

2B FUTURE PROJECTS PRIZE 1

059 A RANDOMISED CONTROLLED TRIAL TO COMPARE EPIDERMAL GRAFTING WITH SPLIT-THICKNESS SKIN GRAFTING FOR WOUND HEALING (EPIGRAAFT TRIAL)

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Introduction: Split-thickness skin grafting (SSG) is an important modality for wound closure. However, the donor site becomes a second, often painful wound, which may take more time to heal than the graft site itself. Epidermal grafting (EG) is an alternative method of autologous skin grafting that harvests only the epidermal layer of the skin by applying continuous negative pressure on the normal skin to raise blisters. This procedure has minimal donor site morbidity and is relatively pain-free, allowing autologous skin grafting in an outpatient setting. We plan to compare EG to SSG and to further investigate the cellular mechanism by which each technique achieves wound healing. Study design EPIGRAAFT is a multicentre, randomised, controlled trial that compares the efficacy and wound-healing mechanism of EG with SSG for wound healing. The primary outcome measures are the proportion of wounds healed in 6 weeks and the donor site healing time. The secondary outcome measure is the difference in wound healing mechanism. Pilot data: The healing outcome between EG and SSG were similar at week 6. EG had faster donor site healing ($p < 0.001$) and lesser donor site morbidity ($p < 0.001$). Greater downregulation of gap junctional proteins was seen in the EG group, suggesting different healing mechanism between these two treatment groups. Forward plan This study is expected to define the efficacy of EG and promote further understanding of the mechanism of wound healing by EG compared to SSG. The results of this study can be used to inform the current best practise for wound care.

Take-home message:

Epidermal grafting is an autologous skin grafting that can be performed in the outpatient setting without anaesthesia. This study shows that EG has similar efficacy with SSG, but with lesser donor site morbidity.

060 EVALUATING SUITABILITY OF ADIPOSE DERIVED STEM CELLS FROM CANCER PATIENTS FOR USE IN BREAST REGENERATION

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Introduction: Adipose derived stem cells (ADSCs) are becoming standard in adipose regeneration. 3D culture models mimic biochemical and biophysical cues of tissue microenvironments. We aim to investigate the regenerative potential of ADSCs from breast cancer patients and identify if autologous ADSCs are suitable and safe for regenerative strategies. Study Design ADSCs harvested from breast cancer patients who have and have not received neoadjuvant therapy and healthy controls will be cultured in 3D. The effect of cancer and cancer treatment will be assessed by comparing the regenerative capacity of these cells by adipogenesis assays (Oil Red O), RT-PCR (PPAR- γ , LPL) and assessing cell viability, proliferation and apoptosis. Pilot Data ADSCs from patient groups of interest were examined by flow cytometry for expression of human markers associated with mesenchymal lineages: CD90, CD105, CD44H, CD73, CD34, CD11b, Glycophorin-CD235a, CD33, CD45. Adipogenic potential was confirmed via induction in differentiation media and quantification of adipocytes by Oil Red O. Forward Plan ADSCs will be cultured on 3D scaffolds to mimic the in vivo microenvironment and adipogenic potential assessed. The secretome of ADSCs during adipogenesis will be examined to identify pro-tumourigenic cytokines released that may stimulate tumourigenesis. The effect of hormonal and cytotoxic therapeutics on ADSC adipogenic potential will be investigated in vitro (3D). While ADSCs offer exciting potential as a regenerative strategy, the potential for autologous use and oncologic safety in breast cancer patients must be addressed before this technology can be translated clinically, providing a novel approach to breast reconstruction for mastectomy patients.

Take-home message:

Current methods of breast reconstruction are significantly limited. This proposed novel approach using ADSCs offers an attractive and potentially superior method of breast reconstruction post mastectomy, thus answering an urgent clinical need for breast cancer patients.

061 UNDERSTANDING THE BIOLOGY OF NEUROBLASTOMA AND TESTING NEW TARGETED THERAPIES USING A NOVEL IN VIVO MODEL: THE CHICK EMBRYO

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Introduction: Neuroblastoma (NB) is the most common extra-cranial solid tumour of childhood, with 50% mortality in high-risk cases. Successful treatment requires therapies that block metastasis and promote differentiation. We use the chick embryo as a preclinical model to test new therapies. Study design Experimentation in chick embryos of this age does not require Home Office licence. Fluorescently labelled NB cells, representing different genotypes, were placed onto the chorio-amniotic membrane of the embryo. Tumours are allowed to develop and retinoic acid (ATRA), CDK4/6 and CDK1 inhibitor therapies were injected into the allantoic sac. The ability of drugs to reduce metastasis was determined

by dissecting the tumours. Tumours were assessed by their morphology and expression of proliferation markers (Ki67). Pilot data Preliminary testing showed all therapies reduced the number of NB tumours formed. Confocal microscopy revealed that cells treated with retinoic acid exhibited neurite process development and were therefore morphologically more differentiated. Ki67 staining of cells indicated that CDK1-i treated cells had significantly lower levels of active proliferation compared to control ($p=0.01$). Forward plan Rigorous testing of new chemotherapeutic agents is essential prior to clinical trials in children. Mouse models are expensive and have a low throughput. We have developed the chick embryo as a validated and inexpensive model suitable for high throughput screening in which biochemical markers and tumour morphology can be assessed. Future plans involve testing a range of drugs and introducing combination therapies. Live imaging will allow us to further understand the effects of the pharmacotherapeutics on NB cells.

Take-home message:

High grade neuroblastoma remains a difficult to treat condition with a mortality rate of over 50%. Screening of novel drugs in the chick embryo model is a fast and cost-effective method of understanding metastatic pathways of neuroblastoma and elucidating the impact of new chemotherapeutics.

062 WITHDRAWN

063 DEVELOPMENT OF A TABLET BASED CONSENT APPLICATION TO IMPROVE INFORMED CONSENT

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Introduction: If consent for surgery is to be valid, patients must be able to recall, understand and weigh up the information provided to allow effective decision making. Our research has shown recall and understanding of consent for elective surgery to be poor, raising concerns about the validity of informed consent. These concerns have led to development of a tablet application (app) to improve patient recall and understanding. This app calculates personalised risk information and includes animations and graphical depiction of personalised consent information. It encompasses the entirety of the informed consent process from information provision to signature. Study design The app will progress through qualitative assessment involving patient and health care professional focus groups, initially separately and then combined. After any subsequent app refinement, a pilot study is planned, prior to a randomised controlled trial. Pilot Data Assessment of informed consent for inguinal hernia surgery has shown recall of 51% and understanding of 39% when consent is obtained through a shared decision making process. The designed app has been subject to initial qualitative assessment by a small number of surgeons, all of whom believe it would improve patient understanding and ensure standardisation of information provision. Forward plan Further qualitative assessment is planned for October 2016 in the form of focus groups. After app refinement, a feasibility study of the app as a tool to improve informed consent for patients is planned. A randomised controlled trial of the app will be designed based on the outcomes of these initial phases of research.

Take-home message:

A tablet application to improve informed consent is to be piloted and subsequently assessed in a randomised controlled trial.

064 A NANOCOMPOSITE POLYMER POSS-PCU (POLYHEDRAL OLIGOMERIC SILSESQUIOXANES AND POLY (CARBONATE-UREA)-URETHANE) FOR THE DEVELOPMENT OF COMPLIANT ENDOVASCULAR STENT-GRAFTS WITH LONG-TERM DURABILITY

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Introduction: Current thoracic endovascular technology suffers from high profile delivery systems, high burdens of material fatigue in areas of maximum 4 dimensional movement, and poor conformability. We have developed a more compliant stent-graft using a nanocomposite polymer POSS-PCU bonded to nitinol. Study design: Based on bench testing as below, solid, porous and woven types of POSS-PCU will be tested to optimise stent-graft design and subjected to burst pressures testing, tensile testing, energy dispersive x-ray analysis, compliance and distention measurement. In situ branching will be performed by direct retro or antegrade puncture facilitated by reliable thermal sealing process. Pilot data: In results so far, POSS-PCU stent-grafts successfully completed accelerated pulsatile fatigue testing in an in vitro accelerated model for 400-million cycles equivalent to 10-years in human body. There was no loss of tensile strength, or compliance and no evidence of thermo-mechanical degradation. The overall compliance of the POSS-PCU stent-graft was $3.3 \pm 0.61\%/mm \text{ Hg} \times 10^{-2}$, which was significantly greater than the ePTFE stent-graft ($2.3 \pm 0.95\%/mm \text{ Hg} \times 10^{-2}$; $P=0.0003$). The ePTFE stent-graft was significantly stiffer with stiffness index $\beta 92.7 \pm 46.1$ compared to POSS-PCU stent-graft ($\beta 39.1 \pm 5.91$; $P < 0.0001$). Forward plan: POSS-PCU possesses superior haemocompatibility, biostability, and antithrombogenicity, owing to its enhanced physicochemical properties and nano-reinforced structure and surface nanotopography. This technology has the potential to address some of the current limitations including developing conforming and compliant stent-grafts to improve long-term durability and reduce the risk of late endoleak and failure.

Take-home message:

This abstract presents an endovascular stent-graft based on a superior biomaterial and has the potential to address some of the limitations of the current devices.

O65 EXOGEN LOW INTENSITY PULSED ULTRASOUND SYSTEM FOR NON-UNION OF FRACTURES – A NATIONAL PROSPECTIVE MULTI-CENTRE STUDY

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Introduction: Non-union is a serious complication of fractures and may occur for various reasons including infection, instability and microvascular disease (smoking, NSAID usage or diabetes). Revision surgery can be challenging and expensive therefore a non-surgical option with comparable outcomes and less risks could improve patient care. EXOGEN is a bone healing device applied by the patient at home. EXOGEN uses low-intensity pulsed ultrasound which activates cell surface receptors resulting in up-regulation of genes and proteins involved in angiogenesis, osteogenesis, bone consolidation and matrix remodelling (COX-2, VEGF and IGF-1). International studies have demonstrated EXOGEN to have union rates of 88% and 86.2%. Study Design Prospective, multi-centre study in centres with ≥ 50 EXOGEN applications since 2012. Follow-up until fractures are classed as united or not-united and requiring further intervention. Data will be collected on a variety of patient and fracture characteristics. Pilot Data $n = 101$ (109 bones/applications) patients 61M:40F with a median age of 48 (21-86) were retrospectively reviewed at a tertiary referral centre. 72/109 (66%) of fractures achieved union after EXOGEN with 46/109 (42%) uniting after 90 days and a further 26/109 (24%) after 180. No complications were noted. Forward Plan Recruitment underway for a prospective multi-centre study to allow analysis of specific fracture cohorts and facilitate better assessment of the efficacy of EXOGEN in non-union. EXOGEN may have a role in reducing the risk (and cost) associated with revision surgery which may improve outcomes in patients with non-union. COX-2 (Cyclooxygenase-2) VEGF (Vascular Endothelial Growth Factor) IGF-1 (Insulin-like Growth Factor-1)

Take-home message:

Exogen may provide a safe, cost-effective and comparable union rates to revision surgery, a national study could validate international findings and improve care for patients suffering with non-union following a fracture.

O66 IN VIVO MONITORING OF VASCULARISATION OF DECELLULARISED SCAFFOLDS IN TISSUE ENGINEERING USING PHOTOACOUSTIC TOMOGRAPHY

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Introduction: Angiogenesis is key to the long-term survivorship of tissue-engineered constructs in vivo. Ability to monitor angiogenesis is therefore crucial to enable researchers and clinicians to determine and compare the therapeutic nature of vascularisation strategies used in tissue engineering. Photoacoustic tomography is a promising non-invasive imaging technology which produces three-dimensional images for in vivo monitoring of angiogenesis. Study design: Decellularised donor trachea will be used as tissue-engineered scaffolds for subcutaneous implantation in murine models. Pro-angiogenic strategies using cell therapy will be applied to the scaffold. In vivo photoacoustic imaging will be carried out to monitor and quantify rate of neovascularisation in different cell therapy groups. Images will be compared to histological analysis for validation of method. Pilot data: Six adult CD1 mice were subcutaneously implanted with decellularised trachea for a period of 15 weeks. Retrieved samples showed good integration of scaffold and photoacoustic images demonstrated high-resolution quantification of angiogenic response. The study showed evidence of progression of neoangiogenesis over an extended period of time without the need to perform terminal procedures or use of invasive contrast dyes. All experiments have been approved by the National Research Ethics Committee and were performed in accordance with national guidelines and university's research policies. Forward plan: Validation of the use of photoacoustic technology to monitor angiogenesis in vivo will allow for reduction of more invasive methods used pre-clinically. It would also have significant impact in supporting its novel use in the observation of tissue integration and angiogenesis of tissue-engineered scaffolds in the clinical setting.

Take-home message:

This novel study into the use of photoacoustic imaging technology in tissue engineering will play a significant role in validating and supporting its future application for the monitoring of angiogenesis in both the pre-clinical and clinical setting.