

**ENGINEERING A BIOCOMPATIBLE MICROSCALE SURFACE TOPOGRAPHY
FOR PROMOTING THE HARD TISSUE IMPLANT'S MECHANICAL
PROPERTIES AND CELL RESPONSE**

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Abstract: *This study evaluated methods to improve the long-term durability and performance of the metallic hard-tissue implant materials under physiological conditions, using the β -type Ti-45Nb (mass%) alloy as an example. The focus was on enhancing surface characteristics, mechanical behavior, and biocompatibility of the bio-metallic alloy through a combination of severe plastic deformation and surface modification techniques. High-pressure torsion (HPT), as a severe plastic deformation procedure, was used to refine the alloy's microstructure, and attained results showed that a significant reduction of the grain size was achieved without inducing phase transformations. Subsequent laser surface treatment was employed to modify the surface chemistry and topography of the investigated alloy, and surface analysis that followed revealed increased roughness and the formation of a passive oxide layer. These microstructural and surface changes led to improved mechanical properties and enhanced bioactivity of the Ti-45Nb alloy in simulated physiological environments. Overall, the combined use of plastic deformation and laser treatment significantly enhanced the performance of Ti-45Nb alloy for biomedical applications.*

Keywords: *metallic biomaterials, microstructural refinement, laser surface modification, surface characteristics, mechanical properties, cytotoxicity, biocompatibility*

1. Introduction

Titanium-niobium alloys have emerged as promising materials for biomedical implants due to their superior mechanical properties and biocompatibility. These alloys address key limitations of conventional titanium alloys, including toxicity concerns and the stress shielding effect associated with the Ti-6Al-4V (mass%) alloy [1-3]. Despite these advantages, further optimization of these alloys is required to ensure long-term implant performance under physiological conditions [4]. Severe plastic deformation (SPD) techniques, such as high-pressure torsion (HPT), are effective methods for enhancing the mechanical properties and biocompatibility of implant materials [5-7]. SPD methods produce an ultrafine-grained (UFG) microstructure by significantly reducing grain size and increasing dislocation density, which in turn improves material properties. Numerous studies have demonstrated that UFG metallic materials exhibit superior physical properties, higher corrosion resistance, and enhanced interactions with cells compared to their coarse-grained (CG) counterparts [6, 7].

Ti-Nb alloys, particularly Ti-45Nb (mass%) alloy, demonstrate excellent biocompatibility and low cytotoxicity, attributed to the inherent properties of titanium and niobium. These characteristics make them suitable for long-term biomedical applications [7, 8]. Consequently, Ti-Nb alloys are considered promising candidates for orthopedic and dental implants, where exceptional bio- and mechanical compatibility with human tissues is essential [9]. However, the surface of the cytocompatible Ti-Nb alloy often necessitates modification to promote osseointegration, as its intrinsic properties do not actively stimulate bone growth [10-12]. Recently, laser surface scanning has attracted significant interest in biomedical engineering. Laser beam irradiation modifies the surface properties of metallic implants, thereby enhancing mechanical performance, corrosion resistance, and biocompatibility in hard-tissue applications [13, 14]. These improvements are

attributed to the formation of specific microstructural and morphological features at the surface, which facilitate integration with surrounding tissues. Furthermore, laser surface processing promotes the development of protective oxide layers, resulting in a bioactive surface that supports improved osseointegration with simultaneous improved corrosion resistance [15-18].

The objective of this study was, therefore, to investigate the effects of microstructural refinement and laser irradiation on the surface topography, mechanical behavior, and cytocompatibility of the Ti-45Nb alloy under simulated physiological conditions.

2. Materials and methods

In the present study, the β -type Ti-Nb alloy was selected as the base material. Analysis of the Ti-45Nb alloy in the as-received hot-extruded condition showed a coarse-grained structure, as presented in previous research [19,20]. However, after its HPT processing, significant grain refinement occurred, transforming the CG into a UFG structure [19, 20].

Subsequently, the unprocessed and HPT-processed specimens were subjected to the laser surface scanning treatment, where both samples were irradiated with output energies of 5 mJ and 15 mJ using a Nd:YAG EKSPLA SL 212/SH/FH laser system operating at a wavelength of 1064 nm. Prior to the surface treatment, the specimens were prepared using standard metallographic procedures, including grinding, polishing, and ultrasonic cleaning.

Surface analyses of the laser-treated alloy samples were carried out using a stereo microscope Stemi 508 Zeiss, with an AxioCam 212 color digital camera. Elemental composition was examined via energy-dispersive spectroscopy (EDS) with an Oxford Inca 3.2 system coupled with SEM JEOL JSM 5800, while phase identification was conducted using X-ray diffraction (XRD) using a Rigaku Ultima IV diffractometer. Surface topography was further evaluated using a non-contact optical profilometer ZYGO NewView 7100.

The mechanical properties of the Ti-45Nb alloy under different processing conditions were evaluated using nanoindentation. Both experimental and theoretical results, based on established methodologies, were considered and presented in previous studies [20-22].

Cytotoxicity of the Ti-45Nb alloy prior to and following structural and surface modification was assessed using MRC-5 human fibroblast cells, as reported previously [21, 22]. Cytotoxicity was determined as the percentage of cell growth inhibition in in vitro assays such as (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide) test (MTT) and Dye Exclusion Test (DET) performed in triplicate for reproducibility [21, 22]. The MTT assay results provided data on the proliferation and viability of MRC-5 cells in contact with the investigated alloy after 48 h of exposure. The DET assay complemented these findings by determining the percentage of dead vs. viable cells.

3. Results and discussion

3.1. Laser surface scanning of the investigated alloy

3.1.1. Surface morphology studies

The study of laser irradiation effects on the alloy's surface properties was primarily focused on the examination of complex interactions of the material surface with the laser beam and the impact of the irradiation-induced high temperatures and rapid accompanying processes on the alloy's surface characteristics. Surface characterization of the laser-treated CG and UFG Ti-45Nb alloy revealed the formation of micrometer-scale structures and distinct surface effects (Figure 1). Laser scanning in air led to specific morphological changes, strongly influenced by the energy distribution during irradiation, which is in accordance with previously described results in the literature [15, 18, 21]. The material heating and melting in the surface and subsurface zones caused partial material removal due to laser ablation processes. Following the end of laser irradiation, the molten material solidified quickly, resulting in characteristic hydrodynamic surface damage effects in the form of ripples and

valleys. Furthermore, the accumulation of molten material led to the formation of periodic wave-like structures, as illustrated in Figures 1b and 1d. Additionally, increased laser pulse energy led to the formation of more distinct surface damage features on the surfaces of both CG and UFG alloy samples. Moreover, profilometric analysis showed that the wave-like structures, which were formed under higher laser output energy, were not uniformly distributed, leading to variations in hydrodynamic surface patterns (Figure 2). Increased laser energy also resulted in deeper and more pronounced ablation damage, as shown in Figures 2b and 2d. The linear profiles indicate that surface damage depth and the ejected material height range from $-0.5 \mu\text{m}$ to $+1.25 \mu\text{m}$, reflecting the ablation process intensity.

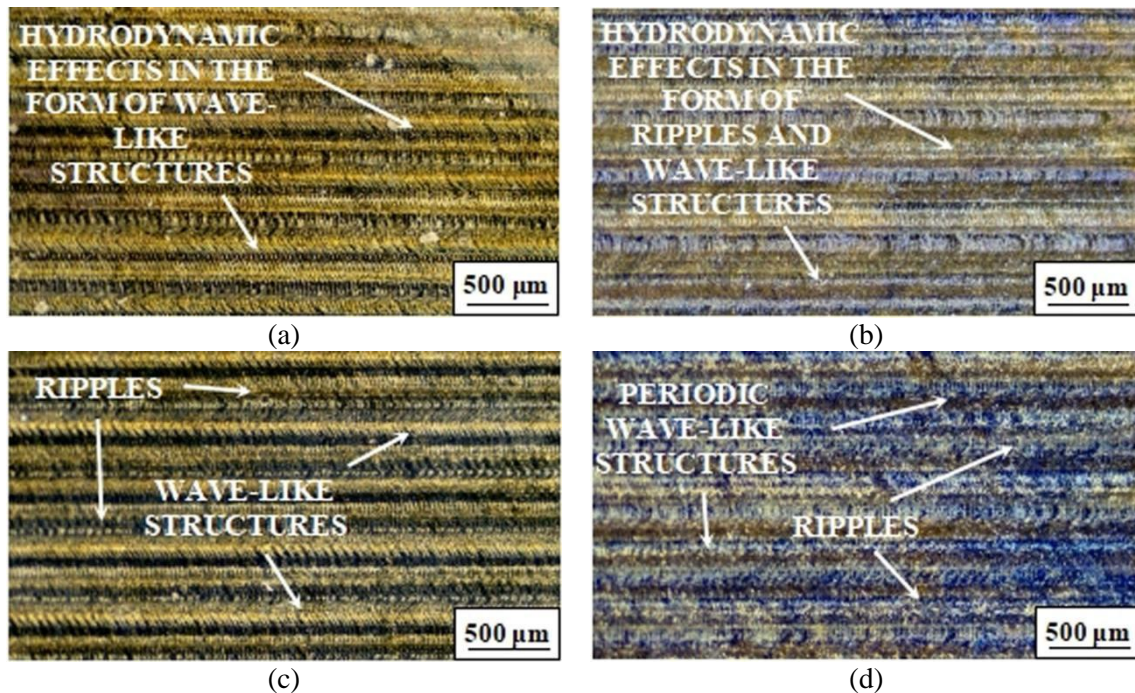


Figure 1. Stereoscopic micrographs of a),b) CG and c),d) UFG Ti-45Nb alloy surface after laser treatment with a),c) 5 mJ and b),d) 15 mJ.

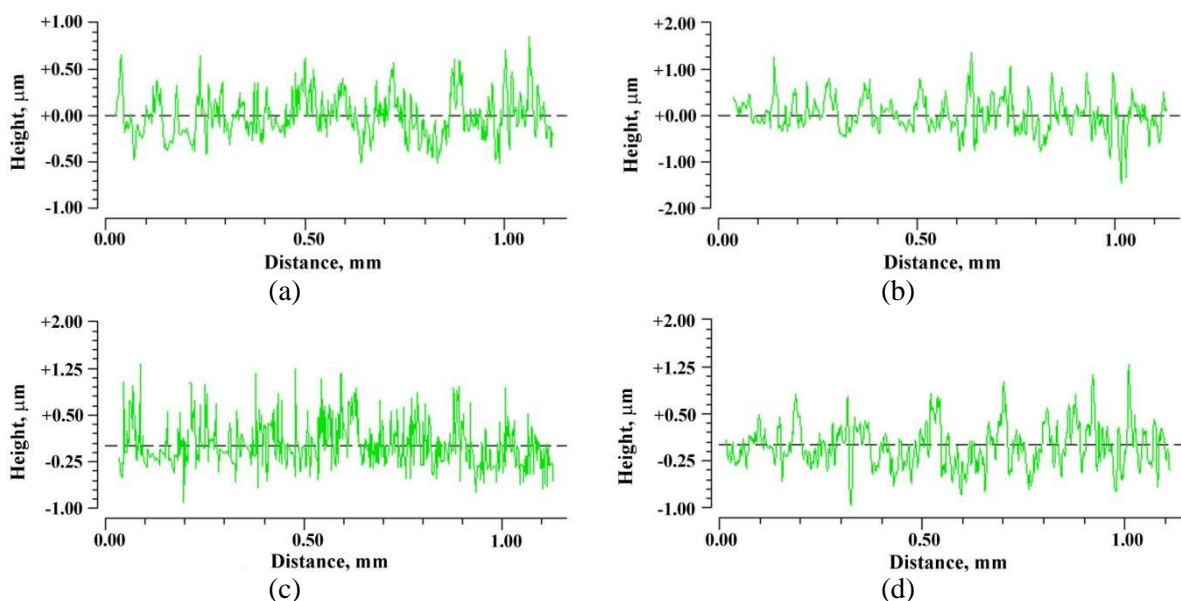


Figure 2. Profilometric analysis of the a),b) CG and c),d) UFG Ti-45Nb alloy surface after laser treatment with a),c) 5 mJ and b),d) 15 mJ [21].

3.1.2. Surface roughness and chemistry studies

Laser surface scanning caused overlapping and redistribution of formed surface damage features, which contributed to increased surface roughness. As shown in the diagram in Figure 3, the laser treatment created, depending on the degree of laser ablation and irradiation penetration, a surface that was rougher compared to the untreated alloy surface. The application of higher-intensity laser output energy produced a surface with more pronounced morphological changes during the irradiation, which resulted in a more significant increase in surface roughness for both CG and UFG samples. Furthermore, the UFG Ti-45Nb alloy exhibited higher roughness values compared to the CG specimens.

Analysis of the CG and UFG Ti-45Nb alloy surfaces after laser treatment in air revealed that changes in the chemical composition of the surface, in addition to morphological changes, were induced as a result of high absorption energy. Results of the EDS analysis demonstrated that the increase in laser pulse energy from 5 mJ to 15 mJ led to an increase in surface oxygen content by more than 30% in the analyzed irradiated areas and further stimulated the surface oxidation process of the material (Figure 4). The obtained results indicate the formation of a stable and thin layer on the alloy surface of Ti and Nb oxides, which is consistent with data available in the literature [6, 9].

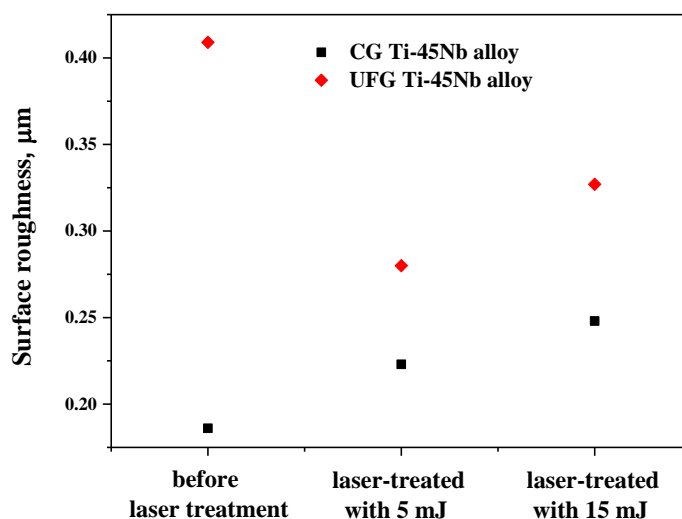


Figure 3. Surface roughness of the CG and UFG Ti-45Nb alloy before and after laser treatment.

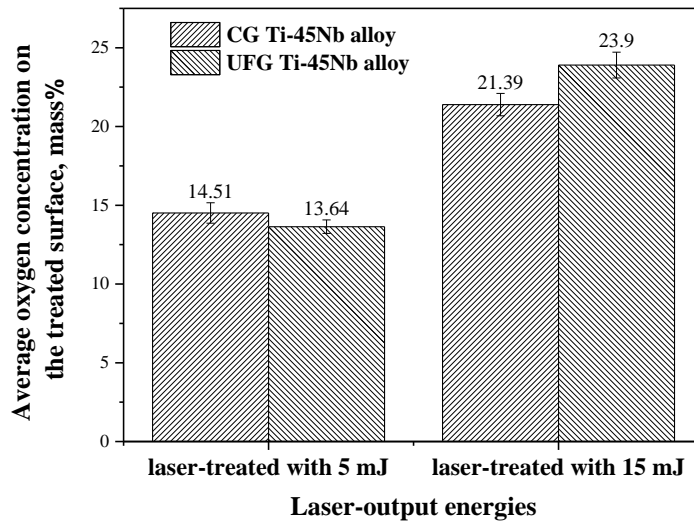


Figure 4. Chemical composition of the laser-treated CG and UFG Ti-45Nb alloy surfaces as a function of the laser output energy.

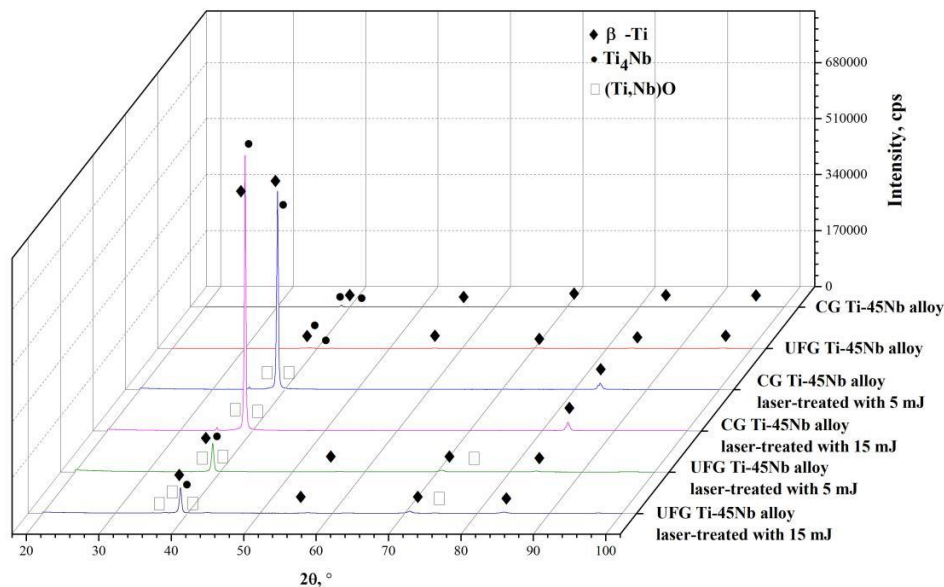


Figure 5. XRD patterns of the CG and UFG Ti-45Nb alloy before and after laser treatment.

Rapid heating and cooling of the irradiated alloy that occurs during the laser treatment can cause phase transformations or recrystallization that alter the alloy’s microstructure and thus affect material properties. Phases identified by XRD in the CG and UFG Ti-45Nb alloy after laser surface treatment showed that phase transformation did not occur, with identical phases present in the alloy’s microstructure pre- and post-laser treatment, despite the attained microstructural and surface modifications (Figure 5). However, laser treatment was observed to promote the formation of (Ti, Nb)O, indicating the formation of a surface oxide layer. This layer, formed on the alloy surface during interaction of the alloy with the laser beam, enhances both the corrosion resistance and biocompatibility of the alloy under physiological conditions [17, 22].

3.2. Investigation of the mechanical properties

Table 1 summarizes both experimental and theoretical ranges of elastic modulus (E), hardness (H), and plasticity (E/H) of different metallic implant materials available in the literature, all of which are, in the case of the investigated Ti-45Nb alloy, increased after the laser irradiation treatment. Based on the previously reported results of our investigations [20], it has been shown that the investigated UFG alloy, before and after the additional laser treatment, exhibits higher values of E , H , and E/H compared to the alloy in the CG condition. Moreover, the comparative analysis showed good agreement between theoretically and experimentally obtained data [20]. Overall, the results of our study showed that the application of severe plastic deformation and laser surface treatment resulted in the optimal improvement of the alloy's surface mechanical properties, which is consistent with findings previously reported in the literature [7, 23, 24].

Similarly to our findings, K.Y. Xie et.al. [24] in their research documented the grain refinement effects on the β -type Ti alloy's E and H values, and showed that HPT processing resulted in a significant increase in alloy hardness from 2.55 GPa to 3.128 GPa, which is comparable to the increase observed in our Ti-45Nb alloy samples. Moreover, the E values observed in our research after HPT processing and surface treatment align with the literature reports for different alloys in the Ti-Nb system, where E values range from 48 GPa to 98 GPa (see Table 1). Furthermore, the results attained during our research indicated that plasticity was significantly improved, which is consistent with the results of the A. Panigrahi et.al. [25] study, where an increase in plasticity following HPT was documented. These results suggest that the grain refinement and laser surface treatment of the Ti-45Nb alloy play a role in reaching the elastic modulus, hardness, and plasticity values favourable to the alloy's applicability in the field of orthopedic and dental implantology.

On the other hand, the literature data presented in Table 1 show that E values for a vast number of metallic biomaterials are in the range from 89 GPa to 246 GPa, suggesting that the investigated Ti-45Nb alloy is better suited for the fabrication of hard-tissue replacements compared to these materials. Moreover, the limited literature data available on the hardness of metallic implant materials indicate that H values can vary within the range of 1.422 to 5.531 GPa, which is consistent with the experimental results and the theoretical calculations for the Ti-45Nb alloy subjected to HPT processing and laser surface modification.

Table 1. Literature data showing the mechanical properties of various metallic biomaterials.

<i>Metallic implant materials</i>	<i>Investigation method</i>	<i>Elastic modulus, E, GPa</i>	<i>Hardness, H, GPa</i>	<i>Plasticity, E/H</i>
<i>Ti-45Nb alloy [20]</i>	Experimental	37 - 91.505	1.81 - 2.949	18.35 - 37.44
	Theoretical	44.21 - 100.01	0.67 - 3.08	23.08 - 106.54
CP-Ti [25]	Experimental	102	2.0	55.56
Ti-6Al-4V [25]	Experimental	110	3.4	32.26
Ti-5Mn-3Mo alloy [26]	Experimental	89 - 100	~3.295 - 3.658	
Co-Cr alloys [27]	Experimental	~ 193 - 246	2.687 - 5.531	
Ti-35Nb [28]	Experimental	84.7 ± 1.2	2.354 ± 0.15 after treatment: 2.471 ± 0.1	
Ti-45Nb [25,29]	Experimental	61 - 72	1.50 ± 0.04	25 - 43.48
	Theoretical	62 - 64		
Ti-13Nb-13Zr alloy [30]	Experimental	62 - 84	(2.462 - 2.795) ± 0.07	
Ti-50Nb alloy	Experimental	79	2.16	
Ti-80Nb alloy		97	1.90	
Ti-90Nb alloy [31]		98	1.80	

Ti-40Nb alloy [32]	Experimental	68 - 102	1.62 - 3.5 after treatment: 2.2 - 3.87	
Ti-25Nb-xSn-xCr alloy [33]	Experimental	min: 66.2 ± 2 max: 78 ± 3	min: 1.93 ± 0.15 max: 2.36 ± 0.13	
Ti-29Nb-13Ta-4.6Zr alloy [34]	Experimental	47.8 ± 0.22	1.922 ± 0.02	
Ti-29Nb-13Ta-4.6Zr alloy [23]	Experimental	64 HPT: 60	2.109 HPT: 2.256-2.942	
Ti-25Ta-25Nb alloy [35]	Experimental	55	1.422	
Ti-36Nb-2.2Ta-3.7Zr-0.30O alloy [24]	Experimental	65 ± 0.5 HPT: 43.3 ± 0.4	2.55 ± 0.05 HPT: 3.138 ± 0.06	

3.3. Biological studies

Cytotoxicity tests were performed on the Ti-45Nb alloy with CG and UFG microstructure, *i.e.* pre- and post-HPT processing, before and after laser scanning to assess its biocompatibility. The combination of MTT and DET tests provided a comprehensive review of the cytocompatible potential of the Ti-45Nb alloy samples prepared under different conditions (Figure 6). MTT test revealed that both CG and UFG Ti-45Nb alloys show lower MRC-5 cell viability before laser treatment. Laser irradiation at 5 mJ and 15 mJ increased cell viability in all cases, with the highest value (134.42%) observed for the UFG alloy laser-treated at 15 mJ. On the other hand, DET test indicates that the lowest MRC-5 cell viability (79.45%) was characteristic of the CG Ti-45Nb alloy before laser treatment. The highest value (94.28%) was observed in the case of UFG alloy after it was laser-treated with 15 mJ. These results suggest that laser surface treatment significantly improves the biocompatibility of the investigated alloy. Namely, MTT and DET results confirm that all tested samples are non-cytotoxic, and the Ti-45Nb alloy demonstrates excellent overall cytocompatibility. These results are in accordance with the research of I. Dimić et. al. [7] where MTT test showed increased MRC-5 cell viability over time when in contact with CP-Ti, Ti-13Nb-13Zr (TNZ), and UFG Ti-13Nb-13Zr (UFG TNZ) alloys, with no cytotoxicity observed. Results of I. Dimić et. al. [7] indicated that after 96 hours, CP-Ti, Ti-13Nb-13Zr, and UFG Ti-13Nb-13Zr alloys promoted cell growth, while UFG CP-Ti influenced slightly lower MRC-5 cell viability. Moreover, DET results confirmed that UFG TNZ alloy outperforms CP-Ti, as a standard implant material [7]. Furthermore, A. C. Bărbîntă et.al. [36] studied the cytotoxicity of new generation titanium alloys (Ti₂₁Nb₆Zr₁₅Ta, Ti₂₅Nb₁₀Zr₈Ta, Ti₁₇Nb₅Zr₅Al, Ti₇Nb₇Zr₂Al) using fibroblast-like cells of the human cell lines. Their study indicated that the new generation alloys showed no cytotoxic effects and supported cell attachment and proliferation, when compared to the conventional alloys (Ti₆Al₇Nb, Ti₆Al₄V), exhibiting higher cell viability and indicating that TiNbZrTa and TiNbZrAl alloys are promising new candidates for biomedical applications [36].

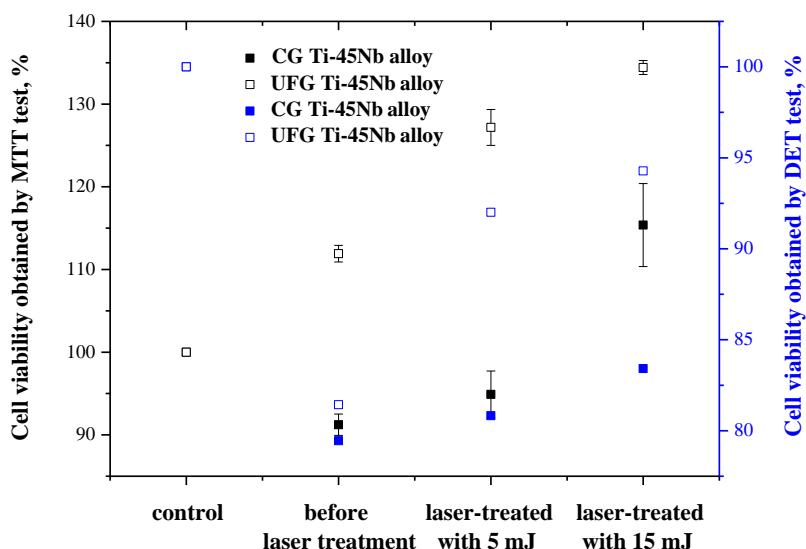


Figure 6. Cell survival rate measured by the MTT and DET assays after 48 h.

As presented in our previous work [21, 22], improved biocompatibility after both treatments (HPT and laser surface scanning) has been observed, and as a result, the UFG structure obtained by HPT enhanced cellular adhesion and proliferation, while laser-modified surfaces, due to altered roughness and surface chemistry, promoted favourable cell interactions. The obtained results also show strong agreement with the literature [37-39]. M. Manjaiah et al. [37] and Y. Jiao et al. [38] showed that thicker surface oxide layers and higher surface roughness, as a result of the metal oxides' presence, improve the alloy's cytocompatibility. The improved cells' attachment and favourable cells' morphology, which are observed during our research on the laser-modified surfaces, are consistent with the work of Z. Zhao et al. [39], who reported enhanced biointegration of the laser-treated Ti-6Al-4V coated with Zr oxides.

In summary, the presented research showed that HPT processing of the alloy primarily improves the alloy's bulk mechanical properties and corrosion behavior through microstructural refinement, while the laser surface treatment of the alloy offers additional advantages at the surface level, particularly in terms of its biological response (see Table 2). Moreover, the presented research indicated that the combined application of both processing methods demonstrates a synergistic effect, making the investigated alloy highly suitable for biomedical applications.

Table 2. Comparative effects of HPT processing and laser surface modification on the Ti-45Nb alloy microstructural, surface, and mechanical properties and biocompatibility.

Properties	HPT processing	Laser surface treatment
Microstructural properties	Ultrafine grains, increased grain boundary density	Local surface structure modification, formation of fine texture
Surface properties	Increased roughness due to structural refinement	More pronounced surface damage features formation, increased surface roughness and oxygen content, oxide layer formation
Mechanical properties	Increase in hardness, elastic modulus, and plasticity due to structural refinement	Significant increase in hardness, slight increase in elastic modulus, and an increase in plasticity at the alloy's surface

		due to changes in the alloy's topography and chemistry
Biocompatibility	Excellent cytocompatibility with increased cell adhesion due to higher surface energy	Excellent cytocompatibility with attained favourable surface roughness and surface oxide layer, beneficial for cell adhesion and proliferation
Primary contribution	Improvement in the overall mechanical properties of the material	Improved biological response of the material

4. Conclusions

Based on the presented results, it can be concluded that by combining the HPT microstructural refinement with the laser surface modification, a significant scientific advancement in the field of titanium-based biomaterials development can be achieved. This approach effectively tailors the mechanical properties, cytocompatibility, and biocompatibility of the metallic implant materials required for their biomedical applications. As a result, these modifications contribute to achieving implant materials with enhanced durability and long-term stability in the human body, thereby improving their performance and lifespan in physiological conditions.

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