Soft tissue ablation by picosecond synchronously-pumped $CdSiP_2$-based optical parametric oscillator tuned to 6.45 µm

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ABSTRACT

Optical parametric oscillators (OPOs) are attractive tools for research on tissue ablation upon infrared irradiation. Here, we report on the performance of several mid-infrared nonlinear crystals, namely type I and type II $AgGaS_2$ (AGS) and type I $CdSiP_2$ (CSP), used in synchronously-pumped OPOs tuned to a wavelength of 6.45 µm, coinciding with the amide II absorption band of proteins. CSP-based OPOs clearly exhibit better performance in comparison to AGS: First, the oscillation threshold with CSP is three (five) times lower than type II (type I) AGS. Second, the idler conversion efficiency is more favourable for CSP and allows reaching 27.5 mW of idler average power, while 13 and 6 mW are obtained with type II and type I AGS, respectively. Such performance makes CSP suitable for high power 6.45 µm surgical applications. Preliminary ablation experiments on liver tissues with our CSP-based OPO highlight the promising future of CSP in medical applications.

Keywords: tissue ablation, synchronously-pumped optical parametric oscillators, $CdSiP_2$, $AgGaS_2$

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1. INTRODUCTION

Investigations on tissue ablation are usually carried out using conventional infrared (IR) laser sources such as Ho:YAG (2.1 μm), Er:YAG (2.94 μm), and CO_2 (10.6 μm) [1-4]. However, significant thermal damage to the tissues surrounding the ablation sites is observed at these wavelengths, which results in an increased number of damaged cells and/or a reduced irradiation of the targeted materials. This problematic triggered a quest for alternative laser sources emitting at more suitable wavelengths. High absorption of the laser radiation is necessary for an optimal ablation of the targeted tissue. Although ablation is also possible at low IR absorption, it is then accompanied by very undesirable and severe thermal damage. Water and proteins account for most of the IR absorption in tissues. For wavelengths around 3 μm, water is the dominant IR absorber and absorption by proteins is negligible, since the IR spectrum of proteins is governed by vibrations involving peptide bonds (O=C-N-H). The most active of these vibrational modes are the C-O stretch at 6.1 μm referred to as Amide-I, the C-N deformation at 6.5 μm referred to as Amide-II, and the C-N stretch with N-H in plane deformation at 8.1 μm referred to as Amide-III. For the wavelengths included between 6.1 and 6.45 μm, where the ablation is based on the denaturation of structural protein due to resonant absorption of amide in addition to explosive vaporization of water due to the resonant absorption of water, the IR absorption of proteins thus far exceeds that of water [5,6]. Numerous previous investigations have highlighted efficient tissue ablation, with low collateral damage, using free electron lasers (FELs) tuned to ~6 μm as IR source [7-9]. However, FELs require dedicated facilities, considerable expertise for their operation, and high costs, which severely limit their usefulness for clinical applications. Novel IR laser sources covering the wavelengths of interest, like optical parametric oscillators (OPOs), are currently developed as alternative to FELs. OPOs are simpler, more practical, and also well suited to the picosecond pulsed ablation regime that is possibly the most effective according to recently proposed mechanisms [9]. Thus, we aim at developing a simple, robust, high power, and stable IR OPO tuned to ~6 μm. Very few non-linear crystals, i.e., $AgGaS_2$ (AGS), $CdSiP_2$ (CSP), and $ZnGeP_2$ (ZGP), allow tuning IR wavelength into the desired range. $ZnGeP_2$ is possibly less practical since it requires pumping by less common sources such as Ho^{3+} lasers emitting wavelengths longer than ~2 μm to avoid residual absorption [10,11]. In this paper, we discuss the performance of CSP-based, and type I and type II AGS-based OPOs with an idler wavelength of 6.45 μm which are pumped by a picosecond Nd:YAG laser. Our first experimental results on the ablation of soft tissues (liver) using a CSP-based OPO are also presented and compared with the literature.

2. EXPERIMENT

The Nd:YAG pump source is described in ref. 12. Briefly, it consists of a 25 Hz flash lamp-pumped Nd:YAG oscillator mode locked at 100 MHz, actively using an acousto-optic modulator (AOM) and passively using a non-linear mirror stabilized with a GaAs plate acting as a two-photon saturable absorber. It is followed by a second AOM, external to the oscillator cavity, filtering out the initial fraction of the pulse train that is non-stationary. Prior to pumping the OPO, the 1064 nm pulse train is amplified via a three-pass amplification stage. The OPO is then pumped by the amplified pulses synchronously and quasi-collinearly, with the pump beam ~2° off the optical axis of the OPO cavity. The synchronously-pumped OPO (SPOPO) cavity consists of two curved mirrors (R= –5 m) for the signal only, separated by 1.5 m and leading to a Gaussian mode with a diameter of 4 mm in the center of the cavity, where the non-linear crystal is placed. Wavelength tuning is achieved by rotating the non-linear crystal (AGS) or by changing its temperature (CSP). The three non-linear crystals used in this experiment were a type II AGS (10×10×10 mm^3) cut at θ=45° and φ=0°, a type II AGS (10×10×10 mm^3) cut at θ=42° and φ=45°, and a type I CSP (cross-section: 6.75×6 mm^2; length: 9.5 mm) cut at θ=90° and φ=45° for non-critical phase-matching.

3. RESULTS

Figure 1 shows the measured OPO idler power at 6.5 μm for the CSP, type I AGS, and type II AGS non-linear crystals as a function of the pump power. CSP shows a slope conversion efficiency of 1.93 %, which is better in comparison to both the AGS crystals, and about twice the power obtained with type I AGS. With CSP, an idler conversion efficiency of 1.7% was measured from 1.064 and 6.5 µm, giving an average power of 27.5 mW. With type II AGS, we obtained a slope conversion efficiency of 1.75 % and an idler conversion efficiency of 1.1 % (13 mW). The type II AGS outperforms the type I AGS that showed a slope conversion efficiency of 0.92 % and an idler conversion efficiency of 0.47%, with 6 mW of idler average power. Also the CSP-based OPO exhibits a pump threshold of ~140 mW, i.e., 3 and 5 times lower than for the type II and type I phase-matched AGS-based OPOs, respectively. Compared to both AGS crystals, the significantly better performance of CSP is attributed to its very high non-linearity. The lower threshold and higher conversion efficiency of type II AGS compared to type I AGS are also expected given the differences between their effective non-linear coefficients as well as the relatively narrow and constant bandwidth of type II AGS in the tuned IR range [13].

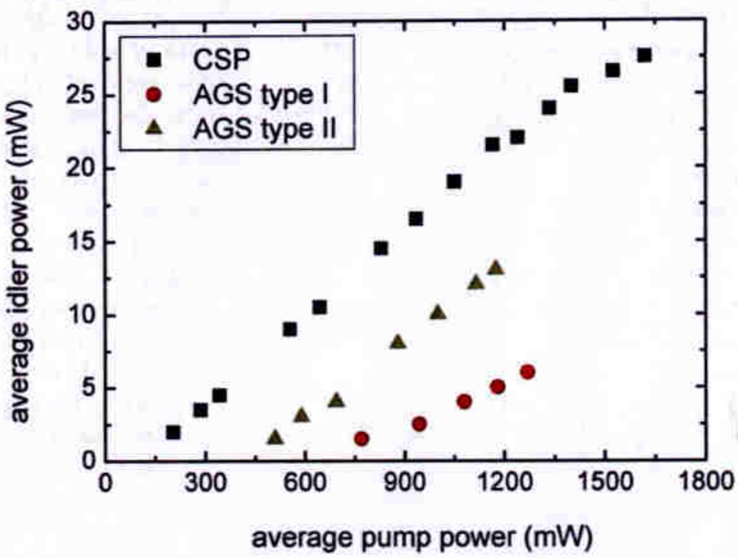

Fig.1: OPO idler power at 6.5 µm based on CSP, type I AGS, and type II AGS non-linear crystals measured as a function of the pump power.

Moreover damages were detected at the surface of AGS crystals for ~1.4 mW average pump power, while no damage was observed for CSP during our experiments. Besides its high nonlinearity compared to AGS, CSP exhibits a thermal conductivity of 13.6 W/mK, which is ~10 times larger than that of AGS (1.4 W/mK) [14], facilitating thermal management and thus yielding highly stable average power.

Preliminary assessments of liver tissue ablation using the CSP-based OPO output have been realized and a picture of a sample is shown in Fig. 2. The IR laser beam was focused using a CaF_2 lens of 100 mm focal length kept normal to the sample surface and high speed and thermal cameras were used to characterize the ablation. The IR beam waist diameter measured using a scanning knife-edge technique [15] was 1250 µm, leading to an average power density of ~2.45 W/cm^2. The fluence of the macro-pulse bunch and of an individual picosecond pulse were ~98 and 0.98 mJ/cm^2, respectively. Exposure time of 100 sec led to thermal damage in the tissue with a temperature rise between 40 and 50°C in the center of the irradiated area, as shown in Fig. 3. This is to be compared with previous ablation experiments performed with a nanosecond ZGP-based OPO (10 ns, 250 µJ, 10 Hz, 2.5 mW), where the fluence in the 60 µm diameter spot reached 8 J/cm^2, the ablation threshold being estimated at ~2 J/cm^2 [16]. The ablation yield was found to be strongly related to the IR absorption in the tissue that varies with the laser wavelength, as explained in the introduction. However, other parameters, such as the macro- and micro-pulse durations, pulse repetition rate, and fluence, also play significant roles in soft tissue ablation. For example, thermal confinement will occur when the pulse duration is shorter than the time it takes for the heat to diffuse in the surrounding volume. This confinement enables strategies for minimizing unwanted thermal damage to tissues adjacent to the targeted area. In this context, it has been demonstrated using a CO_2 laser that pulse duration and shape strongly influence the ablation because of thermal effects, where the IR energy is converted into heat, and of mechanical effects, where the IR light induces shock waves [17]. Macro-pulses with duration in the µs range exhibited a more effective ablation compared to longer pulses (ms), with less thermal damage from the hot vapor plume generated in the ablation channel. Comparative soft tissue ablations using FEL and ZGP-based OPO also demonstrated that the OPO shorter pulse duration increases the ablation efficiency in comparison to the longer FEL pulses [16]. Moreover, the OPO caused similar or less collateral thermal damage in porcine cornea, which strongly supports OPOs as alternative IR sources to FELs, with regard to thermal damage and ablation yield, in addition to the other instrumental advantages described in the introduction. Only a minor influence of the FEL micro-pulse duration varied between 1 and 200 ps was reported by M. A. Mackanos *et al.* [16] and the overall pulse structure can be considered as simpler and determined by the macro-pulse with a duration of 3 to 4 µs. J. T. Walsh *et al.* found that lower pulse-repetition rate leads to a complete tissue cooling between pulses while higher rates lead to a slight increase in damage resulting from the thermal energy accumulation [1].

Fig. 2: Picture of a liver tissue sample after ablation using the CSP-based SPOPO.

Fig. 3: Thermal image of a liver tissue sample during ablation with the CSP-based SPOPO.

Although actual ablation was not achieved in our preliminary experiment because of the large IR beam waist, this work reveals that OPOs are very promising compared to FEL with respect to several ablation parameters such as the energy per macro-pulse and pulse duration. The data highlight the suitability of CSP-based OPOs for medical applications because of their particular temporal structure and of their high average output power. To our knowledge, this paper is the first to report the investigation of tissue ablation with a CSP-based synchronously-pumped OPO. For successful ablation of soft tissues, an appropriate collimation system will have to be installed to reduce the idler beam waist. To this end, we measured the vertical and horizontal waist extension of the IR spot for various propagation distances, using the knife-edge technique. The experimental beam waist can be compared to that of a non-ideal Gaussian beam:

$$w(z) = w_0 \sqrt{1 + \left(\frac{z - z_0}{z_R}\right)^2}, \qquad (1)$$

In this expression, z_R is the Rayleigh length defined by:

$$z_R = \frac{\pi w_0^2}{M^2 \lambda}, \qquad (2)$$

and w the beam diameter, λ the radiation wavelength, w_0 the waist dimension (narrowest spot size), M^2 the beam quality factor, z the axial distance, and z_0 the position of the beam waist.

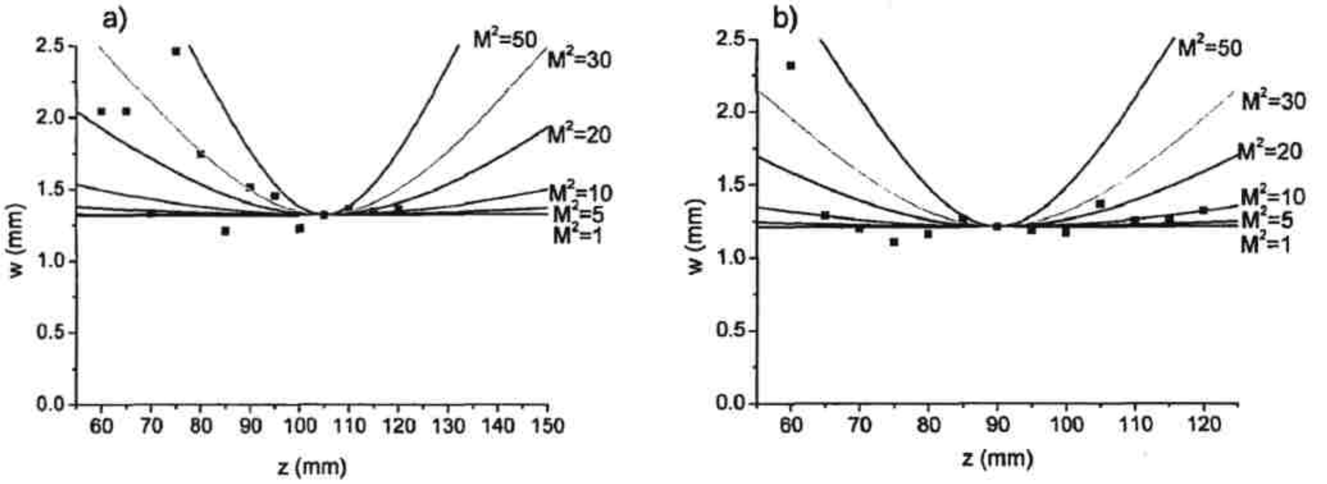

Fig. 4: CSP-based SPOPO beam diameter in the horizontal (a) and vertical (b) planes measured at different positions along the propagation direction. The experimental data (symbols) are compared to the waist of a non-ideal Gaussian beam for different values of the beam quality factor M^2.

In figure 4, non-ideal Gaussian beam diameters are presented for different values of the quality factor M^2 (see Eqs. 1 and 2) along with the experimental data measured in both the horizontal and vertical planes for different positions along the propagation direction. The comparison sets a maximum to the experimental M^2 value to around 10 for both the horizontal and vertical planes. Thus, it appears possible to achieve a beam waist diameter below 0.3 mm by first expending the beam to a diameter of 20 mm and then using a lens with a focal length of 100 mm for focusing on the sample, following:

$$\theta \approx \frac{w_0}{z_R}, \qquad (3)$$

where θ is the beam divergence. In these conditions, the fluence will be raised by a factor 42 to reach 4.1 J/cm^2 and 41 mJ/cm^2 for the macro-pulse bunch and the individual picosecond pulse, respectively. These values are above the estimated threshold for ablation [16]. Apart from its focusability, the performance of our table-top CSP-based SPOPO is close to that of the "free-electron laser high-precision surgical scalpel'' described by Serebryakov *et al.* [5]. Indeed, the laser specifications for surgical applications using the Vanderbilt-FEL were set to 2-3 mJ per macro-pulse with a repetition rate of 30 Hz, which are close to the present OPO system with its 1.1 mJ per macro-pulse at 25 Hz. The shorter macro-pulse duration in the CSP-based OPO system (1 μs) against the FEL (4-5 μs) and the reduced number of micro-pulses (*i.e.*, 100 for the OPO and 10^4 for the FEL) are further arguments in favor of the table-top system for surgical applications.

4. CONCLUSIONS

We have discussed the experimental performance of SPOPOs based on mid-infrared non-linear crystals of CSP and type I and type II AGS. CSP shows clear advantages compared to AGS. First, the oscillation threshold is measured at 140 mW with CSP, that is 3 (5) times lower than with type II (type I) AGS. Second, the idler conversion efficiency (and slope conversion efficiency) is better with CSP giving a 27.5 mW of average power, compared to 13 and 6 mW with type II and type I AGS, respectively. Also, the CSP-based OPO operates without any visible damage, well above the damage threshold for AGS. Finally, CSP affords a better pump depletion and allows stable high power beams thanks to its higher thermal conductivity compared to AGS.

The performance of these non-linear crystals demonstrates the suitability of the CSP-based OPO for surgical applications and preliminary results on liver tissue ablation show that the synchronously-pumped OPO is a viable alternative table-top laser source for the FEL.

Forthcoming work will target modification of the beam waist to increase the fluence on the sample so as to reach efficient tissue ablation with minimal thermal damage. Also, the effects of several experimental parameters on tissue ablation require further investigation in order to develop compact and inexpensive laser systems with clinical relevance.

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