Laser Processing - 2019

Report on a scientific paper

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1 Description of the paper

1.1 Paper links

The paper choose for this report is named "Selective femtosecond laser ablation via two-photon fluorescence imaging through a multimode fiber", the corresponding internet address is **https ://www.osapublishing.org/boe/abstract.cfm ?uri=boe-10-2-423**.

This paper was published by "The Optical society", one of the biggest publisher in optics and photonics around the world. The reference of the papers are **Biomedical Optics Express Vol. 10, Issue 2, pp. 423-433 (2019)** and was found using google scholar. The DOI of the paper is **https ://doi.org/10.1364/BOE.10.000423**.

1.2 Motivations

My interest in this papers in due to various reasons. First of all, I did my bachelor's degree in electrical and biomedical engineering. Electronics and electrical engineering applied to biomedical application are in my scope of knowledge, applying it with this new course on laser processing is therefore very interesting to me. Secondly, this study deals with fiber optics, a matter related to the laboratory of Hiroyuki Tsuda in which I take part here in Keio University. And finally, this paper deals directly with the creation of an application which is a good point to enlighten the practical use of the theory on laser processing.

1.3 Team research background

Below other DOI of papers published by some members of the teams who are from the *Optics Laboratory, School of Engineering, École Polytechnique Fédérale De Lausanne, Lausanne, Switzerland* and *Laboratory of Applied Photonic Devices, School of Engineering, École Polytechnique Fédérale De Lausanne, Lausanne, Switzerland* :

— **https ://doi.org/10.1364/OPTICA.5.000960**
— **https ://doi.org/10.1364/OE.25.011491**
— **https ://doi.org/10.1364/OL.40.005754**
— **https ://doi.org/10.1038/nature05060**

2 Summary of the paper

2.1 Introduction

Nowadays, optical fibers uses in medical application has an increasing role due to the fact that it can conveys light information efficiently and that their dimension are small. Combined with ultrashort pulses, which improve image resolution and quality, and femtosecond laser ablation (FLA), which allows really clean ablation in tissues, a system of ablation guided by two-photon fluorescence (TPF) imaging feedback could be implemented. A problem arise while trying to create this dual system because FLA's required peak intensity is really high, and it can be higher that the maximum peak sustainable by endoscope, causing fibers deterioration and non-linear effects. In order to combine the two techniques (FLA and TPF), new fibers are therefore investigated. Those fibers would be an alternative to the hollow-core photonic crystal fiber (HC-PCFs) which allows micro Joule pulse energy, enough for FLA, but shows limitation. Also to reduce the size and complexity of the endoscope compared to commercially available one, which use additional opto-mecanical components, a technique called Transmission Matrix(TM) is used to focus light while travelling into the fiber.

The hypothesis of creating this new dual system was studied using graded index fibers (GRIN) of 200 μm core and 400 μm core applied to ablation in biological tissues of the cochlea. Firstly, the area of ablation was detected by TPF through the fiber and then the FLA technique processed in the same fiber. The results of the studies validates the possibility of creation of this kind of system with laser beam for which peak intensity can be up to 1.5×10^{13} $[W/cm^2]$. It is important to notify that is it the first time that combining FLA and TPF was made through multi-mode fibers. The importance of this study lies in the fact that it can create new tools of smaller size which on top of that combine two efficient techniques that can perform more precise detection, manipulation and ablation of cells or their components.

2.2 Optical setup

Figure 1 shows the optical setup. It works as follows. Using a high pulse energy laser (upper gray box on the figure) a signal is generated. Then using lenses the signal is collimated and expanded and it is splitted to obtain a reference signal and a signal which will illuminate the sample. After that, with several optical device it is fitted to the core. It is done such that the peak intensity is lower then the damage threshold of the device, in all cases. The higher peak they had was $60[MW/cm^2]$, at the SLM, while the device limit is $0.25[TW/cm^2]$. When the beam exit the fiber it is detected by a CMOS detector, it is also true for the reference. The two signals are compared and a digital hologram is extracted. This hologram will then make possible to compute the Transmission Matrix (TM) by repeating this for 12000 to 46000 inputs angles. The TM of the system is then determined and can be used to focus the light.

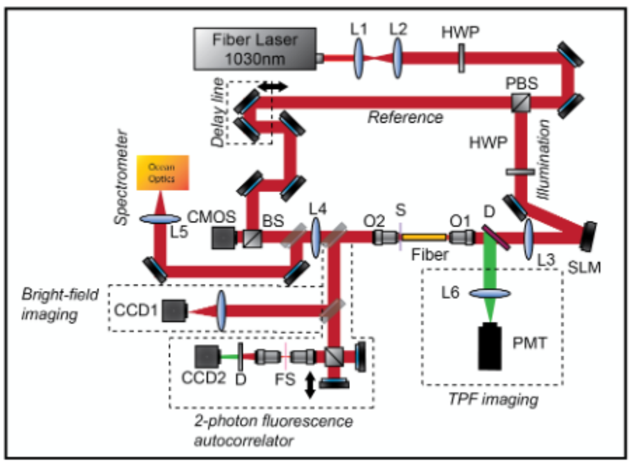

FIGURE 1 – Optical setup for the validation of the hypothesis.

The performance of the fibers under different high intensities, necessary for FLA, are studied through the focused pulse at the level of the distal side. A temporal and spectral analysis of this signal is done. A spectrometer is used for the spectral analysis while for the TPF, mirrors, microscope and objectives are used to collect the fluorescent signal.

2.3 Sample preparation

A biological sample of the internal ear is obtained using mice.

2.4 High peak intensity achieved through the fiber

2.4.1 Result from previous studies

How ultra-short pulses were delivered via multi-core fiber was already investigated by the team. Using the same kind of procedure for laser ablation the team obtained a maximum peak intensity of $4 \times 10^{12}[W/cm^2]$. And they noted an actual loss of power due to the fiber cores. They could only have 14% of the input power. This is were they defined the focusing efficiency of the system as the percentage of the power that is in the focus spot. They then issued the fact that to have a better efficiency they will try the experiments on different fibers.

2.4.2 Optimization, limitations of the system and results

They first studied the focusing efficiency and discovered that using the TM method, already discussed above, with those fibers allowed them to obtain up to 28% of focusing efficiency. The limiting factors being the polarization of certain modes, which given the setup are not taken into account, the coherence gating of their fiber and the non-linear effects that happens. Those non-linear effects in the fiber creates a loss of focusing efficiency because the TM method is designed for linear system and in this non-linear case, its performances decreases.
After this, for the new system built, they recorded both the focus efficiency and the Peak intensity. This is the major result of their study. And it is displayed in Figure 2.

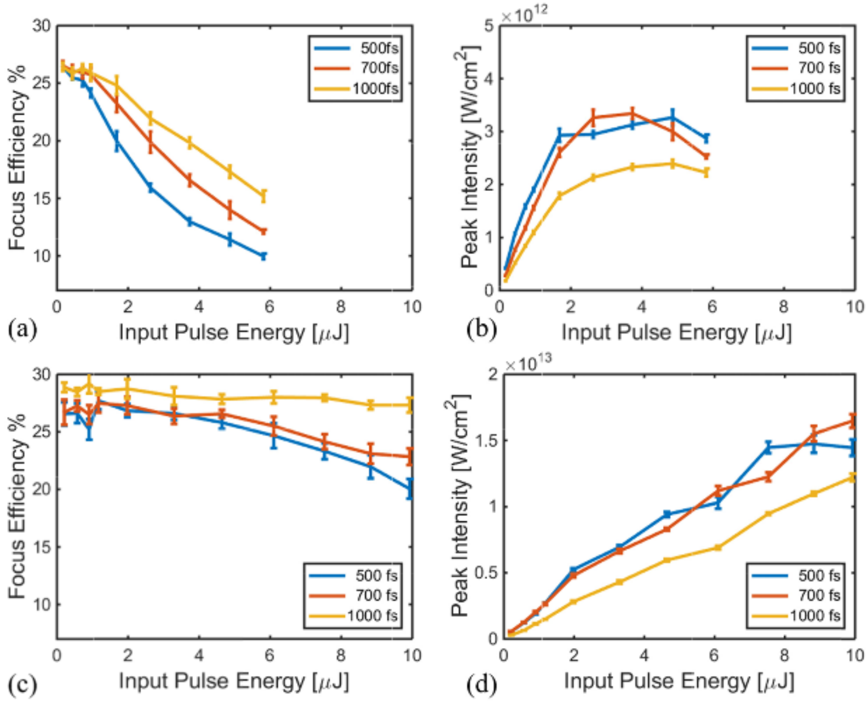

Figure 2 – Focusing intensity and peak efficiency for different pulse duration of 500, 700 and 1000 fs. Figure (a) and (b)correspond to the 200 μm core fiber, while (c) and (d) to the 400μm core fiber

This figure is the most important figure of the paper. This is because the limiting factor of creating their new project by combining FLA and TPF was the non-linear effects and fiber damages is the response of the fiber to high peak intensity pulses needed in FLA. Using their new material, they overcame this problem and made their applications feasible.

It can be observed on figure 2(a) that, for the 200 μm core fiber, the focusing efficiency decline quickly, for all pulses duration, after 1μJ of input. This explains the fact that the value of the peak intensity doesn't increases with the Input Pulse Energy as seen on figure 2(b). Those observation are explained by the fact that there is a spectral and temporal enlargement due to nonlinearities. The maximum value that can be delivered is therefore around 2.5-3$\times10^{12}[W/cm^2]$. Values of input power higher than 6μJ would damage the fiber. For the 400 μm core fiber, the situation is different. The focus efficiency didn't exhibit any particular change, this is confirmed by no spectral and temporal enlargement. Therefore, the Peak Intensity increases in a linear manner with maximum value around 1.5$\times10^{13}[W/cm^2]$.

Using GRIN fibers they demonstrate that a working, efficient system being able to sustain laser ablation and which shows comparable result with HC-PCF ones.

2.5 TPF imagine feedback is combined to FLA

They then demonstrate that the FLA is performed very precisely with the TPF imaging feedback from the same probe. And that, using the 400μm core fiber with peak intensity of $10^{13}[W/cm^2]$, it was possible both the imaging (which for biological tissues needs intensity higher than $10^{12}[W/cm^2]$) and the FLA.

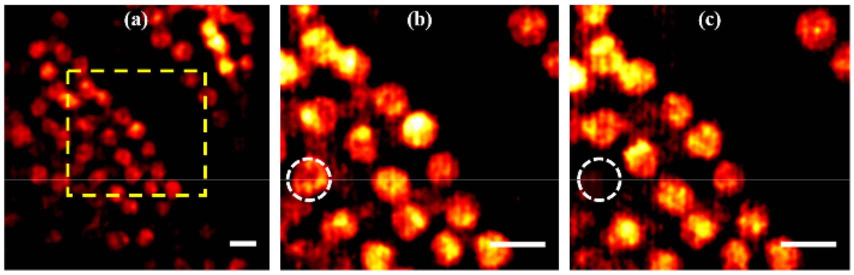

FIGURE 3 – TPF imaging of region where the ablation occurs. On (a) the region, (b) the cell of interest before ablation and (c) after ablation

The figure 3 shows the imaging shows properly the experiment performed. And that the system is functional. Following this they confirmed that the beam only impact the desired are with no effect on the cells in the surrounding.

2.6 Conclusion

This study enlighten a new system with good imaging characteristics and a feasible FLA in addition with no peripherial damage of tissues. The 400 μm core fiber shows the best result and could also be used for other material.

This new system could particularly be applied in various medical sectors. It could give a diagnostic on inner-ear tissues damages. Could be used for microdissection of chromosomes or to care and modify neural tumor.