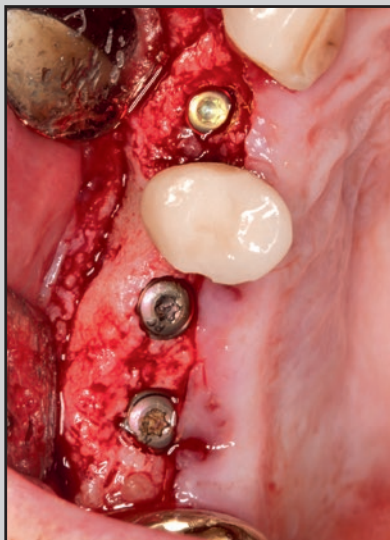
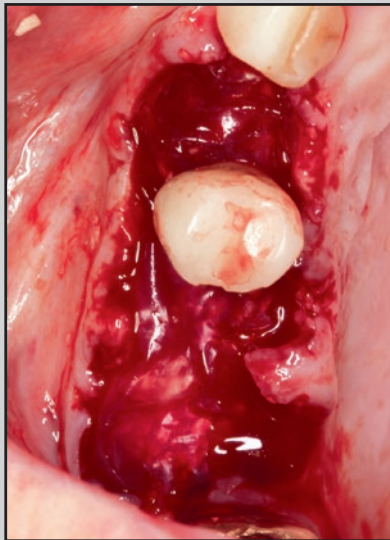
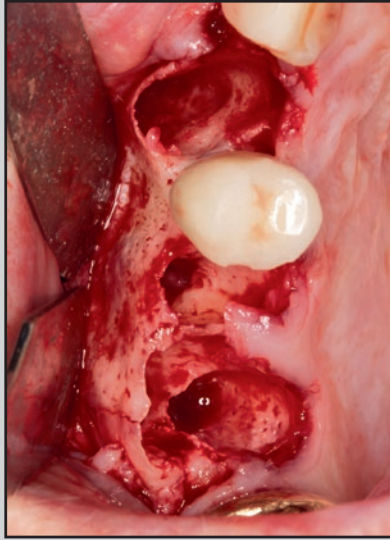




The Use of a Dehydrated, Deepithelialized Amnion-Chorion Membrane in Guided Bone Regeneration Involving Staged Implant Placement: Case Series with a 5-Year Follow-up



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Barrier membranes are critical to the success of guided bone regeneration (GBR). Though not directly involved in bone regeneration, barrier membranes hold bone graft materials at the surgical site during the slow process of bone regeneration and prevent the infiltration of fibrotic gingival tissues that would compromise new bone formation. Many options are available on the market, but membranes derived from placental tissues are gaining rapid adoption due to their unique biologic and handling properties. In this case series, a dehydrated human deepithelialized amnion-chorion membrane (ddACM) was used in combination with freeze-dried bone allograft (FDBA) for two-stage GBR procedures. Data from 1-year and 5-year follow-up appointments are presented, as well as predictable indications for the use of ddACM. Using ddACM with FDBA for GBR cases led to predictable bone regeneration with osseointegrated implants at 5-year postoperative visits. Int J Periodontics Restorative Dent 2021;41:657–662. doi: 10.11607/prd.5602

A variety of barrier membranes are available on the market for guided bone regeneration (GBR), providing clinicians with a plethora of options from which to choose. Ultimately, each case will have specific considerations and require the clinician to devise a patient-centered treatment plan that maximizes positive surgical outcomes while minimizing the potential for treatment failure, patient discomfort, and financial burden. For most cases, clinicians require membrane products that are: effective occlusive barriers to block undesired cellular invasion (ie, gingival and bacterial), easy to handle to facilitate application and reduce chair time, resorbable to obviate the need for removal at a later date, and nonimmunogenic to prevent foreign body responses that will inflame the site and inhibit wound healing.

Barrier membranes derived from placental tissues possess all of these functional characteristics and are gaining rapid adoption due to their unique biologic properties,^{1–3} prompting the present authors to investigate the utility of a dehydrated, deepithelialized amnion-chorion membrane (ddACM) in GBR cases aimed at augmenting dentoalveolar ridge volumes at the time of, or in advance of, implant placement. Derived from the amniotic sac, ddACM has intact basement membranes that are natural occlusive

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barriers found in a variety of tissue throughout the body.⁴ Because the membrane is uniquely flexible and compatible with all periodontal tissue types, it is easy to place over contoured graft materials and can be tucked into tight spaces without needing to trim the membrane before placement. Additionally, ddACM has been shown to contain a variety of active growth factors and cytokines that play critical roles in wound healing and tissue regeneration as well as antimicrobial factors that inhibit bacterial growth.⁵⁻⁷

The following case reports highlight the use of the ddACM (Bio-Xclude, Snoasis Medical), describing its use in two-stage indications.

Case 1

The patient in Case 1 was an 82-year-old woman with an American Society of Anesthesiologists (ASA) II classification, taking calcium channel blockers for cardiovascular issues including hypertension. The patient's previous dental history included a high decay rate with implant placement to replace hopelessly involved teeth. At the time of the procedure, her chief concern was the maxillary right posterior sextant, which presented with significant recurrent decay around teeth 13, 15, and 16 (FDI tooth-numbering system). Due to a poor crown-to-root ratio and inadequate ferrule, the teeth were condemned, leaving strategic extraction and implant placement as the treatment of choice.

Standard surgical protocol was observed, and the patient was anes-

thetized using three carpules of lidocaine 2% (1:100,000 epinephrine). Full-thickness flap elevation was performed, allowing for atraumatic removal of the teeth. The extraction sockets were thoroughly debrided of soft tissue remnants and rinsed with sterile saline (Fig 1a). It was decided at the time of the extraction that a staged approach would be used for implant placement due to the significant amount bone destruction and periapical pathology. Approximately 1.0 cc of mineralized freeze-dried bone allograft (FDBA) was hydrated for 30 minutes, and excess moisture was removed using a 2 × 2 cotton sponge. The FDBA was packed into the extraction sites and covered with a 10 × 20-mm dry ddACM membrane (Figs 1b and 1c). Primary closure was not attempted due to the large extraction sites, as the buccal flap would need to be significantly released and advanced (Fig 1d). The area was rinsed with sterile water (chlorhexidine gluconate is contraindicated because of the inherent biologic properties of the membrane) and allowed to heal by secondary intention to maintain the buccal attached keratinized tissue (Fig 1e).

The sites were reopened approximately 4 months after the initial surgery, revealing complete regeneration (Fig 1f). Regular-connection Bone Level implants (Straumann) were placed at sites 15 and 16 with a narrow-connection Bone Level implant (Straumann) placed at site 13 (Fig 1g). Healing was uneventful, and the implants were restored without incident (Fig 1h). The 5-year postoperative radiographs show bone maintenance (Fig 2).

Case 2

The patient in Case 2 was a 67-year-old man with an ASA II classification who was a non-insulin-dependent diabetic. His chief concern was tooth 24, which had advanced periodontal disease and Class III mobility patterns. The treatment plan included removing the tooth and replacing it with an implant.

The maxillary left posterior sextant was anesthetized with lidocaine 2%, and the tooth was extracted with forceps. Full-thickness buccal and palatal flap elevation from sites 23 to 25 was necessary to expose the horizontal and vertical bony defects (Fig 3a). Immediate implant placement was not possible, as the site required significant augmentation, leaving little chance for a restoratively driven placement or predictability.

The area was thoroughly debrided of soft tissue remnants using a combination of spoons and curettes, followed by irrigation with sterile saline and chlorhexidine gluconate 0.12%. Mineralized FDBA (0.5 cc) was hydrated with sterile saline for 30 minutes prior to tooth removal and was carefully placed in the osseous defect. The site was covered with a ddACM membrane and sutured with 4-0 mild chromic gut sutures (Fig 3b). Primary closure was not achieved; however, healing was uneventful.

The graft was left undisturbed for 4 months before reentry. Full-thickness flap elevation revealed complete healing of the horizontal and vertical defects, enabling a restoratively driven implant placement

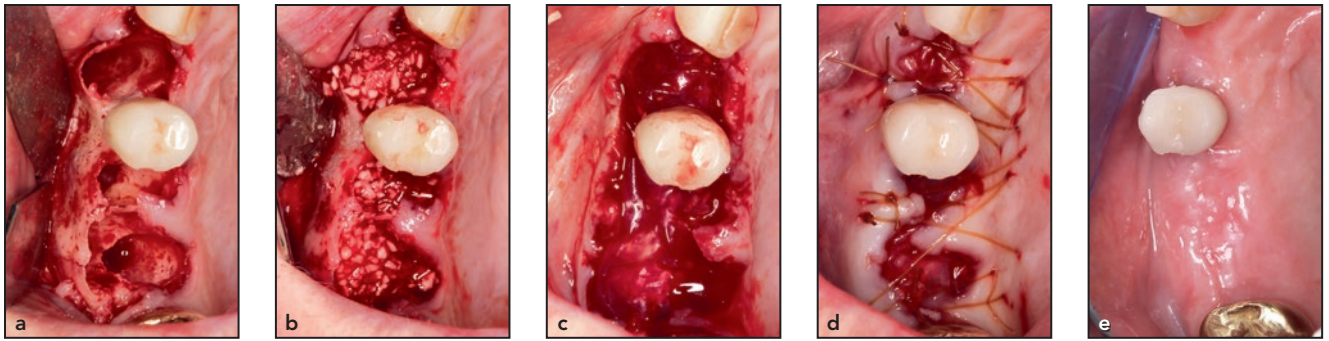
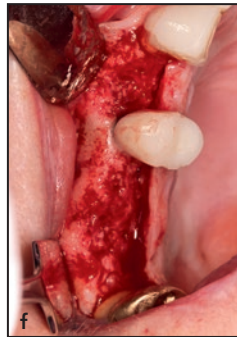


Fig 1 (a) Full-thickness flap reflection, extraction of hopelessly involved teeth, and careful debridement of any soft tissue remnants. (b) Mineralized FDBA was placed in extraction sockets. (c) ddACM was placed to cover the allograft and ridge defects. (d) Sites were closed with 4-0 mild chromic gut sutures using a



combination of interrupted and horizontal mattress techniques. Note the healing by secondary intention. (e) Soft tissue healing. Note complete soft tissue closure. (f) Full-thickness flap elevation revealed regeneration of the defects, enabling predictable implant placement. (g) Placement of regular-connection Bone Level implants in positions 15 and 16. Placement of a narrow-connection Bone Level implant in position 13. (h) Buccal view of the final restoration after 4 months.

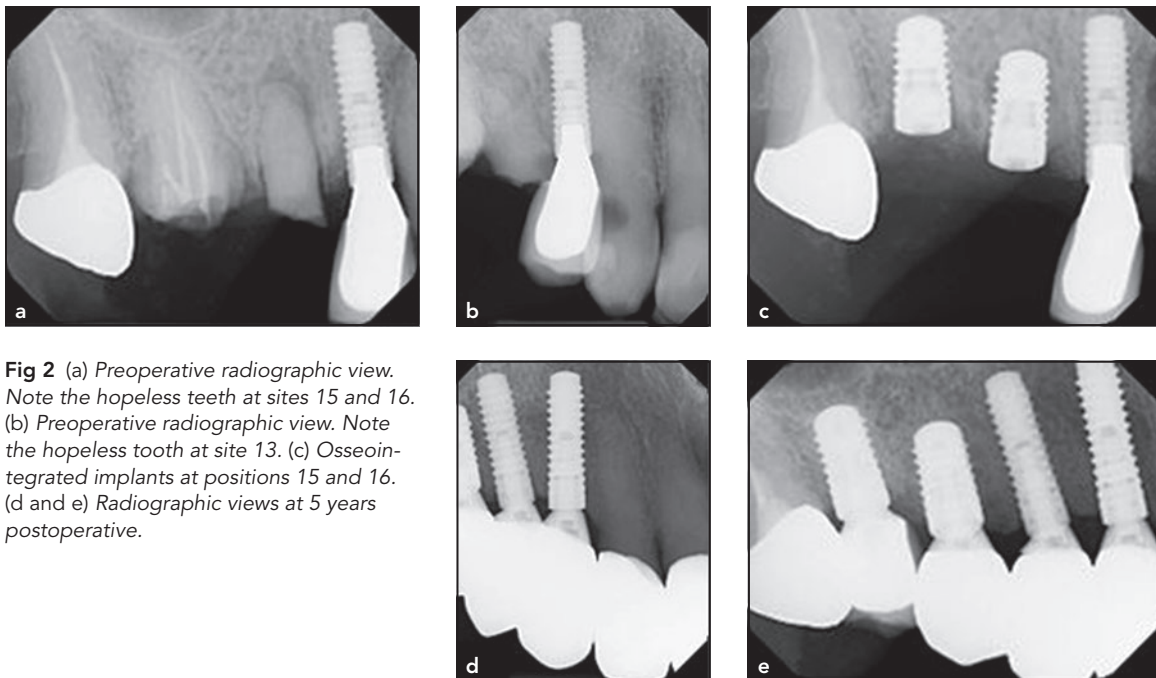


Fig 2 (a) Preoperative radiographic view. Note the hopeless teeth at sites 15 and 16. (b) Preoperative radiographic view. Note the hopeless tooth at site 13. (c) Osseointegrated implants at positions 15 and 16. (d and e) Radiographic views at 5 years postoperative.

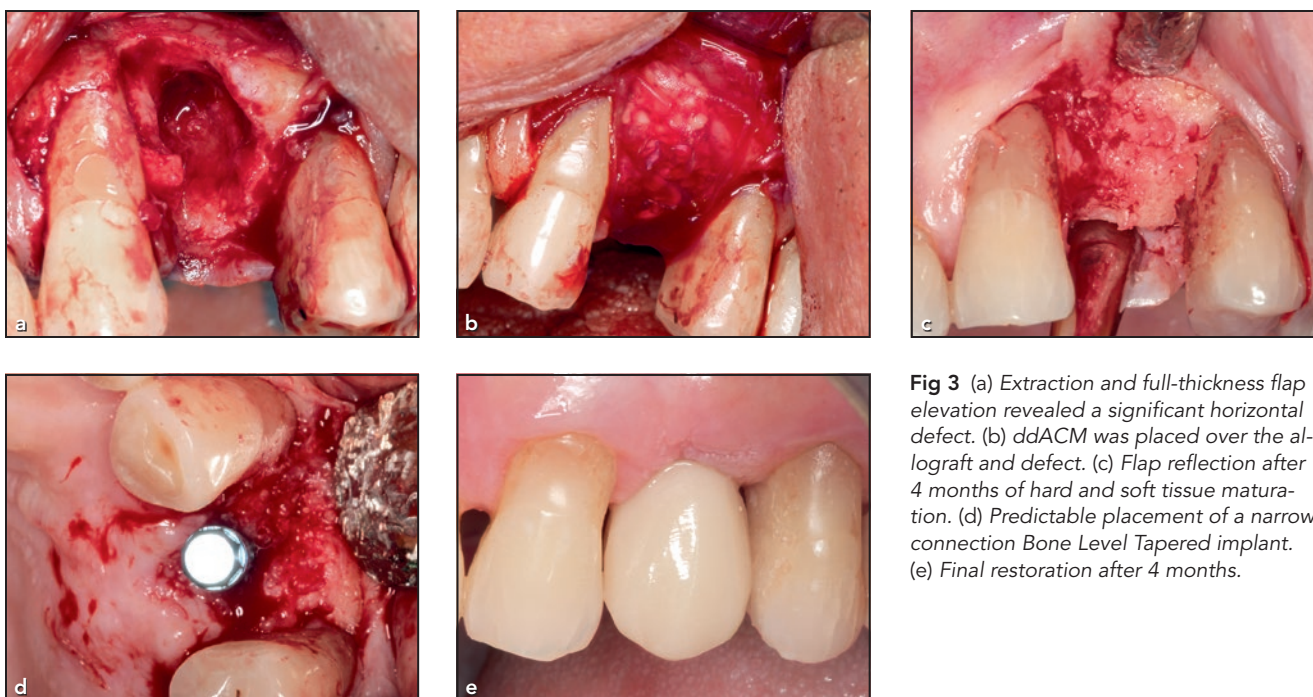


Fig 3 (a) Extraction and full-thickness flap elevation revealed a significant horizontal defect. (b) ddACM was placed over the allograft and defect. (c) Flap reflection after 4 months of hard and soft tissue maturation. (d) Predictable placement of a narrow-connection Bone Level Tapered implant. (e) Final restoration after 4 months.

(Bone Level Tapered implant, Straumann; Fig 3c). Healing was uneventful, and the implant was restored with a porcelain-fused-to-metal crown (Fig 3d). Good bone maintenance was noted in the 5-year post-operative radiographs (Fig 4).

Discussion

As a surgeon, one has a multitude of decisions to make when designing treatment strategies for implant placement and GBR. The final choices are often dictated by the surgeon's skill and judgement, the ability to place the implant in a restoratively driven fashion, and the need to attain adequate initial stability. Various techniques have been introduced through the years that incorporate biologically derived

products and lead to increases in overall bone yield. Platelet-rich fibrin (PRF), for example, is prepared from the patient's own blood to create an autologous fibrin-based clot that can be shaped into a membrane. As the fibrin clot forms, platelets release stored growth factors and cytokines,^{8,9} providing PRF membranes with biologic properties that extend beyond their primary role as a barrier for guided tissue regeneration (GTR)/GBR.

Placental membranes derived from the amniotic sac represent a relatively new class of biologically sourced membrane products in the field of GTR/GBR. Early reports involving the use of placental membranes in periodontal procedures mainly employed amnion-only grafts,^{10,11} whereas ddACM, an advanced version of the original

amnion-only grafts, combines layers of the amnion and chorion to create a deepithelialized and dehydrated laminate membrane. As a commercially available product with a 5-year shelf life at room temperature, ddACM does not require time-consuming chairside preparation, and it can be used without trimming, prehydration, or being secured with suture or tack, making it an attractive alternative to PRF and other membrane products on the market.

The success of placental membranes in GTR/GBR likely stems from the unique properties underlying the biologic role(s) that the amniotic sac plays during gestation. First and foremost, the amniotic sac is the sole barrier between the mother and child, and its ability to serve as a flexible but resilient occlusive bar-

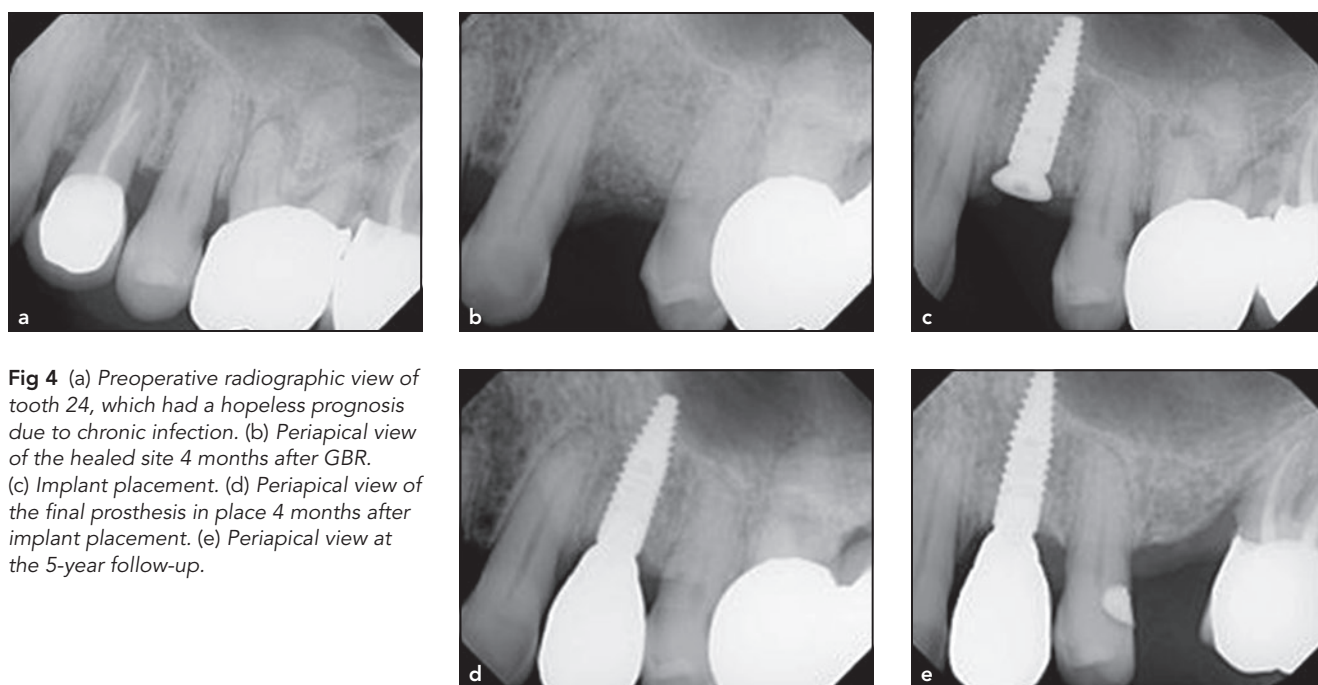


Fig 4 (a) Preoperative radiographic view of tooth 24, which had a hopeless prognosis due to chronic infection. (b) Periapical view of the healed site 4 months after GBR. (c) Implant placement. (d) Periapical view of the final prosthesis in place 4 months after implant placement. (e) Periapical view at the 5-year follow-up.

rier without eliciting a foreign body response by the mother's immune system is a critical aspect of its function throughout the pregnancy.¹² Though the amnion and chorion are comprised of several distinct sublayers, the basement membranes, with interwoven networks of collagen IV and laminins, are comparable to the basement membranes that anchor the epithelial layers of the gingiva, skin, and capillaries,⁴ providing the amnion and chorion with natural barrier functionality (as well as a extracellular cues to guide reepithelialization). Second, the amnion and chorion layers have been shown to contain a plethora of growth factors and cytokines with known roles in tissue repair and wound healing.^{5,13} Unlike the factors present in PRF, which are uniquely balanced to activate acute inflammation and wound healing, the mixture of fac-

tors found in the amniotic sac will support tissue growth to accommodate the increasing size of the developing baby. Similarly, cytokines found in the placental membranes are thought to temper inflammation within the womb as a protective measure, not activate it, as would be the case for cytokines found in PRF. Third, and perhaps most intriguing, the amniotic sac contains antimicrobial factors that are thought to prevent infections within the uterine environment, again reducing the potential for the occurrence of acute situations that would threaten the health of the baby.^{14,15} Beta-defensins (short peptides expressed by cells in the trophoblast sublayer of the chorion) are likely the primary contributors to the antimicrobial properties of the placental membrane, having been shown to inhibit bacterial, viral, and fungal

infections in vitro.¹⁶ Of note, beta-defensins are naturally expressed in the oral cavity, where they are thought to play critical roles in preventing infections, regulating innate and adaptive immunity, and mediating wound healing responses.¹⁶

The cases presented here represent common GBR situations in which patients require significant bone regeneration to ensure successful implant placement and stabilization. Given the critical role barrier membranes play in GBR cases and the accumulating evidence supporting placental membranes in periodontal surgery, the present authors chose to evaluate ddACM in two ridge augmentation procedures. In addition to the successful outcomes of these cases, ddACM was easy to use due to its thin, flexible nature, which allowed facile placement without trimming, and

its ability to be used in open-wound cases where primary closure is not possible.

Acknowledgments

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References

1. Bhushan KS, Singh G, Chauhan G, Prakash S. Amniotic membrane and its structure, features and uses in dentistry—A brief review. *Int J Curr Adv Res* 2015;3:354–360.
2. Rana MP, Mehrotra N. Human amniotic membrane: Hope in periodontal regeneration. *Int J Sci Res* 2016;5:564–569.
3. Choudhury SA, KJ N, Padmanabhan S. Use of placental tissues in periodontics: A review. *IOSR J Dent Med Sci* 2018;17:71–75.
4. Jayadev R, Sherwood DR. Basement membranes. *Curr Biol* 2017;27:R207–R211.
5. Koob TJ, Lim JJ, Masee M, Zabek N, Denozière G. Properties of dehydrated human amnion/chorion composite grafts: Implications for wound repair and soft tissue regeneration. *J Biomed Mater Res B Appl Biomater* 2014;102:1353–1362.
6. Ashraf H, Font K, Powell C, Schurr M. Antimicrobial activity of an amnion-chorion membrane to oral microbes. *Int J Dent* 2019;2019:1269534.
7. Palanker ND, Lee CT, Weltman RL, et al. Antimicrobial efficacy assessment of human derived composite amnion-chorion membrane. *Sci Rep* 2019;9:15600.
8. Nurden AT, Nurden P, Sanchez M, Andia I, Anitua E. Platelets and wound healing. *Front Biosci* 2008;13:3532–3548.
9. Preeja C, Arun S. Platelet-rich fibrin: Its role in periodontal regeneration. *Saudi J Dent Res* 2014;5:117–122.
10. Singh H, Singh H. Bioactive amnion as a guided tissue regeneration (GTR) membrane for treatment of isolated gingival recession. A case report. *Indian J Dent* 2013;4:110–113.
11. Kiany F, Moloudi F. Amnion membrane as a novel barrier in the treatment of intrabony defects: A controlled clinical trial. *Int J Oral Maxillofac Implants* 2015;30:639–647.
12. Kubo M, Sonoda Y, Muramatsu R, Usui M. Immunogenicity of human amniotic membrane in experimental xenotransplantation. *Invest Ophthalmol Vis Sci* 2001;42:1539–1546.
13. Koob TJ, Lim JJ, Masee M, et al. Angiogenic properties of dehydrated human amnion/chorion allografts: Therapeutic potential for soft tissue repair and regeneration. *Vasc Cell* 2014;6:10.
14. King AE, Paltoo A, Kelly RW, Sallenave JM, Bocking AD, Challis JR. Expression of natural antimicrobials by human placenta and fetal membranes. *Placenta* 2007;28:161–169.
15. Noda-Nicolau NM, Poletini J, Marconi C, Peraçoli JC, Miot HA, da Silva MG. Human beta defensins 1, 2 and 3 produced by amniochorion membranes is similar in term and preterm delivery. *Open J Obstet Gynecol* 2017;7:846–857.
16. Diamond G, Ryan L. Beta-defensins: What are they really doing in the oral cavity? *Oral Dis* 2011;17:628–635.