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VASCULARISATION OF COMPOSITE BONE SCAFFOLDS – IN RODENTS WITH "MICROFIL" PERFUSION. SYSTEMATIC REVIEW

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Background and aim. Extensive research in oral and maxillofacial surgery aims to find an ideal alternative to autogenous bone for critical-size bony reconstructions. However, no such material has been found. Despite ongoing challenges, three-dimensional (3D) composite scaffolds show promise in improving vascularisation and bone regeneration by closely mimicking natural bone. A new investigation technique combining "Microfil" perfusion and micro-computed tomography (CT) allows efficient analysis of neovascularisation, bone regeneration, scaffold integration, and quantitative comparisons between studies.

This systematic review aims to investigate the effect of 3D composite scaffolds on new bone formation and vascularisation in critical-sized calvarial defects in rodents using "Microfil" perfusion and micro-CT.

Materials and methods. A comprehensive electronic search was conducted according to the PRISMA guidelines in PubMed and Medline from January 2013 to October 2023 limited to English language publications with available full texts. *In vivo* studies about "vascularisation bone scaffolds" using scaffolds made from a combination of inorganic and organic synthetic materials and analysing the neovascularisation and bone regeneration with "Microfil" and micro-CT techniques were investigated.

Results. The full text of 48 studies was assessed for eligibility, with 8 studies meeting the inclusion criteria. Findings indicate that scaffolds modified with angiogenic and/or osteogenic factors excelled pure scaffolds in vascularisation and bone regeneration ($p<0.01$ for new bone area (NBA), $p<0.05$ for vascularised area (VA) and bone volume fraction (BV/TV), $p=0.051$ for vessel number (VN)). Combining two modifying factors generated even better results ($p<0.01$ for VN and NBA, $p<0.05$ for BV/TV, $p=0.071$ for VA). Moreover, scaffolds with larger pore sizes (>400 μm) indicated a trend towards improved outcomes ($p<0.05$ for BV/TV, $p=0.053$ for VA). Additionally, composite scaffolds showed significantly higher NBA ($p<0.05$) than non-composite scaffolds. Nevertheless, three included studies showed a high risk of bias in at least one category, and all included studies presented missing information in half of the assessed items.

Conclusions. Enhancing vascularisation and bone regeneration in critical-sized calvarial defects using 3D composite scaffolds may benefit from modifications with angiogenic and/or osteogenic factors, especially when delivered together and with larger pore sizes. A properly designed scaffold structure could potentially erase the need for adding angiogenic and/or osteogenic factors. Future studies with larger sample sizes and similar study designs should investigate the optimal morphology as well as osseo- and angioinductive properties of these scaffolds.

Keywords. Bone tissue engineering; composite scaffolds; Micro-CT; Microfil; vascularisation.