ORIGINAL RESEARCH

A histomorphometric study on treated and untreated ceramic filled PEEK implants versus titanium implants: Preclinical in vivo study

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Abstract

Objectives: To investigate the osseo-integrative behavior of untreated (UCFP) and sandblasted ceramic filled PEEK (SCFP) implants in comparison with titanium implants through measurement of bone implant contact (BIC) and bone density (BD).

Materials and methods: Nine implants from each type were inserted into 9 dogs in which every experimental dog received the three different implants in the lower border of the mandible. The animals were euthanized after 3 months and extracting bone blocks containing implants followed by blocks preparation for histological examinations.

Results: BIC and BD were significantly higher in titanium and SCFP compared with UCFP group (p = .007) and (p = .012), respectively. Aluminum blasting increased the bone ingrowth and bone implant contact when compared to machined surfaces of untreated PEEK implants.

Conclusion: In conclusion, sandblasting with 110 μm aluminum oxide particles can be proposed as a suitable surface treatment that enhances hydrophilicity of CFP. Further in vivo animal studies are still needed to confirm the findings of this study.

KEYWORDS
animal experiments, biomaterials, biomechanics, bone implant interactions, finite elemente analysis, material sciences, morphometric analysis

1 | INTRODUCTION

Since the introduction of dental implants, implant technology has been rapidly progressing with frequent production of new designs, materials, shapes, and surface treatments. Implants fabricated from titanium and titanium alloys are considered the gold standard in the field of oral implantology (Abraham, 2014) However, there are

increased concerns that titanium can release metal ions and contribute to varying degrees of local allergic reactions, which have been suggested as a potential factor in dental implant failures that are often misdiagnosed (Chaturvedi, 2013; Harloff et al., 2010) In the presence of high smile line, titanium can pose an esthetic risk, particularly in cases of thin gingival biotype and/or gingival recession (Cosyn, Thoma, Hmmerle, & De Bruyn, 2017; Özkurt & Kazazoğlu, 2011) Additionally, the demand for metal-free reconstructions is burgeoning. It is also claimed that the difference in elastic moduli between titanium implants and surrounding bone may cause stress

Abbreviations: BIC, bone implant contact; CFP, ceramic filled PEEK; CFRP, carbon fiber reinforced PEEK; Peek, polyether ether ketone; RA, roughness average; SAD, surface area density; SCFP, sandblasted ceramic filled PEEK; UCFP, untreated ceramic filled PEEK.

transfer and probably result in peri-implant bone loss (McCracken, 1999).

Accordingly, a variety of alternative implant materials have been proposed. Biocompatibility, osteoconductive, esthetic advantages, and interesting microstructural properties of zirconia ceramics make it a prevalent biomaterial in dental implantology (Al-Amleh, Lyons, & Swain, 2010; Lughi & Sergo, 2010; Sanon et al., 2015). However, mechanical stresses and wetness exposure may have detrimental effects on mechanical properties of zirconia. The exact effect of aging on zirconia is not yet well known. Besides, zirconia implants may be associated with even higher stress peaks to the surrounding bone compared with titanium, due to its higher elastic modulus (210 GPa) (Andreiotelli & Kohal, 2009; Cionca, Hashim, & Mombelli, 2017; Lughi & Sergo, 2010). More recently, high-performance thermoplastic material called polyether ether ketone (PEEK) has been proposed as a potential substrate for manufacturing physiologic dental implants.

Elastic modulus of PEEK is 3.6 GPa and can be further modified by impregnating material with filler particles such as carbon fibers or ceramic particles to achieve a modulus of elasticity close to that of cortical and trabecular bone (Stratton-Powell, Pasko, Brockett, & Tipper, 2016; Toth et al., 2006; Vail, Krick, Marchman, & Sawyer, 2011). Considering the closer match of mechanical properties of PEEK to bone, the stress shielding of PEEK dental implants is less than that of titanium. The process involves reduction in bone volume around an implant due to the shielding effect of physiologic loads by the implant. PEEK is biocompatible, resistant to chemical degradation, high temperatures exceeding 300°C and exhibits strength properties that are comparable to some metals (Kurtz & Devine, 2007) However, when using PEEK as an implant substrate, the greatest challenge is represented by bio-inertness of the material. Based on in vitro studies, unmodified PEEK was proven to be inherently hydrophobic in nature, with a water-contact angle of 80–90°, which will affect the proliferation rate of surrounding cells (Thomas & Cook, 1985; Winkler & Mekayarajjananonth, 1999). A study comparing titanium, PEEK, and zirconia implant materials revealed that PEEK has the lowest bone implant contact, consequently compromising its osseointegration (Koch et al., 2010). Various techniques have been employed to improve the bioactivity of the material, among which are surface coating and surface treatment or a combination of both techniques (Ma & Tang, 2014). Such treatments led to modification of the roughness average values (Ra value) and wettability of material, which were said to influence BIC (Elias, 2011).

To the authors' best knowledge, no previous study investigated the influence of surface treatment on the bioactivity of ceramic filled PEEK (CFP) dental implants in an animal model. Therefore, the aim of the present study was to evaluate the osseo-integrative behavior of untreated CFP (UCFP) and sandblasted CFP implants (SCFP) in comparison with titanium implants in terms of BIC and bone density (BD) in a canine model at a 3-month observation period.

2 | MATERIALS AND METHODS

This animal study was approved by the Animal Ethic Committee, Faculty of Dentistry, Cairo University, Egypt.

2.1 | Sample size

Based on a previous study published by Kim, Kim, Park, and Cho (2009) on beagle dogs with 10-week time point, the average bone contact of titanium implants is 45.3% ± 12.2%. Considering that the average %BIC for low roughness peek is 32.6 ± 11.7 (Stübinger et al., 2013), a total sample size of 21 was required to achieve power of 80% and 5% significant level. This number has been increased to a total sample size of 27 implants (9 in each group) to allow for losses of around 20%.

Accordingly, nine healthy mature male mongrel dogs, aged 9–12 months and with an average weight of 12–15 kg, were used in this experiment. Prior to the study, the dogs underwent complete examination to rule out the presence of any disease. Once recruited, they were fed cooked meat, bread, milk, and water and were kept under clinical observation. At the night of surgery, dogs were deprived of food to prepare them for anesthesia and were weighed before its commencement to calculate the required dose of drugs to be administered.

Each dog received three implants: one Ti (control), one untreated, and one treated PEEK implants (test groups). The implants were placed posteriorly in the premolar–molar region, two on one side and the third one on the other side in a random order.

I-FIX one-piece titanium dental implant with ball abutment (Dentis company, Daegu, South Korea) 2.5 mm in diameter and

FIGURE 1 3d images for scanned implant

13 mm in length was digitally scanned using a high-resolution optical surface scanner (IScan D104i, Imetric, Switzerland). The 3D digital files of the scanned implant were exported in standard tessellation language (STL) format and were used to mill 18 BIO-HPP PEEK implants (Bio High Performance Polymer) (Figure 1) with a macro design matching that of scanned titanium implant using 5 axes milling machine (Shera Werkstoff-Technologie GmbH & Co. KG).

The titanium implant has a moderately rough implant surface with an Ra value of 1.59 µm (Elias, 2011). Nine implants were randomly selected from the eighteen milled PEEK implants and were sandblasted by 110 µ aluminum oxide particles under pressure of 5 bars for 10 s at a fixed distance of 50 mm resulting in Ra value of 1.55 µm (SCFP). The untreated CFP implant (UCFP) has Ra value of 1.46. The previously mentioned Ra values were predetermined based on an invitro study, which evaluated the topography and wettability of filled versus unfilled PEEK as shown in (Table S1) (Elawadly, Radi, El Khadem, & Osman, 2017).

Ultrasonic cleaning of implants was then performed to remove residual Al_2O_3 particles from sandblasting. After cleaning, implants were wrapped and sterilized in autoclave at 134°C under pressure of 2.10 bar for 34 min. The animal surgeries were carried out in the Department of Laboratory Animal Services, Faculty of Veterinary Medicine, Cairo University. Premedication with atropine sulfate 0.05 mg/kg was injected subcutaneously 10–30 min before the surgery for the reduction of salivary and bronchial secretions. Anesthesia was induced with a mixture of xylazine-HCL (1 mg/kg) and ketamine HCL (5 mg/kg) via a 23 g intravenous cannula through the cephalic vein. Anesthesia was maintained by venous drip of 500mg thiopental sodium/500 ml dextrose 5% with drip rate of 28–40 drop/min. The respiratory airway was kept patent by applying an endotracheal tube. A surgical flap was reflected at the inferior border of the mandible, and a pilot drill was used to create the osteotomy site.

After implant insertion, the periosteum was sutured by polyglactin resorbable sutures size 0 (Vicryl, Ethicon). The images of surgical procedure are shown in (Figure 2a–f).

The animals were housed in separate cages in Faculty of Veterinary Medicine, Cairo University. The animals were bathed in 1/1000 Neocidal Diazinone to guard against Ecto-Endoparasitic infection. Further, the dogs were vaccinated by vanguard Canine Parvovirus Coronavirus (CPV-CV) and by Defensor 3 to guard against some infectious diseases and rabies, respectively. During the healing stage, the animals were supplied with balanced food, sufficient amount of water and were kept living in an optimal condition.

2.2 | Histological methods

2.2.1 | Sample preparation

After a healing period of 12 weeks, the animals were euthanized under general anesthesia with an overdose of thiopental.

Mandibular en bloc resections were retrieved and fixed in 10% formaldehyde for more than a week for fixation of specimens. A block of bone containing each implant was then dissected out with fine handsaws, reduced to approximately 1 cm × 1 cm with 2 cm height, and rinsed with water. All specimens were dehydrated with a sequence of ethanol concentrations, cleared with xylene, and embedded in methyl methacrylate at approximately 60°C. Undecalcified 100 µm thick sections through the long axis of all implants were cut in a parallel direction to the long axis of implants using saw hard microtome system (Leica SP1600). For all samples, 1–2 central sections were prepared with a cutting distance of about 400 µm. Only sections representing the implant at full length were included in the analysis. The prepared sections were then glued to semi-transparent acrylic sheets. These sections were ground and polished to 30 µm thickness by an automatic rotary machine containing interchangeable sandpapers of different grit sizes; P400, P1000, P2500 and finally with P4000 (P: ISO/ FEPA Grit designation). Sections were ultrasonically treated with 50% ethanol bath for 30 min to remove 3–5 µm of MMA to expose the underlying mineralized and unmineralized tissues. Sections were stained with Mc Neal's (Wu & Liu, 2012) tetra chrome with equal parts of 0.1% toluidine blue and basic fuchsin to distinguish unmineralized osteoid from fully mineralized bone tissue and provide sufficient preservation of morphological details.

2.2.2 | Quantitative and qualitative assessment

All histological sections were identified with a random numerical sequence in order to codify groups and have analysis performed by the investigator. Sections were viewed using ZEISS stereomicroscope (Stemi sv 6, Carl Zeiss, Germany) with external light source at 2.5× magnification, and digital images were captured using an attached digital color camera. Captured images were analyzed using NIH Image analysis software (ImageJ—Research Services Branch, NIH, Bethesda, MD, USA and Rasb & ImageJ). The study analyzed BIC percentage on the entire implant surface by dividing the regions of BIC on the total implant perimeter (Figure 3). Furthermore, the same sections were captured with light microscope (LEICA DMIL, Germany) for higher magnification of 10× and 20× to compare the outline of implants and type of bone, respectively (Figures 4–6).

BD was calculated using image J software by point counting method.(Wu & Liu, 2012) This technique involves the superimposition of a grid point lattice on the region of interest (ROI), which is represented by chambers of implants, and then counting the number of points in ROI. Each grid point has 0.25 mm surface area. To avoid assessment bias, points were counted in three standard positions; at center, 15° to left, and 15° to right. An average of three readings was then taken to calculate the percentage, which is represented by bone area/total area ×100 (Figure 7).

The Animal Research: Reporting of In Vivo Experiments (ARRIVE) guidelines were strictly followed throughout the study.

FIGURE 2 Surgical Procedure, (a) flap reflection and osteotomy preparation, (b) insertion of 2 implants on one side, (c) insertion of PEEK implant on the other side, (d) shows three implants inserted on both sides, (e) suturing and periosteum closure, and (f) flap closure
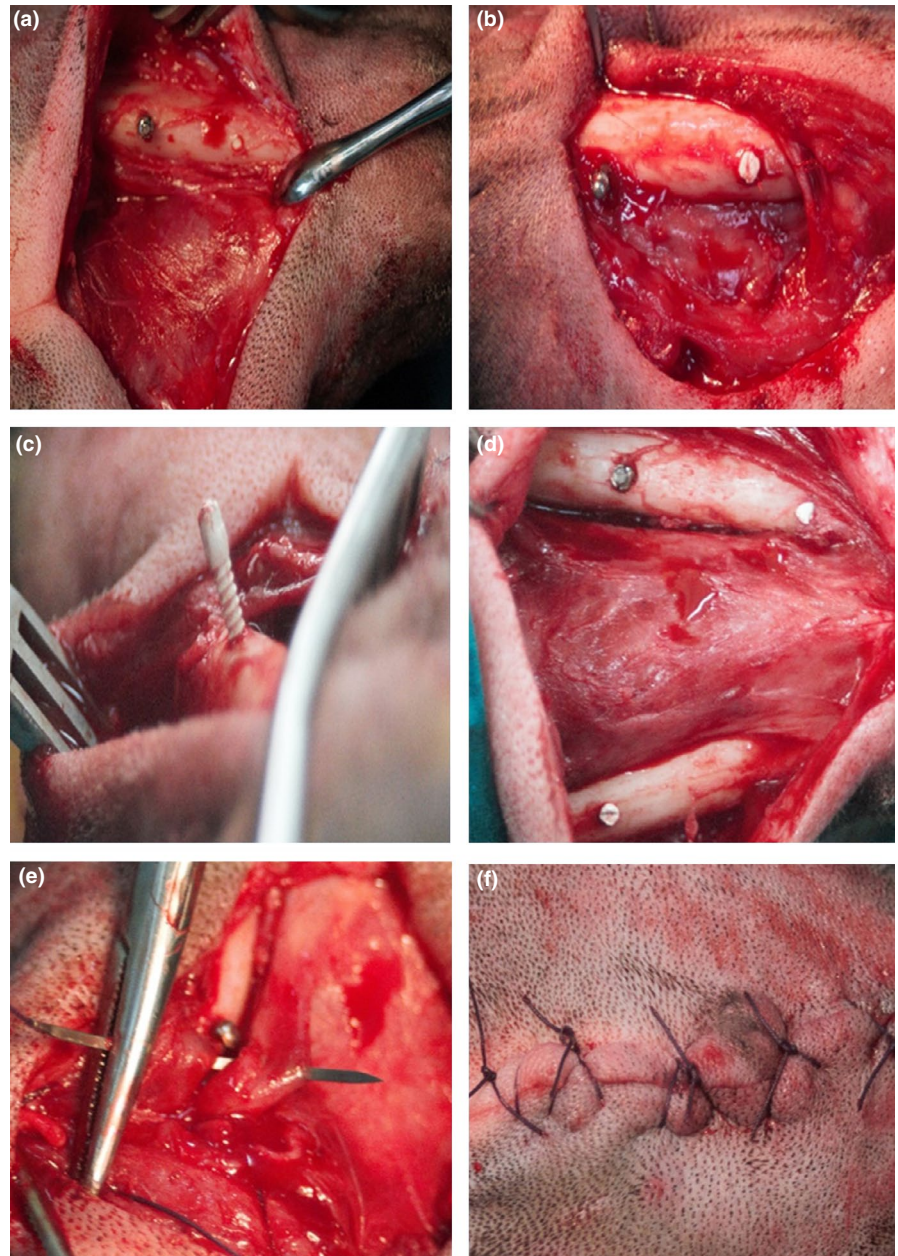
2.3 | Statistical analysis

Data were presented as mean, standard deviation (*SD*), 95% confidence interval (95% CI) median, and range. Data were explored for normality by using Shapiro–Wilk test. Since data were normally distributed, comparison between the study groups was done using repeated measures analysis of variance (ANOVA) test through general linear model (GLM) analysis; with paired *t* test as a posthoc multiple 2-group comparisons after applying Bonferroni correction of multiple comparisons. Two-sided *p* values less than 0.05 were considered statistically significant. All statistical calculations were done using computer program IBM SPSS (Statistical Package for the Social Science; IBM Corp) release 22 for Microsoft Windows. Univariate GLM analysis with repeated measures was performed to compare between the 3-implant types at one single time point considering the within-subject effect. One analysis

was done for BIC and another one for density using 3 level factors for the 3 implants data. No between subject factor and no other co-variates were entered in the analyses. Homogeneity of variance was checked through separate Levene's test and residual plots were visually assessed and the data appeared homogenous.

3 | RESULTS

All animals survived implant surgery and were available for evaluation. Clinical evaluation revealed no local infection or pathology at the implant sites. All implants were clinically stable with a 100% survival rate.

Microscopic examination revealed different thread profiles between titanium and CFP implants, whether treated or not.
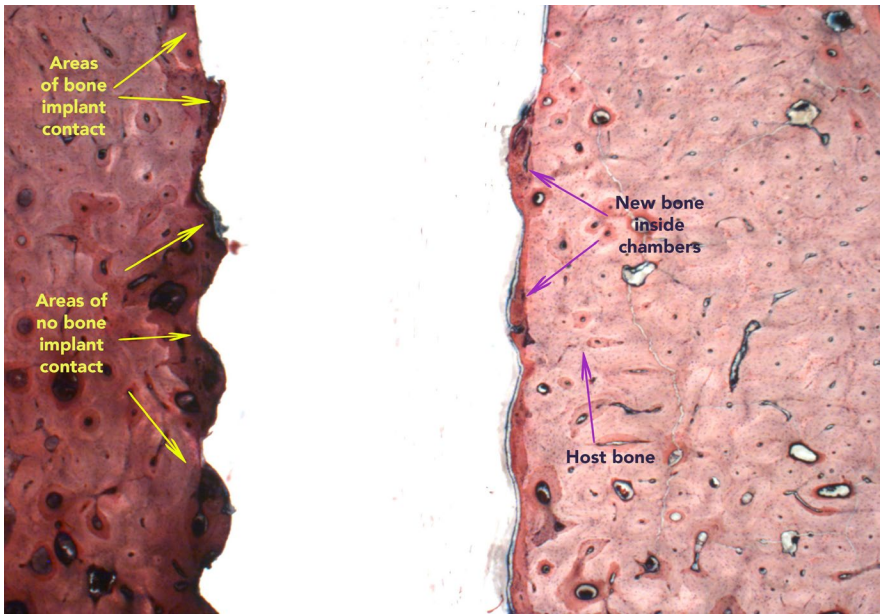
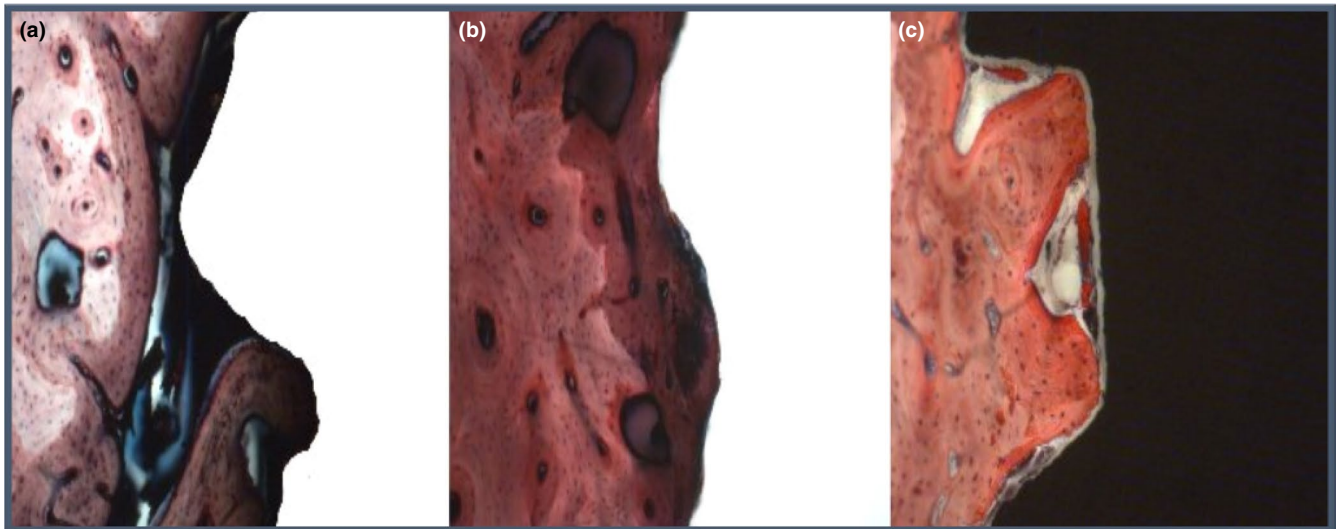**FIGURE 3** Showing the difference between areas of bone contact and non-contact

FIGURE 4 Showing different thread profiles between titanium and CFP implants, (a) untreated CFP, (b) sandblasted CFP, and (c) Titanium implant
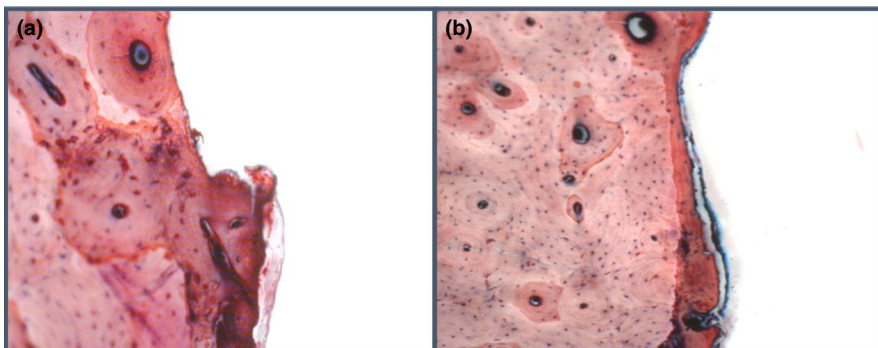

FIGURE 5 Histological images of treated PEEK with different magnifications, a) shows a decrease in the intervening connective tissue layer that surrounds untreated one 10x and b) shows a direct contact of bone to implant surface 20×

Titanium implants showed deep, trapezoid-shaped chambers between consecutive threads, while CFP implants exhibited shallower concave-shaped chambers. New bone apposition with different percentages could be observed into the chambers. In titanium and SCFP, new bone apposition could be observed, especially inside the implant threads close to implant surface. For UCFP, a narrow

FIGURE 6 Histological images with different magnifications, (a) shows untreated PEEK surrounded by intervening layer of connective tissue 10× and (b) a close image shows the direct contact of connective tissue layer to the implant surface 20×
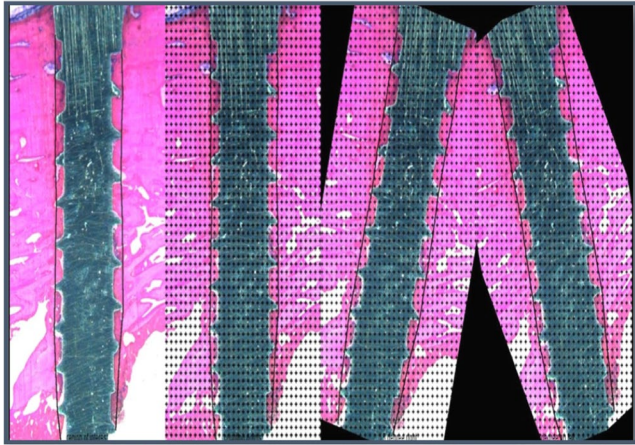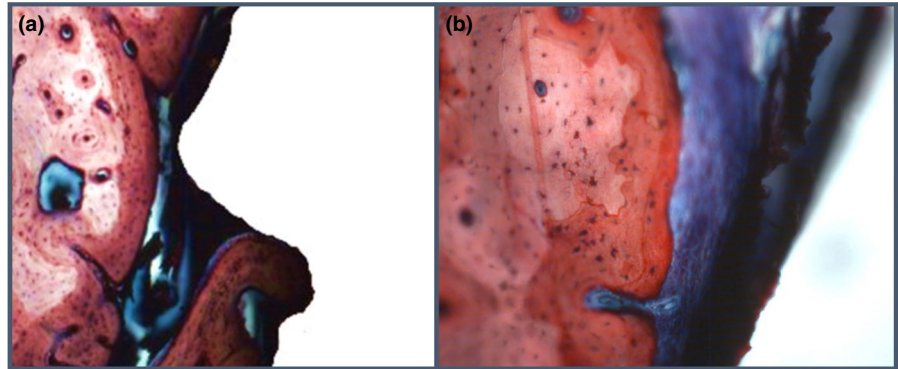

FIGURE 7 Shows point counting methods for BD measurements

intervening layer of connective was found on a larger portion of bone–implant interfaces.

The mean %BIC was 54.0% ± 5.4%, 51.1% ± 7.3%, and 30.9% ± 12.7% for titanium, SCFP, and UCFP groups, respectively (Table 1).

Tests of within-subject effects of BIC factor revealed significant difference (*p = .007*). Pairwise comparisons revealed no significant difference between titanium and SCFP groups (*p = .330*), whereas comparisons between titanium and UCFP, SCFP, and UCFP were statistically significant (*p < .005*) (Table 2).

The mean BD % in the thread area of the titanium group was 55.2% ± 9.9% with a range of 43%–72%. For the SCFP, it was 57.5% ± 11% with a range of 41.5%–78%, whereas for UCFP the value was 36.4%±13.2% with a range of 13.5%–52.2% (Table 3).

TABLE 1 Descriptive statistics, repeated measures ANOVA for bone implant contact data of the tested groups

BIC	N	Mean	SD	95% CI for Mean Lower Bound	95% CI for Mean Upper Bound	Min.	Max.	p value
Titanium	9	54.0%[A]	5.4%	49.9%	58.1%	45.0%	61.2%	.007
PEEK treated	9	51.1%[A]	7.3%	45.5%	56.7%	41.8%	61.0%	
PEEK untreated	9	30.9%	12.7%	21.1%	40.6%	13.5%	52.2%	

Note: SD: standard deviation, CI: confidence interval, min: minimum, max: maximum, capital similar letters not statistically significant, *p* ≤ .05 is statistically significant.

TABLE 2 Pairwise comparison of bone implant contact

Paired samples test

		Paired differences Mean	Std. deviation	Std. error mean	95% confidence interval of the difference Upper	95% confidence interval of the difference Lower	t	df	p value
Pair 1	BIC-titanium–BIC-PEEK treated	2.900%	8.387%	2.796%	−3.547%	9.347%	1.037	8	.330
Pair 2	BIC-titanium–BIC-PEEK untreated	23.157%	16.461%	5.487%	10.504%	35.810%	4.220	8	.009[A]
Pair 3	BIC-PEEK Treated–BIC-PEEK untreated	20.257%	17.808%	5.936%	6.569%	33.945%	3.413	8	.027[A]

Note: [A] Groups with statistically significant difference.

TABLE 3 Descriptive statistics, repeated measures ANOVA for Surface area density data of the tested groups

Surface area density	N	Mean	SD	95% CI for Mean		Min.	Max.	p value
				Lower Bound	Upper Bound			
Titanium	9	55.2%[A]	9.9%	47.6%	62.8%	43.0%	72.0%	.012
PEEK treated	9	57.5%[A]	11.1%	48.9%	66.0%	41.5%	78.0%	
PEEK untreated	9	36.4%	13.2%	26.2%	46.5%	13.8%	54.5%	

Note: SD: standard deviation, CI: confidence interval, min: minimum, max: maximum, capital similar letters not statistically significant, *p* ≤ .05 is statistically significant.

TABLE 4 Pairwise comparison of surface area density

Paired samples test									
		Paired differences							
					95% confidence interval of the difference				
		Mean	Std. deviation	Std. error mean	Upper	Lower	t	df	p value
Pair 1	Density-titanium– Density-peek treated	−2.278%	15.032%	5.011%	−13.832%	9.277%	−0.455	8	.661
Pair 2	Density-titanium– Density-peek un	18.828%	15.456%	5.152%	6.947%	30.709%	3.654	8	.018
Pair 3	Density-peek treated– Density-peek un	21.106%	14.768%	4.923%	9.754%	32.457%	4.287	8	.009

Tests of within-subject effects of BD factor revealed significant difference (*p* = .012). Pairwise comparisons revealed no significant difference between titanium and SCFP groups (*p* = .661), whereas comparisons between titanium and UCFP, SCFP, and UCFP were statistically significant (*p* < .005) (Table 4).

4 | DISCUSSION

Along the journey to develop physiologic, aesthetically pleasing implants with a modulus of elasticity that is close to that of the bone, researchers have attempted the use of PEEK as an implant material. Implants with modulus of elasticity that is close to that bone were suggested to optimize the biomechanical load distribution between implant and surrounding tissue, reduce healing time, maintain bone implant contact, and improve prognosis of treatment. An important area of research when introducing any novel implant material is the creation of a surface that will stimulate the osteoconduction and osteoinduction to sustain a bone implant contact for long-term prognosis of treatment. Implant surface topography is considered as one of the important parameters that significantly influences BIC, which might affect implant stability. Several animal studies reported that surface roughness was mandatory to enhance BIC.

In a previous study, different surface treatments of different PEEK materials were evaluated. The surface roughness and wettability of unfilled (UFP), ceramic filled (CFP), and carbon fiber reinforced (CFRP) PEEK disks were compared. Specimens were either untreated or were surface treated with 50 μ, 110 μ, or 250 μ

aluminum oxide particles. The authors found that the CFRP and CFP specimens treated with 110μ exhibit low contact angles and moderately rough surface (1–1.5 μm) and were thus suggested as potential substrates for fabrication of dental implants (Elawadly et al., 2017; Elias, 2011). Based on the findings of previously described study, CFP was selected because of its favorable surface properties and its white color, which can be considered advantageous in jaw regions of high esthetic demand. Selection of a one-piece implant design was limited by machining technique. An accurate implant–abutment connection is not easily achieved by milling. One-piece design was mandatory for implant placement, nevertheless following implant insertion ball abutment was removed under copious irrigation to allow for pressure-free environment. The minor difference detected in the shape of thread profile between titanium and PEEK implants may be attributed to tolerance of milling burs or limitations of scanning procedures. Yet, it is speculated by authors that such a difference did not influence the results considering that no significant difference was detected in %BIC and BD% between titanium and SCFP.

The present study showed successful osseointegration of unloaded, surface treated SCFP implants in experimental animals at 12-week healing period. SCFP implants showed BIC and BD values comparable to titanium and significantly higher values when compared to UCFP. The most frequently used animal model for dental bone–implant interface studies is rabbits and dogs. A canine model was preferred for this study as it provides a bone microstructure with a trabecular/cortical ratio similar to that found in human mandibles, in addition to similar saliva and microflora (Pearce, Richards, Milz, Schneider, & Pearce, 2007) Yet, irrespective of animal model employed, valuable information can

be retrieved from properly designed animal studies and represent an initial step when introducing any new biomaterial.

It must be mentioned that the present study reports data on healing after three months and without loading. Loading and longer periods of healing may yield different results; however, selected observation period allowed for basic evaluation of the osseo-integrative behavior of the material with proposed surface treatment paving road for further in-depth studies.

The findings of this study are in agreement with previous investigations that surface topography is important to bone tissue response of a dental implant even under loaded or unloaded conditions. Using the BIC and BD ratios as parameter for the degree of osseointegration, it can be stated that aluminum blasting of CFP implants can improve bioactivity and osseointegration of material. Comparable BIC and BD values to that of titanium implants were observed for SCFP and significantly higher than that of UCFP. A thin bone layer covered a relatively large portion of the SCFP. This feature showed that surface roughness of PEEK implants created by aluminum blasting activated the migration, spreading, and proliferation of osteoblasts suggesting contact osteogenesis comparable BD values to titanium could give a lead for continuous bone remodeling in healing chambers and prognosis of implant stability when subjected to load (Molly, 2006).

4.1 | Limitations and recommendations

It is worthy to mention that the present study reports data on healing after three months and without loading. Loading and longer periods of healing may yield different results. However, the selected observation period allowed for basic evaluation of the osseo-integrative behavior of the investigated implants with proposed surface treatment, paving road for further in-depth studies. Future in vivo animal studies under loading conditions and at different observation periods are still needed to confirm the findings of this study and provide a better understanding of the bone healing process surrounding the surface treated peek implants. Micro-CT studies are also recommended to determine the total volume of bone around implants in 3 dimensions. Once proven effective as implant material, randomized clinical trials could be assigned.

The results of this study can be considered as a step forward toward exploring the potentials of using SCFP as an implant substrate. Future in vivo animal studies under loading conditions and at different observation periods are still needed to confirm the findings of this study and provide a better understanding of the bone healing process surrounding the surface treated peek implants. Micro-CT studies are also recommended to determine the total volume of bone around implants in 3 dimensions.

5 | CONCLUSIONS

Sandblasting with 110 μ aluminum oxide particles can be proposed as a suitable surface treatment that enhances hydrophilicity of CFP. Aluminum blasting of CFP results in an increased %BIC and BD when compared to UCFP. SCFP implants can be considered as a new implant material.

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SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section.