



# Thulium fiber laser: ready to dust all urinary stone composition types?

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## Abstract

**Purpose** To evaluate whether stone dust can be obtained from all prevailing stone composition types using the thulium fiber laser (TFL) for lithotripsy. Where applicable, stone dust was further characterized by morpho-constitutional analysis.

**Methods** Human urinary stones were submitted to in vitro lithotripsy using a FiberLase U2 TFL generator with 150 µm silica core fibers (IPG Photonics<sup>®</sup>, IPG Medical<sup>™</sup>, Marlborough, MA, USA). Laser settings were 0.05 J, 320 Hz and 200 µs. A total of 2400 J were delivered to each stone composition type. All evaluated stones had a > 90% degree of purity (calcium oxalate monohydrate, calcium oxalate dihydrate, uric acid, carbapatite, struvite, brushite and cystine). Spontaneously floating stone particles were considered as stone dust and collected for analysis by scanning electron microscopy and Fourier transform infrared spectroscopy.

**Results** Stone dust could be retrieved from all evaluated urinary stones after TFL lithotripsy. Most stone dust samples revealed changes in crystalline organization, except for calcium oxalate monohydrate and carbapatite, which conserved their initial characteristics. Mean maximal width of stone dust particles did not exceed 254 µm.

**Conclusions** The TFL is capable to produce stone dust from all prevailing stone types. Morpho-constitutional changes found in stone dust suggest a photothermal interaction of laser energy with the stone matrix during TFL lithotripsy.

**Keywords** Thulium fiber laser · Lithotripsy · Urolithiasis · Stone dust · Scanning electron microscopy · Fourier transform infrared spectroscopy

## Introduction

In the past decades, rising intervention rates for urinary stones have been reported together with a worldwide rise in prevalence of this disease [1–3]. Application of Holmium:

YAG lasers for lithotripsy in conjunction with flexible ureteroscopy for stone clearance has become a mainstay of treatment in industrialized countries [4]. In recent years, lithotripsy techniques evolved together with refinements to Holmium: YAG laser generators, resulting in a widespread integration of stone dusting techniques for ureteroscopy [5–7]. Stone dusting presents the advantage to form small stone dust particles capable of spontaneous evacuation, obviating cumbersome and time-consuming active extraction of larger stone fragments [8]. A new laser is currently being explored for lithotripsy and seems to be particularly advantageous for the generation of fine stone dust: the Thulium fiber laser (TFL) [9–11].

To date, all observations on TFL lithotripsy found in literature were made on calcium oxalate monohydrate (COM) and uric acid (UA) stones. No study yet evaluated whether the TFL is applicable to other urinary stone types, despite the existence of obvious evidence from preliminary clinical applications. Therefore, we evaluated whether stone dust can be obtained from most common stone composition types using the TFL for lithotripsy in this study. As a secondary

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objective, we aimed to characterize stone dust by scanning electron microscopy (SEM) and Fourier transform infrared spectroscopy (FTIR) analysis.

## Material and methods

Human urinary stones of the following stone composition types were retrieved from a large stone biobank from our institution: COM, calcium oxalate dihydrate (COD), UA, carapatite (CA), struvite (STR), brushite (BR) and cystine (CYS). Stones with a volume of approximately 300 mm<sup>3</sup> and a >90% degree of purity were selected.

Each stone was separately submitted to lithotripsy using a FiberLase U2 TFL generator with 150 µm silica core fibers (IPG Photonics<sup>®</sup>, IPG Medical<sup>™</sup>, Marlborough, MA, USA). Laser settings were 0.05 J (pulse energy), 320 Hz (pulse frequency) and 200 µs (pulse duration). Laser lithotripsy was performed under direct visual control in glass cuvettes filled with saline using a LithoVue flexible ureteroscope (Boston Scientific<sup>®</sup>, Maple Grove, MN, USA) with painting movements of the laser fiber tip over stone samples. After delivery of 2400 J, stone dust was collected as previously described [12]. Briefly, collection of stone dust involved spontaneously floating stone dust particles to evacuate from a 5 mm hole located 2 cm above the bottom of a plastic container upon irrigation. All experiments were performed at room temperature (21 °C) with stones immersed into saline during 24 h before lithotripsy. Only collected stone dust particles were considered for analysis. Remaining stone fragments within the plastic container were discarded.

Morphological and constitutional analysis were performed as previously described [12]. Briefly, for morphological analysis, each sample was separately analyzed with a Zeiss Gemini Supra 55VP SEM (Carl Zeiss<sup>®</sup> AG, Oberkochen, Germany). For constitutional analysis, FTIR was performed with a Bruker Vector 22 spectrometer (Bruker Optics<sup>®</sup>, Marne-la-Vallée, France). The FTIR spectra of the initial stones were compared to the spectra of stone dust after lithotripsy.

Three separate micrographs of each stone dust sample were obtained using SEM with a magnification of 100 ×. The maximal width of the three largest stone dust particles visible on each micrograph was measured using the image processing software ImageJ (Release 1.52, U.S. National Institutes of Health, Bethesda, MD, USA), resulting in nine measures from which the mean maximal width of stone dust particles was determined for each stone type separately.

The study was in accordance with ethical standards of the Helsinki declaration. Statistical analysis and graph plotting were performed with IBM SPSS Statistics 24.0 (IBM Corp<sup>®</sup>, Armond, NY, USA).

## Results

The TFL was capable of disintegration of all evaluated urinary stone types. Stone dust could be retrieved from each urinary stone type. Stone dust samples were of sufficient quantity for an adequate morpho-constitutional analysis.

Table 1 summarizes observations from morpho-constitutional analysis of stone dust samples. For COM and CA, all characteristics from initial stones were preserved. For COD, BR and CYS, traces of the initial stone composition type could be found on FTIR analysis, but all these samples also showed conversion other composition types. Particularly, for COD, the typical bipyramidal organization was hardly ever found in stone dust particles on SEM analysis (Fig. 1a), while FTIR analysis revealed a conversion from COD to COM. The BR stone dust sample showed a partially preserved baguette-like organization on SEM analysis (Fig. 1b), while FTIR analysis revealed a conversion to monetite. The hexagonal organization of CYS was hardly ever found in stone dust particles (Fig. 1c), with profound changes of the typical bands on FTIR analysis. The UA and STR stone dust samples both revealed profound morpho-constitutional changes. Stone dust originating from UA lithotripsy showed a conversion to sodium hydrogen urate monohydrate on FTIR analysis, with a corresponding needle-like organization on SEM analysis (Fig. 2a). Stone dust originating from STR lithotripsy was composed of a pile of randomly configured needles partially attached to each other, corresponding to a conversion to newberyite on FTIR analysis (Fig. 2b).

On SEM analysis, the mean maximal width of stone dust particles was 254 µm (SD 66 µm, range 179–380 µm), 198 µm (SD 23 µm, range 159–234 µm), 116 µm (SD 21 µm, range 84–148 µm), 155 µm (SD 43 µm, range 90–208 µm), 154 µm (SD 15 µm, range 128–174 µm), 213 µm (SD 41 µm, range 141–268 µm) and 244 µm (SD 19 µm, range 222–277 µm) after TFL lithotripsy of COM, COD, UA, CA, STR, BR and CYS, respectively (Fig. 3).

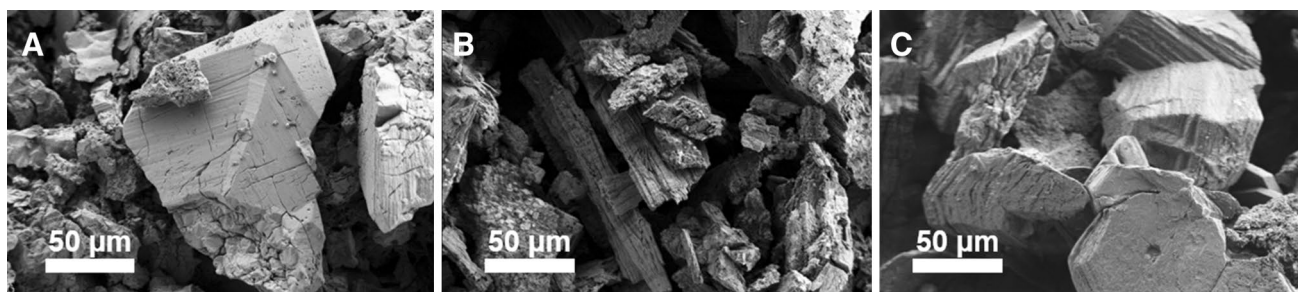
## Discussion

The TFL has recently been compared to Holmium: YAG for laser lithotripsy and presented several advantages that seemed particularly relevant for urinary stone disintegration: broader pulse energy and pulse frequency range, electronically modulable pulse shape and duration range, as well as smaller acceptable fiber core diameters [9]. Low pulse energy and relatively high pulse frequency as well as small core diameter fibers have been repeatedly reported to be best suited for fine disintegration of urinary stones—a

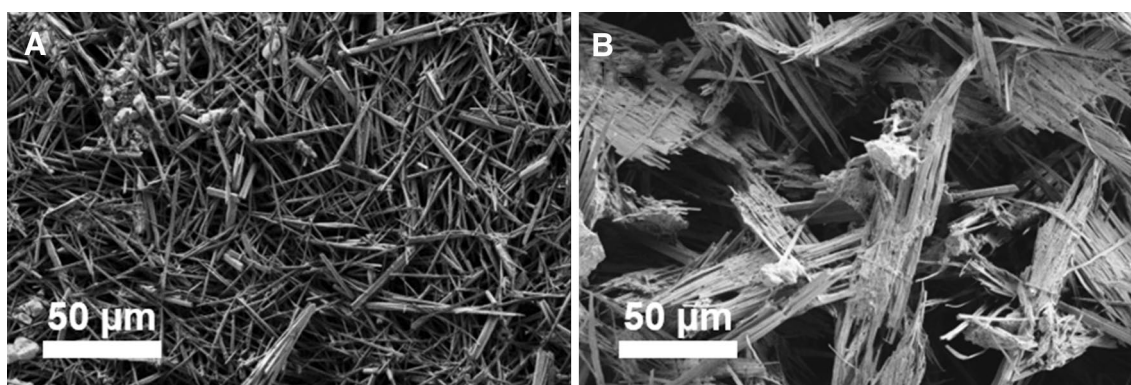
**Table 1** Observations from morpho-constitutional analysis of stone dust after TFL lithotripsy

Stone type	Preserved characteristics from initial stones?	Morphological analysis (SEM)	Constitutional analysis (FTIR)
COM	Yes	Preserved lamellar organization	Preserved major bands at 1617, 1315 and 781 $\text{cm}^{-1}$
COD	Partially	Almost complete loss of bipyramidal organization	Displacement of major bands from 1645 and 1324 $\text{cm}^{-1}$ to 1624 and 1318 $\text{cm}^{-1}$ , respectively, as well as appearance of a prominent band at 781 $\text{cm}^{-1}$ indicating a conversion from COD to COM
UA	No	Altered organization with appearance of a needle-like organization	Major bands at 3603, 1738, 1613, 1531 and 1003 $\text{cm}^{-1}$ , indicating a conversion from UA to sodium hydrogen urate monohydrate
CA	Yes	Preserved organization with spherical particles within more smooth blocks	Preserved major bands at 1035, 604 and 563 $\text{cm}^{-1}$
STR	No	Loss of the encased monodirectional needle organization resulting in a pile of randomly configured needles that are partially attached to each other	Loss of the ammonium bands at 1470 and 1435 $\text{cm}^{-1}$ . Very large and displaced major band at 1014 $\text{cm}^{-1}$ indicating a conversion from STR to newberyite
BR	Partially	Partially preserved longitudinal bague-like organization	Displacement of major bands from 1136 and 1063 $\text{cm}^{-1}$ to 1134 and 1066 $\text{cm}^{-1}$ , respectively, as well as the appearance of major bands at 1002 and 564 $\text{cm}^{-1}$ , as well as additional bands at 1406 and 892 $\text{cm}^{-1}$ , indicating a conversion from BR to monetite
CYS	Partially	Preserved layered organization, with an almost complete loss of the hexagonal organization	Loss of the 1656 $\text{cm}^{-1}$ band, unusually prominent band at 1622 $\text{cm}^{-1}$ and large, prominent and displaced band at 1337 $\text{cm}^{-1}$ , indicating a profound change in crystalline organization

SEM scanning electron microscopy, FTIR fourier transform infrared spectroscopy, COM calcium oxalate monohydrate, COD calcium oxalate dihydrate, UA uric acid, CA carapatite, STR struvite, BR brushite, CYS cystine.

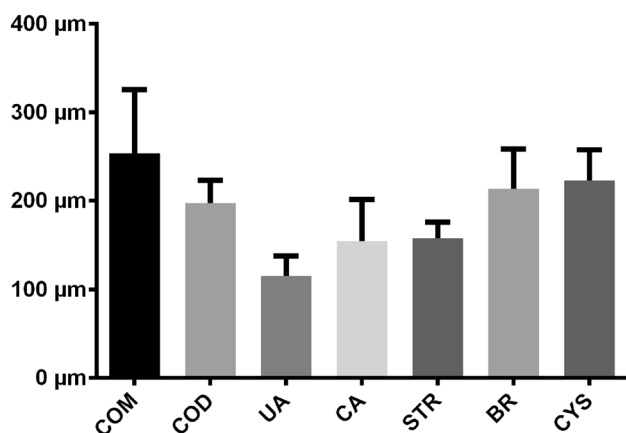


**Fig. 1** SEM analysis of stone dust after TFL lithotripsy (magnification 500 ×). **a** Partially preserved bipyramidal organization of COD. **b**: Partially preserved baguette-like organization of BR. **c** Partially preserved layered and hexagonal organization of CYS



**Fig. 2** SEM analysis of stone dust after TFL lithotripsy (magnification 500 ×). **a** Crystalline reorganization of UA with appearance of needles, corresponding to a conversion to sodium hydrogen urate

monohydrate on FTIR analysis. **b** Crystalline reorganization of STR with appearance of needles partially attaching to each other, corresponding to a conversion to newberyite on FTIR analysis



**Fig. 3** Mean maximal width of stone dust particles after TFL lithotripsy of all evaluated stone composition types. Bars are mean values and whiskers are standard deviations

technique also known as stone dusting [5, 6, 8, 13, 14]. Derived from these observations, the extended operating range of the TFL has been explored in the present study: pulse energy four times lower than lowest Holmium: YAG laser reach (0.05 J vs. 0.2 J, respectively); pulse frequency

four times higher than highest Holmium: YAG laser reach (320 Hz vs. 80 Hz) and a fiber core diameter at least 25% smaller than the safely acceptable lowest core diameter range for Holmium: YAG generators (150 µm vs 200 µm). Pulse duration was electronically controlled by the TFL generator depending on pulse energy and frequency.

Small stone particles originating from TFL lithotripsy were found to spontaneously evacuate upon irrigation in our experimental setup. These small particles were considered as stone dust. This methodology has been recently proven to deliver robust evidence for stone composition changes after Holmium: YAG laser lithotripsy of urinary stones [12], an observation that had also been reported in previous studies [15–17]. In line with these results, most urinary stone samples evaluated in this study showed morpho-constitutional changes with evidence of conversion to differing stone composition types and profound changes in crystalline organization. Only thermodynamically relatively stable stone composition types such as COM and CA conserved their morpho-constitutional characteristics. These observations suggest—a least to some extent—a photothermal interaction of laser energy with the stone matrix during TFL lithotripsy. To the best of our knowledge, this is the first



report on morpho-constitutional changes of most common urinary stone types after TFL lithotripsy. These findings may become of clinical relevance in cases where stone dust would be collected for the purpose of metabolic workup of urinary stone formers, since the etiopathogenic relationship between stone composition and underlying disease may be altered [18, 19].

Stone dust particles were found to be considerably smaller than 500  $\mu\text{m}$  upon SEM analysis. This observation appears of particular interest, since TFL was recently found superior to Holmium: YAG laser for generation of stone particles < 500  $\mu\text{m}$  at equivalent pulse energy and frequency settings [9, 10, 20]. Nevertheless, these in vitro studies should be interpreted with some caution, since a consensus on the exact definition of stone dust has not been met to date. A size limit of  $\leq 250 \mu\text{m}$  has been recently proposed to generally adhere with the definition of stone dust, based on several in vitro analyses [21]. That size range compares to the results of the present study, since mean maximal stone width did not exceed 254  $\mu\text{m}$ . Small deviations for individual stone composition types may be explained by the slightly differing experimental setups. Future studies on stone dust shall evaluate the clinical relevance, applicability and reproducibility of these findings. We, therefore, expect future studies to define best laser characteristics and settings for optimal generation of stone dust particles that would impact on clinical outcomes. How different operating modes of the TFL would impact on stone dusting was not within aims of this study and must be evaluated in separate future studies.

## Conclusions

This study proved the TFL to be capable of disintegration of all prevailing urinary stone composition types into particles considerably smaller than 500  $\mu\text{m}$ . These small particles were considered as stone dust and were observed to spontaneously evacuate upon irrigation in an experimental setup, thus validating the TFL as a promising new technology for stone dusting techniques. Morpho-constitutional changes found in stone dust suggest a photothermal interaction of laser energy with the stone matrix during TFL lithotripsy.

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## Compliance with ethical standards

**Conflict of interest** Dr. Etienne Xavier Keller is a consultant for Olympus, Debiopharm and Recordati. Dr. Vincent De Coninck is a consultant for Boston Scientific, BD Bard and Coloplast. Dr. Steeve Doizi is a consultant for Coloplast and Boston Scientific. Prof. Michel Daudon, PhD, is a consultant for Advicenne. Prof. Olivier Traxer is a consultant for Coloplast, Rocamed, Olympus, EMS, Boston Scientific and IPG Medical.

**Ethical approval** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

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