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Non-invasive in-situ detection of malignant skin tissue and other abnormalities using portable LIBS system with fiber spectrometer and eye-safe erbium glass laser

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Abstract

Portable LIBS, (**L**aser **I**nduced **B**reakdown **S**pectroscopy) systems are capable of real-time material analysis without sample preparation. LIBS systems focus a high peak power laser pulse onto a targeted material to produce a laser spark or plasma. Elemental line spectra is created, collected and analyzed by a fiber spectrophotometer. The line spectra emission data is quickly displayed on a laptop computer display. "Eye-safe" Class I lasers provide for practical in-situ LIBS applications such as detection of malignant skin tissues without the need for eye-protection goggles. This is due to the fact that Megawatt peak power Q-switched lasers operating at 1.54um in the narrow spectral window between 1.5um and 1.6um are approximately 8000 times more "eye-safe" than other laser devices operating in the visible and near infrared.

Key Words: Laser induced breakdown spectroscopy; elemental analysis; fiber spectrophotometer; atomic emission line spectra; laser plasma spark, eye safe laser, detection of malignant skin tissue, portable LIBS system.

Introduction

In this study we establish a medical screening procedure that makes use of a compact "eye-safe" LIBS device capable of real-time in-situ determination of healthy and unhealthy skin tissue without a traditional biopsy [1]. The non-invasive procedure targets human (or animal) skin with a focused Megawatt peak power Class I laser pulse in the "eye-safe" wavelength region between ~1.4um and 1.6um [2]. The laser pulse produces a microscopic plasma spark on the skin surface (Stratum Corneum) that provides line spectra emission of the various elements present. The plasma emission is collected and element lines are instantly identified and measured by a fiber spectrophotometer and laptop computer. Close coupling of multiple spectrophotometer 1mm diameter fused silica signal "pickoff" fibers and plasma yields good signal to noise ratio and low part per million (ppm) level detection of elements. Discrimination between healthy and unhealthy or cancerous skin tissues is accomplished by measuring the relative change in element concentrations as determined by different neighbor element line spectra intensity ratios [1,3,4,5].

Instrumentation

Initial studies were performed with a "breadboard" LIBS system comprised of a Kigre MK-88 high peak power (~0.7 Megawatts) 1.54um Q-switched (5mj/7ns) erbium glass laser with integrated optical beam launch and detection system. This experimental system employed a Stellarnet EPP2000-UV2-14 (200-400nm) fiber spectrometer and a laptop computer loaded with SpectraWiz and laser controller software. A schematic of the device is shown in figure 1. A photograph of the "brassboard" hand held eye-safe erbium glass laser head and beam delivery system is shown in figure 2.

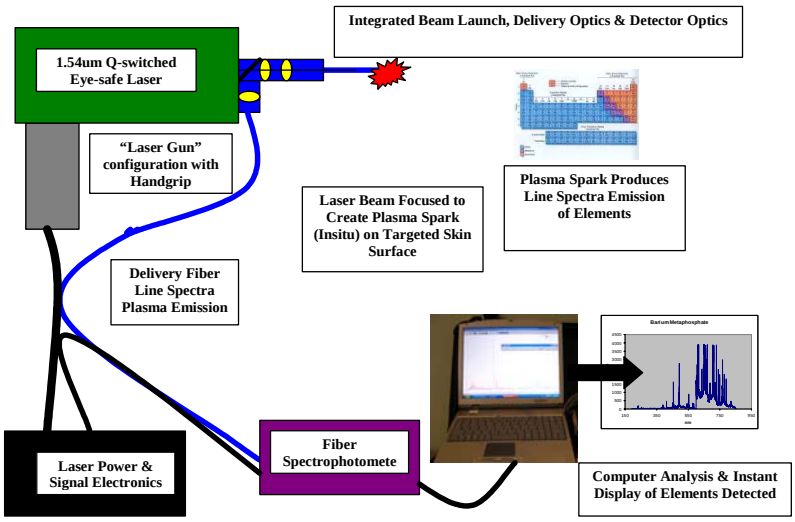

Fig. 1 - Schematic of the eye-safe in-situ LIBS system

Fig. 2 - "Brassboard" hand held laser head and beam delivery system

Experimentation

Our investigations of LIBS elemental analysis of the skin's outer surface began with a search for changes in copper concentration levels. Copper levels in human skin have been reported to be greatly reduced from 163 ppm in healthy skin tissue to 12 ppm in malignant skin tissue [1]. However, mineral concentration values change with skin depth. Higher copper concentration level data reported in other LIBS skin tissue studies were apparently taken from biopsies of deeper skin layers and not from the Stratum Corneum outer skin surface. The plasma spark generated by the LIBS device used in the present study penetrates ~ 25um into the skin's outer surface. Elemental skin analysis studies indicate changes in element concentration with skin depth [5,6]. Figure 3 illustrates increased concentrations of elements such as calcium and potassium in the skin's outer layers and copper and iron concentrations in deeper skin layers [1,3,4,5,6,7,8].

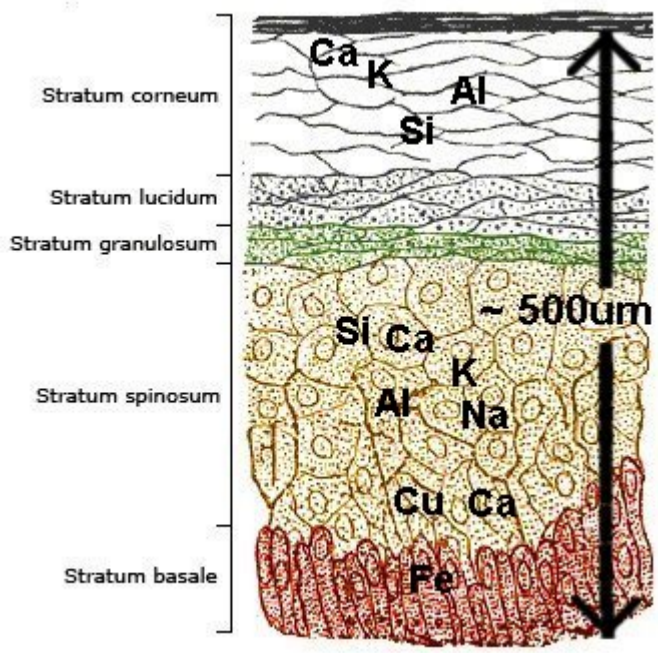

Fig. 3 - General distribution through outer skin layers of selected elements with concentration levels greater than ~100ppm.

Calcium and aluminum exhibit relatively high concentration levels (10-100s ppm) in the skin's outer surface layer with strong peaks near each in the UV part of the spectrum at 393.36 nm and 396.15 nm respectively [3,4, 9,10,11]. The concentration of calcium in malignant skin layers is reported to be nearly double that of healthy skin while the concentration of aluminum is reported to remain relatively constant [1]. The relative intensity of the calcium and aluminum line spectra emission intensity ratios may be a reliable indicator of healthy and unhealthy skin tissues. Tables 1, 2 and 3 show reported

(and estimated) element concentration changes in skin associated with skin cancer and psoriasis [1,3,4,5,6,7,8,12]. Previous studies indicate that we could observe a significant change in the ratio (relative line intensities) of the aluminum and calcium lines for normal in malignant outer stratum corneum skin layer [15,16].

Element	Normal Stratum Corneum Conc. ppm	Malignant Stratum Corneum Conc. ppm	Psoriatic Stratum Corneum Conc. ppm
Al	300	Est. 250	
Ca	273 – 351	Est. 600	841
Cu	2		
Fe	17 - 100		46
Zn	20 - 28		97
Na	1500	Est. 5500	
K	1800		

Table 1. Reported (and estimated) element concentrations for the stratum cornium

Element	Normal Stratum Spinosum Conc. ppm	Malignant Stratum Spinosum Conc. Ppm	Psoriatic Stratum Spinosum Conc. ppm
Al	69	56	
Ca	273 -234	410	727
Cu	163	12	
Fe	35 - 1820	2110	128
Zn	45		50
Na	2600	9370	
K	5840	5150	

Table 2. Reported (and estimated) element concentrations for the stratum spinosum

Element	Normal Stratum Basale Conc. ppm	Malignant Stratum Basale Conc. ppm	Psoriatic Stratum Basale Conc. ppm
Al	69	56	
Ca	273-320	410	1074
Cu	163	12	
Fe	105 - 1820	2110	161
Zn	23		35
Na	2600	9370	
K	5840	5150	

Table 3. Reported (and estimated) element concentrations for the stratum basale

Figure 4 shows LIBS spectra of the outer layer of healthy human skin (back of hand). The element lines identified in figure 4 are consistent with LIBS literature references and the calibration standards shown in figures 5 and 6 [1,8,9,10,11,13,14,17,18]

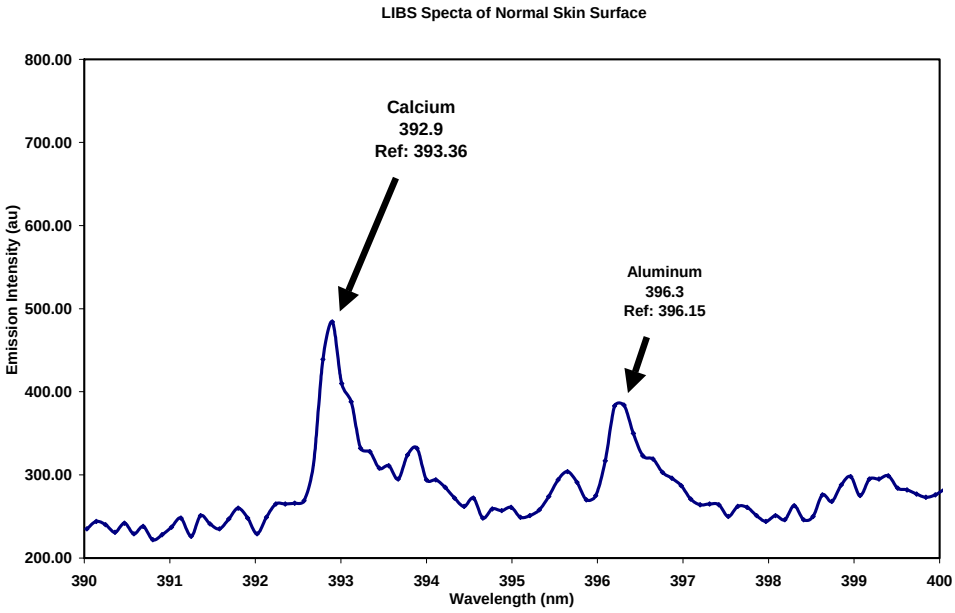

Fig. 4 – LIBS spectra of normal (healthy) human skin in-vivo/in-situ

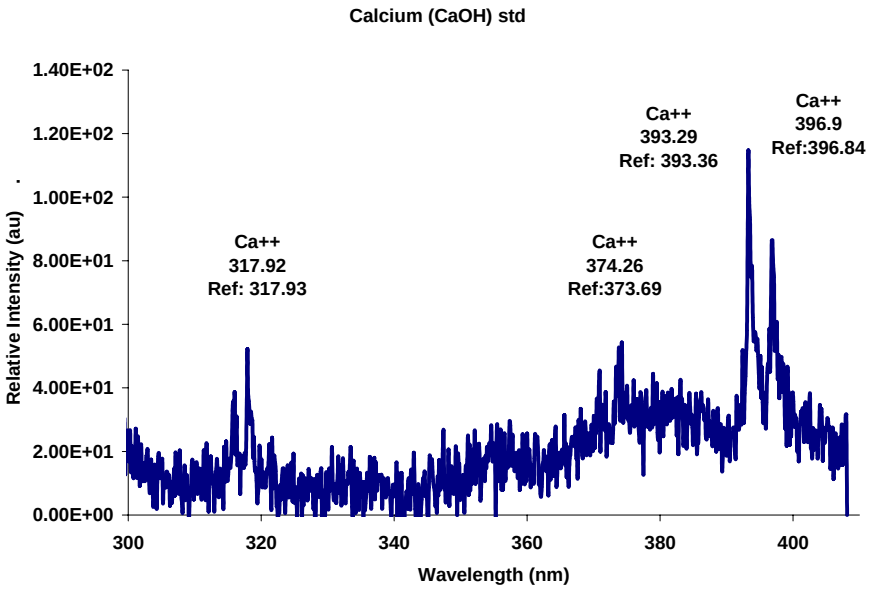

Fig. 5 Calibration of LIBS system calcium lines in-situ

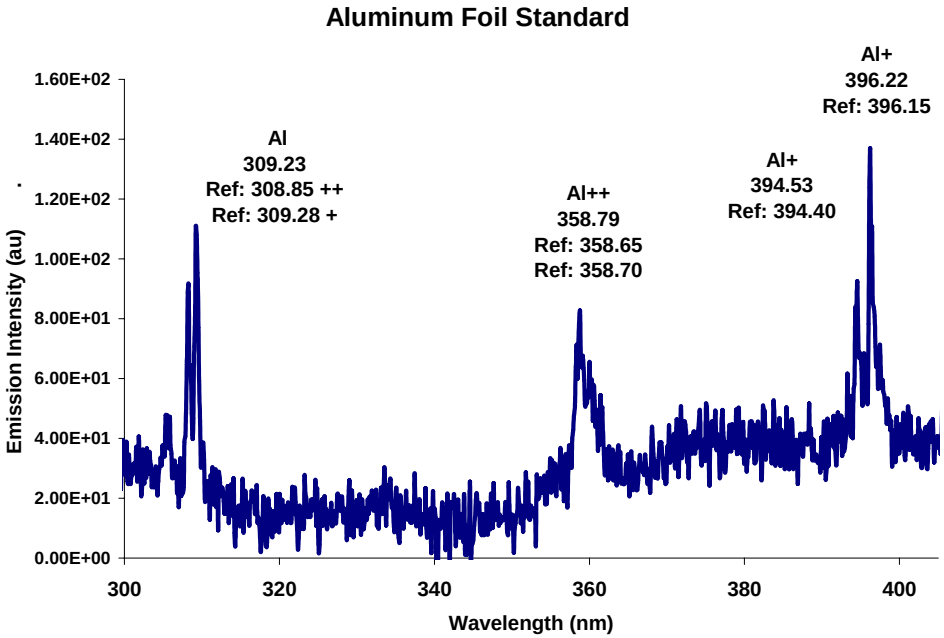

Fig. 6 Calibration of LIBS system aluminum lines in-situ

The UV spectrophotometer used in the initial investigation was configured with a 14 um slit. The wider slit setting allows for better sensitivity and signal-to-noise ratio performance. However, it also degrades instrument line resolution. We estimate the line resolution for the spectra in figures 4, 5 and 6 to be approximately 0.4 nm.

Our approach is to use a type of quasi-quantitative LIBS analysis technique involving observation of the line intensity of neighboring calcium and aluminum peaks. The line intensity will change with the relative concentration of either two different elements or different oxidation states of the same element. In-situ test sample evaluations are quickly gathered and "tagged" preliminarily for further characterized with reference to location and the relative abundance of a given element or element oxidation state [19].

Figure 7 illustrates the estimated change in the line intensities of the calcium and aluminum LIBS spectra expected when a malignant area of stratum corneum skin it tested.

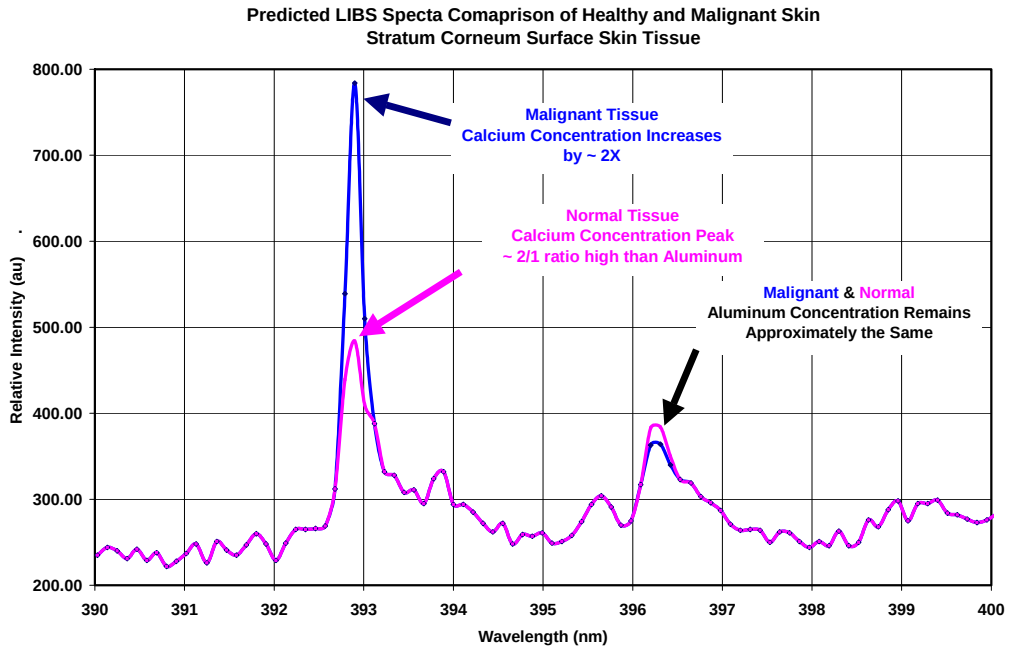

Fig. 7 – Predicted LIBS spectra of malignant and healthy skin in-vivo/in-situ

Future Clinical Studies

Malignant skin tissue samples were not made available for our initial lab testing. A user friendly "brassboard" version of this LIBS system is currently under construction. This prototype LIBS system is to be employed in a Mohs micrographic surgeon's office and used to measure element concentration changes in healthy and malignant skin tissue. The

software and hardware improvements included in the newer brassboard eye-safe LIBS system are expected to increase the line spectra signal to noise ratio. This will provide more reliable LIBS data acquisition and aid the doctor with clinical LIBS skin tissue data comparison and analysis.

Conclusion

We have shown that relative changes in the elemental composition of the human skin may be analyzed with LIBS to discriminate between healthy and unhealthy tissue. Further LIBS system research of this nature, should lead to additional applications. For example, this may be used to detect changes in the composition of the skin that are associated with numerous abnormalities and health issues. These may include the ingestion of drugs or poisons such as amphetamines and pesticides. Skin composition changes may also result from the interaction of two or more prescription drugs. Changes in the composition of the skin are associated with ailments including: abdominal cancer, anemia, back tumors, gastrointestinal bleeding, heart attack, hip cancer, anemia, leukemia, non-Hodgekin's lymphoma, diabetes and sickle cell anemia. The spectrophotometer wavelengths and software may be optimized to detect the specific chemical changes in the human tissues associated with specific abnormalities or health issues.

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