Master Thesis Florian Thamm

Ischemic Stroke Segmentation on CT-Perfusion Data using Deep Learning Methods

Segmentierung von ischämischen Schlaganfällen auf CT-Perfusionsdaten mithilfe von Deep Learning Methoden

Florian Thamm¹²

Supervisors: Leonid Mill¹ M.Sc, Dr. Markus Jürgens², Prof. Dr. Andreas Maier¹

¹Pattern Recognition Lab, Friedrich-Alexander-University, Erlangen-Nuremberg ²Siemens Healthineers AG, Computed Tomography, Research & Developement, Forchheim

Thesis Description

The global second leading cause of death and the third leading cause of disability are cerebrovascular accidents, also known as strokes [1, 2]. According to the American Heart Association, the majority of all strokes are of ischemic nature with a share of 87% [3]. The treatment of patients suffering acute ischemic strokes using thrombolytics remains limited, since thrombolysis involves higher hemorrhagic risks and therefore in cases of large occluded arteries the mechanical/surgical thrombectomy can be the the superior and the preferred method [4, 5]. As a consequence the ability of localizing the ischemic stroke lesion on artery-level is crucial for a successful mechanical recanalization and therefore for the whole treatment by its clinical outcome.[4, 6].

Computed tomography (CT) and magnetic resonance imaging (MRI) represent the most important modalities addressing the diagnosis, management and in particular the exact localization of acute strokes. MRI has gained high acceptance in the evaluation of acute stroke, specifically diffusion-weighted imaging (DWI), which outperforms typical CT applications in terms of precision, but is rather difficult in clinical practice [7, 8]. On the other hand, several CT applications exist: 1) Unenhanced CT is widely used as a first-line imaging tool to identify hemorrhagic insults. 2) CT Angiography (CTA) is mainly used in the identification of intravascular thrombi that can be targeted for thrombolysis and/or mechanical thrombectomy [4, 9]. 3) CT Perfusion (CTP), as well as DWI and in contradiction to unenhanced CT and CTA, is commonly used to localize stroke lesions, by characterizing the bloodflow on tissue-level. This flow is described by a variety of parameters, including the cerebral blood flow (CBF), the cerebral blood volume (CBV), the mean transit time (MTT) and other measures like time to peak (TTP) or time to drain (TTD). These parameters provide an insight into the delivery of blood to the brain parenchyma and enable the distinction between penumbra and the "core" of the critically infarcted tissue, which is of high importance for further revascularization procedures. Therefore, CTP and DWI can be considered as methods, to identify patients thought to be optimal candidates for reperfusion therapies, like the mechanical thrombectomy [9, 10, 4].

Since the segmentation of the core and the penumbra on CTP image data is not standardized, different thresholds for either, the core and the penumbra, have been proposed as state-of-the art methods, while many of them are compared with the DWI as gold standard [11, 12, 13, 14, 15]. These methods do not only differ in their threshold levels, but also on which parameters (typically CBV, CBF, MTT and TTP) they are working on. However, these thresholding methods do neither consider anatomical structures nor spatial relations of the infarcted tissue itself, which may introduce artifacts in terms of small noisy clusters, causing a mismatch between CTP and DWI. It is not unusual to extend the segmentation process by clustering methods in order to avoid this [16, 17].

Image segmentation in general, is a well studied field in image processing and still it remains challenging for many applications. Especially in advanced applications like the segmentation of ischemic infarcted tissues, high precision results are required to provide the best possible patient care and treatment [18, 19]. As a result of the high difficulty, many algorithms and methods were invented in the last years, but deep learning methods first and foremost gained higher attention for their superior performance, e.g [20, 21, 22, 23]. In contradiction to threshold approaches, deep learning methods incooperate spatial information and context into the segmentation.

Master Thesis Florian Thamm

This thesis aims to combine both, robustly extract the segmentation of the ischemic stroke lesion with the use of Deep Learning Methods based on CTP data. Other recently published approaches achieved promising results, but were either using non state-of-the-art segmentation architectures [24] or were using a small number of different perfusion parameters [25, 26]. The thesis at hand, explores the performance of state-of-the-art deep learning models, by not only involving the typical perfusion parameters (CBV, CBF, MTT and TTP), but also by comprising the base line volume (BASE), the maximum intensity projection (MIP) and the average intensity projection (AVG), in order to achieve the best possible segmentation. The thesis also covers a detailed analysis of the network combined with an analysis of the positive or negative impact which comes along with the additional parameters. In summary, the thesis deals with the following points:

- 1. Segmentation of the Critically Infarcted Tissue
 - (a) Pre-Processing
 - (b) Segmentation with Deep Learning
 - (c) Possibly: Post-Processing
- 2. Systematic Parametrization of the Model
- 3. Analysis of the Deep Learning Model
 - (a) Determination of the relevant Perfusion Parameters
 - (b) Possibly: Evaluation of the Artifact-freedom of the Segmentation

References

- [1] Walter Johnson, Oyere Onuma, Mayowa Owolabi, and Sonal Sachdev. Stroke: A global response is needed. Bulletin of the World Health Organization, 94:634–634A, 09 2016.
- [2] A Donnan Geoffrey, Marc Fisher, Malcolm Macleod, and Stephen M Davis. Stroke. *The Lancet*, 371(9624):1612 1623, 2008.
- [3] Dariush Mozaffarian, Emelia J Benjamin, Alan S Go, Donna K Arnett, Michael J Blaha, Mary Cushman, Sandeep R Das, Sarah de Ferranti, Jean Pierre Després, Heather J Fullerton, et al. Heart disease and stroke statistics-2016 update a report from the american heart association. *Circulation*, 133(4):e38–e48, 2016.
- [4] Michel T Torbey and Magdy H Selim. The Stroke Book. Cambridge University Press, 2013.
- [5] Salwa El Tawil and Keith W Muir. Thrombolysis and thrombectomy for acute ischaemic stroke. *Clinical Medicine*, 17(2):161–165, 2017.
- [6] Murugan Palaniswami and Bernard Yan. Mechanical thrombectomy is now the gold standard for acute ischemic stroke: implications for routine clinical practice. *Interventional neurology*, 4(1-2):18–29, 2015.
- [7] Pamela W Schaefer, Javier M Romero, P Ellen Grant, Ona Wu, A Gregory Sorensen, Walter Koroshetz, and Ramon G González. Diffusion magnetic resonance imaging of acute ischemic stroke. In *Seminars in roentgenology*, volume 37, pages 219–229. Elsevier, 2002.
- [8] Maarten G Lansberg, Gregory W Albers, Christian Beaulieu, and Michael P Marks. Comparison of diffusion-weighted mri and ct in acute stroke. *Neurology*, 54(8):1557–1561, 2000.
- [9] Ramon G González, Joshua A Hirsch, WJ Koroshetz, Michael H Lev, and Pamela W Schaefer. *Acute ischemic stroke*. Springer, 2011.
- [10] Michelle P Lin and David S Liebeskind. Imaging of ischemic stroke. Continuum: Lifelong Learning in Neurology, 22(5):1399, 2016.
- [11] Max Wintermark, Reto Meuli, Patrick Browaeys, M Reichhart, J. Bogousslavsky, P. Schnyder, and P. Michel. Comparison of ct perfusion and angiography and mri in selecting stroke patients for acute treatment. *Neurology*, 68(9):694–697, 2007.

Master Thesis Florian Thamm

[12] Max Wintermark, Adam E Flanders, Birgitta Velthuis, Reto Meuli, Maarten Van Leeuwen, Dorit Goldsher, Carissa Pineda, Joaquin Serena, Irene van der Schaaf, Annet Waaijer, et al. Perfusion-ct assessment of infarct core and penumbra: receiver operating characteristic curve analysis in 130 patients suspected of acute hemispheric stroke. Stroke, 37(4):979–985, 2006.

- [13] Pamela W Schaefer, Elizabeth R Barak, Shahmir Kamalian, Leila Rezai Gharai, Lee Schwamm, Ramon G. Gonzalez, and Michael H Lev. Quantitative assessment of core/penumbra mismatch in acute stroke: Ct and mr perfusion imaging are strongly correlated when sufficient brain volume is imaged. Stroke, 39(11):2986–2992, 2008.
- [14] Bruno P Soares, Elizabeth Tong, Jason Hom, Su-Chun Cheng, Joerg Bredno, Loic Boussel, Wade S Smith, and Max Wintermark. Reperfusion is a more accurate predictor of follow-up infarct volume than recanalization: a proof of concept using ct in acute ischemic stroke patients. *Stroke*, 41(1):e34–e40, 2010.
- [15] Bruce CV Campbell, Søren Christensen, Christopher R Levi, Patricia M Desmond, Geoffrey A Donnan, Stephen M Davis, and Mark W Parsons. Cerebral blood flow is the optimal ct perfusion parameter for assessing infarct core. Stroke, 42(12):3435–3440, 2011.
- [16] Andrew Bivard, Patrick McElduff, Neil Spratt, Christopher Levi, and Mark Parsons. Defining the extent of irreversible brain ischemia using perfusion computed tomography. *Cerebrovascular diseases*, 31(3):238–245, 2011.
- [17] Andrew Bivard, Christopher Levi, Neil Spratt, and Mark Parsons. Perfusion ct in acute stroke: a comprehensive analysis of infarct and penumbra. *Radiology*, 267(2):543–550, 2013.
- [18] Maryam Rastgarpour and Jamshid Shanbehzadeh. The problems, applications and growing interest in automatic segmentation of medical images from the year 2000 till 2011. *International Journal of Computer Theory and Engineering*, 5(1):1, 2013.
- [19] Richard Szeliski. Computer vision: algorithms and applications. Springer Science & Business Media, 2010.
- [20] Vijay Badrinarayanan, Alex Kendall, and Roberto Cipolla. Segnet: A deep convolutional encoder-decoder architecture for image segmentation. *IEEE transactions on pattern analysis and machine intelligence*, 39(12):2481–2495, 2017.
- [21] Dan Ciresan, Alessandro Giusti, Luca M Gambardella, and Jürgen Schmidhuber. Deep neural networks segment neuronal membranes in electron microscopy images. In *Advances in neural information processing systems*, pages 2843–2851, 2012.
- [22] Jonathan Long, Evan Shelhamer, and Trevor Darrell. Fully convolutional networks for semantic segmentation. In *Proceedings of the IEEE conference on computer vision and pattern recognition*, pages 3431–3440, 2015.
- [23] Olaf Ronneberger, Philipp Fischer, and Thomas Brox. U-net: Convolutional networks for biomedical image segmentation. In *International Conference on Medical image computing and computer-assisted intervention*, pages 234–241. Springer, 2015.
- [24] David Robben, Anna Boers, Henk A Marquering, Lucianne M Langezaal, Yvo Roos, Robert J van Oostenbrugge, Wim H van Zwam, Diederik Dippel, Charles Majoie, and Aad et al. van der Lugt. Prediction of final infarct volume from native ct perfusion and treatment parameters using deep learning. arXiv preprint arXiv:1812.02496, 2018.
- [25] Christian Lucas, André Kemmling, Nassim Bouteldja, Linda F Aulmann, Amir Madany Mamlouk, and Mattias P Heinrich. Learning to predict ischemic stroke growth on acute ct perfusion data by interpolating low-dimensional shape representations. *Frontiers in neurology*, 9, 2018.
- [26] Mazdak S Abulnaga and Jonathan Rubin. Ischemic stroke lesion segmentation in ct perfusion scans using pyramid pooling and focal loss. In *International MICCAI Brainlesion Workshop*, pages 352–363. Springer, 2018.