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Letter

Laser ablation of Fe_2B target enriched in ^{10}B content for boron neutron capture therapy

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Abstract
The technique of laser ablation in liquids is applied to produce Boron-containing nanoparticles from ablation of a Fe_2B bulk target enriched in ^{10}B isotope. Laser ablation of the target in liquid isopropanol results in partial disproportionation to free Fe and Boron while nanoparticles of Fe_2B are also presented. The nanoparticles are magnetic and can be collected using a permanent magnet. The average size of nanoparticles is about 15 nm. The content of ^{10}B in the generated nanoparticles amounts to 76.9%. The nanoparticles are biocompatible and can be used in boron neutron capture therapy.

Keywords: boron neutron capture therapy, laser ablation, liquids, nanoparticles, bimetallic nanoparticles

(Some figures may appear in colour only in the online journal)

1. Introduction

Neutron capture therapy (NCT) is an actively developing direction of binary technologies of radiation therapy [1]. The NCT method is used for the treatment of inoperable and radioresistant cancers, and in cases where other methods of treatment are ineffective. It is based on the preliminary saturation of cancer cells with elements having a high neutron capture cross-section, and subsequent irradiation of them with low-energy (epithermal) neutrons. The most effective

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is boron-NCT (BNCT), where, to efficiently capture thermal neutrons, one non-radiative boron isotope, ^{10}B is used [1, 2]. Then, the isotope ^{11}B is formed that almost instantly decays to ^{7}Li nuclei and an α-particle with a high linear energy transfer. Both the α-particles and the lithium nuclei produce closely spaced ionizations in the immediate vicinity of the reaction. The mean free path of α-particles and lithium nuclei in biological tissues is of several micrometers, which is comparable with the size of a target biological cell. As a result, the absorption of energy is localized and leads to the death of cancer cells while the cells of healthy tissues are not affected by neutrons. Currently, several boron-containing chemical compounds are used for BNCT procedures. The main disadvantage of these compounds is relatively low boron content. It is desirable to increase the boron content in the used compounds.

To increase efficiency of BNCT some groups use boron-containing nanoparticles that have higher value of B atoms compared to boronophenylalanine and sodium borocaptate (BSH) [3–8]. To produce such functional nanoparticles, chemical methods are used. It leads to formation of NPs with different kinds of additional ions and chemical impurities that makes them impossible to apply directly for biological cells.

Laser ablation is one of the methods for formation of pure nanoparticles, that is especially important for biomedical applications [9–12]. In this case, irradiation of the target is performed usually in water that guarantees generation of NPs without any outsider components.

The best candidates for NCT are not only NPs of boron itself but also its binary compounds, for example, Fe_2B [13]. Fe-B materials doped with rare earth elements, such as Nd, are the strongest permanent magnets. One may expect that NPs of such materials obtained with the help of laser ablation in liquids will retain magnetic properties of the starting material. This would allow the use of external magnets to localize the nanoparticles in the place where they are needed.

Laser ablation of Fe_2B target with natural composition in boron isotopes in liquid acetone has been successfully realized [13]. These NPs are magnetic and can be collected using a permanent magnet. However, even with NPs of Fe_2B the Boron content is about 10%. The ^{10}B content in natural boron is of order of 20%, so the content of ^{10}B active in BNCT process is of 2% by mass of Fe_2B NPs.

In this work we present the results of laser ablation of a Fe_2B target enriched in ^{10}B content with final aim using these NPs in BNCT.

The radiation of an Ytterbium fiber laser with a wavelength of 1060–1070 nm was focused by an objective ($F = 20.4$ cm) onto the surface of the Fe_2B placed into transparent for laser radiation liquid. The laser beam moved along the target surface at the speed of 100–500 mm s^{-1} by galvano system mirrors. Pulse duration was of 200 ns, repetition rate of 20 kHz, pulse energy of 1 mJ and laser fluence on the target was around 6 J cm^{-2}.

Two liquids were tested as the medium for laser ablation, either water H_2O or isopropanol C_3H_8O. The target had a shape of a massive cylinder made of Fe_2B of 35 mm in diameter preliminary enriched in ^{10}B content using a photonuclear reaction with gamma photons. Polymeric walls of the cell were fixed on the target itself and a soda lime glass transparent for laser radiation was fixed on walls at the height of 5 mm above the surface of the cylinder. The cell was included into a flow cell equipped with peristaltic pump.

The NPs morphology was analyzed with a Carl Zeiss 200FE transmission electron microscope (TEM). Diffraction patterns (XRD) of NPs were recorded using x-ray diffractometer Bruker D8 Discover A25 Da Vinci Design, CuK_α radiation with $\lambda = 1.5418$ Å. Isotopic composition of the generated NPs was characterized by mass-spectrometer of secondary ions IMS-4f, CAMECA.

Laser ablation is accompanied by the liquid breakdown above the target surface and formation of plasma. Laser ablation of Fe_2B target in H_2O results in its decomposition to presumably iron hydroxides and formation of some other NPs. These NPs are rusty in appearance, which is probably due to the interaction of Fe with H_2O. The NPs are not magnetic, which means that they contain neither Fe nor Fe_2B NPs [14].

The NPs generated by laser ablation in isopropanol are black in appearance. They are magnetic and can be collected using a permanent magnet. Since biological tests require an aqueous medium for Fe_2B NPs, isopropanol was substituted by H_2O in several cycles. The generated NPs were evaporated on a Si substrate for further mass-spectrometric and x-ray diffraction analysis.

X-ray diffractograms of the initial bulk Fe_2B target is presented in figure 1(a). It coincides with the diffraction pattern for Fe_2B from database Powder Diffraction File-2, version 2011. X-ray diffractograms of the NPs produced by laser ablation of this target in isopropanol are shown in figure 1(b).

The high background in figure 1(b) is due to x-ray luminescence induced by CuK_α radiation in Fe. According to XRD data, Fe_2B compound is partly disproportionated upon laser ablation in isopropanol. Indeed, except for Fe_2B NPs there are also NPs of Fe and stable boron molecules B_{12} and B_{28} made of 12 and 28 atoms of Boron, respectively.

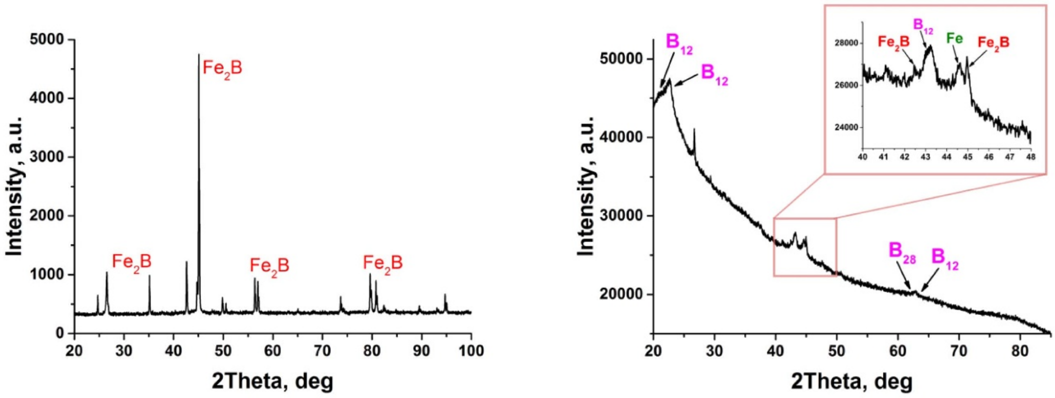
TEM view of nanoparticles generated by laser ablation of Fe_2B target in isopropanol is shown in figure 2.

One can see that NPs are aligned one after another which confirms their magnetism. The aligned NPs are embedded into amorphous halo that presumably consists of the products of Fe_2B decomposition. Amorphous carbon may also be presented since it is formed under laser decomposition of isopropanol. This carbon should not have diffraction peaks in XRD.

A view of the scattered electrons (STEM) of NPs prepared by laser ablation of Fe_2B target in isopropanol is shown in figure 3.

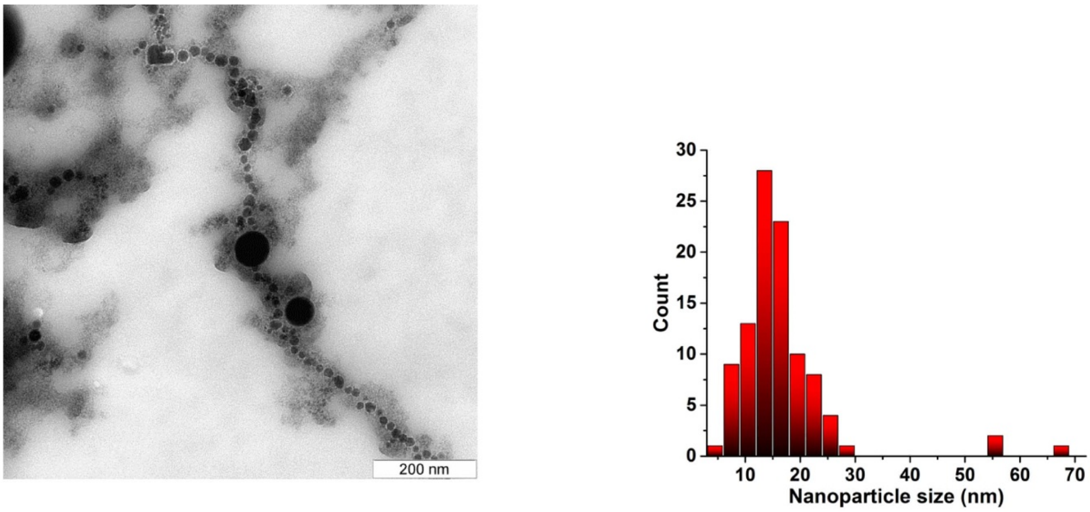
One can see a dense core and a less dense shell around it. An amorphous halo is also made of less dense materials than the core.

Boron nanoparticles of natural isotopic abundance were used as a reference in isotopic measurements. Such nanoparticles were produced by laser fragmentation of industrial powder (size from 200 to 800 nm) in isopropanol. Laser source was the same as in laser ablation of Fe_2B target in liquid (Ytterbium fiber laser). The x-ray diffractogram of the industrial boron powder is shown in figure 4. Broad peaks correspond to amorphous boron while small peaks on amorphous



(a) (b)

Figure 1. X-ray diffractograms of the initial Fe_2B target (a) and NPs generated by laser ablation of this target in liquid isopropanol (b).



(a) (b)

Figure 2. TEM view of NPs produced by laser ablation of Fe_2B target in isopropanol. Scale bar denotes 200 nm (a). Histogram of size distribution of NPs in figure 2 (b).

background correspond to rhombohedral phase of B. Strong narrow peaks at 15 and 28 degrees are the peaks of boron hydroxide $B(OH)_3$.

Isotopic composition of NPs obtained by laser ablation of Fe_2B target in isopropanol was compared with that of industrial boron powder fragmented by laser radiation in isopropanol. The results are shown in table 1.

One can see that the content of ^{10}B in NPs generated by laser ablation of Fe_2B target enriched in this isotope is almost four times higher ^{10}B content in industrial Boron powder. This is advantageous for required amount of NPs for BNCT.

Fe_2B is formed via direct reaction of Fe with B at temperature as low as 900 °C and its melting temperature is 1389 °C [15]. The temperature of the target is much higher during laser ablation. Also, the ablation is accompanied by the formation of plasma. The components of the target, Fe and B, are separated from each other. Not all the components may return to each other after plasma recombination and cooling down of the vapors of surrounding liquid. For this reason the NPs produced by laser ablation of the target are composed not only from Fe_2B, there are elemental Fe and boron, as one can see from figure 1. The disproportionation of the target materials upon laser ablation of two-component targets is rather typical phenomenon especially if the physical properties of the components are very different. For example, disproportionation is observed under laser ablation of Sm_2Co_{17} target in liquid cyclopentanone [16].

Elemental boron possesses numerous allotropes, some of them are presented in the diffractograms in figures 1(b) and 4. New allotropes of boron appear after laser ablation of Fe_2B target, namely, B_{12} and B_{28}. They are not presented in the initial target and could be formed during cooling down the vapors above the target surface.

NPs produced by laser ablation of Fe_2B target were covered by polyethyleneglicol (PEG) for cytotoxic tests. The particles were successfully tested on two types of cell cultures U87

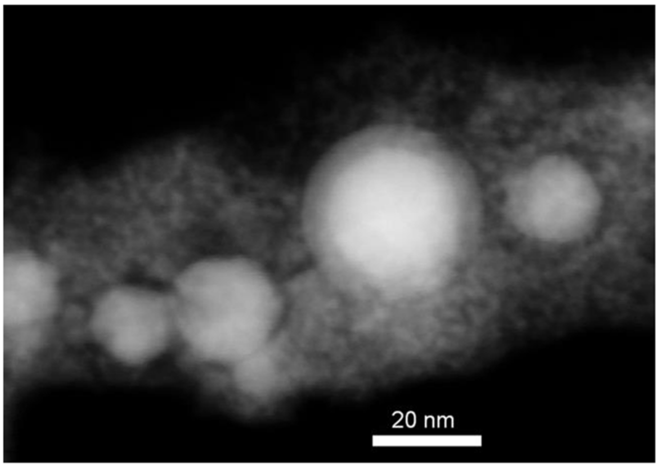


Figure 3. STEM view of NPs obtained by laser ablation of Fe_2B in isopropanol. Scale bar denotes 20 nm.

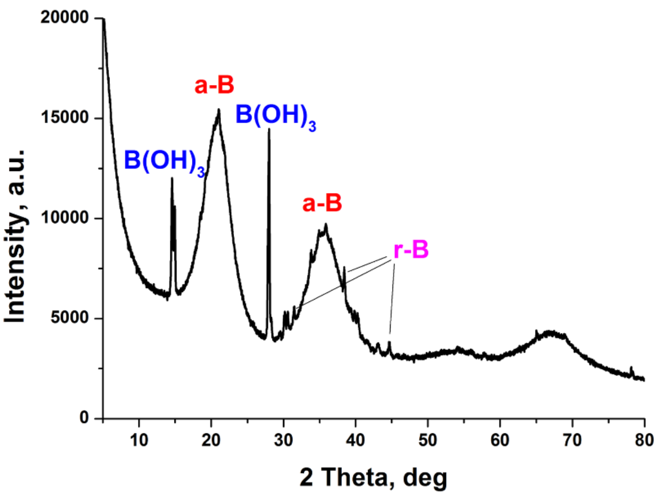


Figure 4. X-ray diffractogram of industrial boron powder. Label 'a-B' indicates amorphous B, 'r-B'—rhombohedral B.

Table 1. Boron content in different samples.

Boron isotope content, %	^{10}B	^{11}B
Industrial B powder	19.2 ± 0.1	80.8 ± 0.1
Ablated Fe_2B nanoparticles	76.9 ± 0.1	23.1 ± 0.1

(human glioblastoma) and SW-620 (human colorectal adenocarcinoma).

Thus, NPs enriched in ^{10}B content have been successfully realized by laser ablation of a bulk Fe_2B target in isopropanol. It was found that NPs contain apart from Fe_2B NPs also NPs of Fe and molecular B_{12} and B_{28} structures. Average size of NPs is about 15 nm, and some of them have core–shell structure. NPs are magnetic and can be collected and directed using a permanent magnet. The content of ^{10}B in laser-produced nanoparticles is as high as 76.9%, which exceeds the ^{10}B content in natural Boron almost by factor 4. The generated nanoparticles are biocompatible and can be used in BNCT.

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