

Back to the future in TBI (Trauma Plenary Session), September 27, 2023, 2:30 PM - 4:10 PM

Background: Spinal cord injuries (SCI) lead to functional alteration with important consequences such as motor and sensory disorders. The repair strategies developed to date remain ineffective. The adipose tissue-derived stromal vascular fraction (SVF) is composed of a "cocktail" of mesenchymal and hematopoietic stem cells with trophic, pro-angiogenic and immunomodulatory effects. Numerous therapeutic benefits were shown for tissue reconstitution, peripheral neuropathy and for the improvement of neurodegenerative diseases. **Methods:** Our strategy is based on an autologous injection of the SVF within 4 hours after SCI. To check our hypothesis, we conducted a pre-clinical study in adult male rats. Contusions performed at thoracic level T10 using an impactor, all the animals were paraplegic. The epididymal fat removed in a second time, then the autologous SVF is purified (>90% of viability), before 1 million of cells are directly injected into the lesion.

Results: Autologous SVF implantation promotes 1) locomotor recovery (BBB test, Ladder rung walking test, Catwalk), 2) H-reflex normalization, and ventilatory frequency adjustment to an isometric exercise. 3) In vivo 7T MRI, shows signs of regeneration and revascularization. We also identified a biomarker for the following of the inflammation. These results were confirmed by 4) immunohistological stainings (angiogenesis with CD31, number of neurons with MAP2 and axonal regeneration with GAP43), and by 5) studying proinflammatory cytokines (IL-1, IL-6, TNF- α) by ELISA.

Conclusions: These encouraging results demonstrate significant recovery post-autologous SVF implantation that could be improved by treadmill exercise. The work is currently being carried out in pigs before moving on to humans.

85

BRAIN AND SPINE 3 (2023) 101794 101840

CLINICAL AND RADIOLOGICAL EFFICACY OF THE MIDLINE LUMBAR INTERBODY FUSION (MIDLIF) IN TREATING PATIENTS WITH DEGENERATIVE SPONDYLOLISTHESIS: FINAL RESULTS OF A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Serghei Borodin^{1,2}, Aureliu Bodiu^{1,2}, Eduard Eftodiev¹, Sergiu Boboico¹, Igor Gherman². ¹Republican Clinical Hospital, Chisinau, Moldova (the Republic of); ²Nicolae Testemitanu State University of Medicine and Pharmacy, Chisinau, Moldova (the Republic of)

Spine Parallel Session v.4, September 28, 2023, 8:30 AM - 10:00 AM

Background: Standard surgical treatment techniques for degenerative lumbar spondylolisthesis involve fixation of the spine with pedicle screws to increase the success of intervertebral fusion. Pedicle screw insertion requires extensive lateral muscle dissection and retraction, resulting in a significant increase in surgery-related morbidity. To overcome some of these drawbacks, the cortical bone trajectory (CBT) pedicle screw fixation and the midline lumbar interbody fusion (MIDLIF) techniques have recently been developed. To date, the clinical efficacy of the MIDLIF technique in the treatment of low-grade degenerative spondylolisthesis is not fully established.

Methods: A prospective randomized controlled trial was conducted between 2017 and 2022 in the Neurosurgery Department of the Republican Clinical Hospital of Moldova. The study analyzed the clinical and radiological efficacy of the MIDLIF arthrodesis technique compared to traditional lumbar interbody fusion techniques used exclusively in the treatment of degenerative lumbar spondylolisthesis. The trial enrolled 112 eligible patients with degenerative low-grade spondylolisthesis, randomly assigned into two groups. The minimum follow-up period was at least 12 months post-operatively. Data from ODI, VAS and SF-12 questionnaires were recorded.

Results: Similar fusion rates were observed in both groups one year after the operation. Midline lumbar interbody fusion provided a significantly better improvement in postoperative relief of the low back pain, and a significantly better functional recovery at 1 year post-operatively. In addition, MIDLIF resulted in significantly less surgery-related morbidity than traditional fusion techniques.

Conclusions: CBT pedicle screw fixation is as effective as traditional transpedicular techniques in achieving successful lumbar interbody fusion. At the same time, MIDLIF provides the typical benefits of a minimally invasive approach such as shorter incision, less bleeding, less need for hemotransfusion, less post-operative pain and faster functional recovery. Thus, it could be a reliable alternative to the traditional fusion techniques in well selected patients with degenerative low-grade spondylolisthesis.

503

BRAIN AND SPINE 3 (2023) 101794 101841

STENT-SCREW ASSISTED INTERNAL FIXATION WITH APEX PUSHING TECHNIQUE FOR KYPHOSING THORACOLUMBAR FRACTURES (SAIFAP)

Stefan Motov^{1,2}, Gregor Fischer^{1,2}, Thomas Forster^{2,3}, Roman Schwizer^{2,3}, Benjamin Martens^{2,3}, Martin Stienen^{1,2}. ¹Department of Neurosurgery, Cantonal Hospital St.Gallen & Medical School of St.Gallen, Switzerland; ²Spine Center of Eastern Switzerland, Cantonal Hospital St.Gallen & Medical School of St.Gallen, Switzerland; ³Department of Orthopedic Surgery, Cantonal Hospital St.Gallen & Medical School of St.Gallen, Switzerland

Spine Parallel Session v.4, September 28, 2023, 8:30 AM - 10:00 AM

Background: Short- or long-segment posterior stabilization with vertebral body stent (VBS) in the index vertebra and cement-augmented pedicle screws (stent-screw assisted internal fixation = SAIF) is a treatment option in kypshing thoracolumbar fractures and may avoid corpectomy in some situations. SAIF was effective in obtaining height restoration, kyphosis correction and pain relief in smaller series with vertebral collapse. There is little information about the effect of the combination of SAIF with the apex pushing technique (APT) to reduce segmental kyphosis.

Methods: We retrospectively included all patients treated at the Kantonsspital St. Gallen between 2016 and 2023 with a surgical technique, which combines the SAIF and APT (SAIFAP). Radiological and clinical data for all patients with osteoporotic, traumatic and pathological fractures who were treated with SAIFAP were obtained. Statistical analysis was performed through SPSS Version 28, IBM. We performed t-tests for independent samples and a Chi-Square tests to explore statistical significance.

Results: We included a total of 48 patients (54% male) with a mean age of 75 years (CI 54;93), ASA score of 2, CCI score of 5 and BMI of 27 kg/m². Twenty-two fractures were osteoporotic (46%, OF types II-V), 20 were traumatic (42%, A3, A4) and 6 were pathological (12%). Most fractures (67%) were located in the thoracolumbar junction and operated with open midline approach (63%; 37% percutaneous, minimally-invasive technique). The mean length of surgery was 171 minutes (SD 54), mean estimated blood loss 436 ml (SD 497). We achieved a mean sagittal angle correction of 5° (SD 11) and sagittal anterior/posterior wall height correction of 6 (SD 8)/4 (SD 6) mm on first follow up after 54 days (SD 28). While the sagittal angle correction (6° (SD 13)) persisted on last follow up after 627 days (SD 465), the anterior/posterior wall height correction declined to 1 (SD 15) and -4 (SD 14) mm, respectively. Surgical complications (junctional/distant fractures, wound infections, wound healing disorders and screw loosening) occurred in 14/44 patients (29%) for whom the follow up was available on last follow up. Patients with traumatic fractures tended to have less complications (n=2, 12.5 %) than patients with osteoporotic (n=6, 33%) or pathological (n=2, 50%) fractures (p=0.68).

Conclusions: In our single-center experience the SAIFAP technique appears to be an effective correction method for kypshing fractures, including those of the thoracolumbar region. However, the initial satisfying correction might be lost in the long-term. Long-term complication rates in elderly patients with osteoporotic and pathological fractures were not negligible.

796

BRAIN AND SPINE 3 (2023) 101794 101842

DEEP LEARNING ON PREOPERATIVE RADIOGRAPHS FOR CLINICAL SUCCESS PREDICTION AFTER SURGERY FOR CERVICAL DEGENERATIVE DISEASE

Caroline Goedmakers¹, Leonie Pereboom², Merel de Leeuw den Bouter³, Rob Remis⁴, Marius Staring⁵, Carmen Vleggeert-Lankamp¹. ¹Leiden University Medical Center (LUMC) department of Neurosurgery, Leiden, Netherlands; ²Faculty of Mechanical, Maritime and Materials Engineering (3mE), Delft University of Technology, Delft, The Netherlands, Delft, Netherlands; ³Delft Institute of Applied Mathematics, Department of Numerical Analysis, Delft University of Technology, Delft, The Netherlands, Delft, Netherlands; ⁴Circuits and Systems Group, Microelectronics Department, Delft University of Technology, Delft, The Netherlands, Delft, Netherlands; ⁵Division of Image Processing of the Leiden University Medical Center, Leiden, The Netherlands, Leiden, Netherlands

Spine Parallel Session v.4, September 28, 2023, 8:30 AM - 10:00 AM

Background: As populations age and the prevalence of cervical spine degeneration rises, the demand for computer-aided diagnostics and prognostics in

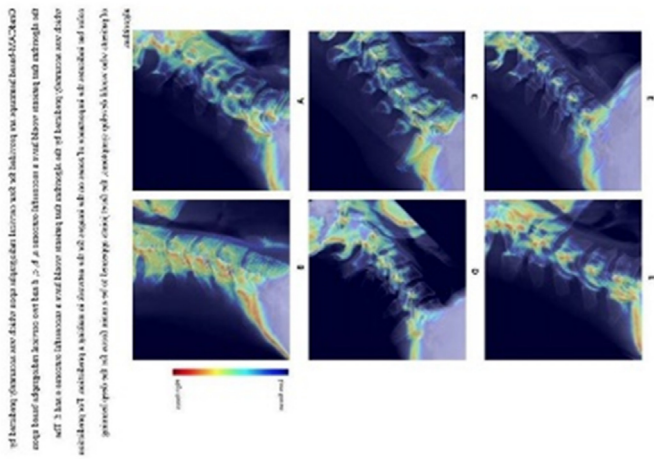
neurosurgery rises. Not all patients benefit from surgical treatment and predicting who will remain challenging. Automating parts of the radiological image analysis process using Machine Learning could provide more accurate, consistent assessment with increased time efficiency, and potentially gain new disease insights. The purpose of this study was to identify which image features on cervical radiographs are important for the prediction of clinical success one year after surgery for cervical disc disease, by developing and validating a deep learning algorithm that predicts clinical success solely based on the radiograph.

Methods: In this prognostic classification study using RCT data a convolutional Neural Network (CNN) was developed on cervical lateral flexion radiographs. After data augmentation 826 images were used for training and 266 for validation, originating from 70 unique clinical records. All patients had Neck Disability Index (NDI) scores available preoperatively and one year postoperatively, and clinical success was based on previously established cut-off values for NDI. The CNN consists of four convolutional layers with ReLU activation function and a maximum pooling function. Fivefold cross-validation was performed and Grad-CAM heatmaps were generated for model interpretation.

Results: The model was able to predict clinical success one year after surgery on cervical flexion radiographs with an accuracy of 71%, sensitivity of 80%, and AUC of 0.80. The Grad-CAM heatmaps illustrated the model focused on the facet joints in the classification process (figure 1).

Conclusions: The model showed good discriminative ability. The Grad-CAM heatmaps of this study show a significant influence of the facet joints, the only synovial-lined, diarthrodial joints in the spine, in the classification process. There is currently no other method available to predict clinical success based on imaging alone for this clinical scenario.

Optional Image



202

BRAIN AND SPINE 3 (2023) 101794 101843

CAR-T CELLS AGAINST THREE NOVEL ANTIGENS SHOW ANTITUMORAL EFFICACY IN EX VIVO PATIENT DERIVED GLIOBLASTOMA ORGANOID

Leopold Diener¹, Nicolas Goedert¹, Marah Alskalani¹, Andrea Cattaneo¹, Camelia Monoranu², Julian Hübner³, Tim Schulz¹, Almuth Keßler¹, Ralf-Ingo Ernestus¹, Carsten Hagemann¹, Mario Löhr¹, Maria Breun¹, Thomas Nerretter³, Vera Nickl¹. ¹Neurochirurgische Klinik und Poliklinik, Sektion Experimentelle Neurochirurgie, Universitätsklinikum Würzburg, Würzburg, Germany; ²Pathologisches Institut, Abteilung für Neuropathologie, Universität Würzburg, Würzburg, Germany; ³Medizinische Klinik II, Universitätsklinikum Würzburg, Würzburg, Germany

Experimental & Clinical Neuro-Oncology (Neuro-Oncology Parallel Session), September 26, 2023, 8:30 AM - 10:00 AM

Background: Glioblastoma (GBM) is the most prevalent malignant brain tumor in adults with limited treatment options. The emerging field of immunotherapies for solid tumors has led to promising experimental and clinical results. However, tumor heterogeneity, antigen escape mechanisms and the complex tumor microenvironment (TME) hinder smooth translation of therapeutics from bench to bedside. Therefore, ex vivo models resembling the precise patient conditions

are needed. Previous work in our lab has identified three suitable antigens (target 1, 2, 3) with stable expression in primary and recurrent GBM. We assessed the effector functions (proliferation and target cell apoptosis) of three different chimeric antigen receptor (CAR) T cell constructs in GBM patient derived organoids (PDOs).

Methods: organoids (PDOs).

Methods: We generated PDOs from freshly resected GBM tissue. Subsequently, CAR-T cells against three targets were produced by transduction of peripheral blood mononuclear cells derived T cells of healthy humans. PDOs were separately incubated with the three CAR-T cell variants and untransduced control T cells at an effector to target ratio of 1:4 and fixated after 24 h, 48 h and 72 h to conduct immunofluorescence staining (T cell proliferation: CD4+/Ki67+, target cell apoptosis: target+/CC3+).

Results: We incubated PDOs of four different patients showing different levels of antigen expression in parental tissue. The PDOs exhibited disintegration and loss of circular shape over time, whereas PDOs treated with control T cells maintained their morphology. High fractions of CD4+ CAR-T cells proliferated homogeneously in all four PDOs (p-value target 1/2/3: 0.0008/<0.0001/<0.0001). CAR-T cells against target 1 and 2 induced significantly increased apoptosis (p value target 1/2/3: <0.0001/0.0439/0.1306, non-significant but trending towards more apoptosis in treated PDOs).

Conclusions: By testing CAR-T cells targeting three steadily expressed GBM antigens, we contribute valuable data of preclinical performance and additionally promote lesser-known antigens by proving them as reasonable target antigens in GBM. However, further ex vivo models like slice cultures or the lasting implementation of a TME in PDOs are necessary to fully understand CAR-T cell effectiveness. Additionally, approaches like a combination of different CAR-T cell constructs and/or the addition of checkpoint inhibitors should be prioritized as next evaluation steps in both ex vivo and in vivo models.

203

BRAIN AND SPINE 3 (2023) 101794 101844

INTRAOPERATIVE MRI-GUIDED RESECTION COMPARED TO 5-ALA-GUIDANCE IN NEWLY DIAGNOSED GLIOBLASTOMA: A PROSPECTIVE CONTROLLED MULTICENTER CLINICAL TRIAL

Constantin Roder¹, Jan Coburger², Moritz Scherer³, Patrick Haas¹, Christian von der Brölie⁴, Marcel Alexander Kamp⁵, Mario Löhr⁶, Christina Hamisch⁷, Marco Skardely⁸, Torben Scholz⁹, Stephanie Schipmann^{10,11}, Julian Rathert¹², Catrin Marlene Brand¹³, Ulrike Ernemann¹, Florian Stockhammer¹³, Rüdiger Gerlach¹², Paul Kremer⁹, Roland Goldbrunner⁷, Ralf-Ingo Ernestus⁶, Michael Sabel⁵, Veit Rohde⁴, Ghazaleh Tabatabai¹, Peter Martus¹, Sotirios Bisdas¹⁴, Oliver Ganslandt¹⁵, Walter Stummer¹⁰, Andreas Unterberg³, Christian Rainer Wirtz², Marcos Tatagiba¹. ¹University of Tuebingen, Germany; ²University of Ulm, Germany; ³University of Heidelberg, Germany; ⁴University of Goettingen, Germany; ⁵University of Duesseldorf, Germany; ⁶University of Wuerzburg, Germany; ⁷University of Cologne, Germany; ⁸Municipal Hospital of Reutlingen, Germany; ⁹Asklepios Hospital Hamburg Nord, Germany; ¹⁰University of Muenster, Germany; ¹¹Haukeland University Bergen, Norway; ¹²Helios Hospital Erfurt, Germany; ¹³Municipal Hospital Dresden, Germany; ¹⁴Lysholm Department of Neuroradiology London, UK; ¹⁵Municipal Hospital Stuttgart, Germany

Experimental & Clinical Neuro-Oncology (Neuro-Oncology Parallel Session), September 26, 2023, 8:30 AM - 10:00 AM

Background: Prospective studies suggest the superiority of intraoperative MRI (iMRI) over 5-aminolevulinic acid (5-ALA) for achieving complete resections of contrast enhancement in glioblastoma. We investigated whether this assumed superiority proofs to be true in a prospective controlled trial.

Methods: A prospective controlled multicenter parallel-group trial with two center-specific treatment arms (5-ALA and iMRI) and blinded evaluation was performed. Safety measurements, including propensity scores, were used to ensure comparability between arms. Main inclusion criteria were unifocal completely resectable glioblastomas. Independent blinded review of pre- and post-operative MRI was performed to assess resectability and extent of resection. The primary endpoint was complete resection in early postoperative MRI. Clinical outcome parameters, including progression-free survival (PFS), overall survival (OS), and quality of life status, were also analyzed.

Results: 314 patients with newly diagnosed glioblastomas were recruited at eleven German centers. We evaluated 127 patients in the 5-ALA and 150 in the iMRI arm in a modified intent to treat analysis. A complete resection, defined as a residual tumor $\leq 0.175 \text{ cm}^3$, was achieved in 90 (78%) of patients in the 5-ALA