EC Dental Science Editor's Column - 2016

Bioengineering of Oro-Maxillo-Facial Soft and Hard Tissues via L-PRF Bio scaffolds

"L-PRF should be considered a "living tissue" preparation for natural guided tissue regeneration and not simply a "growth factor-rich" surgical adjuvant"

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COLUMN ARTICLE

Tissue regeneration and anatomical reconstruction in defects of the oro-maxillo-facial complex have been always a critical and controversial issue. Both, quality and quantity of the regenerated tissues are important to consider, aesthetically and functionally. Practically, the oral surgeon is faced with an ample collection of regenerative techniques and materials to choose from. How can one select the *"ideal" or "best-fit" strategy and procedure for an optimal clinical outcome? Evidence-based studies? Level of evidence?*

Leukocyte and Platelet-Rich Fibrin (L-PRF) is a 3-D autogenous biomaterial derived via simple and rapid centrifugation of wholeblood patient samples, in the absence of anti-coagulants, bovine thrombin, additives or any gelifying agents. A relatively new "revolutionary" advance in second generation platelet concentrate-based therapeutics, clinical effectiveness of L-PRF remains highly-debatable, whether due to preparation protocol variability, limited evidence-based clinical literature and/or inadequate understanding of its bio-components.Nonetheless, L-PRF *can be* indicated as an innovative *tool* for contemporary oro-maxillo-facial tissue regeneration and bioengineering. It is biocompatible, biodegradable, resilient and malleable biomaterial suitable for use inperiodontal and oral surgery.It seems to provide a strong alternativeand possibly cost-effective biomaterial for oral-tissue regenerative procedures. Indeed, existing evidence suggests that L-PRF improves *early* wound healing and promotes post-surgical bone formation and maturation. However, it is noteworthy that a clearer consensus seems to be present, today, regarding its significant beneficial impact on post-surgical pain and discomfort control, regardless the type of procedure. Unlike its predecessors, new L-PRF preparations (clots, membranes and blocks/plugs) tend to function more as biologically-active biomaterials and scaffolds for the delivery of autologous cells, cytokines and growth factors. Thus, L-PRF should be considered a "living tissue" preparation for natural guided tissue regeneration and not simply a "growth factor-rich" surgical adjuvant. Yet, it is safe to say that this remains an un-explored territory in Dental Biomaterial (Dental Bioengineering) Research, in general. In particular, L-PRF preparation protocols require revision and standardization. Furthermore, a good analysis of *intrinsic* rheological properties, bio-components and-function would enhance the validity, comprehension and therapeutic scope of the reported clinical observations; a step closer towards a new era of "*super*" or "smart" dental biomaterials and bioscaffolds.

Citation: Ziyad S Haidar."Bioengineering of Oro-Maxillo-Facial Soft and Hard Tissues via L-PRF Bio scaffolds". EC Dental Science ECO.01 (2016): 17-18.

For the most reproducible and clinically-usable L-PRF clots and membranes (and best possible clinical outcome), the following protocol is recommended:

Collect a 5-9 mL whole venous blood sample into 2-3 sterile 6 mL glass-coated plastic vacutainer tubes (without anti-coagulant).

Centrifuged immediately for 10-12 minutes at 2700-3000 revolutions per minute (rpm) using a high-quality table centrifuge.

Collect L-PRF clot carefully from the middle portion of the tubes. Typically, three compartments should be evident in the tube - **UPPER:** straw-colored acellular plasma (***PPP***), **MIDDLE:** yellowish fibrin clot (***FC***); and **LOWER:** red-colored lower fraction containing red blood cells (***RBCs***). Remove the upper layer to collect the middle fraction; 2 mm below to the lower dividing line.

The collected clot can then be used (quickly) directly as filling material, mixed with bone grating material (L-PRF plug or L-PRF block) or compressed into a strong L-PRF membrane, using a special surgical box designed to prepare it without any damage.

REMINDER: Quick handling is critical to obtain bioactive L-PRF clots charged with serum and platelets.

Our group is currently investigating the potential of incorporating oral-derived mesenchymal stem cells or growth-factor embedded nanoparticles within the L-PRF, as "future" bio-scaffolds, to further boost, with predictability, bone formation, soft tissue healing, treatment time and post-surgical stability, in advanced oro-maxillo-facial surgical procedures such as Periodontally-Accelerated Osteogenic Orthodontics and Distraction Osteogenesis. Our research extends to investigate the potential of L-PRF in reducing the need for prescription drugs following invasive surgical procedures such as third molar extraction and cysts resections. Finally, we are vigorously working on characterizing the physico-chemico-mechanical rheological properties and biological-content variations of L-PRF, alongside partnering up with nurses, physicians and dentists to optimize and standardize the chair-side preparation protocol, for use in several therapeutic indications.

Keywords: Ridge Preservation; Tissue Engineering; Regeneration; Leukocyte; Platelet; Fibrin; Growth Factors; Dentistry; Oral Surgery; Periodontology; Osteogenesis; Grafts