High-scale proteome analysis of oral squamous cell carcinoma with aptamer-based molecular recognition pattern - a feasibility study

ID: 285

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Background:

In order to help individualize therapy principles for oral squamous cell carcinoma (OSCC), analysis of different biomarkers for metastasis, tumor recurrence, resistance mechanism and outcome seems mandatory. Slow Off-rate Modified aptamers as modified DNA aptamers as used in the SOMAScan® (Somalogic, Boulder, USA) with high affinity and high specificity to the respective proteins, may overcome current limitation in proteome analysis. So far, this technology was not evaluated for OSCC. Therefore, aim of this feasibility study is to firstly assess this method to identify distinct proteomic changes in the peripheral blood of patients with OSCC in comparison to healthy control.

Materials and methods:

From pre- and postresection 2ml sera as excess material of a well-defined study cohort (OSCC (n=6) vs. an age-matched healthy control group receiving dental surgery (n=4)) was obtained after informed consent. SOMAscan® analysis (Somalogic, Boulder, USA) was performed. Briefly, novel modified DNA aptamers (SOMAmers) were conducted. Following immobilization and denaturation, SOMAmers were released from associated proteins and hybridized to custom micro-array chips, containing complementary samples to each individual SOMAmer and measured via Cy3 fluorescence intensity.

Results:

The bio-informatic analysis revealed a total of 77 significantly differently expressed proteins (each $p<0.05$) that could discriminate between tumor and healthy control with a 100% accuracy in hierarchical clustering. Furthermore, 76 proteins were dectected that were significantly (each $p<0.05$) differently expressed between pre- and postresection sera samples. In the subsequent canonical pathway-analysis, complementfactors, High-Mobility-Group-Pathway-1 (HMGB-1 proteins), apoptosis signaling, and transcription factors were statistically significant regulatory altered between the pre- and postresection liquid biopsy ($p<0.05$). Especially MYC and TWIST pathways showed significantly differences in up- and downstream of different regulator proteins.

Conclusion:

The quantitative proteome analysis with modified aptamers is feasible and may be used to develop precise serum marker to predict tumor occurrence, progression and recurrence in OSCC.

Pre-operative co-activation of the masseter muscle upon smiling predicts synchronicity of smile development after facial reanimation

ID: 516

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Background:
The synchronicity of the oral commissure movement of a bilateral smile is an important goal for oral reconstruction in facial palsy patients, usually achieved when choosing the contralateral facial nerve as a donor nerve. However, over the years, several studies reported some degree of spontaneity in certain patients using a non-facial donor nerve, indicating that synchronous initiation of the smile might be achievable with other donor nerves. We designed a prospective cohort study to evaluate whether pre-operative involuntary activation of the masseteric nerve upon smiling predicts a synchronous smile development when using the masseteric nerve for reanimation.

Materials and methods:
In a prospective cohort study, we evaluated unilateral long-standing facial palsy patients scheduled for dynamic smile reanimation with a free functional muscle transplant using the masseteric nerve as a donor nerve preoperatively via EMG for an involuntary activation of the masseter muscle upon smiling (co-activation). Postoperatively, six months after noting the first muscle contraction, we evaluated the synchronicity of the bilateral smile development by analyzing slow-motion video sequences of the patients taken while the patients watched funny video sequences. We then correlated the results with the pre-operative EMG.

Results:
We included 30 patients in this prospective study, of which 19 demonstrated involuntary co-activation of the masseter muscle upon smiling, and 11 did not. Postoperatively all patients could demonstrate a voluntary smile. 94% of patients who had pre-operative co-activation showed a synchronous movement of the oral commissure when smiling. In those patients who did not demonstrate co-activation of the masseter muscle upon smiling, 0% showed synchronicity. The pre-operative co-activation of the masseter muscle could predict the outcome regarding synchronicity of the smile with a sensitivity of 99.7%, a specificity of 88.5% and 92.5% positive predictive value, and 99.6% negative predictive value ($p < 0.001$ for all).

Conclusion:
The lack of masseter co-activation with smile predicts a lack of spontaneous involuntary smile after dynamic smile reconstruction using the masseteric nerve.

Quantitative assessment and localization of the hollowing of the temple after craniectomy and cranioplasty - The frontozygomatic shadow

ID: 605

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Background:

Computer-aided design (CAD) cranioplasty implants are shaped with respect to the bony defect. Temporal muscle atrophy following decompressive craniectomy is not taken into account, resulting in a typical contour defect at the temple. This can present an esthetic discomfort for patients and their surroundings. The aim of this work was to assess the precise localization and volume of this hollowing defect, to path the way for a surgical corrective during future cranioplasties.

Materials and methods:

We analyzed CT data of patients who had undergone craniectomy and CAD cranioplasty in our institution between 2012 and 2018. 3D reconstructions of the skin surface prior to craniectomy and at least 6 weeks after cranioplasty were fused and subtracted from each other resulting in a 3D volume of the hollowing defect. Finally, all cases were fused to localize the center of the defect in relation to a reference skull.

Results:

Out of 91 patients, 21 had suitable datasets. Five cases had good cosmetic results; 16 patients had an apparent hollowing defect. Their average defect volume was 5.0 cm^3 ± 4.5 cm^3. The defect localizations were in the area behind the zygomatic process and just below the superior temporal line, covering an area of app. 3x3 cm^2 which we call the frontozygomatic shadow. Surgical attempts of temporal muscle restoration were more often found in reports of good results ($p<0.01$), but also in 50% of reports, whose surgeries resulted in a hollowing defect. Mean time between the two surgeries was 112 ± 43 days. There were no significant differences regarding time between the two surgeries, age or performing surgeon.

Conclusion:

This work supplies evidence for the indication of a surgical corrective during cranioplasty in a small but cosmetically relevant area. Based on our 3D data analysis, future focused surgical strategies such as bone cement augmentation in the area of the frontozygomatic shadow may obtain better aesthetical results here.

Virtual reality planning simplifies accurate resection of skull invading meningeomas and allows manufacturing of a tailored implant prior to operation

ID: 800

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Background:

The resection of skull invading meningeomas usually requires a tumor including craniotomy followed by reconstruction of the defect. We demonstrate the usefulness of Virtual Reality surgical planning for pre-operative manufacturing of a customized implant and Augmented Reality navigation to carry out the precise implant-corresponding craniotomy

Materials and methods:

For the pre-operative 3D-planing, CT- and MRI data were three-dimensionally reconstructed in the Dextroscope and a craniotomy was virtually performed according to the tumor borders. The data containing the simulated craniotomy were then converted to DICOM-format and transferred to the manufacturer of patient specific PMMA skull-implants. The simulation data was also transferred to the navigation system, and we used its image injection feature to carry out the craniotomy precisely as pre-operatively planned.

Results:

In three patients we showed that a 3D planning procedure allows exact simulation of the ideal craniotomy size and shape as well as the pre-operative manufacturing of an implant that matches the defect. Intraoperatively, the augmentation of the planned craniotomy line facilitated carrying out a precise and straightforward craniotomy. The dispensability of intraoperative adjustment of both craniotomy and implant proves, that we achieved optimal implant fitting in all three cases. After a maximum 35-days period of PMMA-related subcutaneous edema all three patients were satisfied with the excellent cosmetic results.

Conclusion:

The demonstrated procedure is feasible, save and a practicable solution. To improve the precision of individual neurosurgical interventions we should take advantage of modern techniques and technology, especially with respect to planning and implementing spatially challenging tasks.

New intraoperative microscopic label-free brain tumour tissue detection by a deep convolutional neural network based on stimulated Raman histology
ID: 60

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Background:
Intraoperative rapid histological tissue sample assessment on a microscopic level is essential for oncological biopsies and surgical resections to determine the presence of tumor and decide on clear tumor margins, respectively. Stimulated Raman histology (SRH), a new label-free optical technology creating virtual haematoxylin-and-eosin-stained images, has been recently shown to enable pathological brain tumor rapid section diagnosis in fresh, unprocessed tumor tissues within a few minutes.[1-3] Here, we developed a new machine learning algorithm (MLA), using a deep convolutional neural network (CNN), enabling the prediction of tumor presence in a rapid automated workflow based on SRH. Further, we tested the validity and reliability of its predictions in a monocenter, prospective clinical trial in patients undergoing neurooncological surgery.

Material and methods:
We employed a MLA using a fully CNN implemented in Tensorflow 2.5. The aim of the CNN was to classify each SRH image according to the following four categories: (1) presence of tumor, (2) cannot exclude tumor, (3) non-tumor tissue and (4) low quality SRH image. To test the validity and reliability of the CNN-based SRH algorithm we conducted a clinical prospective trial approved by the local ethics committee in 94 consecutive neurooncological patients undergoing stereotactic biopsy (SB) and/or surgical resection (SR). Small human brain and tumor tissue samples (1-3 mm^3) for SRH were acquired parallel to regular pathological assessment and squashed onto a histological slide resulting in a flat tissue layer of max. 10 mm^2. Random areas of 2x2 mm within the sample were chosen for SRH and the CNN was applied afterwards. The pathological diagnosis was made in a typical routine histopathological workflow. SRH images were independently reviewed for the presence of tumor. Consistency of CNN-based brain tumor detection was analysed within the sample and the intrasample-reliability of probability values (expressed as mean +/- SD) were determined using Intraclass correlation coefficient (ICC) (single-measurement, absolute-agreement, 2-way mixed-effects model) in cases in which three or more SRH images were acquired per sample.

Results:
The CNN could be successfully established and trained in a dataset of 400 SRH images with an extraction of 2.3 million patches. For the clinical validity and reliability analysis 225 tissue samples were acquired intraoperatively in total (range 1-8 samples per patient), resulting in 593 SRH cases the CNN was applied on. In the vast majority (88.0 %) of cases the CNN could successfully identify tumor (n=468) and differentiate from healthy brain tissue (n=54) at a mean probability value level of 85.5% +/-15.3%) (Figure 1 for illustrative case). Merely in 63 SRH images (10.6 %) the CNN-based detection of brain tumor tissue was classified as unsure and could not surely exclude tumor while 8 SRH cases (1.4 %) were determined as too low of image quality for tumor detection. The CNN-based brain tumor detection and differentiation from healthy brain tissue was found to be consistent within each sample in 87.3 % and showed a good intraclass reliability (0.819, 99% CI 0.749-0.874). The image acquisition and consecutive application of the CNN took in mean 240 seconds per case in total. The pathological

diagnoses of the patients the samples derived from represented the full spectrum of neurooncology surgery ranging from benign to malignant glioma (n=29 patients), various carcinoma and melanoma metastases (n=25), benign to anaplastic meningioma (n=13), pituitary adenoma (n=6), schwannoma (n=2) and other brain tumors (n=11) as well as normal or reactive brain tissue (n=2).

Conclusion:
Our results demonstrate how this new CNN algorithm coupled to SRH can reliably detect the presence of brain tumor independent of entity and dignity and differentiate from healthy brain tissue on a microscopic level in a small fresh tissue sample in less than four minutes in total. It, thus, potentially enables an alternative pathway for intraoperative decision making in neurooncological surgery independent of the traditional more time consuming histopathological rapid sectioning workflow.

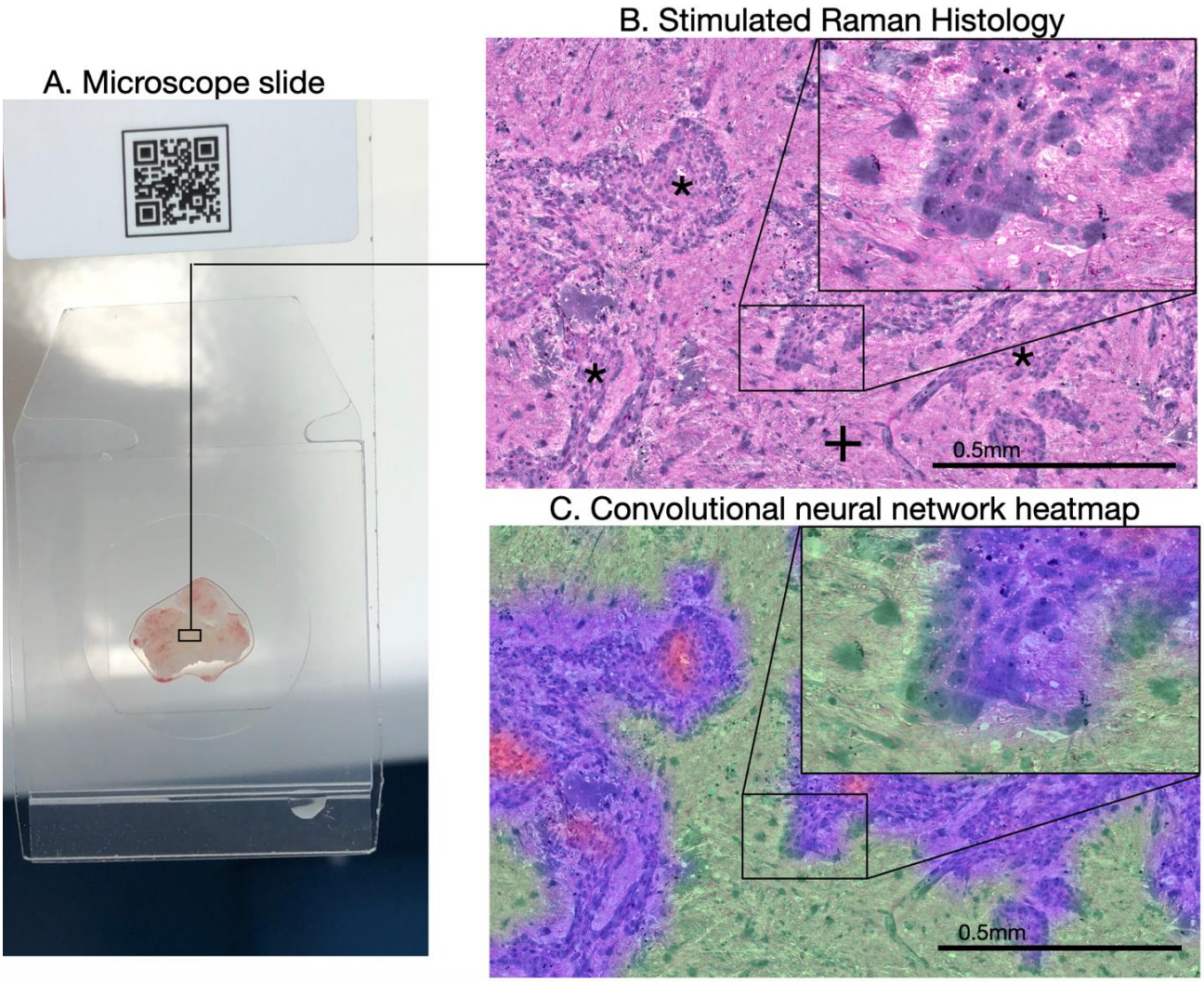

Figure 1. A. Illustrative example of a squashed small tissue sample the surgeon acquired from the tumor margin of a non-small cell lung cancer brain metastasis during surgery to test for residual tumor remnants in the resection bed. B. The 2x2 mm stimulated Raman histology (SRH) image showed tumor tissue clusters (*****) within the surrounding non-tumor brain tissue (**+**). Magnified views show cell nucleus in blue; cytoplasm, collagen fibers, erythrocytes in red with different intensities). C. The corresponding convolutional neural network heatmap could correctly identify the delineation of tumor tissue (colored in purple), non-tumor brain tissue (green) and low-quality (red) within the sample.

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virtual surgical planning and augmented reality in craniofacial surgery - review of the literature and case example

ID: 486

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Background:

Virtual Surgical Planning (VSP) and computer aided design is increasingly used in craniofacial surgery. Mixed Reality Viewers offer new possibilities to further enhance surgical planning. Especially in craniofacial and reconstructive surgery, it may help to balance the risk of the operation against the cosmetic results.

Materials and methods:

We present an overview of the literature and a case of a patient with sagittal craniosynostosis presenting after 1 year of age in which we used VSP and a Mixed Reality Viewer.

Results:

We used virtual surgical planning to prepare the operation. We presented and discussed the preoperative CT scan and 3D photo as well as the virtually planned result interactively with the patient using a mixed reality viewer and patient specific 3D-Models. During the operation, we used patient-specific, disposable guides and splints to speed up the operation and achieve optimal results. The patient was followed up using 3D photography

Conclusion:

Virtual Surgical Planning has the potential to shorten operative time and improve operative results in complex craniofacial cases. The possibility to demonstrate the expected results and the extent of the operation with the use of a Mixed Reality Viewer and Patient-Specific 3D model improves shared decision-making.

Imaging modalities for the diagnosis and treatment of lymphedema
ID: 546

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Background:
Imaging modalities play an integral role in the early diagnosis and treatment of lymphedema by providing quantitative and qualitative interpretations. However, imaging modalities in lymphedema still face various issues. Most methods are lacking a universally standardized protocol for diagnosing and staging, which would be beneficial to improve reproducibility and objectivity.

Materials and methods:
The features of the commonly performed imaging modalities are assessed.

Results:
Lymphoscintigraphy (LS) is generally considered the gold standard in confirming the diagnosis of lymphedema, offering quantifiable assessments of lymphatic fluid transport.
Near-infrared fluorescent imaging, also termed indocyanine green (ICG) lymphography, visualizes superficial lymphatic vasculature effectively. Its main application is to diagnose lymphedema and plan locations for lymphaticovenular anastomosis (LVA) operations.
Ultrasonography is widely performed to exclude venous diseases. High- and ultra-high frequency ultrasound is an effective means for lymphatic and vein mapping before LVA operations.
Magnetic resonance lymphangiography (MRL) diagnoses lymphedema by providing information on lymphatic morphology and function regardless of depth. It depicts fat and fluid excess. MRL reveals possible venous pathology, as well as diagnoses other than lymphedema (recurrent tumor, occult metastasis, lymphangiosarcoma).
Emerging technologies, e.g., bioimpedance spectroscopy, laser tomography, and photoacoustic imaging, can contribute to an earlier diagnosis, a superior treatment plan, and improved outcomes after reconstructive lymphatic surgery.

Conclusion:
Imaging modalities facilitate proper patient-, lymph vessel-, and donor-site selection, which are prerequisites for a successful lymphatic surgery. Each technique has different characteristics and yields specific information. Thus, they have to be indicated accordingly. This presentation will provide the audience an understanding and interpretation of these imaging modalities, and our experience will support physicians in outlining a treatment plan.

presurgical selection of the ideal aneurysm clip
ID: 786

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Background:
Aneurysms occlusion rate after clipping is higher than after endovascular treatment. However, a certain rate of incompletely clipped aneurysms remains. Presurgical selection of the proper aneurysm clips could potentially reduce the rate of incomplete clippings caused by inadequate clip geometry. Aim of the present study was to assess whether preoperative three-dimensional image-based simulation allows for preoperative selection of a proper aneurysm clip for complete occlusion in individual cases.

Materials and methods:
Patients harboring ruptured or unruptured cerebral aneurysms prior to surgical clipping were analyzed. CT-angiography images were transferred to a 3-dimensional surgical planning station (Dextroscope®) which contains computer-graphical models of 58 aneurysm clips. Intracranial vessels and aneurysms were segmented and the virtual aneurysm clips placed at the aneurysm neck. Intraoperative clip selection was documented, and aneurysm occlusion rate was assessed by postoperative digital subtraction angiography.

Results:
Nineteen patients were available for final analysis. In all patients the most proximal clip at the aneurysm neck was the preselected clip. All aneurysms except one were fully occluded as assessed by catheter angiography. One aneurysm had a small neck remnant, which did not require secondary surgery.

Conclusion:
The preselection of a suitable aneurysm clip in a Virtual Reality environment can be translated to the operating room, reduces exploratory tissue dissection and improves intraoperative clip selection. The associated occlusion rate of aneurysms is high.