

EURAPS Research Council 27-28th May 2015



SUMMARY PROGRAMME

Venue: Music Hall, Assembly Rooms, 54 George Street, Edinburgh EH2 2LR
Phone: 0131-220-434 Website: <http://www.assemblyroomsedinburgh.co.uk>

Local Host: Prof. Andrew Hart <Andrew.Hart@glasgow.ac.uk>

Wednesday 27th May 2015

08:30 - 09:00 registration

09:00 - 11:15 Session 1: Clinical

11:15 - 11:30 Break

11:30 – 13:00 Session 2: Tissue Engineering

13:00 – 14:00 LUNCH

13:15 – 13:45 Research Council National Delegates meeting (Music Hall)

14:00 – 15:45 Session 3: Peripheral Nerve / Hand

15:45 – 16:00 Break

16:00 – 18:00 Session 4: General

18:00 – 19:00 drinks tour of Edinburgh

19:00 onward: evening reception at “Beer & Skittles”, 14 Picardy Place, Edinburgh EH1 3JT

Phone 0131-556-1289

Website: <http://www.beerandskittlesbar.co.uk/>

Thursday 28th May 2015

08:00 – 10:50 session 5: Future Directions

10:50 – 11:00 Break

11:00 – 13:00 Symposium: *Microsurgery as a Model for Implementing Tissue Engineering into Clinical Practice*:

Sponsors: Malosa Medical www.malosa.com Cytori Therapeutics www.cytori.com

11:00 – 11:20 Mr. David Soutar (Past-President of EURAPS & BAPRAS) “*The Development & Rollout of Microsurgery into Widespread Clinical Practice, and the Most-Cited Paper in Plastic Surgery*”

11:20 – 11:45 Prof. Stefan Hofer (Wharton Chair of Reconstructive Surgery, University of Toronto & Editor-in-Chief of JPRAS) “*Establishing High Quality Academic Output from a Microsurgical Practise & Where Future Research Should be Focused*”

11:45 – 12:15 Prof. Bruno Péault (Chair of Vascular regeneration, MRC Centre for Regenerative Medicine, Edinburgh, & Professor, David Geffen School of Medicine, Orthopaedic Hospital Research Center, UCLA, California) “*What is a Stem Cell – rationalizing characterization and use in tissue engineering*”

12:15 – 12:45 Prof. Matt Dalby (Professor of Cell Engineering, University of Glasgow) “*Controlling stem and other cells by materials manipulation - what are the translational barriers to clinical implementation*”

12:45 – 13:00 Open discussion on delivering the integration of microsurgery & tissue engineering, and service development opportunities for Plastic Surgery.

13:00 Close of Research Council meeting

14:00 EURAPS Main Meeting Commences (same venue as Research Council)

E-mail: research-council@euraps.org

Website: <http://research-council.euraps.org>

Meeting Supported by Malosa Medical, Cytori Therapeutics, Touch Bionics

Registration via EURAPS Research Council Website / on Arrival



2015 - Session Programme

Wednesday 27th May 2015

Venue: Music Hall, Assembly Rooms, 54 George Street, Edinburgh EH2 2LR

08:30 - 09:00 registration

09:00 - 11:20 Session 1: Clinical

Chairing: Christian Bonde, Copenhagen & Ash Mosahebi, London

09:00-09:04	Andrew Hart	Introduction
09:04-09:12	Ozan Bitik	Analysis of lower breast pole length and nipple-areola complex position following superior pedicle, short horizontal scar breast reduction
09:12-09:20	Burak Kaya	Metamizole: An effective solution for vasospasm
09:20-09:28	Karaca Basaran / Idris Ersin	The free-nipple breast-reduction technique performed with transfer of the nipple-areola complex over the superior or superomedial pedicles.
09:28-09:36	Nina Goesseringer	Intraoperative team approach in order to optimise DIEP reconstruction
09:36-09:44	Rob staruch	Mechanical analysis of Nanocomposite Bipolymer Hydrogel Foams for military wound healing
09:44-09:52	Rossella Sgarzani	Pressure ulcers in patients with spinal cord injuries: concordance between ulcer swab and intra-operative culture for the aetiological diagnosis of infection.
09:52-10:00	Fatih Ceran	Evaluation of the retro-orbital fatty tissue volume in delayed orbital blow-out fractures
10:00-10:08	Petros Konofaos	A comparison of cranioplasty materials using an impact testing model in rabbits
10:08-10:16	Luca Negosanti	Usefulness of magnetic resonance in the diagnosis of osteomyelitis in patients with spinal cord injury (SCI) and pressure ulcers.
10:16-10:24	Cristina Auba	Effect of postoperative brachytherapy and external beam radiotherapy on functional outcomes of immediate facial nerve repair after radical parotidectomy
10:24-10:32	Nicholas Slater	Large contaminated ventral hernia repair using Component Separation Technique with synthetic mesh is safe
10:32-10:40	Mehtap Karamese	Intra-articular platelet-rich plasma injection for the treatment of temporomandibular disorders and a comparison with arthrocentesis

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10:40-10:48	Fatih Ceran	Use of Anastomotic Microvascular Device or Hand-Sewn Anastomoses for Arteriovenous Shunts: An Experimental Study in Rats
10:48-10:56	Rojda Gumuscu	Acellular dermal matrix and dermal flaps in one-stage breast reconstruction after mastectomy
10:56-11:04	CJ Tollan	Intraoperative Laser Doppler Scanning: A comparative study of SIEA and DIEAP flaps
11:04-11:12	Beniamino Brunetti	The propeller transposition flap: a reliable geometrical design to improve the vascular safety of perforator based propeller flaps Withdrawn
11:12-11:15		Open Discussion Time

11:15 - 11:30 Break

11:30 – 13:00 Session 2: Tissue Engineering

Chairing: Prof. Arndt Schilling, Munich & Prof. Dr. Hans-Günther Machens, Munich

11:30-11:39	Zita Jessop	A morphological and biophysical analysis of immature and mature bovine auricular cartilage: Implications for tissue engineering
11:39-11:48	Richard Wong	A Microsurgical Model for Tissue Engineering in the Mouse.
11:48-11:57	Georgina Wellstead / Tom Pidgeon	The Need for Core Outcome Reporting in Autologous Fat Grafting for Breast Reconstruction
11:57-12:06	Zita Jessop	A novel isolation protocol for auricular cartilage derived stem cells (CDSCs) and implications in cartilage tissue engineering
12:06-12:15	Libor Streit	Effect of Sedimentation, Centrifugation and Membrane-Based Filtration on Human Adipose Derived Stem Cell Content and on Viability and Morphology of the Fat Graft
12:15-12:24	Hazem Alfeqy	Prevention of post primary flexor tendon repair peritendinous adhesions using bone wax
12:24-12:33	Volodymyr Protsenko	Replacement of post-resection bone defects in tumors using material based on bioactive glass
12:33-12:42	Mary Frimpong	Investigating the matrix chemistry of human adipose-derived stem cells: the first step toward creating a scaffold for optimal adipose tissue engineering with a biomimetic approach Withdrawn 26/5/15
12:42-13:00		Open Discussion

13:00 – 14:00 LUNCH

13:15 – 13:45 National Delegates Meeting & 2016 Research Council Planning Meeting
Chair: Benedetto Longo Venue: main lecture theatre

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14:00 – 15:45 Session 3: Peripheral Nerve

Chairing: Prof. Andrew Hart, Glasgow & Ms. Eva Placheta, Vienna

14:00-14:08	Maham Hadi	A novel self-assembling nanopeptide hydrogel to deliver cell therapy for peripheral nerve regeneration
14:08-14:16	Suzanne Thomson	Understanding cell and molecular scale events regulating peripheral nerve repair
14:16-14:24	Federico Facchin	Is what we know about the Palmar Fascia enough?
14:24-14:32	Li Yong	An anatomical study of the dorsal branches of the digital nerves
14:32-14:40	Rosanna Ching	Exosomes from adipose-derived stem cells as mediators of nerve regeneration
14:40-14:48	Andrew McKean	Incidence, shoulder outcome and surgical intervention of unilateral obstetric brachial plexus injury in Scottish population
14:48-14:56	Savaş Serel	Functional and Histopathological Study of Prefabricated, Sham and Non-Vascularized Rat Femoral Nerve
14:56-15:04	Lima Sottaz	Engineered growth factor and nanotopography for triggering axonal outgrowth
15:04-15:12	Neil Fairbairn	Light activated sealing of acellular nerve allograft (ANA) for large gap nerve injury
15:12-15:20	John Biddlestone	Tumour-Stroma interactions: Initial findings from an in-vitro tumour-ADSC co-culture model
15:20-15:28	Elisabeth Kappos	Implantation of a Denaturated Cellulose Adhesion Barrier and Finger Function after Plate Osteosynthesis of Longfiner P1 Fractures - Results of a randomized controlled trial
15:28-15:36	Konstantin D. Bergmeister	Effects of selective Nerve Transfers on the Mammalian Motor Unit
15:36-15:44	Jonathan Leckenby	Nerve regeneration through autologous grafts: does the axonal load of the graft affect the outcome?

15:45 – 16:00 Break

16:00 – 18:00 Session 4: General

Chairing: Stefan Hacker, Vienna & Adam Reid, Manchester

16:00-16:08	Parviz Sorooshian	Development of a tissue fibrosis model in the hind limb of the mouse
16:08-16:16	Seon Lee / Tom Pidgeon	The Efficacy of the Cook-Swartz Implantable Doppler in the Detection of Free Flap compromise: A Systematic Review and Meta-Analysis

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16:16-16:24	Gerrit Grieb	Levels of macrophage migration inhibitory factor and glucocorticoids in chronic wound patients and their potential interactions with impaired wound endothelial progenitor cell migration
16:24-16:32	John Biddlestone	The role of hypoxia as a microenvironmental cue in the differentiation of ADSC
16:32-16:40	Ozan Bitik	Composite jejunum/diep flap: a novel rat model of viscerocutaneous flap prefabrication
16:40-16:48	Megan Anderson	Differential Distribution of the Ca (2+) Regulator Pcp4 in the Branchial Arches Is Regulated by Hoxa2
16:48-16:56	Jacqueline Rees-Lee & Cynthia To	Laser speckle imaging (LSI) of tissue blood flow: preliminary results from use during free-flap breast reconstruction
16:56-17:04	Seon Lee	Reporting Quality of Observational Studies in Plastic Surgery Needs Improvement A Systematic Review
17:04-17:12	Giorgio Giatsidis	Short Cyclical Intermittent Stimulations Potentiate Adipogenesis in Soft-tissues
17:12-17:20	Seon Lee / Tom Pidgeon	Levels of Evidence in Plastic Surgery - Bibliometric Trends and Comparison with Five Other Surgical Specialties
17:20-17:28	Pawel Szycha	Inframammary fold correction in two-stage breast reconstruction with the fibrous capsule, together with its vascular and stromal characteristics
17:28-17:36	Aidan Rose	Frequent loss of function mutations in TGFBR1 and TGFBR2 reveal hair follicle bulge stem cells as the cell of origin in cutaneous squamous cell carcinoma
17:36-17:44	Min Wu	E2F1 Reduces Wound Healing by Suppressing Neovascularization through Regulating Endothelial Progenitor Cells Mobilization and Recruitment to the Ischemia Skin Withdrawn
17:44-17:52	Gisella Nele	Bow-tie flap for umbilical reconstruction
17:52-18:00	Wee Lam	Congenital Duplication Differences of the Hand: Insights from Experimental Manipulations of Sonic Hedgehog Signalling and a Proposed Classification System

18:00 – 19:00 drinks tour of Edinburgh – proposed route to be provided on the day

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Thursday 28th May 2015

Venue: Music Hall, Assembly Rooms, 54 George Street, Edinburgh EH2 2LR

08:00 – 10:50 Session 5: Future Directions for Plastic Surgery

Chairing: Benedetto Longo, Rome & Efterpy Dimiri, Greece

08:00-08:10	Galip Gencay Ustun	A systematic review and meta-analysis of free flap safety in the elderly
08:10-08:20	Nanda Kandamany	Approaching 100 Free Flaps for Burn Injuries-Lessons Learned and Refinements of Design in a 16-Year Experience
08:20-08:30	Andrew Hart	In vitro characterisation of a microengineered electroactive polymer conduit for peripheral nerve repair
08:30-08:40	Nadja Menzi	Lipoma-derived Stem Cells (Lmscs) as a Potential Source for Regenerative Medicine
08:40-08:50	Ali Modarressi	Can autologous PRP be used safely and efficiently for adipose derived mesenchymal stem cells culture?
08:50-09:00	Naghmeh Naderi	Effect of nanocomposite polymer fabrication on proliferation and morphology of adipose derived stem cells
09:00-09:10	Grainne Bourke	Early nerve repair for experimental brachial plexus injury
09:10-09:20	Margot Den Hondt	Are we decellularizing too aggressively? The effect of gentle decellularization on rabbit trachea: preliminary report. Withdrawn
09:20-09:30	Alessandro Faroni	Grooved polymer scaffolds with human Schwann-like adipose-derived stem cells towards nerve regeneration
09:30-09:40	Lima Sottaz	MR-Diffusion-based assessment of chronic compression neuropathy treated with adipose-derived stem cells
09:40-09:50	Thomas Reekie	Patient Reported Outcome in a 4-limb Amputee after fitment with i-limb digits Myoelectric Prosthesis
09:50-10:00	Naghmeh Naderi	Effect of pore size and porosity on adipose-derived stem cell behaviour on nanocomposite polymer scaffolds
10:00-10:10	Liam McMorrow	Assessing the potency of CD271-Positive Adipose-Derived Mesenchymal Stem Cells to a Schwann Cell-like Phenotype

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10:10-10:20	Hoda Khorasani	Scientific impact of presentations from the EURAPS and the AAPS meetings; a ten year review
10:20-10:30	Christopher West	A high-throughput approach to identify defined polymer based substrates for tissue engineering using adipose derived perivascular stem cells
10:30-10:40	A. Khan	Radioprotecting free flaps using lentivirally-delivered superoxide dismutase 2 (SOD2) gene therapy
10:40-10:50	Christopher West	Percutaneous delivery of adipose derived pericytes prevents the development of atrophic non-union in a rat model

10:50 – 11:00 Break

11:00 – 13:00 **Symposium: *Microsurgery as a Model for Implementing Tissue Engineering into Clinical Practice***

Chairing: Andrew Hart, Glasgow & Ken Stewart, Edinburgh

Session Sponsors: Malosa Medical www.malosa.com & Cytori Therapeutics www.cytori.com

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13:00 Close of EURAPS Research Council Meeting

14:00 EURAPS Meeting Commences (same venue as Research Council)

EURAPS Research Council is grateful for the essential support of the following exemplary medical companies. Please visit their websites and discuss their products at the meeting:

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SESSION 1: CLINICAL

Chairing: Christian Bonde, Copenhagen & Ash Mosahebi, London

09:00-09:04 Andrew Hart Introduction

09:04-09:12 Ozan Bitik Analysis of lower breast pole length and nipple-areola complex position following superior pedicle, short horizontal scar breast reduction

Ozan Bitik & Hakan Uzun

Hacettepe Universitesi Plastik Cerrahi AD Sekreterliği, Ankara, Turkey

Background: Postoperative changes following superior pedicle breast reduction are closely related to the pattern of skin resection. We have observed that the superior pedicle, short horizontal scar breast reduction technique provides a stable breast shape in the long term. Objectives: We test the validity of our clinical observations through objective analysis of postoperative dimensional changes following superior pedicle, short horizontal scar breast reduction. Methods: Of 42 patients who underwent superior pedicle, short horizontal scar breast reductions between January 2011 and June 2012, 38 (75 breasts) were available for long-term follow-up. The midclavicular point-to-superior areolar border distance (A), the inferior areolar border-to-inframammary fold (IMF) distance (B), and the areolar diameter (C) were measured and recorded at the time of (1) preoperative markings, (2) first postoperative visit, and (3) 2-year postoperative follow-up visit. The specifications of the preoperative markings were recorded to analyze their correlation with actual breast dimensions. Results: The superior border of the nipple-areola complex (NAC) was located, on average, 1.2 cm higher at the first postoperative visit when compared with the markings ($P < 0.001$). The nipple-areola position did not change significantly in the long term ($P = 0.224$). The average postoperative increase in the IMF-to-inferior areolar border distance between the first postoperative visit and the long-term follow-up visit was 0.3 cm ($P < 0.001$). Although statistically significant, this extent of change (4.5%) in the lower pole vertical length was clinically unidentifiable, and pseudoptosis did not occur after superior pedicle, short horizontal scar mammoplasty. Conclusion: Long-term stability of the NAC position and lower breast pole length makes superior pedicle, short horizontal scar breast reduction a predictable and dependable option for primary breast reduction/mastopexy and for a matching procedure.

09:12-09:20 Burak Kaya Metamizole: An effective solution for vasospasm

Burak Kaya, Servet Elcin Alpat, Savas Serel & Hakan Ergun
Ankara University Cebeci Hospital, Turkey

Vasospasm is a major problem during microsurgery, and a variety of pharmacological agents are used to alleviate vasospasm. This study aimed to demonstrate the effect of metamizole on vasospasm and to compare it with lidocaine and papaverine, both of which are commonly used to correct vasospasm. Fifteen female rats were randomly divided into groups 1, 2, and 3, which were the metamizole, papaverine, and lidocaine treatment groups, respectively. Both femoral arteries of all of the rats were dissected, and they were immediately photographed. The pharmacological agents were topically applied to the arteries of the animals in each group. Five minutes after pharmacological agent application, the arteries were photographed again. The images were transferred to a computer and the arteries' diameters were compared statistically. No statistically significant differences were detected among the groups with respect to the arteries' diameters immediately after surgery. All of the groups showed increases in the arteries' diameters after the pharmacological agents were applied. No significant difference was detected between the metamizole and papaverine groups with respect to the

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arteries? diameters following pharmacological agent application, but the arteries? diameters in these two groups were larger than the arteries? diameters in the lidocaine group ($p < 0.001$). These findings show that metamizole, which is very widely used because of its analgesic and antipyretic effects, is as effective as papaverine at alleviating vasospasm. Topically applied metamizole is considered a good alternative to correct vasospasm during microsurgery.

09:20-09:28 Karaca Basaran / Idris Ersin The free-nipple breast-reduction technique performed with transfer of the nipple-areola complex over the superior or superomedial pedicles.

FUNDA AKOZ SAYDAM, IDRIS ERSIN, MEMET YAZAR & AHMET CEMAL AYGIT

Institution: Bagcilar Research and Training Hospital Plastic Reconstructive and Aesthetic Surgery Department, Istanbul, Turkey

INTRODUCTION: Although the free-nipple breast-reduction technique is essentially an amputation, achieving aesthetic results still is important. The authors present their technique for free nipple-areola complex (NAC) transfer over the superomedial or superior pedicle full-thickness flaps in patients for whom a free-nipple technique is inevitable due to certain risk factors. MATERIALS AND METHODS: The study included 25 patients who underwent surgery with the aforementioned method for addressing severe gigantomastia. The patients had a mean age of 43 years (range 34-59 years) and a mean body mass index (BMI) of 35.8 kg/m² (range 28-42 kg/m²). During the operation, the NAC was elevated as a full-thickness skin graft, then transposed to the superior or superomedial pedicles, which had been planned previously. The subsequent stages of the operation thus became a Wise-pattern breast reduction. RESULTS: The mean resection per breast was 1,815 g (range 1,620-2,410 g). Breast projection, shape, and areolar pigmentation were assessed during the follow-up visit. One patient experienced a partial loss of the NAC graft, which healed secondarily, and three patients experienced a patchy hypopigmentation of the NAC. Breast projection and conical structure were observed to be preserved during the follow-up period. CONCLUSIONS: The modified free-nipple technique aimed to convert the reduction procedure to a technique similar to pedicle methods, yielding successful results during the early phases. The full-thickness flap constructed in this way provides more fullness and a maximum contribution to projection in patients who will inevitably undergo breast reduction with the free-nipple method. (This paper was published in Aesthetic Plastic Surgery Journal in 2014)

09:28-09:36 Nina Goesseringer Intraoperative team approach in order to optimise DIEP reconstruction

Maria Rydevik-Mani, Lorenzo Cali-Casi, Antonia Pappadopoulos & Andres Rodriguez Lorenzo
Uppsala University Hospital, Sweden

Introduction: Breast reconstruction with deep inferior epigastric artery perforator (DIEP) flap is considered the gold standard in autologous breast reconstruction. Hence, DIEP flap reconstructions are still regarded as advanced and resource intense surgical procedures, with long operative surgical time. We hypothesize that a team approach with dedicated microsurgical operating staff reduces the operation time and postoperative complications. Materials and Methods: 100 consecutive patients underwent unilateral DIEP reconstruction with a standardized approach. The patients were operated by 1 to 3 microsurgeons. Groups were compared based on the number of microsurgical-trained specialists. A statistical analysis was performed with ANOVA for operating time and chi-square test for complications. Results: 16 patients were operated by a single microsurgical trained specialist, 64 by 2 and 20 by 3. Increasing number of microsurgical-trained specialists was associated with a trend of shorter operating time. The minimum operating time decreased with increasing number of specialists. Overall, flap failure rate was 2%, and both of these cases occurred in the group operated by a single specialists. 9 take backs were performed due to hematoma and 9 cases of venous congestion occurred. There was no significant difference in take back rate between the different numbers of

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participating surgeons. Conclusions: A standardized team approach is needed for optimization of the procedure's workflow during surgery. Team approach may reduce extreme operation times and complication rate. By optimizing the surgical experience available during DIEP flap breast reconstruction ? including trained nurses and theatre set up - operation time can be reduced and efficiency improved. Team approach provides a platform for education and mentorship of less experienced surgeon to decrease the learning curve in a safe manner. Two microsurgical-trained surgeons achieved optimal operation flow with lowest complication risk.

09:36-09:44 Rob Staruch Mechanical analysis of Nanocomposite Bipolymer Hydrogel Foams for military wound healing

Shehan Hettiaratchy, Rory Rickard, Alexander Seifalian & Peter Butler

Introduction Military injuries often include large soft tissue wounds that require a significant amount of long-term reconstruction. Tissue engineering may yield solutions for these complex wounds. Firstly, the aim of this work was to investigate low pressure foam synthesis for production of composite foam scaffolds. Secondly, to compare mechanical properties of synthesised composite hydrogel foam against current clinical foams. We characterised a novel scaffold synthesis method and mechanically tested composite scaffolds. Materials & Methods Polyhedral oligomeric silsesquioxane poly(carbonate-urea) urethane (POSS PCU) and polyhedral oligomeric silsesquioxane polycaprolactone (POSS PCL) were synthesis as per a previously described method. Deacylated Chitosan and Gelatin were purchased from Sigma Aldrich. Gelatin and chitosan were mixed with POSS PCU and POSS PCL in increasing concentrations. In brief polymer solutions were placed into a sealed container. Nitrous oxide gas was delivered through pressurized delivery capsules. Cannister pressure was monitored throughout using a PXM409-350BAUSBH pressure transducer. Polymers were pressurised at room temperature. Polymers were depressurised into a rectangular container and underwent a phase conversion in deionised water. Foams scaffolds were then characterised for pore size, porosity, compressive modulus using a Instron universal testing machine and compared to the industry standard; Granufoam. Results Foams containing POSS PCU, POSS PCL, Gelatin & Chitosan were synthesised as unipolymer and biopolymer composite scaffolds. The addition of Gelatin to POSS PCU created low density high porosity hydrogel foams. The addition of Chitosan to POSS PCL created low density medium porosity foams with superior mechanical properties. The compressive stress at maximal load, CSML, of all novel foams was greater than control foam Granufoam. Furthermore compared to Granufoam the novel foams had higher porosities and lower densities. Conclusions Polymer nanocomposite hydrogel foams were synthesised for a potential injectable application in military wounds. Our foams showed superior mechanical properties to gold standard Granufoam.

09:44-09:52 Rossella Sgarzani Pressure ulcers in patients with spinal cord injuries: concordance between ulcer swab and intra-operative culture for the aetiological diagnosis of infection.

Luca Negosanti, Sara Tedeschi, Donatella Brillanti & Riccardo Cipriani

Plastic Surgery Dpt, S.Orsola Malpighi Hospital, Bologna, Italy

OBJECTIVE: To assess predictive value of ulcer swab specimen culture in identifying etiological agents of infection in patients with spinal cord injury (SCI) and pressure sores. METHODS: Prospective, observational, single-centre study on adult patients with spinal cord injury undergoing surgical debridement and reconstruction for pressure ulcers at Montecatone Rehabilitation Institute from July 2011 to January 2014. Before surgery an ulcer swab specimen was taken with Levine's technique and sent for culture. During surgery bone and soft tissue specimens were collected, and sent for culture and histological evaluation. Results of cultures of swabs and intra-operative specimens were compared. RESULTS: During the study period 64 patients were treated. On admission 37

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patients (58%) had fever, median CRP serum level were 2.3 mg/dL (IQR 1.4-5.2). According to histology of intra-operative specimens, diagnostic certainty of osteomyelitis was present in 53% patients (34/64). Culture of intra-operative specimens yielded monomicrobial infection in 30% and polymicrobial infection in 47% of cases; culture was negative in 23% of cases. The most common microorganisms found were S.aureus, P.mirabilis and P.aeruginosa, which were cultured in 33%, 19% and 12.5% of cases, respectively. Results of culture of swabs and intra-operative specimens were concordant in 25% of cases (16/64). Main reason for non concordance was yielding of a different microorganism (40%), false positive (swab culture positive/intra-operative culture negative) were 13 (20%) and false negative (swab culture negative/intra-operative culture positive) were 10 (15%). At univariate analysis the presence of osteomyelitis was associated with non-concordance ($p=0.001$). CONCLUSION: In our cohort of patients with SCI and infected pressure ulcers, results of culture of swab specimen were predictive of etiology of infective process only in 25% of cases. These findings suggest that ulcer swab specimen culture is not reliable enough to guide the choice of antimicrobial therapy in clinical practice, especially when osteomyelitis is present.

09:52-10:00 Fatih Ceran Evaluation of the retro-orbital fatty tissue volume in delayed orbital blow-out fractures

Ozgur Pilanci, Samet Vasfi Kuvat & Mehmet Sagir
Bagcilar Training and Research Hospital, Istanbul

Introduction: In patients where diplopia and enophthalmia are manifest, surgical intervention is usually indispensable. The pathogenesis of these symptoms usually includes the prolapse of the orbital tissues into the sinus or compression by the surrounding bone structures. Although the retro-orbital fatty tissue, orbital fascia and the muscle tissue can be reduced to the original place after being incarcerated into the maxillary space, it is obvious that the procedure will lead to significant fibrosis in these structures. We have aimed to carry out a quantitative evaluation of the fatty tissue volumes in delayed patients. Materials and Methods: The preoperative and postoperative fatty tissue volume and the changes in this volume were evaluated by using computed tomography on the patients (n: 9) who were consulted to our clinic from other health centers. Results: Although no significant correlation was observed between the prolapsed volume and the postoperative reduction in the fatty tissue, the reduction in the retro-orbital fatty tissue was statistically significant. Conclusion: We think early surgical intervention and surgical trauma are the main factors on retro-orbital fatty tissue volume. Although the prolapsed tissue can be surgically replaced, volume losses in the retro-orbital fatty tissue may be observed during the postoperative period and this situation might be attributed to surgical trauma. We are of the opinion that quantitatively describing the reduction in the volume of the fatty tissue may shed light to the planning of secondary procedures.

10:00-10:08 Petros Konofaos A comparison of cranioplasty materials using an impact testing model in rabbits

Petros Konofaos, Craig Salt & Robert Wallace
University of Tennessee Health Science Center, USA

Introduction: The objective of this study was to evaluate the neuroprotective properties and structural integrity of polymethylmethacrylate (PMMA) and porous polyethylene (PP) in comparison with those of autologous bone grafts by using a rabbit impact model. Material and Methods: The study involved the creation of a 25mm x 20mm oval skull defect in 16 adult New Zealand white rabbits which were randomly divided into four groups (n=4). In three groups, a cranioplasty was performed with the use of either PMMA, PP or with a bone flap. In the control group the animals were not undergone any means of reconstruction. At the end of the 8th week, the animals were sedated and an impact test was performed at the center of each cranioplasty. Then the animals were euthanized and the cranium and

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the brain of each animals were taken for macroscopic and histological evaluation. Results: There was a statistical significant difference among groups for the severity of the hemorrhage ($p=0.022$) and the grade of cranioplasty disruption ($p=0.0045$). There was no significant differences between the groups in terms of the ranges of energy levels delivered at impact testing ($p=0.75$). Autologous bone was found to be the weakest of the materials tested. In this group severe injury resulted at much lower energy levels than was observed in the control, PMMA, or PP groups. Both PMMA and PP were resistant to fracture and disruption. PMMA provided the greatest neuroprotection, followed by PP. Conclusions: This pilot study confirmed both PP and PMMA consistently provided a level of neuroprotection superior to that obtained with a native bone flap, with PMMA to offer the highest protection. The factor most closely associated with neuroprotection was the interface that the cranioplasty material made with the surrounding skull. This bond was the strongest in the PMMA group followed by the PP group.

10:08-10:16 Luca Negosanti Usefulness of magnetic resonance in the diagnosis of osteomyelitis in patients with spinal cord injury (SCI) and pressure ulcers.

Rossella Sgarzani, Sara Tedeschi, Mattia Rizzi & Paolo Morselli
Bologna, Italy

OBJECTIVE To assess usefulness of magnetic resonance (MR) in pre-operative diagnosis of osteomyelitis in patients with spinal cord injury (SCI) and pressure ulcers. **METHODS** Prospective, observational, single-centre study on adult patients with spinal cord injuries undergoing surgical debridement and reconstruction for pressure ulcers at Montecatone Rehabilitation Institute from July 2011 to January 2014. In the 30 days before surgery patients underwent MRI. In MRI criteria for diagnosis of osteomyelitis included cortical bone erosion, abnormal signal of the marrow on T1-weighted and STIR images, soft-tissue edema, deep collections, heterotopic new bone, hip effusion. During surgery bone and soft tissue specimens were collected, and sent for culture and histological evaluation. The histological result of bone intra-operative specimens was the reference for the definitive diagnosis of osteomyelitis. **RESULTS** During study period 85 patients were included in the study. Pre-operative MR was positive for osteomyelitis in 45 cases. According to histology, osteomyelitis was definitively diagnosed in 40 patients. MR findings and histology were concordant in 61% of cases (52/85); 19 false positive (MR positive/histology negative) and 14 false negative (MR negative/histology positive) cases were found. Sensitivity and specificity of MR in the diagnosis of osteomyelitis were 65% and 58% , respectively, with a positive predictive value of 58% and a negative predictive value of 65%. **CONCLUSION** In our cohort sensitivity, specificity, positive predictive value and negative predictive value of MR for the diagnosis of osteomyelitis in patients with SCI and pressure ulcers are lower than previously described. Our findings suggest that MR cannot be considered a reliable diagnostic technique for the diagnosis of osteomyelitis. Further studies are needed to investigate this topic.

10:16-10:24 Cristina Auba Effect of postoperative brachytherapy and external beam radiotherapy on functional outcomes of immediate facial nerve repair after radical parotidectomy

Diego Marre, Alvaro Cabello & Bernardo Hontanilla
Pamplona, Spain

Introduction: Th effect of brachytherapy on facial nerve regeneration has not been studied. On the other hand, there is much controversy regarding the effect of radiotherapy on functional outcomes after nerve repairing. We propose to evaluate the effect of postoperative brachytherapy and external beam radiotherapy on functional outcomes of immediate facial nerve repair after radical parotidectomy. **Patients and methods:** Fifty-three patients underwent total parotidectomy of which 13 were radical with

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sounds were assessed and compared for evaluation of treatment success. Results: There was a statistically significant reduction in pain intensity and joint sound and an increase in mouth opening in the study group when compared with the control group. Conclusions: This study shows that intra-articular PRP injection for the treatment of reducible disc displacement of the TMJ is a more effective method than arthrocentesis.

10:40-10:48 Fatih Ceran Use of Anastomotic Microvascular Device or Hand-Sewn Anastomoses for Arteriovenous Shunts: An Experimental Study in Rats

Samet Vasfi Kuvat & Ozgur Pilanci

Bagcilar Training and Research Hospital, Sokak

Introduction The microsurgery is facing the most brilliant age of its history. The anastomotic microvascular device (AMD) has marked an era in microsurgery over the last two decades. These developments in microsurgery are raising awareness further about the work that we do. We try to maintain our traditions on the other hand. Undoubtedly, our most important tradition is hand-sewn microsurgery (HSM). Microsurgery has been performed by using HSM which remains the most preferred method. The aim of this experimental study was to compare the features of the anastomotic microvascular device and hand-sewn microsurgery on arteriovenous shunts. **Material and Methods** **HSM Group:** Arteriovenous shunt was performed between carotid artery and internal jugular vein by using 10/0 Ethilon (Ethicon Co.) suture with the principles of hand-sewn microsurgery. **AMD Group:** Arteriovenous shunt was performed between carotid artery and internal jugular vein by using the 1-millimeter anastomotic microvascular device. **Results** Arterial anastomosis technically more challenging and not suitable as they have more muscular walls. Anastomotic time is faster with the coupler device compared to hand-sewn technique. Flow Vol ; Ved (cm/sec) ;V max (cm/sec) rates were found significantly higher in the AMD group than HSM group. Endothelialization and wall integrity rates better in AMD group, however, subintimal thickening occurred more in this group. A significant difference was not observed for the presence of inflammatory cells and fibrin escape rates in both groups. **Conclusion** This study has shown that AMD is less thrombogenic, faster than HSM. High quality and durability of vascularization, insignificant foreign body reaction are histopathological advantages of AMD. Costs and arterial challenges are disadvantages for microvascular device use.

10:48-10:56 Rojda Gumuscu Acellular dermal matrix and dermal flaps in one-stage breast reconstruction after mastectomy

Anne Therese Lauvrud, Ulrika Fallbjörk & Malin Sund

Umea Universitet Sjukus, Sweden

Background There are different techniques of immediate reconstruction, but it is currently not established which method is most cost effective, safe and gives the best aesthetic result. Use of acellular porcine matrix (PAM) in one-stage immediate breast reconstruction makes it possible to select a more suitable implant size, which can give better aesthetic results. An option to PAM is using a dermal sling. The aim of this study was to determine the outcome of one-stage immediate reconstruction after breast surgery at our department. **Method** All patients operated with one-stage breast reconstruction volunteered to participate in the study. We used PAM or dermal slings in combination with silicone anatomical implants. **Results** Between January 2010 and January 2015, a total of 34 patients were operated with skin sparing mastectomy combined with one-stage immediate reconstruction. The indication for mastectomies was ductal carcinoma in situ, except one patient undergoing bilateral mastectomy because of diabetic mastopathy. None of the patients had undergone radiotherapy. In 26 patients the nipple areolar-complex sparing (NAC) technique was used. Negative frozen section from underneath NAC was analysed in all these cases preoperatively. The average drainage time was 10 days. Six patients (17,6%) had to remove the implant because of deep

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infections, two of these had been reconstructed with dermal flaps and four with PAM. Conclusion In this small cohort with an average follow-up time of 32 months no significant see any difference between patients operated with PAM or dermal sling in immediate breast reconstruction as a one-stage procedure when considering drainage time, LOS and implant removal rate. However, there was a tendency for more implant removals using PAM. This needs to be verified in a larger cohort with longer follow-up. We consider the methods safe, predictable with good aesthetic results and probably cheaper than 2 stage procedures.

10:56-11:04 CJ Tollan Introoperative Laser Doppler Scanning: A comparative study of SIEA and DIEAP flaps

Iain Mackay

Canniesburn Plastic Surgery unit, Glasgow, Scotland

Introduction The free Deep Inferior Epigastric Artery Perforator (DIEAP) flap is the breast reconstruction of choice in suitable patients. A modification of this is the Superficial Inferior Epigastric Artery (SIEA) flap which leaves less donor site morbidity. The aim of this study was to compare the perfusion of the DIEAP flap and the SIEA flap. **Material and Methods** 10 patients undergoing DIEAP breast reconstruction were scanned intraoperatively using a Laser Doppler Scanner. The lower abdominal flap was raised on four vessels, the DIEAP and SIEA from each side. The laser doppler scanned the lower abdominal skin flap with one vessel supplying the flap and the other three clamped. The four vessels were scanned sequentially. A previous prospective pilot study was undertaken to confirm the feasibility and reproducibility of intraoperative clamp and scan times. The order was randomised and the total scanning time took no more than 35 minutes per patient. **Results** The mean flow associated with DIEAP vessels is higher than that with SIEA vessels ($P=0.007$). There was a significant difference between the zones ($P<0.001$). The DIEAP Hartrampf zones in order of perfusion were 1, 3, 2, 4. This agrees with Dinner's description of better ipsilateral perfusion in the DIEAP flap, rather than Hartrampf's original description of TRAM flap zones. For the SIEA flap there was no statistically significant difference in flow between zones 1, 2 & 3 ($P<0.05$), and all were highly significantly better perfused than zone 4, $P<0.001$. **Conclusions** This study supports previous work confirming that the DIEAP preferentially supplies the ipsilateral hemiflap compared to the SIEA which is better suited for crossing the midline. This study also suggests that the SIEA flap may provide a large skin paddle on a single pedicle with excellent donor site for use in a wide range of reconstructive situations.

11:04-11:12 Beniamino Brunetti ~~The propeller transposition flap: a reliable geometrical design to improve the vascular safety of perforator based propeller flaps~~ ~~Withdrawn~~

11:12-11:15 Open Discussion Time

11:15 - 11:30 Break

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SESSION 2: Tissue Engineering

Chairing: Prof. Arndt Schilling, Munich & Prof. Dr. Hans-Günther Machens, Munich

11:30-11:39 Zita Jessop A morphological and biophysical analysis of immature and mature bovine auricular cartilage: Implications for tissue engineering

Sian Morgan, Emman Combella, Ilyas Khan & Iain Whitaker

Welsh Centre for Burns and Plastic Surgery, Swansea University; College of Medicine & Centre for NanoHealth, Wales

Introduction and Aims Routine clinical use of regenerative medicine technologies to replace lost cartilage is elusive. In part this is due to the 'immaturity' and structural instability of tissue engineered constructs. Our previous work in articular cartilage has shown that maturation of cartilage stabilises tissue inducing profound morphological, structural and biochemical change. Biologically inducing maturation has the potential to provide stable tissue engineered cartilage for aesthetic and reconstructive facial surgery. **Materials and Methods** We used bovine ears (n=5) as a model system to investigate the morphological, histochemical and biomechanical differences between immature (aged 1-3 weeks) and mature (aged 18 months) auricular cartilage. Morphology was evaluated using histological stains (H&E, Alcian Blue and Safranin-O). Cartilage component assays were used to assess water content/biochemical composition and mechanical properties were assessed using cross-linking analysis to determine the effect of maturation on collagen organisation. **Results** We found profound regional differences between the immature and mature study groups when considering - 1) Architecture and cellularity of auricular cartilage (P<0.05) 2) Tissue hydration and proteoglycan content (P<0.05) 3) Elastin content and collagen volume / cross-link configuration. **Conclusion** These findings suggest there are significant differences between immature and mature auricular cartilage. The ability to biologically induce maturation in tissue engineered cartilage offers the potential provide stable tissue engineered cartilage for aesthetic and reconstructive facial surgery.

11:39-11:48 Richard Wong A Microsurgical Model for Tissue Engineering in the Mouse.

Jason Wong

University of Manchester

Introduction: Reproducing functional and viable tissue following injury or disease remains an important goal in the field of tissue engineering. The creation of an arteriovenous (AV) shunt graft within an engineered scaffold has been shown to spontaneously generate vascularized tissue. This vascular conduit directs highly pressured arterial blood into a thinner walled vein graft resulting in hydrostatic gradients that increase angiogenesis, vascular tissue formation with an intricate microcirculation. Understanding the mechanisms that underlie this phenomenon may result in directing growth to specific tissue or organ end-points and may be applicable to the field of reconstructive surgery and tissue transplantation. **Methods & Materials:** The study involved creation of an AV shunt in the leg of the mouse. These AV shunts were placed within a number of custom-designed porous chambers for 2 and 4 weeks. Chambers were weighed and analysed for matrix production, protein deposition and cell infiltration. **Results and Conclusions:** We show that the mouse microsurgical model increases angiogenesis and the volume of tissue generated in the mouse. Proteomic analysis suggests the presence of the AV shunt up-regulates collagen formation, cytoskeletal proteins and down-regulates MAPK/ERK 1, 3 and 5: cell proliferation and differentiation signals. The mouse AV shunt model provides us with a genetic tractability system to interrogate the mechanisms by which new tissue forms from the shunting phenomenon. Identifying these novel mechanisms will allow us to manipulate future tissue engineered tissues for better tissue integration. Funding RCS(Edin)

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11:48-11:57 Georgina Wellstead / Tom Pidgeon The Need for Core Outcome Reporting in Autologous Fat Grafting for Breast Reconstruction

Riaz Agha, Alexander Fowler, Thomas Pidgeon & Georgina Wellstead

Institution not stated

INTRODUCTION There is growing interest in the potential of autologous fat grafting (AFG) for breast reconstruction. This systematic review examines the range of outcomes used across studies of AFG, their definitions and whether there is a need for a core outcome set to aid reporting. **METHODS** Following the protocol of our previous systematic review, a search of 20 databases (1986 to March 2014) returned 35 studies which met the inclusion criteria for our systematic review. These were assessed independently by two authors. Disagreements were resolved by consensus. **RESULTS** Of 35 studies, 27 (77%) were case series, 5 (14.3%) were cohort studies and 3 (8.6%) were case reports. A total of 51 different outcomes were reported. Of these studies, each reported a median of 5 separate outcomes (range 2-14), of which a median of 3 outcomes were defined (range 0-14). A median of 2 outcomes per paper were pre-specified in the study methods (range 0-12) and a median of only 2 outcomes per paper (range 0-12) were both defined and pre-specified. The most commonly reported outcome in studies of AFG was that of 'Operative details?', reported by 26 studies, and 8 different outcome definitions were used. 'Cancer recurrence?' was reported by 20 studies, with the use of 10 different outcome definitions. Overall, there was a poor proportion of defined and pre-specified outcomes that employed a wide range of different outcome definitions. **CONCLUSION** There is a need for a core outcomes set for autologous fat grafting to minimise outcome and reporting bias and aid evidence synthesis.

11:57-12:06 Zita Jessop A novel isolation protocol for auricular cartilage derived stem cells (CDSCs) and implications in cartilage tissue engineering

Mohammad Javed, Sian Morgan, Ilyas Khan & Iain Whitaker

Welsh Centre for Burns and Plastic Surgery, Swansea University; College of Medicine & Centre for NanoHealth, Wales

Introduction Manufactured allogeneic tissue-engineering based technologies have the potential to avoid donor site morbidity. In the case of cartilage, the use of non-related stem cell sources (eg: ADSCs) produces inelastic cartilage, prone to calcification. We present a novel protocol for isolation and characterization of chondroprogenitors (CDSCs) and discuss findings in the context of manufacturing workflow strategies for regenerative medicine therapies. **Methods** Human and bovine auricular cartilage samples were stored at 2-8°C in sterile media (DMEM with 1% gentamycin) and processed within 6 hours using a pronase/collagenase digest. CDSCs were isolated using differential fibronectin cell adhesion assays. CDSCs were expanded and differentiated into chondrocytes under 2D culture (to 70-80% confluence before being detached and cryopreserved) and pellet culture conditions at 37°C 5% CO₂. **Results** Our findings include the first demonstration of CPCs in the chondrium in addition to the perichondrium that had been previously described. Cell digests produced over 50% cell viability using trypan blue staining. The iCELLigence impedance-based cell assay system allowed us to determine optimal conditions for cell growth, proliferation and adhesion in real time. Single CDSCs formed colonies that contained over 64 cells each after 2 weeks. We discuss these results in the context of the manufacturing workflow for autogenous and allogeneic regenerative medicine therapies. **Conclusions** We isolated CDSCs from the chondrium and demonstrated high proliferative and chondrogenic potential. Efficient isolation of CDSCs from human auricular cartilage and optimisation of cell growth and differentiation is a crucial step towards clinical translation.

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12:06-12:15 Libor Streit Effect of Sedimentation, Centrifugation and Membrane-Based Filtration on Human Adipose Derived Stem Cell Content and on Viability and Morphology of the Fat Graft

Josef Jaro, Veronika Jurtkov, Ale Hampl & Jiř Vesel

Department of Plastic and Aesthetic Surgery, Masaryk University, Czech Republic

Introduction: Fat grafting is a promising surgical technique using patient's own adipose tissue for regeneration and augmentation. Adipose-derived stem cells (ASCs) are reported to be responsible for the regeneration. The percentage of viable cells correlates with its ultimate survival volume. The aim of this study was to find differences in selected properties of fat graft when processed by commonly used techniques. Material and Methods: Adipose tissue was harvested from hypo-gastric region in 14 healthy patients by manual liposuction. Aspirated tissue was processed by sedimentation, centrifugation, and membrane-based filtration. In centrifugation protocol, adipose layer was divided to low-density (upper 2/3) and high-density (bottom 1/3) fractions. Volume percentages of the processed fat to the initial volume of lipoaspirate were calculated. The morphology of individual samples was evaluated by scanning electron microscopy and its overall viability was assessed by live-dead assay. Then each sample was enzymatically digested and the isolated cells were counted and seeded on culture plates. The number of adherent cells was assessed using nuclear staining followed by fluorescent microscopy. The stem cell character was confirmed by specific surface marker expression (CD105+, CD90+, CD31-, CD45-) and cell capacity to differentiate into adipogenic and osteogenic lineages. Results: The highest number of isolated ASCs per 1 ml of lipoaspirate was obtained by centrifugation technique from the low-density fraction. The volume of aqueous component was the lowest in the membrane processed fat suggesting high ultimate fat graft survival volume. Overall viability was about the same in all samples. We observed significant structural changes on submicroscopic level of tissue samples - the extracellular matrix was best preserved by sedimentation technique, but the sample was filled with oil drops and residues of disrupted adipocytes. Oil drops were best eliminated by the membrane-based filtration. Conclusions: Centrifugation and membrane-based filtration are effective and profitable processing techniques for fat-grafting.

12:15-12:24 Hazem Alfeqy Prevention of post primary flexor tendon repair peritendinous adhesions using bone wax

Haitham Khashaba, Mohamed Abdelrahman & Ahmed Taha

Canniesburn Plastic Surgery Unit, Glasgow, Scotland

Peritendinous adhesion is an important cause of poor functional outcome after flexor tendon repair. The prevention of these adhesions after flexor tendon repair is still challenging all plastic and hand surgeons. The objective of this study is to evaluate the effect of application of bone wax within the sheath after the tendon repair on the peritendinous adhesion. 50 patients with post traumatic cut of flexor digitorum profundus and superficialis zones 1-4 were randomized into two groups. One is treated with the modified Kessler repair with application of the wax (n = 25), and the other is treated with modified Kessler repair without the wax (n = 25). Each group underwent the same procedure, post operative care and later follow up and evaluations based on regular basis at 3, 6, 12, 18 months. There was a significant decrease in the postoperative adhesions in the group treated with the bone wax combined with the conventional repair in comparison to the control group. There were no significant complications or weakened repair. In contrast, the use of the wax was easy to apply, not bulky, not associated with any allergic reactions or fibrosis and not restricting the tendon gliding movement. Key Words: flexor tendons, bone wax, peritendinous adhesions, prevention.

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12:24-12:33 Volodymyr Protsenko Replacement of post-resection bone defects in tumors using material based on bioactive glass

Volodymyr Chorney & Alexander Ilnitskyi

Institute of Traumatology and Orthopedics NAMS of Ukraine

Introduction: Replacement of post-resection bone defects remains today an unsolved problem. The use of bone autoplasty causes an additional surgical trauma. The use of allogeneic transplant may cause the transfer of infection from the recipients, immunological conflict between donor and recipient, which may become the reason of festering or transplant rejection. In this regard, the new material based on bioactive glass has been developed and introduced into clinical practice. This biocomposite material has a complex (osteoconductive, osteoinductive) mechanism of action. Our aim is to evaluate the results of the use of material based on bioactive glass to replace the post-resection defects of bone in patients with benign tumors and tumor-like diseases. Material and methods: Material based on bioactive glass was used to replace the post-resection defects in 127 patients with tumors and tumor-like bone diseases of different localizations. Biocomposite material was used in the form of beads, plates, gel. Follow-up period was from 3 months to 5 years. Results: In all cases, in 2-4 months after surgery the X-ray has detected signs of incipient replacement of post-resection defect with trabecular bone in the zone of a material injection. During the next follow-ups with the period up to 5 years, a partial or complete replacement of a defect in the zone of a material injection was observed. In all cases, after application of the material based on bioactive glass the postoperative wounds were healed by first intention. Allergic or hypersensitive reaction was not observed. Conclusion: Biocomposite material based on bioactive glass has shown high efficiency in post-resection replacement of bone defects in patients with benign tumors and tumor-like diseases due to its osteoconductive and osteoinductive properties.

12:33-12:42 Mary Frimpong ~~Investigating the matrix chemistry of human adipose-derived stem cells: the first step toward creating a scaffold for optimal adipose tissue engineering with a biomimetic approach~~–Withdrawn 26/5/15

12:42-13:00 Open Discussion

13:00 – 14:00 LUNCH

13:15 – 13:45 National Delegates Meeting & 2016 Research Council Planning Meeting

Chair: Benedetto Longo

Venue: main lecture theatre

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SESSION 3: Peripheral Nerve

Chairing: Prof. Andrew Hart, Glasgow & Ms. Eva Placheta, Vienna

14:00-14:08 Maham Hadi A novel self-assembling nanopeptide hydrogel to deliver cell therapy for peripheral nerve regeneration

Maham Hadi, Alessandro Faroni, Alberto Saiani & Adam J Reid
University of Manchester

Introduction - In recent years, experimental work has focused on delivery of cellular therapies to promote peripheral nerve regeneration. In order to be delivered to the site of injury, cells require a scaffold that will support their survival whilst permitting neurotrophic action. The scaffold should be non-toxic and degradable in a sensible timeframe. Self-assembling nanopeptide hydrogels offer a novel approach to this problem. Our aim was to study the viability of stimulated human adipose derived stem cells (dASC) on a FEFKFEFKK (F9) hydrogel. Materials & Methods - The manufacturing method of F9 was optimised for pH and peptide concentration to enable cell survival and attachment. Viscoelastic properties of F9 with and without cells were assessed by oscillatory rheology. Cell proliferation, viability and cytotoxicity were assessed and compared with Matrigel. Subsequently, BDNF protein expression was quantified with ELISA. Results - F9 peptide can self-assemble to form usable hydrogels with storage modulus of 5000 Pascal with a concentration of 30mg/ml. F9 was found to permit greater proliferation and less cytotoxicity than the Matrigel, whilst cell viability was significantly greater ($P < 0.001$). BDNF expression was significantly greater in the F9 environment than in the Matrigel ($P < 0.01$). Conclusions - This is the first study known to us that demonstrates compatibility of self-assembling nanopeptide hydrogels with human ASC. We hope that it will lead to further exploitation of the potential of this hydrogel in cell delivery particularly in the field of peripheral nerve injury.

14:08-14:16 Suzanne Thomson Understanding cell and molecular scale events regulating peripheral nerve repair

Theo Dejardin, Paul Kingham, Mathis Riehle & Andrew Hart
University of Glasgow, Scotland

Peripheral nerve injury is common (1/1000) and can be functionally devastating. Despite advances in microsurgical repair axonal regrowth across the repair site, and as such functional outcome, remain unsatisfactory. The neurobiology of the nerve repair must be unravelled in order to identify therapeutic targets. Nerve repair has previously been shown to respond to both intrinsic and extrinsic factors and the directionality and rate of axonal regrowth following injury can be enhanced in vitro by growing cells on a patterned surface. Following construction of microtopographically patterned substrates this study used qualitative RT-PCR to demonstrate the downstream genetic effects of this extrinsic mechanical cue. Gene expression was measured at day 0, 1, 2, 5 and 10 following injury, of nerves grown on either the patterned surface or a smooth control, using the Sprague-Dawley in vitro model. Altering the topographical substrate on which nerves were grown resulted in a significant alteration in phenotype and differential expression of the target genes studied. Expression timelines are presented and the molecular pathways are discussed. In cell western and immunofluorescence were used to demonstrate protein expression and localise targets. This study further characterises a useful in vitro model and provides more detail on the complex interactions underlying nerve repair. It highlights some of the downstream molecular effects of microscale patterning, that could be harnessed in the surgical setting by using patterned nerve conduits, and provides further evidence for potential pharmaceutical targets for future clinical translation.

14:16-14:24 Federico Facchin Is what we know about the Palmar Fascia enough?

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Federico Facchin, Luca Lancerotto, Cesare Tiengo & Franco Bassetto

Institution: not stated, Padova, Italy

Background: The palmar fascia is the fibrous system of the hand, which fibers create a complex 3D network through the palm and the fingers. The longitudinal fibers from the palmaris longus tendon spread through the palm in the sub-dermal layer, forming pretendinous bands. The transverse fibers form the proximal transverse ligament and the natatory ligament. The vertical fibers, also called septa of Legueu e Juvara, define seven longitudinal compartments of the midpalmar region of the hand. Dupuytren's contracture is the primary disease affecting the palmar fascia. Its physiopathology and the causes responsible for the high risk of recurrence after surgery are not clearly defined yet. Materials and Methods: The anatomical features of the palmar fascia, in relation to the potential relevance for the understanding of the fibroproliferative tissues diffusion in the Dupuytren's disease, were evaluated in 15 fresh-frozen and fixed cadaver hands. Results: The analysis of the relationship of the three main groups of fibers revealed two different types of interaction. The vertical fibers of the vertical septum ulnar to the flexor tendon apparatus of the III, IV and V fingers are straight and continuous from the skin to the deep layers of the hand. The vertical fibers of other septa are interrupted by the transverse fibers. Conclusion: The continuous vertical fibers could represent for the affected tissue of the palmar fascia a preferred path of progression through the depth of the hand. Hence clarifying the microscopical anatomy of the palm could improve the outcome of the treatment of Dupuytren's disease.

14:24-14:32 Li Yong An anatomical study of the dorsal branches of the digital nerves

Anna Kinsella, Gordon Findlater, Christopher Charles Booth, Simon Parson & Dominique Davidson

Introduction: A particular challenge when operating on Dupuytren's disease is the presence of spiral cords. Their close relationship with the neurovascular bundle, at the base of the finger, can distort the usual anatomy and displace the bundle medially. The dorsal branches (DBs), from the digital nerves (DNs), arise in this area may, if large in diameter, be mistaken for DNs, leaving DNs at risk of injury. Descriptions of the anatomical consistency, origin and diameter of the DBs relative to the DNs vary in the available literature. However a clear understanding of this anatomy is critical to avoid nerve injury during surgery. Materials and Methods: Dissection was performed on 10 fresh-frozen cadaveric hands under 3.0x loupe magnification. The origin of the DB was measured relative to the proximal A1 pulley and to the common digital nerve (CDN) bifurcation. The diameters of the DNs and DBs were measured immediately distal to DB origin, with an eyepiece graticule, and the mean of three measurements was calculated. Results: DBs were found on both sides in the majority of digits (89±3.1% of 100 digits). The DBs originated at or proximal to the A1 pulley in 58%, 11% arose proximal to the pulley and 34% of cases were found distal to the A1 pulley. Relative to CDN bifurcation, the CDN-DB range was 19.8-40.3mm and DB originated most proximally on the ulnar side of the little finger. DBs were consistently more than half the diameter of the corresponding DNs. This was particularly the case for the radial side of the middle finger (DN:DB;1:0.98) and the ulnar side of little finger (DN:DB;1:0.93). Conclusion: Our study provides an anatomical description and comparison of DBs and DNs across all digits of the hand. This knowledge guides safe operative dissection and highlight the use of DBs as suitable nerve donors for repair of damaged DNs.

14:32-14:40 Rosanna Ching Exosomes from adipose-derived stem cells as mediators of nerve regeneration

Peyman Kelk, Mikael Wiberg & Paul Kingham

Umea University, Sweden

Introduction Functional outcome following significant peripheral nerve injury remains poor despite the various treatment options currently available. This impacts considerably on both patients and society

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as sufferers are commonly young workers. We hypothesise that exosomes (small intercellular messaging particles) isolated from adipose-derived stem cells differentiated into a Schwann cell-like phenotype (dASCs) can contribute to the development of new strategies for treating these injuries. Materials and Methods Exosomes were isolated from Schwann cells (SCs) and dASCs cultured from male Sprague-Dawley rats and applied to neurons in vitro. Computerised image analysis was used to assess neurite outgrowth after 24 hours. Exosomal cargo was also investigated using RT-PCR techniques to identify mRNA and microRNA involved in nerve regeneration. Results Neurons incubated with SC and dASC exosomes both showed longer neurites than the control group ($p < 0.05$, one-way ANOVA). RNA was identified in both cell type exosomes including mRNA for GAP43, NF200 and peripherin and the microRNAs miR-1, miR-133a and let7d, all of which have shown a role in nerve regeneration. Conclusions dASC exosomes increase neurite outgrowth in vitro, mirroring their SC counterparts. Both the miRNA and mRNA identified within these exosomes are likely to be instrumental in this increase. These findings illustrate how peripheral nerve injuries could potentially be treated without harvesting a functioning nerve for either a graft or SC culture, and also avoid the problems associated with using stem cells themselves.

14:40-14:48 Andrew McKean Incidence, shoulder outcome and surgical intervention of unilateral obstetric brachial plexus injury in Scottish population

Mr. Mark Gorman, Mr. Timothy Hems & Professor Andrew Hart

Scottish National Brachial Plexus Service & University of Glasgow, Scotland

Introduction: The lack of reported incidence figures and outcome data for obstetric brachial plexus injury (OBPI) at the population level in the UK has an adverse impact on patient & parental counselling, and support, and provides difficulty obtaining adequate, equitable service-level NHS funding. This study aimed to report that data through statistical interpretation of The Scottish National Obstetric Brachial Plexus Injury Service database. Material and Methods: The Service prospectively records relevant demographical, musculoskeletal and plexus injury-specific outcomes. Patient records presenting from March 2002 to June 2013 ($n=373$) were screened ($n=127$ excluded due to inadequate data or incorrect diagnosis) and retrospectively assessed ($n=246$). Birth incidence of unilateral OBPI was estimated and shoulder outcomes (Mallet score), with Narakas Grade and age at recovery of biceps function as prognostic indices, were interrogated using SPSS. Results: OBPI affected >0.4 per 1000 live births; 30% were discharged by age 1 year, indicating spontaneous recovery (none represented subsequently); 70% did not recover. Primary surgical intervention was performed in 26% of cases ($n=13$: nerve exploration, $n=52$: shoulder surgery; indications evolved). Nerve surgery (5%) was performed at a mean age of 5.8 months ($SD=2.4$); further procedures were required in 38% ($n=5$) of this group. Of patients not undergoing nerve surgery 21% required shoulder surgery. Narakas Grade and age at recovery of biceps function were confirmed as prognostic indices for future Mallet scores. The time-course of shoulder recovery is described. Conclusions: Few units have captured longitudinal data for such large numbers of patients in to adolescence. The long-term shoulder outcomes in patients undergoing nerve surgery were encouraging. Nerve surgery was of benefit in severe cases.

14:48-14:56 Savaş Serel Functional and Histopathological Study of Prefabricated, Sham and Non-Vascularized Rat Femoral Nerve

Arsın Ulu, Yıldırım Sara, Aylin Okçu Hepar & Zeki Can

Ankara University, Turkey

Introduction: Nerve injuries often necessitate the use of nerve grafts but inadequate vascularization of the scarred recipient site jeopardizes nerve graft survival. Nerve prefabrication can be a step forward

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to overcome this problem. The purpose of this study was to compare electrophysiologic and histopathologic differences of prefabricated, control and non-vascularized rat femoral nerve grafts and aims to show the feasibility of vascularization of the peripheral nerve by prefabrication. Methods: 36 male Wistar Albino rats were randomly assigned into three groups. Femoral artery, vein and nerve bundles were used. In prefabricated vascularized group, first of all direct contact between femoral artery, vein and femoral nerve was achieved. Femoral nerve was transected and sutured concomitantly after three weeks. In non vascularized group, femoral nerve was transected and sutured and then, isolated with a silastic tube in order to prevent any contact with the surrounding tissues. In control group, no surgical operation to the femoral nerve was performed and this group was used to compare with the other two groups. Histopathologic examination, electrophysiologic evaluation of nerve conduction with amplitude and frequency were performed. Results: Histopathologic assessment revealed that femoral nerves were preserved their integrity with perineural congestion in vascularized group. In non-vascularized group, all femoral nerves were necrotic. Vascularized femoral nerve conduction velocity (NCV) was 35.08 ± 1.34 m/s , compound action potential (CAP) was 0.49 ± 0.11 mV. In control group, NCV was 36.57 ± 1.13 m/s , CAP was 3.02 ± 0.3 mV. There was no nerve conduction and CAP in non-vascularized femoral nerve. Conclusions: Nerve prefabrication with vascularization protects the nerve from trauma and preserve physiological activities compared to non-vascularized nerve. This preliminary research demonstrates the possibility of using nerve graft prefabrication to obtain more stable results in scarred and poor vascularized tissue.

14:56-15:04 Lima Sottaz Engineered growth factor and nanotopography for triggering axonal outgrowth

Silvio Hemmi, Dirk Schaefer, Daniel Kalbermatten & Srinivas Madduri
University Hospital Basel

Introduction: Peripheral nerve injuries affect more than one million people each year and often result in life-long disabilities due to lack efficient therapeutic options. Currently available treatment options are associated with several drawbacks (Madduri et al., 2010). For addressing some of these problems, we have developed dual functional collagen nerve conduits (C-NCs) with trophic and topographical guidance support. Methods: GDNF was engineered with collagen binding domain (CBD-GDNF) and expressed in eukaryotic cells. Resulting recombinant growth factor was loaded into C-NCs reinforced with aligned PLGA microfibers. As a control, unmodified GDNF was loaded into C-NCs. In vitro release kinetics were studied over 28 days followed by bioactivity test. Biological performance of dual functional NC was tested in vitro using chicken embryonic DRG neuronal cells. Results: C-NC scaffolds showed sustained release for both GDNF and CBD-GDNF over 28 days. Interestingly, CBD-GDNF mediated slow and low release with significantly reduced initial burst release when compared to native GDNF. Bioactivity of released growth factor was maintained throughout the entire release period as demonstrated by neuronal differentiation of Neuro-2A cells treated with growth factors release. Topography of the microstructured PLGA scaffold in combination with bioactive interphase determined the direction and extent of axonal outgrowth from DRG explants. As desired, axonal outgrowth from DRGs was perfectly (99%) in line with the aligned fibers. In case of random fibers, axonal growth was distributed in all directions. The latter case was the major hurdle for the target oriented regeneration. Conclusions: C-NC endowed with recombinant growth factor CBD-GDNF and PLGA aligned microfibers hold great potential for promoting peripheral nerve regeneration over critical nerve gaps.

15:04-15:12 Neil Fairbairn Light activated sealing of acellular nerve allograft (ANA) for large gap nerve injury

Joanna Ng-Glazier, Amanda Meppelink, Robert Redmond & Jonathan Winograd
St Johns Hospital, Edinburgh

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Introduction: Photochemical tissue bonding (PTB) uses visible light to create sutureless, watertight bonds between two apposed tissue surfaces stained with photoactive dye. In phase 1 of this 2-phase study, we demonstrated that isografts+PTB resulted in superior outcomes compared to conventional sutured isografts. Following major trauma, demand for autogenous nerve graft may exceed supply. Acellular nerve allograft (ANA) is an alternative although outcomes are typically inferior to autograft. This study aimed to assess the efficacy of PTB when used with ANA. Methods: 20 Lewis rats were randomized into 2 groups (n=10). 15mm left sciatic nerve gaps were repaired using ANA. ANAs were secured using epineurial suture (group 1) or PTB (group 2). Outcomes were assessed using sciatic function index (SFI), gastrocnemius muscle mass retention and nerve histomorphometry. Statistical analysis was performed using ANOVA and Bonferroni all-pairs comparison. To allow an assessment of ANA vs isograft, isograft+PTB and isograft+suture groups from phase 1 were included in the analysis. Results: Following sacrifice, all nerves were in continuity and showed evidence of regeneration. Isografts out-performed ANA in all outcome measures. SFI, Muscle mass retention, nerve fiber diameter, axon diameter and myelin thickness was greater in ANA+PTB compared with ANA+suture, although this was not significant. However, muscle mass retention, nerve fiber diameter, axon diameter and myelin thickness were statistically equivalent to gold standard isograft+suture. Conclusion: The advantage of light activated sealing of isografts vs suture observed in phase 1 appears to be reduced when applied to ANA. This may be related to the lack of schwann cells and neurotrophic factors in ANA. Light activated sealing of ANA may improve performance to an extent where they are equivalent to autograft. This may have important clinical implications when injuries preclude the use of autograft and prove useful when augmenting ANA with Schwann cells and neurotrophic factors.

- 15:12-15:20 John Biddlestone Tumour-Stroma interactions: Initial findings from an in-vitro tumour-ADSC co-culture model
- 15:20-15:28 Elisabeth Kappos Implantation of a Denaturated Cellulose Adhesion Barrier and Finger Function after Plate Osteosynthesis of Longfinger P1 Fractures - Results of a randomized controlled trial

Philipp Esenwein, Martino Meoli, Rahel Meier & Joerg Gr?nert
Institution not stated

Introduction: Adhesions after osteosynthesis of P1 longfinger fractures often lead to dissatisfactory functional outcomes. To prevent adhesions, the use of an adhesion barrier has often been proposed. However, results until now have not been convincing. The aim of this prospective randomised trial was to evaluate the value of a product consisting of denaturised cellulose. Methods: This is a double blinded, randomised controlled trial. Patients were electronically randomised into two groups. The trial included isolated and closed P1 fractures with indication of plate osteosynthesis. Patients who could be treated conservatively and patients with accompanying injuries were excluded from the study. Randomisation into two groups: with or without application of adhesion barrier. Clinical and radiological follow-up after six weeks and six months after surgery. Range of motion was compared to the unaffected opposite side. Primary endpoint was TAM. Secondary endpoint DASH score, as well as ability to work after six weeks and six months, tenolysis and any complications. Results: Out of 367 P1 longfinger fractures treated at this trauma center between 2010 and 2013 42 patients were included. Key baseline characteristics were well comparable between groups. One postsurgical infection was noted in treatment group. One patient in control group had to be reoperated due to screw overlength. Three more patients (one control and two treatment group) refused follow up. Both the mean TAM and DASH values, as well as results of return to work and tenolysis were numerically slightly better for the

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treatment group after six weeks, but the difference did not reach statistical significance and the trend disappeared at the six months evaluation. Conclusion: Results do not support the use of this device. good results of both groups after six months might make an advantage of the treatment group hard to prove due to a ceiling effect.

15:28-15:36 Konstantin D. Bergmeister Effects of selective Nerve Transfers on the Mammalian Motor Unit

Martin Aman, Krisztina Manzano-Szalai, Otto Riedl & Oskar C. Aszmann
Medical University of Vienna

Introduction: Selective nerve transfers (SNTs) change the motor unit by rewiring motor neurons to new functional targets and are used for treating slow nerve regeneration, neuroma pain and improve prosthetic control. This experimental study investigates the effects of SNTs on the different motor unit levels and the course of muscular reinnervation. Methods: In rats the ulnar nerve (UN) was selectively transferred to the long head of the biceps after neurotomy of the motor branch. After 3, 6 or 12 weeks (each N=15), muscle force and motor unit number estimation (MUNE) were analyzed and both biceps processed for muscle fiber typing. Motor neurons were labeled with Fluoro-Ruby in 10 animals with SNT and 10 without. Results: All 55 SNTs were functional and no dropouts occurred. Muscle force, muscle weight and MUNE increased progressively from 3 to 6 to 12 weeks. At 12 weeks muscle force was 88%, muscle weight 97,5% and MUNE 116,8%, all compared to contralateral control. Retrograde labeling showed 172,3% motor neurons compared to control (p= 0.006; t test). Muscle fiber types changed progressively from predominantly intermediate to slow and fast, similar to muscles innervated by the UN. Conclusion: This study shows the high regenerative potential and good functional outcome of SNTs. The rewiring of the motor unit led to impressive changes on all levels, most interestingly to functional and structural hyperinnervation of the muscle. Further studies are currently conducted by our group to optimize SNTs.

15:36-15:44 Jonathan Leckenby Nerve regeneration through autologous grafts: does the axonal load of the graft affect the outcome?

Jonathan Leckenby, Kerstin Rolfe, Jeff Lichtman & Adriaan Grobbelaar
Institute not stated

Introduction: Many factors affect the ability of a nerve to regenerate through a graft. The length of graft, the type of graft and the diameter of the graft have all shown to play a role. The axonal load of a donor nerve affects the outcome however, the impact a graft's axonal load has on regeneration is not clear. The aim of this study was to compare the clinical and histomorphological outcomes of autologous grafts with significantly different axonal counts. The hypothesis is that a graft with a higher axonal count will yield a better outcome. Methods: Transgenic YFP-16 mice were used and surgeries were performed on the Posterior Auricular (PAN) branch of the facial nerve. The rodents were separated into four groups: 1) Sham 2) Direct Nerve Repair (DNR) 3) Small Nerve Graft (SNG) and 4) Large Nerve Graft (LNG). Clinical outcomes were measured by analysis of the recovery of ear movement and histomorphological outcomes were assessed using automated segmentation of serial section electron microscopy (SSEM) images. Data was collected at Post-Operative Weeks (POW) 0, 3, 6, 12, 24 and 48. Results: The DNR group recovered approximately 75% of ear movement and almost 80% of axons regenerated across the repair site over the study period, in comparison to 30% and 33% for the SNG group and 49% and 55% for the LNG group. Conclusion: Grafts with a higher axonal count yielded a significantly better clinical and histomorphological outcome than those with lower axonal counts; this contradicts previous publications suggesting larger diameter grafts result in poorer outcomes. In this study it appears that axonal regeneration through a graft plateaus at approximately six months. SSEM

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provides an invaluable tool to study the behaviour of axons as they regenerate and allow for associated observational factors to be analysed.

15:45 – 16:00 Break

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SESSION 4: General

Chairing: Stefan Hacker, Vienna & Adam Reid, Manchester

16:00-16:08 Parviz Sorooshian Development of a tissue fibrosis model in the hind limb of the mouse

Richard Wong & Jason Wong

Blond McIndoe Laboratories, University of Manchester

Introduction: The stiff finger and hand represents significant morbidity to patients and a menace to hand surgeons and therapists that can arise from any trivial or severe trauma or inflammatory disease process. Our understanding of this problem remains without a unifying pathogenesis and effective solution. We sought to study of the pathogenesis of the stiff finger and hand by developing a mouse model of hand fibrosis, and sought to examine macrophage recruitment and activation in relation to fibrotic signaling and tissue stiffness. Materials & Methods: Our research strategy involved trying to cause hand stiffness in the mouse using two models: a modified bleomycin hand fibrosis model and a cast immobilization model. Macrophage recruitment was assessed by F480 immunohistochemistry and changes in matrix stiffness were assessed by atomic force microscopy in comparison to unwounded controls. Fibrosis PCR array was used to examine pathways of fibrosis. Results: Macrophage recruitment was more extensive in the cast immobilized tissues than those treated with bleomycin and corresponds to matrix fibrotic change. Notable changes in the matrix of skin and subcutaneous tissues were noted in the cast immobilized digits in comparison to bleomycin-treated and control digits. Multiple fibrotic markers were elevated and may indicate a specific macrophage activated phenotype involved in the fibrotic process. Conclusion: This study has identified a new model for digital and hand fibrosis that can be used to investigate novel therapeutics in reducing stiffness in the hand after immobilisation which may relate to aggressive macrophage biology.

16:08-16:16 Seon Lee / Tom Pidgeon The Efficacy of the Cook-Swartz Implantable Doppler in the Detection of Free Flap compromise: A Systematic Review and Meta-Analysis

Riaz Agha, Buket Gundogan, Alexander Fowler & Thomas Bragg

Institution not stated

Background: Reducing free flap failure rates is a key goal of any microsurgical unit. The Cook-Swartz implantable Doppler can be used to monitor flap vascularity. We conducted a systematic review and meta-analysis to compare the efficacy of the Cook-Swartz implantable Doppler with clinical monitoring to prevent flap failure. Methods: A comprehensive literature search was carried out using MEDLINE, EMBASE, PsycINFO, Ebsco, The Cochrane Library, CINAHL, SCOPUS, SciELO, NHS evidence and online clinical trial registers from 1966 until 11th September 2014. Studies comparing flap failure rates in Cook-Swartz implantable Doppler and clinically monitored groups were considered. Screening and data extraction was performed by two independent researchers. Results: Seven articles met the inclusion criteria, involving 3,280 patients and 3,304 flaps. The average failure rate in the clinical group was 3.50% and in the Doppler group was 2.0%. A fixed effects meta-analysis was performed and found a reduced failure rate with the use of the Doppler (OR 0.37, [0.21-0.64], p=0.0005). Conclusions: The Cook-Swartz Doppler has the potential to be a useful adjunct to clinical monitoring of free flaps. Further research is needed to confirm its benefits and refine its indications to optimise cost-effectiveness.

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16:16-16:24 Gerrit Grieb Levels of macrophage migration inhibitory factor and glucocorticoids in chronic wound patients and their potential interactions with impaired wound endothelial progenitor cell migration

David Simons, Lena Eckert, Jurgen Bernhagen & Norbert Pallua
Department of Plastic Surgery, University Hospital RWTH Aachen, Germany
Background: Macrophage migration inhibitory factor (MIF) is a structurally and functionally unique pleiotropic mediator in inflammation. There is now strong evidence that MIF promotes revascularization and is involved in wound healing processes. Methods: A cohort of 33 patients was recruited, including 14 patients with acute and 19 patients with chronic wounds. 21 healthy donors served as a control group. Patients were divided into groups according to the nature of the wound. Both serum and wound fluid samples were collected from each patient, and MIF and cortisol concentrations were determined in serum and wound exudates. Additionally, leukocyte numbers and C-reactive protein levels in patients' sera were routinely monitored. To functionally underscore MIF's potential role in wound revascularization, a chemotaxis assay was adapted to test whether and to what extent serum samples and wound fluids of each group promote the chemotactic migration of endothelial progenitor cells (EPCs). Results: MIF serum levels were significantly higher in chronic wound patients than in acute wound patients. Wound exudates of chronic wounds, however contained a significantly lower concentration of MIF than acute wounds. In chronic wound patients, EPC migration might be delayed, as suggested by in vitro chemotaxis experiments. This observation is likely due to the locally reduced MIF levels in the wound area. Conclusion: We conclude that MIF is correlated with occurrence of chronic wound. The increased MIF levels in the serum of chronic wound patients might be due to MIF's systemic effect of its proinflammatory activities, while its locally decreased levels in chronic wound exudates might be responsible for impaired recruitment of EPCs. Additional prospective data and detailed in vivo models are needed for a more comprehensive understanding of the role of MIF in chronic wound healing.

16:24-16:32 John Biddlestone The role of hypoxia as a microenvironmental cue in the differentiation of ADSC

Late addition

16:32-16:40 Ozan Bitik Composite jejunum/diep flap: a novel rat model of viscerocutaneous flap prefabrication

Emer Ekin, Dicle Yasar Aksu, Ali Aliyev & Ali Emre Aksu
Hacettepe Universitesi Plastik Cerrahi AD Sekreterliđi, Ankara, Turkey

Reconstruction of complex pharyngo-esophageal defects present a major challenge, particularly in soft tissue deficient and previously scarred surgical sites. In recent years, free jejunum flap has emerged as a reliable means of esophageal reconstruction, however it may require cutaneous coverage with an additional flap in extensively scarred, secondary reconstructions. Prefabrication of an intestinal-cutaneous composite flap can potentially solve this problem. In our study, a jejunum/DIEP composite flap was successfully prefabricated based on mesenteric vessels. Surgical details of the prefabrication procedure, micro-angiographic imaging of the neo-vascular anatomy and analysis of histological changes are presented.

16:40-16:48 Megan Anderson Differential Distribution of the Ca²⁺ Regulator Pcp4 in the Branchial Arches Is Regulated by Hoxa2

Shilu Amin, Fabiana Luise, Leo Zeef & Nicoletta Bobola

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Branchial arches are externally visible tissue bands in the head region of all vertebrate embryos. Although initially formed from similar components, each arch will give rise to different head and neck structures. Hox transcription factors control branchial arch identity. We aimed to characterize the molecular control of branchial arch identity in mice. Branchial arch cells were induced to aberrantly express *Hoxa2* following infection using supernatants from Ecotropic-Phoenix packaging cells. Branchial arch cells were then sorted by retroviral gene expression of fluorescent proteins using flow cytometry. Differential RNA expression was determined using microarray. We identified *Pcp4* as a second branchial arch-specific molecular signature. We further show that the transcription factor *Hoxa2* binds to *Pcp4* chromatin and regulates *Pcp4* expression in the second arch. *Hoxa2* is also sufficient to induce *Pcp4* expression in anterior first arch cells, which are *Pcp4*-negative. *Pcp4* is a small calmodulin (CaM)-binding protein, highly expressed in the developing neural system and has the ability to inhibit cell death and to promote neurite outgrowth in vitro. Changes in the synaptic plasticity of cerebellar Purkinje cells are observed in *Pcp4*-null mice. Non-neural effects of *Pcp4* have also been described, including a positive role in the osteoblastic differentiation of bone marrow stem cells and in the differentiation of B cells. Additional experiments will be required to understand the function of *Pcp4* in the development of the second branchial arch. Local modulation of calcium signal transduction is a key determinant of beak shape, linking control of Ca(2+) signaling to variations in craniofacial morphology. The control of *Pcp4* by *Hoxa2*, leading to its expression in the second arch, and the ability of *Pcp4* to modulate Ca(2+) signaling suggest that acquiring second arch identity may partly rely on a differential ability of second branchial arch cells to control Ca(2+) levels.

16:48-16:56 Jacqueline Rees- Laser speckle imaging (LSI) of tissue blood flow:
 Lee & Cynthia To preliminary results from use during free-flap breast reconstruction

Cynthia To, Rodney Gush, John Palmer & Andrew Wilson
Royal Devon and Exeter NHS Trust /University of Exeter, U.K.

Introduction Inadequate tissue perfusion is a major cause of post-operative complications following breast reconstruction. The aims of this pilot observational study were to assess the feasibility of using LSI to assess flap perfusion intraoperatively and to assess its potential clinical usefulness in mapping tissue blood flow to reduce post-operative complications. **Methods** The feasibility of performing LSI (moorFLPI-2) in nineteen reconstructions with DIEP and MS-TRAM flaps (n=16, mean age=50 years; range=32-68 years) was assessed. The clinical usefulness of intra-operative LSI images was assessed by comparing (1) zonal blood flow at the time point of abdominal flap isolated on pedicle and; (2) tissue perfusion post anastomosis and occurrence of post-operative complications. **Results** The feasibility of using LSI intra-operatively was demonstrated and added an average of only 10 minutes to the overall operating time. Areas of perfusion zones (Holm's) above an arbitrary tissue viability threshold (200PU) were calculated (percentage of total zone (Z) area), these were median Z1 (81%); Z2 (67%); Z3 (51%) and Z4 (1%) (p=0.001 for Z4 vs all; p=0.003 for Z1 vs Z3; Z2 vs Z3, ns; Wilcoxon). Good potential was shown for LSI images to guide selection of flap boundaries, regarding avoidance of poorly perfused tissue, and potential to predict skin necrosis and flap ischaemia. **Conclusions** LSI was easily used intra-operatively. These pilot data suggested that LSI has the potential of aiding surgical decisions to avoid the use of poorly perfused tissue and the resultant post-operative complications.

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16:56-17:04 Seon Lee Reporting Quality of Observational Studies in Plastic Surgery Needs Improvement A Systematic Review

Seon-Young Lee, Riaz Agha, Kyung Jin Lee Jeong & Alexander Fowler
University of Southampton, U.K.

Introduction: Our objective was to determine the compliance of observational studies in plastic surgery with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) statement checklist. Methods: All cohort, cross-sectional, and case-control studies published in 5 major plastic surgery journals in 2013 were assessed for their compliance with the STROBE statement. Results: One hundred thirty-six studies were identified initially and 94 met the inclusion criteria. The average STROBE score was 12.4 (range, 2-20.1) with a standard deviation of 3.36. The most frequent reporting deficiencies were not reporting the study design in the title and abstract (30%); describing the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection (24%); describing efforts to address sources of bias (20%); reporting numbers of individuals at each stage of the study (20%); and discussing limitations (40%). Conclusions: The reporting quality of observational studies in Plastic Surgery needs improvement. We suggest ways this could be improved including better education, awareness among all stakeholders, and hardwiring compliance through electronic journal submission systems. Key Words: observational studies, research methodology, reporting quality, STROBE, levels of evidence.

17:04-17:12 Giorgio Giatsidis Short Cyclical Intermittent Stimulations Potentiate Adipogenesis in Soft-tissues

Luca Lancerotto, Franco Bassetto & Dennis Paul Orgill
Institution not stated, Padova, Italy

Abstract Background: External suction has shown to enhance adipogenesis of soft tissues holding the potential to impact current standards in recipient site preparation before fat grafting. Yet, optimal kinetics and duration of treatment have not been determined. Based on our previous preclinical experience, we hypothesized that cyclical-intermittent kinetics may strengthen outcomes of External volume Expansion (EVE). Methods: Fifty twelve-week old wild type mice underwent EVE using a previously described model. Five experimental groups (N=10) investigated different kinetics of EVE (Group A: 2hrs x1time/day x1day; Group B: 2hrs x1time/day x5days; Group C: 2hrs x3times/day x5days; Group-D: 2hrs x5times/day x5days; Group E: 1hr x6times/day x5days). We compared results to contra-lateral controls. Animals were sacrificed 5 days after last stimulation and a skin biopsy was obtained from stimulated/control areas. We used digital pictures for macroscopic analysis. Specimens were analyzed by microscopic methods to assess tissue remodeling, angiogenesis and adipogenesis. Results: All animals well tolerated EVE: no minor/major complications occurred and no significant volume augmentation was observed at a five days follow-up. EVE significantly induced subcutaneous tissue thickening (from 0.4 to 1.2-times higher) and adipogenesis in all groups (from 0.6 to 0.9-times higher) compared to control. Longer and repeated stimulation increased outcomes linearly but shorter frequent intermittent cyclical stimulations showed best performances. Conclusions: EASE seems a promising approach for non-invasive soft tissue induction of adipogenesis before fat grafting. Length and frequency of treatment impact on outcomes, shorter and more frequent stimulations being most effective.

17:12-17:20 Seon Lee / Tom Levels of Evidence in Plastic Surgery - Bibliometric Trends and Comparison with Five Other Surgical Specialties
Pidgeon

Riaz Agha, Mariana Devesa, Katharine Whitehurst & Alexander J Fowler
Institution not stated

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Introduction Categorising research by level of evidence (LEV) is an important evidence-based medicine initiative within Plastic Surgery and more generally. Our objective was to assess how the LEVs in plastic surgery have changed from 2003 to 2013, and how this trend compared with five other surgical specialties. Methods All articles published in the top three general plastic surgery journals by 2013 Thomson Reuters Impact Factor (IF) was conducted for 2003 and 2013. Articles then being labeled as LEV 1-5 as defined by the American Society of Plastic Surgeons and comparisons made with five other surgical specialties. Results Mean LEV for plastic surgery improved by 4.1% from 3.86 (95% confidence interval 3.81-3.91) to 3.70 (95% confidence interval 3.64 to 3.74) in 2003 to 2013 respectively. Journals representing all six surgical specialties improved their mean LEV (range 3.7% to 10.9%). By mean LEV in 2013, Plastic Surgery ranks five out of six, as in 2003. Overall, the specialty journals decreased the proportion of published level five and increased level two and three evidence, except for plastic surgery, where only level three evidence increased significantly. There was a slight trend towards higher LEV with higher weighted or mean IF but this did not reach significance ($p=0.0065$ and 0.079 respectively). Conclusion Plastic Surgery is tending towards higher levels of evidence but the pace of change is slow. The specialty must continue to drive towards higher levels of evidence to improve the corpora of research utilised for evidence-based decision-making.

17:20-17:28 Pawel Szychta Inframammary fold correction in two-stage breast reconstruction with the fibrous capsule, together with its vascular and stromal characteristics

Monika Dzieńiecka & Marek Zadrozny

Polish Mother's Memorial Hospital - Research Institute, Lodz, Poland

Introduction: Fibrous capsule surrounding breast implant has been suggested in clinical trials to be applicable as a soft tissue "capsular" flap. Histological design of fibrous capsule with reliable determination of blood vessels would validate its potential use as a pedicled flap. Our aim was to demonstrate the histological properties of the fibrous capsule in a series of patients undergoing two-stage breast reconstruction, together with clinical application of capsular flap for the inframammary fold correction. Materials and Methods: Prospective study enrolled 16 women treated with two-stage breast reconstruction, who underwent surgical exchange of expander for permanent implant. A small section of fibrous capsule surrounding the expander was meticulously dissected. Specimens were studied with hematoxylin and eosin to evaluate morphological characteristics, van Gieson's stain to evaluate elastic fibers, Masson's trichrome to evaluate collagen fibers and immunohistochemistry with anti-CD31 to evaluate vascularity. Immunohistochemistry was performed on fully automated Ventana BenchMarkGX immunostainer (Ventana Medical System). Subsequently, inframammary fold correction with capsular flap was undertaken for breast asymmetry following bilateral prosthetic breast reconstruction. Results: Microscopic images demonstrated that fibrous capsule contained blood vessels located in the stroma, which in turn was composed of multiple layers of collagen fibers and a smaller amount of elastic fibers. Vessel density was variable, however relatively large quantities of blood vessels were observed in most cases, mainly near its inner surface. Surgical method of the inframammary fold correction with capsular flap is presented. Conclusion: Inframammary fold correction can be safely done with the durable, resistant and well-vascularized fibrous capsule surrounding the breast expander/implant, harvested as a pedicled tissue flap.

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17:28-17:36 Aidan Rose Frequent loss of function mutations in TGFBR1 and TGFBR2 reveal hair follicle bulge stem cells as the cell of origin in cutaneous squamous cell carcinoma

Aidan Rose, Patrizia Cammareri, Owen Sansom & Gareth Inman
University of Dundee, Scotland

Solid tumors are typically considered to evolve over several years, arising from the accumulation of mutations within either stem or differentiated cells. However patients with malignant melanoma treated with inhibitors of oncogenic BRAF (vemurafenib), often present with rapid onset keratoacanthomas and/or cutaneous squamous cell carcinoma (cSCC), driven by paradoxical hyperactivation of the RAS/RAF MAPK pathway. Here, using targeted next generation sequencing, we identify frequent type-1 and type-2 TGF- β receptor (TGFBR1 and TGFBR2) mutations in skin lesions from vemurafenib treated patients. Expanding on this, we discover a similar high frequency of TGFBR1 and TGFBR2 mutations in 98 sporadic cSCC tumor samples. Functional in-vitro analysis reveals these mutations commonly ablate canonical TGF- β Smad signaling and typical TGF- β mediated tumour suppressor responses. In normal tissue, active TGF- β signalling co-localises to hair follicle bulge stem cells within both human and murine skin. Given this, we model hyperactivation of the MAPK pathway (through knockin of BRafV600E or KRASG12D) and the consequences of TGF- β signalling ablation (through the deletion of Tgfb1) targeted to Lgr5+ve bulge stem cells. Whilst BRaf or KRAS activation alone rarely led to cancer, homozygous deletion of Tgfb1 results in rapid aggressive cSCC. Taken together, our results indicate that bulge stem cells can act as the cell of origin for cSCC, and that hyperactivation of the RAS-RAF-MAPK pathway, coupled with loss of TGF- β signalling, are driving events in skin tumorigenesis.

17:36-17:44 Min Wu ~~E2F1 Reduces Wound Healing by Suppressing Neovascularization through Regulating Endothelial Progenitor Cells Mobilization and Recruitment to the Ischemia Skin~~ Withdrawn

17:44-17:52 Gisella Nele Bow-tie flap for umbilical reconstruction

MariaGrazia Moio, Annalena Di Martino & Fabrizio Schonauer
University Federico II Naples

Introduction Absence of the umbilicus may occur as a result of various surgical procedures, such as the correction of gastroschisis, omphalocele or bladder exstrophy. Often the residual scar is located in the mid abdomen, in a position convenient to reconstruct the umbilicus. Based on the assumption that the umbilicus is physiologically made of scar tissue, we present a new technique for umbilical reconstruction, which uses two small flaps designed inside the scar, resulting in a 'bow tie' figure. Materials and methods Three patients were referred to our Plastic Surgery Unit for abdominal surgery sequelae, including the absence of the umbilicus, between 2010 and 2013. Under general anesthesia, scar revision was performed and a 'bow-tie' shaped flap was designed inside the scar tissue to reconstruct the umbilicus. The flap-base was attached to the abdominal fascia, having the vascular supply from it, while two random trapezoidal half-flaps were planned perpendicular to the scar, with the larger edge away from the base. Umbilicus was reconstructed by joining the two flaps. Results In all patients, immediate post operative results showed a natural conical looking neo-umbilicus and no necrosis of the hemi-trapezoidal flaps was observed; these findings were confirmed at six months and one year follow up. In one patient, it was necessary to perform a secondary revision of the abdominal scar, while the other patients were satisfied with the improved symmetry of the abdomen and the reconstructed umbilicus. Conclusions In a context of abdominal surgery sequelae with the absence of

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the umbilicus, bow tie shaped flap allows a good conical umbilical shape without additional donor site scars. Results are long lasting without contracture. Compared to other flaps that can be used to reconstruct the umbilicus, we advocate the 'bow-tie' shaped flap as an easier alternative for umbilical reconstruction.

17:52-18:00 Wee Lam Congenital Duplication Differences of the Hand:
Insights from Experimental Manipulations of Sonic
Hedgehog Signalling and a Proposed Classification
System

Megan Davey

Royal Hospital for Sick Children and the Roslin Institute, Edinburgh

Background: The pathogenesis of preaxial polydactylous conditions in congenital hand differences (CHD) has been attributed to anomalies in Sonic hedgehog (SHH) signalling, which exerts its influence on the posterior digits 2-5 and the ulna. Insights into limb patterning and SHH action has been attained through experimental manipulation of the chicken-wing model through application of SHH-agonist molecules, e.g. retinoic acid (RA). This study aims to further define the boundaries of SHH influences in limb embryogenesis, and suggests a possible embryological classification of certain CHD according to SHH signalling. Methods: Activation of SHH was induced through application of 1µg-5µg of smoothened SHH agonist (SAG) to whole chicken embryos during early limb bud development (15-17HH). Precise induction of ectopic SHH expression was achieved through implantation of RA soaked AG1-X2 beads at the anterior borders of developing limbs. Embryos were dissected at E12 when limbs were fully developed and correlated to human pathological standards and clinical classification systems. Results: Inexact SAG applications caused highly variable morphologies in manipulated limbs, with majority (55%) presenting as preaxial polydactylies in the autopod/hand/foot. A further 10% exhibited limb truncation, particularly shortening/radial dysplasia. Surprisingly, 20% exhibited both preaxial polydactyly combined with a degree of radial dysplasia. Precise ectopic SHH manipulations using RA caused limb malformations in 100% of samples. A weaker effect caused full radial aplasia whereas stronger applications resulted in mirror-image hands including ulna dimelia. Conclusions: Although highly divergent in nature, this study demonstrated that all polydactylous conditions might be caused by a common abnormality in preaxial polarising activity. It is postulated that mirror-image hands/feet, ulna dimelia and radial dysplasia may form one distinct group associated with ectopic SHH signalling in the anterior/preaxial limb bud. We propose a possible embryological classification based on the intensity of preaxial SHH signalling that can correlate to certain CHDs.

18:00 – 19:00 drinks tour of Edinburgh – proposed route to be provided on the day

19:00 evening reception: "Beer & Skittles" 14 Picardy Place, Edinburgh EH1 3JT
Phone 0131-556-1289 Website: <http://www.beerandskittlesbar.co.uk/>

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pedicles whenever possible, choosing flaps which allow combined synchronous surgery on donor and recipient site to minimise operative time, flap design to ensure anastomotic coverage in scarred skin and placing great emphasis on maintaining optimum physiological management of the patient in the first 5 days post operatively. Over our long experience, we have also progressively refined flap design to seek flaps providing thin, flexible skin and soft tissue and optimum donor sites for patients.

08:20-08:30 Andrew Hart In vitro characterisation of a microengineered electroactive polymer conduit for peripheral nerve repair

Andrew Hart, Theo Dejardin, Christopher Martin & Mathis Riehle
The University of Glasgow, Scotland

1. Introduction: Optimising peripheral nerve repair requires a multimodal cell-scale approach. Electronic technologies could enable design-based engineering to precisely regulate electrical fields and microscale topography within bioresorbable polymer conduits. 2. Methods: Rat DRG explant model, culture duration 1-6 weeks. Outgrowth (network area/aspect ratio & angular distribution, axon length/directionality/fascicular morphology; anti- β 3-tubulin & anti-S-100 +/- phase contrast microscopy) was investigated on polymer substrates (PDMS / PCL) under varying [NGF] (10 / 50 / 100ng/ml): A. Microscale surface patterning and stiffness optimisation using poly-L-lysine surface coated PDMS casts (PDMS:curing agent ratio range 40:1 - 10:1; Young's modulus 4.1MPa vs 0.1MPa) / spin coated PCL sheets (biocompatible polymer). B. Electrical field parameter space established using virtual modelling, and wired multichannel stimulation in vitro. Optimal stimulus effect replicated using custom-fabricated wireless devices. C. Nano-fabrication of a micropatterned, wirelessly powered electronic PCL nerve conduit undertaken. 3. Results: A. Stiffness affected axon length & network area, and the response to NGF. Surface micropatterning inverts the NGF growth response on stiff substrate, rigidly controls axonal directionality (12.5 μ m grooves optimal), and improves fascicular morphology, Schwann cell interaction, growth rates, and growth cone morphology. B. Direct currents were cytotoxic, AC stimulation was viable. Optimal parameters included oligo-centiHertz frequencies, and oligo-millivolt potential differences. On unpatterned substrates, axonal outgrowth was significantly determined by stimulation. C. Flexible, biocompatible, stimulating electrodes (75 μ m wide x 700nm deep gold tracks), wirelessly powered by inductance coupling, were successfully engineered within PCL constructs. Stimulation control of axonal outgrowth was achieved. The regenerative benefit of topography dominates over stiffness, NGF, and electrical field. 4. Summary: Nano-fabrication facilities and electronic engineering techniques permit the creation of a biocompatible polymer repair construct that can deliver known, biologically relevant stimulation to a regeneration front, and make fuller use of the powerful, favourable growth control afforded by microscale topography and stiffness modulation.

08:30-08:40 Nadja Menzi Lipoma-derived Stem Cells (Lmscs) as a Potential Source for Regenerative Medicine

Nadia Menzi, Mathias Tremp, Pietro G. di Summa, Laurent Tchang, Rik Osinga, Dirk J. Schaefer & Daniel F. Kalbermatten

Institution: not stated, Basel, Switzerland

Introduction Involvement of adipose-derived stem cells (ASCs) in the development of multiple symmetric lipomatosis (MSL) has been proposed. However, the pathogenesis and pathophysiology of this tumor remains largely unknown. The aim of this study was to characterize lipoma-derived mesenchymal stem cells (LMSCs) from patients diagnosed with MSL and potentially providing new insights into the pathophysiology, pathogenesis and treatment of this disease. Material and Methods Stromal vascular fraction (SVF) was extracted from patients diagnosed with MSL sharing similar phenotypic and clinical characteristics. LMSCs were analyzed by the colony-forming unit-fibroblast

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(CFU-f) assay and flowcytometry using standard markers (CD105 and CD73 (mesenchymal markers), CD31 and CD34 (endothelial markers) and the pan-haematopoietic marker CD45). Furthermore, the potency and power of adipogenic plasticity from LMSCs was evaluated in vitro and compared to human adipose-derived stem cells (hASCs) from healthy donors. Results Three patients diagnosed with either MSL type I or II could be identified for LMSCs analysis. The resulting mean CFU-f frequency was $14.3 \pm 5\%$. Flowcytometric analysis of the LMSCs revealed high levels of CD34 ($70 \pm 9\%$), CD45 ($37 \pm 13\%$) and CD73 ($56 \pm 14\%$), whereas low levels of CD31 ($17 \pm 14\%$) and CD105 ($6 \pm 1\%$) were detected. Furthermore, LMSCs showed the ability to differentiate into multiple lineages and have a significant higher adipogenic differentiation potential than hASCs. Conclusions LMSCs share similar properties to stromal cells with a strong proliferative capacity and adipogenic plasticity. A better understanding of LMSCs features may be useful to regulate their activities, slowing down proliferation and angiogenesis at the source of the MSL.

08:40-08:50 Ali Modarressi Can autologous PRP be used safely and efficiently for adipose derived mesenchymal stem cells culture?

Ali Modarressi, Fatemeh Atashi & Brigitte Pittet
Institution not stated, Switzerland

Introduction: Mesenchymal stem cells derived from adipose tissue (AT-MSCs) are promising candidates for cell therapy and tissue engineering strategies. Currently the use of non-autologous cell culture media (e.g animal-derived or allogenic serum) for clinical applications of mesenchymal stem cells (MSCs) is criticized by regulatory agencies. Autologous platelet-rich plasma (PRP) is proposed as a safer alternative medium supplement for adipose-derived mesenchymal stem cells (AT-MSC) culture. Material/methods: To study the efficiency of PRP on cell proliferation, AT-MSCs were cultured for 10 days in media supplemented with different concentrations of autologous non-activated (nPRP) or thrombin-activated PRP (tPRP) (1%-60%). AT-MSC proliferation, cell phenotype and multipotency capacity were assessed and compared to AT-MSCs expanded in a classical medium supplemented with 10% of fetal bovine serum (FBS). Platelet count and viability in the presence or absence of AT-MSCs, was assessed for up to 10 days of culture. Results: Culture media supplemented with nPRP showed dose-dependent higher AT-MSC proliferation than did FBS or tPRP. 20% nPRP was the most effective concentration to promote cell proliferation. This condition increased 13.9 times greater AT-MSC number in comparison to culture with FBS, without changing the AT-MSC phenotype and differentiation capacity. 57% of platelets were viable up during 10 days of culture. Conclusion: We concluded that 20% autologous nPRP is a safe, efficient and cost-effective supplement for AT-MSC expansion. It should be considered as an alternative to FBS or other non-autologous blood derivatives. It could serve as a potent substitute for the validation of future clinical protocols as it respects good-manufacturing practices and regulatory agencies standards.

08:50-09:00 Naghmeh Naderi Effect of nanocomposite polymer fabrication on proliferation and morphology of adipose derived stem cells

Naghmeh Naderi, Michelle Griffin, Iain Whitaker, Alexander Seifalian
Institution not stated

Introduction: Adipose-derived stem cells (ADSC) have advantageous properties including multi-differentiation potential, angiogenesis and immunomodulation. However, the ideal scaffold for ADSC delivery has not yet been found. We have developed a family of biodegradable and non-biodegradable scaffolds to act as carriers for ADSC. Our biodegradable nanocomposite scaffold is composed of polyhedral oligomeric silsesquioxane POSS nanoparticles incorporated into poly-(caprolactone/carbonate)-urethane/urea (PCL). In this study, we compared POSS-PCL manufactured

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by two different fabrication techniques for ADSC delivery. Methods: POSS-PCL was fabricated using solvent casting or coagulation. Human adipose tissue was processed with collagenase to yield ADSC. Cells were characterised by flow cytometry (P0-P2) and differentiated into osteoblasts, chondrocytes, and adipocytes. 1.5x10⁴ ADSC were seeded on circular disks of POSS-PCL. ADSC viability, proliferation and adhesion were compared between both fabrication methods using immunofluorescence, scanning electron microscopy (SEM), alamarBlue and total DNA analysis. POSS-PCL nanocomposite polymers were characterized using SEM, Atomic Force Microscopy (AFM), contact angle measurements, and mechanical testing. Results: ADSC population was CD34+/CD73+/CD90+/CD105+/CD19-/CD14-/CD45- and able to differentiate into adipocytes, chondrocytes, and osteoblasts. Casted POSS-PCL samples were less stiff and provided a rougher surface than coagulated samples (p<0.01). Additionally, ADSC viability and proliferation was significantly higher on casted scaffolds (p<0.01). ADSC adhered in their rounded morphology at 6 hours to coagulated samples but spread out on casted samples. By 24 hours ADSC had spread out and adhered to both casted and coagulated polymers. Conclusion: ADSC favour casted over coagulated POSS-PCL nanocomposite polymers. Both methods provide suitable biocompatible platforms for ADSC proliferation.

09:00-09:10 Grainne Bourke Early nerve repair for experimental brachial plexus injury

Aleksandra McGrath, Ludmila Novikova, Lev Novikov & Mikael Wiberg
Umea Universitet, Sweden & Leeds General Infirmary U.K.

Neonatal brachial plexus injuries result in significant lifelong upper limb disability. There is often controversy about the timing of exploration and nerve repair in these cases. Knowledge of the central effects of proximal brachial plexus nerve injury and repair are critical to understand the outcomes and plan best treatment strategies. This project was to develop a neonatal brachial plexus model in a rat and evaluate the central effects of early nerve repair. Under anaesthesia a selective left sided brachial plexus injury was performed on day old neonatal Sprague Dawley rats. Retrograde tracing was performed to enable quantitative evaluation of the number of motor neurons in the cervical spinal cord. A time course demonstrating the devastating loss of motor neurons over time (day 2- day 28) was developed. During the second phase of the study the injury and retrograde tracing was repeated in a matched neonatal group. This cohort had primary nerve repair. Improved survival of spinal motor neurons was seen throughout the time course and was statistically significant. Further evaluations of the effects on cellular activity following injury and volume differences on the anterior horn were also performed. In conclusion, injury to the brachial plexus in this neonatal model demonstrated dramatic loss of motor neurons after global injury. Early nerve repair reduced degeneration of motor neurons. This demonstrated the need for further evaluation of early nerve repair in neonatal brachial plexus injury.

09:10-09:20 Margot Den Hondt ~~Are we decellularizing too aggressively? The effect of gentle decellularization on rabbit trachea: preliminary report.~~ Withdrawn 17/5/15

09:20-09:30 Alessandro Faroni Grooved polymer scaffolds with human Schwann-like adipose-derived stem cells towards nerve regeneration

Atefeh Mobasseri, Julie Gough & Adam Reid
The University of Manchester

Introduction - Peripheral nerves have capacity to regenerate after injury, a response controlled

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predominantly by Schwann cells (SC); however, functional outcomes remain unsatisfactory in particular in the presence of a nerve gap and regenerative medicine approaches are sought to improve the neural response. Our strategy aims to combine the use of regenerative cells and synthetic biodegradable scaffolds for the creation of bio-artificial conduits able to form a favorable environment for nerve regeneration. Methods ? We have stimulated human adipose-derived stem cells (ASC) towards SC-like ASC and measured morphology and gene expression (qRT-PCR) of key growth factors at 0/7/14 days of the treatment protocol. Furthermore, we utilised a co-culture model of neurons and SC-like ASC on polymer films, with grooved surface topography, to examine the biological responses. Results ? SC-like ASC demonstrated elongated morphology compared to native SC. We found several neuroglia associated genes to be strongly upregulated following glial stimulation: Nestin, 48 ± 16 fold increase ($n=4$, $*P<0.05$); Brain derived neurotrophic factor, BDNF, 2.03 ± 0.32 fold increase ($n=4$, $*P<0.05$); Glial derived neurotrophic factor, GDNF, 4.93 ± 1.41 fold increase ($n=3$, $*P<0.05$). Conversely, other genes that are related to neuron-glia interactions were strongly down-regulated: Nerve growth factor, NGF expression was reduced by 60% ($n=4$, $***P<0.001$); Neuregulin 1, NRG-1 expression was reduced by 70% ($n=3$, $***P<0.001$); Epidermal growth factor receptor 3 expression, ErB-B3, a receptor for NRG-1, was reduced 60% ($n=3$, $**P<0.01$); Neurotrophin 3, NT-3 expression was almost completely abolished $>90\%$ ($n=3$, $****P<0.0001$). Cellular interaction with the topographical cues were found to improve SC-like ASC morphology, migration patterns and to preferentially direct axonal outgrowth from neurons. Conclusion - this study provides in vitro evidence that human SC-like ASC can be combined with engineered biodegradable polymer scaffolds towards improved nerve regeneration.

09:30-09:40 Lima Sottaz

MR-Diffusion-based assessment of chronic compression neuropathy treated with adipose-derived stem cells

Patricia K. Sieber, Robyn M. Benz, Bram Stieljes & Daniel F. Kalbermatten
University Hospital Basel

Introduction Adipose-derived stem cells (ADSCs) provide a potential therapy of compression neuropathy. In animal studies, evaluation of peripheral nerve injury and therapy monitoring is commonly performed using clinical scoring and histopathological work-up but recent developments in magnetic resonance imaging allow for the direct evaluation of nerve fiber integrity. We present the evaluation of this imaging method, diffusion tensor imaging in the context of chronic sciatic nerve injuries treated with ADSCs. Methods In Sprague Dawley rats (2 groups of 7 rats), a nerve crush injury was performed and animals were observed for four weeks. The chronic sciatic nerve lesion was inflicted using a permanent non-metallic clip on the left side; the contralateral side served as internal control. The 14 animals were injected with either 500?000 ADSCs or growth medium in the epineurium just distally to the clip directly after the trauma. Gait analyses with calculation of the Sciatic-Function-Index (SFI) using a computed track were carried out weekly. At four weeks, the 14 animals were sacrificed and post-mortem imaging was performed on a 3-Tesla scanner. The Fractional Anisotropy (FA), a measure of fiber integrity, was obtained for both sides proximally and distally to the lesion. Results Clinically, there was no difference in SFI between the two groups at 4 weeks. The FA showed no differences between the injured and non-injured side at the proximal site (FA 0.67 vs. 0.65). Distally, the FA was clearly reduced on the injured side (FA 0.65 vs. 0.49). Concordant with the SFI, no FA difference was seen between treated and untreated animals (FA 0.47 vs. 0.50). Conclusion Our preliminary results indicate that DTI may be used to quantitatively assess sciatic nerve injury after treatment using ADSCs in a rat model. Further studies are underway to evaluate DTI-imaging in long term animals that show a therapeutic response.

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09:40-09:50 Thomas Reekie Patient Reported Outcome in a 4-limb Amputee after fitment with i-limb digits Myoelectric Prosthesis

Thomas Reekie, Stephanie Barr, Jennifer Lang & Andrew Hart
Canniesburn Plastic Surgery Unit, Glasgow, Scotland

Introduction: Bilateral hand loss is a functionally and psychologically devastating experience. Hand prostheses have been in use for nearly two millennia, with an 'iron hand' documented to improve cosmesis in 77AD. Advanced myoelectric prostheses now have potential to greatly improve functional and cosmetic outcomes for amputees but benefits quantified near time of fitting, have not been clearly documented over time. Methods: A 45 year old female required 4-limb amputation subsequent to overwhelming Streptococcal sepsis, and ECMO. CMC-level amputation was salvaged using a pedicled groin flap (right) and an ulnar artery perforator flap (left) to preserve recipient vessels for hand transplantation. Once functional recovery had plateaued, the patient was fitted with a unilateral Touch Bionics i-limb. SF36, DASH and EQ-5D questionnaires were administered before the patient was fitted with the prosthesis then 4 & 28 weeks afterwards. Video recording of task completion permitted modified Sollerman Hand Function Testing. Results: Salient surgical details are presented. Task function was good prior to prosthetic fitment. DASH scores show continued improvement over time, which correlate well with improving functional integration. The EQ-5D, which is a measure of general health, also showed a definite improvement, as did the SF36 score. Pre fitting 4 weeks post fitting 28 weeks post fitting DASH 75.83 48.33 28.33 EQ-5D 32321 32321 11311 EQ VAS 86 EQ VAS 90 EQ VAS 94 Modified Sollerman 58 63 67 Conclusion: Adequate characterization of benefit from complex prostheses is impaired by the infrequent and heterogeneous nature of the patient population. Optimal hand salvage with a view to prosthetic fitment and maintaining transplant options is a beneficial primary intervention. Clear objective functional and holistic welfare improvement was seen in this patient after prosthetic fitment, with improved life function while she awaits bilateral hand transplant. A learning curve is apparent in prosthetic benefit.

09:50-10:00 Naghmeh Naderi Effect of pore size and porosity on adipose-derived stem cell behaviour on nanocomposite polymer scaffolds

Naghmeh Naderi, Michelle Griffin, Iain Whitaker & Alexander Seifalian
Institution not stated

Introduction: We have developed a family of scaffolds for ADSC delivery. Our biodegradable nanocomposite scaffold is composed of polyhedral oligomeric silsesquioxane (POSS) incorporated into poly-(caprolactone/carbonate)-urethane/urea (PCL). Geometric variables of a scaffold such as porosity, pore size, and pore morphology can influence cellular behaviour. In this study we investigated the effect of pore size and porosity of POSS-PCL scaffolds on ADSC behaviour. Methods: Human adipose tissue was processed to yield ADSC. Characterisation of ADSC was performed using flow cytometry and differentiation to osteoblasts, chondrocytes, and adipocytes. 1.5x10⁴ ADSC were seeded on POSS-PCL disks fabricated with porogen particles (NaCl) ranging from 25-300 micrometre in size and 25%-75% in concentration. Tissue culture plate (TCP) and nonporous samples served as controls. ADSC proliferation and adhesion on the disks were compared between the different pore sizes and concentrations using scanning electron microscopy (SEM), immunofluorescence, alamarBlue and total DNA analysis. Results: ADSC population was CD34+/CD73+/CD90+/CD105+/CD19-/CD14-/CD45- and able to differentiate into adipocytes, chondrocytes, and osteoblasts. At 14 days: porous POSS-PCL samples were associated with significantly better ADSC proliferation than nonporous controls. 25% NaCl content in the 25-100 micrometre pore size group was associated with significantly worse ADSC proliferation compared to

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any other pore size and porosity. Comparing different pore sizes, 100-200 and 200-300 micrometre group was associated with improved ADSC proliferation in the 50% and 75% NaCl groups, but not 25%. Immunofluorescence and SEM results confirmed these findings. Conclusion: larger pore sizes and porosity are associated with improved ADSC attachment, proliferation, and organisation.

10:00-10:10 Liam McMorrow Assessing the potency of CD271-Positive Adipose-Derived Mesenchymal Stem Cells to a Schwann Cell-like Phenotype

Liam A McMorrow, Alessandro Faroni, R Patrick J Smith & Adam J Reid
University of Manchester

Introduction - The use of cellular therapy to promote peripheral nerve regeneration has demonstrated promising experimental results. Schwann cells (SCs) are the fundamental cell of regeneration; however, they are difficult to culture, proliferate slowly and require harvesting of a donor nerve. Adipose-derived stem cells (ASCs) may provide a suitable alternative source of SCs. ASC stimulation towards a SC-like phenotype requires prolonged culture times and within the heterogeneous ASC population there are subpopulations that are more responsive to this stimulation. Isolation of selected ASC subpopulations may improve the culture process towards a potential clinical therapy. We investigated whether selection of a CD271-positive subpopulation from human ASC (CD271+) would promote a superior SC-like phenotype when compared to an un-enriched ASC population (US). Methods - 3 patients consented for donation of fat tissue, ASCs were extracted before magnetic-assisted cell sorting (MACS) isolation of CD271-positive cells. CD271+ and US populations were characterised by flow cytometry before being stimulated towards a SC-like phenotype. Both groups were compared post-stimulation for their likeness to SC - measuring aspect ratio, proliferation and gene/protein expression at 0, 7 and 14 days of stimulation. Results - CD271+ subpopulation isolation was excellent with MACS. CD271+ expression ranged from 72-90% in the sorted group and 7-15% in the unsorted group. The CD271 population proliferated faster ($P < 0.05$). Stimulation towards a SC-like phenotype was successful and cells took on a spindle-like morphology with CD271 populations demonstrating higher aspect ratio ($P < 0.05$). Gene expression of neurotrophic factors GDNF and BDNF was also significantly ($P < 0.05$) greater in the differentiated CD271+ subpopulation than the US population. Discussion - Our data suggests that selection for CD271-positive ASC may improve efficacy of stimulation to a SC-like phenotype, which will make cellular based therapies for peripheral nerve injury more feasible.

10:10-10:20 Hoda Khorasani Scientific impact of presentations from the EURAPS and the AAPS meetings; a ten year review

Hoda Khorasani & Christian Bonde
Rigshospitalet K, Denmark

Introduction: As new findings within different fields of medicine are more available for physicians worldwide, several societies have been established in order to exchange knowledge and research. It is therefore of interest to investigate which abstracts from the societies' scientific meetings are published in peer reviewed journals. This may be an indicator of the scientific value of the meetings. The aim of this study was to analyze and compare presentations from the annual European Association of Plastic Surgeons (EURAPS) and American Association of Plastic Surgeons (AAPS) meetings in reference to publication status. Material and methods: Based on the abstract booklets from the annual meetings of the two societies, all abstracts presented over a ten year period (2000-2009) were analyzed. The observation period for published abstracts was five years. All abstracts presented were systematically searched for in PubMed and Google Scholar to obtain publication status. The registered data were analyzed based on subspecialty. Weighted chi-square analysis was used to analyze statistically

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significant differences in publication rates for the two societies and for English speaking vs. non-English speaking countries. Results: 72% of the abstracts from the AAPS (n =344) were published in peer reviewed journals. The subspecialty most often resulting in publication was ?Craniofacial surgery? followed by ?Breast surgery? and ?Microsurgery?. Mean time from presentation to publication was 21,6 months (range -60 ? 111 months). The most common journal for publication was Plastic and Reconstructive Surgery (PRS). 68% (n=667) of the EURAPS abstracts were published in peer reviewed journals. The subspecialty most often resulting in publication was ?Microsurgery? followed by ?Clinical studies? and ?Craniofacial surgery?. Mean time to publication for the presentations was 16,8 months (range -67 -111 months). The most common journal for publication was PRS. EURAPS had statistically significant less time to publication when compared to AAPS (p=0,008).No difference between the two societies? publication status was found (p=0,157). No difference between English speaking and non-English speaking countries was found (p=0,931). Conclusion: For both societies it is evident that the majority of the presented abstracts have resulted in publication. After ?The Society for Cardiothoracic Surgery?, AAPS and EURAPS have the highest publication rates for presented abstracts at meetings, indicating a high scientific value of the meetings.

10:20-10:30 Christopher West A high-throughput approach to identify defined polymer based substrates for tissue engineering using adipose derived perivascular stem cells

Ken Stewart, Dave Hay, Mark Bradley & Bruno Peault

The Centre for Regenerative Medicine, University of Edinburgh

Introduction: Tissue engineering is a promising technique in addressing many clinical problems in plastic and reconstructive surgery. Tissue engineering relies upon the identification of biomaterials that allow the stable growth of cells whilst simultaneously supporting their clinical application, however traditional techniques in identifying biomaterials are expensive and laborious. Here we utilise a high-throughput technique that allows rapid and simultaneous screening of a large library of polymers to identify potential substrates for tissue engineering. Methods: Microarrays of 2000+ distinct polymers were created using a specialized contact printer on the surface of standard microscope slides. Perivascular stem cells (PSC) were purified from human adipose tissue using fluorescence activated cell sorting (FACS). PSC were incubated on the microarrays for 24hours to determine those polymers with high binding affinity for PSC. Candidate polymers were further evaluated for their ability to support stable proliferation of PSC whilst maintaining and promoting their ability to generate bone, fat and cartilage. Results: Initial screens identified 5 distinct polymers that specifically and selectively bound PSC (P<0.05). Further evaluation identified polymers that were able to support the long term stable proliferation of stem cell phenotype as assessed by FACS, and also support the subsequent differentiation of PSC into adipo, chondro and osteo-cytes using functional assays. Discussion: This study uses a novel high-throughput approach to identify specific substrates that selectively bind PSC. Further analysis demonstrates individual polymers that support the differentiation of PSC towards specific lineages. These polymers may serve as scaffolds for tissue engineering in plastic surgery.

10:30-10:40 A. Khan Radioprotecting free flaps using lentivirally-delivered superoxide dismutase 2 (SOD2) gene therapy

Aadil A Khan^{1,2}, James Paget^{1,2}, Simon Robinson², Paul Harris¹ and Kevin Harrington¹

¹ Department of Plastic Surgery, The Royal Marsden Hospital, London, UK

² Targeted Therapy Team, Department of Cancer Biology, The Institute of Cancer Research, London, UK

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Adjuvant radiotherapy is harmful to free flaps leading to late adverse effects (LAEs) characterized by fat necrosis, volume loss and contracture often requiring salvage surgery. Using a virally-delivered, free flap gene therapy strategy, this study aims to radioprotect free flaps from LAEs whilst maintaining the oncological efficacy of radiotherapy.

Methods: Lentiviral particles encoding the superoxide dismutase 2 gene (LVSOD2) were generated and used to infect superficial inferior epigastric artery (SIEA) flaps in Fischer (F344) male rats. LVSOD2 was delivered by intra-arterial injection, into the SIEA, performed *ex vivo*. LVSOD2-infected and control flaps were irradiated 1-month post-operatively with 50 Gy/3 fractions. Flap outcomes were measured using clinical, imaging, histological and molecular end-points. A tumour recurrence model was developed by engrafting syngeneic tumour cells into control and LVSOD2 flaps prior to irradiation with 20 Gy/5 fractions.

Results: SIEA flap irradiation with 50 Gy/3 fractions resulted in a depletion of SOD2 protein expression and biochemical activity ($p < 0.01$). LVSOD2 infection resulted in durable transgene expression *in vivo* (6 months). LVSOD2-infected flaps developed significantly less skin paddle contracture ($p < 0.01$), volume loss ($p < 0.001$) and less severe acute/late toxicities as scored using the RadioTherapy Oncology Group (RTOG) scoring system ($p < 0.05$). They also exhibited significantly less fibrosis compared to control flaps ($p < 0.05$) and retained greater reactive oxygen species (ROS) scavenging capacity, and SOD2 protein expression, compared to controls ($p < 0.05$). Tumour recurrence studies demonstrated greater retardation of tumour growth in LVSOD2 flaps compared to controls ($p < 0.05$) and improved animal survival ($p < 0.01$) following radiotherapy.

Conclusions: We demonstrate that free flap gene therapy with LVSOD2 can protect irradiated flaps from LAEs and appears to, paradoxically, radiosensitize recurrent disease. These findings merit further evaluation of this pre-clinical concept for translation.

10:40-10:50 Christopher West Percutaneous delivery of adipose derived pericytes prevents the development of atrophic non-union in a rat model

Tae Tawonsawatruk, Iain Murray, Bruno Peault & Hamish Simpson
The Centre for Regenerative Medicine, University of Edinburgh

Introduction: Atrophic non-union is attributed to biological failure of the fracture repair process. Pericytes are native ancestors of mesenchymal stem cells (MSC), and a promising source of bone progenitors that may provide trophic factors required for fracture healing. We aimed to evaluate whether pericytes could improve healing in an animal model of atrophic non-union and compare them to bone marrow derived MSC (BM-MSC). Methods: Pericytes and MSC were isolated from human adipose tissue and bone marrow, respectively. Seventeen Wistar rats underwent a validated procedure to induce atrophic non-union. Animals were randomly allocated to receive either pericytes ($n=5$), BM-MSC ($n=5$) or no cells ($n=7$). In treatment groups, 5×10^6 cells suspended in PBS were percutaneously injected into the fracture gap 3 weeks after operation. Controls received only PBS injection. Radiographic parameters, histology, micro-CT and biomechanical tests evaluated fracture healing at eight weeks. Results: At eight weeks, animals in cell treatment groups showed evidence of bone healing with only 1/5 in both the pericyte and BM-MSC groups progressing to non-union, whereas 6/7 in control group had developed non-unions. Radiographic parameters showed significant improvement ($p < 0.05$) over the eight-week period in cell treatment groups. Histology demonstrated bone bridges at the fracture gap in the both cell treatment groups. Bone mineral density of the fracture callus in animals injected with PSC and MSC was significantly higher than controls ($p < 0.05$). The biomechanical properties of the callus of the cell treatment groups were comparable and stiffer and stronger than the control group. Discussion: The results from this study demonstrate that pericytes have significant bone regeneration potential in an atrophic non-union model. These cells may have a role in the prevention of atrophic non-union and could enable a paradigm shift in the treatment of

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fractures at high risk of failing to heal and developing non-union.

10:50 – 11:00 Break

11:00 – 13:00 Symposium: *Microsurgery as a Model for Implementing Tissue Engineering into Clinical Practice*

Chairing: Andrew Hart, Glasgow & Ken Stewart, Edinburgh

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11:00 – 11:20 Mr. David Soutar (Past-President of EURAPS & BAPRAS) *“The development & rollout of microsurgery into widespread clinical practice, and the most-cited paper in Plastic Surgery”*

11:20 – 11:45 Prof. Stefan Hofer (Wharton Chair of Reconstructive Surgery, University of Toronto & Editor-in-Chief of JPRAS) *“Establishing high quality academic output from a microsurgical practise & where future research should be focused”*

11:45 – 12:15 Prof. Bruno Péault (Chair of Vascular regeneration, MRC Centre for Regenerative Medicine, Edinburgh, & Professor, David Geffen School of Medicine, Orthopaedic Hospital Research Center, UCLA, California) *“What is a stem cell – rationalizing characterization and use in tissue engineering”*

12:15 – 12:45 Prof. Matt Dalby (Professor of Cell Engineering, University of Glasgow) *“Controlling stem and other cells by materials manipulation - what are the translational barriers to clinical implementation”*

12:45 – 13:00 Open discussion on delivering the integration of microsurgery & tissue engineering, and service development opportunities for Plastic Surgery.

13:00 Close of EURAPS Research Council Meeting

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