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Recent developments and advances of femtosecond laser ablation: Towards image-guided microsurgery probes

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ABSTRACT

In this contribution we review recent developments and advances in femtosecond laser ablation, with a focus on biomedical applications. In recent years, research has focused on further expanding the use of ultrafast laser ablation beyond ophthalmology, addressing needs in other fields such as dental and orthopaedic surgery. Furthermore, new advances in the development of endoscopic probes for ultrafast laser surgery and the integration of spectroscopic analytical imaging techniques for image-guided devices pave the way for other clinical applications, such as otolaryngological surgery of vocal fold scarring, inner ear surgery, and cancer detection and simultaneous tumour removal.

1. Introduction

Laser ablation consists in the selective removal of tissue after exposure to an intense optical field. The mechanisms which govern the ablation process are manifold and depend on the type of radiation employed. When pulsed lasers are used, the effect of the laser pulse on the tissue is strongly influenced by the time scale of the interaction.

In the long pulse duration range (ns or longer), ablation relies mainly on linear absorption and the consequent thermomechanical response of the tissue [1]. One limiting factor of this type of ablation is the wavelength dependence of the optical properties of biological tissues, since it affects the spatial distribution of the deposited and absorbed energy. Therefore, different laser sources are needed for different ablation targets. Moreover, relying on a linear absorption process, heat diffusion in the surrounding tissue would cause non-negligible thermal damage outside the focal volume and along the beam path direction.

On the other hand, if the pulse energy is confined to a sufficiently short time, as in femtosecond pulses, the high photon flux can lead to nonlinear absorption processes. Nonlinear absorption determines the creation of a plasma of free electrons, tightly confined in the focal volume, which is then responsible for the localized tissue disruption. The specific mechanisms underlying material damage caused by ultrashort pulses are diverse and remain the subject of ongoing research, particularly within the field of material science [2]. These mechanisms depend not only on the irradiation parameters but also on the composition of the sample under study. In the case of biological media, such as cells and tissues, the material removal is generally associated to the following processes [3,4]: photochemical and photothermal damage, thermoelastic bubble formation and optical breakdown. These processes arise at different peak intensities and pulse train repetition rate and they are extensively discussed by Vogel et al. in Ref. [3]. They will be briefly summarised in the following. At low intensities and high repetition rate (>MHz), ablation can be caused by a combination of photochemical and photothermal damage. In the first case, phenomena such as dissociation of water molecules and subsequent creation of reactive oxygen species [5] or direct breaking of chemical bonds in other chemical structures like DNA [6], take place. A large number of consecutive pulses are needed to achieve sufficient and fast photochemical damage, therefore a repetition rate in the MHz range must be employed. In the second case, multiple low intensity ultrashort pulses, may lead to thermal cumulative

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ablation, where the material decomposition is caused by denaturation of biomolecules and localized thermal damage to cellular structures.

At high intensities but low repetition rate (<MHz), the thermal relaxation of the plasma is followed by the generation of a transient cavitation bubble whose expansion and collapse are responsible for the permanent ablation damage. Fig. 1 gives a schematic overview of the processes. Since the bubbles have hundreds of nanosecond lifetime, if the laser repetition rate is higher than the bubble collapsing rate, cumulation effects may take place [3]. At extremely high intensities, optical breakdown will occur: the plasma becomes highly absorbing and the high temperature and pressures cause the emission of a shock wave alongside the creation of the cavitation bubble, leading to possible more severe mechanical damages in the surrounding volume.

Relying on nonlinear absorption processes, femtosecond laser ablation not only has the advantage of reducing the collateral thermal damage, which is essential for micro and nanosurgery applications, but it is also applicable even to transparent or low-absorbing materials [7,8]. In this regard, one of the first clinical applications of femtosecond laser ablation was eye surgery, with the development of fs-LASIK (fs-laser assisted in situ keratomileusis) for vision aberrations correction through intrastromal ablation [9]. Unlike conventional LASIK [10], in which a mechanical instrument, the microkeratome, was used to cut a thin corneal flap and expose the underlying stroma for excimer laser ablation, fs-LASIK used a femtosecond laser to replace the microkeratome in the flap creation step. Thanks to the aforementioned advantages of femtosecond ablation, this technique allowed for greater efficiency and predictability, as well as a reduction of surgically induced astigmatism [9,11]. Several other applications have followed fs-LASIK in ophthalmology, with keratoplasty [12,13] and cataract surgery [14] being two examples. In this field, the introduction of femtosecond ablation was mainly directed to the replacement of mechanical tools for a more precise and less invasive surgical procedure. Further details and applications of femtosecond ablation in ophthalmology can be found in the work of Kaz Soong et al. [15] and Hoy et al. [4]. The major reason why this technology has been immediately successful in this field is undoubtedly the easy accessibility of the tissue under study and thus the possibility to use free space laser systems. Being already an established technique, femtosecond ablation in ophthalmology will not be the subject of this review.

The situation is different in other fields, such as dental and orthopaedic surgery: here the applications of ultrafast laser ablation are still confined to the research environment, but they show great potential to be brought into the clinical setting. Therefore, the first section of this review will explore developments of ultrafast surgery of hard tissues, i.e. teeth and bones, and will give an overview of the advantages of using femtosecond lasers for these types of tissue.

In parallel with these developments, major efforts have been made in recent years to translate femtosecond laser ablation into endoscopic applications, which could expand laser-based surgery to difficult-to-access biological tissues and on patients. The limitations and difficulties of this implementation will be addressed in the second section, and an overview of the implemented devices will be provided.

Lastly, this work will discuss a new trend in the field of endoscopy, which is image-guided laser surgery probes. Endoscopy is a standard diagnostic tool in disciplines like otolaryngology, head and neck surgery, or gastroenterology. The possibility of real time imaging of the tissue under investigation is of paramount importance to ensure a correct tissue removal and it could unlock novel procedures, for instance in the field of tumour margin identification and malignant tissue removal.

2. Femtosecond ablation of hard tissue: from dental surgery to bone ablation

The research on laser ablation in dental surgery goes back decades in the past. Similar to ophthalmology, lasers were investigated as a tool to replace the mechanical instruments usually employed in conventional surgical procedures. However, the first efforts to utilize continuous wave or pulsed lasers in the ns to ms range (mainly CO_2 lasers in the infrared or Nd:YAG at 1064 nm) failed due to a number of factors: linear absorption of radiation leads to uncontrolled melting of the dental tissue, carbonization, cracks on the tooth surface and possible necrosis of the pulp due to thermal damage [16]. Other lasers were investigated, especially Er,Cr:YSGG and Er:YAG lasers [17,18], to reduce the thermal effects, however, falling within the water absorption band, shock waves due to rapid evaporation could lead to mechanical damage and superficial cracks [19].

Here, femtosecond lasers came to help thanks to the nonlinear nature of the absorption process. A systematic review on the characteristics and advantages of ultrafast lasers for dentin and enamel ablation was recently published by Lagunov et al. [20]. According to them, the main factors that make this technique appealing in this field are the extremely low heat diffusion in the depth of the tooth, thus reducing possible damages to the dental pulp, the ability to perform precise micromachining due to the confined interaction within the focal volume, and the non-significant modifications of the chemical composition of the tooth surface. A complete study on the effect of ultrafast ablation on human enamel was also conducted by Le et al. [21]. They fully characterized the topographical, compositional and structural modifications induced in enamel by exposure to a 560-fs laser at 1030 nm and 1 kHz repetition rate and they concluded that the surface of enamel did not show any sign of carbonization or cracks and the thermal damage in the surroundings of the ablation site was minimal. They did observe the formation of a thin layer of altered material, due to the melting and re-solidification of hydroxyapatite but the thickness of such layer was below 1 μm. Similar conclusions were drawn by the same group after the characterization of dentin [22]. Within a fluence range between 2 and 14 J/cm^2, the structure and constitution were preserved and no carbonization or cracking of the surface were found. Despite the many advantages of femtosecond lasers for tooth ablation, one limitation that slows down the replacement of conventional tools in clinics is the low speed of ablation. For this reason, a lot of effort has also been spent lately to increase the ablation rate. Most of the studies focused on the optimization of the laser parameters, such as fluence, line scanning spacing and speed, and repetition rate of the laser source in order to maximize

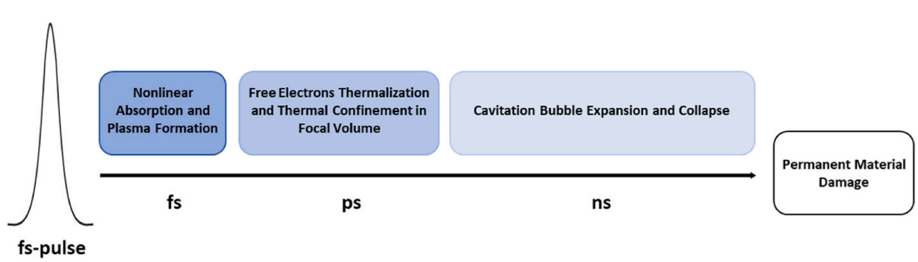

Fig. 1. General scheme of the femtosecond ablation process in the thermoelastic regime. After plasma formation due to nonlinear absorption processes, thermalization of free electrons occurs within few to tens of picoseconds, causing confined heating in the focal volume. The localized temperature rise determines the generation of a cavitation bubble, which expands and collapses within tens to hundreds of nanoseconds, leading to permanent damage in the focal volume.

the ablation efficiency [23–25]. Fig. 2 illustrates examples of ablation craters created on enamel and dentin. An alternative approach, proposed by Loganathan et al. [26], involved instead surface pretreatment of the tooth before ablation (with orthophosphoric acid and Carie care gel), aiming to improve the laser-material interaction, with the result of increasing three times the ablation rate, with respect to untreated tooth. The same group also introduced an effective mathematical model to predict the ablation profile on hard tissues as well as the ablation rate and efficiency [27]. The method is based only on the assumption of a Gaussian laser beam and fluence distribution, so it is applicable to any ultrashort pulse and extendable to all hard tissues in general, therefore useful not only in dental surgery but also in orthopaedic applications.

Laser ablation in orthopaedic surgery has had a similar development to dental surgery because of the close nature of the sample under study. In both cases, ablation involves hard tissue that needs to be removed with low collateral damage and at high speed. In this regard, several studies have examined the properties of femtosecond ablation of bone tissue [28–30] and found comparable results to those obtained on dental tissue; indeed, it has been claimed that the two types of hard tissue undergo the same ablation processes because of their similar constitution [28]. Other investigations also focused on optimizing laser parameters on different bone samples [31–33] with the same goal of increasing ablation efficiency and speed. An exhaustive comparison on the recent achievements in bone ablation for orthopaedic surgery can be found in the work of Li et al. [34]. The authors compared the ablation parameters in several studies and found values of ablation rates between 0.80×10^{-4} and 0.99 mm^3/s for different laser configurations. Although these values are generally lower than those of mechanical drilling instruments, and therefore disadvantageous in situations where high speed is required, femtosecond ablation might be preferable when high-precision operation is needed.

Ultrafast surgery based on femtosecond lasers is thus on his way to replacing, at least to a certain extent, mechanical tools in dental and orthopaedic surgery, and it has proven its advantages with respect to continuous wave and long pulsed laser ablation. However, its acceptance in the clinical environment is restricted in the previous studies by the use of bulky and free space optical systems. The development of flexible surgical probes for efficient delivery of ultrashort pulses would certainly boost the translation of this technique into the clinical setting.

3. Ultrafast laser probes for endoscopic femtosecond ablation

Interest in endoscopic probes for femtosecond ablation has increased in recent years and has been driven by developments in fibre optics. In fact, the main difficulties in implementing femtosecond ablation in an endoscope are related to the transmission of ultrashort pulses through fibre-optic systems. The nonlinear dispersion effects caused by the high peak intensities in conventional optical media, i.e. silica-based fibres, determine a spectral and temporal broadening of the ultrashort pulses, causing a decrease in the peak intensity on the sample site. Furthermore, due to the nonlinearity of the dispersion process, pre-chirping of the pulse to compensate for the broadening is extremely difficult [4].

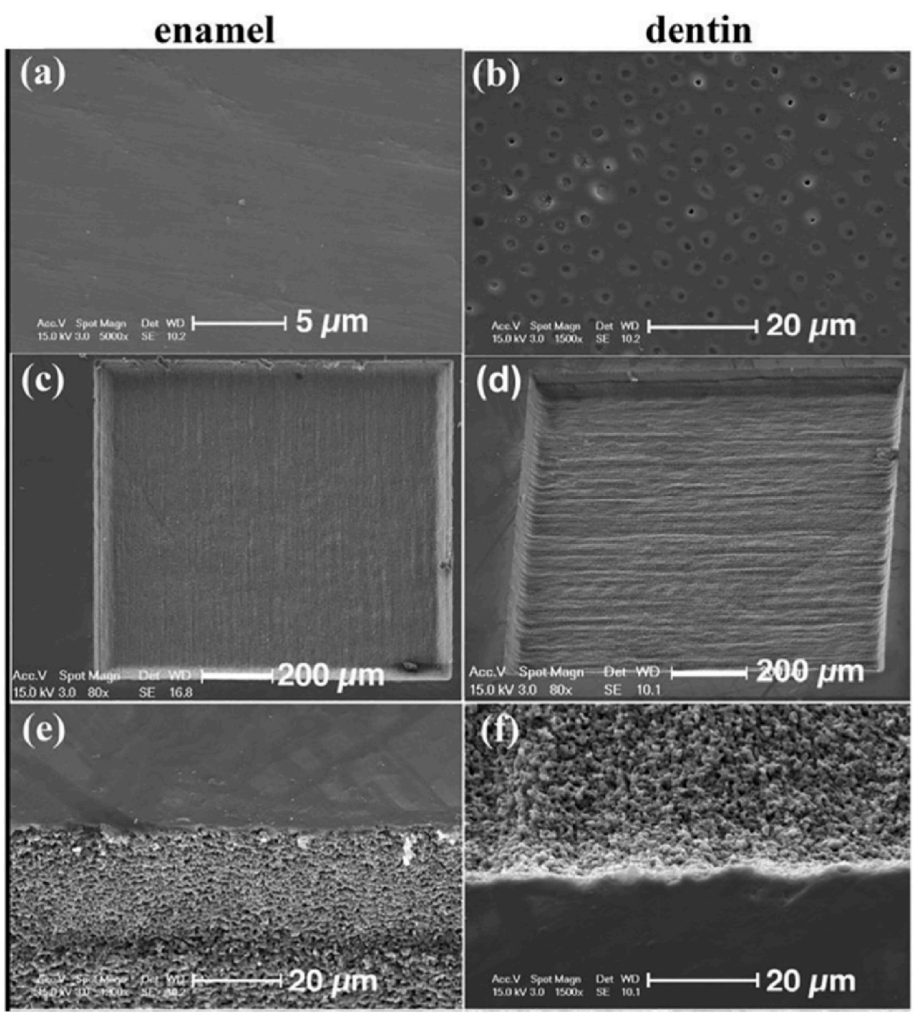

Fig. 2. Scanning electron microscope (SEM) images of enamel and dentin before (a, b) and after (c–f) femtosecond ablation. (e) and (f) show the interface between the ablation area and the pristine material. SEM analysis confirms the absence of collateral damage. Image taken with permission and modified from Ref. [24].

Already more than a decade ago, the commercialization of air-core photonic bandgap fibres fostered the development of ultrafast probes for femtosecond ablation [35,36]. The transmission of the pulses in air allows a strong reduction of the nonlinear effects and permits higher intensities on the sample. However, due to the limited core size (6 μm in the previously cited works) damage to the fibre inlet during coupling is still possible. Another aspect to consider in the development of fibre-optic systems for surgery applications is the size of the probe, which must be minimized to facilitate endoscopic use. The goal of the following generation of fibre probes was thus twofold: to achieve high energy ultrashort pulses transmission and to reduce the size of the delivery probes.

Towards the realization of a miniaturized device, Ferhanoglu et al. [37] developed a 5-mm fibre probe, which employed a piezoelectric tube actuator as scanning mechanism and two aspheric lenses for focusing. The device was much smaller than the previous probes [35,36] and could deliver up to 450 nJ of pulse energy to the sample with ablation speeds up to 4 mm/s. However, it was still limited by damage to the cladding of the 6 μm-core photonic crystal fibre used. Another approach to reduce the size of the probes and, at the same time, the damage caused by high intensities was proposed by Conkey et al. [38]. They realized a lens less endoscope which is based on a multi-core fibre system and it uses wavefront shaping to achieve focusing and scanning without requiring additional components and optics. The idea is to distribute the pulse energy over multiple cores so as to reduce nonlinearities and reach a higher final intensity at the focus. With such device they could efficiently transmit up to 3 μJ pulses with 750 fs pulse duration. An alternative way to deliver higher energetic pulses with minimal nonlinear dispersion is to use larger core hollow-core fibres. Kagome lattice hollow-core photonic crystal fibres (Kagome HCPCF) are a good example in this direction. They were used to build a 5-mm ultrafast laser scalpel, using a piezo-based scanning mechanism and a ZnS micro objective for focusing [39]. In this work a 31 μm-core Kagome fibre was capable of delivering up to 1.2 μJ to the sample, with the main limitation being the nonlinear absorption occurring in the ZnS objective. In a recent work [39], the same group further improved the probe by replacing the ZnS with CaF_2 in the micro objective proving an increase in the maximum allowed peak intensity of a factor of 37. This increase in the available intensity on the sample is crucial to speed up the material removal rate [40] and they demonstrated the efficient ablation of bovine cortical bone with ablation rates greater than 0.1 mm^3/min. They also simulated that, using a higher power laser with the same probe, the removal rate could reach up to more than 2 mm^3/min. Although these values are still lower than conventional laser surgery systems, this ultrafast laser probe can be advantageous in biologically sensitive regions where thermal damage is highly undesirable. An example of application proposed by the group is spinal decompression surgery, where bone spurs must be removed to release pressure on the spinal cord. The high-precision and low collateral damage of femtosecond ablation would be a solution to avoid complications and harm to spinal tissue.

The development of small and efficient ultrafast laser probes paves the way for further applications of femtosecond laser ablation in biomedicine as it gives the possibility of accessing tissues that were impossible to access with the bulk optical systems used until then.

Another example of application is the otolaryngological treatment of scarred vocal folds. After surgical treatment of laryngeal cancer, a common side effect is scarring of the vocal folds, leading to degradation or permanent disruption of vocal function [4]. To restore the viscoelastic properties of this tissue, commonly proposed solutions involve the injection of biomaterials deep into the tissue [41]. However, injection alone does not guarantee localization of the biomaterial in the desired areas, as it tends to spread around. To address this problem, Andrus et al. [42] proposed the use of an ultrafast laser probe to create sub-epithelial voids in the vocal folds tissue, allowing localized injection of bio gels. They developed a miniaturized probe based on a Kagome HCPCF and a custom-built 6 mm diameter objective, able to deliver up to 3.8 μJ pulse energy on the sample. To achieve efficient sub-surface ablation, the objective was designed to have a high numerical aperture of 0.47 and thus allowing tight focusing of the beam into the tissue (with a beam radius of about 1.12 μm). To facilitate the use of the probe in the larynx, they placed a reflective microprism after the lenses to achieve a side-focusing configuration. The probe was tested on ex-vivo porcine hemilarynges demonstrating the ability to create sub-surface voids up to 114 μm deep in the tissue. Finally, they proved the localization of injected biomaterial in the ablated areas, showing the potential of this system for the treatment vocal fold scarring in the clinical setting. Table 1 summarizes the characteristics of the different ultrafast laser ablation probes which have been discussed in this section.

4. Towards nonlinear imaging-guided ultrafast laser ablation

The success of flexible, miniaturized probes for femtosecond endoscopic ablation opens the way for many applications in medicine. However, to take full advantage of the high-precision benefits of this technique, a major step forward would be the implementation of image-guided femtosecond ablation in a “seek and treat manner”. In this way, it would be possible to have real-time monitoring of ablated features and enable ‘seek and treat’ applications. In this direction, nonlinear spectroscopic imaging could help, as it is based on similar ultrafast laser excitation and involves label-free microspectroscopy techniques that do not require staining of the sample, but, at the same time, can provide morphological and chemical information (morphochemical) on a microscopic scale [43]. The simplest implementation of nonlinear imaging is two-photon excited autofluorescence (TPEF), which is fluorescence emission from endogenous tissue fluorophores due to two-photon absorption. This process is found in many endogenous fluorophores in biological media, so it can be a label-free tool to access tissue during and after an ablation procedure. Also, being triggered by ultrashort laser pulses, TPEF could be initiated by the same laser used for femtosecond ablation, provided the pulse energy is reduced. In a recent work, Kakkava et al. [44] have realized such TPEF-guided implementation using the multimodal fibre probe already proposed in Ref. [38] for the selective and guided ablation of cochlear hair cells. They employed the same 1030 nm laser system for both femtosecond ablation and TPEF imaging. The ultrafast probe was used to precisely ablate single cells of approximately 7 μm × 7 μm on an ex-vivo section of organ of Corti and TPEF to monitor the result of the ablation process. In this case, the cellular tissue

Table 1
Comparison between different ultrafast laser probes for femtosecond ablation. The overall diameter of the probe, the maximum deliverable pulse energy at the sample side and the fibre type used as delivery system are compared. ‘n.a.’ stands for ‘not available’ and refers to an information which is not explicitly mentioned in the paper.

Author/Year	Probe diameter [mm]	Maximum deliverable pulse energy [μJ]	Fibre type
Hoy et al. [35]/**2008**	18	0.35	Air-core bandgap fibre
Hoy et al. [36]/**2011**	9.6	n.a.	Air-core bandgap fibre
Ferhanoglu et al. [37]/**2014**	5	0.45	Air-core bandgap fibre
Conkey et al [38]/**2017**	n.a.	At least 3	Multicore fibre
Subramanian et al. [39]/**2016**	5	1.2	Kagome hollow-core photonic crystal fibre
Subramanian et al. [40]/**2021**	5	At least 5	Kagome hollow-core photonic crystal fibre
Andrus et al. [42]/**2022**	6	3.8	Kagome hollow-core photonic crystal fibre

was removed from the cochlea and stained, therefore the fluorescence came from an exogenous fluorophore and not from the pristine tissue. The same group also proposed to combine two imaging modalities and femtosecond ablation for hair cells diagnostics in an intact mouse cochlea, i.e. without the need of extracting the internal tissue [45]. Cochlear hair cells are enclosed in a dense bone structure, so direct access to imaging is limited due to the high scattering properties of bone. The idea of their work was to use femtosecond laser ablation to precisely thin the bone layer shell to a level that would allow TPEF imaging of the underlying cells. In the meantime, the thickness of the ablated layer was supervised by optical coherence tomography (OCT) to prevent undesired damage to the cells. Thanks to the high precision of femtosecond ablation and the supervision of OCT, they could thin the bone layer down to 40 μm, allowing efficient TPEF imaging through the osseous layer. These two examples show how image-guided femtosecond ablation can be useful in the diagnosis and guided therapy of inner ear diseases, which are responsible for most cases of hearing loss and where the high precision of ultrafast laser ablation is essential to achieve the best results.

Another field in which ultrafast laser ablation could benefit from image guidance, and particularly from nonlinear imaging techniques, is cancer diagnostics and treatment. Multimodal nonlinear imaging, i.e. the combination of several nonlinear modalities such as such as TPEF, second harmonic generation (SHG) and coherent anti-Stokes Raman scattering (CARS), have already been proven to be a powerful tool for label-free diagnostics of several types of cancer [46–50]. The use of multiple nonlinear spectroscopic imaging modalities gives insights on different chemical components, such as endogenous fluorophores like elastin, NAD(P)H or FAD (with TPEF), collagen content (with SHG) and lipids (with CARS in the CH_2 stretching region). Combining the image data results in a false-color image that allows to display the morphological and chemical composition (morphochemistry) of native tissue in a label-free manner. Analyzing the multimodal images by machine and deep learning approaches translates the morphochemical information encoded in the multimodal spectroscopic images into medically relevant information in terms of discriminating between healthy and unhealthy tissue [51–53]. Several recent studies have already demonstrated the implementation of such multimodal nonlinear imaging approaches into flexible endoscopic solutions [54–57]. Overall, multimodal nonlinear imaging in the form of fibre probes combined with innovative automated image analysis routines has great potential as a tool for computational spectral histopathology for automatic prediction of tissue type/disease during surgery, opening new possibilities for improved intraoperative disease diagnostics. The additional integration of femtosecond ablation within these systems could be a pathway to novel diagnostic and surgical tools. The precise high-resolution definition of the tumour margins is just the first important step. The synchronous application of a femtosecond laser would allow an exact cutting along these margins with maximal preservation of surrounding healthy tissue, hence, would reduce the morbidity, and would allow better preservation of function. Conventional CO_2 laser surgery, the working horse for instance for head and neck surgery, always produces larger coagulation zones. This prevents not only an accurate histopathological tumour margin definition, but also means that more healthy tissue has to be removed than is necessary from an oncological point of view. The work of Meyer et al. [58] is an example of first implementation of CARS imaging guided femtosecond ablation. In this case, two laser sources were used, a compact fibre laser for CARS microscopy and a femtosecond laser for ablation. The setup was tested for several types of soft tissue, from thin sections to bulk tissue, demonstrating a lateral resolution of about 8

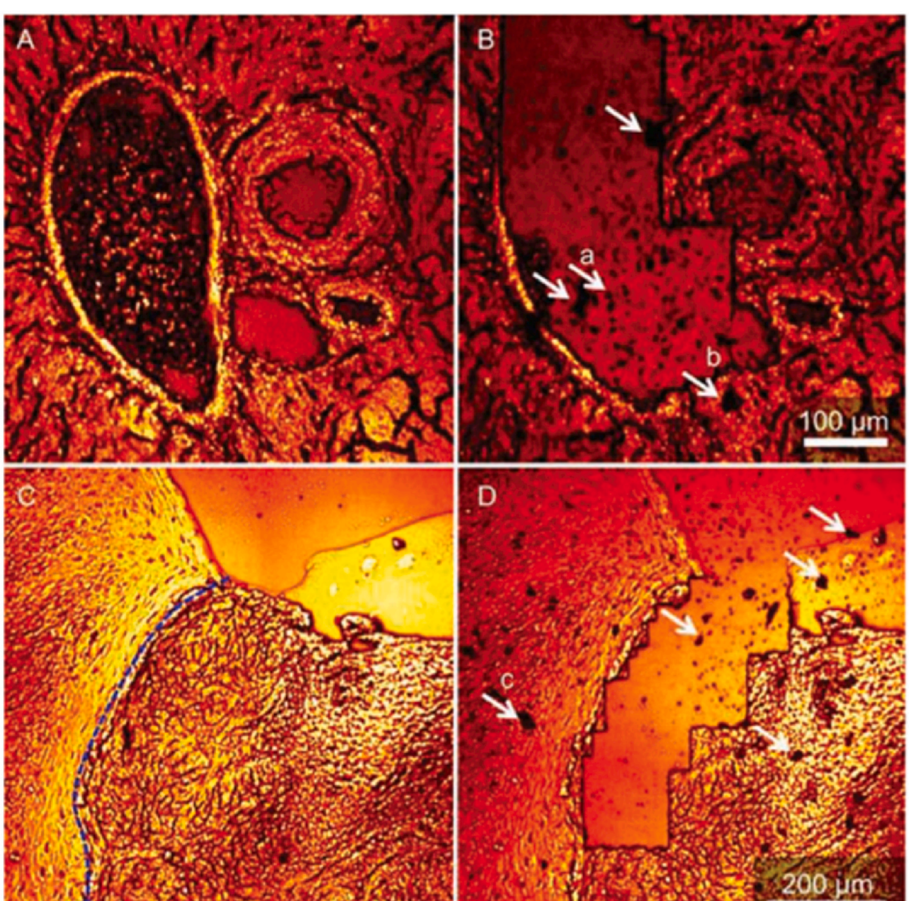

Fig. 3. Example of CARS-guided femtosecond ablation of a murine liver section. (A) CARS image at 2850 cm^{-1} from the portal area of a murine liver section. The portal vein, the hepatic artery and bile duct can be distinguished in the image. (B) Selective ablation of the material within the portal vein. (C) CARS imaging at 2850 cm^{-1} allows the discrimination of normal epithelium (left) from dysplasia (right). (D) Targeted removal of dysplastic tissue by femtosecond laser ablation. The arrows present in (B) and (C) points to some ablation debris. Reproduced from Ref. [58] with permission from the Royal Society of Chemistry.

µm and an axial resolution of 30 µm, when a numerical aperture of 0.4 is used. As shown in Fig. 3, the authors proved the selective removal of specific features in a murine liver section: the molecular specificity of CARS allows discrimination between different tissue conditions, for instance normal epithelium and dysplasia (Fig. 3C), thus enabling precise targeted ablation. A crucial aspect of femtosecond ablation for tumour removal is certainly the formation of potentially harmful debris that can be generated during laser ablation. Here, the ablation procedure must ensure residual tumour tissue with a size smaller than the typical cellular dimension, to reduce the risk of spreading via bloodstream. Future investigations should therefore be conducted to understand the efficacy and safety of this procedure as a cancer treatment tool.

Toward endoscopic implementation of tumour surgery guided by nonlinear multimodal imaging, a recent contribution by Lai et al. [59,60] proposes a handheld endomicroscopic system that combines ultrafast laser ablation with several imaging modalities for head and neck cancer detection and removal. The authors developed a rigid probe with 6 mm in diameter, at least 430 µm field of view and sub-micron resolution for multiphoton imaging (CARS, TPEF and SHG), as well as indocyanine green (ICG) fluorescence detection. The probe is also capable of delivering sub-picosecond pulses up to 0.5 µJ and has demonstrated micrometer-scale ablation of rat liver and chicken meat tissue.

Currently, the successful integration of this technique into practical endoscopic solutions represents a significant challenge for its effective utilization in clinical settings. The need for specialized lasers and detectors, and suitable delivery probes adds complexity and cost to the assembly of CARS-guided endoscopy systems. Additionally, the relatively limited field of view achieved thus far poses challenges in achieving the same level of navigation as with wide field endoscopes. However, in our vision, the development of CARS-guided endoscopic solutions is not an alternative to standard endoscopic devices, but rather a complementary addition.

The use of such devices in the clinical setting also poses the problem of controlling endoscopes with micrometric accuracy. This task can be challenging even for the experienced hand of surgeons, so this field could benefit from the development of robotic arm solutions for surgical applications. The development of increasingly advanced probes can be expected to go hand in hand with robotic control systems that can be used in operating rooms and allow easy handling of these devices even in sensitive or difficult-to-access areas of the body.

5. Conclusion

In this review, we sought to provide readers with an overview of the latest research on femtosecond laser ablation in the biomedical field. We suggested the advantages of this light biological matter interaction technique with respect to conventional laser ablation and the reasons why it has found great success in ophthalmology. Beyond this field, most applications are still confined to the laboratory, but the development of new ultrafast probes and efficient delivery systems is encouraging the translation of this technology into the clinical setting. Because of the slow ablation rates that femtosecond lasers can provide, the main areas where this technique could be advantageous over conventional techniques are those where tissue sensitivity requires minimal collateral damage or where high ablation precision is preferred to speed. The integration or combination with spectroscopic analytical imaging methods into ultrafast laser surgical probes could further facilitate the transfer of this technology to new fields. Further research will be needed to evaluate the efficacy and safety of femtosecond ablation for direct cancer excision, and robotic solutions should be considered when transferring the devices to a real-world surgical application.

Declaration of competing interest

We certify that there is no conflict of interest with any financial or non-financial organization regarding the content discussed in the manuscript.

Data availability

Data will be made available on request.

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