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Pilot study of ex vivo platelet activation using variable added calcium and electric pulse parameters: Growth factor release and clotting features

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Recent research has highlighted multiple opportunities for activated platelet rich plasma (PRP)/platelet gel in wound healing [1]. This entails drawing the patient's blood, centrifuging it to separate the PRP, and activating it by adding bovine thrombin (BT), the current state of the art clinical platelet activator, and CaCl2 to trigger platelet activation (growth factor release and clotting). The activated PRP is then applied onto a patient's wound. While efficient, BT may trigger side effects [2] and create challenges for cost, repeatability and workflow.

Electric pulse stimulation (EPS) is a potential candidate to replace BT by mitigating these drawbacks [3]. While initial studies suggested that EPS required CaCl2 for platelet activation, subsequent research demonstrated that one can achieve growth factor release without clotting with EPS and no added CaCl2 [3]. This observation could open new opportunities for injectable PRP since BT triggers growth factor and clotting and cannot be used for these applications while one could use EPS to activate PRP before injection to facilitate growth factor delivery at the injury site.

The current study reports the relationship between electrical parameters (pulse width, pulse amplitude, conductive vs. capacitive coupling) and CaCl2 level on growth factor release and clotting. Depending upon CaCl2 level and EPS, one can achieve various levels of growth factor release with no clotting or growth factor release with clotting. Furthermore, clotting time and clot mechanical strength may be controlled by choosing appropriate CaCl2 level and pulse parameters. For instance, combining 5.35 mM of CaCl2 with a 1.5 kV, 300 ns pulse triggers no clotting and little growth factor release while applying a 1.75 kV, 5 us pulse causes growth factor release with no clotting. Adding more CaCl2 to the microsecond pulses eventually triggers clotting. This demonstrates the potential for EPS as the first ever designer platelet gel technique.

[1] K. M. Lacci and A. Dardik, "Platelet-rich plasma: Support for its use in wound healing,"Yale J. Biol. Med., vol.83, pp. 1-9, 2010.

[2] D. L. Diesen and J. H. Lawson, "Bovine thrombin: history, use, and risk in the surgical patient,"Vascular, vol. 16, Suppl. 1, pp. S29-36, 2008.

[3] V. B. Neculaes, A. S. Torres, A. Caiafa, B. D-L. Lee, and A. L. Garner, "Platelet activation and growth factor release using electric pulses,"US Patent 9 452 199, Sep. 27, 2016

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