Specific Comments To Authors:

I strongly recommend publication of the article and suggest running a future clinical trial. It has been demonstrated that around the peri-apical lesions in patients treated with bisphosphonates a layer of bone necrosis similar to MRONJ can be created, for which the use of PRF is particularly recommended. It would be interesting to cite this article: Miranda M, Gianfreda F, Raffone C, Antonacci D, Pistilli V, Bollero P. The Role of Platelet-Rich Fibrin (PRF) in the Prevention of Medication-Related Osteonecrosis of the Jaw (MRONJ). Biomed Res Int. 2021 May 13;2021:4948139. doi: 10.1155/2021/4948139. PMID: 34095295; PMCID: PMC8140838. Minor spell check are necessary.

Specific Comments To Authors:

The article is in line with its purpose and explained both the operation and the related subject in detail. I have no additional suggestions.

Answering:

Dear Editor,

Thank you for the opportunity to revise this manuscript. We have amended the manuscript according to the reviewer comments. All changes to the manuscript have been highlighted in yellow below.

We have also amended the figures and their legends and attached as supplementary file with the images in powerpoint.

Conflict of interest and copyright license have been added and the Audio core tip provided.

Generally, the advantages of PRF membranes are their low expense and low risk of body rejection and infection.[40] Not to mention that the use of PRF is recommended in the patients treated with bisphosphonates with periapical lesions to improve bone repair and prevent osteonecrosis.[41] The PRF membrane was used to cover the bony defect in several case reports.[17,18] In accordance with the present case report series, they found that PRF promoted accelerated bone healing evident after 6 months. [15] However, in many of these reports, the through-and-through defect was excluded.[17,18] Moreover, this study incorporated CBCT to evaluate bone healing after using PRF in periapical surgery. The CBCT proved to be superior to

periapical radiographs in sensitivity and specificity.[42,43] The evidence of bone healing was seen in all cases at four months post- surgery, thus reducing the period needed to evaluate the short-term success of surgical endodontic treatment. The CBCT imaging was better than the periapical radiograph in identifying the volumetric changes in the size of the lesion after periapical surgery.[44] Moreover, postsurgical cases that were identified as uncertain or incompletely healed in periapical radiographs can be classified in CBCT imaging.[44] Especially in the third case, the CBCT was better at detecting bone healing after periapical surgery compared to the periapical radiograph.

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Figure 1: Bone regeneration using A-PRF membrane in through-and-through bony defects following periapical endodontic surgery on the maxillary right second premolar: (a) The CBCT shows localized radiolucency surrounding the apex of maxillary right second premolar. The lesion is perforating the labial cortical bone and displaced sinus periosteum upward which is a typical feature of periapical osteoperiostitis. The root canal treatment appears to be overextended with a uniform density; (b) The CBCT shows bony healing of the resected area within four months; (c) A clinical photo of the resected root; (d) A clinical photo of the MTA retro-filling; (e) The PRF membrane handled using a tweezer and placed to seal the bony defect.

Figure 2: Periapical endodontic surgery on the maxillary left second premolar using A-PRF membrane (a) The CBCT shows localized radiolucency surrounding the apex of the maxillary left second premolar in the sagittal section. There is a thin layer of the labial bone surrounding the apex and a displaced sinus periosteum upward which is a typical feature of periapical osteoperiostitis in the sagittal section. The root canal treatment appears to be adequate with a uniform density; (b) The CBCT shows bony healing of the resected area within four months and a normal appearance of the maxillary sinus; (c) A clinical photo of the labial bone before root resection; (d) A clinical photo of the bony defect after resection shows a hollow space adjacent to the maxillary sinus; (e) The PRF membrane is used to seal the bony defect.

Figure 3: Periapical endodontic surgery on the maxillary right lateral incisor A-PRF membrane: (a) The CBCT shows a well-defined radiolucency surrounding the apex of the maxillary right lateral anterior in the sagittal section. The lesion appears to be perforating the labial and palatal bone surrounding the apex in the coronal section. The root canal appears to be adequate and uniform in density; (b) The CBCT shows the bone formation and healing surrounding the apex and bony defect within four months post-operatively in the coronal and sagittal section; (c) A clinical photo shows the resected surface of the root and the bony defect; (d) The placement of bone graft mixed with the blood clot; (e) The PRF membrane is used to seal the defect and hold the bone graft in place.