

# KIDNEY STONE CLASSIFICATION USING MULTIMODAL MULTIPHOTON MICROSCOPY

Matthew GLEESON\*<sup>†</sup>,<sup>1</sup> Joséphine MORIZET<sup>†</sup>,<sup>1</sup> Pierre MAHOU,<sup>1</sup> Michel DAUDON,<sup>2</sup> Dominique BAZIN,<sup>3</sup> Chiara STRINGARI,<sup>1</sup> Marie-Claire SCHANNE-KLEIN<sup>‡</sup>,<sup>1</sup> Emmanuel BEAUREPAIRE<sup>‡</sup>.<sup>1</sup>

<sup>1</sup> *Laboratory for Optics and Biosciences, Ecole Polytechnique, CNRS, Inserm, Institut Polytechnique de Paris, Palaiseau, France;*

<sup>2</sup> *Hôpital Tenon, AP HP, Département de Physiologie, Paris, France;*

<sup>3</sup> *Université Paris-Saclay, CNRS, Institut de Chimie Physique, Orsay, France;*

\*matthew.gleeson@polytechnique.edu

<sup>†</sup> contributed equally; <sup>‡</sup> contributed equally

Keywords: Nonlinear optics, polarization, multiphoton microscopy, kidney stones, calcium oxalate

Kidney stones (KS) affect up to 15% of the global population at least once in their lifetimes with a high chance of re-occurrence<sup>[1]</sup>. Optimizing treatment and recommending subsequent lifestyle changes requires knowledge of the KS physiochemical composition. However, current characterization methods often require extensive sample preparation, expert interpretation or are overly detailed in the context of a clinical setting. Here we present a multiphoton multimodal based classification scheme with small sample amounts, facile preparation, label-free, and easy interpretation. Combining the probabilities of generating two-photon excited fluorescence (2PEF) to indicate protein content, second harmonic generation (SHG) to infer crystalline structure and polarization resolved third harmonic generation (pTHG) to determine birefringence<sup>[2,3]</sup>, we show how common types of kidney stones are distinguishable. Intensity measurements with PMTs and broad wavelength filters of the 2PEF response gave mixed responses across samples suggesting the 2PEF profile should be spectrally characterized. SHG is an effective discriminator for all samples, while pTHG distinguished two common types of calcium oxalate KS. Additionally, we present a pTHG study with a model applicable to imaging the sub-micron structure of KS fragments.

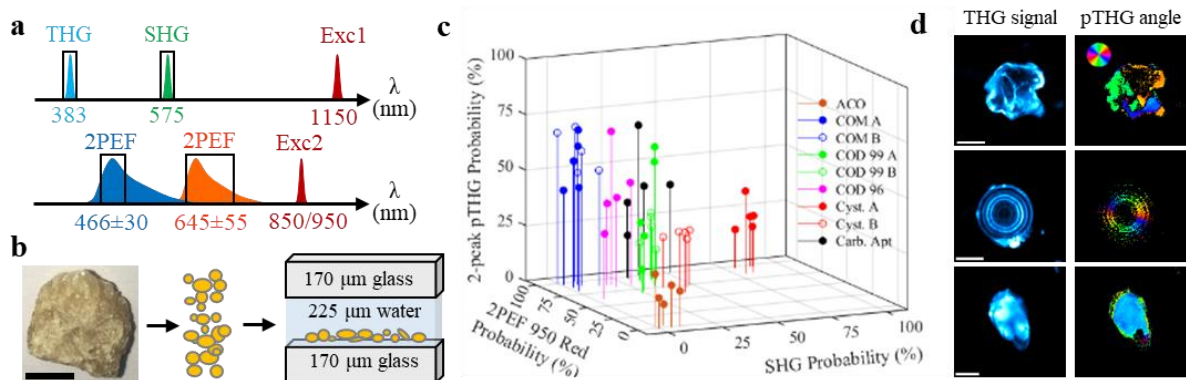


Fig. 1: **a** Signals measured **b** preparation of KS for imaging **c** parametric plot showing how different types of KS occupy different positions on the 3D plot **d** pTHG response of different KS types.

[1]. V. Romero, H. Akpınar, D.G. Assimos, *Reviews in Urology*, **12**(2-3), e86-e96 (2010)

[2]. J. Morizet *et al*, *Optica*, **6**(3), 385-388 (2019)

[3]. J. Morizet *et al*, *Optica*, **8**(7), 944-951 (2021)