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自体富血小板纤维蛋白应用于根尖周炎磨牙即刻种植1例报告及文献复习

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[摘 要] **目的**：将自体富血小板纤维蛋白（PRF）单独应用于根尖周炎磨牙即刻种植，观察其临床疗效并探讨其作用机制，以拓宽其临床应用并为其临床实践提供指导。**方法**：收集1例将PRF单独应用于根尖周炎磨牙即刻种植患者的临床资料，采用锥形束CT（CBCT）和口腔扫描数据三维重建的方法对种植体周围组织改变量进行评估，并结合相关文献分析PRF的治疗方法和治疗效果。**结果**：采用微创拔除患者46患牙行即刻种植的治疗方法。术前取患者自体血液30 mL（3管），将血液置于不含抗凝剂的10 mL玻璃涂层塑料管中，采用3 000 r·min^{-1}离心10 min的方法制备3枚PRF，并将其作为唯一材料充填跳跃间隙。治疗后采用CBCT和口腔扫描三维重建对比分析，术后6个月时，种植体周围骨组织增加203.19 mm^3，颊侧骨高度增加5.83 mm，且颊侧骨组织增加量大于1 mm；术后12个月时，种植体周软硬组织基本保持稳定。**结论**：将自体PRF单独应用于根尖周炎磨牙即刻种植，获得了良好的治疗效果，种植体周骨组织再生且种植体周软硬组织基本保持稳定。

[关键词] 富血小板纤维蛋白；即刻种植；根尖周炎；骨再生
[中图分类号] R781.341 [文献标志码] B

Application of autologous platelet-rich fibrin in immediate implant placement of molar with periapical periodontitis: A case report and literature review

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ABSTRACT **Objective**: To observe the clinical efficacy of autologous platelet-rich fibrin (PRF) application alone in immediate dental implant placement in the molars with periapical periodontitis, and to discuss the mechanism, in order to widen its clinical application and to provide the guidance for its clinical practice. **Methods**: The clinical data of one patient who underwent immediate implant placement in the molars with periapical periodontitis using PRF as the sole material were collected. The changes in the tissues surrounding the implant were evaluated through the three-dimensional reconstruction of cone-beam CT (CBCT) and oral scan data, the therapeutic methods and outcomes of PRF treatment were analyzed combined with the relevant literatures. **Results**: A minimally invasive extraction of the patient's 46 diseased molar was conducted followed by the immediate implant placement. Before surgery, 30 mL of the patient's own blood (3 tubes) was drawn, which was then placed in 10 mL glass-coated plastic tubes

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without anticoagulants. Three PRF were prepared with the blood by centrifuging at 3 000 r·min^{-1} for 10 min. These clots were used as the only filling material for the jumping gap. The postoperative CBCT and oral scan 3D reconstruction results showed that the peri-implant bone tissue was increased by 203.19 mm^3, the buccal bone height was increased by 5.83 mm, and the buccal bone tissue was increased by more than 1 mm at 6 months postoperatively; after 12 months, the soft and hard tissues around the implant remained essentially stable. **Conclusion**: The application of autologous PRF alone in immediate implant placement in the molars with periapical periodontitis achieves favorable treatment outcomes, the peri-implant bone tissue regenerates, and the peri-implant hard and soft tissues remain stable, which providing the new insights into the immediate implant treatment.

KEYWORDS Platelet-rich fibrin; Immediate implant placement; Periapical periodontitis; Bone regeneration

即刻种植可维持牙槽骨的高度和宽度，有利于获得良好的牙龈美学形态，同时可缩短患者的治疗周期，提升患者满意度[1]，现已成为牙齿缺失的有效治疗手段。根尖周炎作为口腔常见病之一，拔除根尖周炎患牙后行即刻种植治疗，拔牙窝中残留的细菌可能影响种植体骨结合，甚至引发种植体周围炎[2-4]。然而，仍有研究[5-8]显示：患牙拔除并彻底清创后行即刻种植，种植体存活率较高，种植体周软硬组织稳定，可获得理想的临床疗效。富血小板纤维蛋白（platelet-rich fibrin，PRF）作为一种自体来源的生物活性材料，已广泛应用于口腔种植领域，临床上常将其与骨替代材料联合应用于拔牙位点保存[9]、引导性骨组织再生术[10]和上颌窦底提升术[11]。本课题组前期研究[12]表明：PRF作为唯一的骨替代材料应用于内窥镜辅助的上颌窦底内提升术可获得良好的临床疗效，提升骨高度平均为6.72 mm。将PRF作为唯一的骨替代材料应用于炎症环境下的小范围骨缺损，亦可获得良好的临床疗效。与既往报道的常用跳跃间隙填充材料，如骨填充材料和脱矿牙本质基质[13]等比较，PRF在促进局部骨缺损修复的同时，可降低骨替代材料导致的术后感染风险，PRF集成骨、抗炎和抑菌作用于一体，具有无免疫排斥反应、制备方法简单且成本低廉等优点。本研究将PRF应用于1例根尖周炎磨牙即刻种植的患者，探讨其临床疗效及作用机制，以拓宽其临床应用并为其临床实践提供指导。

1 临床资料

1.1 一般资料

患者，女性，23岁，主诉“牙冠折裂，牙齿松动”，于2022年2月就诊于本院种植中心，患者全身状态良好，有根管治疗史，否认系统性疾病史和遗传病史。

1.2 专科检查

口内检查：患者38牙位近中阻生；46牙位咬合面可见牙冠折裂，冠折及龈下4 mm，Ⅲ°松动。口腔卫生条件良好。影像学检查：术前锥形束CT（cone beam CT，CBCT）（$CBCT_0$）显示：24和25牙位可见根管充填物；38牙位近中阻生；46牙位冠折，颊侧可见骨缺损，根尖周可见直径约为2 mm的卵圆形透射影。46牙位处牙槽骨宽度为12.7 mm，牙槽嵴顶到下颌神经管的距离为19.6 mm。见图1。

1.3 诊 断

①46牙位冠折；②46牙位慢性根尖周炎；③38牙位近中阻生；④24和25牙位牙体缺损。

1.4 治疗计划

经本院修复科会诊后，建议拔除46患牙行即刻种植治疗。

1.5 治疗过程

与患者沟通治疗方案和相关费用，签署知情同意书。术前嘱患者使用0.12%氯己定漱口水漱口，每次含漱3 min，共3次。术前取患者自体静脉血液30 mL（3管），将血液置于不含抗凝剂的10 mL玻璃涂层塑料管中，3 000 r·min^{-1}下离心10 min（医用离心机，型号：TR-18Plus，江苏创英医疗器械有限公司），在脱细胞血浆与红细胞之间形成的纤维蛋白凝胶（PRF凝胶）中含有大量血小板和白细胞[14]。用镊子将凝胶从管中取出，用无菌剪刀去除附着的红细胞。将PRF凝胶置于医用纱布上，缓慢压缩成PRF膜。

消毒，铺巾，必兰麻醉起效后，微创拔除46患牙，搔刮牙槽窝，生理盐水冲洗，彻底去净残留的肉芽组织和炎性物质。逐级备洞后植入ITI

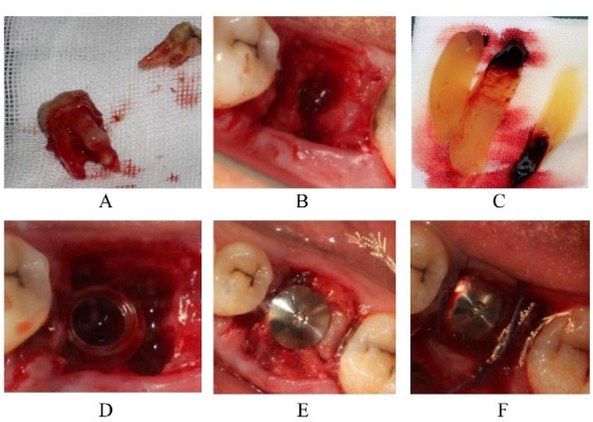
A B C D E

A：Preoperative intraoral photograph；B—D：Preoperative CBCT imaging findings；E：Measurement of available bone height and bone width.

图1 根尖周炎磨牙即刻种植患者术前口内照片和CBCT影像表现

Fig. 1 Preoperative intraoral photographs and CBCT images of one patient with immediate implant placement of molar with periapical periodontitis

Straumman SLActive 4.8 mm ×12.0 mm种植体1枚。3枚PRF压缩成膜后植入跳跃间隙中，缝合创口（图2）。术后即刻CBCT（$CBCT_1$）显示种植体三维位置良好，种植体颊侧颈部可见明显骨缺损（图3）。



A B C D E F

A：Minimally invasive extraction of affected teeth；B：Complete debridement；C：Three pieces of PRF were prepared；D：Implant placement；E：PRF implantation；F：Suture of wound.

图2 根尖周炎患牙即刻种植手术过程

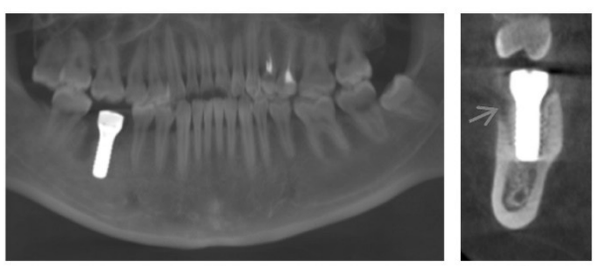
Fig. 2 Immediate implant procedure for teeth with periapical periodontitis

术后6个月复诊时拍摄CBCT（$CBCT_2$），$CBCT_2$显示种植体周有新骨形成，种植体颊侧骨板完整（图4）。共振频率分析显示种植体稳定系数平均为72，种植体骨结合良好。数字化口腔扫描制备模型（图5）。2周后行冠修复治疗（图6）。

术后12个月复诊，CBCT（$CBCT_3$）显示种植体周骨结合良好，颊侧骨板完整，牙冠近远中邻接良好（图7）。

1.6 治疗结果

1.6.1 46牙位种植体周围骨体积改变（peri-implant bone volume changes，BV） 将不同时期的CBCT（$CBCT_1$和$CBCT_2$）导入到骨组织三维重建软件Mimics Research 21.0中进行三维重建并将三维图像成功拟合，如图8和9所示。布尔运算计算结果显示：术后6个月种植体周骨体积增加

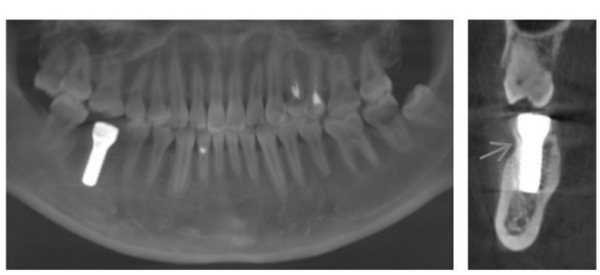


A B

A：Mesial and distal direction；B：Buccal and lingual direction. Arrow indicated a significant bone defect observed at buccal implant neck.

图3 根尖周炎患者术后即刻CBCT影像表现

Fig. 3 Postoperative immediate CBCT images of one patient with periapical periodontitis

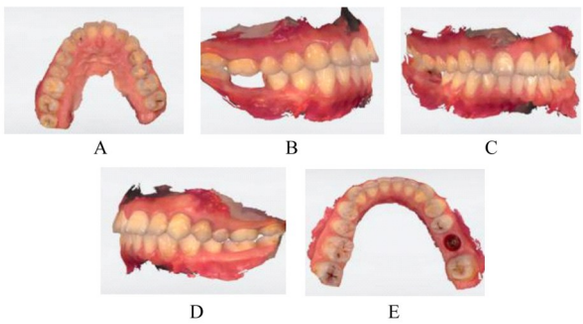


A B

A：Mesial and distal direction；B：Buccal and lingual direction，arrow indicated new bone formation on buccal side of implant with an intact bone plate on buccal side.

图4 根尖周炎患者术后6个月CBCT影像表现

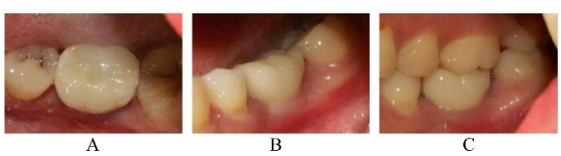
Fig. 4 CBCT images of one patient with periapical periodontitis 6 months after surgery



A：Upper jaw；B－D：Occlusion；E：Lower jaw.

图5 数字化口腔扫描法制取印模

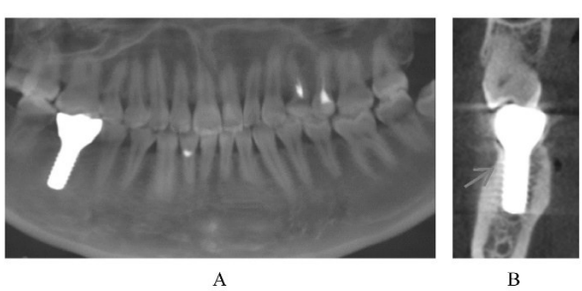
Fig. 5 Impressions obtained by digital oral scanning



A：View of occlusal surface；B：Buccal view；C：Occlusion.

图6 根尖周炎患者冠修复治疗

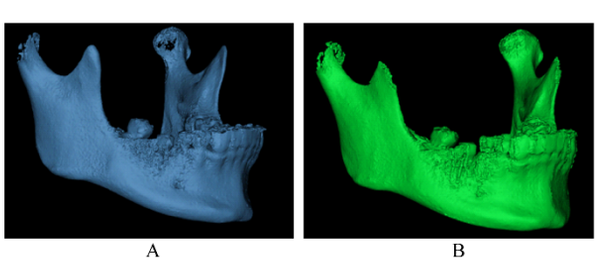
Fig. 6 Crown restoration therapy of one patient with periapical periodontitis



A：Mesial and distal directions；B：Buccal and lingual direction. Arrow indicated mesial-distal proximity.

图7 根尖周炎患者术后12个月CBCT影像表现

Fig. 7 CBCT images of one patient with periapical periodontitis 12 months after sugery

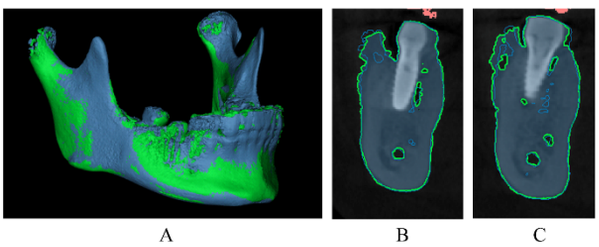


A：$CBCT_1$ three-dimensional reconstruction image；B：$CBCT_2$ three-dimensional reconstruction image.

图8 根尖周炎患者的$CBCT_1$和$CBCT_2$三维重建图像

Fig. 8 Three-dimensional reconstruction images of $CBCT_1$ and $CBCT_2$ of one patient with periapical periodentitis

203.19 mm^3。



A：Three-dimensional image of one patient suffering from periapical periodontitis with successful CBCT1 and CBCT2 fitting；B－C：Cross-sectional images after successful CBCT1 and CBCT2 fitting from buccal to lingual direction.

图9 根尖周炎患者的$CBCT_1$与$CBCT_2$拟合成功的三维图像及截面图像

Fig. 9 3D images and cross-sectional images of successfully fitted $CBCT_1$ and $CBCT_2$ of one patient with periapical periodontitis

1.6.2 46牙位种植体颊侧骨厚度(bone thickness on buccal side，BT）将不同时期CBCT（$CBCT_1$、$CBCT_2$和$CBCT_3$）导入至CS 3D Imaging软件中，分别测量种植体平台处和种植体平台下方2、4、6和8 mm处的BT。将术后即刻、术后6个月和术后12个月颊侧骨组织厚度分别记为BT_1、BT_2及BT_3。相对于术后即刻，术后6个月和术后12个月BT改变量分别记为$BT_{2\text{-}1}$及$BT_{3\text{-}1}$。相对于术后即刻，在术后6个月$CBCT_2$显示种植体颊侧骨缺损已修复，在种植体平台处和平台下方2、4、6及8 mm处骨板厚度增加量分别为1.33、1.10、1.27、1.53和1.13 mm。术后12个月颊侧骨组织约增厚1 mm，未见明显骨吸收。BT及其改变量见表1。BT的测量方法见图10。

1.6.3 46牙位种植体颊舌侧骨高度(height of bucco and lingual bone，BH）将不同时期CBCT（$CBCT_1$、$CBCT_2$和$CBCT_3$）导入至CS 3D Imaging软件中，分别测量种植体平台到颊舌侧骨板最高点的垂直距离，即为BH。将术后即刻、术后6个月和术后12个月骨组织高度分别记为BH_1、BH_2及BH_3。相对于术后即刻，术后6个月和术后12个月骨高度改变量分别记为$BH_{2\text{-}1}$及$BH_{3\text{-}1}$。术后6个月BH增加量为5.83 mm，舌侧骨高度增加较少，为0.24 mm；术后12个月舌侧骨组织发生少量吸收，为0.17 mm。BH及其BH改变量见表2。BH的测量方法见图10。

表1 46牙位种植体术后即刻、术后6个月和术后12个月BT及BT改变量

Tab. 1 BT and BT changes of 46 tooth position implatation immediately after surgery, 6 months after surgery, and 12 months after surgery (*l*/mm)

BT/Height	BT_1	BT_2	BT_3	BT_{2-1}	BT_{3-1}
0 mm	0	1.33	0.87	1.33	0.87
2 mm	0	1.10	0.73	1.10	1.10
4 mm	0.83	2.10	1.80	1.27	0.97
6 mm	1.43	2.97	2.93	1.53	1.50
8 mm	2.00	3.13	3.57	1.13	1.57

BT_1: Bone thickness on buccal side at immediate postoperative period; BT_2: Bone thickness on buccal side at 6 months postoperative period; BT_3: Bone thickness on buccal side at 12 months postoperative period; BT_{2-1}: Amount of change in bone thickness on buccal side at 6 months postoperative period relative to immediate postoperative period; BT_{3-1}: Amount of change in the bone thickness on buccal side at 12 months postoperative period relative to immediate postoperative period.

表2 46牙位种植体术后即刻、术后6个月和术后12个月BH及BH改变量

Tab. 2 BH and BH changes of 46 tooth position implatation immediately after surgery, 6 months after surgery, and 12 months after surgery (*l*/mm)

BH/Position	BH_1	BH_2	BH_3	BH_{2-1}	BH_{3-1}
Buccal	−3.53	2.30	1.90	5.83	5.43
Lingual	1.83	2.07	1.67	0.24	−0.17

BH_1: Height of buccal and lingual bone at immediate postoperative period; BH_2: Height of buccal and lingual bone at 6 months postoperative period; BH_3: Height of buccal and lingual bone at 12 months postoperative period; BT_{2-1}: Amount of change in height of buccal and lingual bone at 6 months postoperative period relative to immediate postoperative period; BT_{3-1}: Amount of change in height of buccal and lingual bone at 12 months postoperative period relative to immediate postoperative period.

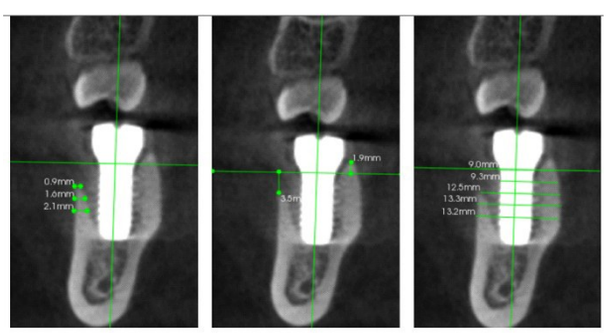
1.6.4 46牙位种植体牙槽骨宽度（width of alveolar socket，BW）将不同时期CBCT（$CBCT_1$、$CBCT_2$和$CBCT_3$）导入至CS 3D Imaging软件中，分别测量种植体平台处和种植体平台下方2、4、6及8 mm处的BW。将术后即刻、术后6个月和术后12个月BW分别记为BW_1、BW_2及BW_3。相对于术后即刻，术后6个月和术后12个月BW改变量分别记为BW_{2-1}及BW_{3-1}。术后6个月，种植体平台下方4、6和8 mm处均出现骨吸收，分别为0.40、0.53和0.01 mm；术后12个月，种植体平台下方4、6和8 mm的骨吸收量进一步增加，分别为0.67、0.57和0.14 mm。BW及其BW改变量见表3。BW的测量方法见图10。

表3 46牙位种植体术后即刻、术后6个月和术后12个月BW及BW改变量

Tab. 3 BW and BW changes of 46 tooth position implatation immediately after surgery, 6 months and 12 months after surgery (*l*/mm)

BW/Height	BW_1	BW_2	BW_3	BW_{2-1}	BW_{3-1}
0 mm	8.97	9.43	9.40	0.46	0.43
2 mm	9.23	9.80	9.90	0.57	0.67
4 mm	12.53	12.13	11.86	−0.40	−0.67
6 mm	13.10	12.57	12.53	−0.53	−0.57
8 mm	12.97	12.87	12.83	−0.01	−0.14

BW_1: Width of alveolar socket at immediate postoperative period; BW_2: Width of alveolar socket at 6 months postoperative period; BW_3: Width of alveolar socket at 12 months postoperative period; BW_{2-1}: Amount of change in width of alveolar socket at 6 months postoperative period relative to immediate postoperative period; BW_{3-1}: Amount of change in width of alveolar socket at 12 months postoperative period relative to immediate postoperative period.



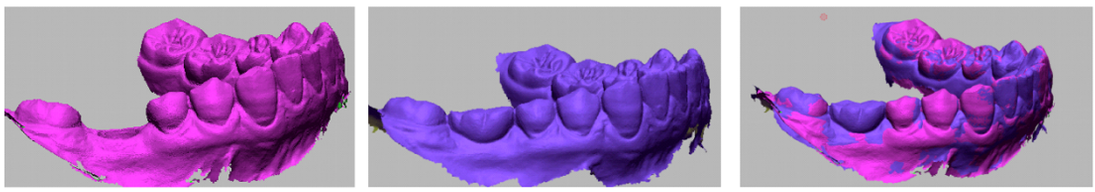
A B C

A: Measurement of bone thickness on buccal side; B: Measurement of height of buccal and lingual bone; C: Measurement of width of alveolar socket.

图10 BT、BH和BW的测量方法示意图

Fig. 10 Schematic diagrams of measurement methods of BT, BH, and BW

1.6.5 46牙位种植体周围软组织稳定性 将术后6个月（修复前）和术后12个月（修复后6个月）所获得的数字化口腔扫描数据导入至Geomagic Design X软件中拟合后进行偏差分析，观察其软组织改变。偏差分析结果显示：种植体周软组织基本保持稳定。见图11。其中，绿色区偏差值在（0±0.5）mm范围内，软组织变化量较少。黄色和红



A B C

A：Oral scan image 6 months after surgery；B：Oral scan image 12 months after surgery；C：A successful fit image.

图 11 根尖周炎患者术后6和12个月数字化口腔扫描图像及拟合图像

Fig. 11 Digital oral scan images and fitted images of one patient with periapical periodontitis 6 and 12 months after surgery

色部分偏差值大于0.5 mm，小于0.8 mm，软组织变化量较大，见图12。

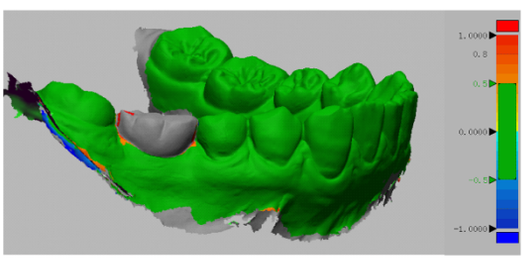


图 12 根尖周炎患者数字化口腔扫描数据拟合后偏差分析图

Fig. 12 Deviation analysis diagram after fitting digital oral scan data of one patient with periapical periodontitis

2 讨 论

在即刻种植的临床实践中，常采用骨替代材料填充种植体与牙槽窝之间的跳跃间隙。骨替代材料作为骨组织形成的支架，在促进种植体周骨组织形成的同时减少了牙槽窝垂直向骨吸收[15]。然而，骨替代材料本身仍存在以下局限性：①骨替代材料缺乏活细胞和生物成分，骨传导性能良好而骨诱导能力欠佳；②骨替代材料缺乏抑菌性成分，术后感染风险较高；③骨替代材料仍存在术后吸收较多及免疫排斥反应等不足。因此，寻找一种具有骨诱导和骨传导性能，并兼备抗炎和抗菌作用的生物材料至关重要。

PRF作为组织再生的生物支架和生长因子库，已广泛应用于骨缺损的修复。富血小板纤维蛋白基质（platelet-rich fibrin matrix，PRFM）释放的血管内皮生长因子（vascular endothelial growth factor，VEGF）可通过细胞外调节蛋白激酶途径（extracellular signal-regulated kinase，ERK）参与内皮细胞有丝分裂反应，改善创面血管生成[16]；同时，PRF可激活转化生长因子β（transforming growth factor-β，TGF-β）信号通路，升高人骨形态发生蛋白2（human bone morphogenetic protein-2，BMP-2）的表达水平，并通过上调成骨分化标志物（Ⅰ型胶原、骨钙素和碱性磷酸酶等）的表达，提高成骨细胞的初始生存能力，促进骨髓间充质干细胞和成骨细胞的增殖、迁移及分化，促进新骨形成[17-20]。此外，PRF可通过增加产生骨保护素（osteoprotegerin，OPG）细胞的数量诱导OPG的表达，提高OPG/RANKL比值进而促进早期成骨细胞分化[21]；PRF在促进白细胞介素6（interleukin-6，IL-6）和肿瘤坏死因子α（tumor necrosis factor-α，TNF-α）表达，发挥免疫调节成骨作用，同时可上调跨膜降钙素受体的表达，抑制破骨细胞的活性[17，22]。因此，PRF在骨增量方面有极大的应用潜力。

本研究将PRF单独应用于根尖周炎磨牙即刻种植，术后6个月$CBCT_2$示种植体颊侧颈部骨缺损已被修复。同时，经三维建模测量分析可得术后6个月种植体周围骨体积增加量为203.19 mm^3，种植体颊侧骨高度明显增加，为5.83 mm，且种植体颊侧骨厚度增加量＞1 mm。术后12个月种植体颈部平台下方4、6和8 mm处的骨吸收量分别为0.67、0.57及0.14 mm，基本接近ELBRASHY等[23]的研究，该研究采用异种骨替代材料充填跳跃间隙，术后6个月牙槽窝平均吸收量为0.59 mm。因此，将PRF单独用于磨牙即刻种植骨增量获得了良好的骨增量效果且术后12个月种植体周骨组织基本保持稳定。

根尖周炎作为口腔常见疾病之一，其优势菌与种植体周围炎优势菌群具有一定程度的相似性。研究[24]表明：根尖周炎患牙拔除后，牙槽窝中残留的细菌，可进一步诱导炎症和骨吸收，增加种

植体失败的风险。故根尖周炎患牙即刻种植的关键是彻底清除拔牙窝中的炎性肉芽组织和感染物，尽量降低术后感染风险。PRF纤维蛋白支架中含有白细胞、血小板和抗菌肽，可抑制细菌增殖并减轻局部炎症反应。研究[25-27]表明：PRF分泌物释放的过氧化氢和抗菌肽，能够抑制牙龈卟啉单胞菌中主要毒力因子——银杏蛋白酶的活性进而抑制残留细菌的生长，增强局部免疫力。同时，PRF中由血小板释放的阳离子多肽CXCL4可与疏水细菌细胞膜结合，使细菌细胞膜穿孔而发生渗透性死亡。PRF可抑制树突状细胞和M1型巨噬细胞激活，促进M2型巨噬细胞极化[28-30]，并降低脂多糖诱导的巨噬细胞中白细胞介素1β（interleukin-1β，IL-1β）、白细胞介素18（interleukin-18，IL-18）和炎症小体的表达，减少由脂多糖激活的RAW 264.7细胞中活性氧自由基（reactive oxide species，ROS）释放，抑制巨噬细胞焦亡进而发挥抗炎作用[31]。因此，本研究采用PRF作为跳跃间隙唯一的填充材料，治疗期间无感染或种植体周围炎发生，且患者术后6个月随访时种植体周围骨结合良好。

种植体周软组织对于保证种植体的长期稳定性和美学效果具有重要作用。当种植体周软组织退缩时，菌斑易堆积，易引起种植体周围黏膜炎或种植体周围炎[32]。本研究将患者术后6个月和术后12个月数字化口腔扫描数据拟合后进行偏差分析，结果显示：大部分种植体周软组织改变量在（0±0.5）mm的范围内，仅有少量软组织改变量在（0.5～0.8）mm，种植体周软组织基本保持稳定。

综上所述，将PRF单独应用于根尖周炎磨牙即刻种植取得了良好的临床疗效，术后6个月CBCT示种植体周骨组织再生且术后12个月种植体周围软硬组织基本保持稳定，为即刻种植治疗提供了新的选择。然而，在本病例中，种植体平台0 mm及平台下方2 mm处颊侧骨组织厚度均＜2 mm，因此种植体颊侧颈部骨组织的稳定性需进一步随访评估。此外，PRF的临床应用仍有一定的局限性，其力学性能较差且降解时间较短，因此PRF常单独应用于小范围的骨缺损，对于较大范围的骨缺损，本文作者建议将PRF与骨替代材料联合应用[18，33]。同时，在组织工程研究中，需进一步优化PRF纤维蛋白支架并延长其降解时间，延缓生长因子的释放，以进一步拓宽其临床应用。

利益冲突声明：

所有作者声明不存在利益冲突。

作者贡献声明：

贾克文负责实验方法设计、调查研究、实验数据分析、实验结果可视化和论文初稿撰写，朱悦萌和陈思宇负责论文的审阅与修订，李明慧、游佳倩和陈升负责软件开发及程序设计及实验结果的可视化，周延民负责研究概念生成、研究资源采集、实验设计验证与核实、研究课题监管及论文审阅与修订。

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