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Chapter

Laser Chemical Elemental Analysis: From Total to Images

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Abstract

This book chapter focuses on laser ablation employed in elemental analysis and discusses the fundamentals and instrumentation of the laser-induced breakdown spectroscopy (LIBS) and laser ablation inductively coupled plasma mass spectrometry (LA-ICP-MS) techniques. The analytical performance of such techniques, challenges related to calibration, and strategies to improve sensitivity are discussed. In addition, the processes involved in data acquisition and imaging for acquiring the elemental spatial distribution are highlighted, and some representative examples in environmental, biological, medical, and forensic researches are presented.

Keywords: LIBS, LA-ICP-MS, imaging, plasma, mass spectrometry, optical emission, laser ablation

1. Introduction

The association of chemistry and light is so old than human being history, most probably raging from the observation of the solar spectrum to spectroscopic analysis, thus allowing the discovery of new and unknown substances. The advent of laser (acronym to Light Amplification by Stimulated Emission of Radiation) has only served to strengthen this natural bond. With the advances in electronics and computational programs, the lasers have a multitude of applications, from proteins (*i.e.* matrix-assisted laser desorption/ionization, MALDI) [1] to elemental analysis (*i.e.* laser ablation inductively coupled plasma mass spectrometry, LA-ICP-MS, or laser-induced breakdown spectroscopy, LIBS) [2]. The applications are dictated by the laser wavelengths, which, in fact, reflect their energies. For example, for biomolecules, like proteins, wavelengths higher than 350 nm are currently used, and for elemental analysis, 213 or 193 nm are most common.

Because of its modulated power, directionality, and temporal coherence, the laser has become a highly versatile tool, and used in a large variety of applications, from the study of how chemical reactions occur, then to initiate chemical reactions upon irradiation to extremely sensitive and selective means to evaluate the presence of chemical substances of interest [3]. Additionally, and as highlighted by the adage "a picture is worth a thousand words" [4], the laser ablation imaging [5] is another excellent option to greatly enhance the understanding of a studied system.

Then, this Chapter is devoted to elemental analysis, focusing on not only laser ablation ICP-MS and LIBS for qualitative and quantitative analysis, but also on imaging the results obtained from those analyses. Particular emphasis is placed on

the discussion regarding the instrumentation, some processes involved in the image acquisition and formation, and also on the analytical results and figures of merit for a diversity of methods involving different areas as geochemical, environmental, biological, medical, and forensic. Some trends aspects and perspectives in the application of laser in chemical analysis are also the focus of this Chapter.

2. Laser-induced breakdown spectroscopy (LIBS)

The spectrochemical analysis exploits the electronic quantized transitions, which are characteristic of each individual element. An energy source (i.e. flame, plasma, laser, arc) can excite atomic species that emit specific wavelengths or frequencies upon returning to their fundamental state. The emitted light is spectrally resolved and detected to determine the elemental composition of the sample. The use of laser for the ablation process in the spectrochemical and elemental analysis was first proposed by Brech and Cross in 1962 [6]. At that time, the luminous plume produced by the ruby laser on the surface of metallic and non-metallic materials was able to remove a small mass of the target in the form of atoms and small particles, but too weak to provide usable spectra. Thus, an auxiliary electrical spark for excitation of vaporized and atomized material was added [7]. This study marks the conception of laser-induced breakdown spectroscopy (LIBS). Although the instrumentation proposed by Brech and Cross was soon commercially available, the interest in using LIBS rise in the 1980s. Advances in technology, more specifically the development of powerful and robust lasers, high-resolution optics, high sensitive detectors, and fast electronics for data acquisition have all contributed to its acceptance in routine analysis and increasing adoption as a cost-effective alternative analytical technique. Besides the ablation of the sample surface, using powerful modern lasers a microplasma is formed that excites the ablated atoms, ions, and molecular fragments. The plasma continues this excitation, and can also vaporize small ablated particles, atomize and excite atoms, ions, and molecules obtaining a rich emission spectrum used for qualitative and quantitative analysis [8]. LIBS is a highly versatile and adaptable spectroscopy technique. It has increasingly become a powerful tool for fast multi-elemental analysis in several fields of applications such as industrial, agriculture, environmental, food, geological, and biomedical. The growing interest on LIBS is probably due to the simplicity of the technique and instrumentation as sampling and subsequent excitation of atoms, ions and molecules rapidly occurs in one step and in the same system, i.e. there is no transportation of ablated material to another instrument as in LA-ICP-MS. It is a universal technique because any type of sample can yield a LIBS spectrum [8, 9]. The most notorious advantages of LIBS are the direct solid analysis capability, the quasi non-destructive analysis, and the portable instruments for analysis in the field. On the other hand, the technique presents limited detectability and it is not useful for trace element analysis unless physical and chemical enhancement strategies are applied to overcome this drawback.

2.1 Fundamentals and principals of operation

In practice, LIBS is a very simple spectroscopic technique to implement. A high-powered density pulsed laser beam is focused through lenses in (liquid or gaseous) or on (solid) the sample to produce dielectric breakdown leading to plasma formation. Plasma is a partially ionized gas containing atoms, ions and free electrons, and electrically neutral. Once initiated, the plasma induces the ablation of a finite quantity of the sample surface to a condition that may then be excited by the energy

supplied by the same pulse or by a subsequent pulse of the laser beam (double pulse strategy) [9, 10]. Excitation is followed by emission of electromagnetic radiation which is collected, often through a fiber optic cable, and directed into a spectrometer where it is spectrally resolved and further instrumentally detected.

The interaction between a laser pulse and mater to create LIBS plasmas involves a process dependent on characteristics of both the laser, *e.g.* wavelength, irradiance and pulse duration, and the sample, *e.g.* gases, liquids, and solids, which can be conductive and non-conductive samples. When the laser pulse in the nanosecond time regime reaches the sample, the dominant mechanism is the thermal ionization process [9, 10]. A process of scattering transfers the laser energy to the lattice of the spot targeted on the sample causing the melting and generation of larger particles, thus enlarging the size distribution of the aerosol particles [11]. Plasma life stages include plasma ignition, plasma expansion and cooling and particle ejection and condensation. The physics of the plasma generation, evolution, and termination processes are complex. In the case of the analysis of solid samples, *i.e.* the majority of LIBS applications, plasma is initiated when the power density of the laser exceeds the breaking limit of a solid surface. In general, irradiance above 10^8 W cm^{-2} is needed. The breakdown is promoted by the intense electric field gradient of the laser, and atoms, ions, and electrons result from the deposition of energy into the target. Afterward, a high-pressure vapor is produced while the plume compresses the surrounding gas. A shockwave at supersonic speed is generated from the surface towards the surrounding atmosphere during vapor expansion. The absorption of the incident laser energy and transfer to the plasma occurs through the inverse Bremsstrahlung absorption involving interactions between free electrons, atoms, and ions. Free electrons in the hot vapor absorb photons from the incident laser increasing their kinetic energy to ionize additional atoms by collisions. The new electrons absorb more photons from the remaining pulse so that a cascade of ionization is generated [8–10]. Plasma is created having distinctive characteristics, high temperatures (10.000 K), and high electron densities (>10^{17} cm^{-3}). The removed material in the ablation process of the solid samples contributes to plasma formation and expansion. In fact, the plasma is only sustained due to the presence of the ablated material [9]. The plasma expands in a similar way the initial breakdown occurs, at supersonic velocities producing a shockwave, also through the process of inverse Bremsstrahlung absorption. Meanwhile, electron number density and temperature of the plasma changes. The remaining laser energy from the laser duration of the pulse is continuously absorbed by the plasma. Collisions with the surrounding gas reduce plasma velocity of propagation, and then plasma cools down by self-absorption and recombination between electrons and ions, generating neutral species and clusters after plasma extinction [8–10]. Part of ablated mass are particles and these particles create condensed vapor, liquid sample ejection, and solid sample exfoliation, not interesting for LIBS analysis [10].

After 10^{-9} s and 10^{-8} s of the ignition, plasma induced by laser in the nanosecond regime becomes opaque due to laser pulse absorption by electrons in the plasma. It reduces the ablation rate because only a fraction of radiation reaches the sample surface. This phenomenon is called shielding and induces a crater with melted and deposited material around it [10]. Meanwhile, plasma is reheated, and the lifetime and size of plasma are higher. On the other hand, ultra-short pulses (femtoseconds) lead minimum plasma shielding and crater with highly defined edges without melted or deposited materials [9, 10]. This regime of pulse is too short to induce thermal effects in the breakdown process. Electronic excitation and ionization, and Coulomb explosion, are the main bond breaking and plasma ignition mechanisms, making the ablation mechanism mostly based on photochemical reactions resulting in vaporization presenting sharper size-distribution solid aerosol than those

generated by nanosecond lasers [11]. In the case of picosecond laser pulses, both thermal and nonthermal processes can occur depending on the laser irradiance.

Initially, the emission spectrum is dominated by a background continuum, while ionic and atomic emission increases with time. The continuum is the main source of background signal (BG) in LIBS, which predominates at the first instants of the plasma life [12]. It is a result of the bremsstrahlung emission (radiant loss of energy due to electron deceleration) and banding (e.g. OH, N_2^+, NH, and NO). A delay time is required to start analytical measurement to avoid high continuous emission. The decrease in the emission intensity of the continuum occurs at a higher rate than the excited atoms or ions in the plasma. Thus, temporal separation is feasible and detectability is improved. In LIBS analysis, the delay time must be experimentally evaluated in order to obtain maximum signal-to-background ratio [12].

Undesirable matrix effects may lead to inaccurate determinations and lower sensitivity. These are usually a consequence of i) physical properties of the sample which change the ablation parameters altering the amount of ablated mass, ii) the presence of an element alters the emission features of another one, and *iii)* the plasma–particle interaction processes, which are time and space-dependent due to the transient nature of the plasma and its spatial inhomogeneity [13]. Elemental fractionation is defined as a non-stoichiometric effect which also depreciates the quality of the results [10, 13]. It occurs when the ablated material failure to represent the real composition of a sample due to preferential evaporation of volatile elements, selective segregation, surface temperature distribution inhomogeneity, among others. Elemental fractionation and matrix effects in laser sampling-based spectrometry methods have been discussed in detail by Zhang et al. [14]. Adequate laser wavelength, energy density, pulse width, and proper calibration using standard reference materials with known composition and matrix-matching strategy can overcome these drawbacks. An advantage of LIBS compared to LA-ICP-MS is fractionation can occur only during ablation, as there is no transportation of ablated material from ablation chamber to excitation/ionization source, or from ICP to mass spectrometer.

Plasma optical thickness is an important parameter in laser-induced plasmas. The emitted radiation is successively reabsorbed by atoms/ions located in the coldest plasma region leading to self-absorption and pronounced non-linear effects [15]. The plasma is called optically thick and usually occurs for the most intense emission lines of elements and for less intense emission lines at higher elemental concentrations.

2.2 Instrumentation

The main components of a generalized LIBS apparatus include (i) laser source; (ii) focusing lenses; (iii) sample support; (iv) optical fiber; (v) spectrometer (vi) detector and (vii) computer for precise control of temporal events, such as: pulse trigger laser and spectrum recording. In the case of a particular application, the specification of each component may be considered and changed. Elements to be monitored, expected concentration, type of analysis (quali or quantitative), sample characteristic (physical state, homogeneity and matrix composition) are common factors to consider when selecting the instrumental specifications.

The laser source generates the laser beam, which main properties are the wavelength and pulse width, both dependent on the laser source and its technological developments. The initial works employing laser in the chemical analysis used visible and infrared (IR) laser sources, such as 693 nm ruby [7, 16] and 1064 nm Nd:YAG (neodymium-doped yttrium aluminum garnet) [17] with a pulse width of μs and ns, respectively. However, further researches demonstrated that the ablation

efficiency of transparent samples using visible or IR wavelengths was harmed due to the poor absorbance of the laser energy by these types of samples.

The evolution of optical technologies led the development of Nd:YAG with wavelengths of 266 and 213 nm by quadrupling and quintupling, respectively, the natural frequency of the Nd:YAG emitted laser. On the other hand, the use of gas excimer as a laser source also enhanced the possibilities of shorter laser wavelengths, such as 193 and 157 nm ArF lasers, which works in the deep-UV region [8–10]. As previously mentioned, the pulse duration is also an important parameter of the laser beam and impacts on the mechanism of interaction between the laser beam and the solid target, the amount of the ablated material, and the crater shape [8–10]. Nowadays, the typical pulsed laser used in LIBS works with a pulse width of nanoseconds or femtoseconds. The best type of laser used for LIBS depends on the application and the desired laser wavelength and pulse duration.

Laser pulses can be focused on the sample using lenses or mirrors. Focal length, diameter, and material are important parameters to achieve minimum spot size (highest power density on target), maximum transmission, and minimum back reflections. For systems requiring an adjustable focus, i.e. lens-to-sample distance may change, a multi-lens system may be required [17]. The collection of the emitted radiation and direct it into the spectrometer is possible by employing lenses and fiber optic or only lenses. Fiber optic transmits the light using total internal reflection, and it is especially useful when the detection system cannot be positioned close to the sample target [17]. A combination of lens and fiber optic is typical as the lens collimates the emitted light improving the focalization into the fiber probe [10].

Once emitted light by the plasma reaches the spectrometer, it is diffracted in order to obtain spectra in terms of signal intensity as a function of wavelength. Czerny Turner is a sequential dispersive system that combines two collimating mirrors and one grating, while Paschen-Runge optics use a concave grating to separate wavelengths allowing simultaneous multielement analysis. Although both designs have been employed in LIBS for many years, Czerny Turner optical mounting is limited by the monoelemental characteristic in which sequential multielemental analysis is impossible in the case of inhomogeneous samples as the elemental composition varies shot to shot, and Paschen-Runge presents relatively low resolution [9]. High-resolution and high spectral coverage devices are essential in LIBS due to the complexity of the emission spectra. Echelle optics combine a low-density grating with a prism and is called an order-sorting device, i.e. light is diffracted in two dimensions. It offers typical spectral bandwidth of 5 pm and high spectral coverage emission, approximately from 200 to 900 nm, which can be recorded with a single laser pulse. In recent years, the Echelle spectrograph has been more extensively used, but require a two-dimensional detector [10, 17].

Detectors devices convert the diffracted optical signal into an electric signal. Photodiodes multiply the current produced by incident light striking photocathode by multiple dynode stages. This is the simplest and inexpensive device but useful only for one-dimensional spatial information from the spectrometer (e.g. Czerny Turner and Paschen-Runge). On the other hand, charge-coupled device (CCD) is constituted by a bi-dimensional configuration of several sensors, each made up of three electrodes over a common substrate of p-type silicon, which allow the acquisition of two-dimensional spatial information obtained by the Echelle system. More recently proposed, intensified CCD (ICCD) is a CCD coupled to microchannel plates to provide time-gated detection of the laser plasma [8–10]. Thus, time-resolved detection down to a few nanoseconds is possible, which is essential to avoid high continuous emission [17].

2.3 Analytical features and strategies to improve sensitivity

The majority of LIBS measurements involve the analysis of solids. Some applications are limited by the relatively low sensitivity of the technique. Limits of detection of LIBS usually range from 1 to 100 parts per million (mg kg^{-1}). Therefore, most applications are focus on major elements, as the technique cannot meet the demands for the detection of trace elemental analysis (parts per billion, μg kg^{-1}). Physical and chemical strategies have been demonstrated to enhance the LIBS detection limits and sensitivity [18]. Increased plasma temperature and electron density are achieved by double-pulse laser method using two laser sources, the use of spatial and magnetic constraint devices, and controlling the atmosphere in which the sample is placed with inert gas (e.g., N_2, Ar, and He) [19]. Nanoparticles (NPs) deposited on surfaces of the solid samples favors ablation processes which mechanisms differ for conductors and insulators samples. For liquid sample analysis, liquid–liquid extraction, liquid–solid conversion, and surface-enhanced LIBS (liquid sample is dried onto the surface of a selected solid substrate before the analysis) have been exploited to overcome problems due to laser-liquid sample interaction, laser energy dissipation, low plasma temperature and sample splashing which depreciate repeatability and reproducibility. The reader is referred to a recent review paper by Fu et al. [18].

The possibility of measuring the molecular emission in LIBS allows the determination of some non-metallic elements from emission bands of diatomic molecules, e.g. fluorine and chlorine have been detected by the emission of CaF, BaF, MgF, CaCl, SrCl, or MgCl [20, 21]. Isotopic analysis based on the discrimination between emission bands of molecules formed by two different isotopes has been reported. The different masses of the isotopes affect the vibrational and rotational energy levels results in molecular isotopic shifts which are exploited in the isotopic determinations [21].

Different data acquisition modes are possible in LIBS analysis and it is selected depending on the goal of the experiment. Using just one laser pulse or using repetitive laser pulses, localized microanalysis with lateral and depth profiling information is easily obtained. For image-based analysis, a generation of a series of plasmas at different positions on the sample following a scan sequence is necessary. Most of LIBS imaging instruments rely on an XY stage that moves the sample instead of moving the laser beam because of a greater collection efficiency from a fixed plasma plume. LIBS imaging analysis is later discussed in this text, and additional information can be found in the review by Jolivet et al. [22].

An important innovation in LIBS is the handheld instruments commercially available for analysis in the field, especially useful when the sample cannot be moved. Some instruments present capability of chemometric analysis by means of proprietary software, video targeting, and an argon purge of atmosphere neighboring the target in order to improve sensitivity. Applications in agriculture, environment, industry, and cultural heritage can provide information to solve important economic and historical issues. An impressive breakthrough of this technique is the use in planetary geology on a Mars mission for remote sensing.

3. Laser ablation inductively coupled plasma mass spectrometry: LA-ICP-MS

With the development of laser technologies and the increasing demand for specific applications in the direct analysis of solids, in 1985 Alan Gray [16] demonstrated the coupling between a ruby laser ablation system with an inductively

coupled plasma mass spectrometer (LA-ICP-MS) for monitoring Si, Al, Fe, Ca, Mg, Na, K, Mn, and Ti in pelletized standard powdered rock samples. Since its application, the area has been growing and one indicator of that is the number of scientific works published: more than 15,000 research papers related to LA-ICP-MS in the last 6 years (source: www.sciencedirect.com, September 10th, 2020).

The interest in the LA-ICP-MS technique is related to its impressive characteristics, such as the possibility to acquire elemental and isotopic information by direct sampling of nano, and even pico or femtograms of solid materials in the micrometric scale, and limits of detection around low parts per million (in some specific cases hundreds of parts per billion). Additionally, the image-based analysis to study sample heterogeneity and elemental or isotopic distribution in a surface contributed to its acceptance [23, 24]. These almost unique characteristics permit the use of LA-ICP-MS in many fields of science, such as geochemistry, forensic, environmental, materials, medical, and biological, in specific applications that were not possible by conventional elemental analysis and sample pretreatment.

3.1 Principles of operation

The LA-ICP-MS technique works based on the coupling of a solid sampling system, the LA system, with a powerful elemental/isotopic analytical technique, the ICP-MS. A high-power laser beam, focused on the sample surface through an optical system promotes a huge and instant increase of the temperature of the target sample and transfers a discrete sample volume to the vapor phase. A solid aerosol is generated in an ablation chamber because of this interaction between the laser beam and the sample, and this process is named laser ablation [2, 25].

The solid aerosol generated carries the information of the elemental and isotopic composition of the sample ablated (analytes and matrix components). To acquire this information in terms of analytical data, the aerosol is transferred to the ICP-MS by a gas stream through a connection tube to the ICP. In the ICP, a high-temperature argon plasma induced by a radiofrequency, the aerosol is digested, and its solid constituents are vaporized, atomized, and ionized [2, 25].

The ions generated into the ICP are extracted, through the interface region, to the mass spectrometer (MS), the instrumental component responsible to separate and detect these ions. After the extraction by the interface region, the ion optics conduces the ion beam up to the mass analyzer device, a high vacuum region in which separation of the ions based on its mass-to-charge ratio (m/z) occurs. The ions are further detected by a specific detector that generates an electric impulse due to the interaction of the ions on its surface [2, 25].

The analytical signal profile observed in a typical LA-ICP-MS analysis is a transient signal characterized, in general, by the counts per second (intensity) of the monitored ion as a function of the ablation time. The specific characteristics of the LA-ICP-MS instruments available for chemical analysis are dependent on each instrumental component type and its principles of operation discussed in the next sub-section.

3.2 Instrumentation and its fundamental characteristics

As mentioned before, the LA-ICP-MS permits different instrumental setups that can impact on mechanisms of the interaction between the laser beam and the solid sample, the separation of the ions in the mass analyzer, and the analytical response of the instrument during analysis. The main components of LA-ICP-MS instrument are the laser source, ablation chamber equipped with a CCD camera, and transport tubing connected to the ICP-MS. The ICP-MS, in turn, can be composed of different

mass analyzer types, which presents specific analytical features, and the detector. The main characteristics of each LA-ICP-MS component are discussed below, focusing on principles of operation, commenting on the potentialities and limitations, as well as its technological developments and improvements.

3.2.1 Laser ablation system

The laser source is the heart of a laser ablation system because it confers the main properties of the laser beam and thus, the main characteristic of the ablated material. It was previously mentioned, in the LIBS section, the coupling between laser radiation and the solid sample surface promotes the ablation depending mainly on the laser wavelength and pulse width. Readers are referred to as sections 2.2 and 2.3. Besides the efficient coupling, these parameters impact the size-distribution of the aerosol particles and the crater shape. In general, the ablation rate increases by increasing the laser energy (shorter wavelengths), and smaller particles of the solid aerosol are obtained using femtosecond lasers, which are required to guarantee the efficiency of the transport and posterior digestion of these particles into the ICP. The most common pulsed laser used in LA-ICP-MS present nanoseconds or femtoseconds pulse width and short wavelengths (e.g. 213 nm, 5th harmonic solid-state Nd:YAG laser).

Different from LIBS which sample holder can be open support, in LA coupled systems, such as LA-ICP-MS, a closed gas-tight compartment denominated ablation chamber is required. The ablation process occurs in the ablation chamber, which presents a transparent window in the wavelength of the laser beam, and the gas streaming transports the aerosol to the ICP. The ablation chamber is coupled to a CCD camera to improve sample visualization and to define the specific position of the sampling target on the sample surface using the LA software. The types of ablation cell designs are vast, including commercial and customized, but some requirements are needed for the efficiency of the role of ablation chambers.

In general, ablation chambers must provide a gas environment that permits an expansion of the aerosol generated to ensure a small-size particle-distribution, and an adequate gas-flow for an efficient transport of the solid aerosol to the ICP avoiding memory and fractionation effects. Thus, the ablation volume, the flow dynamics of the gas stream, and the diameter and length of the transport tube are determinant for the features of an efficient ablation chamber [26]. The carrier gas also plays an important role in chemical analysis. Lighter carrier gases, such as helium, improves the efficiency of the ablation process and particle transportation enhancing sensitivity of the analytical method and reducing drawbacks related to fractionation in the transport process [27]. Recent developments in the design of low dispersion systems, rapid response ablation cells and their impact on bioimaging applications was recently discussed by Van Malderen et al. [28].

3.2.2 ICP and mass analyzer devices

LA system generates a laser beam that is responsible for removing an amount of sample and transferring its constituents to the vapor phase. From this point, is the role of the ICP-MS to analyze this material and provide analytical information regarding its elemental and isotopic composition. Because the analytical entities monitored by ICP-MS are mainly mono-charged positive ions, ICP-MS instruments must first be able to generate ions from the aerosol constituents of the sample. The ICP's are ion sources in which plasmas are produced by the energy transferred from a radiofrequency generator to a gas flow into a concentric quartz tube (torch) via a magnetic field through an induction coil [29]. The plasma has the ability to ionize

most atoms of the elements presented in the periodic table due to its high-temperature (around 10,000 K) and high electron density. The inductively coupled plasma formation mechanism will not be discussed in this chapter, but we encourage the readers to look for it in Thomas, 2013 [30].

As the ions of the sample composition are formed in the plasma, including the analytes and concomitants, they are conducted towards the interface region to enter the mass spectrometer. This interface region is composed of metallic cones, normally two (sampler and skimmer cones) which extracts these ions. Then, ions go to the mass spectrometer via the ion optics, which are a set of electrostatic lenses that conduce the positive ions to the mass analyzer, and deviates the neutral and negative species, as well as the photons [30].

The heart of the mass spectrometer is the mass analyzer. This component has the function to, based on the mass-to-charge ratio, separate the analyte ions from concomitants, permitting the detector count and acquire the abundancy of the specific element under analysis. For this, there are different arranges of mass analyzers with their principles of operation to separate the ions. The most employed mass analyzer types in LA-ICP-MS are quadrupole systems, magnetic sector, and time-of-flight [30].

The quadrupole system is composed of two pairs of metallic bars, positioned oppositely. It operates as a mass analyzer by applying specific direct and alternate current (AC/DC) in the pair of rods that in consequence, for each specific AC/DC applied, only the desirable m/z of the ions presents a stable trajectory in the quadrupole, reaching the detector. The trajectory of the other ions will be unstable and will exit the quadrupole before reaching the detector. This mass selection occurs sequentially, and each m/z determined has an optimum AC/DC voltage applied on the quadrupole. This characteristic, as well as the design of the quadrupole, confers a resolution ranging from 0.7–1.0 *a.m.u*. It is possible to optimize the parameters of quadrupole to increase the mass resolution, but a compromise with the sensitivity must be attempted. This relatively low resolution impacts some applications due to the interferences that can be present in the analysis. Some isobaric and polyatomic species formed in the plasma can present the same m/z of the analyte and then depreciate the accuracy of the analysis. For this, the new quadrupole-based ICP-MS's presents a collision/reaction cell or interface that uses a reactive or non-reactive gas to break polyatomic interference species, reduce their kinetic energy or react with the analyte generating a new analyte ion free of interference, then allowing accurate results. Although the limitations of single quadrupole devices in terms of resolution, the low price, and suitability for most quantitative applications make it the most widely used mass analyzer in ICP-MS analysis. The newest inductively coupled plasma tandem mass spectrometry, popularly called triple-quadrupole ICP-MS presents an additional quadrupole located before the collision/reaction cell. It confers the possibility to filter non-analyte ions in the first quadrupole, preventing the production of unwanted species that could immediately interfere on the m/z of interest and the second mass analyzer to deal with interferences using mass-shift or on-mass strategies. It has shown great results of accuracy in some specific difficult applications for single quadrupole ICP-MS [30].

Another mass analyzer type is the double-focusing magnetic sector technology. This mass analyzer device operates with two analyzers, a magnetic and an electrostatic. This design of mass analyzer presents greater resolution and interference overcoming compared to the quadrupole, and is applied in studies that need this resolution, such as isotopic ratio monitoring and analyte quantification in complex samples. The principles of m/z separation in such mass analyzer are based on the dependence of the deflection angle of the ion beam by a magnetic field to the mass of the ions, and the alignment of the ions with the same m/z in the electrostatic

field, due to its kinetic energy. The combination of these two mechanisms of separation improves the resolution and the precision of the measurements. With a single detector, the mass separation is sequential, by varying the magnetic field in the deflection separation, allowing a specific m/z at a time to reach the outer slit and the detector. But, if this double-focused magnetic sector technology is arranged with an electrostatic sector field followed by a magnetic sector field and a detector plane, known as multi-collector, the detection of the ions is simultaneous and the precision of the ion measurement is improved. This technology is the state-of-the-art instrumentation for high precise and accurate isotopic ratio studies. The disadvantages of the double-focusing magnetic sector technology are related to the price of these instruments and, in the case of multi-collector, the loss of resolution, impacting on the analysis of complex matrices [30].

The last discussed mass analyzer technology is the time-of-flight (ToF) mass analyzer. Its principles of operation are based on the velocity dependence of the ions to the m/z, for ions generated at the same time and with the same kinetic energy. For this, packages of ions are simultaneously introduced in the mass analyzer by a specific ion optics, and, in a flight tube, the package of ions is accelerated due to a constant voltage, through a known distance. As the kinetic energy of the ions is the same, they will reach the detector in different times-of-flight due to their differences in m/z. In general, lighter isotopes reach the detector first, followed by medium m/z ions and, finally, heavier ions. These principles of operation can produce 20,000 mass spectra per second and, in contrast with the quadrupole technology, there is no dependence on the resolution and the sensitivity for the ToF analyzers. So, it came in the scientific community as an instrument with higher resolution compared with the quadrupole system, faster and is applicable not only for isotope ratio studies but also for fast qualitative screening and quantitative analysis of complex matrices [30].

As can be seen, there are many possibilities of LA-ICP-MS setup, whether the LA system, with the properties of the laser source and ablation chamber, or the ICP-MS specificities, such as the ICP conditions, mass analyzer devices, and their particularities, not mentioning the detector types, that are not less important, but were not discussed in this chapter due to de variety of designs in the market. In this way, LA-ICP-MS hardware's designs will provide specific analytical features for each instrument setup, that will be commented in general in the next sub-section, to a better understanding of LA-ICP-MS potentialities and limitations.

An innovative approach that exploits the combination of the two techniques, LIBS and LA-ICP-MS, is known as Tandem LA/LIBS and commercially available (**Figure 1**). It provides simultaneous and complementary information for total and spatially resolved mapping of major and trace elements. Emission spectra are simultaneously monitored from the micro plasma created by the laser during ablation/sampling.

3.3 Analytical features, challenges and limitations

The capabilities of LA-ICP-MS as an analytical technique starts with the characteristics of the LA system. It has the ability to direct sampling with micrometric spatial resolution, varying from 4 to 200 μm in most instruments. As the ablation chamber can move on the axis x and y, the ablation can be performed in spot analysis and also by making ablation lines over the sample area of interest, and this is the sampling principle for image-based LA-ICP-MS applications later discussed [2, 24, 25].

For quantitative applications, and especially using quadrupole-based ICP-MS, the LA-ICP-MS can achieve a precision of 2–5% for the determination

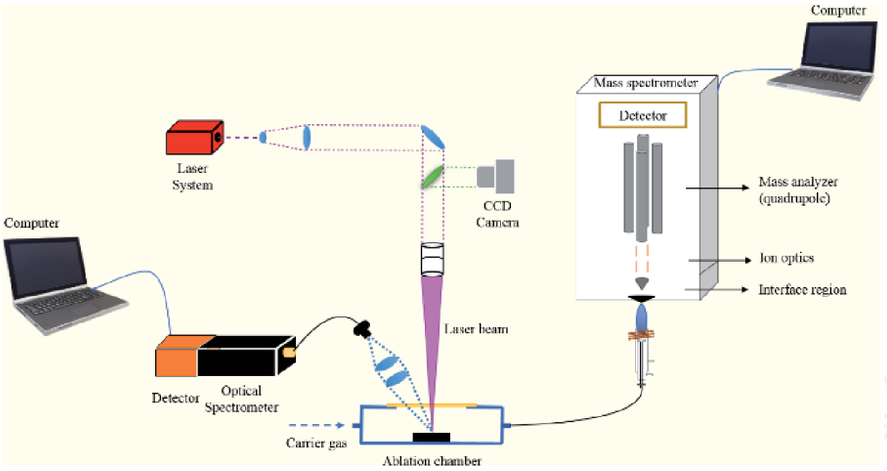


Figure 1.
Schematic diagram of the for simultaneous LIBS and LA-ICP-MS.

of homogeneous elements in solid samples. For isotopic ratio studies and using double-focusing magnetic sector ICP-MS with multi-collector, the LA-ICP-MS allows a precision, in some cases, of 0.001–0.005% in the isotope ratio measurement. For heterogeneous samples, the precision is not the goal of the analysis, but the evaluation of the elemental distribution and its concentration in different areas of the sample [2, 24, 25].

In terms of limits of detection, it varies depending on the sample matrix and instrumental setup employed, usually ranging from hundreds of ng g^{-1} to a few μg g^{-1}. Due to its limit of detection and the low mass ablated, LA-ICP-MS can cover a wide range of concentration, allowing the determination of trace, micro and major elements directly in the solid sample analyzed [2, 24, 25].

Although the potentiality of LA-ICP-MS, there are some drawbacks that the scientific community have devoted effort to overcome, and that the users must give special attention. The critical limitations of LA-ICP-MS are derived from the nature of the interaction between the laser beam and the solid sample and the transport process of the solid aerosol generated through the ICP. Since the mass removed by the laser beam is dependent on the matrix of the sample and the characteristics of LA system and parameters (laser fluence, spot size diameter, and repetition rate), thus, the analytical signal obtained in the ICP-MS is also matrix-dependent. This fact impacts the accuracy of the analytical method, which will be achieved in the condition that the same mass is ablated from the sample and the calibration standards, and the analyte undergoes the same transportation effects and processes in the plasma until be ionized [2, 25].

However, it is not simple to achieve a suitable solid calibration standard for the vast sample matrices that are analyzed by LA-ICP-MS. The ideal condition is the use of certified reference materials (CRMs), but a limited number of matrix types is available as CRM. It is especially difficult for the analysis of heterogeneous and non-powdered samples. To overcome this drawback, the scientific community has been studying different approaches to calibration. The main strategies are the use of matrix-matched materials, such as lab-made standards, by spiking the analytes in the powdered material that has approximately the same composition of the sample, drying and pressing it into a pellet. In the case of non-matrix-matched standards, solution-based strategies are employed, for example, the use of solution nebulization of liquid standard and mixing it with the aerosol of the sample, to calibrate the method. In all these cases, the homogeneity of the standard must be monitored to guarantee the analytical performance of the external calibration procedure. Additionally, internal standardization is usually needed to correct signal

fluctuations during the analysis. A detailed review of calibration strategies for LA-ICP-MS quantification method was written by Miliszkiewicz et al. [31], and can be checked for more information about calibration strategies [2, 25].

Another drawback in LA-ICP-MS analysis is the fractionation that can occur in an ablation procedure or transport process. As previously mentioned in the LIBS section of this chapter, femtosecond UV lasers could suppress this effect, due to the minimization of the thermal process during the ablation. Aligned with the femtosecond UV laser, a well-designed ablation chamber and transport tubing will permit the small size distribution of the aerosol particles, avoiding fractionation during the ablation and the transportation through the ICP. Another point, and not less important, the optimization of the LA-ICP-MS instrument parameters are recommended to guarantee its suitability to the sample matrix analyzed. Such parameters are the laser frequency, spot size diameter, repetition rate, carrier gas flow rate, auxiliary gas flow rate, and radiofrequency power [2, 25].

In spite of these limitations, a careful dealing with LA-ICP-MS analysis, followed by an adequate optimization of the instrumental parameters, monitoring the possible sources of analyte fractionation, and a suitable calibration strategy allow the LA-ICP-MS users to achieve impressive information of solid samples that could not be accessed using traditional solution-based ICP-MS analysis, enlarging the possibilities of application.

3.4 LA-ICP-MS applications

The fields of science that LA-ICP-MS is applicable are vast, including forensic, environmental, materials, biological, geological, etc. Although the image-based analysis using LA-ICP-MS composes the state-of-the-art of this technique, the use of LA-ICP-MS in studies involving total elemental analysis are also useful and confers interesting information about plenty kinds of samples that are pointed out above.

The use of LA-ICP-MS in forensic science can provide information of crime evidence without destructing the sample (usually obtained in a small amount). For example, the elemental composition of tape packaging samples could be used to classify them according to their origin rolls [32], and the elemental composition of glass evidence also allows for forensic crime elucidation [33]. The analyses of difficult to prepare samples are feasible using LA-ICP-MS, which is the case of hair samples. Ash and He [34] demonstrated that LA-ICP-MS was used to understand the poisoning dynamics of thallium in a criminal case, including understanding the increasing of doses of poison and the time interval. Levels of Cu, Zn, and Hg monitored in hair samples of different grizzly bears showed adequate correlation with the duration of salmon consumption and the amount of it [35], which is an important environmental monitoring method of mammal's wildlife.

LA-ICP-MS is applied also in conjunction with separation techniques, such as thin-layer chromatography (TLC), to improve the quality of the data. The use of TLC-LA-ICP-MS could provide quantitative information of gold nanoparticles (AuNPs) by separating them from gold ions, as well as AuNP size information by using a specific mobile phase in the TLC separation [36]. TLC was also employed in fractionation studies of S, Ni, and V in petroleum using LA-sector field ICP-MS [37].

The reader is referred to critical reviews of recent LA-ICP-MS applications, such as by Lobo et al. [38], where isotopic analysis in biological studies are discussed; or Limbeck et al. [39], where the challenges and advances in the quantitative analysis are detailed. Another interesting work by Pozebon et al. [40] demonstrates the use of LA-ICP-MS analysis of biological samples bringing information of novel

developments in instrumentation, methods of calibration, and applications in modern demands, such as single-cell analysis and NP uptake.

4. Elemental distribution imaging via LA-ICP-MS and LIBS techniques

Images are present in daily life of the population in different contexts, such as through the image created by the eyes, enabling observation of the environmental around us; through pictures and photographs that record different personal or historical moments; and also, via magnetic resonance imaging (MRI) or X-ray computed tomography (CT) which contribute to medical diagnostics. In the chemistry context, imaging is a process that transforms the spectral information of atoms and molecules present in the solid sample surface, in a high resolution image through the application of powerful spectral techniques as LA-ICP-MS, LIBS, Raman [41], X-Ray Spectroscopy [42] and Secondary Ion Mass Spectrometry (SIMS) [43].

For the LA-ICP-MS and LIBS techniques, the imaging process occurs through the applications of laser pulses directed at specific regions of the sample surface (*x,y* coordinate), via point by point or continuous lines performing the chemical measurements and obtaining spectral information of the region of interest [22, 44]. In this case, a document (.txt or .log format, for example) is generated for each point or a line containing the signal intensity data of all the elements measured [45]. Due to the complexity and a large number of data obtained, appropriate software for data processing is required to separate the information and generate a data matrix, thus allowing the generation of a final image for each element. A two (2D) or a three (3D) dimensions image can be created for each element in the sample. The 2D image is equivalent just to the surface image and the signal intensity or concentration of the analyte, obtained by the conventional method describe previously. The 3D image can be obtained in two ways, i) analyzing and combining each layer of the sample (volume reconstruction of several 2D images), ii) repeated pulses of laser in the same region, allowing in-depth elemental imaging [46]. The scheme of the imaging process *via* LA-ICP-MS or LIBS can be seen in **Figure 2**.

There are different software for data processing and generation of chemical images, such as Microsoft Excel, LA-iMageS [47], and MATLAB [48]. In the case of LIBS imaging, the use of chemometrics tools has been a great ally in the data treatment due to the complexity of the emission spectra data. Principal component analysis (PCA) and partial least squares (PLS) are commonly used, and also can

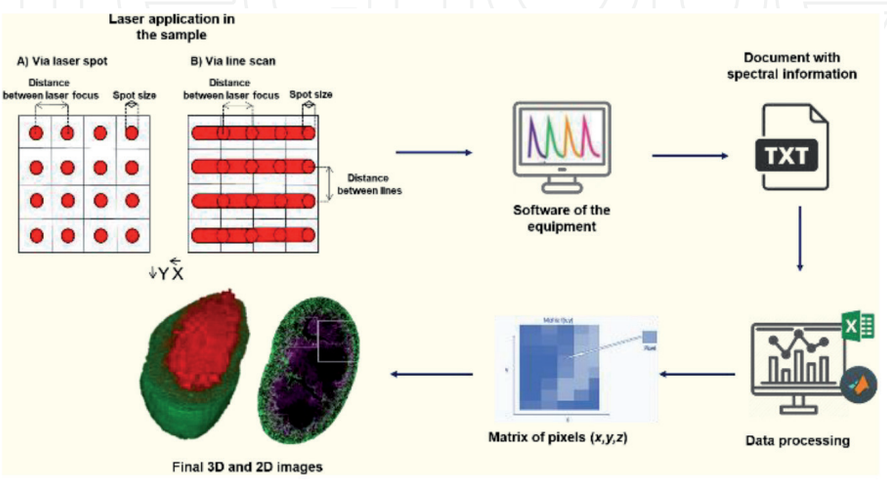


Figure 2.
Steps of the imaging process via LA-ICP-MS and LIBS. Final 3D and 2D nanoparticles images by Gimenez et al. [46], reproduced with permission of Springer Nature.

generate hyperspectral images [22, 49]. The final images are formed by a matrix of pixels, represented by I(*x,y,z*), in which *x,y* are the sample coordinates and *z*, the spectral information. Therefore, the number of pixels that will form the final image will be directly related to the amount of information, image quality, and the spatial resolution that the imaging process can provide.

The spatial resolution is the ability of the imaging method to distinguish two points in the sample surface, also mentioned as lateral resolution. It is correlated to the spot size and line scan direction, the x- and y-resolution. The x-resolution (μm) is related to the scan direction and the pixel size of each data set, obtained by multiplication of the scan speed and the acquisition time. The y-resolution (μm) is correlated to the distance between the lines. Thus, the spatial resolution and, consequently, the pixel size, is a result of the laser spot size, scan speed, acquisition time, and the distance between the measured lines or points. These parameters vary according to the application and optimized instrumental parameters. It is important to mention that LA-ICP-MS and LIBS are considered high spatial resolution techniques [48, 50, 51].

The imaging process has the advantage of accessing spatial and distribution information of chemical species that would not be possible using the conventional method of analysis, as atomic emission spectroscopy (AES) and inductively coupled plasma mass spectrometry (ICP-MS). These techniques usually require sample preparation steps, as decomposition and/or extraction, that cause destruction of the sample and, consequently, of spatial information. One of the major limitations of imaging via LA-ICP-MS and LIBS is the long data acquisition time, varying according to the size of the analyzed sample, scan speed, and laser parameters, as well as making the whole system result in representative images of the system in evaluation [22, 44]. Quantitative imaging based on LIBS and LA-ICP-MS is still a challenge and a controversial topic between researchers. Most methodologies are considered just qualitative or semi-quantitative, but in the literature, it can be observed different studies that aim to developed calibrations and mathematical strategies to transform the relative intensity information into a quantitative image [46, 52]. The applicability of the LA-ICP-MS and LIBS imaging can provide spatial chemical information to solve problems in different areas of science as demonstrated in the next section.

4.1 Applications of elemental distribution imaging via LA-ICP-MS and LIBS

Biomedical researches and clinical diagnosis are some of the most important areas of chemical imaging applications because is necessary to know the chemical specie involved in different diseases and the specific localization in human tissues, thus allowing specific drug development. Recent reviews of LIBS [22] and LA-ICP-MS [53] imaging applied in medical science can be found in the literature.

Moncayo *et al.* applied LIBS imaging of human paraffin-embedded skin samples as complementary biopsy with conventional histopathology sample preparation to detect the differences of the spatial distribution of P, Mg, Na, Ca, Zn and Fe in healthy and malignant skin tissues of cutaneous metastasis of melanoma, Merkell-cell carcinoma (MCC) and squamous cell carcinoma (SCC). In this study, two lens-fibred system and two spectrometers were used to realize the simultaneous detection of all elements. The high-resolution images were obtained using laser shots with 50 μm of step size and an acquisition time of 3 hours for each sample with, approximately, 3cm^2 of the tumor area. As imaging results, high levels of P were observed in all skins in the tumors areas; high levels of Ca and Zn were noticed closest to the tumor and decrease in the areas away from the tumor in the MCC; a gradient level of Ca and Mg in metastatic melanoma and Na, Mg and Zn in

SCC were observed in the left area of the tumor, allowed proper identification and discrimination of the three different skins analyzed by LIBS imaging [54].

Applying quantitative LA-ICP-MS imaging using line scan mode, the spot diameter of 10 μm, 20 μm s^{-1} scan speed, and matrix-matched calibration, Crone *et al.* could evaluate the ineffectiveness of Pt drug-based in bone metastasis treatment in a mouse tibia samples, in which are generally considered an unsatisfactory and scarce treatment. According to the results, there is no efficient transport of the drug into the bones, in which presented lowest concentration of Pt and, the highest concentration were found on the outside of the bone samples, confirming the hypothesis that the Pt drug did not penetrate the bones [55].

Studies involving NPs has increased in the last years because of their versatility of applications, such as in medical science (drug delivery, label method or immunotherapy) and environmental (nutrient or toxic transport) [55–57]. Imaging the distribution of Ag, Cu, and Mn in soybean leaves cultivated in the presence or the absence of AgNPs (40 nm average size) and also using $AgNO_3$ indicated Ag poor translocation to leaves. Additionally, the homeostasis of Mn and Cu is highly affected in plants cultivated in the presence of $AgNO_3$ compared to those cultivated in the presence of AgNPs (**Figure 3**) [56]. Additionally, the study of bio-distribution of NPs is a challenge because of their small size (< 100 nm), so high spatial resolution imaging techniques present as promising assessment tools to evaluation at the cellular level and macroscales.

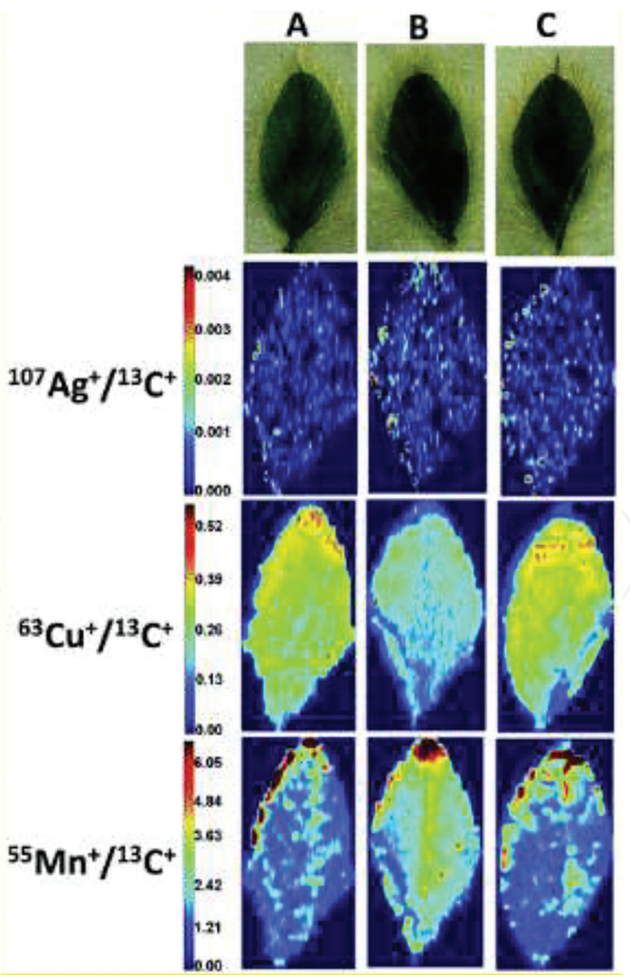


Figure 3.
Ag, Cu and Mn distributions in soybean leaves for the groups (A) control, (B) $AgNO_3$ and (C) AgNPs (total silver at the end of cultivation is 12 mg kg^{-1}), using $^{13}C^+$ as the IS. Each real soybean leaf is presented on the top of this figure [56] - reproduced by permission of The Royal Society of Chemistry [56].

Krajcarová *et al.* used double-pulse LIBS image mapping to verify the spatial distribution of Ag^+ and AgNPs in a small root cross-section of *Vicia faba* and their differences in transport efficiency. Ag^+ ions are toxic for plant tissues and the AgNPs are the most used as an antimicrobial agent in many products applied in plants. However, the later can interfere in the growth and biomass production if absorbed by the roots of the plants. Using a 50 μm of image resolution, the authors observed a clear difference between the localization of Ag^+ ions and AgNPs. AgNPs were found in just one part of root layers, close to the rhizodermis, and had no significant visual effects on the roots, just reduced the lateral root formation. Meanwhile, Ag^+ presented higher signal intensities and homogeneous distribution in the root cortex and caused reduced root lengths, darker color, and absence of lateral roots [58].

LA-ICP-MS imaging and NPs was used by Cruz-Alonso *et al.* to evaluate molecular distribution and quantification in human retina sections of 4 postmortem donors. Gold nanoparticles were applied as antibody-conjugated nanoclusters (Ab-AuNCs) to identify metallothioneins (MTs), which are protective to the neural retinal cells against oxidative stress. The LA-ICP-MS quantitative imaging (expressed in ng of MT g^{-1}) was applied in line scan mode with 10 μm of spot diameter and a matrix-matched analytical curve was used as a calibration strategy. As the sample is a biological tissue, the authors replaced the commercial ablation chamber by an in-house chamber with a reduced internal volume and cell temperature constant at −20°C, keeping the sample integrity. As results, the Ab-AuNCs allowed observed that the MTs present distribution in some principals retinas layers, known inner and outer nuclear layers and ganglion cells layers, as well as a present different concentration between the 4 postmortem donors, which is correlated with the biological diversity characteristics of each individual patient [52].

Different applications of imaging process applied to environmental studies [22], and translocation and accumulation of metals in plant tissues [59]. Paleoclimate and geological researches developed important studies in environmental science aiming to understand climate and environmental impacts using tree rings and speleothems as natural archive samples. These samples present high temporal resolution, allowing temporal reconstruction because changes in environmental or climate conditions can interfere on growth periods and elemental composition. Locosseli *et al.* demonstrated with LA-ICP-MS imaging that the decrease of Pb through the tree rings of *Tipuana tipu* (Fabaceae) could be correlated to the decrease of Pb concentration in gasoline of São Paulo (Brazil). In this study, high-resolution scan mode with x-resolution of 31.5 μm, scan speed varying of 60–100 μm s^{-1}, and LA-iMageS software was used [60].

A limitation in environmental studies is the small sample size that is allowed in the ablation chamber used in LA-ICP-MS, limiting experimental sampling. As an advantage of LIBS imaging, the ablation chamber does not be needed to be closed. Recently, Cáceres *et al.* reported the development of a method that enables the create megapixels elemental image of large speleothems (25 cm long) and coral (8 cm long) surfaces by fast and high-resolution LIBS imaging. Approximately 360,000 pixels $hour^{-1}$ were obtained in a 10 μm of lateral resolution, 100 Hz (100 pixels s^{-1}) as operation speed, and 8 hours per 2D imaging created with LasMap software. It allowed the visualization of fibers and specific regions of coral with the Mg/Ca, Sr/Ca and Na/Ca images, and according to the authors, the speleothems images demonstrated that compositional variations of Sr/Ca and Mg/Ca are not random but they result of variations of paleoenvironmental proxies [61].

As previously mentioned, LA-ICP-MS and LIBS can have the same initial laser system (**Figure 1**), which is a multimodal method in the imaging process.

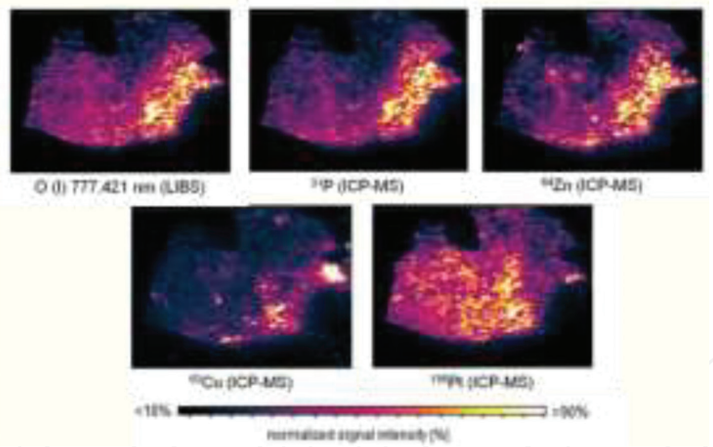


Figure 4.
Multimodal images of human tumor. Adapted from Bonta et al. [62] with permission from The Royal Society of Chemistry.

This approach was applied for Bonta *et al.* to create an elemental mapping of biological tissues with a tumor of human malignant pleural mesothelioma (MPM) (**Figure 4**).

Using a line scan with 40 μm of spot diameter, 40 μm of lateral resolution, 80 μm s^{-1} of scan speed and the software ImageLab to create the images, the authors observed that O, P, Zn, and Cu exhibit similar heterogeneous spatial distribution in the tissue, with high signal intensity in the tumor region, correlated with high number of activated proteins and their cofactors in this area. Different elements were detected in the tumor area, the presence of Pt, originated from common anti-cancer drug cisplatin, was detected in the healthy area, but not in the tumor's region [62]. This information would not be observed using a conventional method of analysis via decomposition.

5. Conclusions

Remarkable research and developments in laser technology and atomic spectrometry have promoted LIBS and LA-ICP-MS techniques to the height of its maturity in terms of both instrumentation and applications. Sensitivity, precision, and accuracy have continuously been improved, and obviously dependent on the experimental configurations used (type of laser, spectrometers, and detectors). These techniques allow the direct analysis of solids which is a significant advantage for the analysis of difficult-to-digest materials. High spatial resolution capacity allows for detailed information of the sample surface composition. All these features result in promising solutions for studies which the spatially resolved elemental information are required to provide a better understanding of the sample with significant advantages over conventional bulk analyses, such as in medical, environmental and technological science. Because LIBS present simpler instrumentation and an interesting trend is the portable instruments particularly attractive for in situ applications such as in agriculture and environmental analysis. Still, some researches focus on quantitative developments and calibration strategies to overcome remaining drawbacks such as the lack of CRMs, matrix effects and fractionation as well as multimodal system and isotopic analysis by LA-ICP-MS.

At this stage of development, we may point out that LA-ICP-MS and LIBS have complementary analytical performances and may be considered as attractive alternatives for the analysis of both bulk samples and elemental imaging distribution.

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