Habilitation Thesis Commentary

This habilitation thesis named ***„Diagnostics and Recanalization Treatment of Ischemic Stroke"*** represents a collection of previously published scholarly works. All these studies focus on different aspects of acute stroke neuroimaging and recanalization treatment. It is comprised of 9 scholarly works (4 *in extenso* and 5 annexes) and it is divided into four main sections. The first section summarizes briefly stroke epidemiology and pathophysiology. The second section is devoted to modern neuroimaging tools in acute ischemic stroke with a special emphasis put on automated detection of early ischemic changes on baseline neuroimaging and clinical utility of the multiphase CTA (mCTA). The third section is devoted to endovascular treatment (EVT) of acute ischemic stroke. Its first part is focused on comparisons of the EVT data from the Czech Republic with the HERMES (*Highly Effective Reperfusion evaluated in Multiple Endovascular Stroke Trials*) meta-analysis. Its second part presents an observational multicenter study assessing the effectiveness and safety of EVT versus best medical management in patients with computed tomography angiography (CTA) detected large vessel occlusion in the anterior circulation and with mild neurological deficit using recent data from comprehensive datasets and propensity score matching. The last section contains fulltexts (pdf) of original publications (annexes) related to the topic of this habilitation thesis.

Acute stroke imaging

Stroke represents a major cause of disability and is the second leading cause of death worldwide. The overall number of strokes has been increasing and it is expected to accelerate over the coming decades. Without major advances in prevention, acute stroke management and treatment the burden and cost of this disease will considerably increase. Patients' selection for recanalization treatment is based on two main pillars: clinical characteristics and baseline neuroimaging. Brain computed tomography (CT) is the most widely used and widespread modality of stroke imaging; non-contrast CT (NCCT), CTA, and CT perfusion (CTP) represent important imaging tools aiding in diagnosis and decision-making on subsequent therapy.

Baseline neuroimaging is also used to determine how much brain tissue is already irreversibly damaged. The most commonly used imaging techniques are CTP and mCTA. Our research team have recently studied a new color-coded mCTA display format, in which all 3 mCTA series are consolidated in a single color-coded map, thereby potentially facilitating and improving

mCTA interpretation. mCTA color-maps therefore constitute a good alternative to facilitate interpretation of collateral status until fully-automated collateral assessment becomes routinely available, particularly for less-experienced readers. The publication (***Utility of Time-Variant Multiphase CTA Color Maps in Outcome Prediction for Acute Ischemic Stroke Due To Anterior Circulation Large Vessel Occlusion***) and **Annex 1** and **Annex 2** are dedicated to this subject in detail.

Acute stroke treatment

The treatment of acute ischemic stroke (AIS) has undergone dramatic changes in last decade. Randomized controlled clinical trials have demonstrated that the EVT represents a highly effective and safe treatment. In order to confirm a broad applicability of EVT in the anterior circulation large vessel occlusion strokes and to establish the treatment effect at a national level, we compared the Czech EVT data with the patient-level meta-analysis "HERMES" (*publication:* ***Mechanical Thrombectomy Performs Similarly in Real-World Practice: A 2016 Nationwide Study from the Czech Republic***).

EVT represents a standard of care for AIS due to large vessel occlusion, but level 1A guideline recommendations for EVT are currently restricted to patients with National Institutes of Health Stroke Scale (NIHSS - a scale assessing the severity of neurological deficit) ≥6. The aim of our observational multicenter study (*publication:* ***Thrombectomy vs. Medical Management in Low NIHSS Acute Anterior Circulation Stroke***) was to assess the effectiveness and safety of EVT versus best medical management in patients with CTA detected large vessel occlusion in the anterior circulation and NIHSS≤6 (=mild neurological deficit) using data from comprehensive datasets and propensity score matching. Additionally, the **Annex 3** is devoted to our single-centre experience with patients' selection for EVT based on automated CTP analysis and it also compares our EVT results with CTP-based randomized controlled trials. The **Annex 4** represents a first comprehensive nationwide questionnaire-based evaluation of all stroke centres in the Czech Republic performing EVT in 2016. The **Annex 5** summarizes the technical EVT results from the year of 2016.

Applicant's contribution:

1) **Detection of ischemic changes on baseline multimodal computed tomography: expert reading vs. Brainomix and RAPID software (Section 2.1):** the applicant designed and conceptualized the study, performed the imaging reading of all included patients (in co-operation with dr. Petra Cimflová), analysed and interpreted the results, wrote 50 % of the first draft of the paper and work on paper revisions.

2) **Utility of Time-Variant Multiphase CTA Color Maps in Outcome Prediction for Acute Ischemic Stroke Due To Anterior Circulation Large Vessel Occlusion (Section 2.2):** the applicant participated in the study design, read the scans of all patients included in the study, participated in the statistical analysis and data interpretation, wrote the first draft of the paper with dr. Johanna Ospel (30%).

3) **Mechanical Thrombectomy Performs Similarly in Real-World Practice: A 2016 Nationwide Study from the Czech Republic (Section 3.1):** the applicant designed and conceptualized the study, performed the data mining, analysed and interpreted the results, wrote 80 % of the first draft of the paper and led work on paper revisions.

4) **Thrombectomy vs. Medical Management in Low NIHSS Acute Anterior Circulation Stroke (Section 3.2):** the applicant co-designed the study (with dr. Charlotte Zerna and prof. Michael D. Hill), interpreted the results, wrote 60 % of the first draft of the paper and co-participated on paper revisions with dr. Charlotte Zerna.

5) **Permeability surface area product analysis in malignant brain edema prediction – A pilot study (Annex 1):** the applicant designed and conceptualized the study, led the imaging lab team, analysed and interpreted the data wrote 70 % of the first draft of the paper and led work on paper revisions.

6) **Displaying Multiphase CT Angiography Using a Time-Variant Color Map: Practical Considerations and Potential Applications in Patients with Acute Stroke (Annex 2):** the applicant participated in image selection for the paper (50%), wrote the first draft of the "technical" paper in co-operation with dr. Johanna Ospel.

7) **Single-Centre Experience with Patients Selection for Mechanical Thrombectomy Based on Automated Computed Tomography Perfusion Analysis-A Comparison with Computed Tomography Perfusion Thrombectomy Trials (Annex 3):** the applicant designed and conceptualized the study as a senior author, performed the scan reading of all included patients, participated in data analysis and interpretation, wrote 40 % of the first draft of the paper and participated in the paper revisions.

8) **A Comprehensive Nationwide Evaluation of Stroke Centres in the Czech Republic Performing Mechanical Thrombectomy in Acute Stroke in 2016 (Annex 4):** the applicant designed, conceptualized and led this study, analysed and interpreted the data, wrote 80 % of the first draft of the paper and led work on paper revisions.

9) **Mechanical Thrombectomy for Acute Ischemic Stroke in Czech Republic: Technical Results from the Year 2016 (Annex 5):** the applicant participated in study design, participated in data acquisition and design of statistical analysis, revised the manuscript for intellectual content (10%).

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