EURAPS Research Council

11TH EURAPS RESEARCH COUNCIL MEETING

24-25 MAY 2023
STOCKHOLM, SWEDEN

ABSTRACT BOOK

SESSION 1
REGENERATIVE / HAND

EURAPS Research Council

Abstract No.: 102 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Non-invasive Mechano-regeneration of Skeletal Muscle and Restoration of Function in a Rat Model of Critical Volumetric Muscle Loss Injury

Introduction:
Volumetric muscle loss (VML) injury is among the very first causes of chronic disability from combat-related injuries. Injured Service members frequently face a long, challenging path of rehabilitation and only occasionally are able to fully recover initial muscle function. Skeletal muscles do not regenerate after VML injury and currently available therapeutic options are still inadequate.
Our research focuses on a new paradigm that target mechano-sensitive cell and tissue pathways to induce regeneration of injured muscles.
Here, we tested whether these therapies can induce skeletal muscle regeneration and restoration of function in a rat model of critical volumetric muscle loss injury (VML).

Materials and Methods:
Female Sprague Dawley Rats (n= 10/group) underwent a critical VML to their tibialis anterior (TA) muscle. Control animals received no treatment, while experimental groups receive muscle therapy targeting mechano-sensitive pathways for one week. At 2 weeks and 4 weeks follow up, measured outcomes included isometric torque and fatigue resistance of injured TA muscles, treadmill perfomance, TA morphology (MRI), and muscle histological and molecular characteristics.

Results:
At the 4 week follow up,treated animals recovered significantly more isometric torque (73±19% of pre-injury baseline) than controls (47±24%) [$p<0.05$].
Resistance to fatigue was also significantly higher in the treated animals (89±25% of pre-injury baseline) than in controls (57±28%) [$p<0.05$].
Treadmill endurance was higher in the experimental group (98±58%) than in the control group(41±35%) [$p<0.05$].
Gross volume of the TA muscle did not significantly differ, although histological and molecular analysis confirmed signs of tissue regeneration as opposed to fibrosis.

Conclusions:
In a rat study, therapies targeting mechano-sensitive pathways significantly improved muscle recovery (torque, fatigue resistance, and endurance) after a critical VML.
If confirmed in larger animal models/human studies, this approach could re-define the standard-of-care in acute trauma management and best practice in rehabilitation of wounded warriors with muscle injuries.

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Abstract No.: 77 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Altered pathways of keratinization, extracellular matrix generation, angiogenesis and stromal stem cells proliferation in patients with systemic sclerosis

Introduction:
Systemic Sclerosis (SSc) is a connective tissue disease characterized by endothelial dysfunction, abnormal autoantibodies production and fibroblast activation, with progressive cutaneous and visceral involvement. The exact pathogenesis of this disorder is still under investigation. Many pathological pathways between the cells and extracellular matrix (EMC) have been identified, yet what causes the activation of pro-fibrotic myofibroblasts, and ECM deposition remains to be clarified. The aim of this study was to identify potential functional pathways implied in SSc pathogenesis and markers of SSc-related vasculopathy and fibrosis.

Materials and Methods:
We performed skin biopsies on 3 SSc patients and 3 healthy controls (HC). RNA was extracted from each sample and was used to generate sequencing libraries that were sequenced according to proper transcriptomic analyses. Afterwards, gene set enrichment analysis (GSEA) of differentially expressed genes (DEGs) was performed on the entire list of genes that forms the RNA-seq expression matrix. Furthermore, digital cytometry was used to infer cell fractions from our RNA-seq samples.

Results:
GSEA showed that gene signatures of HC were associated with stromal stem cells proliferation, cytokine-cytokine interaction, macrophage-enriched metabolic network, while common signatures in SSc samples were linked to cornification, keratinization, retinoblastoma and tumour suppressor 53 signaling. We also found that DEGS were specifically expressed in epithelial stem cells (EpSC), fibroblasts, pericytes and vascular endothelial cells (VEC) and that increased cellular subsets in SSc included keratinocytes and fibroblasts, while EpSC and VEC were decreased.

Conclusions:
RNA-sequencing and DEGs comparison highlighted that genes associated with keratinization, ECM generation, negative stromal cell cells proliferation and angiogenesis are upregulated in SSc patients and that cellular interactions are aberrant in this population. This suggests that valuable biomarkers of fibrosis and vasculopathy in SSc could be identified and eventually be used as future therapeutic targets.

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Abstract No.: 27 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Tissue origin of cytotoxic natural killer cells dictates their differential roles in regeneration and progenitor cell survival

Introduction:
Regeneration of amputated digit tips relies on mesenchymal progenitor cells and their differentiation into replacement bone and tissue stroma. Natural killer (NK) cells have well-characterized roles in antigen-independent killing of virally infected, pre-tumorous, or stressed cells; however, the potential for cytotoxic activity against regenerative progenitor cells is unclear. Here, we demonstrate the importance of NK cells in regeneration and that the effects of these cells depend on tissue origin.

Materials and Methods:
Amputation of the distal one-third of the terminal phalanges was performed on aged matched 8-10 week old immunodeficient NSG mice. Two digits per hind paw (digits 2 and 4) were amputated. Digit number 3 functioned as an uninjured control. Adoptive cell transfer (ACT) of flow cytometry purified splenic NK (SpNK) or thymic NK (ThNK) cells from C57BL/6 mice were injected via the tail vein. Changes in hard and soft tissue volume were assessed using microCT and histology. To determine immune cell presence and receptor expression in the regenerating digit tip we used immunofluorescent staining and flow cytometry.

Results:
We confirmed NK cell recruitment to the regenerating digit tip. NK cell cytotoxicity was observed against osteoclast and osteoblast progenitors. ACT of ThNK cells induced apoptosis with a reduction of osteoclasts, osteoblasts, and proliferative cells, resulting in inhibition of regeneration. By contrast, ACT of splenic NK cells showed reduced cytotoxicity towards progenitor cells and improved regeneration. Adoptive transfer of NK cells deficient in NK cell activation genes identified that promotion of regeneration by SpNK cells requires Ncr1, whereas inhibition by ThNK cells is mediated via Klrk1 and perforin.

Conclusions:
These findings yield insight into mammalian digit tip regeneration and demonstrate the importance of NK cells on regenerative ability. Successful future therapies aimed at enhancing regeneration will require a deeper understanding of progenitor cell protection from NK cell cytotoxicity.

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Abstract No.: 9 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : CLINICAL APPLICATIONS OF TISSUE ENGINEERING ANNO 2023. FACTS OR STILL FICTION?

Introduction:
Tissue engineering (TE) was introduced almost 30 years ago as a strategy for regenerating human tissues using a biomimetic scaffold seeded with cells and bioactive molecules. The potential applications seemed endless and the expectations sky high. A stem cell based tissue-engineered trachea construct was reported in a clinical setting a decade ago. However it led to consistent failure and most patients died. This widely reported hoax consumed the euphoria on TE.
Despite promising laboratory findings, the complexity of the human body, scientific hurdles, and lack of persistent long-term funding still hampers its translation toward clinical applications.
So 30 years after its conception, what are the current clinically applied tissue-engineered medical products relevant to plastic surgery, if any?

Materials and Methods:
We performed a literature research, and included articles published from 1991 to 2022, according to the PRISMA protocol, using databanks PubMed, Cochrane Library, Web of Science, and Clinicaltrials.gov.. Owing to the scarcity of clinical, randomized, controlled trials and case studies, we extended our search toward a broad surgical spectrum.

Results:
Despite a plethora of promising translational studies, only two clinical studies reported on experimental and biomimetic techniques to engineer long-lasting constructs for clinical translation. We review these first-in-human clinical reports on three-dimensional (3D) and functional durable tissue-engineered constructs and compare the materials and methods used to other constructs that are so far still ‘lost in translation’.

Conclusions:
The concept of generating 3D tissue-engineered constructs and organs based on autologous molecules and cells is intriguing. The first translational tissue-engineered products and techniques have been clinically implemented. However, despite the 30 years of research and development in this field, TE is still in its clinical infancy. Multiple experimental, ethical, budgetary, and regulatory difficulties hinder its rapid translation. Nevertheless, the first clinical applications show great promise and indicate that the translation toward clinical medical implementation has finally started.

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Abstract No.: 99 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Alpha1-Antitrypsin treatment for improving autologous fat graft survival

Introduction:
Fat grafting is performed in a wide range of reconstructive and rejuvenative surgical procedures. However, grafted adipose tissue undergoes 10-90% resorption, often leading to uneven and unaesthetic outcomes. Adipose cells are a major metabolic entity and are highly responsive to inflammatory stimuli; graft resorption is thus affected by the degree of inflammation, rate of reoxygenation, percent local necrosis and proportion of viable stem cells. Alpha1-antitrypsin (AAT) is a circulating tissue protective glycoprotein that is appropriately elevated during inflammatory conditions. In the context of cell and tissue grafting, AAT redirects inflammation toward physiological resolution, reduces local ROS levels, reduces necrotic events and averts the drive for fibrosis. Unlike most anti-inflammatory approaches, AAT allows mature blood vessel formation under diminished processes of inflammation, while maintaining immunocompetency. These attributes provide an intriguing opportunity to explore AAT therapy for maximizing autologous fat graft survival. Aim: To examine fat graft survival in wild-type (WT) mice and mice transgenic for human AAT (hAAT+/+).

Materials and Methods:
Inguinal adipose tissue (0.3 ml) was transferred from WT mice to a surgical pocket under the scalp of either WT or hAAT+/+ mice. Dynamic graft volume was determined by MRI for 90 days. Histology was performed at selected time points.

Results:
On day 10, grafts from the AAT group exhibited mature RBC-containing blood vessels, whereas grafts from the WT group depicted sites of edema and hemorrhage. On day 90, grafts in the WT group exhibited necrosis, atypical graft tissue architecture and inferior viability compared to the AAT group. At all-time points, hAAT+/+ mice displayed less signs of inflammation, and lower rates of fibrosis and capsule formation.

Conclusions:
Study results support adopting AAT therapy for improving autologous fat graft survival. Further studies are needed to explore treatment protocols, as well as the prospect of graft preconditioning, larger fat grafts and human fat samples.

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Abstract No.: 41 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Push-through filtration of emulsified lipoaspirate over a 500µm mesh filter significantly reduces the amount of stromal vascular fraction and mesenchymal stem cells.

Introduction:
Mechanical isolation of stromal vascular fraction (SVF) intends to separate the regenerative component from its surroundings and obtain a high cellular viability and yield. Emulsification is currently the most used disaggregation method and is effective in disrupting adipocytes and fragmenting extracellular matrix. Subsequent push-through filtration of emulsified adipose tissue to further liquify the tissue is a step that removes parts of the extracellular matrix that is not sufficiently micronized. This step might therefore affect the SVF and adipose derived mesenchymal stem cells (MSC) quantity in the sample.

Materials and Methods:
Eleven lipoaspirate samples from healthy non-obese women were harvested and emulsified. One half of the sample was filtered through a 500µm mesh filter while the other half was left unfiltered. Paired samples were processed and analyzed by flowcytometry to identify cellular viability, SVF and MSC yield.

Results:
Push-through filtration reduced the amount of SVF cells by on average 39.65 ± 5,67 % ($p<0,01$). It also significantly reduced MSC counts by on average 48.28 ± 6.72 % ($p<0,01$). Filtration did not significantly affect viability ($p= 0,118$).

Conclusions:
This study has shown that retention of fibrous remnants by push through filters removes ECM containing an important amount of SVF and MSC from emulsified lipoaspirates. As long as there is no stronger evidence on the dose-effect relationship of SVF-based therapies, isolation methods should aim to preserve SVF and its micro-environment as much as possible. Proper matching of disaggregation and purification of the lipoaspirate is key to obtain optimal SVF yields in mechanical isolation methods for SVF based therapies.

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Abstract No.: 46 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : An Elastic Porous Injectable Scaffold enabling 3D shaping of autologous adipose tissue grafts and improving long-term volume retention

Introduction:
Autologous adipose tissue (AAT) graft has been widely used for correcting soft-tissue defects and reconstructing soft-tissue volumes. However, variable cell death leads to unpredictable outcomes with graft volume retention varying between 25% and 80%In addition, grafted AAT is liquid and fails to create 3D projected shapes, limiting clinical application.
We have developed an Elastic Porous Injectable (EPI) 3D scaffold biomaterial based on modified biodegradable cellulose, which has similar mechanical properties than AAT. In addition, its elastic properties allow it to be 3D structured after injection, while mechanically protecting grafted cells.
For the first time, we co-grafted AAT with the EPI Scaffold in mice and investigated cell viability, shape and 3D projection, as well as volume retention over a period of 1 year.

Materials and Methods:
AAT was harvested from CD1 mice and mixed in a 1:1 ratio with the EPI Scaffold. Cell survival was measured in vitro. The composite mix was injected subcutaneously in mice, and manually shaped. The projection index and the volume were measured with MRI and local tissue response was analysed by histology. Control mice were injected only with AAT.

Results:
EPI Scaffold significantly improves AAT survival (+56%). Histology shows good bio-integration of the biomaterial, without foreign body reaction. Only the composite mix enables to create a stable 3D projected shape (constant projection index at 0.5-0.6 after injection vs. drop to 0.1 at 6 months for AAT control). 1-year after injection, volume of the composite mix is still 92% of the initial volume, whereas it is not measurable anymore for the AAT control.

Conclusions:
The co-grafting of the EPI Scaffold with AAT enables to create stable adipose tissue volumes with 3D projected shapes. EPI Scaffold is available off-the-shelf and does not require specific preparation steps prior minimally invasive injection, ensuring its clinical translational potential.

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Abstract No.: 62 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : The Effect on Patient Anxiety of the Timing of Tendon Repair at the Flexor Zone 2B Level

Introduction:
Although early primary repair is the best option for flexor tendon injuries, it may not always be performed. Emergency surgery or waiting to be operated on can cause anxiety for the patient. However the effect of the repair time of flexor tendons on patients' pre- and post-surgical anxiety levels has not been studied. It is aimed to investigate the anxiety levels among various groups of patients having primary or delayed primary repair.

Materials and Methods:
Between June 2020 and June 2021, 77 patients who were operated for isolated flexor tendon injury in zone 2b level were divided into three groups: Tendon repair after 0-6 hours (Group 1), 6-24 hours (Group 2), and 24-72 hours (Group 3). State-trait anxiety scale 1 (STAI 1) and VAS were administered just before the surgery and STAI 1, STAI 2, VAS, and the 40-item quality-of-recovery scale (QoR40) were administered 7–10 days after surgery.

Results:
Eighty-one flexor tendons of the 77 patients—Group 1 (n = 28), Group 2 (n = 30), and Group 3 (n = 19)—were repaired. The median STAI 1 value (52.5) in the preoperative period was statistically higher than the other groups. It was observed that anxiety decreased significantly after surgery in Group 1 compared to the other groups.

Conclusions:
Urgent surgery causes more anxiety in patients preoperatively. Many benefits of reducing anxiety before surgery have been shown in the literature. Compliance with the follow-up process after surgery, patient comfort, decreased need for analgesics, and positive postoperative psychological and somatic states are among them. It is recommended that flexor tendon repair should be delayed for six hours to reduce patient anxiety if urgent repair is not required.

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Abstract No.: 13 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Modified Flexor Digitorum Superficialis Slip Flap Technique as Alternative to Double-Loop Tendon Graft in A4 Pulley Reconstruction

Introduction:
In digital A4 pulley reconstruction, double loop repair around the middle phalanx with autologous tendon grafts is one of the most preferred methods. However, for this, an autologous tendon graft needs to be taken from a distant location. The aim of this study is to compare the pulley reconstruction performed with the 'Modified Flexor Digitorum Superficialis (FDS) slip flap method', which might be good alternative to classical techniques and eliminates the need for tendon grafts from distant regions, with the classical loop technique.

Materials and Methods:
Patients who underwent 6-thread primary flexor digitorum profundus (FDP) repair and acute A4 pulley reconstruction within one week after sharp flexor zone II injury between November 2020 and May 2021 were included. They were divided into two groups as those repaired using the double loop tendon graft technique (Group 1, n=15) and the modified FDS slip flap technique (Group 2, n=19). [Figure 1] Total active movements (TAM), and Q-DASH test scores of the patients at 1 and 6 months postoperatively were recorded.

Results:
It was observed that there was a statistically significant difference in the mean TAH and QDASH test between 1st and 6th months for groups 1 and 2 ($p<0.05$). However, TAM 1st and 6th months values were statistically similar between Groups 1 and 2. Also it was observed that there was statistically similar between Groups 1 and 2 in terms of QDASH 1st and 6th months survey averages.

Conclusions:
The modified FDS slip flap technique and the conventional technique have never been compared in the literature, and our study showed that functional results similar to the conventional technique can be obtained. The modified FDS slip technique is considered a simple, rapid, and low donor site morbidity procedure and is seen as an alternative technique to other techniques that can be used in flexor pulley reconstruction.

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Abstract No.: 100 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : A Novel Functional Assessment of Rodent Peripheral Nerve Regeneration using a Swim Test

Introduction:
Functional tests are required to assess the efficacy of therapeutic approaches optimizing peripheral nerve regeneration. Currently available experimental tools are complex, expensive, lack reliability and are difficult to perform. Here we evaluated a swim test for monitoring functional recovery following peripheral nerve lesion in rats.

Materials and Methods:
A total of 18 male Lewis rats were randomly assigned to groups and underwent either sciatic transection ("RES";n = 6), transection and direct repair ("TSR"; n = 6), or repair with a 10 mm reversed nerve autograft ("GFT"; n = 6). A glass tank (150 x 15 x 46 cm) filled with water and a multi-angle mirror arrangement was placed in front of a high-speed camera. Swims and static sciatic index (SSI) were recorded and analysed over 16 weeks. Gastrocnemius muscle weight ratio and nerve-specific histomorphometry were examined at endpoint.

Results:
The swim test was able to identify nerve injury in all parameters (horizontal excursion, ankle joint range of motion [ROM], swim toe spread [SwTS] and SSI; all $p<0.01$). SwTS and SSI demonstrated constant recovery over time, with superior sensitivity of the SwTS in differentiating between repair and no repair groups (at 16 weeks: RES vs. TSR $p=0.1973$; RES vs. GFT $p=0.0608$). ROM, maximum ankle angulation, toe spread and horizontal excursion increased in all groups. Gastrocnemius muscle ratio revealed significant atrophy after transection, but not in repair groups ($p<0.0001$). Toluidine blue staining, S-100 and NF-200 immunohistochemistry confirmed axonal remyelination without significant differences between the repair groups.

Conclusions:
The swim test is an advanced multi-angular video motion analysis tool creating objective and reproducible functional outcome evaluation using a natural rat behaviour, i.e. swimming. The swim test provides a simple setup, fast testing sessions and a low cost motion analysis setup which can be expanded to wading and other functional trials.

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SESSION 2
BREAST / GENERAL

EURAPS Research Council

Abstract No.: 59 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Preliminary experience with volume assessment in breast asymmetries using external 3D printed sizers

Introduction:
Breast volume assessment is essential for surgical planning in patients with breast asymmetry.
In search of a valuable method, we propose an external 3D printed breast sizer, which is accurate, easy to use, and acceptable for the patient.

Materials and Methods:
In collaboration with a 3D printing company, a set of breast sizers prototypes was developed with a reverse engineering process using anatomical MENTOR® CPG™ implants.
The sizers were used for preoperative breast volume assessment in patients undergoing breast asymmetry corrective surgery. Breast resection volumes and breast implants volumes were also recorded.
Patients' satisfaction with breast symmetry preoperatively and postoperatively was evaluated with a 10-point Visual Analogue Scale. At the six months follow-up, the authors re-evaluated breast symmetry using the 3D Sizers.

Results:
From 2019 to 2021, 35 patients were operated. Patients with Poland syndrome, unilateral amastia, chest wall deformities, or requiring breast augmentation and contralateral reduction concurrently, were excluded. Twenty-eight patients were included in the present study, thirteen differential breast reductions, twelve differential breast augmentations, and three unilateral breast reductions.
The volume difference measured with the 3D Sizers preoperatively was compared to the differential volumes used to correct the breast asymmetry. Mann-Whitney U test showed no significant difference (p-value: 0.72).
Mean preoperative satisfaction with breast symmetry was 3.79, while mean postoperative satisfaction was 8.79. T-test showed a significant difference ($t = -15.22$, $p = < .00001$).
Postoperative re-evaluation with the 3D printed sizers at 6 months follow-up showed a perfect volume matching between the breasts in all the patients.

Conclusions:
Our 3D printed sizers have proven to be accurate in volume difference measurement for breast asymmetries corrective surgery planning. They are non-invasive, easy to use and well-accepted by patients.
Furthermore, digital files for 3D printing can be made available for download and printed everywhere by other surgeons.

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Abstract No.: 74 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Capsulectomy versus capsulotomy to treat breast capsular contracture: a comprehensive review and analysis

Introduction:
Many studies investigating the treatment of capsular contracture after implant-based breast surgery have been published. However, there have been only a few comparative studies between capsulectomy and capsulotomy. The authors performed a comprehensive literature review to compare recurrence rates between capsulectomy and capsulotomy. Surgical complications were reviewed as secondary outcome .

Materials and Methods:
A systematic review of Pubmed/embase was performed between December 2021 and January 2022 aiming at all articles assessing recurrence rate and surgical outcomes for capsulectomy and capsulotomy. Inclusion criteria were clinical studies with Baker III or IV capsular contracture treated by capsulotomy or/and capsulectomy, reporting the main outcome. Excluded from the study were publications not dealing with capsular contracture and review articles. Recurrence and overall complication rate were obtained by dividing the sum of the patients who had a recurrence or a complication by the total number of patients who had the same operation technique.

Results:
Twelve studies, published between 2000 and 2021, were included – representing a total of 3836 patients. The techniques identified from these studies were classified in five groups: capsulotomy, capsulotomy with change of plane, anterior capsulectomy, total capsulectomy and unspecified capsulectomy. The overall recurrence rates were 23% for capsulotomy, 7.9% for capsulotomy with change of plane, 24% for anterior capsulectomy, 11% for total capsulectomy and 2.6% for unspecified capsulectomy. The overall complications rates were 16% for capsulotomy, 2% for capsulotomy with change of plane, 6% for anterior capsulectomy, 13.8% for total capsulectomy and 3% for unspecified capsulectomy.

Conclusions:
While total capsulectomy, and capsulotomy with change of plane seem to offer the lowest recurrence rate, their success is mitigated for potentially higher complication rates. Taking into consideration the high heterogeneity of the data, no conclusion on the superiority of one technique over the other can be made. Further studies are required to determine appropriate capsular contracture treatment.

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Abstract No.: 71 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Breast Implant Illness - patients outcome in a study on 220 patients

Introduction:
Since the 1960s, there have been repeated speculations describing a correlation between breast implants and systemic diseases. Most studies up to now have neither been able to confirm nor refuse this correlation. The problem still exists today and has been named “breast implant illness”.
Our study describes the systemic diseases that have occurred after the augmentation and the changes in the symptoms after explantation.

Materials and Methods:
Over a period of 4 years, we performed an explantation of the implants including the capsule en bloc on 220 patients.
Data collection was carried out with a questionnaire pre-operatively and 6 months postoperatively.
Data collection included questions concerning the symptoms, whose intensity was to be indicated on a scale of 1 to 10. the existence of tattoos (size and number of colours) and piercings. We divided the patients collective in a collective with tattoos and one without and correlated the patients outcome.
The capsule was histologically examined for ALCL, CD 30 and CD117.

Results:
During data collection 6 months after surgery, 92% of all patients reported a considerable improvement. Over 95% of patients suffered from a fatigue syndrome. 30% of patients had Hashimoto thyroiditis preoperatively, which improved postoperatively. 43% of the patients had increased hair loss, which normalised completely postoperatively.
53% of the patients were tattooed.
In 5% of cases, the CD30 test was positive without the presence of ALCL. In 80% of cases, the CD117 test was positive.

Conclusions:
Due to the multiple symptoms, the patients had consulted several different doctors before the explantation. All kinds of differential diagnoses were excluded preaoperative. The correlation to the breast implants therefore always remained the diagnosis by exclusion and the ultima ratio for the patients to alleviate their symptoms, However, the existence of a positive CD117 test might be indicative of an immunological correlation.

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Abstract No.: 104 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : In Vitro Comparison of Lymphangiogenic Potential of Hypoxia Preconditioned Serum (HPS) and Platelet-Rich Plasma (PRP)

Introduction:
Strategies for therapeutic lymphangiogenesis are gradually directed towards the use of growth factor preparations. In particular, blood-derived growth factor products including Hypoxia Preconditioned Serum (HPS) and Platelet-rich Plasma (PRP) are both clinically employed for accelerating tissue repair and received considerable attention in the field of regenerative medicine research. In this study, their lymphangiogenic potential is investigated and analyzed comparatively.

Materials and Methods:
Proteomic analysis of HPS, PRP and non-hypoxia-preconditioned serum (NS) from 9 volunteers included 3 pro- (VEGF-C, PDGF-B, bFGF) and 3 anti-lymphangiogenic (TSP-1, PF-4, Endostatin) growth factor ELISA measurements. Further investigation included the stimulation of human lymphatic endothelial cells (LECs) from 3 donors with HPS, PRP and NS following migration and tube formation assays. Finally, we tested the blood-derived secretomes in terms of lymphatic vessel sprouting in an ex vivo murine lymphatic ring assay from 3 CD1 mice.

Results:
We found higher pro-lymphangiogenic growth factor concentration (VEGF-C, PDGF-B and bFGF) in HPS in comparison to non-hypoxia-preconditioned (normal) serum (NS) and PRP. Migration of lymphatic endothelial cells (LECs) was promoted considerably with HPS and PRP, but was the greatest with dilution of HPS to 40% (HPS-40%) compared to NS and PRP. Tube formation of LECs was investigated for microvessel generation and showed with HPS-10% stimulation the highest number of tubes, branching points, greater tube length and also cell covered area which indicates higher proliferative effects of HPS-10% compared to NS and PRP. Finally, we tested the effects of the blood-derived secretomes in a 3D ex vivo lymphatic ring assay, which puts HPS-40% with the highest number of generated sprouts compared to NS and PRP.

Conclusions:
Our findings demonstrate a superior lymphangiogenic potential of a new generation blood derived secretome by hypoxic preconditioning of peripheral blood cells - a method which offers a novel alternative to PRP.

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Abstract No.: 90 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Using artificial intelligence to write skin cancer patient clinic letters: a study using ChatGPT

Introduction:
Clinical letters are an important means of communication between healthcare providers and patients. The aim of this study was to assess the readability, factual correctness, and humanness of clinical letters generated by the ChatGPT chatbot, developed by OpenAI. To our knowledge, this is the first description of using artificial intelligence (AI) to generate clinical letters.

Materials and Methods:
The ChatGPT chatbot was instructed to write 38 different and increasingly complex clinical letters at a 6th-grade reading level (UK 11-12 years). Readability was assessed using established readability measures, including SMOG and the Flesch Reading Ease index. The factual correctness and humanness of the letters were also evaluated by clinicians using Likert scales (0 – 10 with 10 being perfect). Linear regression was used to investigate the effect of providing 'general commands', 'specific guidelines' or 'general guidelines' to ChatGPT and the resulting impact on correctness and humanness.

Results:
ChatGPT-generated text had an average readability age of USA 9th grade (UK 14-15 years old). The overall correctness score was 7 and overall humanness score was 7. Weighted kappa values for correctness and humanness were 0.80 and 0.77, respectively. Correctness and humanness scores varied by cancer type, with worse Likert scores for melanoma letters compared to those for basal cell carcinoma (BCC) and worse Likert scores for humanness scores for squamous cell carcinoma and melanoma compared to BCC. General commands, specific guidelines, and general guidelines were not significant predictors of correctness or humanness.

Conclusions:
We demonstrate that it is possible for AI to generate clinical letters which are factually correct, readable to the general population and have high human-like qualities. While further research and refinement is needed, this innovation has the potential to significantly reduce clinician and secretarial work load as well as improving the accessibility and standardisation of information sent to patients following their clinic attendance.

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SESSION 3
VISUAL ABSTRACTS / WOUND

EURAPS Research Council

Abstract No.: 82 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Glass surface promotes differentiation and migration of keratinocytes: a fast-tracked and additive-free approach to deliver readily initiated epidermal cells favorable for wound repair applications

Introduction:
Satisfactory repair of difficult-to-heal skin wounds represents a great challenge with high economic burden. Several reports supported the use of cultured autologous keratinocytes. However, normal keratinocytes require a long time to be propagated in culture, which hinders the attempts to release sufficient amounts of autologous cells to patients within a clinically accepted timeframe.

Materials and Methods:
We compared the effect of two standard commercially available cell culture substrates, plastic and collagen I, with glass on human keratinocytes for 10 days. The effect of these substrates on keratinocytes differentiation was studied on cell viability and migration, gene expression and protein synthesis.

Results:
At day 10, keratinocytes cultured on glass exhibited higher viability compared to plastic and collagen I. Scratch wound assay revealed glass and collagen I enhanced keratinocytes migration potential compared to plastic. qPCR data showed upregulation in the expression of epidermal differentiation markers (KRT1, 10, 14, Involucrin, Stratifin & Loricrin) in keratinocytes cultured on glass (p-value ≤ 0.05). Our immunocytochemistry results showed intense cytokeratin 14 staining in keratinocytes on glass and the cells acquired an enlarged and squamous-like morphology typical to cornified epidermal cells in comparison to the keratinocytes grown on plastic. Moreover, human thrombospondin 1 (TSP-1), an extracellular glycoprotein that inhibits angiogenesis was significantly attenuated in keratinocytes cultured on glass compared to plastic and collagen I.

Conclusions:
These preliminary findings provide evidence that, glass as a culture substrate promotes the epidermal differentiation of keratinocyte monolayers. Improved migration and vascularization are key features in re-epithelizing cells to restore wounded skin effectively. Further validation is needed specifically on the effect of glass on aspects such as metabolic activity, proliferation, and the spatial arrangement of keratinocytes.

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Abstract No.: 48 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Towards an Advanced Therapeutic Medicinal Product, Autologous Keratinocytes in Solution for Difficult-to-Heal Skin Wounds

Introduction:
Keratinocytes-based therapy represents a potential solution for patients with difficult-to-heal skin wounds, which is considered as an advanced therapy medicinal product by the European Medicines Agency (EMA). We aimed at achieving a protocol for complete, EMA compliant, workflow.

Materials and Methods:
The first study compared the effect of the xenofree enzyme TrypLE Select deactivated by phosphate buffered saline, to Trypsin deactivated by media with foetal calf serum in isolating keratinocyte from human skin. The second study compared the effect of four media that are xenofree and chemically defined or has bovine protein extract (KSFM), on cell growth and characterization. The third study compared the effect of transferring the cells at 4oC in 4 different solutions: saline, saline with 2.5% human serum albumin, xenofree media and KSFM. The cells were evaluated for viability, adherence and protein production.

Results:
Trypsin workflow showed slightly higher viability of isolated keratinocytes as well as higher expression of cytokeratin 14 (CK14). Total cell number, cell production of metalloproteases 1 and 10 and gene expression of keratinocyte markers p63, CK14, filaggrin and survivin was similar after the cells were cultured for one week. Similarly, the activity of the apoptotic marker caspase3 after isolation or the apoptotic genes bax, Bbcl2 and slug after one week in culture was comparable. Next, we studied the effect of four media types on the propagation of keratinocytes. The most efficient cell media types were the xenofree media EpiLife® and KSFM. Interestingly, the cell viability was higher with EpiLife® media. For the cell transfer, saline with 2.5% human serum albumin showed higher cell number and viability, while KSFM showed higher cellular adherence after 24 hours. Nevertheless, no difference could be noticed when the cells were immuno-characterized for CK14 or involucrin.

Conclusions:
A complete validated workflow for keratinocytes isolation, propagation and transportation was reported according to the clinical guidelines.

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Abstract No.: 106 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : The Effect of Remote Ischemic Postconditioning on Stasis Zone in Acute Burn: Experimental Study

Introduction:
Stasis zone is the encircling area of the coagulation zone which is a critical area determining the depth and width of the necrosis in burn patients.We performed an experimental study to find out the effect of remote ischemic postconditioning,systemically and locally,on the stasis zone in burn model.

Materials and Methods:
Thermal injury was applied on dorsum of rats (n=48) according to the previously described 'comb burn'model.The rats were divided into 4 groups and injections were done:Group 1:Local injection of NS.Group 2: Systemic injection of NS.Group 3: Local injection of RIpS. Group 4: Systemic injection of RIpS. All 4 groups were sub-grouped as a (n=6 rats) (specimens were taken after 24 hours) and b(n=6 rats)(specimens were taken and macroscopic analysis were done) . Biochemical evaluation was done with NS and RIpS to calculate the levels of endothelial nitric oxide synthase(eNOS),inducible nitric oxide synthase(iNOS) and heme oxygenase-1(HO-1) by ELISA. Immunohistochemical evaluation was performed to the specimens taken from the sub-group a of all groups.Histological scoring system(HSCORE) was used to calculate the immune reaction of anti-nuclear factor-like 2(anti-Nrf-2) to nuclear factor-like 2(Nrf-2) Microscopic evaluation was done to the specimens taken from sub-group b in all groups to find out the quantitative amount of capillary count,inflammatory cell count,fibrosis gradient and epithelial thickness.

Results:
There was a statistical significant difference between NS and RIpS among eNOS, iNOS and HO-1 levels.($p<0.01$)HSCORE for Nrf-2 was statistically higher in Groups 3 and 4 compared to Groups 1 and 2.Macroscopic stasis zone tissue survival percentage was statistically high on Group 4(46%). ($p<0.05$)There was a statistical significant difference between groups 1-2 and groups 3-4 among capillary count,inflammatory cell count,fibrosis gradient and epithelial thickness($p<0.05$).

Conclusions:
RIpC has been indicated to be helpful in salvaging stasis zone on acute burn injuries with the control of the ischemia-reperfusion pathways.

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Abstract No.: 81 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Growth factors healing in the chronic wounds

Introduction:
The management of chronic wounds is a challenge for the practitioner. Advances in biomedical engineering and genetic engineering have allowed the appearance of new molecules such as growth factors. The intra-lesional injectable form of recombinant human epidermal growth factor has recently been approved and introduced in several countries for the treatment of diabetic foot ulcers. However, the use of growth factors in chronic wounds is very little studied. The aim of this work is to study its clinical and therapeutic effects of intra-lesional injection in chronic wounds.

Materials and Methods:
We injected twice a week for a maximum of 8 weeks of one ampoule diluted in 5 ml of saline with a regular clinical monitoring of the local and general condition and systematic photographs with the EKARE software, the information collected through a data sheet.

Results:
The sex ratio was 3:1 and the average age was 47 years with extremes of 29 and 59 years. The average duration of evolution of the lesions was 2.5 years with extremes ranging from 6 months to 5 years. The chronic wound was healed for 2 patients and reduced by 60 % on the average for the others. The adverse effects observed were mainly pain at the injection site in 80% of patients and dizziness in 30% of cases. No cases of chills, fever, local infection or nausea/vomiting were observed.

Conclusions:
This study shows that treatment with intra-lesional growth factor can be beneficial for patients with chronic wounds, for whom there is no specific therapy. Wound healing was thus stimulated. Future controlled studies are needed to further evaluate the possible impact of this promising therapy, as these wounds remain an unresolved medical problem and a significant economic burden for medical care systems.

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Abstract No.: 34 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Anti-fibrotic effect of adipose-derived stem cells on fibrotic scars

Introduction:
Sustained injury, through radiotherapy, burns or surgical trauma, can result in fibrosis, displaying an excessive deposition of extracellular matrix (ECM), persisting inflammatory reaction, and reduced vascularization. The increasing recognition of fibrosis as a cause for disease and mortality, and increasing use of radiotherapy causing fibrosis, stresses the importance of a decent anti-fibrotic treatment. Our aim was to obtain an in-depth understanding of the complex mechanisms underlying fibrosis, and more specifically, the potential mechanisms-of-action of adipose-derived stomal cells (ADSCs) in realizing their anti-fibrotic effect.

Materials and Methods:
A systematic review of the literature using PubMed, Embase and Web of Science was performed by two independent reviewers.

Results:
The injection of fat grafts into fibrotic tissue, releases ADSC into the environment. ADSCs' capacity to directly differentiate into key cell types (e.g., ECs, fibroblasts), as well as to secrete multiple paracrine factors (e.g., hepatocyte growth factor, basis fibroblast growth factor, IL-10), allows them to alter different mechanisms underlying fibrosis in a combined approach. ADSCs favor ECM degradation by impacting the fibroblast-to-myofibroblast differentiation, favoring matrix metalloproteinases over tissue inhibitors of metalloproteinases, positively influencing collagen organization, and inhibiting the pro-fibrotic effects of transforming growth factor-β1. Furthermore, they impact elements of both the innate and adaptive immune response system, and stimulate angiogenesis on the site of injury (through secretion of pro-angiogenic cytokines like stromal cell-derived factor-1 and vascular endothelial growth factor).

Conclusions:
This review shows that understanding the complex interactions of ECM accumulation, immune response and vascularization, is vital to fibrosis treatments' effectiveness like fat grafting. It details how ADSCs intelligently steer this complex system in an anti-fibrotic or pro-angiogenic direction, without falling into extreme dilation or stimulation of a single aspect. Detailing this combined approach, has brought fat grafting one step closer to unlocking its full potential as a non-anecdotal treatment for fibrosis.

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Abstract No.: 79 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Micro-needling and Topical Retinol Palmitate in Burn Wounds: A New Remedy for an Old Problem?

Introduction:
Despite advances in therapy, the mortality and morbidity rates associated with burn injuries remain significant. This experimental study aims to prevent necrosis in the zone of stasis following burn injury using micro-needling and vitamin A, which are known to promote skin regeneration.

Materials and Methods:
24 male Wistar albino rats were randomly allocated into four six-rat groups. After intraperitoneal anesthesia, the rat's dorsal skin was burned using the comb method. The groups were control, micro-needling (Dr), micro-needling plus topical retinol palmitate (Dr+VitA), and retinol palmitate monotherapy (VitA) groups. After 28 days of close observation, wound areas were quantified and histologically investigated using images and tissue samples. The thickness of reepithelization, neoangiogenesis, polymorphonuclear leukocyte infiltration, collagen production and structure were all investigated in tissue samples.

Results:
The Dr group showed a statistically significant decrease in wound area and a gain in weight ($p<0.05$). Clinical zone of stasis (ZOS) survival was only detected in micro-needled groups. With nearly full reepithelialisation, the Dr group exhibited the least degree of PMNL infiltration and angiogenesis. Importantly, micro-needled groups increased collagen type 1 synthesis rather than type 3 production. The collagen alignment in the regenerated skin was substantially comparable to that of undamaged skin. In all of these cases, RP had no discernible curative effect.

Conclusions:
ZOS, the salvageable tissue among Jackson's three zones, is metabolically active after burns, but unpredictable inflammation and coagulation may cause necrosis over time. Salvaging it prevents the burn from expanding, reducing mortality and morbidity. Although micro-needling might seem to be extra source of trauma for ZOS, it has been proven by this study to improve the odds of ZOS making it through the process by reducing both inflammation and necrosis.

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SESSION 4
WOUND / BURN

EURAPS Research Council

Abstract No.: 67 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Directing adipose derived stem cells into epidermal-like cells through epigenetic modifiers-based protocol

Introduction:
Adipose derived stem cells (ADSCs) have obtained the attention in skin regeneration and wound healing for their ease of isolation, and their abundance in adipose tissue. Stem cells differentiation into specific lineage requires to enhance or repress gene activation to alter cellular phenotype , metabolic state and function. Unfortunately, the differentiation process is not always efficient especially when targeted cells do not belong to the same lineage of the stem cell origin. Epigenetic modifications play a crucial role in guiding cell development and differentiation including DNA methylation and histone deacetylation. Investigating the effect of the histone deacetylase inhibitor suberoylanilide hydroxamic acid (SAHA) or DNA methylation 5-Aza-2'-deoxycytidine (AZA) on the differentiation efficiency is crucial to improve the cell therapy for skin replacement in burn wounds.

Materials and Methods:
ADSCs were isolated from healthy individuals undergoing breast reduction and abdominoplasty. Cell viability, after cells being treated with SAHA or AZA, was determined and the cells were subjected to differentiation induction media (0.5 nM bone morphogenetic protein 4 (BMP-4), 0.3 mM L-ascorbic acid 2-phosphate, 1.3 µM hydrocortisone, 5 nM all-trans-retinoic acid and 0.3nM recombinant human epidermal growth factor (EGF)) for 7 days. Epidermal markers such as filaggrin and involucrin were screened at the molecular level while immunofluorescence evaluation were conducted for both KRT5 and KRT14.

Results:
Our preliminary results showed that treating ADSCs with SAHA or AZA has no effect on their viability. Following the epidermal differentiation induction, ADSCs which was pretreated with SAHA showed a trend of increase on the expression of both filaggrin and involucrin genes as well as on the expression of KRT5 and KRT14 protein.

Conclusions:
Our preliminary results support our assumption that pretreating ADSCs with SAHA might enhance the epidermal differentiation efficiency which could improve the stem cell-based therapy for the management of difficult-to-heal wounds.

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Abstract No.: 51 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : MIGRATION MODULATION FOLLOWING SOLUBLE IL-6 RECEPTOR TREATMENT FOR NORMAL HUMAN DERMAL FIBROBLASTS AND ADIPOSE-DERIVED STEM CELLS 2D CULTURES

Introduction:
Interleukin-6 (IL-6) is a key player in wound healing, through its dual pro and anti-inflammatory role depending on the intracellular signaling pathway. In vivo setups, cells can express gp130 and IL-6 can act as a proinflammatory cytokine through soluble IL-6 receptor present within the microenvironment. The aim of this study was to evaluate phenotype modulation following soluble IL-6 receptor treatment on fibroblasts and adipose-derived stem cells.

Materials and Methods:
Normal human dermal fibroblasts (NHDF) and adipose-derived stem cells (ADSC) from donors with matching characteristics were used. Migration assessment was performed using Ibidi inserts. Each insert chamber was seeded with one cell type, thus creating a gap between NHDF and ADSC. Following seeding, proliferation was blocked using mitomycin C before incubating for 2 hours with 10 ng/mL of soluble IL-6 receptor. Four cell treatment constructs were created: negative control (no treatment); either NHDF or ADSC with soluble IL-6 receptor; and both cell types treated. Following treatment, the inserts were removed allowing cell migration and data collected at different time points: imaging and cytokine level assessment (TGFβ1, TGFβ3 and VEGF). Moreover, the experiment was repeated with cell trackers for the two cell types and immunocytochemistry was used to assess different markers, such as TGF β1RII, SMAD2/3, SMAD 1/5/9 and SMA.

Results:
Variation in sprouting from the two cell fronts, migration pattern and gap closure were seen, mainly for the construct with NHDF soluble IL-6 receptor treatment and no treatment for ADSC. Although cytokine levels vary between cell treatment constructs at both 24 and 72h following treatment, there were no statistical difference between conditions.

Conclusions:
Due to differences especially for cell treatment construct without ADSC IL-6 pro-inflammatory trans-signaling pathway activation, the experimental design reveals the potential of migration modulation via IL-6 signaling pathway on different cell types relevant in wound healing process.

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Abstract No.: 21 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Amino acid buffered hypochlorite facilitates debridement of porcine infected burn wounds

Introduction:
Removal of necrotic tissue is a vital step in the treatment of full-thickness burn wounds, with surgical debridement being the most effective method. Since minor burn wounds are typically treated on an outpatient basis where surgical capabilities can be limited there is a need for alternative treatment options. In this study we aim to evaluate the use of amino acid buffered hypochlorite (AABH) as a chemical enhancement for wound debridement in a porcine infected burn wound model.

Materials and Methods:
A total of 60 full-thickness burn wounds, 3 cm in diameter, were created on four pigs using a standardized burn device. The wounds were inoculated with 107 colony-forming units (CFU) of S. aureus. The experimental groups included wounds debrided with a plastic curette, wounds debrided after pretreatment with AABH, and control wounds wiped with gauze. Wounds were treated twice per week for three weeks. Debridement, healing, and infection parameters were evaluated over time.

Results:
After one week, but not after two and three weeks, the curette and AABH groups had higher debrided weights compared to control ($p<0.05$). Percentage of wound area adequately cleared from necrotic tissue was higher in the AABH-group compared to the curette-group and control, after one week. The earliest healing was measured in the AABH group after two weeks (5 % of wounds), which also had the most healed wounds after three weeks (55 %). In both the AABH and the curette groups, bacterial load had fallen below 105 CFU/g after two weeks. No CFU were detectable in the AABH group after three weeks. The AABH-group was also the easiest to debride.

Conclusions:
Our results indicate that AABH facilitates wound debridement and could be a helpful addition to an effective treatment modality for removal of necrotic tissue in full-thickness burns.

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Abstract No.: 96 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Tissue engineered construct consisting of mSVF, MIF-2 plus its small molecule agonists and methacrylated gelatin hydrogel

Introduction:
The reconstruction of the dermis and hypodermis is subject to intense research and has a particular meaning for patients with full thickness tissue defects. Tissue engineering (TE) concepts offer modern solutions to boost body-own resources with low morbidty. A hitherto neglected cell source for TE is mechanically-isolated stromal vascular fraction (mSVF), which circumvents present regulatory boundaries. Herein, a TE construct consisting of 1. mSVF, 2. a reparative, anti-inflammatory, balance-tipping protein called MIF-2 3. supplemented by an innovative small molecule agonists (SMA) loaded on a 4. light-inducible, firmness-tunable hydrogel called methacrylated gelatine (GelMA) is introduced with the goal to restore a vascularized dermis-hypodermis layer

Materials and Methods:
Subcutaneous adipose tissue from human donors and rats was processed and characterized by various methods. Proliferation and maturation mSVF was investigated in a novel in vivo supermicrosurgical arteriovenous shunt model in rats. Next, mSVF was loaded on GelMA under various settings followed by viability assays and morphologic characterization. Finally, rMIF-2 and SMA were added with analysis of release patterns.

Results:
Mechanical SVF showed significant numbers of mesenchymal stromal cells. In rats, mSVF vascularized by an arteriovenous shunt of the saphenous artery and vein gained weight over time, proliferated and differentiated in de novo adipocytes. Besides rich growth factor release, mSVF stably expressed FABP4 with time-dependent up-regulation of ERK1/2 phosphorylation. Mechanical SVF loaded on GelMA remained viable over a course of 21 days in vitro with clear signs of cell spreading. Finally, recombinant MIF-2 protein was gradually released from mSVF-GelMA constructs.

Conclusions:
Our experiments reveal a promising mSVF-MIF-2-GelMA construct designed by a collaboration of plastic surgeons, biochemists and material scientists that may serve as a dermis-hypodermis layer in deep tissue wounds. While several parameters have been studied, the construct needs further evaluation with regards to optimization of rMIF-2 and SMA release kinetics and wound healing effects in vivo.

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Abstract No.: 56 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Histone deacetylase inhibitor alters adipose derived stem cells fate transition toward epidermal lineage

Introduction:
Histone acetylation is one of the epigenetic modifications which plays a crucial role in cell proliferation and differentiation. Induction of histone hyperacetylation modulates gene transcription which is responsible for directing the fate of stem cells. We applied a pharmacological approach for manipulating histone acetylation through the inhibition of histone deacetylases using Suberoylanilide hydroxamic acid (SAHA). Understanding the regulation of molecular mechanism will lead to potential therapeutic targets for various skin injuries.

Materials and Methods:
Adipose derived stem cell line (ASC52) was used as the study model. The cells were treated with SAHA for 3 days, Cell viability and HDAC activity were evaluated. Cell cycle was analysed along with molecular characterization of both G2/M transition check point and p53 pathway. Microarray analyses were conducted to uncover the safety and regulatory pathways that might be affected with the treatment and the data was validated by qPCR.

Results:
Our results showed that cells treated according to our protocol had no change in viability or cell cycle progression while HDAC enzymatic activity was reduced. The molecular analysis showed a significant increase in CCND1, p21 and MDM2, and a significant decrease in p53 gene expression. Interestingly a significant increase of DNAJB6 gene expression were reported which is the regulatory gene of epidermal markers K8/K18. Microarray analysis showed 74 up regulated and 40 downregulated differentially expressed genes. The top five enriched pathways from Reactome pathway analysis were related to extracellular matrix organization, nitic oxide metabolism for the downregulated genes, and the regulation of insulin-like growth factor (IGF) transport and uptake for the upregulated genes which were related to tissue development and modeling. qPCR data was consistent with microarray results.

Conclusions:
Epigenetic pharmaceuticals are promising intervention which supports the transition potential of stem cells. SAHA is an attractive target to modulate stem cells fate to improve the clinical outcomes.

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Abstract No.: 45 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Cell-Based Skin Grafting

Introduction:
The cell-based skin grafting (CBSG) has been developed as a state-of-art approach for skin regeneration. The aim is to provide autologous cells, isolated from a skin biopsy, as a regenerative solution for patients suffering from severe skin loss or difficult-to-heal skin wounds. The technique involves the collaboration of the surgical team with cell biologists to conduct the isolation of the skin cells and the application of cell suspension to the wound inside the operation room, in a 3-hour procedure.

Materials and Methods:
Twenty patients participated in the study. The patients had difficult-to-heal wounds, for which one or more classical management approaches were applied and were not successful.
Split thickness skin biopsy is obtained and a special protocol for rapid keratinocyte isolation is performed in the mobile cell isolation unit, which is transferred to the operation room during the procedure. The keratinocytes are isolated, counted and resuspended in a solution at a specific concentration per wound surface area. The bed wound is prepared and a special, patient-tailored, moist chamber is applied to cover the wound edge and the cell solution is injected inside the chamber. The patient is followed up weekly.

Results:
Most of the patients had their wound size decreased by 50% in 2 weeks. The overall success rate for complete healing was 90%. The wound healing followed the natural healing pattern; i.e. from the periphery to the center, The developed skin resembles the colour and texture of surrounding normal skin.

Conclusions:
Hereby we are reporting a new method for keratinocyte isolation and application, in a bedside procedure, for difficult-to-heal skin wounds. The concept of mobile cell isolation unit can be extended to other applications in the future.

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Abstract No.: 83 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : microRNAs as therapeutic targets in human wounds

Introduction:
Wound healing is a fundamental biological process comprising three sequential and overlapping phases, that is, inflammation, proliferation, and remodeling. This delicate repair process is often disrupted in chronic venous insufficiency patients, resulting in venous ulcers (VUs) characterized by persistent inflammation and proliferative phase initiation failure. MicroRNAs (miR) represent a group of short (~22 nt) noncoding ribonucleic acids that have been identified as regulators of complex gene networks. Manipulating miRs critical for the disease pathogenesis could offer a prominent therapeutic effect.

Materials and Methods:
Patients with VUs, which persisted for more than 4 months despite conventional therapy, were enrolled in this study. Tissue samples were collected from the lower extremity at the nonhealing edges of the ulcers by using a 4-mm biopsy punch. Healthy donors were recruited to study normal wound healing. Biopsies were taken Day 0,1 and 7.
RNA was extracted from biopsies, and data of miRNA and mRNA-sequencing was analyzed.

Results:
We identified 17 pathologically relevant miRs that exhibited abnormal VU expression and displayed their targets enriched explicitly in the VU gene signature. Intermeshing regulatory networks controlled by these miRs revealed their high cooperativity in contributing to chronic wound pathology characterized by persistent inflammation and proliferative
phase initiation failure. Furthermore, we demonstrated that miR-34a, miR-424 and miR-516 upregulated in VU, cooperatively suppressed keratinocyte migration and growth while promoting inflammatory response. By combining miR expression patterns with their specific target gene expression context, we identified miRs highly relevant to VU pathology.

Conclusions:
Our study identified several miRs relevant to VU pathology, which opens the possibility of developing innovative wound treatment that targets pathologically relevant cooperating miRs to attain higher therapeutic efficacy and specificity.

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SESSION 5
HEAD & NECK

EURAPS Research Council

Abstract No.: 80 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : The Analysis of Angular and Densitometric Changes in the Aging Middle Face Skeleton by Using 3D Computed Tomography

Introduction:
Catabolic changes in the facial skeleton with aging and accompanying loss of bone dencity have been suggested as the most important etiologic factor in facial aging. In this study; it is aimed to investigate retrospectively the angular and densitometric changes in the midface skeleton due to aging and to investigate the process of aging the middle face by examining the facial computed tomography scans applied to different age, group and sex.

Materials and Methods:
This study comprised 120 patients who underwent maxillofacial computed tomography (CT) between 2008-2015. Three age groups were determined; young (20-39 y/o), the middle-aged (40-64 y/o), and the elderly (≥ 65) . 20 females and 20 males from each age group were retrospectively analyzed. 3D reconstructions of maxillofacial CT scans were obtained. The 3 angles (glabellar angle, maxillary angle, piriform angle) and piriform aperture area determined for the evaluation of the midface projection were calculated on 3D reconstructions. Bone densities in orbital, nasal, maxillary and zygomatic bones, were measured with Quantitative Computed Tomography (CBCT) method.

Results:
As a result of angular measurements, maxillary angle decreased significantly with the progressive age in the male patient population. In the female patient population, the glabellar angle values showed a significant decrease trend with ageing. In both genders, the pyriform aperture area was significantly increased with age. Bone density measurements showed a significant decline in all areas, with progressive age groups in both genders.

Conclusions:
With the advancing age, dramatical morphological changes observed in middle face. It was also determined that loss of angular projection was correlated with loss of bone density in related areas. In elderly patient group, relatively high loss of bone density has been observed. Therefore, in this patient group, osseous interventions for the middle face should be avoided if not necessary or these interventions should be well planned and meticulously applied.

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Abstract No.: 57 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Nasal Morphological Changes Due To Maxillary Advancement Surgery: Should We Consider While Doing Rhinoplasty?

Introduction:
Because of close relationship between soft tissues in nasolabial region and maxilla, changing the maxilla position with orthognathic surgery leads to changes in shape and functions of nose. Aim of this study is cephalometric evaluation of morphological changes in 3-dimensional structure and projection of nose after maxillary advancement surgery.

Materials and Methods:
Patients who underwent isolated maxillary advancement surgery, mandibular orthognathic surgery with maxillary advancement between 2018-2022 were examined. Nasofrontal angle and nasolabial angle values were compared with ImageJ on preoperative and postoperative 6th month photographs of patients using cephalometric points and correlation of advancement amount with angle changes was analyzed.

Results:
Maxillary advancement with mandibular orthognathic surgery were performed in 37 patients, isolated maxillary advancement was performed in 4 of 41 patients(21 women,20 men) included in this study. Mean age of patients was 24.93±4.98 years. Mean postoperative follow-up period was 34.7±15.07 months. Mean maxillary advancement amount was found to be 5.65±1.79 millimeters(mm). Mean value of preoperative nasofrontal angle was 140.17±7.35, postoperative nasofrontal angle was 132.39±8.37 degrees. Mean value of the preoperative nasolabial angle was 112.93±12.21, postoperative nasolabial angle was 123.07±12.22 degrees.
After maxillary advancement surgery, it was observed the nasofrontal angle decreased and the nasolabial angle increased in all patients, and these changes were statistically significant($p<0.05$). There was no correlation between amount of advancement and change in angle between 21 patients with 5 mm or less advancement and 20 patients with more than 5 mm advancement.

Conclusions:
Nasal changes occur due to Le Fort I osteotomy and maxillary advancement surgery are more complex than thought. For this reason, it is believed nasal changes that may occur due to maxillary advancement surgery should definitely be taken into account in patients who will undergo rhinoplasty simultaneously with orthognathic surgery to prevent undesirable functional and aesthetic results.

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Abstract No.: 103 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Fabrication of 3D personalized composite nanocellulose auricular subunits using the suspended layer additive manufacturing (SLAM) technique: Implications for facial reconstruction

Introduction:
Conventional 3D bioprinting techniques extrude a bioink onto a flat surface. While this provides acceptable resolution for simple structures that do not require supports, it is inadequate when building large, complex, clinically relevant structures due to ‘spreading’, fragility and poor shape fidelity.

The recently described suspended layer additive manufacturing (SLAM) self-healing fluid-gel matrix ameliorates these issues and enables the printing of complex, clinically relevant structures using low-viscosity bioinks. This allows the use of a wider range of biomaterials such as alginate, nanocellulose and hyaluronic acid.

We describe our experiences of refining this technique to fabricate personalized 3D auricular and nasal subunits for use in facial reconstruction.

Materials and Methods:
MRI .DCM files of clinically relevant full size auricular and nasal subunits were converted to .STL files.

Using a Cellink BIOX the .STL files were printed with a composite nanocellulose-alginate-hyaluronic acid bioink into a 0.5% agarose fluid gel bath.

Printed subunit accuracy was determined by rescanning with a Creaform 3D scanner and the CAD geometric dimensions compared. Extruded filament accuracy was characterised using light microscopy. Compressive elastic modulus of the material was determined with a Tinius Olsen material tester.

Results:
The composite bioink had high shape fidelity when 3D printed into the agarose bath and produced constructs that retained comparable dimensions to initial scans. The constructs were able to be removed with ease. The crosslinked bioink had similar elastic modulus to non-printed.

Conclusions:
In this study we show that nanocellulose composite bioinks are compatible with suspended layer additive manufacturing (SLAM). This technique is suitable for fabrication of support-free personalized clinical scale 3D auricular and nasal subunits and overcomes the problems of spreading and poor shape fidelity that occur in conventional bioprinting. Our promising results indicate that the SLAM technique is likely to be a viable method to produce bio printed constructs for surgical implantation

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Abstract No.: 92 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : HISTOLOGICAL AND IMMUNOLOGICAL EVALUATION OF THE OSTEOGENIC EFFECTS OF COMPACT BONE DELIVERED STEM CELL ON SPONGIOSIS BONE IN THE RAT ZYGOMATIC ARC DEFECT MODEL

Introduction:
In stem cell applications, apart from bone marrow and adipose tissue, compact bone is also used as an alternative. However, studies on this subject are limited. In our study, we investigated the effect of stem cell derived from compact bone on rat zygomatic arch defect.

Materials and Methods:
Fifteen rats were included in the study. 5 rats were sacrificed to obtain stem cells before the experiment. The rats were divided into 2 groups with 5 rats each. Group I: Compact bone-derived stem cell applied, group II: Adipose tissue-derived stem cell applied. The right zygomatic arch defect was created in rats in both groups. Zygomatic bones were decellularized by cryosurgery. Stem cells were transferred to zygomatic bones. The number of stem cells, stem cell differentiation, and superficial markers obtained from the groups were examined. Histologically, cell structure, osteocyte count and osteopontin scores, the elemental composition of the groups, percentages of resemblance to the intact bone, osteocyte numbers, and cells were examined by electron microscopy of the bones in the groups after sacrification.

Results:
The morphology of the cells in group I was found to be healthier. The number of osteocytes was 97.56±15.4 and 132.93±10.8 in group I and group II, respectively. ($p<0.05$) The osteopontin score was 3.47±0.73 and 65±0.64 in group I and group II, respectively.($p<0.05$) In the electron microscope examination, the morphologies of the cells in group I was seen as more normal. Osteocytes counts were 10.7±2.8 and 6.1±1.2 in group I and group II, respectively. ($p<0.05$) Morphological similarity percentages to normal bone were 88.4% and 79.6% in group I and group II, respectively.($p>0.05$)

Conclusions:
Stem cells obtained from compact bone gave positive results in zygomatic arch defect. This method can also be used as an alternative in stem cell applications.

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Abstract No.: 58 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Evaluation of the regenerative capacity of pediatric PRP in Oro-Nasal fistulas: efficacy, safety and comparison of the biochemical composition

Introduction:
Platelet-rich-plasma (PRP) is widely used in the surgical field due to its known ability to stimulate tissue regeneration and wound healing. To date, some studies described its regenerative properties in the cleft/palate (CP) surgery as a factor responsible for reducing the complication rate,
No study has ever analyzed the concentration of the analytes responsible for those regenerative abilities in PRP samples and quantified the differences between pediatric and adult PRP. The authors present a preliminary series of oro-nasal fistulas treated preoperatively with PRP infiltration and the results of the comparison analysis of PRP samples.

Materials and Methods:
5 patients (range between 1 and 9 years old), with non syndromic CP diagnosis, were included in non-randomized experimental study with a diagnosis of a secondary OnF. All patients in general anesthesia underwent PRP infiltration in the peri-fistulous labrum and neighboring areas of the palate. PRP samples were prepared using single-spin technique and 0.2ml were analyzed with Luminex assays, comparing analytes expression between PRP-pediatric (PRP-p) and PRP-adult (PRP-a).

Results:
For the first time, we analyzed the biochemical composition of the PRP-p, growth factors, chemokines and cytokines involved in regenerative, inflammatory and wound repair processes, demonstrating a real difference composition from PRP-a. 17 factors were up-regulated in PRP-p, in particular, IL-1b, SDF-1a and IL-6 (80-120 fold change), IL-2, EGF, IL-17a and IFN-a (14-24 fold change) and other ten factors (2-10 fold change) compared to PRP-a. We also observed a dimensional reduction of the defect after the infiltration of PRP varying between 50% and 20% (mean value 34,8%) associated with increased consistency of periorificial tissues.

Conclusions:
Our preliminary results showed a substantial difference between the PRP samples, demonstrating better properties of PRP-p and encouraging its possible use in management of patients with non-syndromic OnF with standard surgical procedures.

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Abstract No.: 52 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : IMPROVING FUNCTIONAL OUTCOMES AFTER SURGICAL TREATMENT OF UNILATERAL LARYNGEAL TUMORS, A RETROSPECTIVE STUDY OF 43 HEMILARYNX RECONSTRUCTIONS.

Introduction:
Unilateral advanced tumors on one vocal fold usually are treated by total laryngectomy. Due to the functional impairment and profound effect on quality of life caused by a total laryngectomy, every attempt to avoid this must be made. We present the outcomes of our modified protocol of hemi-larynx reconstruction using a prefabricated trachea segment since trachea has a similar hollow fibrocartilaginous structure, lined with respiratory epithelium. The prefabrication occurs by inset of a 2-unit radial forearm free flap.

Materials and Methods:
We collected data from patient records from 43 patients with advanced unilateral chondrosarcoma of the cricoid cartilage or unilateral SCC of the glottis
who underwent a hemilarynx reconstruction from January 2003 till January 2023 and performed a retrospective statistical analysis of patient characteristics, subjective speech quality, swallowing function, overall survival, conversion rate to total laryngectomy, presence of a tracheostomy, presence of a jejunostomy, tumor recidive, recidive-free survival, and occurrence of aspiration pneumonia. Nelson-Aalen estimates were used to construct cumulative incidence curves for conversion, tracheostomy, Jenunostomy and recidive, treating death without the specific event as a competing risk. Kaplan-Meier curves were used for overall survival and recurrence-free survival

Results:
We present a good subjective speech quality in 53.49%, remaining presence of jejunostomy in 50.95%, 10-year overall survival in 77.77%, conversion rate in 14.61%, remaining tracheostomy in 34.70%, tumor recidive in 5.19%, 10-year recurrence-free survival in 70.53%, hospitalization aspiration pneumonia in 21.43% - of treated patients.

Conclusions:
The combined use of the tracheal autotransplant with the radial forearm flap approaches the desired optimal reconstructive morphology after repair of extended hemilaryngectomy defects and prevents a total laryngectomy in selected cases, this way improving functional outcomes and quality of life when compared to a conventional total laryngectomy.

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SESSION 6
VISUAL ABSTRACTS MISCELLANEOUS

EURAPS Research Council

Abstract No.: 11 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Donor Nerve Selection in Free Gracilis Muscle Transfer; Comparing Cross-Face Nerve Graft, Motor Nerve to the Masseter and the Dual Innervation Concept: A Systematic Review and Meta-Analysis of Clinical Outcomes

Introduction:
One of the critical factors in facial reanimation is selecting the donor nerve. The most favored neurotizers are the contralateral facial nerve with a cross-face nerve graft (CFNG) and motor nerve to the masseter (MNM). A relatively new dual innervation (DI) method has shown successful results. This study aimed to compare the clinical outcomes of different neurotization strategies for free gracilis muscle transfer (FGMT).

Materials and Methods:
The Scopus and WoS databases were queried with 21 keywords. Three-stage article selection was performed for the systematic review. Articles presenting quantitative data for commissure excursion and facial symmetry were included in meta-analysis, using random-effects model. ROBINS-I tool and Newcastle-Ottawa scale were used to assess bias and study quality.

Results:
The literature search produced 2454 titles, 147 articles containing FGMT were systematically reviewed. Most studies indicated CFNG as the first choice. MNM was primarily indicated in bilateral palsy and in elderly. Clinical outcomes of DI studies were promising despite lower in numbers. 13 studies including 435 observations (179 CFNG, 182 MNM, 74 DI) were eligible for meta-analysis. The mean change in commissure excursion was 7.15mm (95% CI: 4.57-9.72) for CFNG, 8.46mm (95% CI: 6.86-10.06) for MNM, and 5.18mm (95% CI: 4.01-6.34) for DI. In pairwise comparisons, a significant difference was found between MNM and DI ($p=0.0011$), despite the superior outcomes described in DI studies. No statistically significant difference was found in resting and smile symmetry ($p=0.625$, $p=0.780$).

Conclusions:
CFNG is the most preferred neurotizer, and MNM is a reliable second option. Outcomes of DI studies are promising; but more comparison studies are needed to draw conclusions. Our meta-analysis was limited by incompatibility of the usable data. Consensus on a standardized assessment system would add value to future studies.

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Abstract No.: 47 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Spontaneous and dynamic smile restoration after long-standing facial paralysis is effective in elderly: a systematic review.

Introduction:
For longstanding facial paralysis, gracilis free muscle transfer (GFMT) is a frequently used flap to reconstruct smile. A dual-innervation technique, consisting of a cross-facial nerve graft (CFNG) along with masseteric nerve (MN) coaptation could provide a marriage between strength and spontaneity of smile. However, the effectiveness in elderly is not clear. We investigated the benefit of GFMT with dual-innervation in comparison to single innervation focusing on smile spontaneity and effectiveness in elderly.

Materials and Methods:
A systematic review was performed in accordance with the PRISMA guidelines. Articles published from 1995 to 2021 were searched in MEDLINE, Embase and Cochrane library.

Results:
We retrieved 568 studies of which 12 were found eligible. In these 12 studies, 341 patients were treated with GFMT. Dual GFMT innervation resulted in a spontaneous smile in the majority of patients. Dual GFMT innervation showed faster reinnervation compared to CFNG ($p = 0.035$). Dual GFMT innervation showed a trend towards better spontaneous smile compared to MN, although statistics were lacking. Elderly (> 60 years) treated with dual GFMT innervation had an increase in the number of visible maxillary teeth of three postoperatively compared to an increase of one in juniors ($p = 0.03$). Patients > 50 years showed a trend towards a longer reinnervation time compared to juniors , although statistics were lacking.

Conclusions:
Dually innervated GFMT results in a spontaneous smile in adults and elderly. Dual GFMT innervation shows faster reinnervation compared to CFNG and shows a trend towards a better spontaneous smile compared to MN. Dual GFMT innervation is effective in elderly. However, patients > 50 years show a trend towards longer reinnervation time. We encounterd a heterogeneity of reporting methods. The use of standardised protocols is required for further research.

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Abstract No.: 107 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : hPL-human adipose-derived stem cells in IKVAV-functionalised hydrogel conduit (Biogelx): an innovative delivery strategy to improve peripheral nerve repair

Introduction:
Adipose-derived stem cells (ADSC) are nowadays one of the most exploited cells in regenerative medicine. They are fast growing, capable of enhancing axonal elongation, support and locally stimulate Schwann cells (SC) and protect de-innervated muscles from atrophy after a peripheral nerve injury.

Materials and Methods:
With the aim of developing a bio-safe, clinically translatable cell-therapy, we assessed the effect of ADSC pre-expanded with human platelet lysate (hPL) in an in vivo rat model, delivering the cells into a 15 mm critical-size sciatic nerve defect embedded within a laminin-peptide-functionalised hydrogel (Biogelx-IKVAV) wrapped by a poly-"ℇ" -caprolactone (PCL) nerve conduit for a time period of 6 weeks

Results:
ADSC retained their stemness, their immunophenotype and proliferative activity when tested in vitro. At six weeks post implantation, robust regeneration was observed across the critical-size gap as evaluated by both the axonal elongation (anti-NF 200) and SC proliferation (anti-S100) within the Biogelx-IKVAV filled PCL conduit. All the other experimental groups manifested significantly lower levels of growth cone elongation. The histological gastrocnemius muscle analysis was comparable with no quantitative significant differences among the experimental groups.

Conclusions:
Taken together, these results suggest that ADSC encapsulated in Biogelx-IKVAV are a potential path to improve the efficacy of nerve regeneration. New perspectives can be pursued for the development of a fully synthetic bioengineered nerve graft for the treatment of peripheral nerve injury.

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Abstract No.: 65 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : THE MINI-INCISION APPROACH TO THE FACIAL ARTERY AS A RECIPIENT VESSEL IN HEAD AND NECK RECONSTRUCTION

Introduction:
In mid-face defects being operated on under elective conditions, an extra incision is required in the submandibular region to reach the facial artery as a recipient vessel and creating barely visible small scars should be one of the main purposes in these cases. Disturbing additional facial scars related recipient area can be prevented using the mini-incision approach described below.

Materials and Methods:
This study includes 18 patients who were operated on with a mini-incision technique for mid-face reconstruction. The average preparation time of the recipient area, average scar length, and follow-up duration of the patients were recorded. The Modified Vancouver Scar Scale was used to evaluate scar quality one year after operation.

Surgical Technique
The facial artery was detected 1 cm below the mandible and the exact localization of the mini-incision was specified. The facial artery was ligated as distally as possible after a sufficient range of motion to the vessel was provided. The artery was released towards the distal end and taken out from the existing incision. A subcutaneous or trans-buccal tunnel was created from the defect area to the recipient area. The free flap pedicle was passed to the anastomosis site. Anastomoses were performed approximately at or above the skin level. The pedicle was pulled towards the distal end to return the anastomosed vessels to their anatomic planes.

Results:
The technique was performed for maxillary and total nasal reconstruction. The mean follow-up time was 18 months. The mean preparation time of the recipient area was 30 minutes. The patients' mean scar length was 17 mm (13 – 22 mm), and the mean Modified Vancouver Scar Scale was 1.33 (0 – 4).

Conclusions:
With mini-incision approach, the pedicle length required was shortened, a well-qualified, barely visible in an area that could be hidden below the mandible can be obtained.

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Abstract No.: 18 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Breast implants selection

Introduction:
Breast augmentation is one of the most frequently performed procedure in plastic surgery. According to ISAPS statistics, in 2020, 1,624,281 surgeries of this type were performed worldwide. The key point of this procedure is the proper implants selection. It is mainly the surgeon who decides on the implant type and size. This may result in patient dissatisfaction and the desire to replace the implants. In the literature, the number of cases of implants replacement due to the wrong selection ranges from 5.9% to 17.6% (average 12.9%). We present our own method of implants selection, which allows to obtain a very high patient satisfaction rate.

Materials and Methods:
A retrospective analysis included 3,585 patients who underwent breast augmentation in the period from January 2011 to May 2021. The selection of breast implants was done one month before surgery, in front of large mirrors, based on the use of the Vectra 3D (Canfield Ltd.) The entire process was carried out by a qualified medical consultant. Patients chose the implant volume based on external sizers. The surgeon's role was to determine the implant parameters respecting the patient's volume preferences. The patient was carefully educated regarding the anatomical factors affecting her choice.
The follow-up period ranged from 1 to 10 years. The percentage of patients who decided to replace the implants due to the wrong choice was assessed.

Results:
3585 patients aged 19 to 58 (average 34) with a BMI of 19 to 28 (average 21) were examined. Ten patients (0,28%) decided to replace the implants due to the wrong selection.

Conclusions:
The use of the described method of implants selection resulted in the lowest percentage of patient dissatisfaction in the literature.
The system is based on patient’s education and on the patient's decision concerning the volume of implants.

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Abstract No.: 75 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Routine drainage in reduction mammaplasty: Is it necessary? A comparative study

Introduction:
Drains are often used in order to reduce seroma and hematoma occurrence. We compared our outcomes on the use of drains in breast reduction. We hypothesized that drains are not necessary for this procedure.

Materials and Methods:
This retrospective study included 756 consecutive patients who underwent breast reduction surgery due to breast hypertrophy. The Wise pattern with an inferior or superior pedicle technique was performed in all cases. Patients were divided on the basis of drain use.
The study group (n=270) included breast reduction surgery performed without drains. The control group (n=486) underwent the procedure with drains.
The mean age of the patients was 45.4±13.6 years in the undrained group and 45.6±12.1 years in the drained group. The mean body mass index (BMI) was 27.6±3.5 kg/m2 in the undrained group and 28.1±3.2 kg/m2 in the drained group. Patients received a follow-up for an average of 4.2±6.4 months.

Results:
Demographics were similar between the two groups with respect to comorbidities (16.7% vs 12.7%, p=0.292), but the resection weight was significantly heavier in the drained group (607.2g vs 686.8g, p=0.001). Operative time was significantly longer in the drained group (120.1 vs 131.9 minutes, p<0.001).
We did not observe any significant difference among any complications, hematoma rates (3.7% vs 5.9%, p=0.434), infections (11.1% vs 15.6%, p=0.187), wound dehiscence (11.3% vs 12.4%, p=0.517), nor other specific complications. Multivariate analysis for any complication did not reveal any significant predictive factor, but BMI ≥30 kg/m2.

Conclusions:
Drains in breast reduction surgery are not needed as they do not reduce any postoperative complications according to our analysis. They might increase costs and patients' discomfort.

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Abstract No.: 35 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : The impact of body-mass index on autologous breast reconstruction: A systematic review.

Introduction:
The aim of the study was to investigate Body Mass Index (cm2/kg) effect on postoperative complications at the recipient site among women who have had autologous breast reconstruction based on free abdominal-based flaps. Also to determine whether there is a BMI threshold where autologous breast reconstruction may not be recommended.

Materials and Methods:
Adhering to the PRISMA guidelines, studies were identified with searches of Medline via PubMed and EMBASE via OVID. All studies reporting recipient site complications after autologous breast reconstruction, using either Deep Inferior Epigastric artery Perforator flap, Transverse Rectus Abdominis Musculocutaneous flap and Superficial Inferior Epigastric Artery flap were included. BMI was stratified according to World Health Organization classification and furthermore defined as obese (BMI 30) and non-obese (BMI <30). Data regarding postoperative outcome were combined for pooled analyses.

Results:
Twenty studies met the inclusion criteria, and a total of 10512 patients and 11456 flaps were included. Pooled analyses showed significant increased minor- and major complication- and loss of reconstruction rates when comparing the obese group to the non-obese group. Stratifying BMI according to WHO revealed significantly higher odds ratio for minor complications for all 3 groups of obesity when compared to the normal weight group. The risk of loss of reconstruction was significantly higher for the class III obese group when compared to the normal weight.

Conclusions:
The obese population has an increased risk of both minor- and major complications and loss of reconstruction compared to the non-obese population. Despite increased minor complication OR for the obese group, autologous breast reconstruction may still be the best option for this population. However, BMI 40 is the recommended surgical threshold, where the risk of loss of reconstruction is eightfold increased.

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Abstract No.: 112 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Identifying common immunological mechanisms in fibrosis: an immunophenotypic analysis of the capsular response to silicone

Introduction:
Silicone is implanted widely in plastic surgery but the resultant immune response is poorly understood and may lead to fibrosis and lymphomagenesis. We set out to characterise the immune response to silicone using an in vivo mouse model of capsular fibrosis. The primary hypothesis was that smooth and textured silicone surfaces elicit differing cellular, transcriptomic and proteomic immune responses.

Materials and Methods:
A model of capsular fibrosis was developed by implanting smooth and textured silicone breast implant shells into the dorsum of C57BL/6JWT mice. Implant capsules were excised at serial post-operative time points prior to morphometric, flow cytometry, immunohistochemical, RNA-seq and proteomic characterisation.

Results:
Median capsular thicknesses increased between early and late time-points with collagen laid down during the first 2 weeks (w) post-implantation then static. Immunohistochemistry demonstrated early CD45+ (pan-leukocyte) and F4/80+ (macrophage) capsular infiltration that subsequently declined. Flow cytometry provided further evidence for smooth implant immunogenicity with T- (CD3+, CD4+ and CD8+), dendritic and NK cell increases seen at 4 w alongside greater macrophage responses.

RNA-seq found adipogenesis, oxidative phosphorylation, fatty and bile acid metabolism hallmark pathways upregulated in textured capsules at 12 w. Smooth capsules discordantly upregulated myogenic and fibrotic pathways but downregulated the cell cycle. IL6 and IL10 were elevated in capsules at all time-points. Proteomic and RNA-seq correlation demonstrated fat metabolism to be increased in textured as compared to smooth implant capsules but less clarity evident for immune-related proteins.

Conclusions:
Smooth and textured implant surfaces elicited different and temporally dynamic immune responses. Immunogenicity of smooth implant capsules was matched with a transcriptomic propensity for fibrosis but not proliferation. Textured implant capsules upregulated lipid metabolism divergently and this may have modulatory implications for the immune response. Further work is necessary to correlate the findings of the in vivo experiments against pathological human capsular tissue.

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Abstract No.: 3 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : BREAST IMPLANT-ASSOCIATED SQUAMOUS CELL CARCINOMA: AN EVIDENCE-BASED SYSTEMATIC REVIEW

Introduction:
With the recent safety communication issued by The Food and Drug Administration, squamous cell carcinoma breast-implant associated (BIA-SCC) became part of the wide plethora of breast implant capsule (BIC) related conditions. With the current paper we present a review of the cases of BIA-SCC reported in the literature, in order to pave the way for more specific guidelines.

Materials and Methods:
From September to October 2022, we completed a systematic review of the literature on Pubmed, Cochrane and Scopus. Eight-hundred-sixty-three articles were identified. After removing all the duplicates and all the papers not strictly regarding BIA-SCC, thirteen articles were considered eligible to be reviewed, for a total of sixteen cases.

Results:
Eleven patients (79%) received bilateral augmentation, five (21%) bilateral or unilateral reconstruction following mastectomy due to breast cancer (two cases) or benign disease (three cases). Prosthesis were mostly in silicone (nine patients), six patients had saline implants, in one case the implant type was not reported. Years of implantation ranged from the 1970s to 2016. Implant’s surface was smooth in four cases, texturized in three cases and not reported in nine. The length of time from the prosthesis implantation to the clinical presentation of symptoms was less than ten years in two patients (12.5 %), a minimum of ten years in thirteen patients (81.25%) and unknown in one. History of capsular contracture was detected in eight patients (50%), while previous surgical revisions, exchange of implants or implant exposure, extrusion or infection were reported in seven cases (43.75%).

Conclusions:
The paucity of literature available on BIA-SCC does not allow us to come to definitive conclusions. What we can certainly infer is that early detection of symptoms is pivotal in the treatment decision-making. Besides, annual clinical check-ups, along with US assessment, would be a reliable option for BIA-SCC screening in asymptomatic patients.

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Abstract No.: 26 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : A new fasciocutaneous flap model identifies a critical role for endothelial Notch signaling in wound healing and flap survival

Introduction:
Flap surgery is a common treatment for severe wounds and a major determinant of surgical outcome. Flap survival and healing depends on adaptation of the local flap vasculature.

Materials and Methods:
Using a novel and defined model of cutaneous flap surgery, we demonstrate that the Notch ligand Delta-like 1 (Dll1), expressed in vascular endothelial cells, regulates flap arteriogenesis, inflammation and flap survival. Utilizing the stereotyped anatomy of dorsal skin arteries, ligation of the major vascular pedicle induced strong collateral artery development by end-to-end anastomosis in wildtype (wt) mice, which supported flap perfusion recovery over time.

Results:
In mice with heterozygous deletion of Dll1, collateral artery formation was strongly impaired, resulting in aberrant vascularization and subsequent necrosis of the tissue. Furthermore, Dll1 deficient mice showed severe inflammation in the flap dominated by monocytes and macrophages. This process is controlled by endothelial Dll1 in vivo, since the results were recapitulated in mice with endothelial-specific deletion of Dll1.

Conclusions:
Thus, our model provides a platform to study vascular adaptation to flap surgery and molecular and cellular regulators influencing flap healing and survival.

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Abstract No.: 110 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Superior Epididymal Artery Based Paraepididymal Adipofascial Flap: A Novel Experimental Adipofascial Flap Model in the Rat

Introduction:
Flap surgery is widely performed in reconstructive surgery. Experimental research is vital to improve flap viability. However, the number of flap models for animals is still limited. In this study, we define a new adipofascial flap in rats that can be used to investigate pedicled flap and/or adipofascial flap physiology.

Materials and Methods:
Eight Wistar male rats were used. Under deep anesthesia, paraepididymal adipofascial flaps were harvested. Flap perfusion was assessed using a near-infrared fluorescence imaging system. The length of the flap and the diameter of the flap pedicle were measured.

Results:
All animals (n=8) had sufficient sizes of paraepididymal fat pad and no animals were lost. The only postoperative complication was testicular hematoma, which was observed in 2 animals. The maximum length of the harvested paraepididymal adipofascial flap was 9.7 cm with a mean of 6.6 cm. The maximum width of the flap was 3.3 cm with a mean of 2.6 cm. The mean pedicle diameter of the paraepididymal adipofascial flap was 1.1 mm. Near-infrared fluorescence imaging revealed adequate perfusion in all flaps.

Conclusions:
The number of reported adipofascial flap models in animals is low, and they are mostly limited to flaps based on epigastric vessels. Superior epididymal artery-based paraepididymal adipofascial flap can be used as a pedicled flap model for studies focusing on adipofascial and/or pedicled flap physiology. Uncomplicated surgical technique and short operative time make this flap a valuable alternative to other flap models.

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SESSION 7
WOUND / REGENERATIVE

EURAPS Research Council

Abstract No.: 33 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : A prospective dual-centre intra-individual controlled study for the treatment of burns comparing dermis graft with split-thickness skin auto-graft

Introduction:
The STSG technique has been used for 150 years in surgery with limited improvements. Its drawbacks are well known and relate to donor site morbidity and recipient site cosmetic shortcomings (especially mesh patterns, wound contracture, and scarring). The Dermal graft technique has emerged as an interesting alternative, which reduces donor site morbidity, increases graft yield, and has the potential to avoid the mesh procedure in the STSG procedure due to its elastic properties.

Materials and Methods:
A prospective, dual-centre, intra-individual controlled comparison study. Twenty-one patients received both an unmeshed dermis graft and a regular 1:1.5 meshed STSG. Scar assessments were done using The Patient and Observer Scar Assessment Scale (POSAS) and a Cutometer Dual MPA 580 on both donor and recipient sites. These were also examined histologically for remodelling and scar formation.

Results:
Dermal graft (DG) donor sites and the STSG donor sites healed in eight and 14 days, respectively ($p<0.005$). Patient-reported POSAS showed better values for colour for all three measurements, i.e., three, six, and 12 months, and the observers rated both vascularity and pigmentation better on these occasions ($p<0.01$). At the recipient site, ($n=21$) the mesh patterns were avoided as the DG covered the donor site due to its elastic properties and rendered the meshing procedure unnecessary. Scar formation was seen at the dermal donor and recipient sites after six months as in the standard scar healing process.

Conclusions:
The DG technique, besides potentially rendering a larger graft yield, reduced donor site morbidity, as it healed faster and with better cosmesis than the standard STSG. Due to its elastic properties, the DG procedure eliminated the meshing requirement (when compared to a 1:1.5 meshed STSG). This promising outcome presented for the DG technique needs to be further explored, especially regarding the elasticity of the dermal graft and its ability to reduce mesh patterns.

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Abstract No.: 22 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Immunosilencing of human keratinocytes using US11 vectors and associated proteins to reduce future skin allograft rejections

Introduction:
The use of allogeneic skingrafts remains one of the standard therapies for temporary wound coverage in burn patients, but carries the risk of graft rejection. Immunomodulation of allogeneic grafts would be desirable without interfering with the immune response of the recipient organism. The human cytomegalovirus uses various strategies to evade the immune response of the recipient organism. The encoding unique short glycoprotein 11 (US11) gene has a key role in immune evasion. The aim of this proof-of-concept study was to investigate the potential of US11 proteins to reduce major histocompatibility (MHC) class I expression and thereby alloreactivity of human keratinocytes.

Materials and Methods:
Human primary keratinocytes were transfected with an US11-vectors and the reduction of MHC class I expression was quantified by Western blot, real-time PCR and flow cytometry. Keratinocytes were stimulated with recombinantly produced US11 protein and analogous quantification of MHC class I reduction was performed. To evaluate the in vivo potential of US11-stimulated keratinocytes, co-cultures with human peripheral blood mononuclear cells (PBMC) were performed. Finally, allogeneic skin samples were treated with the recombinant US11 proteins to investigate the influence on MHC class I expression in a complex tissue.

Results:
Transfection of keratinocytes with US11 vectors showed a 33% reduction in MHC class I expression at 24 hours with a return to baseline levels at 48 hours. Treatment with the recombinant protein demonstrated a 33% reduction after 6 hours. In co-cultures with PBMC, a reduced interferon gamma concentration was detected by enzyme-linked immunosorbent assays. Treatment of skin samples also showed reduced MHC class I expression after 7 days.

Conclusions:
In conclusion, the proof-of-concept study demonstrated that recombinant US11 proteins can be used as a biopharmaceutical to reduce the alloreactivity of human primary keratinocytes. Further investigation and studies are required to evaluate the potential of a US11-based biopharmaceutical in vitro and in vivo.

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Abstract No.: 30 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Mesenchymal Stem Cell-Derived Exosomes Combining with Bone Grafts Ameliorate Bone Regeneration in Mandibular Defects

Introduction:
Mesenchymal stem cells (MSCs) are known to play an important role in osteogenesis and it has been shown that their mechanism of action is based on the paracrine signaling through exosome secretion. The use of MSCs in the clinic is limited due to the short lifespan of cells, the difficulty of storage, and the risks of tumorogenesis and microthrombosis. Therefore, it is thought that MSCs-derived exosomes may be very useful in this context. Exosomes of dental pulp-derived stem cells (DPSCs), which are more readily obtained than MSCs, are predicted to be similarly beneficial for bone regeneration. In the current literature, the capacity of DPSC-derived exosomes to repair mandible defects when used with xenografts has not yet been demonstrated, especially in a large animal such as a rabbit. The aim of this study was to evaluate the effect of using DPSC-derived exosomes combined with xenografts on bone regeneration in a rabbit mandible bone defect model.

Materials and Methods:
Ten New Zeland white rabbits were included and right hemimandibles served as the control group (xenograft + saline) while the left was the experimental group (xenograft + exosomes). Histomorphometry and Micro-computed tomography (Micro-CT) analysis were performed.

Results:
In histomorphometric studies, more new bone formation was observed in the experimental group (4.87 ± 36 0.78) compared to the control group (2.87 ± 0.41, p=0.00). It was observed that the number of osteoblasts and the formation of new bone matrix increased in the experimental group, and inflammation and collagen connective tissue synthesis were less. Micro-CT analysis revealed that there was no statistically significant difference in new bone volume and new bone surface among the groups, but bone mineral density, trabecular thickness and separation were higher in the experimental group ($p<0.05$).

Conclusions:
DPSC-derived exosomes combined with xenografts ameliorated new bone formation for repairing critical-size defects in the rabbit mandible.

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Abstract No.: 94 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Vascularization of tissue engineered cartilage - Sequential in vivo MRI display functional blood circulation

Introduction:
Establishing functional circulation in bioengineered tissue after implantation is vital for the delivery of oxygen and nutrients
to the cells. Native cartilage is avascular and thrives on diffusion, which in turn depends on proximity to circulation. Here, we investigate whether a gridded three-dimensional (3D) bioprinted construct would allow ingrowth of blood vessels and thus prove a functional concept for vascularization of bioengineered tissue.

Materials and Methods:
Twenty 10 × 10 × 3-mm 3Dbioprinted nanocellulose constructs containing human nasal chondrocytes or cell-free controls were subcutaneously implanted in 20 nude mice. Over the next 3 months, the mice were sequentially imaged with a 7 T small-animal MRI system, and the diffusion and perfusion parameters were analyzed.

Results:
The chondrocytes survived and proliferated, and the shape of the constructs was well preserved. The diffusion coefficient was high and well preserved over time. The perfusion and diffusion patterns shown by MRI suggested that blood vessels develop over time in the 3D bioprinted constructs; the vessels were confirmed by histology and immunohistochemistry.

Conclusions:
We conclude that 3D bioprinted tissue with a gridded structure allows ingrowth of blood vessels and has the potential to be vascularized from the host. This is an essential step to take bioengineered tissue from the bench to clinical practice.

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Abstract No.: 108 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Hypoxia Preconditioned Serum (HPS) Promotes Osteoblast Proliferation, Migration and Matrix Deposition

Introduction:
Hypoxia preconditioned serum (HPS) is a new-generation blood-derived secretome that provides a therapeutic tool for bioactively supporting tissue repair by promoting angiogenesis/lymphangiogenesis, proliferation/migration of fibroblasts and dermal skin regeneration. In this study, we employed HPS on human osteoblasts to examine its biological effects.

Materials and Methods:
Human osteoblasts from 3 donors were stimulated with 2 HPS concentrations (10% and 40%) and analyzed on day 2 and 4 compared to controls (cell media only). Analysis included cell viability assays (cell counts and LDH assay), migration assay, ELISA measurements of Osteoprotegerin (OPG) and sRANKL (soluble Receptor Activator of NF-κB Ligand), ALP (alkaline phosphatase)-enzyme activity and ossification assessment through Alizarin-Red staining.

Results:
Compared to controls, a time- and dose-dependent (up to 14.2× higher) proliferation of osteoblasts was observed after 4 days of HPS-40% stimulation with lower LDH-levels detected than controls, indicating the absence of cytotoxic/stress effects of HPS on human osteoblasts. With regards to cell migration, it was found to be significantly faster with HPS-10% after 72h compared to controls. Culture supernatant analysis showed significant upregulation of OPG with higher dosage (HPS-10% vs. HPS-40%) and longer duration (2d vs. 4d) of HPS stimulation. There was no detection of anti-osteogenic sRANKL after 4 days of HPS stimulation. ALP-activity was found to be upregulated, dose-dependently, after 4 days with HPS-40%. When assessing ossification capacity through Alizarin-Red staining, HPS dose-dependently achieved greater (up to 2.8× higher) extracellular deposition of calcium-phosphate with HPS-40% compared to controls.

Conclusions:
We were able to demonstrate a substantial osteogenic response to HPS treatment via the promotion of proliferation, migration and matrix deposition of human osteoblasts which suggests a possible activation of bone tissue production in vivo. Therefore, HPS holds the potential of promoting bone regeneration.

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Abstract No.: 78 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : miRNome and proteome profiling of human keratinocytes and adipose derived stem cells proposed miRNA-mediated regulations of epidermal growth factor and interleukin 1-alpha

Introduction:
Wound healing is regulated by complex crosstalk between keratinocytes and other cell types across the skin. Keratinocytes provide a cell-transplantation solution for non-healing wounds as autologous applications. Adipose-derived stem cells (ADSCs) have shown potential for differentiation into epidermal cells and involvement in wound healing. The differentiation process still needs further characterization based on understanding cell-cell cross communication.

Materials and Methods:
In this study, a 7-day direct co-culture model comprising of human keratinocytes and adipose-derived stem cells (ADSCs) at a 1:1 ratio is proposed. Molecular and immunocytochemical screening of epidermal differentiation markers revealed direct co-culture promoted differentiation of ADSCs toward the epidermal lineage. As major mediators of cell communication, miRNome and proteome profiles in the cell lysates of cultured human keratinocytes and ADSCs were explored through experimental and computational analyses. Potential miRNA-mediated gene and protein regulations that can alter the fate of ADSCs to differentiate into keratinocyte-like cells were extracted.

Results:
GeneChip® miRNA microarray, identified 378 differentially expressed miRNAs (DEmiRNAs); of these, 114 miRNAs were upregulated and 264 miRNAs were downregulated in keratinocytes. According to miRNA target prediction databases and the Expression Atlas database, 109 skin-related genes corresponding to 26 upregulated miRNAs in keratinocytes were obtained. Pathway enrichment analysis revealed 14 pathways including vesicle-mediated transport, signalling by interleukin and others. Proteome profiling showed significant upregulation of the epidermal growth factor (EGF) and Interleukin 1-alpha (IL-1α) compared to ADSCs.

Conclusions:
Integrated analysis, through cross-matching the differentially expressed miRNA and proteins proposed two potential pathways for regulations of epidermal differentiation; the first is EGF-based through the downregulation of miR-485-5p and miR-6765-5p and/or the upregulation of miR-4459. The second is mediated by IL-1α overexpression through four isomers of miR-30-5p and miR-181a-5p.

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Abstract No.: 17 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Fibroblast growth factor FGF-21 is crucial for the revascularization of white adipose tissue grafts

Introduction:
Autologous fat grafting is a common procedure in reconstructive and aesthetic surgery. Fat survival is the major clinical outcome and it is crucially determined by a rapid and proper blood supply of the grafts, which best prevents volume loss due to resorption. This study aimed at investigating the function of fibroblast growth factor FGF-21, a hepatokine with metabolic and pro-angiogenic activity, in the revascularization process of white adipose tissue grafts.

Materials and Methods:
Subcutaneous white adipose tissue was harvested from 4 FGF21-knockout (KO) mice and 4 C57BL/6J wild-type (WT) control mice and cut into samples with standardized dimensions (0.5x0.5x0.5 mm). Thereafter, the samples were transplanted into the dorsal skinfold chamber of corresponding FGF21-KO (n = 8) and WT recipient animals (n = 8) to study graft revascularization by means of repeated intravital fluorescence microscopy over an observation period of 14 days. The perfused area of the grafts(mm^2), functional capillary density (cm/cm^2), vessel diameter (μm), red blood cell (RBC) velocity (μm/s), shear rate (s-1) and blood flow (pL/s) were repeatedly evaluated. All values were expressed as means±SEM. Statistical significance was accepted for $p<0.05$.

Results:
A delay in revascularization of FGF21-KO mice transplanted white adipose tissue was demonstrated, as indicated by a significantly reduced perfused graft area (1.6±0.9%) at day 6 when compared to controls (12.4±5.1%). This resulted in a significantly lower final functional microvessel density within the grafts (249±11cm/cm^2 vs. 361±15cm/cm^2). Moreover, vessel maturation was equally impaired in FGF21-KO mice, as shown by the larger diameters of newly formed graft microvessels on day 14 (13.1±0.3µm vs. 11.7±0.1µm).

Conclusions:
The findings suggest that FGF21 plays a pivotal role in white adipose tissue graft revascularization. Therefore, this hepatokine represents a promising target for the development of novel strategies to increase graft vascularization and eventually graft survival.

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Abstract No.: 105 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Xenogenic implantation of Human Adipose Matrix results in adipose tissue formation and survival in mice conditioned with External Volume Expansion

Introduction:
Conditioning of a fat grafting site with External Volume Expansion (EVE) can increase adipose graft survival. In this study, non-immunocompromised mice were conditioned with EVE before and after grafting of a human adipose matrix (HAdMx) and long-term adipose tissue survival was assessed.

Materials and Methods:
Thirty-four wild type (C57BL/6J) mice provided 68 recipient sites separated into four treatment groups. Thirty-four sites were pre-conditioned with EVE for five days before grafting of 300 μL HAdMx. Half of these sites were immediately post-conditioned for five days after grafting (Imm-HAdMx group) and 17 were delayed post-conditioned for five days starting 28 days after grafting (Del-HAdMx group). Thirty-four sites were not conditioned and were subcutaneously injected with 300 μL of saline (n=17; Sal group) or HAdMx (n=17; HAdMx group). Tissue harvested 12 week after grafting was analyzed.

Results:
Compared to the unconditioned HAdMx group, the Imm-HAdMx and Del-HAdMx groups showed significantly higher adipose volume retention ($p=0.02$ and $p<0.0001$, respectively), greater angiogenesis ($p=0.04$ and $p=0.02$, respectively), and lower macrophage infiltration ($p=0.002$ and $p=0.003$, respectively). The Del-HAdMx group also showed significantly greater presence of Adipose Stem Cells than the HAdMx group ($p=0.01$). Conditioning significantly increased the molecular expression of LPL, PPAR-γ and VEGF, as verified with PCR and Western blotting analysis.

Conclusions:
Modulation of the recipient site microenvironment with the mechanical forces exerted by EVE promoted angiogenesis and augmented adipogenesis and survival of the neo-adipose tissue. Recipient site conditioning with EVE, particularly when post-conditioning was applied at a delayed time point, permeated adipose tissue formation and survival of a transplanted xenogenic adipose matrix. This experiment highlights the potential of EVE to be used as an adjuvant to optimize fat grafting.

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Abstract No.: 1 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Nanofat contains functional microvessel segments that boost tissue vascularization

Introduction:
Nanofat injections are a frequently applied technique in the field of plastic surgery due to the grafts' regenerative effects that may improve scar quality and rejuvenate skin. However, the underlying mechanisms have not been fully clarified. Therefore, with the present study we investigated nanofat grafts in a murine dorsal skinfold chamber model.

Materials and Methods:
The subcutaneous inguinal fatpad of green fluorescent protein (GFP)+ C57BL/6 male and female donor mice was used to generate nanofat. The nanofat was subsequently injected intracutaneously into dorsal skinfold chambers of gender-matched GFP− wild-type mice. Vascularization and tissue composition of the grafted nanofat were analyzed by means of repeated intravital fluorescence microscopy, histology and immunohistochemistry over a 14-day observation period.

Results:
The freshly generated nanofat still contained surviving perilipin+ adipocytes surrounded by Sirius red+ collagen fibers. Moreover, intact CD31+/GFP+ vessel segments could be detected. These segments survived transplantation into the dorsal skinfold chamber and developed interconnections to the surrounding CD31+/GFP− host microvasculature. Thus, the grafted nanofat rapidly vascularized and formed new microvascular networks with a high functional microvessel density on day 14 without marked differences between male and female mice.

Conclusions:
Even though further research is warranted to confirm the findings of this study, the results suggest that nanofat effectively boosts tissue vascularization. Hence, nanofat may represent a versatile and clinically feasible resource for many applications in tissue engineering and regenerative medicine.

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SESSION 8
NERVE

EURAPS Research Council

Abstract No.: 111 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Increasing Translatability of Cell Therapy for Peripheral Nerve Injury; Investigating SPIONs and HPL in vitro.

Introduction:
Peripheral nerve injury (PNI) from cancer or trauma is common (~1/1,000 population) and devastating. Only 40-50% of patients achieve meaningful recovery following direct, graft or conduit microsurgical repair. Schwann cells provide structural guidance and growth factor secretion for regenerating axons; currently, extraction of Schwann cells necessitates sacrifice of nerve. Adipose derived stem cells (ADSC) are a proposed cell therapy to bioengineer nerve conduits. Patient safety factors pose challenges to clinical translation; end cell site and behaviour must be determined, whilst animal products pose disease transmission risk.

Materials and Methods:
Our group established a nerve conduit rat model, featuring topography and Super Paramagnetic Iron Oxide Nanoparticle (SPION) labelled ADSC. At 14 days, ex vivo, MicroCT image achieved resolution better than 5 μm. This study investigates green, 200nm SPION effects (0.01mg/ml and 0.1mg/ml concentration) on Human ADSC with HPL supplement (FBS ADSC control). ADSCs were harvested in accordance with Human Tissue Act(2004) and Biobank(304). Growth assay assessed proliferation, flow cytometry confirmed CD markers, with Cell Profiler morphology analysis.

Results:
98% of ADSCs exhibited nanoparticle uptake. Stemness CD markers 90,105 and 73 were retained at 0.01mg/ml and 0.1mg/ml SPIONs. ADSC with 0.01mg/ml SPION labelling and HPL were associated with an increase in proliferation ((P=<0.0001 Mann Whitney) n=2) and spindle like morphology ((P=<0.0001 Mann Whitney) n=2).

Conclusions:
These preliminary studies are promising; retention of ADSC CD markers, increase in cell proliferation and increase in spindle cell morphology may facilitate clinical translation of cell therapy.

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Abstract No.: 4 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Evaluation of a guided nerve repair using multi-lumen aligned nanofibrillar collagen scaffold in a rabbit model

Introduction:
When coaptation in large peripheral nerve defects can be challenging, autologous nerve grafts or various biomaterials can be used with different advantages. The aim of our study is to examine different biomaterials based on multi-lumen aligned nanofibrillar collagen scaffolds (BB) in nerve regeneration.

Materials and Methods:
A 2 cm sciatic nerve defect was created in the right hindlimb of 25 rabbits. The animals were divided in 5 different treatment groups. Group A underwent an autologous nerve graft, Group B followed a secondary healing approach, Group C had a nerve replacement with a BB collagen scaffold inserted in a neurotube (N), Group D followed the previous biomaterials BB+N enriched with silver nanowires (Ag), and Group E underwent an application of electrical stimulation at the BB+N+Ag biomaterial. All rabbits were examined by electromyography (EMG), and the compound muscle action potential (CMAP) values of both limbs were obtained after periods of 6 and 12 weeks. Histopathological examination of the gastrocnemius muscles was performed at 12 weeks.

Results:
At the midterm evaluation, CMAP of groups A, B, C, D, E were 16.7%, 0%, 13.4%, 12% and 9.2% ($p<0.05$ between group A and C vs B), while at the final evaluation CMAP were 26.7%, 0%, 24%, 27.7% και 26.1% respectively ($p<0.05$ between A, C, D, E vs B).
The histology of the specimens demonstrated that the group A had the least atrophy of the muscle fibers, almost similar was the group E, followed by the groups C and D with more extensive muscle atrophy and initial adipose degeneration. Group B had demonstrated major muscle atrophy and fat deposition.

Conclusions:
Multi-lumen aligned nanofibrillar collagen scaffolds into a neurotube may provide similar results as autologous nerves. The addition of silver nanowires and electrical stimulation could enhance and expediate the process of nerve regeneration.

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Abstract No.: 36 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Axonal components of the lumbosacralis plexus.

Introduction:
Nerve transfer surgery is a well-established and commonly used surgical treatment option for peripheral nerve injuries and root avulsion injuries when direct coaptation is not possible. The motor fiber count of the recipient as well as the donor nerve is an important prerequisite for successful nerve transfers. While a quantitative analysis of the brachial plexus' motor and sensory axons has been recently reported, similar data for the lumbosacral plexus does not exist. In this study we aimed to analyze the motor and sensory fiber count of nerves arising from the lumbosacral plexus.

Materials and Methods:
The lumbosacral plexus was investigated at multiple levels, reaching from the spinal roots to terminal muscular and sensory branches. Nerve samples were harvested in 10 human cadaver specimens within 24 hours post-mortem. The samples were then processed and subjected to a double immunofluorescence staining protocol using antibodies against choline-acetyltransferase (ChAT) and neurofilament (NF). NF labels all axons, while ChAT identifies motor axons, thus making it possible to distinguish motor and sensory axons in nerve cross sections.

Results:
Our recently established double immunofluorescence staining protocol was successfully used on nerve samples harvested from cadaver specimens within 24 hours post-mortem. We counted over 300000 nerve fibers in the spinal roots Th12 – S4 and investigated the axonal composition of major peripheral nerves, including the femoral nerve (total axons 75273 ± 6158, motor axons 5621 ± 303), the obturator nerve (total axons 20473 ± 2660, motor axons 2880 ± 505), the tibial nerve (total axons 70907 ± 11731, motor axons 6081 ± 1086), the common peroneal nerve (total axons 40393 ± 3742, motor axons 2133 ± 411) and their branches.

Conclusions:
The presented data contributes to the advanced understanding of the axonal composition of peripheral nerves arising from the lumbosacral plexus.

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Abstract No.: 7 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Hyperbaric oxygen treatment promotes axonal outgrowth

Introduction:
Hyperbaric oxygen (HBO) is a promising therapeutic approach to promote peripheral nerve regeneration. Underlying mechanisms of action are poorly understood resulting in inconsistent treatment protocols and unclear indications. The present study evaluated the effects of single or repeated HBO treatment alone or in combination with nerve growth factor (NGF) on PC12 cells. Cell proliferation, survival and differentiation (neurite outgrowth) were analyzed.

Materials and Methods:
PC12 cells were exposed to a single session of HBO (90min) or daily sessions on four consecutive days. Five groups were studied with or without NGF stimulation: control (21% oxygen), 100% oxygen at 1.0 ATA (atmosphere absolute), 2.0 ATA, 2.5 ATA or 3.0 ATA. Brightfield imaging, live/dead assay, cell proliferation using alamar blue reagent and axonal outgrowth using immunostaining of tubulin beta-III were performed.

Results:
Single dose of HBO treatment enhanced the proliferation of PC12 cells without NGF at all pressure conditions compared to control($p<0.05$). In contrast, repeated HBO sessions without NGF stimulation increased dead cell count at 2.0ATA, 2.5ATA and 3.0ATA compared to control($p<0.01$). Of note, repeated HBO treatment in NGF-stimulated PC12 cells resulted in maintained cell numbers and significant increase in axonal outgrowth as evidenced by tubulin beta-III staining ($p<0.05$). However, 3.0 ATA impeded axonal outgrowth in all groups.

Conclusions:
While single HBO exposure significantly increased cell numbers in cells without NGF stimulation, repeated HBO decreased cell count and induced cell death. Interestingly, NGF exhibited neuroprotective effects against oxidative stress-mediated cell death in PC12 cells. In fact, repeated HBO treatment (1-2.5 ATA) resulted in significant stimulation of axonal outgrowth in NGF-stimulated cells. These results hold great promise for neural repair and regeneration applications. Further research is needed for investigating the underlying mechanisms of NGF-HBO mediated functional effects in vitro and in a rat model of sciatic nerve injury.

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Abstract No.: 12 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Using adipose stem cell spheroids with fibrin hydrogel-assisted delivery for peripheral nerve repair: an experimental study

Introduction:
The current treatment options of peripheral nerve injuries, despite substantial advancements, are still unsatisfactory. One promising approach is fibrin-hydrogel nerve conduits (FNCs) loaded with human adipose stem cells (hASCs) for nerve guidance, protection and for local release of neurotrophic factors (TNFs). The combination of FNCs and ASCs showed promising results in vitro and in vivo for nerve regeneration. Within this context, ASCs based spheroids are emerging for enhanced cytokine profile. However, their therapeutic effect on nerve regeneration is unknown. Thus, the present study aimed for fabrication and characterization of hASCs spheroids for nerve tissue engineering applications.

Materials and Methods:
Spheroids based on hASC (passage 4 to 5) were generated using agarose microwell mould. For identifying the optimal culture conditions, various cell seeding densities (i.e., 1000 or 2000, 3000 and 4000 cells/spheroid) were used and the cultures were maintained over seven days. Subsequently, the spheroids were characterized by measuring the size, growth kinetics and intracellular ATP content.

Results:
hASC spheroids have been well established. In general, the size and the ATP levels correlated to the cell seeding density. After a 24-hour period of compaction, the spheroid-size and the ATP content remained stable over 7 days for low-density spheroids. For the high density (i.e., 4000 cells/spheroid), the size and the ATP content showed a marked decline in the last days of culture (day 6 and 7).

Conclusions:
We successfully established optimal conditions for formation of hASC spheroids for seven days. Monitoring the growth of spheroids with their size and ATP levels revealed early changes in spheroid viability. To further validate this model, NTFs expression profile will be analysed. Subsequently, spheroids will be combined with FNCs for treating the sciatic nerve injury in rats.

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SESSION 9
BREAST / MICROSURGERY

EURAPS Research Council

Abstract No.: 95 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Long-term nanoparticle treatment of seromas: a comparative rat model study

Introduction:
Seroma formation is a common postoperative complication. While the best solution has yet to be found, recent focus has been put on bioglass/ceria nanoparticles (NPs) for seroma treatment. Although significant early seroma reduction has been shown, little is known about long-term efficacy of NPs. Therefore, the aim of this study was to assess the long-term effects of NPs in reducing seroma formation, and to understand their underlying mechanism.

Materials and Methods:
Seroma was surgically induced bilaterally in the axillary areas of 20 Lewis rats. On postoperative day (POD) 7, seromas were aspirated on both sides. In 10 rats, one side was treated with NPs, while the contralateral side received only the buffer solution of the NPs. In the other 10 rats, one side was treated with fibrin glue, while the other was left untreated. Seroma fluid, blood and tissue samples were obtained at defined time points. At euthanasia (POD 42), blood and tissue samples were harvested and biochemical, histopathological and immunohistochemical analyses were undertaken.

Results:
NP-treated sides showed no seroma formation after application on POD 7, compared to fibrin-treated sides, where 60% of the rats had seromas on POD 14, and 50% on POD 21. At endpoint, NP-treated sides showed significant macroscopic differences compared to other groups: absent cavities and increased adhesions (NP-treated sides had adhesion scores of 2 - 3 vs. 0 - 1 for the fibrin and untreated sides, $p <= 0.03$).

Conclusions:
Not only do NPs significantly reduce early manifestations of seroma, they also lead to long-term increased adhesion formation and prevent cavity formation. These findings emphasize the adhesive properties of NPs and underline their therapeutic potential in a clinical setting.

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Abstract No.: 23 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Influence of tamoxifen treatment on genetic factors of breast carcinogenesis - an in vitro study with adipose-derived stem cells

Introduction:
According to the current guidelines, anti-hormonal therapy with tamoxifen plays a crucial role in estrogen receptor-positive breast carcinoma. The spectrum of autologous breast reconstruction ranges from autologous fat grafting to complex microsurgical procedures. There is currently no conclusive recommendation regarding tamoxifen-treated patients and autologous fat grafting. Especially the influence of adipose-derived stem cells (ASC) on the tumor bed and a possibly increased recurrence rate as a result, are critically discussed. The aim of the present study was to investigate the effect of tamoxifen on the gene expression of a variety of genes involved in tumorigenesis, cell growth and transformation included in breast carcinogenesis.

Materials and Methods:
Human ASC, MCF-10A cells, MCF-7 cells as well as BT-474 cells were cultured individually or in co-cultures. Cell cultures were treated daily with 5 µM, 15 µM or 25 µM tamoxifen for 48 and 96 hours. Gene expression was quantified using PCR arrays, covering a total of 84 genes of breast carcinogenesis. PCR arrays covered genes of the following eight biological pathways: angiogenesis, apoptosis, cell cycle, cellular senescene, DNA damage and repair, epithelial-to-mesenchymal transition, hypoxia signaling, metabolism as well as telomeres and telomerase.

Results:
Studied genes showed overall an increased expression in mammary carcinoma cell lines with increasing time of treatment and concentrations of tamoxifen. This effect could be further enhanced for individual genes by co-cultivation with ASC. The molecular biological results of the present study partly provided controversial results to the previous clinical data. In general, tamoxifen medication might be a crucial factor for cell growth and cancer recurrence.

Conclusions:
The broad acceptance of tamoxifen in the adjuvant setting could not be argued on the base of the presented in vitro results. Although a higher take rate of fat grafts might be assumed, a discontinuation of tamoxifen medication prior to autologous fat grafting should be discussed.

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Abstract No.: 91 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Capsular inflammation after immediate breast reconstruction - Gene expression patterns and inflammatory cell infiltration in irradiated and non-irradiated breasts

Introduction:
Capsular contracture following post-mastectomy radiotherapy (PMRT) is commonly seen in patients undergoing implant-based immediate breast reconstruction (IBR). Further understanding of the underlying biology is needed for the development of preventive or therapeutic strategies. Therefore, we conducted a comparative study of gene expression patterns in capsular tissue from breast cancer patients who had received versus those who had not received PMRT after implant-based IBR.

Materials and Methods:
Biopsies from irradiated and healthy non-irradiated capsular tissue were harvested during implant exchange following IBR. Biopsies from irradiated (n = 13) and non-irradiated (n = 12) capsules were compared using Affymetrix microarrays to identify the most differentially regulated genes. Further analysis using immunohistochemistry was performed in a subset of materials to compare the presence of T cells, B cells, and macrophages.

Results:
Enrichment testing using Gene Ontology (GO) analysis revealed that the 227 most differentially expressed genes were mainly involved in an inflammatory response. Twenty-one GO biological processes were identified [$p < 0.05$, false discovery rate (FDR) < 5%], several with B-cell-associated inflammation. Cell-type Identification by Estimating Relative Subsets of RNA Transcripts (CIBERSORT) analysis identified macrophages as the most common inflammatory cell type in both groups, further supported by immunostaining of CD68. Radiation remarkably increased B-cell infiltration in the capsular region of biopsies, as quantified by immunostaining of CD20 ($p = 0.016$).

Conclusions:
Transcript analysis and immunohistochemistry revealed inflammatory responses in capsular biopsies regardless of radiotherapy. However, the radiation response specifically involved B-cell-associated inflammatory responses.

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Abstract No.: 98 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Dermal Nipple-Areolar Complex Perfusion through Full Thickness Circumareolar Scars in bilateral Two-Stage Nipple Sparing Mastectomy: dynamic anatomical similarities in dermal neoangiogenesis in human clinical and porcine experimental results

Introduction:
In large breasts, surgeons remain reluctant to perform nipple-sparing mastectomy (NSM) due to higher risk of nipple-areola-complex (NAC) necrosis. Delayed procedures enhance blood supply to NAC in multiple stages. Neovascularization through circumareolar scars in pigs provides sufficient dermal NAC perfusion without necrosis after 4 weeks delay. The purpose of this study is to investigate the similarity between a porcine model and clinical human results in neovascularization to NAC after staged NSM. Neoangiogenesis is shown dynamically by near-infrared fluorescence imaging.

Materials and Methods:
Seven BRCA patients (14 NAC) with large breasts were offered a bilateral two-stage reduction through Wise pattern incisions followed by prosthetic reconstruction after 3 months. Delayed NSM is simulated in 25 nipples (3 pigs) with a 4 weeks-interval. The nipples undergo a full thickness circumareolar incision onto the muscular fascia with preservation of underlying glandular perforators. In the second stage NSM is performed. A silicone sheet is introduced in the mastectomy plane to prevent NAC revascularization by wound bed imbibition. Near-infrared fluorescence with indocyanine green (ICG) is used to assess perfusion patterns.

Results:
No NAC necrosis is seen in 14 human and in 25 porcine NAC. The alteration in perfusion pattern is similar in humans as in pigs. ICG-scan shows complete alteration of NAC perfusion pattern from V1 (subjacent gland) to V4 pattern (capillary fill following devascularization exhibiting a predominant arteriolar capillary blush without distinct larger vessels) in all human and porcine nipples. Complete reperfusion through circumareolar scars takes about three minutes in humans and five minutes in pigs.

Conclusions:
NAC delay reverses glandular perfusion similarly to adequate dermal neovascularization in pigs as in humans. This pilot study suggests that a clinical study in humans with a 4-weeks interval would be feasible. From an anatomical point of view a 4-weeks interval would broaden the indications for this staged technique to therapeutic NSM.

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Abstract No.: 97 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Reconstruction of the human nipple-areolar complex: A novel tissue engineering approach

Introduction:
Reconstruction of nipple-areolar complex (NAC) after breast cancer surgery is challenging because it does not always provide optimal long-term aesthetic results. Generating an NAC using tissue engineering techniques is therefore an alternative option to recreate a specific 3D morphological unit, covered with an in vitro regenerated epidermis and thereafter skin-grafted on the reconstructed breast.

Materials and Methods:
NACs (n=24) were harvested from 15 cadaveric donors and decellularized (n=15) with detergents. Cellular clearance and extracellular matrix (ECM) preservation were confirmed by histology as well as by DNA, ECM proteins, growth factors and residual SDS quantification. Biocompatibility was evaluated 30 days after subcutaneous implantation of native (n=5) and decellularized (n=5) scaffolds in rats. Cytocompatibility was assessed by seeding fibroblasts on the hypodermal side of the scaffold, while keratinocytes were seeded on the epidermal side, using the Reconstructed Human Epidermis (RHE) technique.

Results:
Decellularized NAC showed a preserved 3D morphology and appeared white. After decellularization, a DNA reduction of 98,3% ($p<0.001$) and the absence of nuclear and HLA stainings at the histology confirmed the complete cellular clearance. ECM microarchitecture and composition were preserved, associated with a low amount of SDS residues, as well as the detection and decrease of growth factors. Biocompatibility was confirmed by the absence of rat anti-human IgG at 30 days of implantation in the decellularized group (4/5) in comparison to the native group (0/5). Seeded fibroblasts showed an increasing proliferation until 7 days of culture and a similar viability to the control cells. RHE technique allowed to recreate a keratinized pluristratified epithelium after 7 days of culture.

Conclusions:
Tissue engineering allowed to create acellular NACs preserving their specific architecture and matrix proteins while maintaining their cell growth potential and ability to regenerate skin epidermis.

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Abstract No.: 70 **Category:** General Research **Time:** -

Event : 11th EURAPS Research Council Meeting, STOCKHOLM, Sweden, 24-25 May 2023

Title : Novel robot-assisted microsurgery – what does the learning curve look like?

Introduction:
A new robotic system has been developed specifically for microsurgery to allow the surgeon to use the same microsurgical instruments and microscope as by hand, called the MUSA (MicroSure, Eindhoven, The Netherlands). As with other robotic systems, general advantages are filtering tremors and motion scaling. The current study aims at describing the introduction of robot-assisted microsurgery in a high-volume center and evaluate the learning curve for robot-assisted microsurgery in relation to the previous microsurgery experience.

Materials and Methods:
Participating doctors were divided into three groups based on previous microsurgical experience. Each doctor performed ten sessions in a microsurgery lab. During each session, the doctor performed one anastomosis by hand and one with robot assistance. Artificial vessels with a diameter of 2 mm were used and anastomosed with six single 9-0 sutures. Data was collected on time spent at anastomosis, anastomosis quality, the surgeon's self-evaluation of performance, stress level, and the ergonomic experience.

Results:
Time spent at the first robot-assisted anastomosis ranged from 28 – 79 minutes. After five sessions, all participants, regardless of group, had cut their time to half. Reported effort at the first anastomosis performed with robot assistance ranged from 20 to 12 on a scale from 20 (very high) to 0 (very low), but for the fifth, it ranged from 20 to 4. The experienced microsurgeons needed less effort over time with each robot-assisted anastomosis than the inexperienced group.

Conclusions:
The learning curve for robot-assisted microsurgery is steep for all groups, and inexperienced doctors can learn robot-assisted microsurgery. However, the quality of anastomosis and the effort needed for the anastomosis differed between groups, and experienced microsurgeons had an advantage. When assessing the quality of anastomosis, the surgeons in training made fewer mistakes with robot assistance than with hand sewn.

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