

### DIPLOMARBEIT

"Liquid-assisted femtosecond laser ablation of hybrid oxide nanoparticles with potential application in medical imaging diagnosis"

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### Abstract

Medical imaging technologies such as mammography, magnetic resonance imaging and computed X-ray tomography play a leading role in the diagnosis of breast cancer. However clinical application of this multimodal approach is still problematic due the lack of appropriate commercial contrast agents showing capabilities to distinguish between malignant tumours and benign abnormal masses. Hybrid nanoparticles, which contain in the same structure magnetic and radiopaque elements are a promising alternative for the generation of these multimodal contrast agents due to their unique characteristics, such as: high biocompatibility, contrast enhancement efficacy, cost effectiveness and colloidal stability in the physiological environment.

Liquid-Assisted Pulsed Laser Ablation (LA-PLA) of solid target materials has proved as an efficient synthesis method to produce a wide range of stable nanoparticles in a variety of liquid solutions. A major part of this work is production of nanoparticles by femtosecond laser treatment. This method consists in the laser ablation of custom-made ceramic plates of binary mixed metal oxides, FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub>, submerged in water or ethanol.

Ablation threshold fluences of these target materials could be correlated with the optical interference by laser-generated bubbles. Impact ionization and avalanche breakdown are responsible for the material excitation. There, defect densities play a crucial role in generating free electrons in the conduction bands resulting in avalanche ionization. The decreasing threshold series of FeTaO<sub>4</sub> - Fe<sub>2</sub>WO<sub>6</sub> - FeBiO<sub>3</sub> may suggest an increasing defect density with energy levels close to the conduction band edges. This trend is supported by the target morphologies observed by SEM.

The evaluation of the NPs focussed on the chemical composition and crystallinity. The deviation of the Fe content of the NPs from the original target materials was negligible with  $Fe_2WO_6$ ,  $FeBiO_3$  in contrast to  $FeTaO_4$  where drastic Fe losses were observed both in water an ethanol. Oxygen losses were detected for all three materials.

The nanoparticle morphology correlated well with the observed crystallinity. That means that crystalline NPs exhibited non-spherical shapes. This is observed with FeBiO<sub>3</sub> in both liquids. The only difference was, that the majority NP size was greater in ethanol than in water. In contrast, only amorphous NPs were generated in the case of FeTaO<sub>4</sub> in both liquids. Only for Fe<sub>2</sub>WO<sub>6</sub>, the nature of the fluid shows an influence on the crystallinity: the NPs in water were crystalline and in ethanol amorphous.

This morphological and stoichiometric correlations with the chemical nature of the target and the fluid still need further investigations due to the complexity of the ablation process of solids in liquid contact.

### Zusammenfassung

Medizinische Bildgebungstechnologien wie Mammographie, Magnetresonanztomographie und Computertomographie spielen bei der Diagnose von Brustkrebs eine führende Rolle. Die klinische Anwendung dieses multimodalen Ansatzes ist jedoch nach wie vor problematisch, da es an geeigneten kommerziellen Kontrastmitteln fehlt, die in der Lage sind, zwischen bösartigen Tumoren und gutartigen zu unterscheiden. Hybrid-Nanopartikel, die in der gleichen Struktur magnetische und röntgenopake Elemente enthalten, sind aufgrund ihrer einzigartigen Eigenschaften eine vielversprechende Alternative zur Erzeugung dieser multimodalen Kontrastmittel, wie z.B.: hohe Biokompatibilität, Kontrastverstärkung, Wirksamkeit, Wirtschaftlichkeit und kolloidale Stabilität im physiologischen Umfeld.

Die flüssigkeitsunterstützte gepulste Laserablation (LA-PLA) von festen Targetmaterialien hat sich als effiziente Synthesemethode zur Herstellung eines breiten Spektrums stabiler Nanopartikel in einer Vielzahl flüssiger Lösungen bewährt. Ein wesentlicher Teil dieser Arbeit ist die Herstellung von Nanopartikeln durch Bearbeitung mit dem Femtosekundenlaser. Diese Methode besteht in der Laserablation maßgeschneiderter Keramikplatten aus binären Mischmetalloxiden, FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub>, die in Wasser oder Ethanol eingetaucht sind.

Ablationsschwellenfluenzen dieser Targetmaterialien konnten mit der optischen Interferenz durch lasergenerierte Blasen korreliert werden. Stoßionisation und der Lawinenionisation sind für die Materialanregung verantwortlich. Dort spielen Defektdichten eine entscheidende Rolle bei der Erzeugung freier Elektronen in den Leitungsbändern, die zu einer Lawinenionisation führen. Die abnehmende Schwellenreihe von FeTaO<sub>4</sub> - Fe<sub>2</sub>WO<sub>6</sub> - FeBiO<sub>3</sub> kann auf eine zunehmende Defektdichte mit Energieniveaus nahe der Leitungsbandkanten hindeuten. Dieser Trend wird durch die von SEM beobachteten Targetmorphologien Die unterstützt. Auswertung der Nanopartikel konzentrierte sich auf die chemische Zusammensetzung und Kristallinität.

Die Abweichung des Fe-Gehaltes der NPs von den ursprünglichen Targetmaterialien war bei  $Fe_2WO_6$ ,  $FeBiO_3$  im Gegensatz zu  $FeTaO_4$ , wo drastische Fe-Verluste sowohl in Wasser als auch in Ethanol beobachtet wurden, vernachlässigbar. Für alle drei Materialien wurden Sauerstoffverluste festgestellt.

Die Morphologie der Nanopartikel korrelierte gut mit der beobachteten Kristallinität. Das bedeutet, dass kristalline NPs nicht-kugelförmige Formen aufweisen. Dies wird mit FeBiO<sub>3</sub> in beiden Flüssigkeiten beobachtet. Der einzige Unterschied war, dass die NP-Größe der Mehrheit in Ethanol größer war als in Wasser.

Im Gegensatz dazu wurden bei FeTaO<sub>4</sub> in beiden Flüssigkeiten nur amorphe NPs erzeugt. Einzig bei Fe<sub>2</sub>WO<sub>6</sub> zeigt die Beschaffenheit der Flüssigkeit einen Einfluss auf die Kristallinität: Die NPs in Wasser waren kristallin und in Ethanol amorph.

Diese morphologischen und stöchiometrischen Korrelationen mit der chemischen Natur des Targets und der Flüssigkeit bedürfen aufgrund der Komplexität des Ablationsprozesses von Festkörpern im Flüssigkeitskontakt noch weiterer Untersuchungen.

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# Chapter 1

## Introduction

### **1.1 Motivation**

The number of breast cancer (BC) cases increases significantly worldwide. In 2013, breast cancer has shown the highest incidence for the female population in European Union with 92 600 deaths (16% of all cancer-related deaths in women) [1]. In modern medicine, various types of medical imaging technologies have been developed which play a central role in breast cancer diagnosis and therapy planning. In order to enhance sensitivity and to obtain high resolution of anatomical images, general imaging guidelines require the application of a contrast agent (CA) to distinguish a pathologic tissue from a normal one and to give information about anatomy of diseased tissue [2]. Current commercially produced contrast agents still suffer from many drawbacks including low specificity and sensitivity. Thus the risk of accumulation and toxicity in patients is an unresolved issue. Therefore, the development of new multimodal imaging contrast agent (MCA) has the potential to minimize the toxicity risks (compared to commercial contrast agents) for the patient health and to decrease the cost of diagnosis [3][4].

Different approaches have been used to generate such multimodal contrast agents. Through progress in nanoscience, it is possible to create a new class of multimodal CAs that are capable of providing more detailed information about diseased tissue. In this context, nanoparticles (NPs) have gained significant attention as next-generation MCAs because desired size of the NPs can be established, biocompatible behaviour, establishing of high contrast efficacy for the detection and cost effectiveness [5].

Various chemical approaches have been developed to produce NPs. These methods usually require expensive and/or toxic chemicals as well as controlled atmospheres and often failed to be transferred from the laboratory scale to industrial production. Wet-chemical synthesis also requires long purification steps which are not always suitable for nanoparticles synthesis and the surface of the NPs usually remains contaminated [6].

In this context, it is necessary to find stable, ecological, and low-cost methods that allow pure(r), single-step production. A promising technique for the generation of hybrid NPs is Liquid-Assisted Pulsed Laser Ablation (LA-PLA). This technique is a cost-effective and fast method for the synthesis of a wide range of stable NPs. LA-PLA is a simple and more environmentally friendly method without the requirement of stabilizing agents. In this single step generation, NPs are synthesized directly in a liquid medium without contaminations and byproducts. This attractive route combined with deionized water enables biological and medical applications.

This thesis is the part of the N.I.M.B.L.I.S project which is concentrated on collaborative research between the University of Vienna and University of Madrid. The main goal of this project is to fabricate novel nanoparticle-based multimodal contrast agents (MCAs) designed specifically for their use in breast cancer screening by combining different resonance imaging techniques.

### **1.2 Objectives**

The aim of this work is to design and optimize the fabrication of nanoparticles. Our approach is to use Liquid-Assisted Pulsed Laser Ablation (LA-PLA) to generate NPs that could be the basis of contrast agent production. These nanoparticles are made of ceramics combining a magnetic iron oxide, such as maghemite ( $\gamma$ -Fe2O3) or magnetite (Fe3O4), and an oxide phase of a radiopaque metallic element with high atomic weight, such as wolfram (W), tantalum (Ta) and bismuth (Bi). The photoelectric properties of e.g. BFO have generated much interest, mostly because of its favourable low bandgap of only 2.7 eV.

In addition, the NPs will be developed to meet the acceptable ratio between concentrations of radiopaque chemical elements and the iron-based element. This allow these hybrid NPs to have adequate performance as multimodal CAs.

Medical application of inorganic NPs requires long-term colloidal stability in the physiological environment, and therefore it is challenging to acquire control over the NPs sizes and dispersibility in solution. The NPs tend to aggregate to minimize total surface energy and due to fact that NPs are magnetic in nature, there is an additional contribution from inter-particle magnetic dipolar attraction that tends to destabilize the colloidal dispersion further.

Suitable surface functionalization of the particles and choice of stabilizing agent are crucial to achieving sufficient repulsive interactions between particles to prevent aggregation and obtain a thermodynamically stable colloidal solution [7].

In the present work, we have used citric acid (CA) to form a stable aqueous and ethanol dispersion of nanoparticles. Citric acid is known to stabilize an aqueous dispersion of magnetite nanoparticles and due to steric reasons there is a high probability of having one or two of the three carboxylic groups free for subsequent reactions in the liquid medium, allowing thus further functionalization [8]. We explored the composition and characteristics of the produced NPs in two different solutions of citric acid-distilled water and ethanol. In addition, we determined the ablation threshold fluence induced by femtosecond pulsed laser ablation.

### **1.3 Nanoparticles**

Nanotechnology includes the design, creation, and exploitation of materials at the nanometer range (10 - 100 nm), either by scaling up from single groups of atoms or by refining or reducing bulk materials [9]. Nanoparticles (NPs) are one of the most widely studied nanomaterials and according to research studies, nanoparticles have gained significant attention as next-generation MCAs [5]. Due to their large surface area to volume ratio and unique magnetic, electrical and optical properties, they can be used in fields such as nanomedicine. Remarkable properties of NPs are based on the size effect. Materials at the micrometer range typically expose the same properties as the bulk form; however, at the nanometer range the materials can possess completely different structural, thermodynamic, electronic, spectroscopic, electromagnetic and chemical features [10]. This uncommon behavior can be explained by the fact that the quantity of atoms localized on the NPs surface becomes more significant in case of the nanometer scale materials.

Although the nanoparticles possess the fascinating properties, their production is still challenging because it is challenging to overcome the large surface energy, a result of huge surface-to-volume ratio. Second, control of size distribution of the fabricated nanoparticles is an issue, invariable size distribution, morphology, crystallinity, chemical composition and microstructure which altogether result in desired physical properties. Third, agglomeration and coarsening during the manufacturing of stable nanoparticles is unavoidable [10].

Nanoparticles can be synthesized by two approaches: top-down and bottomup [10]. Commonly, top-down approach begins with a bulk material that is scaled down into its constituent parts. On the other hand, the bottom-up approach is based on synthesis of the required nanoproducts from atomic or molecular components. Although, these two approaches play a significant role in the nanoscience, they can cause structural defects, crystallographic damage and generation of impurities [10].

Iron oxide nanoparticles are one of the widely studied and researched nanomaterials for biomedical application. Eight types of iron oxide are identified, among which maghemite ( $\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) and magnetite (Fe<sub>3</sub>O<sub>4</sub>) are very promising candidates with unique biochemical, magnetic and catalytic properties [11][12][13][14][15]. The crystal structure of these two oxides can be defined as close-packed plane of iron cations with oxygen anions occupying interstitial tetrahedral or octahedral sites. Magnetite and maghemite materials possess an inverse spinel structure that consists of a cubic-close-packed arrangement of oxygen ions. In stoichiometric magnetite, Fe(III) ions are distributed between octahedral and tetrahedral sites, whereas Fe(II) ions are positioned in octahedral sites leaving no vacant places. On the other hand, in stoichiometric maghemite, Fe(III) ions are located at all tetrahedral sites and 5/3 octahedral sites, leaving vacancies (Fig. 1) [13][16].



Figure 1: Crystal structure of the a) magnetite b) magnemite, where the black balls are  $Fe^{2+}$ , the green balls are  $Fe^{3+}$  and the red balls are  $O^{2-}$  molecules

Nanoparticles possess chemical and physical properties that are not typical of neither the bulk nor the atom form. Large surface-to-volume ratio and quantum size effects of magnetic nanoparticles display superparamagnetism and quantum tunneling effects[14]. Magnetite or maghemite obtains superparamagnetic properties when the nanoparticle is smaller than a certain threshold size, usually below 15 nm. In this superparamagnetic regime, magnetite and maghemite nanoparticles display extraordinary high contrast effect for magnetic field [13], and loss of magnetism after removal from the magnetic field [14]. For biomedical applications, superparamagnetic  $\gamma$ -Fe<sub>2</sub>O<sub>3</sub> and Fe<sub>3</sub>O<sub>4</sub> nanoparticles need to possess following properties: (1) uniform particle size (5-20 nm) (2) to be non-toxic (3) high biodegradation and biocompatibility in the human body and (4) stability in colloidal solutions [11][13][14].

All above mentioned properties are influenced by production mechanism of superparamagnetic iron oxide nanoparticles (SPIONs). For example, in MRI contrast agent applications, these SPIONs should have high saturation magnetization value and certain relaxation rate. Saturation magnetization values are a measure of the magnetic moment, so higher values produce more magnetic susceptibility, and therefore stronger MRI signals. The magnetization value of SPIONs is affected by the size of the particles (highest magnetization value occurs in the 6-20 nm particle range), by the spacing between the nanoparticles (in case of coating process) and by crystalline structure of iron oxide. Relaxation rate shows the ability of a CA to increase the relaxation rate of surrounding water protons, in principle increase the efficiency with which image contrast is created. Taking all factors into account, it is essential to choose a production process of SPIONs leading to one or more of the above mentioned properties [11].

Diverse techniques have been used to produce these SPIONs such as coprecipitation methods [14][11][17][18], sol-gel methods [18][17] or hydrothermal process [18][17]. Although these methods are commonly used, they possess some disadvantages: in case of co-precipitation method, it is very hard to control the size, morphology and composition of desired nanoparticle [12], sol-gel is a high-cost method [19], with hydrothermal technique is hard to control the process, thus problems of reliability and reproducibility are also present [19].

NPs of metals with high atomic number (Z) are another important and promising example of nanomaterials with applications in production of CAs. They are promising contrast agents especially for X-ray computed tomography (CT). During this process, the accelerated electrons release electromagnetic radiation in the form of X-ray radiation and the maximum energy is limited by the energy of the incident electron. Generally, materials that possess higher density ( $\rho$ ) or high atomic number (Z) show better absorption of X-rays. The correlation is given in the equation for X-ray absorption coefficient ( $\mu$ ) [20]:

$$\mu \approx \frac{\rho Z^4}{AE^3} \tag{1}$$

where A represents the atomic mass and E is the X-ray energy. The  $Z^4$  factor allows for contrast levels of several orders of magnitude between different tissues and types of contrast agents. When the energy of an incident X-ray is equal or slightly greater than the binding energy of the K-shell electron of the atom, an increase in absorption is established.

Various studies show that NPs made from metals with high atomic number, such as bismuth (Z = 83) [21], tungsten (Z = 74) [22][23] and tantalum (Z = 73) [24][25] with respectively suitable K-edge energy values (90.5, 69.5 and 67.4 *KeV*) can be used in medical imaging as CAs in replacement of commercial agents. The selection of these chemical radiopaque elements is based on the larger number of electrons, which provide an enhanced contrast. It is also important to note that these high-Z CAs can generally reduce radiation exposure to treated person [5]. The NPs used as X-ray contrast agents and to be marketable should meet the following expectations and requirements: contrast enhancement, stable in aqueous solution and identification of key physicochemical properties to identify properties of intravenously injected nanomaterials [25].

Biocompatible magnetic and radiopaque NPs show great potential to be used as new NPs-based-MCAs. New designed hybrid MCAs would include diverse chemical elements or Nano-sized entities showing magnetic properties, as well as different X-ray absorption possibilities.

One research group suggested the preparation of core–shell iron oxide/ bismuth oxide nanocrystals by precipitation. Nanocrystals have been synthesized in aqueous medium without and with stabilization agent-polyethylene glycol. [26][27] In another work, bismuth ferrite BiFeO<sub>3</sub> NPs have been produced via a simple hydrothermal route with KOH as mineralizer and Ethylenediaminetetraacetic acid as the chelating agent [28].

Other studies suggested the synthesis of Fe<sub>3</sub>O<sub>4</sub>/TaOx Core/Shell Nanoparticles using sol-gel method. Fe<sub>3</sub>O<sub>4</sub> NPs were synthesized by thermal decomposition of an iron–oleate complex and incorporated into reverse micelles. Subsequently tantalum(V)ethoxide was added, initiating the sol–gel reaction and leading to formation of NPs which were finally chemically modified [29]. Furthermore, synthesis of Fe<sub>3</sub>O<sub>4</sub>/WO<sub>3</sub> core–shell structures by facile solvothermal epitaxial growth combined with a mild oxidation route was demonstrated [30].

Above mentioned conventional chemical methods are quite complex and mostly require expensive and/or toxic chemicals, stabilizing agents and long purification procedures. Regardless of the chemical synthesis method, there is a possibility of surface contamination by surfactants, by-products and unreacted starting agents. These contaminations reduce the purity of NPs, which is key factor for biomedical applications.

Therefore, an alternative, greener synthesis route for generation of these NPs is required. Considering the benefits of superparamagnetic iron-oxide NPs and radiopaque elements as contrast agents for imaging technique, liquid-assisted pulsed laser ablation (LA-PLA) was proposed in this work as alternative route to produce multimodal CAs consist of FeBiO<sub>3</sub>, Fe<sub>2</sub>WO<sub>6</sub> and FeTaO<sub>4</sub>.

### 1.4 Liquid-Assisted Pulsed Laser Ablation (LA-PLA)

### **1.4.1 Introduction**

The invention of Lasers (Light Amplification by Stimulated Emission of Radiation) in the 20th century started a revolution in science, technology and industry. Today, it is almost impossible to find a field in science not affected by this invention. Laser and laser technology have become a field of science of their own. The history of the laser starts with Albert Einstein's 1917s work "*Quantum Theory of Radiation*". Therein, Einstein gave the theoretical concept and predicted the possibility of lasers [31]. In 1928, Kopfermann and Ladenburg first experimentally verified Einstein's theory – stimulated emission. [32] Finally in 1960, Theodore Maiman, working at Hughes Research Laboratories managed to build a working laser using synthetic ruby [33]. Starting in the 1960's, laser systems with various pulse durations have been produced, from microseconds down to nanosecond, picosecond and finally femtosecond. The race for the shortest pulse duration has reached its maximum by generation and discovering of attosecond ( $10^{-18}$  s) pulses [34].

Pulsed laser ablation (PLA) with nanosecond and picosecond/femtosecond laser pulses has shown great potential in micro- and nano-processing, nanotechnology, cleaning of surfaces from contamination and biomedicine [35]. Laser ablation of materials can be performed in various media: in liquids, in air and in vacuum [36].

Various research groups have confirmed material synthesis by laser ablation in liquids [37][38] and according to Amendola and his research group this technique can be categorized in top-down and bottom-up approaches [39]. Compared with liquid media such as alcohol, acetone and sodium dodecyl sulfate [40], deionized water has the following benefits: (1) excellent properties for the production of contrast agents [41]; (2) ability to produce NPs with high surface purity [42]; (3) long-term stability of synthesized NPs [39]. Dolgaev et al. have shown that LA-PLA can produce NPs of various chemical elements such as Au, Ag, Ti and Si [43].

These groups have confirmed that this powerful technique has extraordinary potential with an uncomplicated preparation procedure, free from any organic contaminants.

This single-step synthesis method possess many benefits: it can be performed in various liquid solutions and can produce a wide variety of nanomaterials, it is compatible with the 12 principles of "green chemistry" since it does not require the use of toxic chemical precursors, it is a low-cost, easy and fast method, because it does not require long reaction times, high temperatures, or multi-step chemical synthetic procedures [39][38].

As a starting point, it is crucial to understand the core mechanisms of LA-PLA and the impact of laser working parameters (e. g. wavelengths, pulse duration, repetition frequency) on NP properties (size, shape, crystallinity). Although LA-PLA enables the production of NPs, the mechanisms and the dependence on processing parameters are still not well understood. Considering all properties and potential, major benefit of LA-PLA over conventional chemical synthesis methods, is the possibility to synthesize NPs in deionized water without any toxic chemicals.

Produced NPs are free of contaminants and therefore applicable as multimodal CAs in imaging techniques. For that reason, this technology is well suited to the aim of this project which is to design and optimize a synthesis route to fabricate biocompatible multimodal nanoparticles.

### 1.4.2 The formation mechanism of NPs by Liquid-Assisted Pulsed Laser Ablation (LA-PLA)

The core mechanism of liquid-assisted pulsed laser ablation at different time scales contains several phases including e.g. ablation, formation of plasma plume, cavitation bubble development and nucleation.

## 1.4.2.1 The pulse propagation and absorption process in liquid medium

A schematic illustration of the formation mechanism of NPs by LA-PLA is shown in Figure 2. In this work a femtosecond Ti:Sapphire laser was applied.



Figure 2: Schematic illustration of NPs formation mechanism by LA-PLA (A-F)

Laser-matter interaction starts with laser pulse propagation through a liquid medium (Fig. 2 B). The absorption of laser light occurs inside a surface layer predominantly by free electrons realized by linear process (Fig. C) [44][45].

This is accompanied by the excitation and ionization of the target and heating of free electrons by inverse Bremsstrahlung process [45]. In case of fs pulses, the instantaneously excitation of electrons is present and electrons thermalize on time scale of ~100 fs [46]. Fast energy relaxation within the electronic system, thermal diffusion and energy transfer to the lattice occurs due to electron-phonon coupling [45]. During excitation and thermalization process, the lattice remains cold. After electron-phonon relaxation period, the irradiated lattice is heated up [46].

A two-temperature model (TTM) is frequently applied to describe this process, considering that the free electrons and lattice possess their own temperatures [46][47][44][45]. This model describes the energy exchange between free electrons and the lattice in which energy absorbed by electrons initiate an increase of electron temperature establishing the electrons thermal equilibrium. Thereafter lattice temperature increases as a consequence of interaction between heated electrons and lattice. Heat transfer takes place through the heat conduction mechanisms [47]. After laser-material interaction, material removal may occur. For the femtosecond pulse duration regime, many ablation mechanisms are suggested and still discussed. Significant temperature difference between the irradiated surface and ambient system cause strong heat dissipation of target, resulting in a material ablation.

Classical thermodynamics is the most common approximation used to describe material ablation [39]. Thermodynamic mechanism explains material detachment from the surface with three processes: evaporation, 'normal' boiling and explosive boiling [44][39] [48]. Explosive boiling occurs when the surface region is rapidly heated up to its critical temperature. The superheated surface undergoes a rapid transition from a heated liquid to a mixture of vapor and liquid droplets [44][39]. However, this process cannot be applied in case of fs laser due to faster material ejection, thus it is not possible to establish thermodynamic equilibrium [39]. Due to this fact "fragmentation" is proposed as detachment mechanism. This process involves decomposition of solid surface into numerous fragments such as hot atoms, vapor and liquid bubbles in disequilibrium [39].

Although thermodynamic mechanism provides information about the first phase of material detachment from the target, some unclear points are related to the effect of photoionization, of photomechanical stress and of plasma confinement on the crater surface due to the liquid buffer. Photoionization could contribute to material detachment by coulombic explosion [39]. For the duration of ablation mechanism two shock waves are emitted to relax excess energy [48]: one propagates into the material surface and another one spread out through a liquid with a supersonic velocity. During propagation through a liquid, shock wave dissipates a certain amount of the energy heating at this way liquid and target and may create material detachment from the crater [39][48][49].

However, we are sure that our target material behaves more like a dielectric than metal due to fact that the bulk ceramic probes consist in binary metallic oxides.

The fundamental mechanisms of the ablation of dielectric materials by fs laser pulses has indicated a fast impulsive ejection of ions due to an electrostatic disintegration of the surface before the major part of the total photon flux absorbed is finally relaxed as thermal energy into the target. [50] Analysis of the ablation mechanisms on dielectric materials have shown that the laser energy is primarily deposited in the electronic system with the result of a dense, overcritical electron hole plasma. The initial electron population is formed due to multiphoton absorption from the valence band or defect states present within the band-gap. Further free-carrier absorption on the trailing edge of the laser pulse develops an avalanche mechanism for electron multiplication and very efficient energy deposition into the carrier gas [50].

Recent experiments with fs laser pulses also showed that the process of laser ablation becomes more deterministic due to the generation of conduction band electrons by multiphoton absorption [46]. A schematic representation of the possible processes in laser irradiated dielectric materials is depicted in Fig. 3.



Figure 3: Potential physical phenomena induced during ultrafast laser excitation of dielectric materials[50]

The initial electron population developed at the target surface is further affected by photoemission, surface charging, trapping, drift in the charge-induced field, recombination, and diffusion. Repetitive irradiation relieves a defect generation process that will enhance the initial electron production by providing new ionization sites. The effect of such incubation processes is dual. Defect accumulation induces a decrease in the ablation threshold and finally leads to a transition between the (initial) gentle to a strong phase in dielectrics [50]. Following incubation, the energy deposition ended to be localized in the laserinduced electron-hole plasma during the initial gentle phase and absorption is enhanced in an extended defect-affected region corresponding to the strong phase.

The temporal behaviour of the free electron density due to photon absorption in the conduction band N(t) can be described by [46]:

$$\frac{\partial N(t)}{\partial t} = P(I) + \beta N(t) - \gamma N^2(t) - \zeta N(t)$$
<sup>(2)</sup>

Here, N(t) presents electron density in conduction band, P(I) is the multiphoton ionization rate,  $\beta$  Avalanche ionization coefficient,  $\gamma$  coefficient of inelastic electron-electron scattering, and  $\zeta$  coefficient of electron-phonon scattering. Equation 2 shows that band gap has a major influence on its ablation efficiency. For an increasing bandgap, the relative weight of the avalanche process is greater than that of multiphoton ionization. Still, multiphoton ionization provides a deterministic seed electron production for the subsequent avalanche process and consequently for shorter pulses, the statistical character of the ablation is reduced [46].

### 1.4.2.2 Plasma plume, cavitation bubble formation and NP nucleation

Due to increased temperature and photoionization, the detached material consists of various species such as ions, molecules, clusters and liquid drops. This newly formed high pressure-temperature area is denoted non-equilibrium plasma plume. In case of ablation in liquid, plasma plume is confined to a near-surface region by the liquid barrier, which decrease the cooling rate at the boundary between solid surface and detached material, because the strong-heated detached material can deliver thermal energy to the target [39].

The plasma starts to expand close to adiabatic [51] at very high velocity followed by a shock wave and eventually cools down, emitting its energy quickly to the liquid and to the target (Fig. 2 D) [39][49]. These conditions initiates the formation of first small nanofragments, which represents a precursor (nuclei) for further nucleation and subsequent growth at a later stage [52][49][51]. The energy transfer from plasma plume to surrounding liquid initiates another effect of the liquid confined plasma, formation of cavitation bubbles (Fig. 2E) [39]. For the duration of bubble expansion, large pressure and temperature difference between surrounding liquid and bubble occurs and induces bubble collapse.

As demonstrated in several studies, at some stage in bubble expansion, the synthesized various species penetrates inside the bubbles [51][49][53][54]. Subsequently, after the reaching of maximum expansion, size of bubbles starts to decreas and NPs are moved to the borderline of bubble and accumulate (Fig. 2 F). When the bubble is fully collapsed, all nanoparticles are released into the liquid [49]. Consequently, two distinct kind of particles are formed. Small primary NPs are dispersed in whole bubble volume and may diffuse to the bubble boundary. Thus, these primary NPs are identified outside the cavitation bubble before its collapse occurs. At the other side, secondary, larger NPs are generated due to collision of primary nanoparticles and they reach its mass maximum at the upper part of the bubble [54]. Additionally, growth and agglomeration of NPs take place in solution [39][51]. For the period of growth released metal species coalescence creating characteristic polycrystalline structure of metallic NPs. Growth of the NPs can be extended due to high stability of colloidal nanoparticle solution [55] and in a case of high tendency to liquid medium [56]. Depending on the metal target, it is possible to obtain two different formation of NPs: 1) pure metallic NPs in case of pure metal target or 2) oxide-hydroxide nanostructures formed by metal composite [37].

One research group demonstrated on Al<sub>2</sub>O<sub>3</sub> target that nucleation can occur only after cooling of the cavitation bubble in the range of tens of microseconds after the laser pulse interaction with target (Fig. 4) [57]. The possibility of following the cavitation bubble composition as well as the thermodynamic parameters is a key issue. The ablated matter is atomized, or only contains small molecules. If the nucleation arises in a bubble confined by the liquid, the nucleation is driven by the gas temperature and the density fluctuation.

Starting from a hot atomized gas, the growth of large molecules and then small clusters is possible only when the temperature decreases sufficiently, after a few microseconds. From the rotational and vibrational spectra of the AlO molecules it is shown that the plasma turns into a hot neutral gas with a temperature of 3400 K after 2  $\mu$ s causing a fast oxidation of Al atoms. The quick oxidation of the Al atoms leading to AlO molecules is in good agreement with the density functional theory (DFT) calculations in which only small molecules are stable when the temperature is higher than 3000 K [58].



Figure 4: Main stages occurring during pulsed laser interaction with matter .(Al<sub>2</sub>O<sub>3</sub> target in 50 ml pure deionized water @355nm, 5ns, 10 Hz) [57]

### 1.4.2.3 Mechanism of laser-generated cavitation bubbles

Laser-generated cavitation bubbles leads to deformation and erosion of the solid target [59][60]. The liquid properties such as density, surface tension, viscosity, compressibility and vapour pressure are crucial in this process. For example, influence of surface tension stabilizes bubbles so that they are able to achieve larger volumes [61][62]. At the other side, higher surface tension effect cause higher erosion of the cavitation [63][64]. Figure 5 represent suggested mechanism which defines the majority of this phenomena.



Figure 5: Surface tension effect on cavitation behaviour [64]

There is a correlation between the total impact energy, bubble cluster size and relative erosion rate with surface tension. The erosion rate and bubble cluster size increase with increasing of surface tension, while in case of open beaker test erosion rate decreases slightly due to insufficient surface tension and then increases.

The cavitation bubble plays an important role in particle formation, as it confines the primary particles and redeposits them to the target. Agglomeration occurs for the confined particles in the induced second bubble. Additionally, upon the collapse of the second bubble a jet of confined material is ejected perpendicularly to the surface. Suggested kinetic influence the final particle size distribution and determine the quality of the resulting colloids [65].

One research group analysed the spatiotemporal kinetics during LA-PLA by X-ray radiography (XR) which permit to probe the process on length scales from nanometers to millimeters with microsecond temporal resolution. X-ray radiography films have been taken during the ablation process on a flat silver target. The radiographs (Fig. 6a) show a hemispherical transmission increase (bright area) within the forming bubble. At maximum expansion at  $110 \,\mu s$  (first highlighted frame in Fig. 6a) the bubble shape is perfectly hemispherical and appears homogeneous with no indication of strong concentration of ablated mass. During collapse the shape does not change significantly, while, however, a weak neck forms close to the interface and the height retracts faster than the width (indicated by an arrow) [65].



Figure 6: a) Averaged X-ray radiographs of the bubble kinetics at selected delays after laser impact, some critical frames are highlighted: the largest extension of the first bubble at 110 µs; shrinking of the first bubble at 156 µs; second bubble (rebound) at 227 µs; jet formation after the second bubble has collapsed at 320 µs. Brighter pixels correspond to higher X-ray transmission; b)Plot of the lateral and vertical bubble radius as function of delay. Error bars are in both cases similar. The solid line is a simulation according to the Rayleigh-Plesset equation [65]

Figure 6b shows the derived bubble radius in height and lateral extension. The observation of the collapse event is smeared out due to the limited time resolution of the singularity in wall motion. The smallest quantifiable radius is 0.3 mm as compared to the maximum bubble radius of 1.1 mm. A second bubble (rebound) peaks at 260  $\mu$ s and contains structured contrast features, the nature of which is not easily identified [65]. The first bubble is well described by the general bubble dynamics in the Rayleigh-Plesset picture (bold line in Fig. 2b), while the second bubble has a critical deviation from this behaviour [65]. The internal structure at 227  $\mu$ s with areas of different densities could mark the interaction of the collapsing bubble with continued boiling at the hot target surface. In fact, at the collapse point the size of the remaining cavity approached the size of the laser spot on the target [65].

Therefore, a singular collapse and subsequent expansion as in sonoluminescence cannot be expected [65]. One can assume, repetition rate of the laser system have influence on bubble size, which is problematic for high productivity processes due to the shielding and scattering effect of the laser energy. [66]

### 1.4.2.3 Impact of Cavitation Bubble Dynamics on NP size

The detailed formation process of nanoparticles after laser ablation is still unclear. Direct physical investigation methods such as shadowgraphy or light scattering techniques are unfortunately limited. Different research groups used in-situ small angle X-ray scattering (SAXS) technique to study the size distribution of nanoparticles and the relation between cavitation bubble dynamic and NPs growth after pulsed laser ablation in liquid [65][54][53].

The used experimental scheme is shown in Fig. 7. Nd:YAG laser was used to ablate a gold ribbon in a water-filled ablation chamber. For the detection of ablated species with inside the bubble region, a horizontal x-ray beam intersects the ablation region with an x-ray focus in the vertical and horizontal direction. The scattered intensity was recorded by a pixel detector Pilatus. The central beam block was equipped with a p-i-n diode, which allowed recording the x-ray transmission through the sample with high time resolution on an oscilloscope. The x-ray beam was centred on the laser path. The cavitation bubble was scanned by vertical movement of the set-up relative to the fixed x-ray beam [54].



Figure 7: Sketch of the setup with the metal rib-bon inside the water chamber. Two 75 lm Kap-ton foils seal the chamber and act as x-ray windows [54]

According to this universal technique, distribution of NPs size in the cavitation bubble can be plotted in respect to time and position (bubble height). Figure 8 shows a sketch of time-resolved SAXS during laser ablation of gold sample in water.



*Figure 8: Sketch of involved species in laser-induced cavitation bubble during its largest extension* [54]

NPs formation appears inside a cavitation bubble. When cavitation bubble reaches its maximum size, SAXS signals confirmed two different particle species: primary particles of about 8–10 nm diameter starting from the bottom of the bubble target and can also be found outside the cavitation bubble in the free liquid and secondary particles due to collision of primary particles in the range of 45 nm diameter which have highest density in the upper part of the cavitation bubble but do not penetrate into the liquid [54].

Another research group studied also the formation of NPs within the laser-induced cavitation bubble in situ, using small angle X-ray scattering with high spatiotemporal resolution. In this experiment the ablation from a silver target immersed in water has been induced by a nanosecond laser. The scattering distribution of ablated nanoparticles of different size and agglomeration state can be considered. A real model-independent quantity is the scalar Porod invariant P [53]:

$$P = \int_{0}^{\infty} I(q)q^{2} dq = 2\pi \Delta \rho^{2} r_{e}^{2} \Phi(1 - \Phi)$$
(3)

where I(q) present the scattering distribution, q is scattering vector,  $r_e$  is the classical electron radius and  $\Delta \rho$  present the density difference. This equation allows deriving the particle filling fraction  $\Phi$  from an integral over the scattering curve weighted by  $q^2$  without the need for any assumptions on particle shape and size. At low filling fractions  $\Phi \ll 1$  the invariant is proportional to the total mass. For compact particles the scattering distribution  $I(q)q^2$  for a hierarchy level shows a maximum at a characteristic q which is inversely proportional to the particle size [53]. So a partial integral over  $I(q)q^2$  gives a good approximation for the mass fraction at this size.

Two different particle species were observed: compact primary particles of 8-10 nm developed directly after the laser ablation and distributed all over the bubble

volume in the time of bubble expansion, and bigger, secondary (or agglomerated) particles of 40-60 nm in size [53]. Comparison between the development of mass of the agglomerates and primary particles versus the bubble expansion is shown in Figure 9. The secondary particle mass increased at the bottom of the bubble close to the ablated area on the target due to agglomeration of primary NPs captured during the first collapse of confined cavitation bubble[53].



Figure 9: Comparison between the growths of mass of the agglomerates and primary particles versus the bubble expansion for several characteristic delays. (The line displays the X-ray transmission at a height of 0.17 mm) [53]

The particle abundance is strongly linked to cavitation bubble dynamics: during maximum elongation of the cavitation bubble, the primary particle mass goes through a maximum and reappears in the rebound, probably then contained in agglomerates [53]. Vice versa, the total mass of agglomerates is relatively weak in the first bubble, but it increases strongly within the rebound. Although most of the ablated material is trapped inside the bubble and follows its oscillation, there is a certain fraction of primary particles and agglomerates which can be localized outside the bubble [53]. This indicates that bubble–liquid interface is penetrable by the ablated matter. Primary particles may enter the liquid already during the bubble expansion phase possibly due to high ejection velocities. Agglomerates stay inside the bubble with highest concentration close to the target surface and are released by the bubble only after its collapse [53].

The size of primary particles and agglomerates does not strongly depend on time and position, the average size of primary particles slightly decreases with higher distance to the target. Furthermore, there is a slight tendency for growth of primary particles and agglomerates during the first rebound [53].

### 1.5 Application of the laser produced NPs

Nowadays, contrast enhancement imaging techniques, such as X-ray computed tomography (CT), digital mammography (DM) and magnetic resonance imaging (MRI) are the most sensitive methods which are commonly used in diagnosis of breast cancer. In these techniques, tumour detection relies on the contrast enhancement produced in MRI and X-ray images after injection of a commercial contrast agent (CA), such as water-soluble iodinated molecules (DM and CT), and gadolinium III chelates (MRI). The precision of contrast enhanced DM is generally high but in case of increased risk of BC the sensitivity is much lower.

However, by using these techniques, one can obtain information such as tumor size and to define possible extension of BC enhanced MRI, has higher sensitivity but due to low gadolinium biological specificity, it is possible to receive falsepositive results. Considering the specificity, sensitivity and complementarity of contrast enhanced DM and MRI techniques, it would be possible to combine these two diagnostic tests. The development of new multimodal imaging contrast agent (MCA) has the potential to minimize the toxicity (compared to commercial contrast agents) risks for the patient health and to decrease the cost of diagnosis. Moreover, these CAs have to respond efficiently to different electromagnetic or ultrasound energies, so that they can be used by multiple imaging modalities depending on the needs of a given breast examination.

## Chapter 2

## **Experimental section**

### 2.1 Metal targets synthesis

Bulk ceramic probes, consisting in binary metallic oxides, were used as target for the synthesis of the nanoparticles. Magnetic iron oxide, such as maghemite  $(\gamma$ -Fe<sub>2</sub>O<sub>3</sub>) or magnetite (Fe<sub>3</sub>O<sub>4</sub>) is combined with an oxide phase of a radiopaque metallic element with high atomic weight: Ta (Z = 73), W (Z = 74), Bi (Z = 83), with respectively suitable K-edge energy values (67.4, 69.5 and 90.5 *KeV*). Following binary oxide targets were produced for this research: FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, and FeBiO<sub>3</sub>.

A traditional ceramic synthesis process was used for the synthesis of the bulk ceramic targets. In this process, firstly, commercial powdered metal oxides (Fe<sub>2</sub>O<sub>3</sub>, WO<sub>3</sub>, Bi<sub>2</sub>O<sub>3</sub>, and Ta<sub>2</sub>O<sub>5</sub>,) were weighed according to the corresponding formulations. Mixtures were subjected to a milling process in a ball mill (ZrO<sub>2</sub> balls stabilized with Y<sub>2</sub>O<sub>3</sub>) to homogenize their composition. Secondly, green cylindrical samples (diameter 1 cm, height 1 cm) were obtained via a dry pressing process at room temperature and pressing pressure of 2500 t/cm<sup>2</sup> using a commercial laboratory hydraulic press.

Thereafter, obtained samples were sintered in laboratory muffle furnace. In this process, each obtained metallic oxide sample was exposed to the adequate temperature (FeBiO<sub>3</sub>, 750 °C; Fe<sub>2</sub>WO<sub>6</sub>, 1050 °C, FeTaO<sub>4</sub>, 1400 °C).

Then, they were treated by superficial laser melt mixing with a diode-pumped Nd:YAG laser (Powerline E20, Rofin; c/o R. Lahoz, Centro de Química y Materiales de Aragón, University of Zaragoza – CSIC, Zaragoza, Spain) delivering pulses of ca. 50 ns pulse width. The laser heads were fitted with a galvanometer beam steering system and coupled to a flat-field lens of 160 mm focal distance providing a spot size of ca. 30  $\mu$ m. The pulse repetition rates ranged from 20 to 200 kHz, at output power values from 0.1 to 20 W. These conditions resulted in irradiance values between 0.5 and 100 MW/cm<sup>2</sup>. Scanning rates were varied between 500 and 3000 mm/s. Finally, the samples were grinded and polished.

### 2.2 Laser setup

For the ablation experiments and synthesis of NPs an amplified Ti:Sapphire laser system was applied (Fig. 10). It delivers sub-30 fs pulses at a repetition rate of 5 kHz centered at 790 nm and with beam diameter of 12.06  $\mu$ m (for water) and 12.21  $\mu$ m (for ethanol) measured with the knife-edge method [67].

The samples were treated with fluences in the range from 0.78-7.03 J cm<sup>-2</sup> and at a constant number of pulses N=1000 at room temperature and atmospheric pressure in deionized water and in ethanol (Absolute, Sigma Aldrich), for the determination of threshold fluence. Laser ablation of three ceramic plates of binary mixed metal oxides (Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub> and FeTaO<sub>4</sub>) was carried out at room temperature at atmospheric pressure in deionized water and in ethanol. The diameter of the ablated area is measured by using an Olympus STM-MJS optical microscop and laser fluence was derived from the diameter. Pulse thresholds  $F_{th}$ are evaluated by the D<sup>2</sup>-lnF method described in section 3.3

Nanoparticles were produced by irradiating the targets in a scanning mode for 20 minutes with a fluence of  $3.9078 \text{ J cm}^{-2}$  (production of NPs in water) and  $3.768 \text{ J cm}^{-2}$  (production of NPs in ethanol), also 1000 pulses per site. The synthesis was carried out in a closed reactor with four different solutions: 1) 20 ml H<sub>2</sub>O + 0.5 % citric acid; 2) 20 ml H<sub>2</sub>O + 0.05 % citric acid; 3) 20 ml C<sub>2</sub>H<sub>5</sub>OH + 0.5 % citric acid; 4) 20 ml C<sub>2</sub>H<sub>5</sub>OH + 0.05 % citric acid.

To observe the samples response to amplified fs-laser irradiation the diameter of the ablated area is measured by using optical microscopy and laser fluence was derived from the knife-edge diameter. Pulse thresholds  $F_{th}$  are evaluated by the D<sup>2</sup>-lnF method described in section 3.3.





*Figure 10: (a) A photograph of the amplified fs-laser setup b) Plastic vessel with optical window* 

a)

### 2.3 Beam profiling: cutting edge technique

In order to investigate the spot-size dependence of laser generated thresholds it is important to obtain information about irradiated area which is quantified by the Gaussian beam radius w. For the evaluation of the beam radius, the cuttingedge technique was applied. A razor blade was scanned through the beam in x and y direction as schematically presented on the Figure 11 and transmitted energy as a function of razor blade position (x' and y') was determined with a detector. The same procedure was repeated for different z-positions. Figure 11 shows a schematic model of a cutting-edge technique.



Figure 11: Scheme of the "cutting edge" method for the determination of the Gaussian beam radius wo and the beam quality parameters. [46]

To calculate the power for photodiode illumination following integral was used [67]:

$$P_{pd}(r,z) = \int_{-\infty}^{x} dx' \int_{-\infty}^{+\infty} dy' I(x',y') = \\ = \underbrace{I_{0}(z)}_{=\frac{x/2}{w(z)^{2}\pi}} \underbrace{\int_{-\infty}^{x} dx' \exp\left(-2\frac{x'^{2}}{w(z)^{2}}\right)}_{=\frac{w(z)}{2}\sqrt{\frac{\pi}{2}}(1+\operatorname{erf}(\sqrt{2}\frac{x}{w(z)}))} \underbrace{\int_{-\infty}^{+\infty} dy' \exp\left(-2\frac{y'^{2}}{w(z)^{2}}\right)}_{=w(z)\sqrt{\frac{\pi}{2}}} = \frac{P}{2}\left(1+\operatorname{erf}\left(\sqrt{2}\frac{x}{w(z)}\right)\right)$$
(4)

where  $r_0$  present the position of the edge of the blade, z is the distance from the focal plane,  $I_0$  is the intensity at the centre of the beam, w is the beam waist radius and  $erf(x) = \frac{2}{\sqrt{\pi}} \int_0^x dx' exp(-x2)$  is the Gaussian error function.

From fitting this equation to experimental data, w(z) can be obtained. In addition, w(z) in a Gaussian beam is assumed by:

$$w(z) = w_0 \ \sqrt{1 + (Z/Z_R)^2}$$
(5)

where  $w_0$  present the Gaussian beam waist radius and  $z_R$  the Rayleigh range. By fitting this equation to the w(z) values, the beam is fully characterized by  $w_0$  and  $z_R$  and the beam diameter can be calculated for an arbitrary distance from the focus. We obtain a Gaussian beam radius of  $w_0$ =12.06 and 12.21 µm for the experiments in water and in ethanol, respectively.

# 2.4 Threshold fluence determination

Femtosecond laser beams are commonly described with a Gaussian radial distribution. The radial fluence distribution is presented in Figure 12.



*Figure 12: Radial fluence distribution in a Gaussian laser profile. F*<sup>0</sup> *is maximal fluence, Fth is threshold fluence, wo represents Gaussian beam radius [46].* 

The energy density needed to ablate material is the ablation threshold fluence *Fth* and *F*<sub>0</sub> is maximal laser fluence. If the maximal fluence *F*<sub>0</sub> exceeds threshold fluence *Fth*, the material will be ablated and a crater with the diameter *D* will be formed. The ablation threshold fluence can be determined from various hole diameters. The squared diameter of the ablated zone  $D^2$  is correlated to the Gaussian beam radius *w*<sub>0</sub>, the maximum laser fluence *F*<sub>0</sub> and the threshold fluence *F*<sub>th</sub>, by [46]

$$D^{2} = 2w_{0}^{2} \ln \left(\frac{F_{0}}{F_{th}}\right)$$
(6)

If the beam radius is known, laser fluences can be calculated from the energies via Equation:

$$F_0 = \frac{2E_0}{\pi w_0^2} \quad (7)$$

From a plot of squared diameter of the ablated area versus laser fluence  $F_{0}$ , the beam diameter can be obtained from the slope and the threshold fluence  $F_{th}$  from the intercept with the horizontal axis (Fig. 13) [68][46] [69].



Figure 13: Squared diameters of the ablated areas in the dependence on the laser fluence [46]

### **2.5 Analytical Techniques**

### 2.5.1 Optical microscopy

After 10 minutes of ultrasonic cleaning, ablation cavity diameters were evaluated by Olympus STM-MJS optical microscope.

### 2.5.2 SEM

In Scanning Electron Microscopy (SEM) a focused beam of high-energy electrons is used to generate signals at the surface of solid targets. The signals that originate from electron-target interactions give information about the target including morphology and composition of the target. These signals include secondary electrons (SE) and backscattered electrons (BSE) which are commonly used for imaging purposes.

For determining the chemical composition of the sample surface X-rays are detected with an Energy Dispersive X-ray spectrometer (EDX). Characteristic acceleration voltages for microscopic studies are U = 5 - 20 kV, which correspond to a wavelength of the electrons  $\lambda_e = 8.7 - 17.3$  pm. In this work a Zeiss Supra 55 VP SEM was used.

### 2.5.3 TEM, SAED and EDX

The particle size, size distribution and morphology were determined by transmission electron microscopy (Philips CM200 TEM,  $LaB_6$  cathode, acceleration voltage of 200 kV). One of the advantages of this technique is the easy sample preparation: a small amount of colloidal specimen is placed on a carbon-coated copper grid and allowed to evaporate at room temperature.

Subsequently, the grid is transferred to a high vacuum chamber and the sample is irradiated with a very thin beam of accelerated electrons. Depending on the sample density, some of the electrons are either scattered and transmitted or interacts directly with the atoms in the specimen.

After receiving a TEM image, a selected area can be further examined by electron diffraction (SAED). The diffraction pattern originates from the focused electron beam, which is scattered by the specimen lattice.

According to Bragg's law, it is possible to record various spots in the pattern and determine the specimen's phases [70].

With this technique, one can examine a very small sample area. SAED provides structural information about the nature and crystallinity of the produced NPs. The diffraction pattern were studied by intensity profile analysis selected area diffraction (PASAD; University of Vienna, C. Gammer) and microscopy software (Gatan, Inc.). To provide compositional information of the NPs, energy dispersive X-ray spectroscopy (EDX) is used. Interaction of a focused beam of electrons with a specimen generates X-rays. A EDX detector is typically incorporated into a TEM and allows the detection and separation of the characteristic X-rays in the form of energy spectra.

The spectra are analyzed with appropriate EDX software, delivering quantitative information about elemental composition. EDX analysis can be invasive and is usually applied after TEM examination.

### 2.5.4 XRD

X-ray diffraction (XRD) is a powerful and rapid method for phase identification of a crystalline structure. Incident X-rays photons interacts with the specimen, creating a diffraction pattern according to Bragg's law [71]:

$$n\,\lambda = 2\,d\,\sin\theta\tag{8}$$

Here, *n* represents an integer number,  $\lambda$  is the wavelength of the X-ray photons, *d* is the spacing between the crystal planes, and  $\theta$  is the incident angle of the X-ray beam.

The result of the X-ray analysis is a diffractogram which shows the intensity of the diffracted X-ray beams as a function of the diffraction angle (2 $\theta$ ). Positive identification of the crystalline material is based on a comparison between a reference diffraction patterns database and the experimental results. XRD measurements were made with a Bruker D8-advanced with a LYNXEYE Sistrip detector. Samples were prepared by dropping the colloidal dispersion on a silicon wafer covered with vaseline and drying. The NPs in ethanol had to be dried and transferred into water. XRD patterns were recorded from 10° to 120° ( $\theta/2\theta$ ) with a measurement time of 60 minutes. The spectra were analyzed by using the software Match.

## Chapter 3

# **Results and discussion**

### **3.1 Characterization of targets**

The morphology of the target materials depends strongly on the composition. FeTaO<sub>4</sub> consists mostly of 2-3 $\mu$ m sized grains (Fig. 14A). A special size distribution is found with Fe<sub>2</sub>WO<sub>6</sub> (Fig. 14B). It shows platelets with thicknesses of the order of 200nm with edges of ca. 4 $\mu$ m. In between those, spherical features with diameters of ca. 1-2 $\mu$ m are located. The other extreme in the series of the investigated targets is shown by FeBiO<sub>3</sub> (Fig. 14C). Agglomerates of particles with <200nm diameter are characteristic.



Figure 14: Scanning electron micrographs of targets. A) FeTaO4, B) Fe2WO6 and C) FeBiO3

XRD patterns of FeTaO<sub>4</sub> (Fig. 15a) displays the presence of four different crystalline phases: two iron-tantalum oxide phases, Fe<sub>0.5</sub>Ta<sub>0.5</sub>O<sub>2</sub> and FeTa<sub>2</sub>O<sub>6</sub>, with tetragonal symmetry (P4<sub>2</sub>/mnm), and Fe<sub>2</sub>Ta<sub>4</sub>O as additional phase with cubic symmetry (Fd-3m). Several peaks correspond to the iron oxide phase hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>). The elemental composition analysed by EDX (Table 1) indicated that the chemical composition deviates from the intended stoichiometry of FeTaO<sub>4</sub>. The Ta content is almost double vs. the theoretical value, whereas the oxygen content does not deviate too much.

The XRD pattern of  $Fe_2WO_6$  suggested the presence of two crystalline iron wolframate phases attributed to the  $Fe_2WO_6$  majority phase with orthorhombic symmetry (Pbcn) and to  $FeWO_4$  with a monoclinic symmetry (P 2/c). (Fig. 15b). In this case, the elemental composition is near to the theoretical stoichiometry.

The XRD pattern of FeBiO<sub>3</sub> shows a phase with rhombohedral symmetry (R3c) and two additional phases of Fe<sub>4</sub>Bi<sub>2</sub>O<sub>9</sub> and Fe<sub>0.5</sub>Bi<sub>12.5</sub>O<sub>20</sub> with orthorhombic symmetry (Pbam) (Fig. 15c). Several peaks of the iron oxide phase hematite ( $\alpha$ -Fe<sub>2</sub>O<sub>3</sub>) were detected. Elemental composition of the FeBiO<sub>3</sub> target indicated a strong deviation from stoichiometry. The oxygen content is more than three times as high as expected in FeBiO<sub>3</sub>. The content of Bi is 50% higher than the theory.

	Fe(%)	<b>O(%)</b>	Ta(%)	W(%)	Bi (%)	Me/Fe		O/(Me+Fe)	
							Formula		Formula
FeTaO <sub>4</sub>	10.32	70.36	18.32	-	-	1.8	1.0	2.5	2.0
Fe <sub>2</sub> WO <sub>6</sub>	18.74	70.39	-	10.9	-	0.6	0.5	2.4	2.0
FeBiO <sub>3</sub>	6.48	82.29	-	-	9.97	1.5	1.0	5	1.5

Table 1: EDX analysis results of targets. Atomic percentages, atomic ratios. Me: high atomic number metals (Ta, W, or Bi). "Formula" means that the ratio is referred to the formula stoichiometry.



Figure 15: XRD analysis of targets of: a) FeTaO4, b) Fe2WO6 and c) FeBiO3

The optical properties of the targets are decisive for the interaction with the laser radiation of 1.55 eV. If the dielectrics exhibit band gaps of >1.55 eV a resonant one-photon transition and excitation is impossible. Ultrashort pulse may allow the impact/avalanche ionization based on a finite concentration of defects or multiphoton excitation.

Material	Band Gap [eV]		Reference
FeBiO3	2.7	-	[72]
Fe <sub>2</sub> WO <sub>6</sub>	2.4	-	[73]
FeTaO <sub>4</sub>	2.2	-	[74]
WO <sub>3</sub>	2.6 - 2.9	sintered	[75]
Ta <sub>2</sub> O <sub>5</sub>	4.7	anodic	[76]
Bi <sub>2</sub> O <sub>3</sub>	2.85 - 2.6	orthorhombic tetragonal	[77]
Fe <sub>2</sub> O <sub>3</sub>	2.1	anodic	[78]

#### Table 2: Band gap

The single oxide components and the mixed oxides show all gaps greater than the photon energy (Table 2). Unstoichiometric mixed oxides can be treated in a simple linear approximation based on the mixed matter theory. The expected value of the oxide bandgaps can be appreciated by a linear combination of the band gaps of the single oxides [73].

### 4.1 Ablation behaviour

The most important parameter describing the ablation behaviour of a solid is the ablation threshold fluence  $F_{th}$ . Its determination was performed by the  $D^2$  vs.  $\ln F$  technique described in Chapter 2.4. The slope of this representation is correlated directly to the laser spot radius on the sample surface. In this experimental work, these slopes have been calculated on the basis of spot radii determined by the cutting-edge technique described in Chapter 2.3. The plotted fluence values were also calculated based on the measured pulse energies and the cutting-edge spot radii. All experiments in both water and ethanol were carried out at a fixed pulse number of N = 1000. (Fig. 16).



Figure 16: Squared diameter of the ablation area versus logarithm pulse fluence (D<sup>2</sup> versus logF) in water and in ethanol. a) FeTaO4. b) Fe2WO6. c) FeBiO3. The lines are the fitted according to eq. 5.

The extrapolation of values near to the thresholds in the low fluence regime resulted in threshold fluences  $F_{th,l}$  collected in Fig. 16 and Table 3. A trend to lower threshold could be observed in the series FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub>. A value for FeBiO<sub>3</sub> was omitted in Fig. 16 and Table 3 since only one value pair existed in the low fluence regime. However the results in both liquids may suggest the lowest  $F_{th,l}$ .

In the higher fluence regime, second linear data regions could be observed which can be extrapolated to a set of higher threshold fluences  $F_{th,h}$  than the before described  $F_{th,l}$  (Fig. 17 and Table 3). The same threshold trend as in the low fluence regime ( $F_{th,l}$ ) was observed in the high fluence regime, but shifted to higher values.  $F_{th,h}$  values decreased also according to the series FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub>.



Figure 17: Ablation threshold fluences. "Low" fluence range:  $F_{th,l}$  "High" fluence range:  $F_{th,h}$  (compare Figure 15)

	$F_{th,l} (H_2 O)$ $[J cm^{-2}]$	$F_{th,h} (H_2O, EtOH)$ [J cm <sup>-2</sup> ]
FeTaO <sub>4</sub>	0.62	0.79
Fe <sub>2</sub> WO <sub>6</sub>	0.43	0.69
FeBiO <sub>3</sub>	-	0.49

Table 3: Low (F<sub>th,l</sub>) and high (F<sub>th,h</sub>) threshold fluence

This shift to higher thresholds a high fluence can be correlated with the optical interference by laser-generated bubbles. The results suggest that the size and lifetime of the bubbles (and the any secondary bubbles) depend strongly on the fluence.

At high fluences, the size and lifetime of the primary and/or secondary bubbles interfere with the next incoming laser pulse at a repetition rate of 5 kHz (Fig. 18). In this regime, the fluctuating curvature and the strong refractive index differences between the liquid and the vapour in the bubble may lead to strong refraction. Thus, the effective fluence arriving on the sample is reduced in contrast to the case where the bubbles have a low lifetime in the low fluence regime so that the following laser pulse can arrive at the surface without any losses.



Figure 18: Bubble dynamics at high (F<sub>h</sub>) and low (F<sub>l</sub>) fluences

The threshold trend for the three materials cannot be explained by different absorptivities based on the band gaps (Table 2) which do not vary significantly in the range of 2.2-2.7 eV. With a photon energy of 1.55 eV single photon absorptions are impossible. A two-photon process should become more probable with decreasing band gap. The observed threshold series did not support this expectation.

On the other hand, impact ionization and avalanche breakdown, may be responsible for the material excitation. There, defect densities play a crucial role in generating free electrons in the conduction bands resulting in avalanche breakdown. The decreasing threshold series of FeTaO<sub>4</sub>, Fe<sub>2</sub>WO<sub>6</sub>, FeBiO<sub>3</sub> may suggest an increasing defect density with energy levels close to the conduction band edges (Fig. 19). This trend in defect densities is supported by the surface morphologies observed by SEM (Fig. 13).

Obviously FeTaO<sub>4</sub>, exhibits a much lower grain boundary density, i.e. with higher grain sizes  $2-3\mu m$ , than the other extreme of FeBiO<sub>3</sub> with grain sizes of < 200 nm.

The influence of the nature of the liquids is minor in comparison to the effects of the solid material compositions. The regions of significant optical bubble interference with the incoming laser beam show a slight dependence on the liquid nature. Possibly the viscosity and the surface tension may influence the bubble dynamics and thus the fluence attenuation.



Figure 19: Single photon excitation probability dependent on the defect density. Band to band excitations are improbable (would need two photon transitions

### 4.3 Characterization of synthesized NPs

# 4.3.1 Characterization of NPs synthesized in aqueous solution of citric acid

The synthesis of NPs was performed in aqueous solution with 0.05 % citric acid. The NPs characterization was performed with TEM, SAED and EDX. Focus was on the chemical composition and crystallinity. Figure 20 shows TEM micrographs and electron diffraction pattern (SAED) of  $FeTaO_4$ ,  $Fe_2WO_6$  and  $FeBiO_3$  nanoparticles produced in distilled water with 0.05 % citric acid.

		Fe (%)	O (%)	W (%)	Ta (%)	Bi (%)
H <sub>2</sub> O	FeTaO <sub>4</sub>	5	75	-	20	-
	Fe <sub>2</sub> WO <sub>6</sub>	27	57	18	-	-
	FeBiO <sub>3</sub>	10	76	-	-	14
EtOH	FeTaO <sub>4</sub>	5	70	-	25	-
	Fe <sub>2</sub> WO <sub>6</sub>	28.6	54.2	17.2	-	-
	FeBiO <sub>3</sub>	12.5	72.5	-	-	15

Table 4: EDX results of NPs synthesized in water and ethanol

		FeTaO <sub>4</sub>		Fe <sub>2</sub> WO <sub>6</sub>		FeBiO <sub>3</sub>	
		Target	NPs	Target	NPs	Target	NPs
H <sub>2</sub> O	Me/Fe	1.8	4.0	0.6	0.7	1.5	1.4
	O/(Me+Fe)	4.4	3.0	2.4	1.3	5.0	3.2
EtOH	Me/Fe	1.8	5.0	0.6	0.6	1.5	1.2
	O/(Me+Fe)	4.4	2.3	2.4	1.2	5.0	2.6

 Table 5: Atomic percent ratios. Comparison between targets and NPs in water and ethanol.

 Me: high atomic number metals (Ta, W, or Bi).



Figure 20a: FeTaO4 TEM micrographs and electron diffraction pattern (SAED) of NPs produced in water



Figure 20b: Fe<sub>2</sub>WO<sub>6</sub> TEM micrographs and electron diffraction pattern (SAED) of NPs produced in water.



Figure 20c: FeBiO<sub>3</sub> TEM micrographs and electron diffraction pattern (SAED) of NPs produced in water.

Figure 20a depicts TEM micrographs of the prepared FeTaO<sub>4</sub> particles. They show a spherical morphology without chain formation or aggregation. SAED images indicated amorphous states. EDX indicated that all NPs possess the same composition, Ta oxide doped with iron (Table 4). The ratio of Ta/Fe increased from the target composition of 1.8 to 4.0 in the NP's (Table 5). Obviously, most of the Fe has been lost during the ablation and formation process. Additionally, signals of Cu and Yb were also observed (not shown in Table 4). Cu signals can be ascribed to the TEM Cu grid. Yb is probably present due to contamination. EDX analysis also indicates some loss of oxygen, an O/(Ta+Fe) ratio of 3.0 versus 4.4 of the target.

The Fe<sub>2</sub>WO<sub>6</sub> particles appeared as a majority of small NPs with diameters of less than 40 nm (Fig. 20b). Few larger NPs occurred. The small NPs exhibit shapes deviating from perfect sphericity. This is supported by electron diffraction (SAED) patterns with sharp spots indicating crystalline Fe<sub>2</sub>WO<sub>6</sub> particles. The EDX analysis detected almost the same metal stoichiometry of the Fe<sub>2</sub>WO<sub>6</sub> NPs and the target (Table 4). Oxygen, however, was lost in the NP generation process analogously to FeTaO<sub>4</sub>. EDX analysis resulted in a reduction of the O/(W+Fe) ratio from 2.4 down to 1.3.

The FeBiO<sub>3</sub> NPs show agglomeration of a majority of small mostly nonspherical particles of less than 50 nm and few larger consisting of tight agglomerates of small NPs (Fig. 20c). The electron diffraction pattern (SAED) indicated crystalline particles in accordance with the non-spherical morphology. EDX indicated that the Bi/Fe ratio is practically the same as that of the target material (Table 5). Again, oxgen losses occurred.

# 4.3.2 Characterization of NPs synthesized in ethanol solution of citric acid

The synthesis of NPs was performed in an ethanol solution with 0.05 % citric acid. Figure 21 shows  $FeTaO_4$ ,  $Fe_2WO_6$  and  $FeBiO_3$  nanoparticles directly produced in ethanol with 0.05 % citric acid.



Figure 21a: FeTaO<sub>4</sub> TEM micrographs and electron diffraction pattern (SAED) of NPs produced in ethanol.



*Figure 21b: Fe2WO6 TEM micrographs and electron diffraction pattern (SAED) of NPs produced in ethanol.* 



Figure 21c: FeBiO<sub>3</sub> TEM micrographs and electron diffraction pattern (SAED) of NPs produced in ethanol.

TEM micrographs of FeTaO<sub>4</sub> particles in ethanol showed spherical morphology (Fig. 21a). This finding is supported by SAED results indicating mainly amorphous states. The composition of the nanoparticles was confirmed by EDX which indicate that all NPs possess the same composition. EDX data showed an even greater excess of Ta versus Fe than in the generation in water (Table 5). The loss of oxygen is somewhat greater than in water.

TEM also showed spherically shaped  $Fe_2WO_6$  nanoparticles (Fig. 21b.). EDX analysis suggested that the metal ratio was well preserved in the NPs, accompanied by a similar loss of oxygen as in the water case.

The FeBiO<sub>3</sub> NPs exhibited crystallinity (Fig. 21c) with mainly non-spherical shapes. The vast majority showed sizes of at least 20 nm. Very few had a smaller diameter. This is in strong contrast to the generation in water, where the majority exhibited diameters below 50 nm. Electron diffraction patterns (SAED) prove their crystallinity. The metal ratio Bi/Fe is near to that of the target like in the case of water, and also in the case of Fe<sub>2</sub>WO<sub>6</sub> in both liquids. Also, the behaviour of the oxygen loss is comparable to water

Actually, oxygen losses were observed with all three NP materials, slightly more in ethanol than in water.

# Chapter 4

# Conclusion

The morphology of the target materials  $FeTaO_4$ ,  $Fe_2WO_6$  and  $FeBiO_3$  depended strongly on the composition. A trend of larger grain sizes of 2-3µm down to small values of <200 nm diameter was observed in the series  $FeTaO_4 - Fe_2WO_6$  -  $FeBiO_3$ .

A trend to lower laser ablation thresholds could be observed in this series. The shift to higher threshold fluences could be correlated with the optical interference by laser-generated bubbles. The results suggested that the size and lifetime of the bubbles depend strongly on the fluence. At high fluences, the size and lifetime of the bubbles interfere with the following incoming laser pulse. In this regime, the fluctuating curvature and the strong refractive index differences between the liquid and the vapour in the bubble may lead to strong refraction. Thus, the effective fluence arriving on the sample is reduced in contrast to the case where the bubbles have a low lifetime in the low fluence regime so that the following laser pulse can arrive at the surface without any losses.

The threshold trend for the three materials cannot be explained by absorptivities based on the band gaps which do not vary significantly in the range of 2.2-2.7 eV. With a photon energy of 1.55 eV two-photon processes are necessary and become more probable with decreasing band gap.

On the other hand, impact ionization and avalanche breakdown, may be responsible for the material excitation. There, defect densities play a crucial role in generating free electrons in the conduction bands resulting in avalanche breakdown. The decreasing threshold series of  $FeTaO_4 - Fe_2WO_6 - FeBiO_3$  may suggest an increasing defect density with energy levels close to the conduction band edges. This trend is supported by the target morphologies observed by SEM.

The evaluation of the NPs focussed on the chemical composition and crystallinity. The deviation of the Fe content of the NPs from the original target materials was negligible with  $Fe_2WO_6$ ,  $FeBiO_3$  in contrast to  $FeTaO_4$  where drastic Fe losses were observed both in water an ethanol. Oxygen losses were detected for all three materials.

The NP morphology correlated well with the observed crystallinity (Fig. 22). That means that crystalline NPs exhibited non-spherical shapes. This is observed with FeBiO<sub>3</sub> NPs in both liquids. The only difference was, that the majority NP size was greater in ethanol than in water.



Figure 22: Schematic comparison of crystallinity of produced NPs in water and ethanol

In contrast, only amorphous NPs were generated in the case of  $FeTaO_4$  in both liquids.

Only for  $Fe_2WO_6$ , the nature of the fluid shows an influence on the crystallinity: the NPs in water were crystalline and in ethanol amorphous.

This morphological and stoichiometric correlations with the chemical nature of the target and the fluid still need further investigations due to the complexity of the ablation process of solids in liquid contact.

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