

OESOPHAGEAL TISSUE ENGINEERING – ADVANTAGES OF STAGED IMPLANTATION IN A LARGE ANIMAL MODEL

Edward Hannon¹, Federico Scottoni¹, Koichi Deguchi¹, Luca Urbani¹, Claire Crowley¹, Carlotta Camilli¹, Toby Proctor³, Ellie Phylactopoulos¹, Simon Eaton¹, Paola Bonfanti¹, Mark Lowdell², Paolo De Coppi¹

¹UCL Great Ormond St Institute of Child Health, London, UK, ²Department of Haematology, Royal Free Hospital, University College London Centre for Cell, Gene and Tissue Therapeutics, London, UK, ³Department of Biochemical Engineering, University College London, Bernard Katz Building, London, UK

Aims of the study: Tissue engineering may offer a solution to oesophageal replacement in children. We have demonstrated orthotopic single stage implantation of decellularised porcine oesophageal scaffolds is possible in a rabbit model however vascularisation of the graft remained a challenge. We aimed to explore if a staged approach with initial heterotopic implantation in a pedicle muscle flap led to improved graft vascularisation.

Methods: Decellularised scaffolds were produced from piglet oesophagi. First stage surgery (figure 1A) involved implantation of the scaffold in a muscle pedicle flap based on the superior epigastric vessels, tunnelled under the skin and positioned heterotopically in the neck of New Zealand white rabbits.

3-4 weeks after heterotopic implantation a 1.8 cm section of cervical oesophagus was resected and the vascularised scaffold mobilised on the pedicle flap and anastomosed in an orthotopic position with 6.0 non absorbable sutures. Open gastrostomy was performed to allow early post operative feeding. Rabbits were scheduled at humane end points and specimens stained before histological analysis.

Main Results: Heterotopic implantation was well tolerated and staged surgery feasible. At second stage, scaffold and muscle flaps were macroscopically well vascularised – figure 1B. Handling properties of the scaffold were much improved compared to previous single stage procedures with better retention of sutures and improved anastomoses.

Survival was limited by granulation tissue ingrowth within the scaffold and luminal obstruction (figure 1C). Histology (figure 1D) demonstrated improved scaffold vascularisation compared to single stage surgery with new vessels invading the scaffold (arrows) and improved migration of host cells into the ECM of the scaffold.

Conclusions: A 2 stage approach to implantation of tissue engineered oesophageal scaffolds improves vascularisation and cell migration into the extracellular matrix. Management of luminal over granulation needs consideration but may be reduced with a shorter interval between operative stages.

