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RESEARCH AND EDUCATION

Osteoblast cell behavior on polyetheretherketone dental implant surfaces treated with different grit size aluminum oxide particles: An in vitro analysis

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ABSTRACT

Statement of problem. The hydrophobic and bioinert nature of polyetheretherketone (PEEK) implants needs to be addressed for successful osseointegration.

Purpose. The purpose of this in vitro study was to evaluate the osteoblast cell behavior on PEEK implant surfaces treated with airborne-particle abrasion using different grit size aluminum oxide (Al_2O_3) particles.

Material and methods. Disk-shaped specimens (n=96) were prepared from medical grade PEEK rods and were distributed into 4 groups (n=24) of untreated PEEK (PEEK 0), airborne-particle abrasion using 50-μm Al_2O_3 particles (PEEK 50), airborne-particle abrasion using 110-μm Al_2O_3 particles (PEEK 110), and airborne-particle abrasion using 150-μm Al_2O_3 particles (PEEK 150). The surface characteristics were assessed using water contact angle (WCA) measurements and scanning electron microscopy (SEM). MG-63 osteoblast cells were cultured, and the biocompatibility of PEEK was assessed using a CellTiter-blue cell viability assay and florescence staining at day 1, 3, and 7. The specimens were stained with Alizarin red to assess the osteoblast cell differentiation on day 10 and 14. The Levene test was used to test the homogeneity of variances. One-way and Welch ANOVA with post hoc corrections were used to assess the overall statistical significance of differences among the groups (α=.05).

Results. The lowest mean WCA was demonstrated in PEEK 150 (49.25 ±5.51) and the highest in PEEK 0 (89.14 ±4.24) ($P<.001$). SEM images of PEEK 150 illustrated a more complex structure with a large area of globular outcroppings throughout the surface. PEEK 150 showed the highest cell metabolic activity at each time point with florescence staining showing a substantial cell confluence at day 3 and 7. Although PEEK 150 did not show a significant increase in cell proliferation, the number of cells attached was significantly higher than other groups ($P<.05$). PEEK 110 and 150 also showed a substantial increase in the extent of mineralization.

Conclusions. Airborne-particle abrasion using moderate Al_2O_3 grit size (110- or 150-μm) improved the hydrophilicity and osteoblast cell behavior on PEEK implants. (J Prosthet Dent 2025;133:531-539)

Intimate and stable bone-to-implant contact is essential for the long-term survival of dental implants, and various strategies have been proposed to enhance the implant surface topography, thereby promoting cellular responses and impeding active inflammatory responses.[1–3] Titanium and its alloys have been widely

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Clinical Implications

Airborne-particle abrasion with moderate Al_2O_3 grit size may be a promising strategy for addressing the bioinert and hydrophobic attributes of medical grade PEEK implants.

accepted as an implant biomaterial because of their high mechanical strength and good biological properties.[4] Surface modifications of titanium implants have been reported to improve cell compatibility, thus promoting osseointegration.[3,5,6] However, the disadvantages of titanium implants include hypersensitivity reactions and stress-shielding effects.[7–9] In addition, the high modulus of elasticity of titanium may eventually lead to loss of bone-to-implant contact.[10]

Polyetheretherketone (PEEK), a semi-crystalline thermoplastic polymer, offers several advantages, including superior mechanical strength, excellent biocompatibility, and stable physical and chemical properties.[11,12] However, the clinical application of PEEK implants has been limited because of its hydrophobic and bioinert nature.[13] An unmodified PEEK implant surface offers fewer osteoconductive and bioactive attributes than titanium.[14] Hence, different strategies, including physical and chemical modifications, have been adopted to improve the bioactivity of PEEK.[15,16] While PEEK augmentation with bioactive coatings has been reported to enhance its osteogenic potential, its inherent instability has raised concerns.[17] Thus, additional strategies to improve the bioactivity of PEEK are needed.

The airborne-particle abrasion of titanium implants presents a micro-rough surface that promotes osseointegration[18–20] and can be accomplished with different particles including aluminum oxide (Al_2O_3), titanium dioxide (TiO_2), and silicon dioxide (SiO_2).[20–22] Airborne-particle abrasion using Al_2O_3 has been reported to improve the biomechanical characteristics of titanium implants.[22] Moreover, the residual alumina particles have been reported to provide dual-functional (osteogenic and bactericidal) effects on the titanium implants.[23] The varying sizes of Al_2O_3 particles may alter the surface topography, subsequently influencing the cell behavior and mechanical properties of implant biomaterials.[24–27] Variation in the grit sizes of Al_2O_3 particles has recently been reported to influence osteoblast cell behavior on titanium implants.[20]

While the enhancing impact of airborne-particle abrasion on titanium implant characteristics has been well-documented, its influence on PEEK implant biomaterial remains unclear. Thus, the purpose of this in vitro study was to evaluate the osteoblast cell behavior on PEEK implant surfaces treated with Al_2O_3 airborne-particle abrasion. The null hypothesis was that the airborne-particle abrasion with Al_2O_3 of different grit sizes would not influence the hydrophilicity or osteoblast cell behavior on PEEK implant surfaces.

MATERIAL AND METHODS

Ninety-six disk-shaped specimens (Ø12×2 mm) were prepared from medical grade PEEK rods (Ketron PEEK 1000; Mitsubishi chemical group) and were distributed into 4 groups (n=24) of untreated PEEK (PEEK 0), airborne-particle abrasion using 50-μm Al_2O_3 particles (PEEK 50), airborne-particle abrasion using 110-μm Al_2O_3 particles (PEEK 110), and airborne-particle abrasion using 150-μm Al_2O_3 particles (PEEK 150). The airborne-particle abrasion was performed for 30 seconds at 0.4 to 0.6 MPa. All specimens were cleaned in an ultrasonic cleaner (EMAG Ultrasonic cleaner Emmi-H30; EMAG-AG) using distilled water for 15 minutes and were sterilized at 121 °C for 20 minutes.

To estimate the hydrophilicity of PEEK, static water contact angles (WCAs) were measured by using a contact angle goniometer (OCA 40; Data Physics instruments GmbH) at room temperature.[28] A 30-μL droplet of distilled water was placed on specimens, and digital images were made after the droplet stabilization. Subsequently, the images were analyzed by using an image processing software program (Software SCA 202V.3.61.4; Data Physics instruments GmbH). The surface topography of the PEEK specimens was assessed by using a field emission scanning electron microscope (SEM) (ZEISS EVO MA10; ZEISS Microscopy) at 2 kV. The images were obtained at ×300 and ×1000 magnification.

Human osteoblastic osteosarcoma cells (MG-63, CRL-1427; ATCC) were used to determine the biocompatibility of untreated and treated PEEK specimens. Cell suspension droplets containing 3×10^5 cells per 100 μL of cell culture medium (D5796, Dulbecco modified Eagle medium, DMEM; Sigma-Aldrich) were placed on the surface of each specimen in 24-well plates, and the cells were allowed to attach for 3 hours in a humidified incubator containing 5% CO_2. Then, 1 mL of cell culture medium was added until the specimens were completely submerged. Equivalent procedures were performed on glass cover slips for the negative and positive control groups. In the negative control group, cell lysis was achieved with 1% Triton X-100 (Sigma-Aldrich). Cell biocompatibility was assessed at day 1, 3, and 7.

A Cell Titer-blue cell viability assay (Cell Titer-blue; Promega) was used to estimate the metabolic activity of cells on specimens.[29] Briefly, at predetermined time points, 200 μL of staining solution was added in 24-well plates containing specimens and were incubated for 4 hours. The cell metabolic activity was estimated by using a spectrophotometer plate reader (Infinite 200 Pro; TECAN) at 560- to 590-nm wavelength.

The alterations in cell morphology and attachment were qualitatively assessed by using fluorescence staining.[30,31] The cells were fixed with 4% paraformaldehyde for 20 minutes at room temperature, and the cell permeabilization was attained using 0.3% Triton X-100 for 10 minutes at room temperature. Subsequently, the specimens were stained at room temperature in the dark for 30 minutes with a green, fluorescent dye (Phalloidin-iFluor Reagent; abcam) to mark actin filaments and 4′,6-diamidino-2-phenylindol (DAPI) (ThermoFisher Scientific) for nuclei. A confocal laser scanning microscope (CLSM) (Leica TCS SP8; Leica Microsystems) and a digital software program (Imaris x64 6.2.1; Bitplane) were used for the qualitative analyses. Cell adhesion was estimated at day 1 by counting the number of cells per field of view, and the cell proliferation rate was calculated at day 3 after normalization to the cells reported at day 1.

Osteoblast cell differentiation between the groups was assessed by estimating the amount of mineralization using alizarin red staining (ARS). After adequate cell confluence, the cells on the specimens were allowed to differentiate in an osteogenic differentiation medium (DMEM supplemented with 10% FBS, 1% penicillin and streptomycin, 10 mM β-glycerophosphate, 100 nM dexamethasone, and 50 μg/mL ascorbic acid) for 10 and 14 days. The cells were fixed with 4% paraformaldehyde for 20 minutes at room temperature and subsequently incubated in 2% ARS solution (Sigma-Aldrich) for 30 minutes in the dark. The extent of mineralization was quantified by extracting the ARS dye from the specimens submerged in 10% acetic acid and 20% methanol at room temperature for 30 minutes, and the absorbance was measured at 405 nm using a spectrophotometer plate reader.

Data were analyzed using a statistical software program (R version 4.3.1; R Foundation for Statistical Computing). The Kolmogorov-Smirnov test was used to assess the normality of data, and the homogeneity of variances was evaluated using the Levene test. A variation of variance was demonstrated in data for the cell viability, proliferation, and mineralization (Supplemental Table 1, available online). Hence, the Welch analysis of variance (ANOVA) followed by the Games-Howell test were used to compare the means between the groups. However, a variation of variance was not observed in the data for WCA measurements and cell adhesion (Supplemental Table 1, available online). Hence, 1-way ANOVA followed by the Tukey test were used to compare the means between the groups (α=.05).

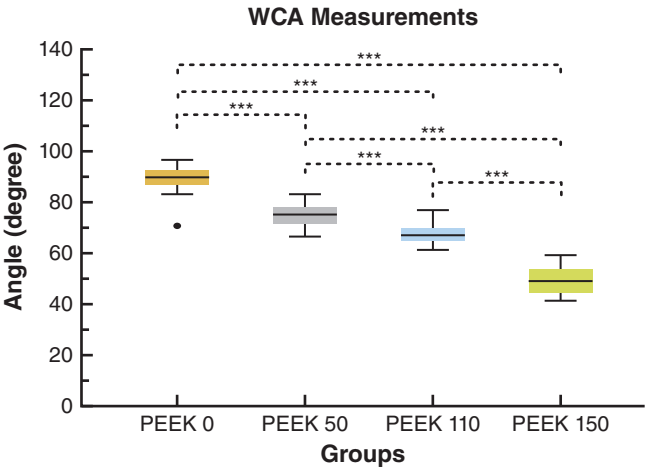

Figure 2. Mean differences in WCAs among four tested groups. ***P<.001. PEEK, polyetheretherketone; WCAs, water contact angles.

RESULTS

Figure 1 illustrates the mean WCAs of untreated and treated PEEK implant surfaces. The lowest mean WCA was found in PEEK 150 (49.25 ±5.51) and the highest in PEEK 0 (89.14 ±4.24) (Supplemental Table 2, available online). The Tukey post hoc test showed significant difference (P<.001) between the treated and untreated groups (Fig. 2). Figure 3 illustrates the SEM images of untreated and treated PEEK specimens at ×300 and ×1000 magnification. PEEK 0 showed a uniform regular surface with smooth appearance. However, small patches of grooves were observed throughout the surfaces (Fig. 3). In contrast, the treated PEEK showed uniform irregular surfaces with the presence of grains and voids. Notably, PEEK 150 showed a complex structure with large areas of globular outcroppings.

Figure 4 shows differences in cell metabolic activity between the untreated and treated PEEK implant surfaces. At

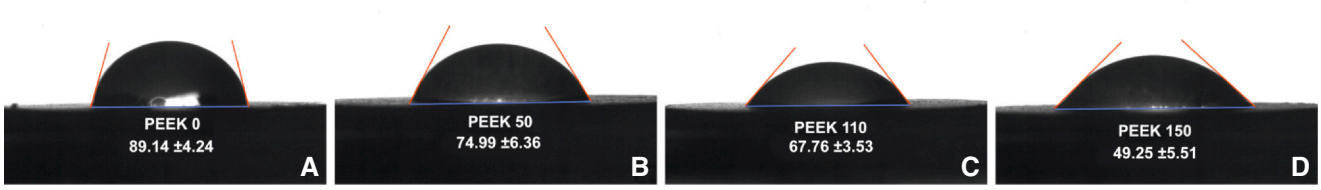

Figure 1. Water contact angles of untreated and treated PEEK implant surfaces. A, PEEK 0 (untreated PEEK). B, PEEK 50 (airborne-particle abrasion using 50-μm Al_2O_3 particles). C, PEEK 110 (airborne-particle abrasion using 110-μm Al_2O_3 particles). D, PEEK 150 (airborne-particle abrasion using 150-μm Al_2O_3 particles). Al_2O_3, aluminum oxide; PEEK, polyetheretherketone.

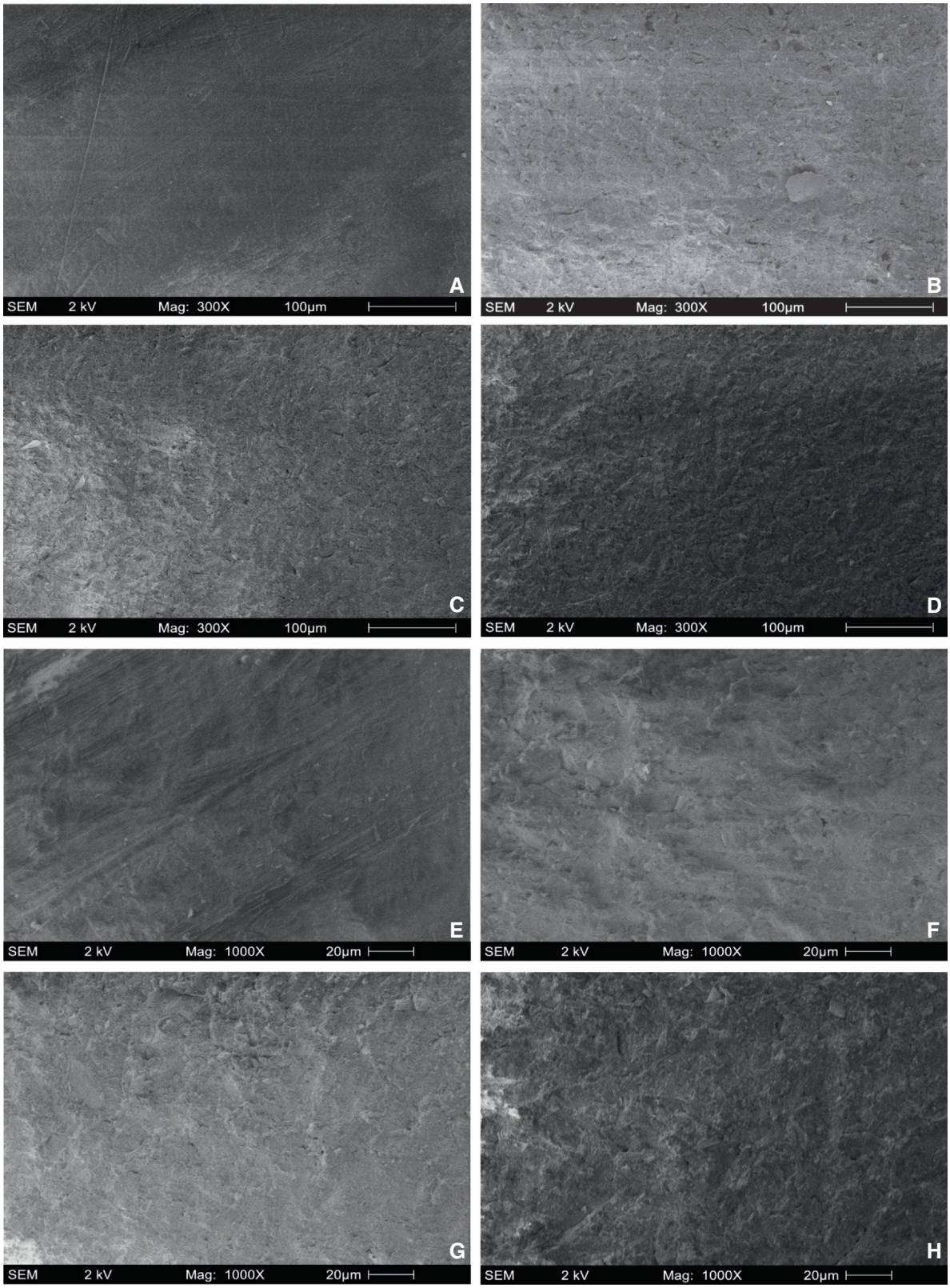

Figure 3. Scanning electron microscopy images of untreated and treated PEEK implant surfaces. (original magnification ×300 and ×1000). A, E, PEEK 0 (untreated PEEK surface). B, F, PEEK 50 (airborne-particle abrasion with 50-µm Al_2O_3 particles). C, G, PEEK 110 (airborne-particle abrasion with 110-µm Al_2O_3 particles). D, H, PEEK 150 (airborne-particle abrasion with 150-µm Al_2O_3 particles). Al_2O_3, aluminum oxide; PEEK, polyetheretherketone.

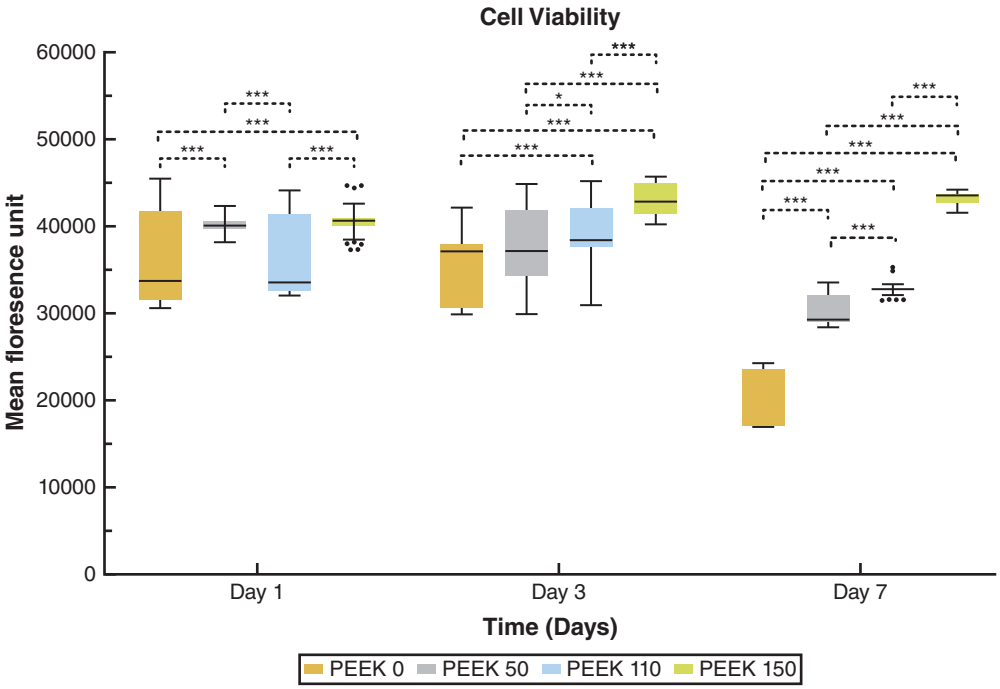

Figure 4. Cell metabolic activity of MG-63 cells cultured on untreated and treated PEEK implant surfaces at day 1, 3, and 7. *P<.05, ***P<.001. PEEK, polyetheretherketone.

day 1, the highest mean metabolic activity was observed in PEEK 150 and the lowest in PEEK 0 showing significant difference (P<.001) (Supplemental Table 3, available online). However, no significant differences were observed between groups, PEEK 0 and PEEK 110 and PEEK 50 and PEEK 150 (P>.05) (Fig. 4). Similar findings were observed at day 3, wherein the highest cell metabolic activity was found in PEEK 150 and the lowest in PEEK 0 (Fig. 4). The Games-Howell test revealed significant differences between PEEK 150 and other tested groups (P<.001). However, no significant differences were found between PEEK 150 and the positive control group (P=.067) (Supplemental Table 3, available online). At day 7, all tested groups showed significant differences (P<.001) except between PEEK 150 and the positive control group (P=.946). While PEEK 0 showed the lowest cell metabolic activity, its activity reduced as compared with day 1 and 3 (Fig. 4). Overall, PEEK 150 had the highest cell metabolic activity suggesting improved cell viability at each time point that increased further throughout the tested time points (Supplemental Table 3, available online).

Figure 5 illustrates the morphology changes and cytoskeleton F-actin fiber organization of MG-63 cells cultured on untreated and treated PEEK surfaces. At day 1 and 3, the cells in the treated groups showed an elongated fibroblastic spindle-shaped morphology with a prominent cell confluence that was evident in PEEK 110 and PEEK 150. In contrast, the cells in PEEK 0 had a round and irregular morphology. At day 7, the cells in the treated groups had a better-assembled dense actin-based cytoskeletal network than PEEK 0. Moreover, the cells were highly confluent and showed a systematic elongation of actin filaments with intimate cell-to-cell adherence (Fig. 5).

The results of cell adhesion and proliferation are presented in Figure 6 and Supplemental Table 4 (available online). The number of cells per field of view was highest in PEEK 150 (169.1 ±22.55) and lowest in PEEK 0 (101.4 ±15.26) (P<.001). No significant difference was observed between PEEK 150 and PEEK 110 (P>.05). The cell proliferation was highest in PEEK 50 (83.6 ±28) and lowest in PEEK 0 (−13.9 ±9.058) with PEEK 0 showing significant differences as compared with other groups (Supplemental Table 4, available online). The difference between PEEK 50 and PEEK 110 was statistically significant (P<.001), but PEEK 50 and PEEK 150 groups were statistically similar (P=.197) (Fig. 6).

The results of the mineralization assay are presented in Figure 7 and Supplemental Figure 1 (available online). At day 10, the lowest mineralization rate was observed in PEEK 0 (0.141 ±0.05) and the highest in PEEK 150 (0.254 ±0.16) (P<.001), with PEEK 110 and PEEK 150 being statistically similar (P=.758). At day 14, the highest mineralization rate was observed in PEEK 150 (0.327 ±0.09) with no significant difference compared with PEEK 110 (P=.902). However, PEEK 110 and PEEK 150 showed a substantial improvement in the mineralization rate as compared with day 10 (Fig. 7). In contrast, PEEK 0 and PEEK 50 showed a reduction in mineralization rate at day 14 as compared with day 10 (Supplemental Table 5, available online).

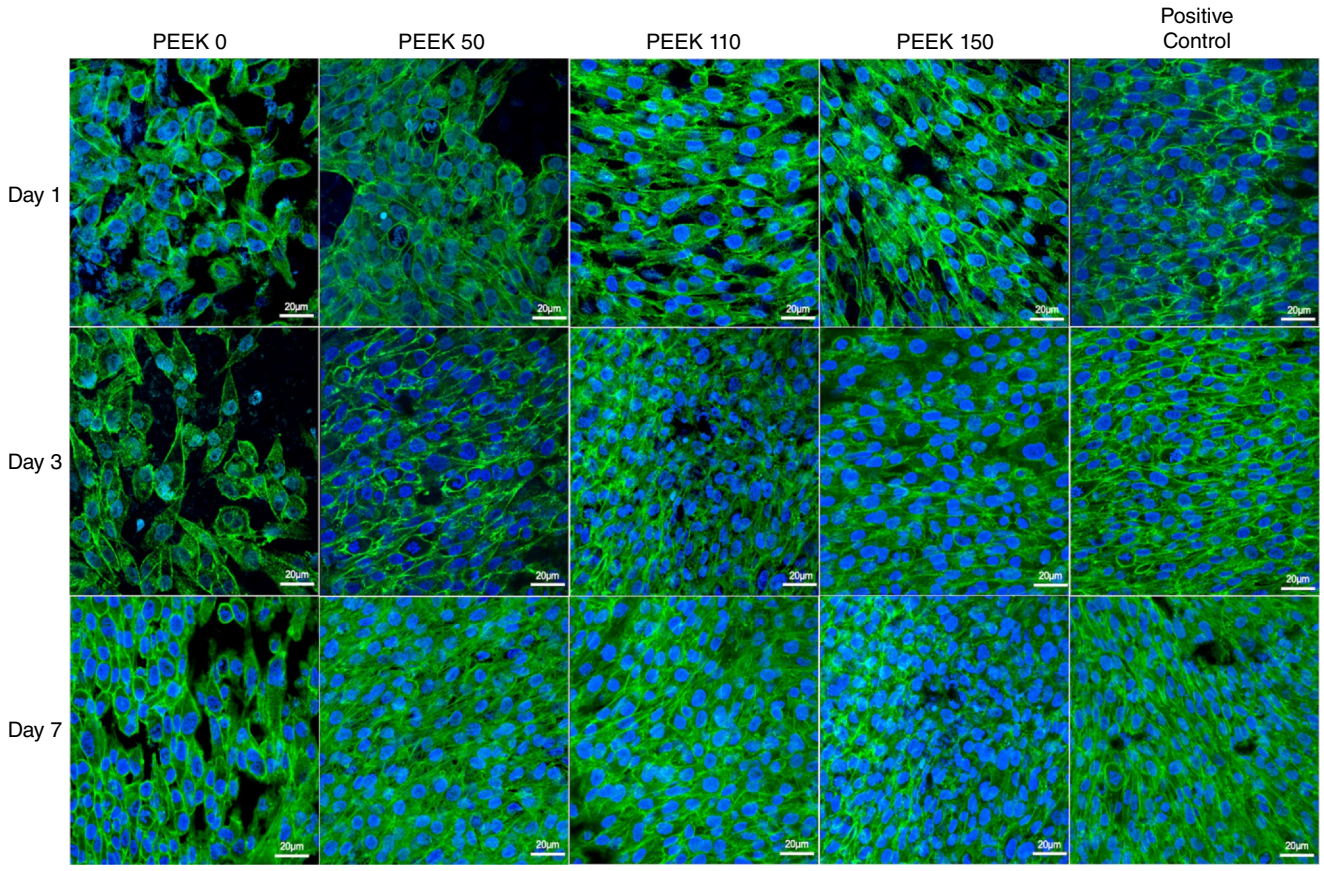

Figure 5. Confocal laser microscopy images showing morphology changes and cytoskeleton F-actin fiber organization of MG-63 cells cultured on untreated and treated PEEK dental implant surfaces at day 1, 3, and 7. PEEK 0, untreated PEEK; PEEK 50, airborne-particle abrasion using 50-μm Al_2O_3 particles; PEEK 110, airborne-particle abrasion using 110-μm Al_2O_3 particles; PEEK 150, airborne-particle abrasion using 150-μm Al_2O_3 particles; Positive control, MG-63 cultured on cover glass, Scale bar: 20-μm. PEEK, polyetheretherketone.

DISCUSSION

Based on the findings of the present study, the airborne-particle abrasion with Al_2O_3 of different grit sizes improved the hydrophilicity of PEEK, subsequently affecting the osteoblast cell behavior. Moreover, using moderate grit size (110- or 150-μm) for airborne-particle abrasion is a favorable approach on PEEK implants, as it improved the osteoblast cell adhesion, proliferation, and differentiation at the tested time points. Thus, the null hypothesis that airborne-particle abrasion with Al_2O_3 of different grit sizes would not influence the hydrophilicity or osteoblast cell behavior on PEEK implant surfaces was rejected.

The hydrophobic nature of PEEK implants limits their suitability for clinical applications. The findings of this study showed improvement in the hydrophilic nature of PEEK after the airborne-particle abrasion that further significantly improved in PEEK 150. This was attributed to the increase in porosity established by Al_2O_3 particles, subsequently providing more surface area for wetting. Although PEEK 50 and PEEK 110 showed moderate hydrophilic properties, the results significantly improved as compared with PEEK 0. These findings of hydrophilicity were consistent with those of a previous study.[15] Moreover, the measurements obtained were similar to those of titanium (58.5 ±4.9).[28] The findings were not consistent with those of Stoilov et al,[20] suggesting that variations in the grit sizes of Al_2O_3 did not influence the hydrophilicity of titanium implants. However, direct comparison with titanium is challenging because of inherent differences in the material composition.

The SEM analysis of treated PEEK showed uniform irregular surfaces with the presence of grains and voids, thus modifying the surface topography of PEEK. The observed difference in the topographical pattern corresponded with the findings of hydrophilicity. PEEK 150 illustrated several globular protuberances that established the micro-irregular surfaces essential for protein adsorption and cell contact within the biological environment. The microscale irregularity further increased the fibrin matrix formation during cell-implant interaction.[6] Moreover, previous studies[15,18–20] reported that the micro-rough implant surfaces transformed the cell-implant interaction, influencing osseointegration.

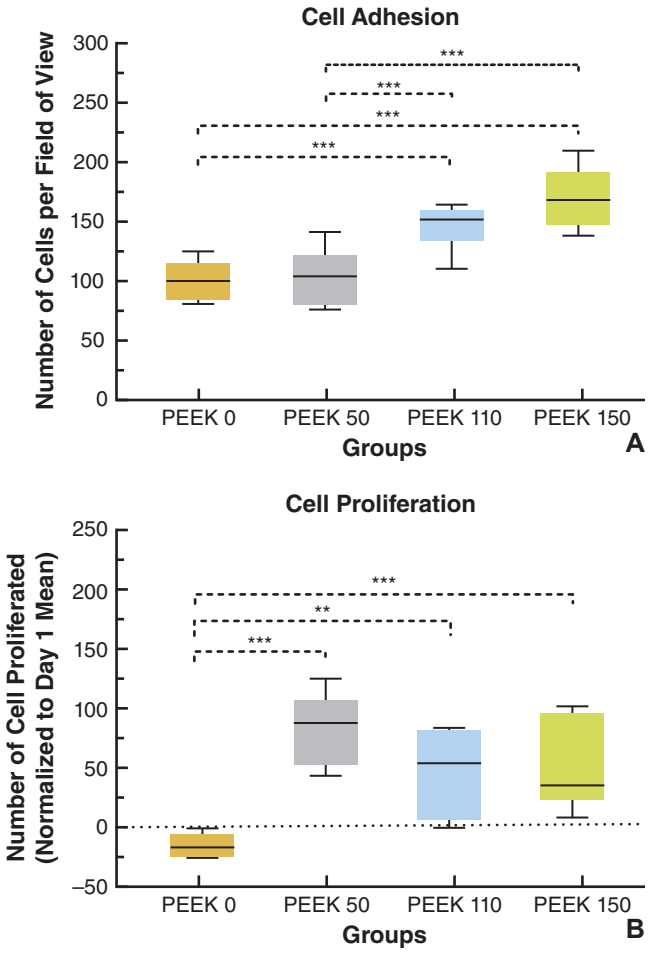

Figure 6. Mean differences in cell biocompatibility of MG-63 cells cultured on untreated and treated PEEK dental implant surfaces at day 1 and 3. A, Cell adhesion. B, Cell proliferation. ***P*<.01, ****P*<.001. PEEK, polyetheretherketone.

The data regarding osteoblast cell biocompatibility were obtained by analyzing the cell viability, cell adhesion, morphology, and proliferation. Both PEEK 110 and PEEK 150 showed a substantial improvement in cell adhesion over PEEK 0 and PEEK 50, attributed to an increase in surface-to-volume ratio, thus facilitating more sites for cell attachment. Furthermore, the airborne-particle abrasion resulted in a local plastic strain, thus inducing the residual compressive stress essential for promoting osteoblast cell adhesion, proliferation, and differentiation.[19] The negative cell proliferation in PEEK 0 was primarily attributed to the reduced cell adhesion, implying that the untreated PEEK surface was unfavorable for cell adhesion, subsequently affecting cell proliferation. In the present study, PEEK 50 showed a substantial increase in cell proliferation, whereas it was reduced in PEEK 150, attributed to cell confluence in PEEK 150, subsequently limiting space for cell proliferation. Stoilov et al[20] reported that the cell proliferation rate on titanium implants was inversely proportion to the size of Al_2O_3 particles. Porrelli et al[25] recently reported that the airborne-particle abrasion of PEEK implants resulted in higher cell adhesion and lower proliferation than with titanium implants. In this study, the cell proliferation was not obtained after day 3 because of cell confluence, making it challenging to calculate the precise number of cells.

Another finding was that PEEK 150 showed a substantial improvement in cell metabolic activity at every time point, attributed to increased cell adhesion and proliferation. Notably, PEEK 0 showed the lowest metabolic activity throughout the time points and the activity reduced from day 1 to 7, suggesting that the airborne-particle abrasion using moderate grit sizes may alter the PEEK surface attributes, subsequently creating favorable settings for nutrients and waste exchange between the cells and the environment, consistent with previous studies.[14–16,32] Moreover, the findings were also consistent with the morphologic findings assessed with florescence staining. Although cells in PEEK 110 and PEEK 150 attained the highest cell confluence, no major difference was observed, consistent with a study[33] reporting an improvement in the cell viability of titanium implants after treatment with airborne-particle abrasion.

The ability of osteoblasts to differentiate influences the speed and the rate of bone formation.[34] The present study determined that the mineralization rate in PEEK 0 was lower than other tested groups and did not increase over time, which was consistent with previously reported studies.[35] In contrast, both PEEK 110 and PEEK 150 showed the highest mineralization rate that increased significantly from day 10 to 14, indicating improved osteogenesis. This mineralization rate was attributed to the increase in cell numbers until day 14 and was consistent with a previous study[33] that reported an improvement in the mineralization rate of titanium implant surfaces after airborne-particle abrasion with alumina. However, these findings were not consistent with a previous reported study[20] in which the high mineralization rate were observed even on titanium surfaces that had been airborne-particle abraded with small particles sizes. However, whether these effects were directly caused by surface physicochemical properties or indirectly by selective protein adsorption is unclear.

Limitations of the present study included that the impact of particulate dimension above 150 μm were not investigated. Notably, PEEK hydrophilicity and osteoblast behavior significantly improved after airborne-particle abrasion with Al_2O_3 using 110-μm and 150-μm grit sizes. Moreover, larger particles may lead to adverse effects, since increased roughness promotes bacterial cell adhesion, as reported by Barkarmo et al.[36] However, the assessment was performed using a single species in separate experiments. Another limitation was that the influence of airborne-particle abrasion on PEEK implants was assessed by using a single cell line in an in vitro setting. Thus, future studies should assess performance across different co-culture conditions to simulate

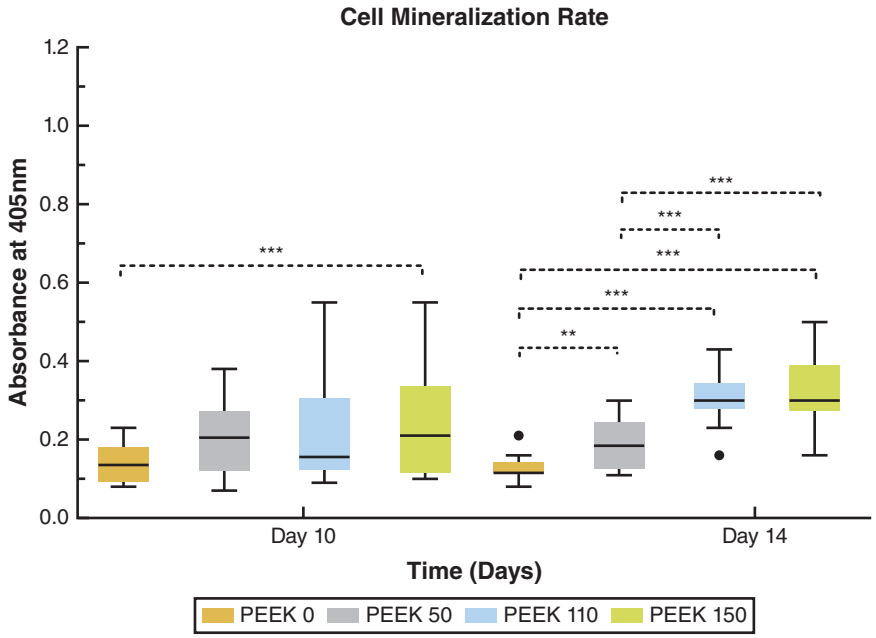

Figure 7. Mean differences in extent of mineralization of MG-63 cells cultured on untreated and treated PEEK implant surfaces at day 10 and 14. ***P*<.01, ****P*<.001. PEEK, polyetheretherketone.

the complex interactions between cells and microbes encountered clinically.

CONCLUSIONS

Based on the findings of this in vitro study, the following conclusions were drawn:

1. Airborne-particle abrasion with Al_2O_3 is a promising strategy for addressing the bioinert and hydrophobic attributes of PEEK implants. However, the particulate dimensions of Al_2O_3 substantially impact the surface attributes of PEEK, influencing the osteoblast cell behavior.
2. Using moderate grit size (110- or 150-μm) for airborne-particle abrasion is a favorable approach on PEEK implants as it enhanced the hydrophilicity and subsequently promoted osteoblast cell adhesion, proliferation, and differentiation.

APPENDIX A. SUPPORTING INFORMATION

Supplemental data associated with this article can be found in the online version at doi:10.1016/j.prosdent.2024.02.024.

REFERENCES

1. Liu Y, Rath B, Tingart M, Eschweiler J. Role of implants surface modification in osseointegration: A systematic review. *J Biomed Mater Res A*. 2020;108:470–484.
2. Goldman M, Juodzbalys G, Vilkinis V. Titanium surfaces with nanostructures influence on osteoblasts proliferation: A systematic review. *J Oral Maxillofac Res*. 2014;5:e1.
3. Bosshardt DD, Chappuis V, Buser D. Osseointegration of titanium, titanium alloy and zirconia dental implants: Current knowledge and open questions. *Periodontol 2000*. 2017;73:22–40.
4. Li J, Jansen JA, Walboomers XF, van den Beucken JJ. Mechanical aspects of dental implants and osseointegration: A narrative review. *J Mech Behav Biomed Mater*. 2020;103:103574.
5. Guizzardi S, Galli C, Martini D, et al. Different titanium surface treatment influences human mandibular osteoblast response. *J Periodontol*. 2004;75:273–282.
6. Kligman S, Ren Z, Chung CH, et al. The impact of dental implant surface modifications on osseointegration and biofilm formation. *J Clin Med*. 2021;10:1641.
7. Singh R, Lehl G, Hussain AB, et al. Prevalence of titanium hypersensitivity in patients with titanium implants: A systematic review and meta-analysis. *J Pharm Bioallied Sci*. 2021;13:S1345–S1349.
8. Poli PP, de Miranda FV, Polo TOB, et al. Titanium allergy caused by dental implants: A systematic literature review and case report. *Materials (Basel)*. 2021;14:5239.
9. Sumner DR. Long-term implant fixation and stress-shielding in total hip replacement. *J Biomech*. 2015;48:797–800.
10. Brizuela A, Herrero-Climent M, Rios-Carrasco E, et al. Influence of the elastic modulus on the osseointegration of dental implants. *Materials (Basel)*. 2019;12:980.
11. Najeeb S, Zafar MS, Khurshid Z, Siddiqui F. Applications of polyetheretherketone (PEEK) in oral implantology and prosthodontics. *J Prosthodont Res*. 2016;60:12–19.
12. Skirbutis G, Dzingutė A, Masiliūnaitė V, Šulcaitė G, Žilinskas J. A review of PEEK polymer's properties and its use in prosthodontics. *Stomatologija*. 2017;19:19–23.
13. Dondani JR, Iyer J, Tran SD. Surface treatments of PEEK for osseointegration to bone. *Biomolecules*. 2023;13:464.
14. Najeeb S, Khurshid Z, Zohaib S, Zafar MS. Bioactivity and osseointegration of PEEK are inferior to those of titanium: A systematic review. *J Oral Implantol*. 2016;42:512–516.
15. Ourahmoune R, Salvia M, Mathia TG, Mesrati N. Surface morphology and wettability of sandblasted PEEK and its composites. *Scanning*. 2014;36:64–75.
16. da Cruz MB, Marques JF, Peñarrieta-Juanito GM, et al. Bioactive-enhanced polyetheretherketone dental implant materials: Mechanical characterization and cellular responses. *J Oral Implantol*. 2021;47:9–17.
17. Zheng Z, Liu P, Zhang X, et al. Strategies to improve bioactive and antibacterial properties of polyetheretherketone (PEEK) for use as orthopedic implants. *Mater Today Bio*. 2022;16:100402.
18. Gil FJ, Planell JA, Padros A, Aparico C. The effect of shot blasting and heat treatment on the fatigue behavior of titanium for dental implant applications. *Dent Mater*. 2007;23:486–491.

19. Gil FJ, Pérez RA, Olmos J, Herraez-Galindo C, Gutierrez JL, Torres-Lagares D. The effect of using Al_2O_3 and TiO_2 in sandblasting of titanium dental implants. *Journal of Materials Research*. 2022;37:2604–2613.
20. Stoilov M, Stoilov L, Enkling N, et al. Effects of different titanium surface treatments on adhesion, proliferation and differentiation of bone cells: An in vitro study. *J Funct Biomater*. 2022;13:143.
21. Barfeie A, Wilson J, Rees J. Implant surface characteristics and their effect on osseointegration. *Br Dent J*. 2015;218:E9.
22. Yurttutan ME, Keskin A. Evaluation of the effects of different sand particles that used in dental implant roughened for osseointegration. *BMC Oral Health*. 2018;18:47.
23. Gil J, Pérez R, Herrero-Climent M, Rizo-Gorrita M, Torres-Lagares D, Gutierrez JL. Benefits of residual aluminum oxide for sand blasting titanium dental implants: Osseointegration and bactericidal effects. *Materials (Basel)*. 2021;15:178.
24. Hussain SM, Hess KL, Gearhart JM, Geiss KT, Schlager JJ. In vitro toxicity of nanoparticles in BRL 3A rat liver cells. *Toxicol In Vitro*. 2005;19:975–983.
25. Porrelli D, Mardirossian M, Crapisi N, et al. Polyetheretherketone and titanium surface treatments to modify roughness and wettability - Improvement of bioactivity and antibacterial properties. *J Mater Sci Technol*. 2021;95:213–224.
26. Heo YY, Um S, Kim SK, Park JM, Seo BM. Responses of periodontal ligament stem cells on various titanium surfaces. *Oral Dis*. 2011;17:320–327.
27. Neoh KG, Hu X, Zheng D, Kang ET. Balancing osteoblast functions and bacterial adhesion on functionalized titanium surfaces. *Biomaterials*. 2012;33:2813–2822.
28. Gheisarifar M, Thompson GA, Drago C, Tabatabaei F, Rasoulianboroujeni M. In vitro study of surface alterations to polyetheretherketone and titanium and their effect upon human gingival fibroblasts. *J Prosthet Dent*. 2021;125:155–164.
29. Parizi MK, Doll K, Rahim MI, Mikolai C, Winkel A, Stiesch M. Antibacterial and cytocompatible: Combining silver nitrate with strontium acetate increases the therapeutic window. *Int J Mol Sci*. 2022;23:8058.
30. Rodríguez-Lozano FJ, López-García S, Sánchez-Bautista S, Pérez-López J, Raigrodski AJ, Revilla-León M. Effect of milled and lithography-based additively manufactured zirconia (3Y-TZP) on the biological properties of human osteoblasts. *J Prosthet Dent*. 2023;130:889–896.
31. Majhi R, Majhi RK, Garhnayak L, et al. Comparative evaluation of surface-modified zirconia for the growth of bone cells and early osseointegration. *J Prosthet Dent*. 2021;126:92.e1–92.e8.
32. Elawadly T, Radi IAW, El Khadem A, Osman RB. Can PEEK be an implant material? Evaluation of surface topography and wettability of filled versus unfilled PEEK with different surface roughness. *J Oral Implantol*. 2017;43:456–461.
33. Lukaszewska-Kuska M, Wirstlein P, Majchrowski R, Dorocka-Bobkowska B. The effects of titanium topography and chemical composition on human osteoblast cell. *Physiol Res*. 2021;70:413–423.
34. Rutkovskiy A, Stensløkken KO, Vaage IJ. Osteoblast differentiation at a glance. *Med Sci Monit Basic Res*. 2016;22:95–106.
35. Lee SS, Huber S, Ferguson SJ. Comprehensive in vitro comparison of cellular and osteogenic response to alternative biomaterials for spinal implants. *Mater Sci Eng C Mater Biol Appl*. 2021;127:112251.
36. Barkarmo S, Longhorn D, Leer K, et al. Biofilm formation on polyetheretherketone and titanium surfaces. *Clin Exp Dent Res*. 2019;5:427–437.

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CRediT authorship contribution statement
Amit Gaikwad: Conceptualization, Funding acquisition, Methodology, Investigation, Data curation, Formal analysis, Software, Visualization, Writing-original draft preparation. **Marjan Kheirmand Parizi**: Methodology, Investigation, Data curation, Formal analysis, Validation, Visualization, Writing-reviewing and editing. **Andreas Winkel**: Conceptualization, Funding acquisition, Resources, Methodology, Validation, Project administration, Supervision, Writing-reviewing and editing. **Meike Stiesch**: Conceptualization, Funding acquisition, Validation, Supervision, Writing-reviewing and editing.

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