Göteborg, 2021

Microcirculation in tissue repair: from microsurgery to 3D bioprinting

Akademisk avhandling

Som för avläggande av medicine doktorsexamen vid Sahlgrenska akademin, Göteborgs universitet kommer att offentligen försvaras i hörsal Arvid Carlsson, Medicinaregatan 3, Göteborg, fredagen den 26 Mars 2021, klockan 13.00

av Matteo Amoroso

Fakultetsopponent: Docent Martin Halle, Institutionen för molekylär medicin och kirurgi, Karolinska institutet, Stockholm

Avhandlingen baseras på följande delarbeten

I. **Amoroso M**, Özkan Ö, Özkan Ö, Bassorgun CI, Ögan Ö, Ünal K, Longo B and Santanelli di Pompeo F. "The Effect of Normovolemic and Hypervolemic Hemodilution on a Microsurgical Model: Experimental study in Rats." Plast Reconstr Surg. 2015 Sep; 136:512-519

II. **Amoroso M**, Özkan Ö, Bassorgun CI, Ögan Ö, Ünal K, Longo B, Santanelli di Pompeo F and Özkan Ö."The Effect of Normovolemic and Hypervolemic Hemodilution on a Perforator Flap with Twisted Pedicle Model: Experimental study in Rats." Plast Reconstr Surg. 2016 Feb; 13:339e-346.

III. **Amoroso M**, Apelgren P, Elander A, Säljö K and Kölby L. "The effect of hemodilution on free flap survival: a systematic review of clinical and experimental studies." Clin Hemorheol Microcirc. 2020 Vol.75(4), pp.457-466

IV. **Amoroso M**, Apelgren P, Säljö K, Montelius M, Strid Orrhult L, Engström M, Gatenholm P and Kölby L. "Vascularization of 3D Bioprinted Fat – Functional and Morphological Studies of Self-assembly of Blood Vessels." Submitted.

V. Apelgren P, **Amoroso M**, Säljö K, Montelius M, Lindahl A, Strid Orrhult L, Gatenholm P and Kölby L. "In Vivo MRI Reveals Functional Vascularization of Gridded 3D Bioprinted Cartilaginous Constructs." Submitted.

SAHLGRENSKA AKADEMIN
INSTITUTIONEN FÖR KLINISKA VETENSKAPER

GÖTEBORGS UNIVERSITET

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Microcirculation in tissue repair: from microsurgery to 3D bioprinting

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Abstract

Microsurgical reconstruction is challenged by two main shortcomings: Perfusion Related Complication (PRC) and donor site morbidity. In the first 3 studies of this thesis, we aimed to provide solutions to PRC-problems, investigating hemodilution as a tool able to increase blood flow in flap microcirculation. In study I, we investigated the beneficial effect of hemodilution on the blood flow of a perforator free flap in a rat model and in study II, hemodilution was examined in a perforator pedicle flap. Overall, study I and study II showed that hemodilution improved flap survival. Study III, a systematic review of the current literature on hemodilution in microsurgery, demonstrated a lack of relevant clinical research on this topic in both clinical and experimental studies. The second part of this thesis aimed to investigate vascularization in 3D bioprinted constructs, a crucial step for bringing this technology into clinical practice, and thereby contribute to a solution to donor site morbidity. In both study IV (3D bioprinted microfractured fat) and V (3D bioprinted cartilage), the constructs were transplanted to nude mice and examined by longitudinal Magnetic Resonance Imaging, histology and immunohistochemistry. Results showed a perfusable vascular network growing around and into the constructs. In study IV, human blood vessels formed spontaneously from fragments of blood vessels in the lipoaspirate used for bioprinting. The blood vessels interconnected with the circulation of the host. In study V, the grid structure itself proved important for vascularization from the host. To summarize, this thesis shows that hemodilution could improve flap viability in microsurgical reconstructions but there is a lack of support for its effect in clinical studies. Vascularization of 3D bioprinted constructs can be achieved by printing with microfractured human fat. By printing in a gridded structure, vascularization can be further stimulated.

Keywords: Microsurgery, Hemodilution, Microcirculation, 3D bioprinting, Tissue regeneration

ISBN 978-91-8009-144-2 (PRINT)
ISBN 978-91-8009-145-9 (PDF)