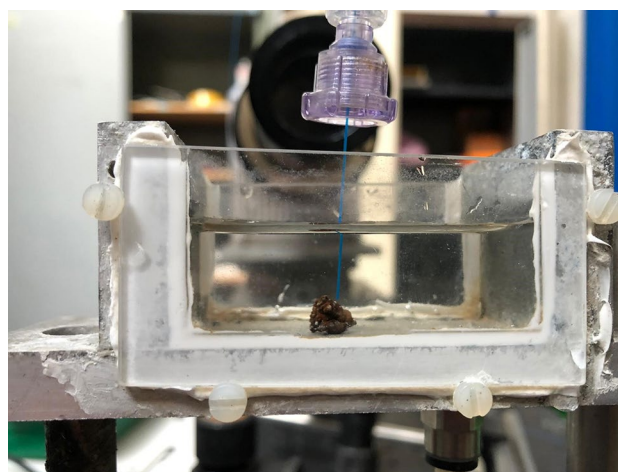


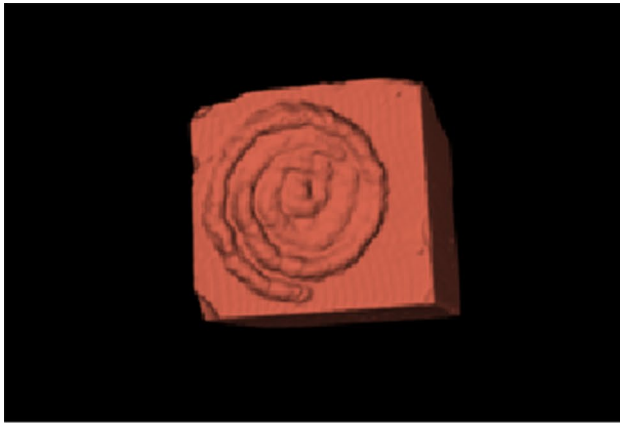
Fig. 1 Experimental setup: filled cuvette with a vertically immobilized 272 μm core-diameter laser fiber in contact with the stone for single-pulse laser emission

Measurement method

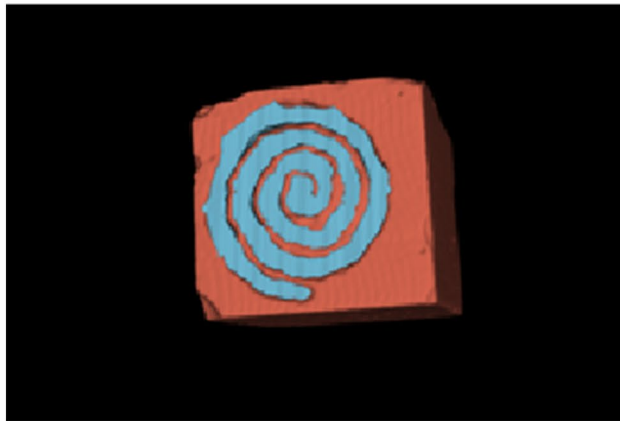
Figure 3 presents the stone samples and the three-dimensional reconstruction by segmentation for each type of stone (COM, UA, and Cys). We separately quantified each ablation volume per laser pulse, using 3D Slicer [11], a free open-source software designed for segmentation (MRI, CT scan). Figure 2 presents the sequence of logical operations used for volume measurement. Using the segment editor of 3D Slicer, we used the program feature "threshold effect" to create two segments labelled "air" and "stone": it uses an adjustable density scale, based on the Hounsfield units, to define a segment (volume) that will fit with the sample ("stone" segment). The "air" segment is then created, with an opposite threshold density scale, to obtain a segment that fills the three craters. Finally, the "logical operator" tool subtracted air and stone to get the three ablation craters made by the single pulse laser emissions. Then, we used the "split into segment" module to separate the different volumes into three independent segments. At the end of the measurement, we got each volume by "segment quantification" module. Given the ablation volume per pulse (AVP), we calculated the required energy to treat 1 mm^3 of stone (division of PE by AVP).

Time of laser lithotripsy estimation

Given the REs, we evaluated the theoretical lasing time for various maximum diameters and volumes, using the sphere formula ($4/3\pi R^3$). The estimated volume represents a sphere included in a cube ($R^3/2$). We provide two



(a) Segmentation of the stone phantom



(b) Segmentation of the air in the spiral crater



(c) Compilation of logical operations to get only spiral crater volume

Fig. 2 Method of segmentation using 3D Slicer to assess ablation volumes based on DICOMs' non-enhanced CT scan. First, segmentation of the stone (a), then segmentation of the air of the spiral crater (b) and compilation of both to get ablation volume (c)

durations: T and $T + 30\%$. The second one intends to estimate the duration of lithotripsy, including the inaccuracy rate due to the dissipation of energy, the “start and stop” effect (pedal activation of the laser generator) and the movements of the patient due to ventilation. We provide 0.6, 0.8 and 1 J PE with 15 Hz of pulse rate to estimate the lasing time to fit with “dusting” and “popcorning” laser settings.

Statistical analysis

For the ablation volumes and the RE, a two-tailed Student's t test was used to show statistical significance between laser settings and stone types. P values of less than 0.05 were regarded as statistically significant.

Results

Ablation volumes

All settings considered, ablation volumes per pulse (AVP) for COM were significantly lower than those for UA and Cys ($p=0.002$ and $p=0.03$, respectively). AVP for Cys was significantly lower than those for UA ($p=0.03$). Those results remained consistent after stratifying according to the energy delivered (Table 1).

Considering the specific pulse energies, 1 J and 0.8 J resulted, respectively, in fourfold and twofold higher AVPs for COM than 0.6 J. AVPs with 1 J and 0.8 J were 2-fold and 1.5-fold higher for Cys, and 2.5-fold and 2-fold higher for UA than 0.6 J, respectively. At 0.6 J pulse energy, AVP for COM was more than tenfold and fivefold lower than those for UA and Cys, respectively. This difference decreased non-proportionally with the elevation of pulse energy (Table 1).

Energy needed to ablate 1 mm³ of stone (RE) (Fig. 4, Table 2)

All settings considered, mean (\pm SD) REs for COM (24 ± 9 J) were significantly higher than those for Cys (7.6 ± 3 J) and UA (2.5 ± 0.7 all $p < 0.001$, Table 1).

Considering the specific pulse energies, 1 J pulse energy resulted in a twofold lower RE compared to 0.6 J and a 50% lower RE compared to 0.8 J for COM. For Cys, 1 J pulse energy resulted in a 25% lower RE compared to 0.6 J and a 20% lower RE compared to 0.8 J. For UA, 1 J pulse energy resulted in a 50% lower for UA compared to 0.6 J and a 15% lower RE compared to 0.8 J (Fig. 2). At 0.6 J pulse energy, RE for COM was more than tenfold and fourfold higher than those for UA and Cys, respectively.

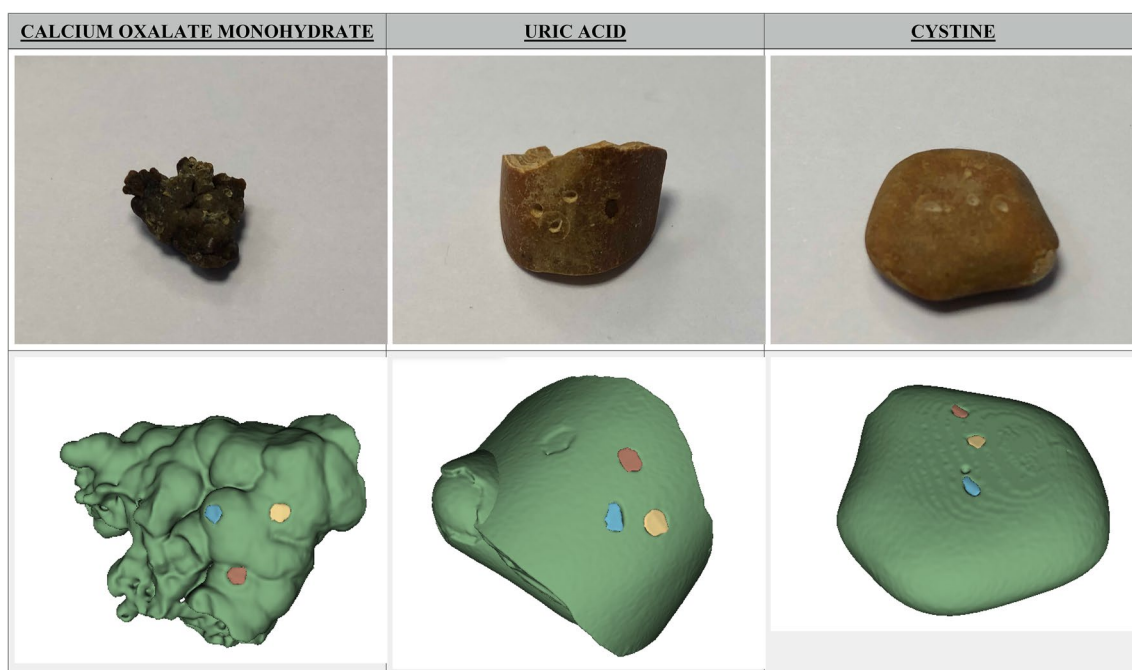


Fig. 3 Stone samples (upper part) after laser emission and 3D Slicer reconstruction (lower part) by segmentation and a separate quantification of each pulse ablation volume

Table 1 Ablation volume per pulse (μm^3) beyond stone type and pulse energy in contact mode

Stone type	Volumes (μm^3) (mean \pm SD)			
	Energy (joules)			All energies combined
	0.6	0.8	1	
Calcium oxalate monohydrate	17.7 \pm 2	35.6 \pm 8 ($p=0.01$)	71.1 \pm 17 ($p=0.01$)	35.9 \pm 20
Cystine	85.3 \pm 8	136.9 \pm 71 ($p=0.6$)	168.3 \pm 48 ($p=0.04$)	101.1 \pm 47
Uric acid	198.1 \pm 44	360.1 \pm 123 ($p=0.012$)	507.4 \pm 120 ($p=0.07$)	126.2 \pm 30
<i>p</i> value				
COM vs cystine	0.01	0.004	0.1	0.03
COM vs UA	0.08	0.016	0.025	0.002
Cystine vs UA	0.05	0.07	0.07	0.03

Relying on RE values, we were able to obtain hypothetical treatment duration times for stones of different compositions and sizes, as reported in Supplementary Fig. 5 and Table 3.

Discussion

We estimated in this laboratory study the ablation volumes for each single laser pulse according to both pulse energy and stone composition. Ablation volumes increased, although not proportionally, with the increase of pulse energy, and were higher in COM stones and lower in UA ones, with Cys stones in-between. As a consequence, we were able to

calculate the volume needed to ablate 1 mm^3 of stone in ideal experimental conditions according to the aforementioned parameters.

Three-dimensional evaluation of stone burden and ablation volume

The improvements in the 3D evaluation of stone volume and the ongoing evolution from maximum diameter to 3D stone burden have not been translated yet into current clinical practice [12-14]. To the best of our knowledge, laser ablating efficacy was never precisely estimated in terms of stone volume, and no clear and reproducible methodology is available at this regard [15-17]. To overcome this

Delivered Energy to treat 1mm³ of stone

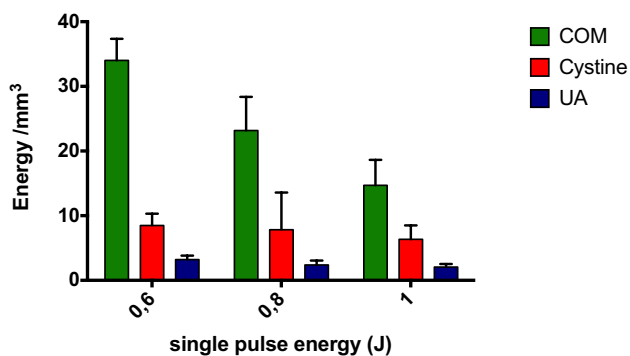


Fig. 4 Required energy to treat 1 mm³ beyond stone type and pulse energy in contact mode

Table 2 Required total energy for 1 mm³ lithotripsy beyond stone type and pulse energy

Stone type	Required energy for 1 mm ³ lithotripsy (joules)			
	Energy (J)			
	0.6	0.8	1	All combined
Calcium oxalate monohydrate	34±3.3	23,2±5.2	14.7±3.9	24±9
cystine	8.5±1.8	7.8±5.8	6.4±2.2	7.6±3
Uric acid	3.2±0.6	2.4±0.7	2±0.5	2.5±0.7
p-value				
COM vs cystine	24±9 vs 7,6±3			<0,0001
COM vs UA	24±9 vs 2,5±0,7			<0,0001
UA vs cystine	2,5±0,7 vs 7,6±3			<0,0001

knowledge gap, we developed an experimental model based on software-based 3D volume segmentation and single pulse delivery of the laser energy. The main challenge of this study was represented by the accurate assessment of small volumes in irregular human stones. In this regard, 3D volume segmentation served as a reliable solution for both these purposes (Figs. 2, 3). This method of 3D volume segmentation uses density (threshold) segmentation because we can easily differentiate kidney stones (+ 500 HU) from urine (clinical situation) or air (laboratory experiments) on computerized tomography (CT scan). CT scan is well known in clinical practice for its accuracy, especially for urinary stone pre-operative stone evaluation, including low-dose CT scan. Consequently, we tried retroactively from clinical practice to use a CT scan-based method to evaluate the ablation volumes. Moreover, our method is also supported by the fact that stone HU density on non-contrast CT scan is recognized as an effective

method to predict stone type, except for differentiating COM and calcium oxalate dihydrate (COD) [18].

Required energy to treat 1 mm³ of stone

In stone surgery, RE has been gaining attention, based on the same design than in benign prostatic obstruction laser procedures: Holmium and Greenlight Laser Enucleation of the Prostate (HoLEP and GreenLEP) has adopted the delivered energy as an effectiveness criteria, even more during the learning curve [19, 20]. Consequently, the evaluation of an endoscopic stone procedure and surgeons may rely on the delivered energy for a stone volume. In this regard, our results are in line with the previous report by Mekayten et al. [21], which reported that in average 13 J is needed to ablate 1 mm³ of a stone of ~ 1000 HU.

We also showed that COM stones required more RE than Cys and UA stones. Previous studies compared the mechanical properties of human and artificial kidney stones (begostone). Because of the density (kg/m³), it was harder to create a fissure in COM stones than is UA stones, as well as hard versus soft BegoStones [22]. Drawing a parallel, hard stones may be tougher to break than soft ones. That could explain our findings on the higher RE for COM than for Cys and UA. More recently, Molina et al. found that only calcium phosphate stones needed less energy than COM and UA [23]. In this study (100 patients), only seven cases presented with UA stones and one with cystine stone. Most of the cases were calcium oxalate stones (64%), revealing monohydrate ones needed more laser energy than dihydrate stones. This confirms that the less dense a stone, the less is the laser energy required. Teichman et al. supported the same results and proposed that COM stones decompose at a higher temperature than Cys and UA stones (204 versus 100 °C), to explain the higher pulse energy required to fragment COM stones [24]. They also confirmed a significant correlation between the cumulative laser energy and stone location (kidney), volume and calcium component. Finally, power was also associated with RE in their study, and trading high pulse energy will need less total delivered energy for treatment (dust or fragment). This represents a compromise between the size of produced fragments and the lasing time, following the idea that “dusting” (high-frequency–low pulse rate) produces smaller fragments than “fragmentation” settings (low-frequency–high pulse rate) [25]. This may be relevant also on the surgeon’s technique, but it is well admitted that “dusting” mode tries to create small fragments that could be spontaneously evacuated [26].

Surgical planning of endoscopic stone procedures

The estimation of the energy needed to ablate that we provide in this current study may turn out useful for

Table 3 Energy and lithotripsy duration besides stone type, maximum diameter or volume and laser settings

For COM	Diameter (mm)	Volume (mm ³)	0,6J-15Hz			0,8J-15Hz			1J-15Hz		
			Total J	Time	Time+30%	Total J	Time	Time+30%	Total J	Time	Time+30%
	1	0,5	17	1,1sec	1,5sec	11	0,7sec	1sec	7	0,5sec	0,6sec
	2	4	135	9sec	12sec	90	6sec	8sec	56	3,8sec	4,9sec
	3	13,5	460	30sec	40sec	300	20sec	26sec	190	13sec	17sec
	4	32	1080	1,2min	1,56min	720	48sec	1min	450	30sec	39sec
	5	62,5	2120	2,35min	3min	1400	1,6min	2min	879	59sec	1,3min
	6	108	3660	4min	5,3min	2400	2,7min	3,5min	1519	1,7min	2,2min
	7	171,5	5800	6,5min	8,4min	3850	4,3min	5,6min	2412	2,7min	3,5min
	8	256	8680	9,6min	12,5min	5750	6,4min	8,3min	3600	4min	5,2min
	9	364,5	12350	13,7min	17,8min	8200	9min	11,8min	5127	5,7min	7,4min
	10	500	16950	18,8min	24,5min	11230	12,5min	16,2min	7032	7,8min	10,2min

For Cys	Diameter (mm)	Volume (mm ³)	0,6J-15Hz			0,8J-15Hz			1J-15Hz		
			Total J	Time	Time+30%	Total J	Time	Time+30%	Total J	Time	Time+30%
	1	0,5	4	0,2sec	0,3sec	2,9	0,2sec	0,3sec	3	0,2sec	0,3sec
	2	4	28	1,9sec	2,4sec	23	1,6sec	2sec	24	1,6sec	2sec
	3	13,5	95	6,3sec	8,2sec	79	5,2sec	6,8sec	80	5,3sec	7sec
	4	32	225	15 sec	19sec	187	12sec	16sec	190	13sec	16sec
	5	62,5	440	29sec	38sec	365	24sec	32sec	371	25sec	32sec
	6	108	760	51 sec	66sec	631	42sec	55sec	642	43sec	56sec
	7	171,5	1206	1,3min	1,7min	1002	1,1min	1,4min	1019	1,1min	1,5min
	8	256	1801	2min	2,6min	1496	1,7min	2,2min	1521	1,7min	2,2min
	9	364,5	2564	2,8min	3,7min	2130	2,4min	3,1min	2166	2,4min	3,3min
	10	500	3517	3,9min	5,1min	2922	3,2min	4,2min	2971	3,3min	4,3min

For UA	Diameter (mm)	Volume (mm ³)	0,6J-15Hz			0,8J-15Hz			1J-15Hz		
			Total J	Time	Time+30%	Total J	Time	Time+30%	Total J	Time	Time+30%
	1	0,5	1,5	0,1sec	0,1sec	1,1	0,1sec	0,1sec	1	0,1sec	0,1sec
	2	4	12	0,8sec	1sec	9	0,6sec	0,8sec	8	0,5sec	0,7sec
	3	13,5	41	2,7sec	3,5sec	30	2sec	2,6sec	27	1,8sec	2,3sec
	4	32	97	6,5sec	8,4sec	71	4,7sec	6,2sec	63	4,2sec	5,5sec
	5	62,5	189	12sec	16sec	139	9,3sec	12sec	123	8,2sec	11sec
	6	108	327	22sec	28sec	240	16sec	21sec	213	14sec	18sec
	7	171,5	519	35sec	45sec	381	25sec	33sec	338	23sec	29sec
	8	256	775	52sec	1,1min	569	38sec	49sec	505	34sec	44sec
	9	364,5	1104	1,2min	1,6min	810	54sec	1,2min	718	48sec	1min
	10	500	1514	1,7min	2,2min	1111	1,2min	1,6min	985	1min	1,4min

pre-operative planning of laser lithotripsy procedures: by knowing the stone volume and of the stone composition or density, and hypothesizing a 20–30% dissipation of energy due to inefficiently delivered pulses (inaccuracy or “stop and start” effect) and patient movements, it is theoretically possible to estimate the duration of surgical procedures (Table 3). This percentage could be greater or lower regarding the surgeon’s experience or technique and the surgical conditions (localization of the stone, visualization, adverse events). Moreover, the lower the gap between the estimated and observed total energy during the procedure itself might serve as a proxy of lithotripsy efficiency, as well as the proficiency of the surgeon. Supplementary Fig. 5 shows an exponential

relation between the ablation time and the diameter of the stone. These results are supported by our volumetric evaluation: doubling the diameter of the cube means multiplying by eight the volume of the sphere included in the cube. That may justify again the importance of a volumetric assessment.

Limitations

Our study is not devoid of limitations. First, our study evaluated ablation volume using ideal experimental conditions, which are substantially different from the current clinical practice; each pulse was delivered cutting the laser fiber beforehand, whereas during intracorporeal lithotripsy the

laser fiber gradually deteriorates without the possibility of cutting it after each pulse. Moreover, we used contact mode for the delivery of laser energy: if on the one hand this provided the highest delivery of energy to the stone, on the other we might have overestimated the ablation volume as compared to clinical practice. In such conditions, the fiber tip is not always in contact with a clear locus at the surface of the stone for various reasons: surgical conditions, visualization, irrigation and retropulsion, surgeon's ability or mode of treatment. Hence, limiting contact mode may reduce fiber degradation or fracture and burnback effects [27–29]. It should be noted that our choice was driven by the necessity to guarantee the highest reproducibility in the experimental setting: it would have not been possible to observe the same distance between the laser fiber tip and the stone due the irregularity in both surface and dimensions of the real human stones that we used in our experiments. Conversely, the possibility of using human stones allowed us to have more realistic estimates.

For the specific purpose of this study, we used a low-power, short-pulse laser generator that may represent a limitation. First, numerous practitioners use low-power generators for endocorporeal lithotripsy. Then, even high-power frequency dusting techniques have been more effective than low-power frequencies in a laboratory study. However, we cannot state about the superiority of high-power over low-power devices. In clinical practice, microbleeding, visualization of the fiber tip degradation, and production of fragments > 1 mm are the limitations of high-power Ho:YAG generators, including Moses technology, which will be probably managed in the near future (suction devices, optimization of the vapor bubble shapes) [30–34]. The Moses technology has recently showed a greater ablation weight in soft artificial BegoStones (contact mode or 1 mm distance) than short- or long-pulse mode. Those results were not maintained against hard stones, at any distance, which is contradictory to Aldoukhi et al.'s study [35, 36]. Considering these controversial data, we recognize the Moses technology could be associated with greater ablation volume, especially in a distance mode. Concerning the long pulse duration (LP), Sroka et al. found similar ablation volumes compared to short pulse but a deeper crater with LP, regardless of the laser settings [37]. LP presents controversial data about the popcorning efficiency; so we cannot conclude on this specific aspect [31, 38]. On the contrary, LP has shown a lower retropulsion and fiber degradation than during short pulse [25, 39]. Regarding those findings, we recognize the interest of an LP Ho:YAG generator, but we cannot assure that an LP Ho:YAG device would have presented higher ablation volumes and, as a consequence, lower RE. Furthermore, we did not evaluate other laser fibers than 272 μm core-diameter laser fiber (200 μm or 365 μm), which could provide additional data for surgical planning.

Conclusion

This *in vitro* study shows for the first time a volumetric evaluation of Ho:YAG efficiency by the ablation volume per pulse on human stone samples. Calcium oxalate monohydrate needs tenfold and fivefold higher laser energy to treat the same volume than uric acid and cystine, respectively. High pulse energy will need less total delivered energy to dust but will produce bigger fragments, traducing the compromise which has to be done in clinical practice. The required energy to treat may represent a valuable information in surgical planning and post-operative accuracy evaluation.

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Author contributions FP and EV: equal contribution: protocol development, data collection and management, data analysis, manuscript writing and editing. LB: protocol development, data collection and management, manuscript editing. CC: protocol development, data collection. MD: protocol development, data collection. SD: protocol development, manuscript writing and editing. OT: protocol development, data analysis, manuscript writing and editing.

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Compliance with ethical standards

Conflicts of interest The authors declare that they have no conflict of interest. However, Olivier Traxer has declared as being a consultant for Boston Scientific Corporation, Coloplast, Wolf, B-Braun, IPG photonics, Lumenis, Olympus and Rocamed. Steeve Doizi has declared as being a consultant for Boston Scientific Corporation and Coloplast.

Research involving human participants or animals This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent This article does not contain any studies with human participants or animals performed by any of the authors. Human stone samples were used in this study, with the informed consent of each patient.

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