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Collection of Abstracts

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Workshop on the ICT Contribution to the Development of Clinical Applications

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The workshop will be organised by the

Computer Vision Lab (CVL) / Technische Universität Wien

in cooperation with the

Computational Imaging Research Lab, Department of Biomedical Imaging, and Image-guided Therapy & Medical Imaging Cluster / Medical University of Vienna.

General Chair: Melanie Gau

Industry-Academia Partnerships and Pathways (IAPP) – Marie Curie Actions

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ABOUT THE WORKSHOP

The *Workshop on the ICT Contribution to the Development of Clinical Applications* held at Technische Universität Wien brought together researchers and ICT students in the fields of medical computing, machine learning, and computer vision from different scientific and research institutions in order to establish a network and share and discuss their latest research and developments in their fields.

COLLECTION OF ABSTRACTS

LANGS, G.: BIG DATA IN MEDICAL IMAGING: THE ROLE OF MACHINE LEARNING

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Clinical routine data is a rapidly growing potential source of insights into the course of disease and the effect of treatment. Its scale is vast compared to individual studies, and the variability observable in the routine population covers a wide range of biology, disease-, and treatment paths. There are several recent advances in machine learning that make it a powerful tool for using these data to understand relationships among observable variables, and patient parameters relevant for clinical decisions. In this talk we will discuss three techniques that contribute to making routine data accessible. Weakly supervised learning can minimize the need for manual expert annotations, and can map image level information to specific positions in the image. Prediction models enable the linking of multivariate characteristics to future treatment response, and unsupervised learning allows for the identification of groups in the patient population that share similar disease progression characteristics. The talk will show results to give an intuition about these methods, and will discuss specifics to medical imaging data that are different to the general computer vision domain.

PLANINC, R.: COMPUTER VISION IN ACTIVE AND ASSISTED LIVING

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Active and Assisted Living (AAL) supports seniors to live independently in their own homes as long as possible, supporting them by technology. The motivation for using technology is based on the increased life expectancy of humans, whereas the number of births is decreasing - resulting in the demographic change. Thus results in an increased need of caretaker resources and increased costs in the health care system. AAL provides countermeasures in order to reduce costs and caretaker resources by supporting elderly people to stay independently, detecting critical events and critical health conditions as early as possible in order to provide immediate help. The area of AAL can be divided into systems providing comfort, autonomy enhancement or emergency assistance.

Due to the emerging 3D sensors, critical events can be detected, while respecting privacy aspects. In order to reliably detect falls, the scene is automatically analyzed and the behavior of persons is modeled. Thus allows to detect falls, but also changes in the daily behavior of older adults, allowing for immediate help. Moreover, in the area of autonomy enhancement the use of 3D sensors allows to analyze ergonomical aspects as well as stress at the workplace. Due to the use of the sensor, physical and mental

problems (e.g. back problems, burnout) should be prevented already at an early stage. In order to foster health in private homes, exergames based on the mobility of the user can be provided in order to motivate the user, while not overburdening them. Thus allows to provide highly personalized games, based on the users' mobility.

SCHLEGL, TH.: DEEP LEARNING IN LARGE-SCALE RETINAL IMAGING

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In recent years, deep learning has become state of the art in various machine-learning tasks as for instance image and audio recognition. It is further applied successfully to natural language processing and machine translation problems. Most recently, convolutional neural networks outperformed even humans on several image classification tasks. Deep learning methods show their power if huge amounts of labeled training data are available. However, often in medical image analysis the amount of annotated training data is scarce. Because the annotation process of medical images is time-consuming, needs clinical expert knowledge and thus is difficult to obtain. We identify different machine-learning approaches, which tackle the problem of limited amounts of annotated training data. If only limited amounts of voxel-level annotated training data are available, one can perform unsupervised pre-training utilizing convolutional neural networks or convolutional restricted Boltzmann machines. This type of pre-training can be performed on any kind of imaging data – even on data of different sites or on imaging data showing very different object classes (e.g. natural images). If a larger annotated dataset of a different site is available, supervised pre-training can be performed using convolutional neural networks for the pre-training and for the fine-tuning phase. In cases, where no voxel-level annotations but corresponding clinical reports are available, semantic information of object classes and semantic concepts of corresponding location information can be used as target labels ("semantic descriptions"). Classifiers trained in a weakly supervised fashion based on these semantic descriptions outperform weakly supervised trained classifiers where only the presence of object classes within an image volume is encoded. We present experiments using convolutional neural networks and convolutional restricted Boltzmann machines and discuss different model architectures and visual and location specific inputs. We further compare and discuss qualitative and quantitative results of the different learning approaches.

BÜHLER, K.: ALGORITHMS IN DAILY CLINICAL PRACTICE: CHALLENGES AND APPROACHES

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Development of applications for use in daily clinical routine has special requirements not only in terms of robustness of an algorithm and its results, but also in respect to the available hardware infrastructure and strict time constraints which have to be considered. In classical image analysis research these aspects are seldom addressed, leading to a gap between results published by the research community and solutions being finally implemented in applications supporting clinical routine.

I will present two examples from our projects with AGFA Healthcare: Semantic Labeling of the Spine and Full Body Tracking of Arteries. Both solutions have been optimized towards supporting radiologists in a clinical environment with high time pressure. This has been achieved by an extremely high level of automation and an algorithm design that is adaptable to the available computational resources.

References

1. David Major, Jiri Hladuvka, Florian Schulze, Katja Bühler „Automated Landmarking and Labeling of Fully and Partially Scanned Spinal Columns in CT Images". Medical Image Analysis Volume 17, Issue 8, December 2013, Pages 1151–1163
2. Major, D., Novikov, A., Wimmer M., Hladuvka, J. and Bühler, K. "Automated Slice-Based Artery Identification in Various Field-of-View CTA scans". Proceedings of EG VCBM 2015
3. Hladuvka, J., Major, D. and Bühler, K. "Bone Profiles: Simple, Fast, and Reliable Spine Localization in CT Scans", 2nd MICCAI Workshop on Computational Methods and Clinical Applications for Spine Imaging 2014. Lecture Notes in Computational Vision and Biomechanics, Vol. 20, 2015
4. Jiří Hladůvka, David Major, Katja Bühler. *Method, apparatus and system for localizing a spine.* WO Patent App. PCT/EP2013/055,233. EP Patent App. EP20,120,159,593. US2015036909 (A1). WO2013135812 (A1). CN104395930 (A)
5. David Major, Jiří Hladůvka, Katja Bühler. *Method, apparatus and system for automated spine labeling.* WO Patent App. PCT/EP2013/065,457; EP Patent App. EP20,120,177,656. US2015173701 (A1). WO2014016268 (A1). CN104641397 (A)

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SCHWARTZ, E.: SPATIO TEMPORAL MODELLING IN BRAIN DEVELOPMENT

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Understanding patterns of brain development before birth is of both high clinical and scientific interest. However, despite advances in reconstruction methods, the challenging setting of in-utero imaging renders precise, point-wise measurements of the rapidly changing fetal brain morphology difficult.

We propose a pipeline based on spectral surface matching to build longitudinal comparable models of fetal brain development in the second and third trimester of gestation. We show how to deal with bad measurement quality due to image noise, motion artefacts and ensuing segmentation and registration errors by enforcing spatial regularity during the estimation of parametric models of cortical expansion. The resulting models accurately capture the morphological and temporal properties of fetal brain development. From these, we find interesting correlations between brain development in utero and established knowledge of both post-natal and evolutionary cortical expansion as well as morphological cortical variability in adults.

DIFRANCO, M.: DIGITAL PATHOLOGY INFORMATICS IN CLINICAL IMAGING

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Advances in diagnostic imaging are creating opportunities for in-vivo disease characterization. Imaging modalities including multi-parametric MRI (fMRI, DCE-MRI, DW-MRI, MR spectroscopy, MR elastography), nuclear medicine (PET-CT, SPECT-CT, PET-MR), ultrasound (3D US, US elastography) and optical imaging (OCT, Photo-acoustic CT) are moving beyond a regime of anomaly detection towards in-vivo tissue characterization, or "Virtual Biopsy". Validation of these tissue characteristics requires comparison of in-vivo imaging with ex-vivo tissue analysis, which can be carried out using digital pathology. Challenges to the success of this validation include spatial alignment between in-vivo and ex-vivo images, substantial differences in image resolution and dimensionality, variability in image acquisition protocols, differing

image representations (e.g., functional, morphological, anatomical), and the need for expert annotations from each modality. This work presents a case study in digital pathology validation of clinical PET/MR imaging in prostate cancer, including a physician-guided 2D-3D registration tool and a machine learning framework for disease characterization in digital pathology slides.

LICANDRO, R.: AUTOMATIC MRD ASSESSMENT IN FLOW CYTOMETRY OF DIFFERENT LEUKAEMIA TYPES IN CHILDREN: AN OVERVIEW

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Leukaemia is a disease induced by genetic alterations of blood progenitor cells, which influences the hematopoiesis, resulting in the proliferation of undifferentiated (leukaemic) cells. The Minimal Residual Disease (MRD) value encodes the ratio between leukaemic and the amount of intact cells observed. It is a powerful predictor for treatment response and thus used as diagnostic tool for planning patient's individual therapy. The focus of the cancer research projects at the Computer Vision Lab at the TU Wien lies on automatically assessing the MRD in Acute Lymphoblastic Leukaemia (ALL - Project AutoFLOW) and Acute Myeloid Leukaemia (AML - Project FlowCLUSTER) in children, to reduce subjectivity, interoperator variability and to increase reproducibility in the daily routine.

The data is acquired at different time points of treatment using the laser based Flow CytoMetry (FCM) technique. It requires stained blood or bone marrow cells of a patient, the antigens of which are marked using a combination of specific fluorescence-labelled antibodies. Dependent on the antigen expression of a single cell, different fluorescence signal patterns are detectable. The challenges in automatic MRD assessment lie in the detection of small cell populations (low MRD) composing about 0.1% of the amount of different cell types observed, in the limited number of cells in the test tube and in the influencing factors for MRD assessment, which emerge from treatment- or age-related variances of the regeneration status of bone marrow precursors. A further focus of research lies in automatically assessing the development and changes of cell populations. In a first step we analyse time-specific population models at different time points of treatment. For future work we aim to estimate a mean trajectory of cell population development for predicting possible treatment outcome or to use it as a prior in the classification procedure of leukaemic cells.

ROTA, P.: FIXED BOUNDARY DECISION IN FLOW CYTOMETRY MRD ESTIMATION

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Acute Lymphoblastic Leukemia (ALL) is the most common malignancy in children and despite the good and reliable available therapy, relapse is still the main cause of treatment failure (~ 15% of cases). In order to evaluate the response of the patient to the treatment, flow-cytometry is one of the fastest and reliable assessing instruments. The analysis consists in introducing the bone marrow sample into the flow cytometer which will produce a multi-parametric reading for each cell. Afterwards clinicians can visualize a combination of 2D scatterplots pruning hierarchically the cells which are considered healthy, and eventually counting the blasts (leukemic cells). The ratio between blasts and a sample subset named intact is called Minimal Residual Disease (MRD) and it is used to evaluate the treatment response at

different time points. However, the analysis of this data requires highly trained operators and, in some cases, even among them the consensus is missing.

In this work we investigate the viability of three traditional Machine Learning methods for the automation of such procedure. The considered methods are: Gaussian Mixture Model (GMM), Support Vector Machine (SVM) and Deep Neural Networks (NN). The first method uses the GMM to model the distribution of cells from a training set in the multi-dimensional space, the model is then used as likelihood in a Bayes decision framework. The SVM is applied directly to a feature vector composed by the readings of each cell. Deep learning is also applied directly on the extracted channels using a stacked auto-encoder architecture. The results of the three methods are promising in absolute terms but still not good enough for clinical applications. The main motivation is the high variability among leukemic phenotypes that leads to a coarse estimation in low MRD cases. The solution is an adaptation stage during the test phase which is presented in Michael Reiter's presentation.

References

1. Rota, Paolo, Florian Kleber, Michael Reiter, Stefanie Groeneveld-Krentz, and Martin Kampel. "The Role of Machine Learning in Medical Data Analysis. A Case Study: Flow Cytometry." In Proceedings of the International Conference on Computer Vision Theory and Applications.
2. Rota, Paolo, Stefanie Groeneveld-Krentz, and Michael Reiter. 2015. "On Automated Flow Cytometric Analysis for MRD Estimation of Acute Lymphoblastic Leukaemia: A Comparison among Different Approaches." In Bioinformatics and Biomedicine (BIBM), 2015 IEEE International Conference on, 438–41. IEEE.

REITER, M.: ASSESSMENT OF FLOW CYTOMETRY DATA USING A COMBINATION OF GAUSSIAN MIXTURE MODELS

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We propose a supervised learning approach to automatic quantification of cell populations in flow cytometric samples. One sample contains up to millions of measurement vectors with a dimensionality between 10 and 20. Normally, each measurement vector corresponds to a single cell in the biological sample. Identifying biologically meaningful cell populations is essentially a clustering problem, however, standard clustering methods are impractical, because size, shape and location of corresponding clusters may vary strongly between samples mainly due to phenotypic differences and inter-laboratory variations. In our holistic approach, we implicitly employ the structural information (such as relative locations and shape of sub-populations). A new input sample is reconstructed by a linear combination of artificial reference samples each represented by Gaussian Mixture Models (GMM), in which for each Gaussian component the class label of the corresponding cluster of observations is known. The reference samples are calculated from a larger set of training samples by non-negative matrix factorization and can be regarded as the basis of a lower dimensional feature space, in which input samples are reconstructed. We show a method for calculating the feature space transformation based on minimization the L_2 distance defined between two GMM. The feature space representation of the sample is then used to assign each observation to one of the specified sub-populations by a Bayes decision. We present classification results on a database of about 170 patients with Acute Lymphoblastic Leukaemia (ALL), where high accuracy in the prediction of relatively small leukaemic populations is crucial. The approach is not limited to our application. It can be employed wherever analysis of large, multi-dimensional, numerical data of a specific class of samples with related structure has to be performed.

(cf. *Pattern Recognition* DOI: 10.1016/j.patcog.2016.04.004)

BIRKFELLNER, W.: COMPUTER AIDED DIAGNOSIS, HIGH PERFORMANCE COMPUTING DURING INTERVENTION

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Intra-fractional respiratory motion during radiotherapy leads to a larger planning target volume (PTV). Real-time tumor motion tracking by two-dimensional (2D)/3D registration using on-board kilo-voltage (kV) imaging can allow for a reduction of the PTV though motion along the imaging beam axis cannot be resolved using only one projection image. We present a retrospective patient study investigating the impact of paired portal mega-voltage (MV) and kV images on registration accuracy. Material and methods. We used data from 10 patients suffering from non-small cell lung cancer (NSCLC) undergoing stereotactic body radiation therapy (SBRT) lung treatment. For each patient we acquired a planning computed tomography (CT) and sequences of kV and MV images during treatment. We compared the accuracy of motion tracking in six degrees-of-freedom (DOF) using the anterior-posterior (AP) kV sequence or the sequence of kV-MV image pairs.

Results. Motion along cranial-caudal direction could accurately be extracted when using only the kV sequence but in AP direction we obtained large errors. When using kV-MV pairs, the average error was reduced from 2.9 mm to 1.5 mm and the motion along AP was successfully extracted. Mean registration time was 188 ms.

Conclusion. Our evaluation shows that using kV-MV image pairs leads to improved motion extraction in six DOF and is suitable for real-time tumor motion tracking with a conventional LINAC.

VOGL, W.-D.: LONGITUDINAL MODELING FOR DISEASE AND TREATMENT RESPONSE PREDICTION

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We present a method to predict treatment response patterns based on spatio-temporal disease signatures extracted from longitudinal spectral domain optical coherence tomography (SD-OCT) images.

We extract spatio-temporal disease signatures describing the underlying retinal structure and pathology by transforming total retinal thickness maps into a joint reference coordinate system.

We propose two approaches to obtain a predictive model based on the aligned signatures. The first model is a multi-variate sparse generalized linear model regression. The second one is an ensemble tree method, denoted as Extremely Randomized Trees, which is based on Random Forests.

Both algorithms are capable of predicting if a disease will recur in the future.

Results: Experiments demonstrate that the models identify predictive and interpretable features in the spatio-temporal signature. In initial experiments recurrence vs. non-recurrence is predicted with a ROC AuC of 0.83 for branch retinal vein occlusion and 0.79 for central retinal vein occlusion. Mapping coefficients from the generalized linear model resp. feature importance from the ensemble trees model back to retinal maps allows for interpretation by clinicians.