Biohybrid materials: inspired by nature to repair bones

G Perale[1,2]

[1] *Industrie Biomediche Insubri SA, Mezzovico-Vira, CH.* [2] *Department of Innovative Technologies, School of Applied Sciences and Arts of Southern Switzerland SUPSI, Manno, CH.*

INTRODUCTION: Evidence of clinical needs related to bone reconstruction dates back to ancient Egypt. A more rigorous scientific approach has been followed since 1889, when "modern" scientists started to focus their efforts on what can be defined as the early bone tissue engineering [1]. Nature here provides the key inspiration to new generation devices, where a composite approach is taking the lead by the smart combination of bio- and nano-technologies to replicate the intimate bone structure. The goal of a new approach is hence to combine the biocompatibility and tissue integration of natural materials with the possibility to tune mechanical and physical properties typical of synthetic ones: composite grafts best mimic the real nature of healthy human bone, being rigid and elastic, compact but porous, dense but viable to cells and vessels [2].

METHODS: A newly developed bone substitute, commercially named SmartBone®, was designed following a new concept of bottom-up composite approach, starting from bovine bone-derived mineral matrix mainly made of calcium hydroxyapatite ($Ca_5(PO_4)_3(OH)$), reinforced with bioresorbable aliphatic block-co-polymers (poly-lactide-ε-caprolactone) and RGD-containing collagen fragments as cell supporting biomacromolecules that increase cell viability and hydrophilicity, thus enhancing biocompatibility and osteointegration [2]. Medical grade components are mixed via a proprietary nanoemulsion physical-chemical process that allows obtaining the final device. 2 years of preclinical studies where followed by 4 years of clinical multi-centric studies, where bone regeneration in a wide range of defects from different patients was assessed by means of state-of-art imaging and histologic techniques [3].

RESULTS: Clinical and histologic evidences provided details on the *in vivo* behaviour of such a xeno-hybrid composite device: once grafted it soaks up blood, thus starting microcoagulation to occur inside the graft itself and hence enhancing graft integration. First weeks are then needed for cellular colonization of the graft, which is also enhance by the presence of collagen fragments that offer a viable environment for cells to spread onto; meanwhile, this time lag is also necessary for the degradation of the thin polymeric film, which progressively fades away leaving mineral structure for cells to consolidate and promoting the formation of new living bone (also by means of formation of new vessels); the following couple of months is needed for the integration of the graft with the native patient bone, thanks also to vascularization and new bone formation inside the graft. The remodelling process is hence completed.

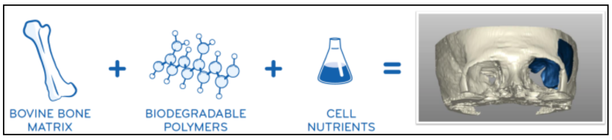

Fig. 1: choosing the right components to mimick the composite structure of natural bone to manufacture custom-made devices for regenerative surgery.

DISCUSSION & CONCLUSIONS: *Aim of an ideal bone graft is to allow its substitution by means of new growing healthy bone from the patient himself. Mother nature offers wide inspiration not only for intimate structure of innovative devices but also on regeneration processes and pathways that have to be walked down by these devices. The choice of composite approach runs along the track of bio-inspiration where, for bone engineering specifically, a composite mixture of natural minerals and synthetic polymers and signalling molecules allows mimicking at best the target tissue while also ensuring the right integration time. Success of such a bio-inspired approach is confirmed by the complete remodelling process, clinically evidenced by complete substation of grafted biomaterials with healthy human bone.*