LIBS based Tissue Differentiation for Er:YAG Surgical Laser

Fanuel Mehari[1,2], Benjamin Lengenfelder[1,2], Robert Figura[1], Florian Klämpfl[1] and Michael Schmidt[1,2]

[1]*Friedrich-Alexander-Universität Erlangen-Nürnberg (FAU), Institute of Photonic Technologies (LPT), Konrad-Zuse-Straße 3/5, 91052 Erlangen, Germany*

[2]*Erlangen Graduate School in Advanced Optical Technologies (SAOT), Paul-Gordan-Straße 6, 91052 Erlangen, Germany*

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Abstract: The analytical technique laser-induced breakdown spectroscopy (LIBS) is becoming an attractive technique in the field of medicine. One emerging application is the differentiation of biological tissues in real-time during laser surgery. This work attempts to further investigate the use of LIBS together with a surgical Er:YAG laser. The main goal here is to investigate the effect of body fluids as potential contaminants during LIBS based differentiation of soft tissues. Furthermore, the work attempts to exploit the use of the surgical laser as a cleaning laser and compares the effect when only the LIBS laser is used for tissue differentiation. The study shows that body fluids have a significant influence on the LIBS spectra and that a surgical laser might serve as an in-vivo cleaner leading to improved tissue classification during laser surgery.

1 INTRODUCTION

Lasers have become one of the most important tools used in modern medicine. Due to the unique intrinsic properties of laser light, such as monochromaticity, focusability and high intensity, lasers are being used in general surgery (Walter, 1999) as well as in specialized disciplines like dermatology (Goldberg., 2013), and ophtalmology (Solomon, 2009). One of the most common lasers used as laser scalpel is the Er:YAG since it offers very high absorption in water and thus efficient processing for all tissue types. The advantages laser surgery brings about include providing a sterile surgery technique along with highly precise treatment areas with little to no thermic damage. However, the laser scalpel lacks any feedback including tactile information and it becomes difficult to operate without inflicting damage to critical tissues such as muscle or nerves. This problem leads to the investigation of various feedback modalities providing tissue discrimination for laser surgery. As a consequence, optical based techniques for tissue discrimination have gained significant interest. One of the optical techniques that is drawing attention for a feedback system is LIBS. LIBS uses a pulsed laser to generate a plasma plume which vaporizes a small volume of a given specimen. Using a spectrometer, the plasma decay emission spectrum is analyzed and then used to identify and quantify the constituent elements the specimen is made of (Cremers and Radziemski., 2013). LIBS has been successfully used to analyze various kinds of tissues under ex-vivo conditions, including biological tissues such as bone and cartilage (Mehari, 2014). Nevertheless, the fact that in-vivo conditions profoundly differ from those outside the body has to be taken into consideration. Tissue surfaces inside the body can be contaminated with body fluids containing various elements that could have an influence on the obtained LIBS spectra.

2 OBJECTIVES

In this work, the influence of simulated in-vivo conditions (by putting a thin saline layer on top of the tissue samples) on the LIBS classification is first investigated without the usage of a surgical laser (single-pulse). In addition, it considers the use of a conventional surgical Er:YAG laser as a cleaning instrument to free the tissue's surface from liquid contaminants prior to LIBS analysis as one possible way to minimize the influence of body fluids (double-pulse). First, the LIBS spectra of contaminated and dry fat and muscle tissue is evaluated without the usage of

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a Er:YAG laser. Second, a conventional surgical Er:YAG laser is used in combination with LIBS analysis for contaminated and dry fat and muscle tissue.

3 MATERIALS AND METHODS

3.1 Single-pulse LIBS

Figure 1 shows a schematic overview of the setup used for single-pulse. The experimental setup essentially consists of three major components and several auxiliary devices. The centerpiece is a Nd:YAG (532 nm) laser whose laser beam is focused onto the tissue samples. Light signals from the LIBS plasma are collected using an array of convex lenses and an optical fiber cable that is connected to a spectrometer for detecting and analyzing the signals. The array of convex lenses for LIBS signal collection is focused onto the tissue surface and aligned with the laser focus. For signal transport to the spectrometer a multimode UV grade fiber cable was used. Spectral analysis is performed with an Echelle spectrograph (Andor Mechelle 5000) of resolving power $\frac{\lambda}{\Delta\lambda} = 6000$. The tissue samples were placed in a petri dish that was put on a XYZ-translation stage to be able to move around the sample in 3D.

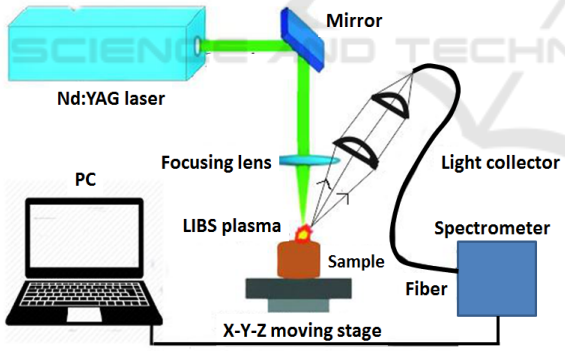

Figure 1: Optical setup for single-pulse LIBS.

3.2 Double-pulse LIBS

An adjusted setup is implemented for LIBS experiments following a laser pulse of a surgical Er:YAG laser (2.94 μm, Glissando, *WaveLight*(TM)), Erlangen, Germany). The Nd:YAG laser in the single-pulse experiments was used. The Er:YAG laser is operated at a repetition rate of 10 Hz with a pulse duration of 350 μs and a pulse energy of 200 mJ. To use it for LIBS experiments in this study, the laser head is fixed steady next to the moving stage and directed onto the tissue sample in a 45° angle. The Er:YAG laser's focus lies slightly above the sample surface. Moreover, it is aligned with the focus of the Nd:YAG laser to ensure that both lasers hit the same area on the tissue surface for one measurement. In order to synchronize the two lasers, a pulse detector for infrared light (DoroTek Lab Bench Detector, $2-12\,\mu$m) is used to detect the reflected light of the Er:YAG laser beam incident on the sample's surface. Similarly to the first setup, this signal is then used to trigger the pulse generator. Subsequently, the pulse generator triggers the Nd:YAG laser with a temporal delay of 100 μs. This delay combined with an internal processing delay of approximately 300 μs from flashlamp triggering to Q-switch activation, ensures that the Nd:YAG laser always fires after the Er:YAG laser's pulse has ceased.

3.3 Sample Preparation and Data Analysis

Fat and muscle tissue samples were extracted from bisected ex-vivo pig heads at the Department of Oral and Maxillofacial Surgery University Hospital Erlangen. Using a knife, the tissues were cut into nearly rectangular pieces of about $5-8$ mm thickness for LIBS measurements.

An isotonic saline solution (9 g NaCl per liter) is used to create a thin liquid layer on the tissue surface to partly mimic a layer of body fluids present at in-vivo conditions, for example, during general surgery. Using a small medical syringe, a few droplets of saline solution are applied onto the tissue surface to be able to spread the liquid in such a manner to establish a consistent liquid layer thickness of approximately $20-30\,\mu$m (measured by OCT) that stays steady over the course of the double-pulse LIBS experiments.

For the LIBS experiments, 6 tissue samples of each, muscle and fat tissue, are measured in both LIBS setups. Each tissue sample is measured 100 times, where one half of the measurement set is obtained under dry conditions and the other one with a saline solution. Therefore, 600 LIBS measurements are taken in each of the experimental setups.

The experimental data obtained from LIBS measurements of the tissue samples is subsequently prepared to undergo different statistical analysis techniques to investigate the effect of the saline solution and the cleaning effect of the surgical laser. Here, statistical analysis is performed to observe the similarity and differences among the tissues investigated under different conditions. As a first step, Principal Component Analysis (PCA) is used to reduce the high dimensionality of the data before Linear Discriminant Analysis (LDA) is performed on the data to classify each

data set into groups. As a final step, the method of Receiver Operating Characteristics (ROC) determines the performance of the classification by LDA. Important values for performance assessment of ROC analysis are the sensitivity (true positive rate), specificity (false negative rate).

4 RESULTS AND DISCUSSION

4.1 Single-pulse LIBS

Figure 2 shows the average LIBS spectrum for dry fat and muscle tissue, which are compared. Due to the fact that fat tissue contains a very high amount of carbon (Woodard and White, 1986), the maximum intensity peak in the LIBS spectrum can be observed at 247.85 nm which corresponds to the emission line of carbon species (Kramida and Ralchenko,). Further we observe a smaller peak at 279.55 nm that corresponds to the emission line of magnesium (Mg) which is contained in fat tissue in a small amount (Woodard and White, 1986). Comparing these values to the average spectrum of muscle tissue, the carbon peak obtained from muscle is significantly smaller which is expected due to the relatively much lower carbon amount in this tissue type. The magnesium peak is stronger in the muscle spectrum. On the other hand, the LIBS spectrum of fat shows several significant peaks in the spectral region 385 – 390 nm which are observed to a much lower extent for muscle tissue. This peak region corresponds to carbon-related molecular emissions from CN (with band head at approximately 388.42 nm) which is related to the higher carbon content of fat tissue. Other peaks of interest for successful tissue differentiation are the sodium peak (Na) at 589 nm, the hydrogen peak at 656.3 nm and the oxygen peak (O) at 777.4 nm. While the sodium and the hydrogen peaks are very comparable for muscle and fat tissue regarding the intensity, the oxygen peak is much stronger observed for muscle tissue. Next step is to compare the spectra of the tissues with saline layer (Figure 3).

The most prominent change in the spectrum is easily observed in the carbon peak at 247.85 nm for muscle and fat tissue. Due to the liquid on the tissue surface, the LIBS laser does not ablate as much tissue material as without the liquid, because the laser energy is now absorbed by the tissue as well as the liquid leading to a smaller amount of energy deposited into the tissue material. Hence, there are less carbon species ionized in the plasma plume. In the same way, a decrease in the intensity values of the magnesium and the CN peak can be observed. At the same time,

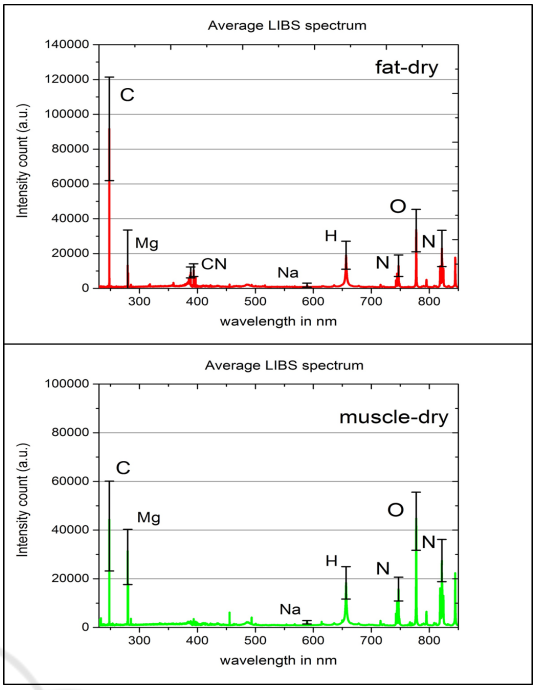

Figure 2: Measured single-pulse LIBS spectra for dry fat and muscle tissue.

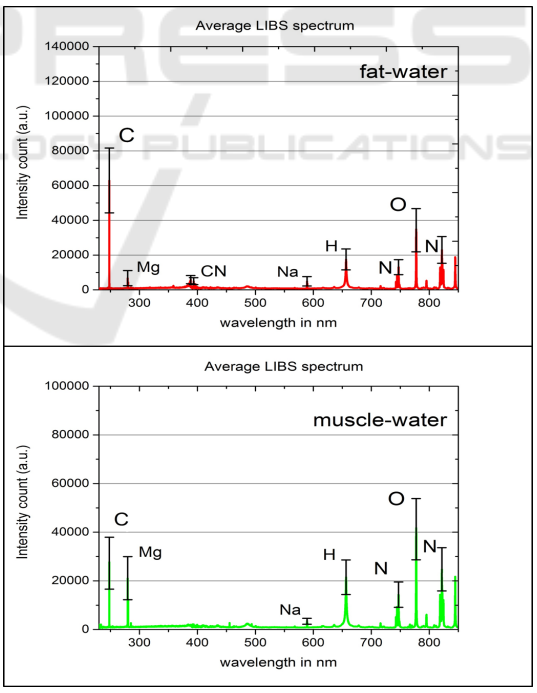

Figure 3: Measured single-pulse LIBS spectra for contaminated fat and muscle tissue.

the sodium peak at 589 nm increases, which can be explained reliably by the use of saline solution that contains 0.9 % of sodium chloride. The increased so-

dium peak proves the assumption that the elements contained in the saline solution will have an impact on the obtained LIBS spectra of the tissue.

4.2 Double-pulse LIBS using Er:YAG Laser

Analyzing the average LIBS spectrum of dry (Figure 4) and wet fat tissue (Figure 5) first, it can be observed that the C and CN peaks significantly change. This is due to the saline solution layer on the tissue surface preventing carbonization of the underlying tissue, so that less carbon species were ablated and detected in the plasma plume. In addition to that, the sodium (Na) peak at 589 nm increased slightly due to the sodium content of the saline solution, which occured to a similar extent in the spectra of the single-pulse setup.

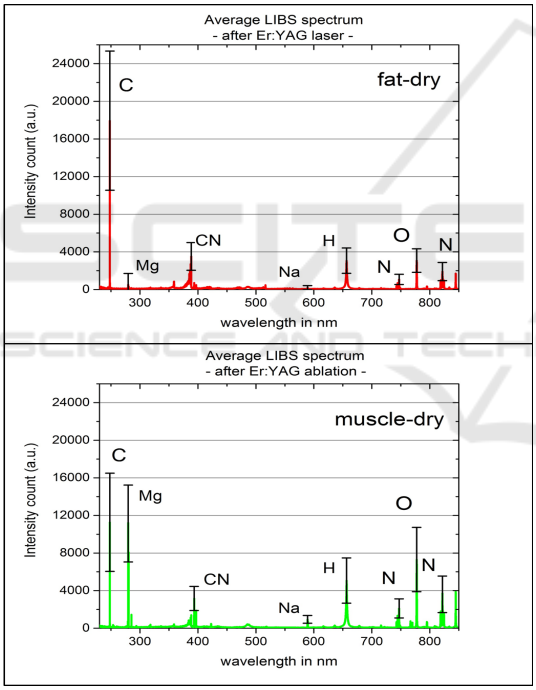

Figure 4: Measured double-pulse LIBS spectra for dry fat and muscle tissue.

Similar to the observations made for fat tissue, the C and CN peaks significantly decreased in comparison to the average spectrum of dry muscle tissue taken in this setup. This can be explained again by the saline solution layer on the tissue surface lessening the process of carbonization by the Er:YAG laser. Moreover, an increase of the sodium, hydrogen and oxygen peaks is observed (Figure 5). Although this may indicate that the Er:YAG laser did not ablate all of the saline solution prior to LIBS analysis, there is

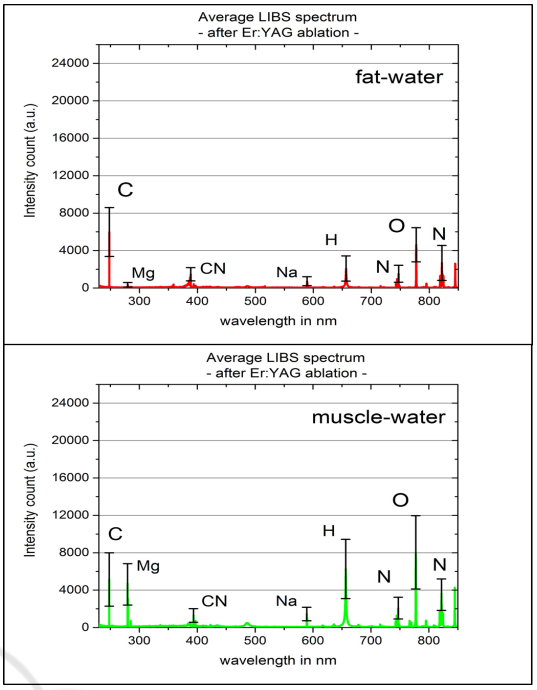

Figure 5: Measured double-pulse LIBS spectra for contaminated fat and muscle tissue.

another scenario potentially contributing to this behavior. Since the Er:YAG laser pulse is incident shortly before the LIBS laser, ablated material by the first laser pulse is ejected perpendicularly to the surface and could interfere with the following LIBS laser. The Er:YAG laser could ablate the saline solution, whose ablated particles are then ionized by the Nd:YAG laser and therefore detected in the plasma plume. This would explain that the Er:YAG laser indeed is able to clean the tissue surface, however, the ablated material is also detected.

4.3 Classification Results

Here, we will only focus on the differentiation of the same tissue type under the two conditions. This is because the differentiation between the two tissue types under the two conditions should not be difficult as their elemental composition is different and hence the effect of the saline layer is not expected to interfere to a level that diminishes their difference. This assumption is in agreement with the results in table 1 which gives an overview on the classification results for single-pulse and double-pulse LIBS. It shows the sensitivity, specifity and AUC (area under curve for ROC analysis). Classification performance is very good for single-pulse LIBS which is considered as disadvantageous since the same tissue type should

Table 1: Classification results for single -and double-pulse LIBS. The sensitivity, specificity and AUC values are shown.

	Sample Combination	Sensitivity	Specificity	AUC
Single-pulse LIBS	**Fat-dry / Fat-water**	0.9967	0.9933	0.9987
	Muscle-dry / Muscle-water	0.9133	0.9400	0.9792
	Fat-dry / Muscle-dry	0.9967	0.9933	0.9987
	Fat-water / Muscle-water	0.9967	0.9933	0.9995
Double-pulse LIBS	**Fat-dry / Fat-water**	0.8000	0.8600	0.8629
	Muscle-dry / Muscle-water	0.8267	0.7567	0.8364
	Fat-dry / Muscle-dry	0.9733	0.9767	0.9911
	Fat-water / Muscle-water	0.9300	0.9267	0.9613

not be differentiated. Comparing the average values of sensitivity, specificity and AUC for both LIBS setups used, it becomes obvious that the classification performance decreases for each classifier when the Er:YAG laser is used. The cleaning effect of the Er:YAG laser causes the average AUC level to drop by around 13 % differentiation for fat and muscle tissue.

5 SUMMARY

The experimental results obtained in this study are expected to lay the groundwork for future soft tissue differentiation under in-vivo conditions after the LIBS technique has proven in recent studies to have the potential for successful ex-vivo tissue differentiation.
The results in this study have shown promising prospects for future in-vivo tissue differentiation using LIBS. Considering that different kinds of body fluids or liquids can be present on tissue surfaces during surgery, it was shown that a thin saline solution layer applied onto the surface has a significant influence on LIBS spectra of fat and muscle tissue. Furthermore, the study indicates that an ER:YAG laser pulse prior to the LIBS laser pulse can serve as an in-vivo surface cleaner leading to improved tissue classification.
In future, the influence of other possible body fluids such as blood needs to be addressed to fully understand and evaluate the potential of LIBS to perform in-vivo tissue differentiation in the future. In addition to that, the potential influence of the liquid layer thickness has to be investigated and other types of tissue such as nerve and skin tissue have to be taken into consideration for those investigations.

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