Histopathologic assessment of soft tissue healing around Polyetheretherketone and Titanium abutments. A Randomized and controlled human study

Abstract

Aims
The establishment of peri-implant mucosa is crucial for dental implant success, involving a sequence of biological events leading to tissue barrier formation. While titanium has been the traditional choice for abutments, alternatives like PEEK show comparable healing outcomes in pre-clinical and clinical studies. This randomized clinical trial aims to compare the histological and inflammatory reactions of Polyetheretherketone (PEEK) and titanium abutments in individuals with partial posterior maxillary edentulism.

Methods
Systemically healthy adults were consecutively enrolled. Following implant placement (44x 8mm, 3P implants, B&B Dental, San Pietro in Casale, Italy), participants were randomly assigned to receive either titanium or PEEK abutments. After a healing period of 5 months, a minimally invasive biopsy procedure was performed, and immunohistochemical analysis of inflammatory infiltration was carried out.

Results
Twenty-two implants were placed in the posterior maxillary region of enrolled patients. Both abutment groups exhibited similar degrees of inflammatory infiltrate ($p > 0.05$). Dystrophic calcifications were slightly higher in the PEEK group ($p = 0.26$). Immunohistochemical analysis revealed comparable percentages of CD3+ T cells, CD20+ B cells, CD38+ and CD68+ cells between the two groups ($p > 0.05$). A trend of a less marked infiltrate was observed around titanium, particularly at the mesial side (26.66% vs. 6.75%, $p = 0.02$).

Conclusions
PEEK and titanium abutments demonstrated similar peri-implant soft tissue responses. The histological findings did not reveal a significantly increased inflammatory reaction associated with Polyetheretherketone. While a trend of less marked infiltrate around titanium was observed, further long-term observations are crucial for a definitive assessment of PEEK abutment suitability.

DOI

10.23805/JO.2025.702

Authors

N. Discepoli[1,]
R. Mirra[1]
I. De Rubertis[1]
R. Ricciardi [1]
N. La Francesca[2]
C. Bellan[2]

1Unit of Periodontics, Department of Medical Biotechnologies, University of Siena, Siena, Italy
2Unit of Pathology, Department of Medical Biotechnologies, University of Siena, Siena, Italy

Keywords

Polyetheretherketone, dental implant, healing.

INTRODUCTION

The establishment of the peri implant mucosa is a key factor for dental implant treatment success. Soft tissue healing after surgical implant placement comprises a sequence of well-established biological events, from the blood clot (coagulum) to the granulation tissue and the eventual establishment of both a mature barrier epithelium and a connective tissue compartment (lamina propria)(1,2). Recruitment of inflammatory cells and angiogenesis regulates and sustains the whole process. The latter leads to the formation of a tissue barrier after a healing period of 6 weeks, as it was demonstrated by a pre-clinical ex vivo protocol (2). In human biopsies, Tomasi and coworkers described the soft tissue interactions with the titanium surface during a healing period of 12 weeks. At the end of the experimental period, sparse inflammatory cell infiltrate was still detectable(3), suggesting that after that period the resolution of the inflammatory process was still ongoing. The commercially pure titanium (c.p) has been used as elective material for the transmucosal portion (abutments) of dental implants mainly due to its high biocompatibility (property to bind to living tissue) and resistance to corrosion (4,5). Albeit it is still considered the material of choice (6), other alternative materials have entered the market, primarily for aesthetic and technical reasons. Polyehereterketone (PEEK) began its biomedical application in orthopedic surgery with a high rate of success (7,8) and more recently it has been used in the dental field as a material for temporary abutments. In vitro evidence has demonstrated the high biocompatibility of PEEK for both human gingival epithelial keratinocytes and fibroblasts (9,10). Moreover, a pre-clinical ex vivo investigation, performed on Labrador dogs, has compared soft and hard tissue healing of PEEK and titanium abutments, after an observation period of 4 months. Similar dimensions of the peri-implant mucosa width and similar locations of the soft tissue in relation to the implant shoulder were observed (11). From a clinical standpoint, available evidence suggests that the comparison of PEEK and titanium abutments does not unveil any difference in terms of soft and hard tissue healing, after 3 months of observation (12,13). The main objective of the current investigation is therefore to compare the histological and inflammatory reaction of PEEK and titanium abutments in a cohort of individuals over a 5 months healing period.

MATERIALS AND METHODS

Study design

The current investigation was designed as a randomized clinical trial, university-based, single centre, parallel arm with an allocation ratio of 1:1. The experimental protocol was conducted at the Department of Medical Biotechnologies, Unit of Periodontology, Università degli Studi di Siena (Siena, Italy), in collaboration with the Unit of Pathology. The protocol was approved by the University Hospital of Siena Ethics committee (Siena, Italy) (Sezione Area vasta Toscana Sud Est, n°16481). Enrolled participants were provided detailed information on the study and signed a written consent prior to the treatment. All the clinical procedures were carried out in accordance with the Helsinki Declaration and following amendments. The current investigation is registered at ClinicalTrials.gov (NCT046623333).

Participants

Patients referring to the Unit of Periodontology were consecutively screened and those with a clinical and radiographic diagnosis of partial posterior maxillary edentulism with at least one tooth missing were considered eligible. Periodontal status was examined with a full periodontal chart and the available bone volume was outlined and recorded in accordance to CBCT images. The enrolment was completed by fulfilling the following inclusion criteria:

a. men and non-pregnant women, age >18;
b. otherwise systemically healthy patients;
c. at least 2mm of Keratinized mucosa at the experimental site;
d. absence of periodontal pockets (PPD>4mm with Bleeding on probing);
e. full mouth Plaque score <25%;
f. patients willing and fully capable of complying with the study protocol.

Patients with one or more of the following characteristics were excluded from the study:

a. heavy smoking (>10 cigarettes/day);
b. pregnancy;
c. present infectious disease;
d. osteoporosis or use of drugs that influence bone metabolism;
e. inability to perform oral hygiene maneuvers;
f. interventions;
g. Implant procedure.

The residual bone height at the sites where implants had to be inserted was measured with CBCT scan image. Two grams of amoxicillin were administered to each patient 1 hour prior to implant placement. All the surgical procedures were carried out by an experienced periodontist. After full thickness flap elevation, the first drill was used to perforate the residual cortical bone. The recipient sites were prepared based on the manufacturer's protocol. Implants were inserted (4x 8mm, 3P implants, B&B Dental, San Pietro in Casale, Italy). According to the randomization list, patients received either an undersized (4mm) healing titanium (TAb) or PEEK abutment (PAb) abutment. All abutments were connected using a torque of 15 Ncm; the mucoperiosteal flap was then repositioned and adapted using a non-resorbable 6-0 suture ensuring transmucosal healing. Patients were prescribed a

non-steroidal anti-inflammatory agent for three days (Ibuprofen 600mg), systemic antibiotic for 5 days (Amoxicillin and clavulanic acid) and Chlorhexidine 0.12% mouth rinse for one week. Sutures were removed seven days after surgery.

Biopsies procedure

Five months after implant placement, a minimally invasive and standardized biopsy procedure was performed. A circumferential incision around the existing abutment was performed with a 6,2 mm diameter cylindrical blade (Mucotome, Omnia spa, Italy). The blade was used to harvest a soft tissue sample 1 mm wide from the existing sulcus, around experimental abutments, parallel to the abutment surface. Immediately thereafter and according to the site-specific gingival height, a larger diameter abutment was screwed (titanium abutments 6mm diameter) for both experimental groups. The specimen orientation (Vestibular-V, Mesial-M, Distal-D, Palatal-P) was guaranteed by embedding them in marked cassettes. Each tissue sample was fixed in 4% buffered formalin for at least 24 hours. All included patients then proceeded with the restorative prosthetic treatment plan established according to their individual needs.

Study Outcomes

The degree of intensity of the inflammatory cell infiltrate, its extent, the presence of calcifications and the site of greater inflammation, either vestibular, palatal, mesial or distal were assessed.

Clinical Variables

Prior to soft tissue sampling, all enrolled subjects received an additional full periodontal chart. Bleeding on probing (Bop) (14), presence of plaque (PS) and probing pocket depth (Ppd) were evaluated by a calibrated examiner, using a UNC 15 periodontal probe and a pressure of 0.25 N, six sites around each experimental abutment (15).

Histological preparation and Immunohistochemical analysis of inflammatory infiltration

In both the Test and Control groups, a semi-quantitative method to assess the extent of inflammatory cell infiltration on Hematoxylin & Eosin (H&E) slices was employed, assigning scores ranging from 0 to 3 (0: Very Low; 1: Low; 2: Moderate; 3: Intense). Additionally, it was determined whether the infiltration was localized or diffuse. Immunostaining for CD20 (CONFIRM anti-CD20 (L26) Primary Antibody, Roche Diagnostics), CD3 (CONFIRM anti-CD3 (2GV6) Primary Antibody, Roche Diagnostics), CD38 (Confirm anti-CD38 (SP149) Primary Antibody, Roche Diagnostics), and CD68 KP-1 (Confirm anti-CD68 (KP-1) Primary Antibody, Roche Diagnostics) was conducted using the Automatic sample preparation system BenchMark ULTRA (Ventana, Roche Diagnostic, Monza, Italy), following the manufacturer's instructions. This process aimed to provide a more detailed characterization of the inflammatory infiltrate. Immunohistochemical analysis was performed exclusively on samples exhibiting non-physiological inflammation. Each cellular sub-population was assigned a percentage value relative to the total inflammatory cells. Furthermore, their location—whether epithelial (designated as 0), subepithelial (designated as 1), or perivascular (designated as 2)—was assessed. The presence or absence of dystrophic calcifications was documented in both groups.

Sample size

The difference between experimental groups in mononuclear inflammatory cells counts was the outcome variable for establishing the sample size. Type I error was settled at 0.05 and Type II error at 0.8. According to previous evidence (16), and considering a common standard deviation of 0.24 (17) a sample size of 11 abutments for group was calculated (command "power", Stata IC 15).

Randomization and allocation concealment

A clinician, not previously involved in patients selection, allocated the distribution of the two experimental abutments (TAb and PAb) according to a simple randomization list with a 1:1 ratio. The sequence was generated with specific software (command "rndseq", Stata 15 IC). Sealed and numbered envelopes containing the randomization codes were opened immediately after implants were uncovered during the second stage surgery.

Statistical methods

Statistical analysis was performed using a dedicated software (STATA IC, version. 15, StataCorp LP, TX, USA). Continuous variables were expressed as mean and confidence interval at 95% (IC95%, Wilson) and categorical variables as proportion and confidence interval (IC95%). Normal distribution was assessed by Shapiro Wilk test for normality ($p<0.05$) and, accordingly, intergroup differences were assessed with the Student T test or Wilcoxon signed rank test ($p<0.05$).

RESULTS

Twenty-two implants were placed in the posterior maxillary region of recruited participants (65.5 ± 1.8 years old; 50% females;) Prior to soft tissue specimens' collection, both objective evaluation and inspection did not reveal soft tissue edema, erythema nor suppuration. The implants healed without complications. Absence of plaque, bleeding on probing and increased periimplant probing depths was assessed.

Histological and immunohistochemical variables

As shown in Table 1, there were no statistically significant differences in the intensity or in extent

VARIABLE		CONTROL (n= 11)	TEST (n= 11)	P VALUE
Intensity (P [95%CI])	VERY LOW	0.13 (0.02-0.57)	0.18 (0.04-0.53)	0.66
	LOW	0.5 (0.18-0.82)	0.45 (0.19-0.75)	
	MODERATE	0.25 (0.06-0.65)	0.36 (0.13-0.68)	
	INTENSE	0.13 (0.01-0.57)	.	
Extent (P [95%CI])	LOCALIZED	0.50 (0.18-0.82)	0.63 (0.31-0.87)	0.55
	DIFFUSED	0.50 (0.18-0.81)	0.36 (0.13-0.68)	
Calcifications (P [95%CI])	PRESENT	0.25 (0.06-0.65)	0.45 (0.19-0.75)	0.26
	ABSENT	0.75 (0.35-0.94)	0.55 (0.25-0.81)	
Site of greater inflammation (P [95%CI])	VESTIBULAR	0.25 (0.06-0.65)	0.18 (0.04-0.53)	0.58
	PALATAL	0.50 (0.18-0.82)	0.54 (0.25-0.81)	
	DISTAL	0.13 (0.01-0.57)	0.27 (0.08-0.61)	
	MESIAL	0.13 (0.01-0.57)	.	

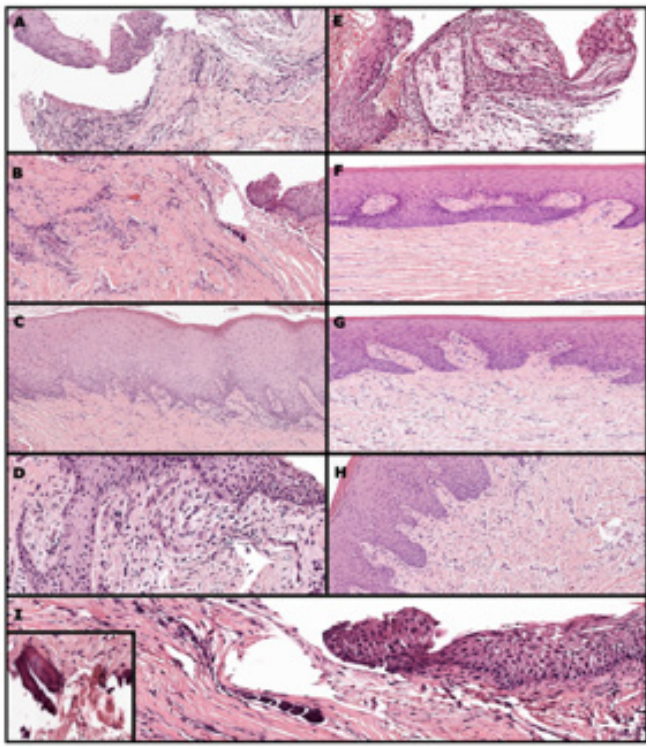
Tab. 1 Assessment of inflammatory infiltrate and dystrophic calcifications

VARIABLE	GROUP	V	P	D	M
CD2O (Mean [95%CI])	C	21.25 (-10.82-53.32)	21.67 (6.58-36.75)	13.75 (0.16-27.34)	18.33 (-28.69-65.36)
	T	29.37 (16.26-42.49)	26.88 (13.67-40.08)	25.83 (10.12-41.55)	18.75 (-14.61-52.11)
CD3 (Mean [95%CI])	C	26.25 (6.36-46.14)	36.67 (21.95-51.38)	38.75 (12.46-65.03)	36.67 (-15.04-88.38)
	T	30.62 (18.10-43.15)	28.13 (-4.84-52.34)	30.83 (18.23-43.43)	40 (33.50-46.49)
CD38 (Mean [95%CI])	C	23.75 (-4.84-52.34)	16.67 (12.38-20.95)	17.5 (-7.23-42.24)	26.66Δ (-4.59-57.92)
	T	18.13 (6.74-29.50)	16.25 (5.59-26.90)	15 (0.16-29.84)	6.75Δ (2.99-10.51)
CD68KP-1 (Mean [95%CI])	C	26.25 (-0.04-52.53)	25 (12.15-37.85)	30 (-4.37-64.37)	15 (-17.86-47.86)
	T	21.88 (-4.84-52.34)	23.75 (11.56-35.94)	28.22 (-1.84-58.50)	34.5 (0.45-68.54)

Abbreviations: C, control group; T, test group; V, vestibular; P, palatal; D, distal; M, mesial.
Δ, p value < 0,05 for intra-group comparisons.

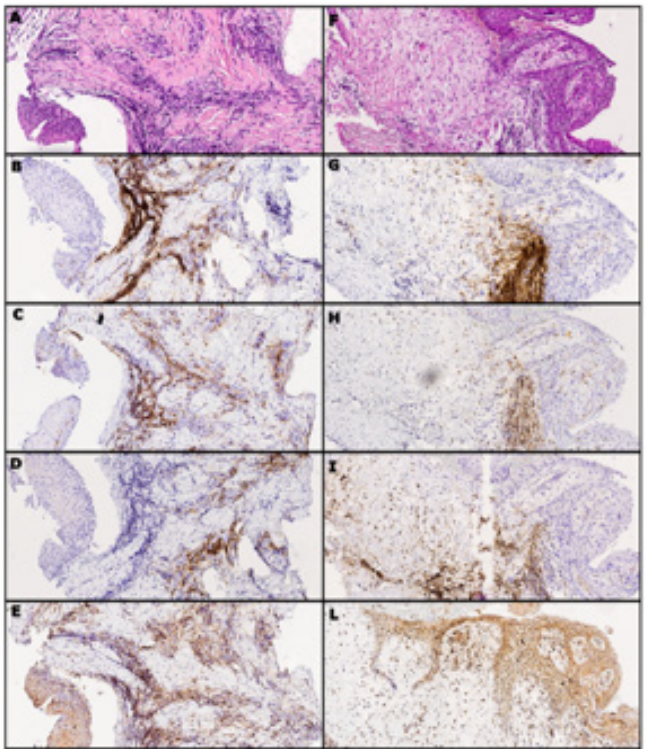
Tab. 2 Distribution of each inflammatory subcellular population

of the inflammatory infiltration. Despite a higher percentage of dystrophic calcifications in the test group, the value was not significant (p-value = 0.26) (Figure 1). Interestingly, the palatal site was found to be the site of greater inflammation for both intervention groups (Figure 2). The distribution of each inflammatory subcellular population is described in Table 2. The immunohistochemical analysis was carried out only on



Evaluation of the inflammation variability in gingival soft tissue, at different sides, in the test group (A: Palatal site, 15x; B: Vestibular site, 10x; C: Distal site, 10x D: Mesial site, 24x;) and control group (E: Palatal site, 10x; F: Vestibular site, 10x; G: Distal site, 10x H: Mesial site, 10x). Dystrophic calcification in gingival soft tissue were found (I: 20x); Occasional large calcifications can be noticed (I Inset: 40x).

Fig. 1 Gingival inflammation and calcifications



Comparative investigation of inflammatory sub-populations on test group (A-E) and control group (F-L) demonstrated a superimposable inflammatory process (A, F: H&E, 13x; B, G: anti-CD 20, 11x; C, H: anti-CD3, 11x; D, I: anti-CD38, 11x; E, L: anti-CD68 KP-1, 11x)

Fig. 2 H&E and immunohistochemical stains performed on the palatal side of both groups

samples that displayed inflammation considered non-physiological. Intragroup comparisons demonstrated a statistically significant greater percentage of plasma cells (CD38+ cells) at the mesial site in the control group (26.66% versus 6.75%, p-value = 0.02) (Figure 3).

Table 3 highlighted the frequency distribution of each marker according to their location. Mononuclear inflammatory cells densities at the epithelial, subepithelial and perivascular levels displayed no statistically significant differences between the two intervention groups (p-value>0.05).

DISCUSSION

The current histopathological investigation demonstrated that there are no differences between titanium and PEEK abutments for what concerns the level of soft tissue inflammation and cellular densities surrounding the abutments, after a healing period of 5 months. Histological and immunohistochemical analyses of biopsy material, which are extremely accurate measures to evaluate soft tissue responses to different types of abutment materials (13), confirmed indeed that the inflammatory cell tissue infiltrate resulted qualitatively similar between the two experimental groups. However, a tendency of a less marked infiltrate was observed around titanium tissue specimens, albeit the difference was not statistically significant. The latter finding was mirrored by a less represented sub-epithelial and peri-vascular infiltrate around titanium abutments. Moreover, higher proportions of dystrophic calcifications were detected in specimens in the test group. The latter result may reflect the mixed response, pro-inflammatory and anti-inflammatory, generated by PEEK (18), that favors a more prolonged, chronic inflammatory process. During chronic inflammation, the establishment of an alkaline and anoxic environment and the increase in phosphatases, favor the formation and deposition of calcium salts. In the present investigation, as in the vast majority of cases, dystrophic calcifications did not manifest clinically. Seldomly, however, they can cause enlargement and ulceration of the overlying mucosa and result palpable. Although a marked delay in the healing time of venous skin ulcers of the lower limbs presenting dystrophic calcifications has been demonstrated (19), to date, the influence of calcium salts deposition on the healing peri-implant soft tissues has not been fully investigated. When examined histologically, even in the absence of clinical signs and symptoms of inflammation, all specimens analyzed displayed, to a similar extent, a certain degree of inflammation. Such results are in line with currently available literature evaluating the healing pattern of peri-implant mucosa(13,20,21). Recent evidence demonstrated that neovascularization and recruitment of inflammatory cells, characterizing

MARKER	SITE	CONTROL GROUP				TEST GROUP			
		V	P	D	M	V	P	D	M
CD20 (P [95%CI])	0	.	.	.	.	.	.	.	.
	1	16.7 (9.97-90)	14.3 (7.14-76.5)	20 (9.43-90.5)	14.3 (2.44-90.9)	25 (10.7-74.9)	35.7 (25.6-88.9)	30 (13.6-86.4)	14.3 (1.93-84.9)
	2	16.7 (9.97-90)	28.6 (11-74.4)	20 (9.43-90.5)	28.6 (9.08-97.6)	41.7 (25-89.2)	21.4 (13.6-86.4)	30 (13.6-86.4)	42.9 (15.1-98)
CD3 (P [95%CI])	0	25 (19.1-97.4)	14.3 (7.15-76.4)	20 (9.43-90.5)	14.3 (2.44-90.9)	25 (10.7-74.9)	21.4 (1.1-74.4)	.	28.6 (7.96-92)
	1	8.33 (2.56-80.9)	21.43 (14.6-85.4)	20 (9.43-90.5)	28.6 (9.08-97.6)	41.7 (25-89.2)	35.7 (25.6-88.9)	40 (21.9-93.4)	28.6 (7.96-92)
	2	.	7.14 (1.84-68.1)	.	.	.	.	20 (6.58-78)	.
CD38 (P [95%CI])	0	.	.	.	.	.	.	.	.
	1	16.7 (9.97-90)	14.3 (7.15-76.5)	22.2 (9.06-90.9)	14.3 (2.43-90.9)	16.7 (5.23-66.7)	14.3 (5.41-66)	11.1 (18.6-76.7)	.
	2	16.7 (9.97-90)	28.6 (23.5-92.9)	22.2 (9.06-90.9)	28.6 (9.08-97.6)	50 (33.2-94.8)	42.9 (33.9-94.6)	44.4 (23.3-98.1)	57.4 (.)
CD68KP-1 (P [95%CI])	0	.	.	.	.	8.3 (1.34-60)	7.14	.	14.3 (1.94-84.9)
	1	25 (19.1-97.4)	21.4 (1.39-58.9)	20 (9.43-90.5)	14.3 (2.43-90.9)	50 (33.2-94.8)	35.7 (14.6-85.4)	40 (21.9-93.4)	28.6 (7.98-92)
	2	8.3 (25.6-80.1)	21.4 (14.6-85.4)	20 (9.43-90.5)	28.6 (9.08-97.6)	8.3 (1.34-60)	14.3 (5.4-66)	20 (6.58-78)	14.3 (1.94-84.9)

Abbreviations: 0, epithelial; 1, subepithelial; 2, perivascular; C, control group; T, test group; V, vestibular; P, palatal; D, distal; M, mesial.

Tab. 3 Distribution of immunohistochemical markers according to their location

the early phases of the healing process of peri-implant mucosa, guide the maturation of peri-implant soft tissue (3,22). The results obtained in the present study are in agreement with those of previous reports demonstrating that no significant differences are identifiable when comparing connective tissue infiltrates at experimental titanium and PEEK abutments, regarding the distribution of mononuclear inflammatory cells(13). Analysis of the inflammatory infiltrate revealed that CD3 + T cells were the most abundant immune cell type and that they predominated over CD20+ B cells, in both intervention groups. Accordingly, it has been thoroughly proven that the inflammatory infiltrate in healthy peri-implant mucosa is dominated by T lymphocytes and that this cell lineage regulates the local immune response (23,24). However, when compared to titanium, soft tissue samples obtained from PEEK abutments presented higher levels of infiltrating CD3 and CD20+ cells, even if this difference was not significant. The latter result may reflect the inhibitory role of titanium on T and B cell reaction (25). In addition, densities of B cells resulted similar for both examined abutment materials and never reached substantial proportions. Several pieces of evidence demonstrated that a marked B cell response is detectable in both periodontitis (26,27) and peri-implantits(28,29). However, a paucity of B lymphocytes promotes a stronger acute inflammatory reaction and prolongs angiogenesis, therefore negatively affecting the kinetics of the healing process(30). Moreover, the proportion of T and B cells was similar to that of macrophages, in both intervention groups. Macrophages exhibit several functions in wound healing, such as angiogenesis and elimination of degraded tissue or cell components and contribute

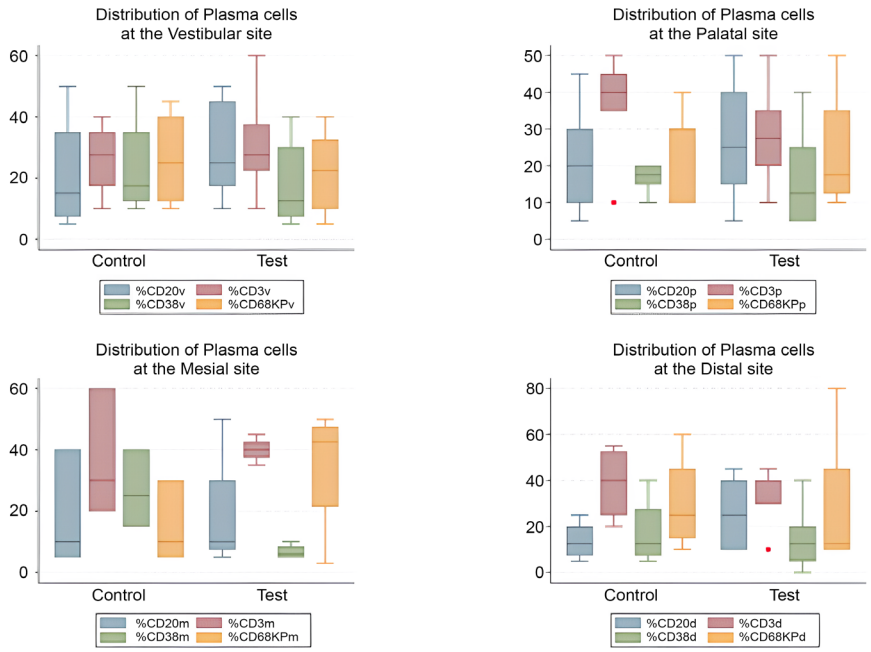


Fig. 3 Immunohistochemistry of CD20+, CD3+, CD38+ and CD68KP+ cells from soft tissue collected from Titanium and PEEK abutments.

to the resolution of the process of inflammation(31). Indeed, the inhibition of CD68K+ cells reaction is known to delay the healing response (32). Furthermore, a higher proportion of CD38+ cells was observed in the control group, particularly at the mesial site. Nevertheless, this statistically significant difference lacks clinical relevance, as the immunohistochemical analysis, performed only in the presence of inflammation, was conducted on a limited number of samples in the test group. Histopathological investigations on soft tissue response to PEEK as an alternative to titanium abutments are scarce. Most comparative data available on soft tissue response to different abutment materials arise from preclinical studies (33,34) or they are based on clinical surrogate variables alone (35). Nevertheless, given the data presented, conducting additional studies on this topic would be appropriate. In order to properly interpret the current results, it must be noted that the present study did not consider different healing times. Previous clinical reports pinpointed that a healing period of 8 weeks allows for the formation of a mature peri-implant soft tissue(36–38). However, a reduction in inflammatory cell counts is detectable with increasing healing time(3). Therefore, different time points and a larger sample size are rendered important to further evaluate the long-term peri-implant stability and to investigate a possible reduction in inflammatory cell densities with increasing healing time.

CONCLUSIONS

In conclusion, the present study demonstrated that both examined abutment materials displayed a similar healing outcome and a comparable peri-implant soft tissue response. The histological findings did not reveal a significantly increased inflammatory reaction associated with Polyetheretherketone. A longer observation period is needful for a definitive assessment of the long-term suitability of PEEK abutments.

Conflict of interest statement

This research received no specific grants from funding agencies in the public, commercial, or not-for-profit sectors. The authors deny any conflict of interest related to this study.

Author contribution statement

Nicola Discepoli (Data Analysis, Methodology, Writing – original draft), Raffaele Mirra (Conceptualization, Writing – original draft), Isabella De Rubertis (Data curation, Writing – original draft), Renata Ricciardi, (Data curation, Investigation), Noemi La Francesca (Investigation), Cristiana Bellan (Supervision).

Data availability statement

The data sets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval statement

Approved by the University Hospital of Siena Ethics Committee (Siena, Italy), Area Vasta Toscana Sud Est, protocol number 16481.

Acknowledgment

B&B Dental Implant Company provided materials and partially supported this research project by supplying the healing abutments.

REFERENCES

1. Salvi GE, Bosshardt DD, Lang NP, Abrahamsson I, Berglundh T, Lindhe J, et al. Temporal sequence of hard and soft tissue healing around titanium dental implants. Periodontol 2000. 2015;68(1):135–52.
2. Berglundh T, Abrahamsson I, Welander M, Lang NP, Lindhe J. Morphogenesis of the peri-implant mucosa: An experimental study in dogs. Clin Oral Implants Res. 2007;18(1):1–8.
3. Tomasi C, Tessarolo F, Caola I, Piccoli F, Wennstr€ Om JL, Nollo G, et al. Early healing of peri-implant mucosa in man. J Clin Periodontol [Internet]. 2016;43:816–24. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jcpe.12591
4. Steinemann SG. Titanium - The material of choice? Periodontol 2000. 1998;17(1):7–21.
5. Gittens RA, Olivares-Navarrete R, Tannenbaum R, Boyan BD, Schwartz Z. Electrical implications of corrosion for osseointegration of titanium implants. J Dent Res. 2011;90(12):1389–97.
6. Sanz M, Klinge B, Gil Acoforado J, Bienz SP, Cosyn J, De Bruyn H, et al. Biological aspects: Summary and consensus statements of group 2. The 5 th EAO Consensus Conference 2018. Clin Oral Impl Res [Internet]. 2018;29:152–6. Available from: https://onlinelibrary.wiley.com/doi/10.1111/clr.13274
7. Toth JM, Wang M, Estes BT, Scifert JL, Seim HB, Turner AS. Polyetheretherketone as a biomaterial for spinal applications. Biomaterials. 2006;
8. Seaman S, Kerezoudis P, Bydon M, Torner JC, Hitchon PW. Titanium vs. polyetheretherketone (PEEK) interbody fusion: Meta-analysis and review of the literature. Journal of Clinical Neuroscience. 2017.
9. 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. Journal of Prosthetic Dentistry. 2021;
10. Ramenzoni LL, Attin T, Schmidlin PR. In vitro effect of modified polyetheretherketone (PEEK) implant abutments on human gingival epithelial keratinocytes migration and proliferation. Materials. 2019;12(9):1–12.
11. Rea M, Ricci S, Ghensi P, Lang NP, Botticelli D, Soldini C. Marginal healing using Polyetheretherketone as healing abutments: an experimental study in dogs. Clin Oral Implants Res. 2017;28(7):e46–50.
12. Koutouzis T, Richardson J, Lundgren T. Comparative soft and hard tissue responses to titanium and polymer healing abutments. Journal of Oral Implantology. 2011;37(SPEC. ISSUE):174–82.
13. Enkling N, Marder M, Bayer S, Götz | Werner, Stoilov M, Kraus D. Soft tissue response to different abutment materials: A controlled and randomized human study using an experimental model. Clin Oral Impl Res [Internet]. 2022;33:667–79. Available from: https://onlinelibrary.wiley.com/doi/10.1111/clr.13932
14. O'Leary TJ, Drake RB, Naylor JE. The Plaque Control Record. J Periodontol. 1972;
15. Lang NP, Nyman S, Senn C, Joss A. Bleeding on probing as it relates to probing pressure and gingival health. Vol. 18, J Clin Periodontol. 1991.
16. Enkling N, Marder M, Bayer S, Götz W, Stoilov M, Kraus D. Soft tissue response to different abutment materials: A controlled and randomized human study using an experimental model. Clin Oral Implants Res. 2022;33(6):667–79.
17. Kraus D, Götz W, Bayer S, Frentzen M, Marder M, Albrecht D, et al. Novel method to obtain human non-separated histological samples for the assessment of peri-implant soft tissue response: A feasibility study. Clin Oral Implants Res. 2021;32(4):401–9.
18. Trindade R, Albrektsson T, Galli S, Prgomet Z, Tengvall P, Wennerberg A. Bone immune response to materials, part I: Titanium, peek and copper in comparison to sham at 10 days in rabbit tibia. J Clin Med. 2018 Dec 1;7(12).
19. Enoch S, Kupitz S, Miller DR, Harding KG. Dystrophic calcification as a cause for non healing leg ulcers. Int Wound J [Internet]. 2005 Jun;2(2):142–7. Available from: http://www.ncbi.nlm.nih.gov/pubmed/16722863
20. Pongnarisorn NJ, Gemmell E, Tan AES, Henry PJ, Marshall RI, Seymour GJ. Inflammation associated with implants with different surface types. Clin Oral Implants Res. 2007 Feb;18(1):114–25.
21. Milinkovic I, Krasavcevic AD, Jankovic S, Sopta J, Aleksic Z. Immunohistochemical analysis of soft tissue response to polyetheretherketone (PEEK) and titanium healing abutments on dental implants: a randomized pilot clinical study. BMC Oral Health. 2022 Dec 1;22(1).
22. Berglundh T, Abrahamsson I, Welander M, Lang NP, Lindhe J. Morphogenesis of the peri-implant mucosa: an experimental study in dogs. Clin Oral Implants Res [Internet]. 2007 Feb [cited 2023 Sep 2];18(1):1–8. Available from: https://pubmed.ncbi.nlm.nih.gov/17224016/
23. Tonetti MS, Imboden M, Gerber L, Lang NP. Compartmentalization of inflammatory cell phenotypes in normal gingiva and peri-implant keratinized mucosa. J Clin Periodontol [Internet]. 1995 [cited 2023 Sep 4];22(10):735–42. Available from: https://pubmed.ncbi.nlm.nih.gov/8682919/
24. Seymour GJ, Greenspan JS. The phenotypic characterization of lymphocyte subpopulations in established human periodontal disease. J Periodontal Res [Internet]. 1979 [cited 2023 Sep 10];14(1):39–46. Available from: https://pubmed.ncbi.nlm.nih.gov/153961/
25. Wang X, Li Y, Feng Y, Cheng H, Li D. Macrophage polarization in aseptic bone resorption around dental implants induced by Ti particles in a murine model. J Periodontal Res [Internet]. 2019 Aug;54(4):329–38. Available from: https://onlinelibrary.wiley.com/doi/10.1111/jre.12633
26. Berglundh T, Donati M. Aspects of adaptive host response in periodontitis. J Clin Periodontol [Internet]. 2005 [cited 2023 Sep 10];32 Suppl 6(SUPPL. 6):87–107. Available from: https://pubmed.ncbi.nlm.nih.gov/16128832/
27. Donati M, Liljenberg B, Zitzmann NU, Berglundh T. B-1a cells and plasma cells in periodontitis lesions. J Periodontal Res [Internet]. 2009 Oct [cited 2023 Sep 10];44(5):683–8. Available from: https://pubmed.ncbi.nlm.nih.gov/19453855/
28. Berglundh T, Zitzmann NU, Donati M. Are peri-implantitis lesions different from periodontitis lesions? J Clin Periodontol. 2011 Mar;38(SUPPL. 11):188–202.
29. Gualini F, Berglundh T. Immunohistochemical characteristics of inflammatory lesions at implants. J Clin Periodontol [Internet]. 2003 Jan;30(1):14–8. Available from: http://doi.wiley.com/10.1034/j.1600-051X.2003.300103.x
30. Oliveira HC, Popi AF, Bachi ALL, Nonogaki S, Lopes JD, Mariano M. B-1 cells modulate the kinetics of wound-healing process in mice. Immunobiology [Internet]. 2010 Mar [cited 2023 Sep 8];215(3):215–22. Available from: https://pubmed.ncbi.nlm.nih.gov/19457571/
31. Brancato SK, Albina JE. Wound macrophages as key regulators of repair: origin, phenotype, and function. Am J Pathol [Internet]. 2011 [cited 2023 Sep 10];178(1):19–25. Available from: https://pubmed.ncbi.nlm.nih.gov/21224038/
32. Koh TJ, DiPietro LA. Inflammation and wound healing: the role of the macrophage. Expert Rev Mol Med [Internet]. 2011 [cited 2023 Sep 10];13. Available from: https://pubmed.ncbi.nlm.nih.gov/21740602/
33. Rea M, Ricci S, Ghensi P, Lang NP, Botticelli D, Soldini C. Marginal healing using Polyetheretherketone as healing abutments: an experimental study in dogs. Clin Oral Implants Res [Internet]. 2017 Jul 1 [cited 2023 Sep 4];28(7):e46–50. Available from: https://pubmed.ncbi.nlm.nih.gov/27080305/
34. Caballé-Serrano J, Chappuis V, Monje A, Buser D, Bosshardt DD. Soft tissue response to dental implant closure caps made of either polyetheretherketone (PEEK) or titanium. Clin Oral Implants Res. 2019;30(8):808–16.
35. Koutouzis T, Richardson J, Lundgren T. Comparative Soft and Hard Tissue Responses to Titanium and Polymer Healing Abutments. Journal of Oral Implantology [Internet]. 2011 Apr 1;37(sp1):174–82. Available from: https://meridian.allenpress.com/joi/article/37/sp1/174/2391/Comparative-Soft-and-Hard-Tissue-Responses-to
36. Salvi GE, Bosshardt DD, Lang NP, Abrahamsson I, Berglundh T, Lindhe J, et al. Temporal sequence of hard and soft tissue healing around titanium dental implants. Periodontol 2000 [Internet]. 2015 Jun 1 [cited 2023 Sep 2];68(1):135–52. Available from: https://pubmed.ncbi.nlm.nih.gov/25867984/
37. Vignoletti F, De Sanctis M, Berglundh T, Abrahamsson I, Sanz M. Early healing of implants placed into fresh extraction sockets: an experimental study in the beagle dog. III: soft tissue findings. J Clin Periodontol [Internet]. 2009 Dec [cited 2023 Sep 2];36(12):1059–66. Available from: https://pubmed.ncbi.nlm.nih.gov/19929957/
38. Borie M, Lambert F, Lecloux G, Bosshardt D, Barrantes A, Haugen HJ, et al. Peri-implant soft tissue integration in humans – influence of materials: A study protocol for a randomised controlled trial and a pilot study results. Contemp Clin Trials Commun [Internet]. 2020 Sep;19:100643. Available from: https://linkinghub.elsevier.com/retrieve/pii/S2451865420301277