# Tissue Response of PEEK Healing Abutment vs Titanium Healing Abutment: A Systematic Review and Meta-Analysis

**Dr. Anushka Tripathi[1], Dr. Shanmuganathan N[2*], Dr. Madhan Kumar S[3], Dr. Parthasarathy N[4], Dr. Chathurika G[5], Dr. Prathiyun Umashankar[6]**

[1,5,6]PG Resident, Department of Prosthodontics, Sri Ramachandra Dental College and Hospital, Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai - 600116, Tamil Nadu, India.

[2*]Professor and Head, Department of Prosthodontics, Sri Ramachandra Dental College and Hospital, Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai - 600116, Tamil Nadu, India.

Email: shanmuganathan.n@sriramachandra.edu.in

[3]Professor, Department of Prosthodontics, Sri Ramachandra Dental College and Hospital, Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai - 600116, Tamil Nadu, India.

[4]Associate Professor, Department of Prosthodontics, Sri Ramachandra Dental College and Hospital, Sri Ramachandra Institute of Higher Education and Research (SRIHER), Chennai - 600116, Tamil Nadu, India.

*ABSTRACT*

**Background:** Healing abutments guide peri-implant soft tissue maturation and establish a biologic seal. Titanium is standard, but aesthetic concerns, hypersensitivity, and plaque retention have prompted use of polyetheretherketone (PEEK). This systematic review and meta-analysis compared peri-implant tissue responses to PEEK versus titanium healing abutments.

**Methods:** Four databases including PubMed/MEDLINE, Scopus, Embase, and Cochrane Central were searched from January 2000 to November 2025. Human randomized controlled trials, clinical studies and animal experiments directly comparing PEEK and titanium were included. Outcomes included histological, immunohistochemical, biochemical and clinical parameters. Risk of bias was assessed using RoB 2.0, ROBINS-I and SYRCLE. Random-effects meta-analysis was performed in Stata 17.

**Results:** Twelve studies were included (nine human trials, three animal studies). No significant differences were observed for neutrophil infiltration, CD20, CD3, pathological load, probing depth, bleeding on probing, plaque index or marginal bone loss. CD68-positive macrophage infiltration (mean difference 0.89; 95% CI 0.43–1.35; $I^2$=0%) and aMMP-8 levels (mean difference 2.18; 95% CI 0.40–3.96; $I^2$=85%) were higher around PEEK without associated clinical deterioration.

**Conclusions:** PEEK and titanium healing abutments show largely comparable peri-implant tissue responses. PEEK may provide aesthetic and plaque-related benefits, while elevated macrophage activity and matrix remodelling markers indicate a distinct biologic response of uncertain clinical significance. Long-term, high-quality RCTs are needed to determine effects on peri-implant health and implant survival.

**Keywords:** Dental implants, Dental abutments, Polyetheretherketone, Titanium, Biocompatible materials, Tissue healing, Inflammation, Peri-implantitis

**How to cite this article:** Tripathi A, Shanmuganathan N, Madhan Kumar S, Parthasarathy N, Chathurika G, Umashankar P. Tissue Response of PEEK Healing Abutment vs Titanium Healing Abutment: A Systematic Review and Meta-Analysis. Int J Drug Deliv Technol. 2026;16(19s): 799-816. DOI: 10.25258/ijddt.16.19s.94

**Source of support:** Nil.

**Conflict of interest:** None

## INTRODUCTION

Healing abutments are essential prosthetic components that guide peri-implant soft-tissue maturation and help establish a biologic seal at the implant–tissue interface. Titanium healing abutments remain the clinical gold standard because of their proven biocompatibility, favourable mechanical properties and reliable long-term outcomes [1]. Their widespread use is supported by evidence of stable soft-tissue integration and preservation of marginal bone levels which are key determinants of implant success [2]. However, aesthetic limitations, potential hypersensitivity reactions and plaque accumulation have driven interest in alternative materials [3].

Polyetheretherketone (PEEK) has emerged as a promising substitute due to its tooth-coloured appearance, low plaque affinity and favourable mechanical properties [4]. Several human studies have assessed peri-implant soft-tissue responses to PEEK compared with titanium. Milinković et al. in a split-

mouth pilot study reported a stronger inflammatory infiltrate around PEEK with increased $LCA^+$ and $CD68^+$ cells, whereas titanium elicited a milder, B-cell–predominant response [5]. In contrast, Discepoli et al. found no significant differences in inflammatory infiltrate or immune cell composition after five months with only a minor mesial trend favouring titanium [6]. Using an experimental model, Enkling et al. demonstrated no differences in clinical parameters, microbial colonization or cytokine expression concluding that both materials provided comparable peri-implant tissue stability [7].

Additional clinical trials support PEEK as a viable alternative healing abutment material. Shomurodov and Mirkhusanova observed similar marginal bone remodelling and bacterial load for customised PEEK and titanium abutments, alongside lower bleeding on probing and reduced plaque accumulation with PEEK [8]. Likewise, Liegeois et al. reported comparable performance between PEEK and titanium, while adhesive resin abutments were associated with greater inflammatory infiltration and bone remodelling [9]. Long-term prospective data further indicate that polymer-based abutments including PEEK do not compromise peri-implant soft- or hard-tissue health compared with titanium [8-10].

Overall, available evidence suggests largely comparable peri-implant healing outcomes for PEEK and titanium, although isolated findings indicate that PEEK may elicit stronger inflammatory responses in certain contexts. Therefore, the current systematic review aims to synthesise human and animal evidence comparing tissue responses in relation to PEEK and titanium healing abutments.

## MATERIALS AND METHODS

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines and was prospectively registered in the Open Science Framework (OSF) (https://osf.io/yvbxn) [11].

### Research question and eligibility (PICO)

The objective was to evaluate and compare peri-implant soft-tissue responses to polyetheretherketone (PEEK) versus titanium healing abutments in humans and animals. Eligibility criteria were defined using the PICO framework: **Population:** human clinical studies (randomized controlled trials and prospective/retrospective studies) involving dental implants restored with healing abutments and animal studies; **Intervention:** transmucosal placement of PEEK healing abutments; **Comparator:** titanium healing abutments; **Outcomes:** peri-implant tissue response including histological outcomes (inflammatory infiltrate, epithelial attachment, connective tissue organization) and clinical outcomes (bleeding on probing, probing depth, plaque index, marginal bone changes and cytokine or bacterial profiles).

### Literature search and study selection

Electronic searches were performed for studies published from January 2000 to November 2025 in PubMed/MEDLINE, Scopus, Embase and the Cochrane Central Register of Controlled Trials. Search strategies combined MeSH and free-text terms related to PEEK/polyetheretherketone, titanium, healing abutments and peri-implant tissue response. Gray literature was searched in OpenGrey, ProQuest Dissertations and Theses and ClinicalTrials.gov. Manual searches were conducted in relevant implant dentistry journals. Two independent reviewers screened titles/abstracts and assessed full texts. Disagreements were resolved by consensus with a third reviewer. Study authors were contacted for clarification or missing data when required.

### Inclusion and exclusion criteria

Inclusion criteria were: (1) human and animal studies directly comparing PEEK and titanium healing abutments; (2) randomized controlled trials, controlled clinical trials or prospective observational studies; (3) reporting clinical, radiographic, microbiological, immunohistochemical or histological outcomes; and (4) minimum follow-up of four weeks. Exclusion criteria were: case reports, case series (<5 patients), in vitro studies, narrative reviews, studies lacking a comparator group, studies with non-separable PEEK and titanium data, conference abstracts and letters to the editor.

### Data extraction, quality assessment, and analysis

Two authors independently extracted data using a standardized Excel form. Cross-verification was performed by senior reviewers. Risk of bias was assessed using RoB 2 for RCTs [12], SYRCLE for animal studies [13] and ROBINS-I for non-randomized studies [14] with disagreements resolved by discussion. Meta-analysis was performed in Stata 17 using random-effects models. Heterogeneity was evaluated using $I^2$ with sensitivity (excluding high-risk studies) and subgroup analyses (follow-up duration; conventional vs customized abutments) planned a priori if needed. Publication bias was assessed using funnel plots and Egger's regression test.

## RESULTS

### Study selection

A total of 190 articles were identified through electronic database searches with no additional records retrieved from trial registries. After removal of duplicate records (n = 32), 158 titles and abstracts were screened. Of these, 132 were excluded as they did not meet the eligibility criteria. Twenty-six full-text articles were assessed for eligibility, and 14 were excluded including nine in-vitro studies and five narrative reviews. Ultimately, 12 studies fulfilled the inclusion criteria and were incorporated into the qualitative synthesis **(Figure 1).**

The detailed database search strategies including search fields and number of articles retrieved from Medline, Scopus, Embase, Web of Science and the Cochrane Library are presented in **Supplementary Table 1.**

**Characteristics of included studies**

The twelve studies included in this review comprised nine human trials [5-9, 15-21] and three animal experiments **(Table 1 and 2).** Human studies encompassed randomized controlled trials, split-mouth randomized trials, controlled experimental models, a pilot molecular analysis and a randomized trial with an observational arm. Sample sizes ranged from five patients in molecular pilot work to over fifty implants in larger trials. Participants were generally systemically healthy adults with partially edentulous sites in the posterior maxilla or mandible, interforaminal mandible or esthetic anterior regions. Most studies required ≥2–3 mm of keratinized mucosa and excluded patients with uncontrolled systemic disease, heavy smoking or active periodontal pathology.

Interventions primarily compared polyetheretherketone (PEEK) healing abutments with titanium abutments as the reference standard. One molecular study evaluated grade 4 titanium, grade 5 titanium, zirconia and PEEK within the same patients. Follow-up varied widely: 24 hours for early molecular gene-expression assessments to 6 months for clinical trials evaluating soft-tissue stability and esthetics. Histology-based evaluations typically occurred at 8–12 weeks or 3–5 months.

Reported outcomes were multidimensional. Clinical measures included probing depth, plaque accumulation, bleeding on probing, peri-implant mucosal height, keratinized mucosa width, pink esthetic score and patient-reported pain. Radiographic marginal bone levels were assessed with standardized periapical radiographs or cone-beam computed tomography. Histological/immunohistochemical analyses evaluated inflammatory infiltrate, epithelial/subepithelial cell infiltration, collagen orientation, rete peg morphology, vascular density (CD34) and immune cell phenotypes (CD3, CD20, CD38, CD68, LCA). Microbiological profiles were quantified using qPCR or DNA–DNA hybridization. Biochemical and molecular outcomes included peri-implant sulcular fluid aMMP-8 (ELISA), cytokines (IL-1β, IL-6, IL-10, TNF-α) and wound-healing gene expression (COL-I/III/IV, MMP-1, TIMP-1, TGF-β1, FN, RAC-1, αSMA, CXCL-1) through RT-qPCR (ΔΔCt). One trial assessed microcirculation with laser Doppler flowmetry and tissue oximetry.

The three animal studies [19-21] (two canine, one miniature pig) evaluated peri-implant mucosal dimensions, marginal bone resorption, inflammatory responses and multinucleated giant cells over 4–16 weeks using non-decalcified ground sections (toluidine blue/basic fuchsin) and calibrated histomorphometry. Only direct PEEK–titanium comparisons were extracted for quantitative synthesis.

**Quality Assessment of Included Articles**

**Risk of Bias**

Eight RCTs [5-9, 10-16, 18], three animal studies [19-21] and one non randomised trial [17] were included in this systematic review. Among the eight RCTs assessed using the ROB 2.0 tool, the majority demonstrated a low risk of bias across all domains. Two studies presented some concerns due to selective reporting, but overall they were judged as having low risk **(Figure 2a).** The three animal studies evaluated using the SYRCLE tool showed a moderate risk of bias, largely related to random sequence generation and outcome measurement. While baseline characteristics, allocation concealment and outcome assessment were judged to be at low risk, uncertainties in randomization and blinding contributed to an overall unclear risk rating **(Figure 2b).** The molecular pilot study was assessed using the ROBINS-I tool. This study showed moderate risk of bias due to confounding and measurement of outcomes, while other domains including participant selection, intervention classification and handling of missing data were judged at low risk **(Figure 2c).** Overall, most of the included studies demonstrated acceptable methodological quality with the clinical studies providing stronger evidence and the animal and molecular studies contributing supportive but more limited data.

**Quantitative Assessment of Included Studies**

Eight human studies meeting the inclusion criteria were included in the quantitative synthesis. For immune cell markers, pooled analysis showed no significant difference in CD20 expression between PEEK and titanium (mean difference [MD] −0.65; 95%

CI −2.42 to 1.11) **(Figure 3a).** In contrast, CD68 expression was significantly higher around PEEK abutments (MD 0.89; 95% CI 0.43 to 1.35) with no heterogeneity ($I^2$=0%; p=0.71) **(Figure 3b).** CD3 expression did not differ significantly (MD −0.06; 95% CI −1.38 to 1.25), although heterogeneity was high ($I^2$=87%; p=0.001) **(Figure 3c).** Biochemical meta-analysis showed significantly higher aMMP-8 levels with PEEK (MD 2.18; 95% CI 0.40 to 3.96) with substantial heterogeneity ($I^2$=85%; p=0.01) **(Figure 3d).**

Histological outcomes were largely comparable. Neutrophil infiltration in connective tissue showed no significant difference between groups (MD −0.49; 95% CI −1.06 to 0.08) with no heterogeneity ($I^2$=0%; p=0.56) **(Figure 4a).** Total pathological load also did not differ significantly (MD 0.40; 95% CI −0.09 to 0.88) with low heterogeneity ($I^2$=0%; p=0.44) **(Figure 4b).** Collectively, these findings indicate similar overall inflammatory burden between materials, while suggesting greater macrophage activity and matrix remodelling around PEEK reflected by elevated CD68 and aMMP-8.

Clinical outcomes at follow-up periods of ≥2 months were likewise comparable between the groups. Plaque index showed no significant difference (MD 1.00; 95% CI −0.47 to 2.47), but with considerable heterogeneity ($I^2$=87.96%; p=0.001) **(Figure 5a).** Marginal bone loss outcomes also demonstrated no significant difference (MD 0.60; 95% CI −0.04 to 1.23) with no heterogeneity ($I^2$=0%; p=0.51) **(Figure 5b).** Probing depth did not differ significantly (MD −2.49; 95% CI −6.34 to 1.36), although heterogeneity was substantial ($I^2$=92.79%; p=0.00) **(Figure 5c).** Bleeding on probing similarly showed no significant difference (MD −0.71; 95% CI −5.52 to 4.10) with high heterogeneity ($I^2$=97.45%; p=0.00) **(Figure 5d).** Overall, clinical indices were comparable, but variability in protocols, follow-up and populations likely contributed to heterogeneity.

## DISCUSSION

Healing abutments play a fundamental role in shaping peri-implant soft tissues and maintaining the integrity of the implant–tissue interface [22]. Titanium healing abutments remain the standard of care because of well-established biocompatibility and mechanical stability. However, the increasing use of polyetheretherketone (PEEK) has raised questions regarding comparative soft-tissue responses [23]. This systematic review and meta-analysis synthesized evidence from nine human clinical studies and three animal experiments directly comparing PEEK and titanium healing abutments across clinical, histological and molecular outcomes.

Across included studies, findings were not fully consistent. Milinković et al. reported that PEEK induced a stronger inflammatory infiltrate dominated by histiocytes and plasmacytes, whereas titanium was associated with a milder B-cell–mediated response [5]. Conversely, Discepoli et al. observed no significant differences in overall inflammatory infiltrate or immune cell composition after five months with only a minor mesial trend favouring titanium [6]. Other trials including Enkling et al. and Shomurodov et al. reported broadly comparable clinical performance with PEEK showing potential advantages such as reduced bleeding on probing, lower plaque accumulation and improved microcirculation recovery [7, 8]. Liegeois et al. similarly found that PEEK performed comparably to titanium, while adhesive resin abutments triggered greater inflammatory cell infiltration and bone loss [9].

Variability likely reflects heterogeneity in study design, sample size, follow-up duration and abutment type (prefabricated vs customized) as well as differences in prioritized endpoints (molecular, histologic, clinical, radiographic). Despite these differences, the totality of evidence suggests broadly similar peri-implant tissue responses to PEEK and titanium, with PEEK offering practical advantages in aesthetics and possibly plaque control without clear compromise of peri-implant health within available follow-up.

Risk of bias assessments indicated that most randomized controlled trials [5-16, 18] were at low risk, whereas animal and molecular pilot studies [17, 19-21] showed moderate risk mainly related to confounding and limited blinding.

Quantitatively, the meta-analysis indicated no statistically significant differences between PEEK and titanium for key clinical parameters (plaque index, probing depth, bleeding on probing and marginal bone levels), although heterogeneity was substantial for several clinical indices. This likely reflects differences in protocols, follow-up intervals and patient factors such as smoking exposure, keratinized tissue dimensions and oral hygiene. Histological and immunohistochemical synthesis showed similar neutrophil infiltration, overall pathological load and adaptive immune markers (CD20 and CD3) between materials. In contrast, CD68-positive macrophage infiltration and aMMP-8 expression were higher around PEEK abutments suggesting increased innate immune activity and matrix remodelling. Importantly, these molecular differences did not translate into

clinically detectable adverse outcomes in soft-tissue inflammation or marginal bone change during the assessed timeframes.

These findings align with previous reviews of polymer-based and alternative abutment materials which generally report comparable clinical outcomes to titanium for plaque accumulation and marginal bone loss, despite occasional signals of heightened inflammatory cell presence [24, 25]. Several reviews have also highlighted potential advantages of PEEK including improved aesthetics and reduced bacterial adhesion, possibly related to surface characteristics such as lower surface free energy [26, 27]. Nonetheless, some experimental and animal evidence has raised concerns that PEEK surfaces may be associated with multinucleated giant cells or fibrous tissue interposition in certain models prompting uncertainty about long-term biological behaviour [28, 29].

Overall, available evidence indicates that PEEK healing abutments can achieve soft- and hard-tissue stability comparable to titanium in the short to medium term. The consistent observation of increased macrophage activity and aMMP-8 levels around PEEK suggests a distinct biologic response, but its clinical relevance remains uncertain. Current data support PEEK as a reasonable alternative when aesthetics and plaque resistance are prioritized, although long-term randomized evidence is required to determine whether early molecular differences influence implant survival or peri-implant health over time [30, 31].

**Recommendations for future research**

Future RCTs should standardize abutment selection and peri-implant outcomes, use blinded assessors and follow patients beyond five years. Consistent histologic/immunohistochemical/biochemical endpoints (macrophages, infiltrates, metalloproteinases) and control of patient factors (keratinized mucosa, systemic health, smoking, oral hygiene) are essential.

**Clinical implications**

PEEK healing abutments are a viable alternative to titanium when aesthetics or plaque resistance are priorities. Clinical outcomes (probing depth, bleeding on probing, plaque index, marginal bone levels) appear broadly comparable within available follow-up. Although higher CD68 infiltration and aMMP-8 expression have been reported with PEEK, these have not been associated with adverse clinical outcomes in the short to medium term. PEEK may be preferred in esthetically demanding anterior regions or in patients with suspected titanium sensitivity, provided and routine peri-implant maintenance and meticulous plaque control are maintained. Long-term monitoring remains advisable until stronger survival data are available.

**CONCLUSION**

From this systematic review and meta-analysis, it can be concluded that the available evidence suggests PEEK and titanium healing abutments produce largely comparable peri-implant tissue responses, although PEEK may induce stronger macrophage activity and matrix remodelling at the molecular level. Long-term clinical trials are required to determine whether these biological differences have consequences for implant survival and peri-implant health.

**REFERENCES**

1. Halim FC, Pesce P, De Angelis N, Benedicenti S, Menini M. Comparison of the Clinical Outcomes of Titanium and Zirconia Implant Abutments: A Systematic Review of Systematic Reviews. J Clin Med. 2022 Aug 28;11(17):5052. doi: 10.3390/jcm11175052. PMID: 36078982; PMCID: PMC9456707.
2. Alexander R, Liu X. Soft tissue integration around dental implants: A pressing priority. Biomaterials. 2026 Jan;324:123491. doi:10.1016/j.biomaterials.2025.123491.
3. Kheder W, Al Kawas S, Khalaf K, Samsudin AR. Impact of tribocorrosion and titanium particles release on dental implant complications — A narrative review. Jpn Dent Sci Rev. 2021 Nov;57:182-9. doi:10.1016/j.jdsr.2021.09.001.
4. Moharil S, Reche A, Durge K. Polyetheretherketone (PEEK) as a Biomaterial: An Overview. Cureus. 2023 Aug 29;15(8):e44307. doi: 10.7759/cureus.44307. PMID: 37779776; PMCID: PMC10536400.
5. 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 Nov 11;22(1):484. doi: 10.1186/s12903-022-02536-0. PMID: 36368972; PMCID: PMC9652880.
6. Discepoli N, Mirra R, De Rubertis I, Ricciardi R, La Francesca N, Bellan C. Histopathologic assessment of soft tissue healing around Polyetheretherketone and Titanium abutments: A randomized and controlled human study. J Osseointegr. 2025;17(1). doi:10.23805/JO.2025.702.

7. 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 Jun;33(6):667-679. doi: 10.1111/clr.13932. Epub 2022 May 2. PMID: 35467040.
8. Shomurodov K, Mirkhusanova R. Comparative evaluation of soft tissue reaction to titanium and polyetheretherketone customized healing abutments: a split-mouth randomised clinical trial. Galician Med J. 2024 Sep 10;31(4). doi:10.21802/e-GMJ2024-A23.
9. Liegeois L, Borie M, Lecloux G, Van Hede D, Lambert F. Influence of Implant Component Materials on Peri-Implant Soft Tissue Healing: A Comparative Histological and Immunohistochemical Study in Humans. Clin Oral Implants Res. 2025 Mar;36(3):397-409. doi: 10.1111/clr.14391. Epub 2024 Dec 16. PMID: 39676638.
10. French D, Ofec R, Levin L. Long term clinical performance of 10 871 dental implants with up to 22 years of follow-up: A cohort study in 4247 patients. Clin Implant Dent Relat Res. 2021 Jun;23(3):289-297. doi: 10.1111/cid.12994. Epub 2021 Mar 25. PMID: 33768695; PMCID: PMC8359846.
11. Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021 Mar 29;372:n71. doi:10.1136/bmj.n71.
12. Sterne JAC, Savović J, Page MJ, Elbers RG, Blencowe NS, Boutron I, Cates CJ, Cheng H-Y, Corbett MS, Eldridge SM, Hernán MA, Hopewell S, Hróbjartsson A, Junqueira DR, Jüni P, Kirkham JJ, Lasserson T, Li T, McAleenan A, Reeves BC, Shepperd S, Shrier I, Stewart LA, Tilling K, White IR, Whiting PF, Higgins JPT. RoB 2: a revised tool for assessing risk of bias in randomised trials. *BMJ* 2019; **366**: l4898.
13. Hooijmans CR, Rovers MM, de Vries RB, Leenaars M, Ritskes-Hoitinga M, Langendam MW. SYRCLE's risk of bias tool for animal studies. BMC Med Res Methodol. 2014 Mar 26;14:43. doi: 10.1186/1471-2288-14-43. PMID: 24667063; PMCID: PMC4230647.
14. Sterne JAC, Hernán MA, Reeves BC, Savović J, Berkman ND, Viswanathan M, Henry D, Altman DG, Ansari MT, Boutron I, Carpenter JR, Chan AW, Churchill R, Deeks JJ, Hróbjartsson A, Kirkham J, Jüni P, Loke YK, Pigott TD, Ramsay CR, Regidor D, Rothstein HR, Sandhu L, Santaguida PL, Schünemann HJ, Shea B, Shrier I, Tugwell P, Turner L, Valentine JC, Waddington H, Waters E, Wells GA, Whiting PF, Higgins JPT. ROBINS-I: a tool for assessing risk of bias in non-randomized studies of interventions. BMJ 2016; 355; i4919; doi: 10.1136/bmj.i4919.
15. Koutouzis T, Richardson J, Lundgren T. Comparative soft and hard tissue responses to titanium and polymer healing abutments. J Oral Implantol. 2011 Mar;37 Spec No:174-82. doi: 10.1563/AAID-JOI-D-09-00102.1. Epub 2010 Jun 16. PMID: 20553131.
16. Liegeois L, Borie M, Lecloux G, Van Hede D, Lambert F. Influence of Implant Component Materials on Peri-Implant Soft Tissue Healing: A Comparative Histological and Immunohistochemical Study in Humans. Clin Oral Implants Res. 2025 Mar;36(3):397-409. doi: 10.1111/clr.14391. Epub 2024 Dec 16. PMID: 39676638.
17. Borie M, Lecloux G, Bosshardt D, Barrantes A, Haugen HJ, Lambert F, Bacevic M. 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. 2020 Aug 15;19:100643. doi: 10.1016/j.conctc.2020.100643. PMID: 33083628; PMCID: PMC7554019.
18. Pilloni A, Marini L, Gagliano N, Dellavia C, Pellegrini G, Henin D, Zeza B, Rojas MA. Molecular Analysis of Peri-implant Soft Tissue Response to Different Abutment Materials in Humans: A Pilot Study. Int J Oral Maxillofac Implants. 2024 Dec 11;39(6):235-249. doi: 10.11607/jomi.10910. PMID: 38788134.
19. Maté Sánchez de Val JE, Gómez-Moreno G, Pérez-Albacete Martínez C, Ramírez-Fernández MP, Granero-Marín JM, Gehrke SA, Calvo-Guirado JL. Peri-implant tissue behavior around non-titanium material: Experimental study in dogs. Ann Anat. 2016 Jul;206:104-9. doi: 10.1016/j.aanat.2016.03.005. Epub 2016 Apr 1. PMID: 27045596.
20. 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 Aug;30(8):808-816. doi: 10.1111/clr.13487. Epub 2019 Jun 12. PMID: 31125452.
21. 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 Jul;28(7):e46-e50. doi: 10.1111/clr.12854. Epub 2016 Apr 15. PMID: 27080305.

22. Ruhstorfer M, Güth JF, Stimmelmayr M, Waltenberger L, Schubert O, Graf T. Systematic review of peri-implant conditions and aesthetic outcomes of customized versus conventional healing abutments. Int J Implant Dent. 2024 Dec 11;10(1):61. doi: 10.1186/s40729-024-00581-8. PMID: 39661263; PMCID: PMC11635071.
23. Mosharraf R, Fathi A, Rismanchian M, Ghasemi E, Givehchian P. Customized versus titanium healing abutments for preimplant tissue healing in fresh socket implants: A systematic review. Dent Res J (Isfahan). 2025 May 22;22:20. doi: 10.4103/drj.drj_479_23. PMID: 40502444; PMCID: PMC12155395.
24. Laleman I, Lambert F, Gahlert M, Bacevic M, Woelfler H, Roehling S. The effect of different abutment materials on peri-implant tissues: a systematic review and meta-analysis. Clin Oral Implants Res. 2023 Sep 26. doi:10.1111/clr.14159.
25. Lin GH, Lee E, Barootchi S, Rosen PS, Curtis D, Kan J, Wang HL. The influence of prosthetic designs on peri-implant bone loss: An AO/AAP systematic review and meta-analysis. J Periodontol. 2025 Jun;96(6):634-651. doi: 10.1002/JPER.24-0144. Epub 2025 Jun 9. PMID: 40489290; PMCID: PMC12273757.
26. Papathanasiou I, Kamposiora P, Papavasiliou G, Ferrari M. The use of PEEK in digital prosthodontics: A narrative review. BMC Oral Health. 2020 Aug 2;20(1):217. doi: 10.1186/s12903-020-01202-7. PMID: 32741366; PMCID: PMC7398079.
27. Pidhatika B, Widyaya VT, Nalam PC, Swasono YA, Ardhani R. Surface Modifications of High-Performance Polymer Polyetheretherketone (PEEK) to Improve Its Biological Performance in Dentistry. Polymers (Basel). 2022 Dec 16;14(24):5526. doi: 10.3390/polym14245526. PMID: 36559893; PMCID: PMC9787615.
28. Mishra S, Chowdhary R. PEEK materials as an alternative to titanium in dental implants: A systematic review. Clin Implant Dent Relat Res. 2019 Feb;21(1):208-222. doi: 10.1111/cid.12706. Epub 2018 Dec 27. PMID: 30589497.
29. Reinedahl D, Johansson P, Galli S, Kjellin P, Albrektsson T, Wennerberg A. Review of PEEK implants and biomechanical and immunological responses to a zirconium phosphate nano-coated PEEK, a blasted PEEK, and a turned titanium implant surface. Am J Dent. 2022;35:152-60.
30. Schwitalla A, Müller WD. PEEK dental implants: a review of the literature. J Oral Implantol. 2013 Dec;39(6):743-9. doi: 10.1563/AAID-JOI-D-11-00002. Epub 2011 Sep 9. PMID: 21905892.
31. Reddy KUK, Seth A, Vuppuluri A, Verma PC, Narala SKR, Babu PJ, Saravanan P. Exploring the bio-mechanical behavior of PEEK and CFR-PEEK materials for dental implant applications using finite element analysis. J Prosthodont Res. 2025 Jan 10;69(1):41-48. doi: 10.2186/jpr.JPR_D_23_00296. Epub 2024 May 22. PMID: 38777753.

**Table 1: Characteristics of included studies**

| Author and Year | Study design | Sample size | Patient demographics and | Implant site characteristics | Type, design and surface features of healing abutments |
|---|---|---|---|---|---|
| Discepoli N, et al. 2025 [6] | Randomized controlled clinical trial; | 22 implants (11 PEEK, 11 titanium) | Systemically healthy adults, mean age 65.5 ± 1.8 years, 50% female; patients with partial posterior maxillary edentulism | CBCT confirmed available bone volume; ≥2 mm keratinized mucosa; no active periodontal disease; posterior maxilla as implant site. | Titanium abutments (control) vs PEEK abutments (test); 4 mm healing abutments connected with 15 Ncm torque; transmucosal healing; **surface details:** standard machined titanium vs medical-grade PEEK |
| Shomurodov K, et al. 2024 [8] | Split-mouth randomized | 20 patients; 52 implants (27 | Mean age 48.4 ± 7.5 years (range | Bilateral edentulous sites in posterior maxilla and mandible; sufficient | Customized healing abutments (CHAs) designed |

| | | | | | |
|---|---|---|---|---|---|
| | controlled clinical trial | Ti CHAs, 25 PEEK CHAs) | 36–62); 12 males, 8 females; 2 light smokers (<10 cigarettes/day); all systemically healthy | bone height; ≥2 mm keratinized mucosa | with ExoCAD and milled: grade 5 Titanium (SIC invent AG, Switzerland) vs medical-grade PEEK (JUVORA Ltd., UK); polished and sterilized before placement |
| Milinković I, et al. 2022 [5] | Randomized pilot clinical study, split-mouth design | 11 patients; 22 implants placed; 20 implants analyzed (1 patient excluded) | Mean age 49 years; 27% female, 73% male; predominantly non-smokers (64%); systemically healthy | Partial edentulism in posterior maxilla/mandible; ≥2 mm keratinized mucosa; no active periodontal disease | PEEK healing abutments (test) vs Titanium healing abutments (control); C-TECH implants, 3.8–4.3 mm diameter; healing abutments 4.3 mm wide, different heights (2–4 mm), transmucosal; both connected at 10 Ncm torque. |
| Enkling N, et al. 2022 [7] | Controlled prospective randomized experimental human study (split-mouth design) | 20 edentulous patients; 40 experimental abutments placed (10 per material group: Titanium, Zirconia, Feldspar-veneered Zirconia, PEEK) | Mean age 64.6 ± 10.1 years; 12 females, 8 males; healthy; | Edentulous anterior mandible (interforaminal region); sufficient bone without grafting; exclusion: smoking >10 cigarettes/day, osteoporosis, systemic diseases affecting bone metabolism | Custom-designed hollow-cylinder experimental one-piece abutments; 4 materials tested: Titanium (grade 5), Zirconia, Zirconia veneered with Feldspar ceramic, PEEK (PEEK CLASSIX®); lateral windows (2.3 mm) allowed mucosal ingrowth; mounted on SICace® titanium implants |
| Koutouzis T, et al. 2011 [15] | Prospective randomized controlled clinical trial | 16 patients; 22 implants (11 titanium, 11 polymer/PEEK) | Mean age: Test 59.1 ± 12.6 yrs, Control 54.2 ± 13.6 yrs; 6M/2F in test group, 4M/4F in control; non-smokers; | Posterior to canines in maxilla or mandible; adequate bone volume (≥4.1 mm diameter, ≥8 mm length implants) | Straumann Bone Level Implants (4.1–4.8 mm diameter, 8–12 mm length); Healing abutments: Titanium RC Healing Abutment (conical, D 4.5 |

| | | | | | |
|---|---|---|---|---|---|
| | | | systemically healthy. | | mm, H 6 mm) vs Polymer RC Healing Abutment (customizable, D 7 mm, PEEK) |
| Liegeois L, et al. 2024 [9] | Randomized controlled comparative clinical study | 37 implants placed; 35 soft tissue samples analyzed (11 Ti, 13 Resin, 11 PEEK) | Adults ≥18 years; systemically healthy (ASA I/II); | posterior maxilla or mandible; ≥3 mm keratinized mucosa; non-smokers or light smokers (<10 cig/day); excluded: uncontrolled diabetes, autoimmune disease, bisphosphonate/denosumab use, pregnancy, immunocompromise | Custom experimental abutments designed with large platform for standardized soft tissue harvesting; manufactured in Grade 5 titanium, resin (Optibond FL), and medical-grade PEEK; torque applied at 15 Ncm; non-submerged healing |
| Borie M, et al. 2020 [16] | Multi-part randomized controlled clinical trial | **Planned:** 180 patients (30 per RCT × 6 RCTs); **Pilot:** 9 patients, 10 implants (titanium only) | Mean age 58.8 years (range 35–77); 5 males, 4 females; non-smokers | sites mainly in premolar/molar region; bone quality mostly type 2–3; implant diameter 4.1 mm, length ≥8 mm | Experimental CAD/CAM custom abutments (Ti, PEEK, PMMA, Zi, Co–Cr, LD, PICN); in pilot: titanium grade 4 only; designed for punch biopsy retrieval; fixed at 10 Ncm in non-submerged approach |
| Pilloni A, et al. 2024 [17] | Pilot prospective human study | 5 patients; 20 implants (4 different abutment materials per patient) | Adults undergoing implant therapy; systemically healthy | peri-implant soft tissue biopsies collected; implant sites not detailed beyond adequate tissue for biopsies | Experimental healing abutments made of Grade 4 titanium, Grade 5 titanium, zirconia, and polyetheretherketone (PEEK); custom-made; transmucosal; standardized design for biopsy harvesting |
| Chokaree P, et al. 2024 [18] | Randomized controlled trial (parallel-group) with additional | 22 patients total: 12 randomized (6 prefabricated, 6 customized), 10 | Adults ≥18 yrs; mean age ≈ 58.5 yrs; 9 females, 13 males; mostly non-smokers | single-tooth extraction sites with intact buccal walls; anterior, premolar, and posterior regions of maxilla/mandible | Group 1: Prefabricated titanium healing abutments (cylindrical, 5–6.5 mm diameter). |

| | | | | | |
|---|---|---|---|---|---|
| | prospective observational arm | observational customized (posterior) | | | Group 2: Customized PEEK healing abutments (CAD/CAM based on CEJ cross-section, concave transmucosal profile, emergence angle 20–30°, ~4 mm tall). |
| Maté-Sánchez de Val JE, et al. 2016 [19] | Animal experimental study (dog model) | 6 dogs; 48 implants (24 reinforced PEEK abutments, 24 titanium abutments) | Healthy male American Foxhounds (~1 year, 14–15 kg) | bilateral mandibular premolars and first molars extracted; implants (3.5 mm × 10 mm, Bredent Blue Sky) placed in fresh extraction sockets | Test: reinforced PEEK abutments (SKY elegance, Bredent). Control: titanium abutments. Both connected immediately post-extraction with platform switching. Torque: 30 Ncm. |
| Caballé-Serrano J, et al. 2019 [20] | Preclinical animal experimental study (miniature pigs, split-mouth design) | 7 Goettinger miniature pigs; 42 implants placed (Ti, Zr, Zr+Al) with Ti or PEEK closure caps | Healthy pigs, ~25 months old, ~50 kg | maxillary anterior region; implants: cpTi grade 4, Y-TZP zirconia, ATZ (zirconia + alumina); standardized placement and submerged healing | Titanium closure caps (screwed, machined cpTi) vs PEEK closure caps (PEEK-classix™, Invibio; press-fit, untreated surface) |
| Rea M. et al. 2016 [21] | Preclinical animal experimental study (dog model) | 6 Labrador dogs; 24 implants (4 types of healing abutments per animal) | Healthy, ~4 years old, 25–26 kg | bilateral extraction of mandibular premolars and first molars followed by implant placement after 4 months of healing | (i) Titanium (Ti). (ii) PEEK bonded to a titanium base (Ti-P). (iii) Pure PEEK (P). (iv) Roughened PEEK (P-R, burr-treated). Implants: 10 mm × 4 mm (CLC Conic, CLC Scientific, Italy). |

**Table 2: Primary and second variables assessed in the included studies**

| Author and Year | Follow-up duration | Outcomes measured | Quantification method for tissue response | Important findings | Inference |
|---|---|---|---|---|---|
| | | | | | |

| | | | | | |
|---|---|---|---|---|---|
| Discepoli N, et al. 2025 [6] | 5 months | **Clinical indices:** Plaque score, bleeding on probing, probing depth. **Histology:** Inflammatory cell infiltrate, dystrophic calcifications, site of inflammation. **Immunohistochemistry:** CD3+ T cells, CD20+ B cells, CD38+ plasma cells, CD68+ macrophages. | Histology with Hematoxylin & Eosin staining, semi-quantitative scoring of infiltrate intensity (0–3) and extent (localized vs diffuse). Immunohistochemistry for CD20, CD3, CD38, CD68 with % distribution of cell sub-populations and localization (epithelial, subepithelial, perivascular). | No statistically significant differences in inflammation between PEEK and titanium. Dystrophic calcifications slightly higher in PEEK group (p=0.26). Titanium showed trend toward less marked infiltrate, especially mesially (26.66% vs. 6.75%, p=0.02). - CD3+ T cells were predominant immune cells in both groups. | Both groups showed similar peri-implant soft tissue healing. PEEK did not cause significantly increased inflammatory reaction compared to titanium. Long-term studies are needed to confirm PEEK suitability. |
| Shomurodov K, et al. 2024 [8] | 3 weeks after CHA placement | **Clinical indices** (bleeding on probing, probing depth, plaque index)**; radiographic bone resorption** (CBCT); **peri-implant crevicular fluid biomarkers** (IL-1β, IL-6, IL-10, TNF-α, aMMP-8)**; microbiological profile** (7 periodontal pathogens via qPCR); **microcirculation and oxygenation** (laser Doppler flowmetry, optical tissue oximetry, wavelet analysis) | Clinical indices measured with periodontal probe; plaque index scoring system. CBCT for marginal bone resorption. ELISA for cytokines and aMMP-8. qPCR for bacterial detection. Laser Doppler flowmetry (blood flow, vasomotor activity); optical tissue oximetry (oxygen saturation, consumption). | No significant differences in bone resorption, cytokines, or bacterial load between groups. PEEK showed lower bleeding on probing (10.24% vs 12.42%, p=0.012), lower probing depth (2.28 mm vs 2.63 mm, p=0.004), and lower plaque index (1.20 vs 1.52, p=0.001). PEEK demonstrated faster recovery of microcirculation and oxygenation (faster relief of ischemia/hypoxia) . aMMP-8 was significantly higher in PEEK group (0.50 ng/ml vs 0.39 ng/ml, p=0.001) but | Both Ti and PEEK CHAs supported healthy peri-implant tissue response. PEEK showed better short-term outcomes in plaque control, bleeding, and microcirculation, without clinically adverse inflammatory response. PEEK can be considered a promising alternative to titanium for CHAs. |

| | | | | | |
|---|---|---|---|---|---|
| | | | | remained within normal limits. | |
| Milinković I, et al. 2022 [5] | 3 months | **Clinical indices:** probing depth (PD), clinical attachment level (CAL), bleeding on probing (BOP), plaque index (PI). **Histology:** presence and intensity of inflammatory infiltrate (epithelial, subepithelial). **Immunohistochemistry:** LCA+, CD3+, CD20+, CD68+ cell counts. | **Histology:** HE staining, qualitative (yes/no) and semi-quantitative scoring of infiltrate intensity (light/medium/intense). **Immunohistochemistry** with avidin-biotin-peroxidase complex; antibodies: LCA, CD3, CD20, CD68; 50 cells counted per antibody (200 per sample), analyzed in ImageJ. | Epithelial infiltrate observed in 100% of PEEK vs 20% of Ti sites (p=0.004). Subepithelial infiltrate: intensive in 100% of PEEK vs light/medium in Ti (p=0.046). Higher LCA+ and CD68+ cells in PEEK (p=0.001, p=0.020). Higher CD20+ and CD3+ cells in Ti (p=0.006, p=0.010). Clinically, BOP and PI were slightly but significantly higher in PEEK, though not clinically relevant (<15%). | PEEK induced a more pronounced inflammatory response dominated by histiocytes and plasmacytes, while titanium induced a milder response dominated by B-cells. Despite histologic differences, clinical tissues were free of relevant inflammation. Findings suggest cautious interpretation due to small sample size. |
| Enkling N, et al. 2022 [7] | 3 months | **Clinical:** Bleeding on probing (BoP), probing depth (PD), plaque index (PI), visible inflammation. **Histology:** Mononuclear and neutrophil cell counts, collagen fiber quality, rete peg quality. **Microbiology:** 6 periodontal pathogens in peri-implant sulcular fluid. **Molecular:** Cytokine (IL-1β, IL-6, IL-8, IL-10) mRNA expression. **Biochemical:** aMMP-8 levels in | **Histology:** toluidine blue staining of non-separated resin-embedded specimens; quantitative cell counts (mononuclear and neutrophils per 0.056 mm² at 50× magnification); semi-quantitative grading of collagen fibers and rete pegs (scale 1–3). **mRNA expression by qPCR** (ΔΔCt method normalized to GAPDH). aMMP-8 measured | No significant differences among groups for BoP, PD, PI, bone level changes, neutrophil counts, collagen fibers, or rete pegs. Feldspar abutments had significantly fewer mononuclear inflammatory cells vs titanium (p=0.032). PEEK abutments exhibited slightly higher aMMP-8 levels and weaker | All tested abutments, including PEEK, elicited acceptable soft tissue responses after 3 months of healing. No adverse inflammation or bone loss was associated with PEEK. Differences were minor and not clinically significant. |

| | | | | | |
|---|---|---|---|---|---|
| | | PISF.<br>**Radiographic:** Marginal bone level change. | by ELISA.<br><br>**Microbiological load assessed** by DNA–DNA hybridization (checkerboard).<br>**Radiographs** calibrated and analyzed by blinded examiners. | collagen fibers, but not statistically significant.<br><br>No differences in cytokine expression or bacterial load.<br><br>Some abutments failed (fracture/deformation) during healing or retrieval, mainly PEEK and feldspar, due to thin-walled design. | Short-term findings suggest PEEK and feldspar are promising alternatives, but long-term data are required. |
| Koutouzis T, et al. 2011 [15] | 3 months | **Clinical:** Plaque index, Bleeding on probing (BoP), Probing depth (PD), Peri-implant mucosa height (PMH), Keratinized mucosa width.<br>**Radiographic:** Marginal bone level changes. | Clinical measurements with calibrated periodontal probe (Hu-Friedy PCP 15).<br>Standardized periapical radiographs analyzed using digital image processing (ImageJ, NIH).<br>Bone level measured as distance from abutment-fixture junction to bone contact. | At 2 weeks: PEEK had less plaque (20.5% vs 40.9%) and more sites with PD ≤ 3 mm (87.9% vs 47%) than titanium ($p<0.05$).<br>No significant differences at 3 months in plaque, BoP, PD, PMH, or keratinized mucosa width.<br>Marginal bone level change minimal and similar between groups (PEEK −0.02 ± 0.2 mm vs Titanium −0.25 ± 0.4 mm). | Both PEEK and titanium healing abutments demonstrated comparable short-term peri-implant soft and hard tissue responses.<br>PEEK did not increase risk of marginal bone loss or soft tissue recession in the first 3 months. |
| Liegeois L, et al. 2024 [9] | 8 weeks | **Clinical:** plaque index, keratinized tissue height, soft tissue thickness.<br>**Radiographic:** peri-implant bone loss (mesial/distal).<br>**Histology:** plasmocytes, PMNs, lymphocytes, macrophages.<br>**Immunohistochemistry:** CD3+, CD20+, | H&E staining for plasmocytes/PMNs.<br>Immunohistochemistry with antibodies (CD3, CD20, CD68, CD34).<br>Semi-quantitative scoring (0–3 scale).<br>CD34-stained slides digitized and analyzed with ImageJ for blood vessel density/area. | Resin abutments showed significantly more macrophages (CD68+) in connective tissue ($p=0.04$) and higher neutrophils in epithelium ($p=0.03$).<br><br>Resin group had greater peri- | PEEK and titanium abutments demonstrated similar and favorable peri-implant tissue responses after 8 weeks, while resin induced stronger |

| | | | | | |
|---|---|---|---|---|---|
| | | CD68+, CD34+ (blood vessels). **SEM:** plaque accumulation on abutments. | SEM scoring of plaque accumulation (0–4 scale). | implant bone loss (0.82 ± 0.10 mm) compared to Ti (0.07 ± 0.18 mm) and PEEK (0.27 ± 0.30 mm, p=0.04).<br><br>No significant differences between Ti and PEEK in soft tissue inflammation, bone loss, or plaque accumulation.<br><br>Blood vessel density and epithelial T/B cells were comparable across all groups. | inflammatory infiltrates and higher bone loss. Resin should be used cautiously for transmucosal applications, whereas PEEK appears comparable to titanium in short-term host response. |
| Borie M, et al. 2020 [16] | 8 weeks | **Clinical:** keratinized tissue height, soft tissue thickness, plaque index, adverse events. **Histology:** sulcus depth, epithelial attachment, connective tissue attachment. **Immunohistochemistry:** CD3, CD20, CD68, CD34 (planned). **SEM:** cell adhesion, plaque, fibers. **TEM:** connective tissue-implant interface (planned). | Non-decalcified histology with toluidine blue-fuchsin; histometric measurements with Zeiss ZEN pro software.<br><br>SEM for surface morphology & residual cells.<br><br>IHC for inflammatory/vascular markers (semi-quantitative scoring).<br><br>TEM planned for PEEK samples. | Pilot with titanium: well-defined epithelial and connective tissue barrier; sulcus depth mean 0.61 mm, epithelial attachment 2.68 mm, connective tissue 1.06 mm.<br><br>SEM showed epithelial and connective cells on abutment surfaces; plaque/calculus mainly coronal.<br><br>IHC: strong Langerhans cells in epithelium, mild–moderate inflammatory infiltrate in connective tissue.<br><br>Protocol validated for future material comparisons. | Custom abutment design and biopsy method feasible and reproducible in humans. Titanium showed stable early soft tissue integration at 8 weeks. The protocol will allow robust future comparisons across abutment materials (including PEEK). |

| | | | | | |
|---|---|---|---|---|---|
| Pilloni A, et al. 2024 [17] | 24 hours | **Molecular:** gene expression of COL-I, COL-III, MMP-1, TIMP-1, TGF-β1, FN, ITGA4, ITGA5, ITGB1, RAC-1, COL-IV, αSMA, IL-6, CXCL-1 | Real-time quantitative PCR (RT-qPCR) of peri-implant soft tissue biopsies (compared to baseline gingival control samples) | COL-I significantly downregulated in Grade 4 Ti and Zr vs control.<br><br>MMP-1 and TIMP-1 increased in all groups, lowest in Grade 4 Ti.<br><br>FN, RAC-1, COL-IV, and αSMA downregulated, especially in Grade 4 Ti.<br><br>IL-6 and CXCL-1 lowest in Grade 4 Ti, suggesting reduced inflammation.<br><br>PEEK showed higher inflammatory and matrix remodeling gene expression than Grade 4 Ti and Zr. | Grade 4 Ti and zirconia induced the most favourable early molecular response, with lower expression of inflammatory and fibrotic genes. PEEK and Grade 5 Ti were associated with less favourable molecular profiles at 24 hours. |
| Chokaree P, et al. 2024 [18] | 6 months | **Clinical:** Horizontal and vertical soft tissue alterations (mean buccal change, papilla height, midfacial height).<br>**Volumetric:** Buccal and total volume variation.<br>**Radiographic:** Marginal bone change (mesial and distal).<br>**Esthetic:** Pink aesthetic score (PES).<br>**Patient-centered:** Pain score (NRS). | Digital intraoral scans at baseline, 1, 4, and 6 months; STL superimposition (Geomagic Control X, Materialise Magics).<br><br>Linear & volumetric changes calculated in mm/% with 3D colour maps.<br><br>Radiographic bone level measured on standardized periapical radiographs with PACS software. | Both groups showed soft tissue dimensional changes, but customized abutments had better trends.<br><br>At 6 months: Customized group showed less reduction in papilla height (PHv −0.73 mm vs −1.18 mm in prefabricated), and less PES reduction (−0.33 vs −2.75; p=0.022). | Customized PEEK healing abutments preserved peri-implant papillae and soft tissue contours better, improved esthetics, and reduced patient discomfort compared to prefabricated titanium abutments. Hard tissue outcomes were similar. |

| | | | | | |
|---|---|---|---|---|---|
| | | | PES (0–14) evaluated by calibrated examiner.<br><br>Pain recorded on NRS (0–10) at prosthesis insertion, 2 h, and 24 | Buccal volume loss smaller in customized group at 1 and 4 months ($p<0.05$), but not significant at 6 months.<br><br>Pain significantly lower in customized group at insertion (0.6 vs 3.4; $p=0.003$).<br><br>Marginal bone changes minimal and not significantly different between groups. | Customized abutments are advantageous for immediate implants, especially in esthetic regions. |
| Maté-Sánchez de Val JE, et al. 2016 [19] | 8 weeks | - Clinical healing outcomes.<br>- Implant stability (ISQ values).<br>- Histology: soft tissue seal, collagen fiber orientation, inflammatory cell distribution.<br>- Histomorphometry: bone-to-implant contact (BIC), peri-implant mucosa dimensions (PM-Bc, PM-Lc, PM-buccal-IS, PM-lingual-IS, IS-Bc, IS-Lc).<br>- Radiographic bone levels. | - Histology: toluidine blue staining of ground sections.<br>- Histomorphometry with calibrated digital imaging (Leica, MIP software).<br>- Radiographs analyzed using ImageJ.<br>- ISQ measured by Osstell Mentor. | - Both groups achieved stable osseointegration with no implant loss.<br>- No significant differences in BIC between groups.<br>- Reinforced PEEK abutments showed significantly greater soft tissue stability: higher PM-Lc (3.71 ± 0.18 mm vs 2.91 ± 0.03 mm, $p=0.012$) and PM-lingual-IS (3.57 ± 0.38 mm vs 2.65 ± 0.43 mm, $p=0.015$).<br>- Titanium showed more buccal bone loss compared to PEEK.<br>- ISQ values similar between groups. | Reinforced PEEK abutments demonstrated comparable osseointegration to titanium and superior preservation of peri-implant soft tissue dimensions and lingual bone levels. PEEK appears to be a biocompatible and effective alternative to titanium abutments in experimental models. |
| Caballé-Serrano J, et al. 2019 [20] | 4 and 8 weeks | - **Histology:** presence of multinucleated giant cells (MNGCs).<br>- | - Ground sections (80 µm) stained with toluidine blue/basic fuchsin. | - Healing uneventful, no inflammatory infiltrates | PEEK closure caps triggered a significantly stronger |

| | | | | | |
|---|---|---|---|---|---|
| | | **Histomorphometry:** MNGC count (small: 2–5 nuclei; large: >5 nuclei) per surface unit.<br>**- Compartmental analysis:** external (soft tissue vs bone contact), internal (cap surface vs implant surface). | - Light microscopy with calibrated measurements of MNGC counts normalized to surface length.<br>- Nonparametric repeated-measures ANOVA and Wilcoxon tests for group comparisons. | observed.<br>- MNGCs found on both Ti and PEEK caps, but significantly more MNGCs on PEEK surfaces in soft tissue (p=0.0008–0.0016), bone region (p=0.016–0.003), and internal compartment (p=0.014–0.0088).<br>- Ti showed direct bone contact, while PEEK consistently had an interposed fibrous layer.<br>- PEEK caps occasionally showed misfit due to press-fit design. | multinucleated giant cell response than Ti, though without overt inflammation. Findings suggest possible foreign body-type reaction to PEEK, highlighting the need for cautious use and long-term validation before routine clinical application. |
| Rea M. et al. 2016 [21] | 4 months | **- Histology:** marginal soft tissue dimensions (PM-IS, PM-B, PM-JE, JE-B), bone crest resorption (IS-C, IS-B), junctional epithelium extension.<br>**-** Clinical healing observations. | - Histometric analysis of buccolingual ground sections stained with toluidine blue.<br>- Measurements taken with Nikon Eclipse Ci microscope and digital image software. | - Buccal bone resorption significantly greater at Ti-P (1.0 ± 0.3 mm) vs Ti (0.3 ± 0.4 mm, $p<0.05$).<br>- No significant differences between pure PEEK and roughened PEEK.<br>- Dimensions of peri-implant mucosa and location of soft tissues relative to implant shoulder were similar across all groups.<br>- Junctional epithelium did not extend apically beyond the implant shoulder in any group. | PEEK (pure or roughened) showed comparable soft tissue integration to titanium. Ti-PEEK hybrid abutments exhibited more buccal bone resorption, but overall peri-implant mucosal dimensions were preserved. PEEK can be considered a potential alternative abutment material, though hybrid Ti-PEEK |

| | | | | | |
|---|---|---|---|---|---|
| | | | | | designs may pose risks. |

**Figure 1: PRISMA flow diagram**