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# Scaffold-free three-dimensional graft from autologous adipose-derived stem cells for large bone defect reconstruction

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**Background:** Long bone non-union is one of the most challenging pathologies in orthopedics surgery. We then assessed the feasibility and safety of human autologous scaffold-free osteogenic three-dimensional (3D)-graft (derived from adipose-derived stem cells, ASCs) to cure a bone non-union in extreme clinical and pathophysiological conditions.

**Methods:** Human ASCs (obtained from subcutaneous adipose tissues) were incubated in osteogenic media and supplemented with demineralized bone matrix to obtain the scaffold-free 3D osteogenic structure as confirmed *in vitro* by histomorphometry, volumetric bone mineral density, BMP-2 quantification and surface analysis for osteogenesis and mineralization. The 3D "bone-like" structure was finally transplanted for patients with bone tumor and bone pseudarthrosis to assess the clinical feasibility, safety and efficacy. Although minor clones with structural aberrations (clonal trisomy 7 in 6%–20% of cells) were detected in the undifferentiated ASCs, the osteogenic differentiation significantly reduced these clonal anomalies.

**Results:** The final osteogenic product was stable, did not rupture with forceps manipulation, did not induce donor site morbidity and was easily implanted directly in the bone defect. No acute (impaired wound healing, pain, inflammatory reaction and infection side effects) or long-term side effects (tumor development) were associated with the graft up to 4 years post-transplantation.

**Conclusions:** We report for the first time that autologous ASC can be fully differentiated into a 3D osteogenic-like implant without any scaffold and can safely promote osteogenesis in extreme conditions of bone non-union, leading to restoration of bone anatomy and function. A prospective controlled trial is needed for clinical relevant indications to clinically assess the 3D osteogenic-like implant.

## Biography

Denis Dufrane has completed his MD and PhD in Cell Therapy in 2000 and 2006, respectively, from the University Catholique De Louvain. He developed a translational "bench to bedside" model from relevant preclinical animal models to clinical practice. He was, up to 2015, the Head of the Tissue and Cell Therapy Center at the university clinical hospital Saint-Luc, Brussels, Belgium. He is currently the chief scientific officer and the co-founder of Novadip Biosciences. He has published more than 46 manuscripts in peer-reviewed journals, presented 38 invited lectures and has more than 120 communications and patents with more than 1300 citations.

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