RESEARCH ARTICLE

Improving Biocompatibility and Mechanical Properties of Titanium Implants in Orthopedic Surgeries: The Role of Machining Depth in Enhancing Surface Interaction with Bone Tissue

Sayyed Mohammadreza Sedehi, PhD Student; Mohammadreza Farahani, PhD

Research performed at University of Tehran, Tehran, Iran

Received: 1 December 2024 *Accepted: 20 July 2025*

Abstract

Objectives: This study comprehensively examined the influence of cutting depth during dry milling on the structural, mechanical, and biocompatibility characteristics of commercially pure titanium. The primary objective was to evaluate how variations in cutting depth can alter the crystallite size, microstrain, and wear resistance, as well as to investigate their correlation with essential biocompatibility parameters including cellular interactions, osteointegration potential, and corrosion resistance in a simulated body fluid environment. Understanding these interrelations is crucial for improving the overall performance of titanium implants used in biomedical applications.

Methods: Pure titanium specimens were precisely machined at cutting depths of 0.1, 0.2, and 0.3 mm under dry conditions, ensuring that all other machining parameters remained constant. The structural characteristics were analyzed using X-ray diffraction to determine crystallite size and microstrain variations. Wear resistance was evaluated through sliding wear tests that quantified material loss, while biocompatibility performance was assessed via immersion tests in simulated body fluid. This evaluation included corrosion resistance measurements, quantification of calcium–phosphate deposition on the surface, and analysis of the initial interactions with osteoblast-like cells to determine cellular affinity and bioactivity.

Results: The experimental results indicated that increasing the cutting depth led to a significant reduction in crystallite size (28, 50, and 25 nm for 0.1, 0.2, and 0.3 mm, respectively) and a corresponding increase in microstrain (0.0011, 0.0011, and 0.009). Specimens machined at cutting depths of 0.2 and 0.3 mm exhibited superior wear resistance, with lower weight losses (7.9 and 5.3 mg) compared with the 0.1 mm specimen (12.1 mg). Biocompatibility assessments revealed that higher cutting depths enhanced corrosion resistance, promoted calcium–phosphate deposition, and improved osteointegration potential.

Conclusion: optimizing the cutting depth to 0.2–0.3 mm during dry milling can substantially improve both mechanical performance and biocompatibility, offering valuable guidance for implant manufacturing and long-term in vivo functionality.

Level of evidence: I

Keywords: Biocompatibility, Machining, Simulated body fluid (SBF), Titanium

Introduction

Over the past few decades, the demand for joint replacement has increased rapidly, with an estimated 90% of individuals over the age of 40 affected by degenerative or inflammatory joint diseases.[1] Issues such as bone weakening (osteoporosis),[2] joint inflammation (osteoarthritis),[3] inflammation of the synovial membrane (rheumatoid arthritis),[4] and cartilage weakening (chondromalacia)[5] cause the loading of bone to deteriorate, potentially leading to the degradation of mechanical properties, pain, and loss of function.[6] Total joint replacement (TJR) addresses these problems by replacing load-bearing or malfunctioning joints with artificial joints or implants.[7] A bioimplant is an artificial device designed to restore the function of a natural organ

Corresponding Author: Mohammadreza Farahani, School of Mechanical Engineering, College of Engineering, University of Tehran, Tehran, Iran

Email: mrfarahani@ut.ac.ir

THE ONLINE VERSION OF THIS ARTICLE
ABJS.MUMS.AC.IR

or tissue without adversely affecting other parts of the body. These components can be implanted into the human body, enabling natural biological processes such as stable bone formation to enhance quality of life and longevity.[8] This demand has prompted researchers to develop biomaterials capable of replicating bone-like characteristics such as toughness and strength.[9] Titanium alloys have become increasingly prevalent in medical applications, including orthopedic and dental implants, due to their favorable properties.[10] High corrosion resistance, an excellent strength-to-weight ratio, low elastic modulus, high biocompatibility, and low density make titanium alloys the material of choice when reliability, performance, and long-term durability are essential.[11] The chemical and physical properties of human body fluids are uniquely distinct from other natural environments,[12] and these characteristics can significantly influence the performance of metals, potentially triggering adverse biological responses. Moreover, the manufacturing process of an implant plays a critical role in determining its in-service behavior and must achieve superior quality to ensure optimal performance within the human body. According to Gravie et al., corrosion behavior is largely determined by the properties of the machined surface in saline environments.[13] In the context of orthopedic implants, the surface quality of machined components plays a decisive role in determining their compatibility and osseointegration with the host tissue.[14] Achieving the desired surface roughness and, consequently, high-quality machined parts requires precise control of machining parameters, cutting tool condition, and the machining environment.[15] Corrosion and wear resistance are directly influenced by surface quality. These factors are critical determinants of an implant's service life within the host.[16] Jiang Wan et al. developed a hierarchical model demonstrating that the superior mechanical performance of load-bearing biomaterials, such as bone and shell, arises from their optimized multi-level structural organization.[17] Their study emphasized that, despite the relatively weak mechanical properties of their constituent phases, these biological materials achieve high toughness and strength through structural hierarchy rather than relying solely on the intrinsic strength of their materials to withstand biological loads. Similarly, Prakash et al. reported that rake angle and cutting speed have a substantial effect on the corrosion behavior of mild steel.[18] Their findings indicated that reducing the rake angle increases the corrosion rate in saline environments, whereas increasing the cutting speed decreases it.[19] Additionally, metallic implants may loosen over time, leading to undesirable effects such as toxicity and adverse biological reactions.[19] Over the past two decades, implants for biomedical applications have undergone rapid and significant advancements. In terms of biocompatibility, titanium is superior to other metallic materials due to the formation of a stable passive titanium oxide layer on its surface.[20] Other desirable properties of titanium include its low elastic modulus, lightweight nature, and reduced artifact generation in computed tomography and magnetic resonance imaging compared with other orthopedic metals.[20] Ti-6Al-4V is the most widely used titanium alloy in surgical applications; however, despite its excellent performance and corrosion resistance, high concentrations of metal ions have been detected in tissues surrounding implants, raising concerns about the long-term safety of this alloy.[20] In the machining of biomedical implants, all manufacturing conditions and parameters significantly influence the mechanical properties and biocompatibility of the final components. Factors such as the presence or absence of coolant,[21,22] the feed rate,[23,24] and machining time[25,26] directly affect the surface characteristics and microstructural features of the material. Although cutting depth can influence machining time and production costs, its primary significance lies in its critical role in enhancing the mechanical properties and biocompatibility of machined titanium components for biomedical applications. In many cases, however, manufacturers overlook the long-term implications of these factors, sacrificing the quality of mechanical and biocompatibility properties particularly in sensitive components such as implants in favor of reducing production time and costs. The cutting depths selected for this study (0.1, 0.2, and 0.3 mm) were based on practical considerations for future projects aimed at utilizing recycled titanium machining chips. These depths correspond to the final phase of machining, specifically the finishing stage, ensuring an appropriate surface finish for biomedical applications while minimizing thermal effects associated with higher cutting depths. Excessive heat generation during titanium machining can degrade metallurgical properties, a concern of critical importance in implant manufacturing.[27,28] Therefore, the chosen cutting depths represent a careful balance between achieving the desired surface quality and preserving the metallurgical integrity of the material. This research forms part of a broader investigation into the machining of implantable components for the human body, requiring precise control of material removal to ensure that the resulting material properties and recyclability remain as close as possible to the ideal condition. The present study addresses existing scientific gaps in previous research, particularly concerning the influence of cutting depth on the long-term performance and biocompatibility of implants. The findings demonstrate that the choice of cutting depth can directly impact implant design by enhancing surface properties, improving production efficiency through optimized machining processes, and ensuring compliance with regulatory standards for implant safety, biocompatibility, and durability. These insights can inform the development of safer, longer-lasting, and more effective implants for clinical use.

Materials and Methods

In this study, four mm-thick commercially pure titanium sheets were machined at cutting depths of 0.1, 0.2, and 0.3 mm using a milling machine. The surface properties and biocompatibility of the machined specimens were subsequently evaluated. These cutting depths were selected to assess their influence on surface and microstructural characteristics, with particular emphasis on the effects of internal stresses and wear rates under varying machining conditions. Milling was performed in a climb milling mode without the use of coolant. Carbide cutting tools with a TiN coating were employed to reduce corrosion and wear during titanium machining. The choice of cutting tool is critical for achieving optimal surface quality and dimensional accuracy in machined components. The chemical composition of the titanium sheets, machining parameters, and process schematic are presented [Tables 1, 2 and Figure 1].

Table 1. Chemical Composition of the Used Sheet

Element	Ti	O	Fe	N	C	Si	Density (g/cm³)
Weight %	Balance	0/27	0/05	0/03	0/02	0/02	4/51

Table 2.Machining Conditions

Parameter	Valeu
Feed rate (mm)	0.1
Cutting depth (mm)	0.1 – 0.2 – 0.3
Tooltip radius (mm)	0.1
Cutting tool rotation (rpm)	800
Machining Direction	Climb
Cooler	-

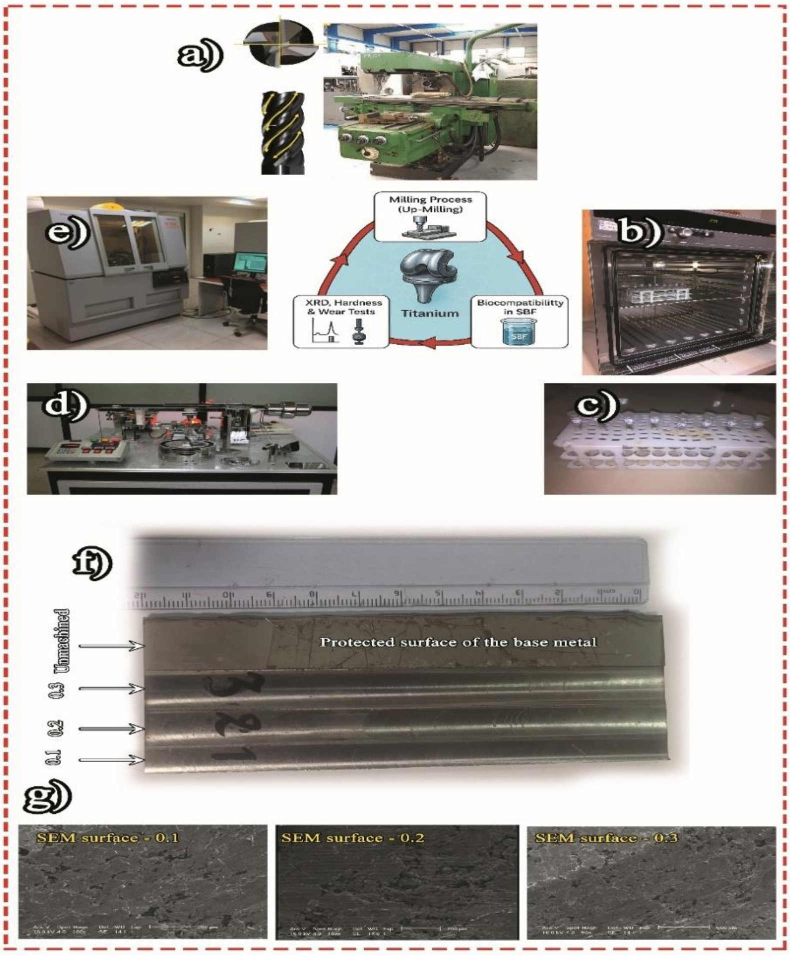

Figure1. Schematic and experimental procedure: a) The machining system, b) The incubator device for placing the samples in simulated body fluid (SBF), c) The method of fixing the samples in the holder for placement in the incubator, d) The wear test system of the pin-on-disk type, e) The XRD device used in this experiment, f) Produced samples, g) SEM images of the machined surfaces

Evaluation of Mechanical Properties and Biocompatibility

To evaluate the biocompatibility of the specimens and their potential to support bone growth, an immersion test was performed in simulated body fluid (SBF). The composition of this solution, compared with human blood plasma, is presented [Table 3]. For each test, specimens were placed in 15 mL containers, and 10 mL of SBF was added. The containers were then transferred to an incubator maintained at 37 °C with a 5% CO_2 atmosphere. The immersion period lasted 28 days, during which the solution in each container was replaced every two days to prevent sedimentation and maintain ion concentrations. At the end of the test, specimens were removed, rinsed thoroughly with distilled water, dried, and prepared for subsequent mechanical and biological evaluation. To further analyze the phases present in both the machined specimens and the separated chips, X-ray diffraction (XRD) was performed using an Explorer instrument (GNR, Italy) under operating conditions of 40 kV and 30 mA, under ISO/IEC 17025:2017 standards.

Table 3.Comparison of Simulated Body Fluid and Human Blood Plasma Compositions

Parameter	Simulated Body Fluid (SBF)	Human Blood Plasma
Na+	142.00	142.00
K+	5.00	5.00
Mg2+	1.50	1.50
Ca2+	2.50	2.50
Cl-	147.96	103.8
HPO42-	1.00	1.00
SO42-	0.50	0.50
HCO3-	4.20	27.0

Results and Discussion

Body Simulator Test

The specimens underwent a 28-day immersion in simulated body fluid (SBF) to evaluate their potential for promoting bone element growth. Bone-like deposits were visibly observed on the surfaces, and energy-dispersive X-ray spectroscopy (EDS) confirmed the presence of calcium (Ca) and phosphorus (P) as newly formed elements [Figures 2 and 3]. A positive response to simulated body conditions is generally indicated when the Ca/P ratio approaches that of human bone (~1.67).[29] The measured ratios for specimens 1, 2, and 3 were 1.89, 1.84, and 2.05, respectively, indicating that all three exhibited a favorable response. Cutting depth significantly influenced the final surface characteristics, which in turn affected bone element growth in the SBF environment.[30] Machining without coolant generates heat and promotes surface oxidation, both of which influence the surface's interaction with simulated body fluid. Among the specimens, the one machined at a 0.3 mm cutting depth exhibited the highest bone element deposition. This was attributed to its increased surface roughness, which provides a greater contact area for bone cell adhesion and growth. Additionally, oxidation from coolant-free machining likely produced a titanium oxide layer, a feature known to enhance biocompatibility and stimulate bone formation. In contrast, specimens with shallower cutting depths tended to have smoother surfaces, reducing contact area and thereby limiting cell adhesion and bone element growth. Considering both surface characteristics and oxidation effects, the 0.3 mm cutting depth offered the most favorable conditions for bone element deposition. Two factors may explain the finer phosphorus particles observed on specimens machined at all three depths. First, deeper machining increases surface roughness, which can catalyze phosphate ion adsorption and deposition, providing numerous nucleation sites for particle formation. Second, the absence of coolant elevates surface temperature during machining, promoting the development of a thin titanium oxide layer that further facilitates phosphate deposition.[31,32] Enhancing biocompatibility remains a critical step in the development of next-generation metallic biomaterials. Titanium and its alloys are widely employed in orthopedic and dental applications due to their superior fatigue strength, low elastic modulus, excellent corrosion resistance, and remarkable ductility. However, because of its bioinert nature, titanium is not ideal for long-term clinical use, as it cannot form a direct bond with living bone during the early stages of implantation. Various strategies have been explored to improve the biological performance of implant surfaces, among which oxidation has received considerable attention. This surface modification technique can produce bioactive, porous, and adhesive coatings on implants,[32] facilitating surface reactions with simulated body fluid and leading to faster, more uniform phosphate ion deposition. Together, these effects create optimal conditions for the growth of fine phosphorus particles, which may enhance implant biocompatibility[33-40] Finer phosphorus particles, in particular, are thought to more effectively stimulate bone tissue formation and accelerate the osteointegration process.[41]

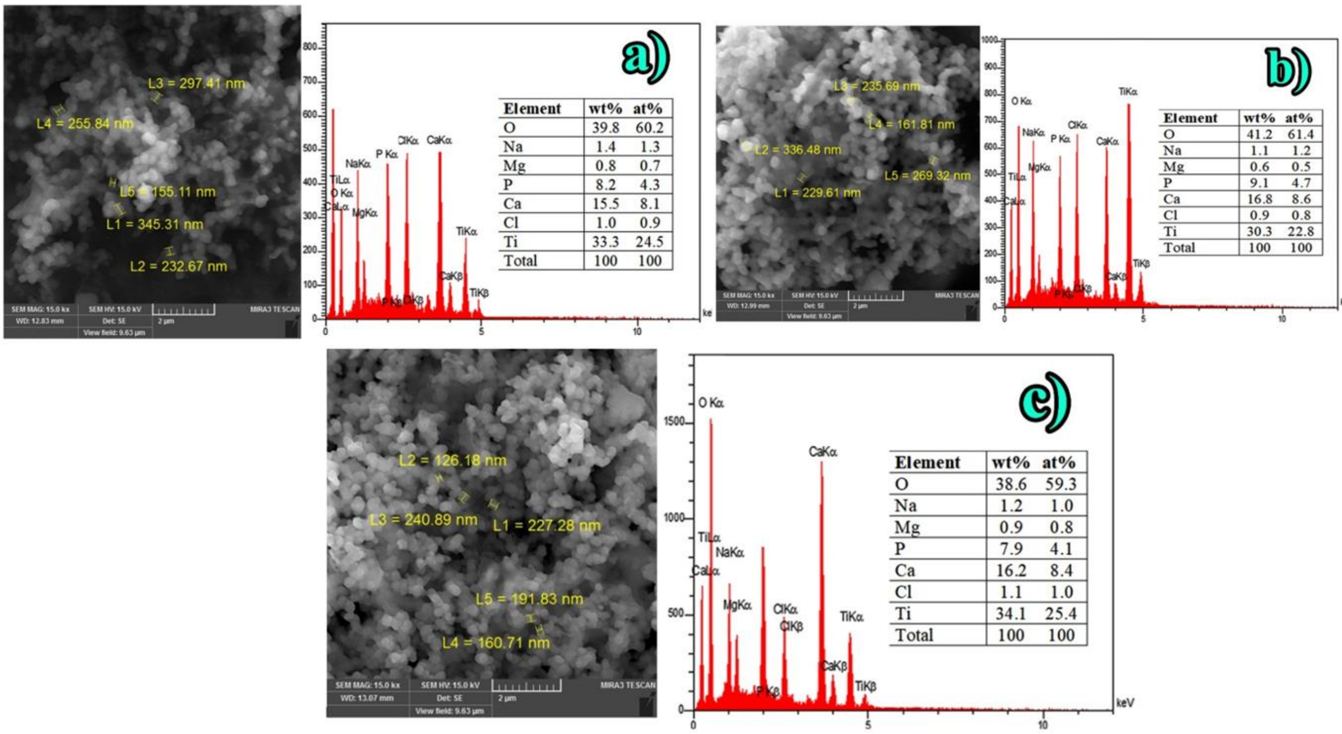

Figure 2. SEM & EDS of: a) sample 1 - b) sample 2 - c) sample 3

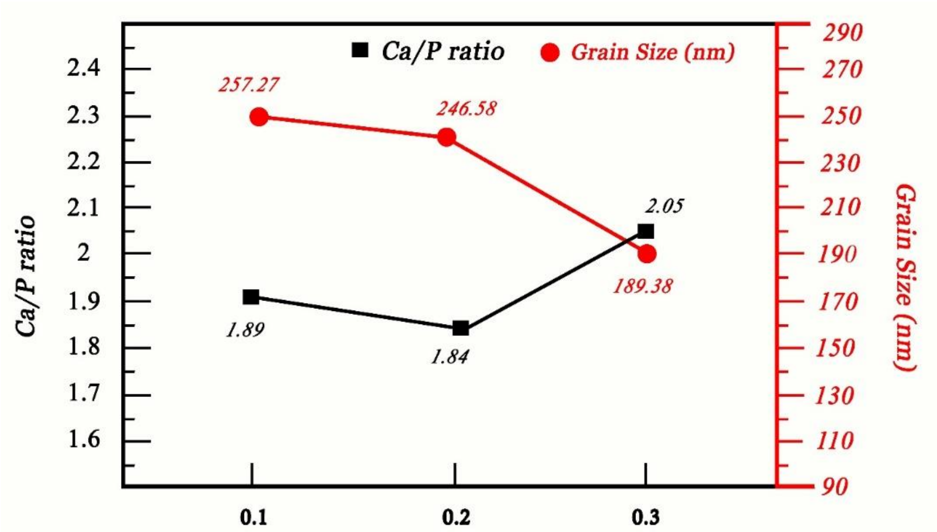

Figure 3. Results of the analysis of the presence and size of bone-related elemental particles: the elemental composition of calcium and phosphorus from EDS confirms the surface bioactivity in all three samples, with Sample 3 exhibiting the highest surface calcium-to-phosphorus ratio after SBF immersion and the smallest particle size

XRD

XRD patterns and data obtained from the three manufactured specimens revealed notable peak shifts and clear correlations between crystal structure and the material's physical properties [Figure 4, Table 4]. The disappearance of diffraction peaks at 2θ angles of approximately 35° and 65° after milling is likely attributable to the formation of residual stresses and structural modifications in the titanium surface. These stresses can alter crystallite size and increase microstrain, leading to the attenuation or complete disappearance of specific characteristic peaks in the XRD profile.[42] The formation of new surface layers induced by the milling process plays a critical role in the observed XRD patterns. A comparison between the unmilled specimen and those subjected to milling reveals the emergence of the 224 phase at approximately 82°, corresponding to titanium oxide, in the machined samples.[43,44] Variations in the intensity of the primary diffraction peak at 40° can be attributed to the combined effects of residual stresses, surface structural modifications, and changes in crystallite size and microstrain among the samples. Notably, both the shallow milling depth (sample 1) and the deep milling depth (sample 3) exhibited a marked reduction in peak intensity. This phenomenon may be explained by the Grain Refinement Saturation effect, wherein the microstructure reaches a limit of refinement and defect formation, beyond which further adjustments to cutting parameters such as cutting depth do not significantly alter the structural characteristics.[45] For shallow milling depths, surface-dominated effects such as strain hardening, defect formation, and residual stress accumulation are the primary contributors to the reduction in peak intensity. At deeper milling depths, the combined effects of elevated thermal input, intensified plastic deformation, and residual stress similarly disrupt the microstructure, leading to phenomena such as grain refinement saturation, increased dislocation density, and enhanced defect formation. Consequently, the reductions in peak intensity observed at both shallow and deep cutting depths arise from converging mechanisms, including residual stress accumulation, surface defect generation, and the inherent limits of grain refinement during mechanical processing. These findings underscore the critical influence of machining parameters on the surface integrity and structural behavior of biocompatible materials such as titanium, as they directly affect long-term performance in biomedical applications. Variations in cutting depth can modify surface characteristics and alter the biological response of the material, ultimately influencing implant performance in the physiological environment.[46] In medical applications, selecting an appropriate machining depth is essential to balance mechanical durability with biocompatibility. Surface modification techniques such as machining, grinding, polishing, and chemical etching are commonly employed to enhance implant performance. Each mechanical fabrication method alters the material's topography, roughness, and residual stress state, which can, in turn, significantly influence cellular responses.[46] The formation of new surface layers induced by the milling process appears to be a contributing factor to the observed XRD behavior. Variations in the intensity of the primary diffraction peak at 40° can be attributed to the combined effects of residual stresses, surface structural modifications, and differences in crystallite size and microstrain among the specimens. Notably, both the shallow (Sample 1) and deep (Sample 3) machining depths exhibited a marked reduction in peak intensity, likely due to elevated residual stress levels and more pronounced surface microstructural alterations. This finding supports the hypothesis that machining-induced surface integrity factors play a critical role in determining the XRD response of titanium alloys. Residual stress refers to the internal stress retained within a material in equilibrium with its surroundings in the absence of any external load. Such stresses have a substantial impact on mechanical performance, influencing properties such as hardness and wear resistance.[44] Accurate extraction of residual stress using a suitable and reliable method is of great importance. Owing to its non-destructive nature, surface sensitivity, and phase selectivity, X-ray diffraction (XRD) is one of the most widely applied techniques for this purpose. However, residual stress measurement via XRD is not straightforward,[47] and the relatively shallow penetration depth of the method,[46] may limit its effectiveness for evaluating stresses at greater subsurface depths. In XRD analysis, broadening of the highest-intensity peak is primarily attributed to small grain size and lattice distortion.[48] Recent studies have demonstrated that grain size plays a decisive role in the generation and distribution of residual stress.[47] Due to the short distance between grain boundaries, a dual relationship exists: grain refinement accelerates residual stress development, but also improves the material's capacity for stress relaxation. This balance directly influences the final mechanical performance.[49] Furthermore, increased intensity of the primary XRD peaks is associated with an increase in particle size within the specimen.[50] Based on the conducted analyses and the observations in Figure 4, it can be concluded that machining parameters have a direct impact on the surface integrity of titanium specimens. Similar studies have reported that such effects may manifest as increased surface roughness, altered wettability, changes in surface energy, and reduced biocompatibility resulting from decreased osteoblast adhesion and proliferation.[51,52] These effects are particularly critical in materials intended for sensitive applications such as biomedical implants. A key aspect of this study, and similar research, is the ability to accurately estimate grain size, identify internal stresses, and determine crystallite size and microstrain in machined specimens. In the first stage, these analyses are conducted by evaluating changes in the width and intensity of diffraction peaks, which provide reliable data. Based on previous studies and the present findings, these analytical results are in strong agreement with experimental observations, confirming their validity.[53,54] In biomedical applications, particularly for implants, grain size is a critical factor influencing both the biological and mechanical performance of a component.[55] Fine-grained structures typically exhibit higher hardness, improved corrosion resistance, and enhanced interaction with body tissues, as smaller grains provide surfaces that promote superior protein adsorption and cell adhesion.[56] Therefore, precise control of the machining process, coupled with scientific analysis of microstructural changes, can not only improve the mechanical and biological properties of implants but also significantly enhance their lifespan and safety.

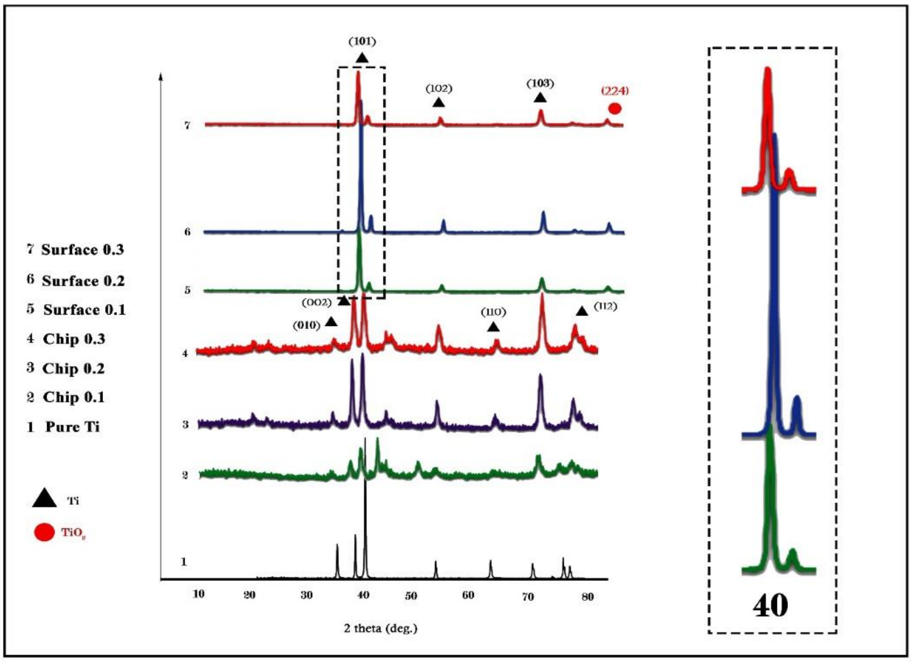

Figure 4. Phase Variation Chart in XRD Test

Table 4. Comparison of Crystallite Size and Lattice Microstrain Extracted from XRD Test

Sample	(mm) Crystallite size	Microstrain	Weight loss due to wear (mg)
0.1	28	0.0011	12.1
0.2	50	0.0011	7.9
0.3	25	0.009	5.3

In the second specimen, machined at an intermediate milling depth, conditions were more favorable for enhancing crystal alignment, resulting in a marked increase in the intensity of the primary diffraction peak at 40°. In the first specimen, machined at a depth of 0.1 mm, the crystallite size and microstrain were measured at 28 nm and 0.0011, respectively. This specimen exhibited a mass loss of 12.1 mg over a sliding distance of 250 m. The combination of small crystallite size and low microstrain indicates a compact and robust microstructure, which typically correlates with higher hardness and improved wear resistance.[57,58] These properties are fundamental in medical applications, where resistance to wear and corrosion directly influences the longevity and functional performance of implants.[59] The second specimen, machined at a depth of 0.2 mm, exhibited a crystallite size of 50 nm and a microstrain of 0.0011, with a wear mass loss of 7.9 mg over a sliding distance of 250 m. The increase in crystallite size may indicate reduced hardness and relative toughness compared with Sample 1, contributing to the lower wear rate. This change may result from internal structural stabilization under mechanical loading, although it could also reflect a shift in wear behavior relevant to implant durability. Sample 3, machined at a depth of 0.3 mm, had a crystallite size of 25 nm and a microstrain of 0.009, with a wear mass loss of 5.3 mg over a sliding distance of 250 m. The reduction in crystallite size, combined with increased microstrain, suggests elevated internal stresses that may compromise hardness. While such changes could enhance corrosion resistance, wear performance might be adversely affected in long-term applications. Overall, the XRD analysis and wear test results confirm that milling depth significantly influences the microstructural and functional properties of commercially pure titanium, with direct implications for the design and performance of medical components.[60]

Finally, given titanium's sensitivity to high temperatures, optimizing machining parameters such as cutting speed, depth of cut, and machining strategy—is essential for achieving the desired properties in medical implants.[61-63] The present findings indicate that selecting an appropriate milling method can optimize titanium implant performance according to specific application requirements. To further elucidate the relationship between machining parameters and implant performance, future research should focus on: (i) investigating the effect of machining on the osseointegration process through in vivo studies; (ii) examining the fatigue behavior of implants in simulated biological environments under cyclic mechanical loading;

and (iii) developing parametric predictive models to assess the influence of machining on the mechanical and biological properties of implants. Such studies will contribute to improved implant design and enhanced longevity and efficiency in clinical applications.

Conclusion

Enhancing the biological properties of implants remains a significant challenge in their design and manufacturing. Minimizing the use of harmful materials during production and reducing manufacturing costs can improve the suitability of implant structures for large-scale industrial application. This study examined the effect of varying machining depths on the biocompatibility of commercially pure titanium specimens, yielding the following key findings:

1- Cutting depth in dry machining has a substantial influence on the microstructure and biocompatibility of commercially pure titanium. XRD analyses revealed that specimens machined at a shallow cutting depth (0.1 mm) exhibited smaller crystallite sizes (28 nm) and lower microstrain values (0.0011). This denser and less-damaged microstructure is likely to contribute to improved biological performance.

2- Specimens machined at a moderate cutting depth (0.2 mm) displayed an increase in crystallite size to 50 nm, while microstrain remained unchanged. These structural variations may reflect the effect of cutting depth on the crystal lattice and, consequently, the material's biocompatibility.

3-Deeper machining (0.3 mm) produced smaller crystallite sizes (25 nm) but a marked increase in microstrain (0.009). Simulated body fluid (SBF) tests confirmed that changes in cutting depth altered biocompatibility, likely due to modifications in the material's microstructural integrity.

4- Overall, cutting depth is a critical parameter influencing the biocompatibility of commercially pure titanium. Selecting an appropriate machining depth can significantly enhance the biological response of the material, underscoring its importance in the design of medical implants. Further research is needed to fully elucidate the influence of machining processes on the biocompatibility of titanium-based biomedical devices.

Acknowledgement

The authors would like to express their gratitude to Ms. Mohaddeseh Moradagholi (IRAN-Zahedan) for her constructive feedback and support during the preparation of this work.

Authors Contribution: Authors who conceived and designed the analysis: Mohammadreza Farahani/ Authors who collected the data: Sayyed Mohammadreza Sedehi/ Authors who contributed data or analysis tools: Sayyed Mohammadreza Sedehi, Mohammadreza Farahani/ Authors who wrote the paper: Sayyed Mohammadreza Sedehi, Mohammadreza Farahani

Declaration of Conflict of Interest: The authors do NOT have any potential conflicts of interest for this manuscript.

Declaration of Funding: The authors received NO financial support for the preparation, research, authorship, and publication of this manuscript.

Declaration of Ethical Approval for Study: This article does not require an ethics approval code.

Declaration of Informed Consent: This article contains no confidential information pertaining to individuals or relevant institutions.

Sayyed Mohammadreza Sedehi PhD Student [1]
Mohammadreza Farahani PhD [1]

1 School of Mechanical Engineering, College of Engineering, University of Tehran, Tehran, Iran

References

1. Li Y, Yang C, Zhao H, Qu S, Li X, Li Y. New developments of Ti-based alloys for biomedical applications. Materials (Basel). 2014;7(3):1709-1800. doi: 10.3390/ma7031709.
2. Graul I, Marintschev I, Pizanis A, et al. Triangular Screw Placement to Treat Dysmorphic Sacral Fragility Fractures in Osteoporotic Bone Results in an Equivalent Stability to Cement-Augmented Sacroiliac Screws A Biomechanical Cadaver Study. J Clin Med. 2025;14(5):1497. doi: 10.3390/jcm14051497.
3. Mekrane FZ, Ouladsine R, Barkaoui A, Ghandour R. Prognostics of the knee osteoarthritis induced by cyclic loading activities. A model-based analysis. Comput Methods Biomech Biomed Engin. 2025:1-14. doi: 10.1080/10255842.2025.2456993.
4. Maeda K, Yoshida K, Nishizawa T, et al. Inflammation and bone metabolism in rheumatoid arthritis: molecular mechanisms of joint destruction and pharmacological treatments. Int J Mol Sci. 2022;23(5):2871. doi: 10.3390/ijms23052871.
5. Soundharya V, Arthi R, Suresh Kumar I, Hari Haran A. Enhanced Bone Marrow Aspirate Concentrate (BMAC) Preparation Strategy in the Management of Chondromalacia Patella: A Case Report. Cureus. 2024;16(4):e59321. doi: 10.7759/cureus.59321.
6. Geetha M, Singh AK, Asokamani R, Gogia AK. Ti based biomaterials, the ultimate choice for orthopaedic implants–A review. Progress in materials science. 2009;54(3):397-425.
7. Perren SM, Pohler OE, Schneider E, eds. Titanium as implant material for osteosynthesis applications. In: Titanium in Medicine: Material Science, Surface Science, Engineering, Biological Responses and Medical Applications 2001 (pp. 771-825). Berlin, Heidelberg: Springer Berlin Heidelberg.
8. Long MJ, Rack HJ. Titanium alloys in total joint replacements a material science perspective. Biomaterials.1998; 19(18):1621-39. doi: 10.1016/s0142-9612(97)00146-4.
9. Jin W, Chu PK. Orthopedic implants. Encyclopedia of biomedical engineering. 2019;1(3):425-39.
10. Sidambe AT. Biocompatibility of advanced manufactured

titanium implants A review. Materials (Basel). 2014;7(12):8168-8188. doi: 10.3390/ma7128168.

11. Niinomi M. Design and development of metallic biomaterials with biological and mechanical biocompatibility. J Biomed Mater Res A.2019;107(5):944-954. doi: 10.1002/jbm.a.36667.
12. Chen Q, Thouas GA. Metallic implant biomaterials. Materials Science and Engineering: R: Reports. 2015;87:1-57.
13. Gravier J, Vignal V, Bissey-Breton S. Influence of residual stress, surface roughness and crystallographic texture induced by machining on the corrosion behaviour of copper in salt-fog atmosphere. Corrosion Science. 2012;61:162-70.
14. Saptaji K, Gebremariam MA, Azhari MA. Machining of biocompatible materials: a review. The International Journal of Advanced Manufacturing Technology. 2018;97(5):2255-92.
15. Mhamdi MB, Boujelbene M, Bayraktar E, Zghal A. Surface integrity of titanium alloy Ti-6Al-4V in ball end milling. Physics Procedia. 2012;25:355-62.
16. Festas A, Ramos A, Davim JP. Machining of titanium alloys for medical application-a review. Proceedings of the Institution of Mechanical Engineers, Part B: Journal of Engineering Manufacture. 2022;236(4):309-18.
17. Wan X, Hu A, Li M, Chang C, Mao D. Performances of CaSiO3 ceramic sintered by Spark plasma sintering. Materials Characterization. 2008;59(3):256-60.
18. Prakash M, Shekhar S, Moon AP, Mondal K. Effect of machining configuration on the corrosion of mild steel. Journal of Materials Processing Technology. 2015;219:70-83.
19. Beltrán V, Lazzarini M, Figueroa R, Sousa V, Engelke W. In situ endoscopic analysis of vascular supply and regenerated alveolar bone in β-TCP grafted and ungrafted postextraction sites before implant placement: A prospective case-control study. Biomed Res Int. 2019:2019:2797210. doi: 10.1155/2019/2797210.
20. Balasubramanian R, Nagumothu R, Parfenov E, Valiev R. Development of nanostructured titanium implants for biomedical implants–A short review. Materials Today: Proceedings. 2021;46:1195-200.
21. Davis R, Singh A. Performance study of cryo-treated end mill via wet, cryogenic, and hybrid lubri-coolant-milling induced surface integrity of biocompatible Mg alloy AZ91D. Proceedings of the Institution of Mechanical Engineers, Part C: Journal of Mechanical Engineering Science. 2021;235(23):7045-61.
22. Bruschi S, Pezzato L, Ghiotti A, Dabalà M, Bertolini R. Effectiveness of using low-temperature coolants in machining to enhance durability of AISI 316L stainless steel for reusable biomedical devices. Journal of Manufacturing Processes. 2019;39:295-304.
23. Madyira DM, Laubscher RF, Van Rensburg NJ, Henning PF. High speed machining induced residual stresses in Grade 5 titanium alloy. Proceedings of the institution of mechanical engineers, part L: journal of materials: design and applications. 2013;227(3):208-15.
24. Bertolini R, Bruschi S, Ghiotti A, Pezzato L, Dabalà M. The effect of cooling strategies and machining feed rate on the corrosion behavior and wettability of AZ31 alloy for biomedical applications. Procedia Cirp. 2017;65:7-12.
25. Fouzia H, Mamoun F, Naouel H, et al. The effect of milling time on the microstructure and mechanical properties of Ti-6Al-4Fe alloys. Materials Today Communications. 2021;27:102428.
26. Singh B, Saxena KK, Dagwa IM, Singhal P, Malik V. Optimization of machining characteristics of titanium-based biomaterials: approach to optimize surface integrity for implants applications. Surface Review and Letters. 2025;32(04):2340008.
27. Patil S, Jadhav S, Kekade S, Supare A, Powar A, Singh RK. The influence of cutting heat on the surface integrity during machining of titanium alloy Ti6Al4V. Procedia Manufacturing. 2016;5:857-69.
28. Mamedov A, Lazoglu I. Thermal analysis of micro milling titanium alloy Ti–6Al–4V. Journal of Materials Processing Technology. 2016;229:659-67.
29. Cengiz B, Gokce Y, Yildiz N, Aktas Z, Calimli A. Synthesis and characterization of hydroxyapatite nanoparticles. Colloids and Surfaces A: Physicochemical and Engineering Aspects. 2008;322(1-3):29-33.
30. Noordin MY, Jiawkok N, Ndaruhadi PY, Kurniawan D. Machining of bone: Analysis of cutting force and surface roughness by turning process. Proc Inst Mech Eng H. 2015;229(11):761-8. doi: 10.1177/0954411915606169.
31. Pesode P, Barve S. Biocompatibility of Plasma Electrolytic Oxidation Coated Titanium Alloy for Biomedical Applications. Bionanoscience. 2025;15(2):232.
32. Tanabe I, Goi Y, Tanabe Y. Research on oxidation phenomenon during titanium machining and its prevention. Journal of Machine Engineering. 2020;20.
33. Soe YH, Tanabe I, Iyama T, Abe Y. Control of tool temperature using neural network for machining materials with low thermal conductivity. Journal of Machine Engineering. 2010;10.
34. Ribeiro Filho SL, Lauro CH, Bueno AH, Brandao LC. Influence cutting parameters on the surface quality and corrosion behavior of Ti–6Al–4V alloy in synthetic body environment (SBF) using Response Surface Method. Measurement. 2016;88:223-37.
35. Brunette DM, Tengvall P, Textor M, Thomsen P,eds. Titanium in medicine: material science, surface science, engineering, biological responses and medical applications. Berlin: Springer; 2001.
36. Urbani G, Lombardo G, Santi E, Consolo U. Distraction osteogenesis to achieve mandibular vertical bone regeneration: a case report. Int J Periodontics Restorative Dent. 1999;19(4):321-31.
37. Esposito M, Hirsch JM, Lekholm U, Thomsen P. Biological factors contributing. Eur J Oral Sci. 1998;106(3):721-64. doi: 10.1046/j.0909-8836..t01-6-.x.
38. d'Hoedt B, Schulte W. A comparative study of results with various endosseous implant systems. Int J Oral Maxillofac Implants. 1989;4(2):95-105.
39. M Salonen MA, Oikarinen K, Virtanen K, Pernu H. Failures in the osseointegration of endosseous implants. Int J Oral Maxillofac Implants. 1993;8(1):92-7.
40. Mericske-Stern R, Zarb GA. Overdentures: an alternative implant methodology for edentulous patients. Int J Prosthodont. 1993;6(2):203-8.
41. Bozorgi A, Khazaei M, Soleimani M, Jamalpoor Z. Application of nanoparticles in bone tissue engineering; a review on the

molecular mechanisms driving osteogenesis. Biomater Sci. 2021;9(13):4541-4567. doi: 10.1039/d1bm00504a.

42. He Y, Zhou H, Zhao Y, et al. Investigating the thermal stability of compressive residual stress in a gradient nanostructured austenitic stainless steel by in-situ XRD and TEM. Materials Characterization. 2024;207:113610.
43. Tamarani A, Zainul R, Dewata I. Preparation and characterization of XRD nano Cu-TiO2 using sol-gel method. InJournal of Physics: Conference Series 2019 (Vol. 1185, p. 012020). IOP Publishing.
44. Ramazani M, Farahmandjou M, Firoozabadi TP. Effect of nitric acid on particle morphology of the nano-TiO2. International Journal of Nanoscience and Nanotechnology. 2015;11(2):115-22.
45. Sedehi SM, Khosravi M, Yaghoubinezhad Y. Mechanical properties and microstructures of reduced graphene oxide reinforced titanium matrix composites produced by spark plasma sintering and simple shear extrusion. Ceramics International. 2021;47(23):33180-90.
46. Prosolov KA, Khimich MA, Sharkeev YP. Surface Treatments and Residual Stress: Assessing the Implications for Biocompatibility in Titanium Implants. Russian Physics Journal. 2023;66(1):116-23.
47. Bemporad E, Brisotto M, Depero LE, Gelfi M, Korsunsky AM, Lunt AJ, Sebastiani M. A critical comparison between XRD and FIB residual stress measurement techniques in thin films. Thin Solid Films. 2014;572:224-31.
48. Liu J, Liang C. Microstructure characterization and mechanical properties of bulk nanocrystalline aluminium prepared by SPS and followed by high-temperature extruded techniques. Materials Letters. 2017;206:95-9.
49. Cao L, Sengupta A, Pantuso D, Koslowski M. Effect of texture and grain size on the residual stress of nanocrystalline thin films. Modelling and Simulation in Materials Science and Engineering. 2017;25(7):075004.
50. Yogamalar R, Srinivasan R, Vinu A, Ariga K, Bose AC. X-ray peak broadening analysis in ZnO nanoparticles. Solid State Communications. 2009;149(43-44):1919-23.
51. Akbas O, Reck L, Jahn A, Hermsdorf J, Stiesch M, Greuling A. Effect of Different Sandblasting Parameters on the Properties of Additively Manufactured and Machined Titanium Surfaces. In Vivo. 2025;39(3):1767-1785. doi: 10.21873/invivo.13979.
52. Umar Farooq M, Pervez Mughal M, Ahmed N, Ahmad Mufti N, Al-Ahmari AM, He Y. On the investigation of surface integrity of Ti6Al4V ELI using Si-mixed electric discharge machining. Materials (Basel). 2020;13(7):1549. doi: 10.3390/ma13071549.
53. Himabindu B, Devi NL, Kanth BR. Microstructural parameters from X-ray peak profile analysis by Williamson-Hall models; A review. Materials Today: Proceedings. 2021;47:4891-6.
54. Kibasomba PM, Dhlamini S, Maaza M, et al. Strain and grain size of TiO2 nanoparticles from TEM, Raman spectroscopy and XRD: The revisiting of the Williamson-Hall plot method. Results in Physics. 2018;9:628-35.
55. Veljović D, Čolić M, Kojić V, et al. The effect of grain size on the biocompatibility, cell–materials interface, and mechanical properties of microwave-sintered bioceramics. J Biomed Mater Res A. 2012;100(11):3059-70. doi: 10.1002/jbm.a.34225.
56. Kasaeian-Naeini M, Sedighi M, Hashemi R. Severe plastic deformation (SPD) of biodegradable magnesium alloys and composites: A review of developments and prospects. Journal of Magnesium and Alloys. 2022;10(4):938-55.
57. Ramezani M, Ripin ZM. An overview of enhancing the performance of medical implants with nanocomposites. Journal of Composites Science. 2023;7(5):199.
58. Strunz P, Kunčická L, Beran P, Kocich R, Hervoches C. Correlating microstrain and activated slip systems with mechanical properties within rotary swaged WNiCo pseudoalloy. Materials (Basel).2020;13(1):208. doi: 10.3390/ma13010208.
59. Tjandra J, Alabort E, Barba D, Pedrazzini S. Corrosion, fatigue and wear of additively manufactured Ti alloys for orthopaedic implants. Materials Science and Technology. 2023;39(18):2951-65.
60. Jiang W, Zhao W, Deng L, Zhou T, Qiu T. Research on theoretical and experimental investigations of burr formation mechanism in micro-milling process of medical ploy-L-lactide. Journal of Manufacturing Processes. 2024;117:1-3.
61. Yazar KU, Mishra S, Karmakar A, Bhattacharjee A, Suwas S. On the temperature sensitivity of dwell fatigue of a near alpha titanium alloy: role of strain hardening and strain rate sensitivity. Metallurgical and Materials Transactions A. 2020;51(10):5036-42.
62. Antil P, Kumar Antil S, Prakash C, Krolczyk G, Pruncu C. Multi-objective optimization of drilling parameters for orthopaedic implants. Measurement and Control. 2020;53(9-10):1902-10.
63. Singh B, Saxena KK, Dagwa IM, Singhal P, Malik V. Optimization of machining characteristics of titanium-based biomaterials: approach to optimize surface integrity for implants applications. Surface Review and Letters. 2025;32(04):2340008.