An Automated Tool for Prediction of Secondary Hemorrhage in Stroke.

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PURPOSE — Current treatment of acute ischemic stroke focuses on reperfusion of infarcted tissue. Patients who might benefit from reperfusion are usually identified through assessment of mismatch between the volumes of irreversibly damaged and critically hypoperfused tissue (a.k.a. tissue-at-risk). However, reestablishing blood flow to tissue that had experienced a significant and prolonged deprivation of oxygen and nutrients bears the risk of hemorrhagic transformation (HT). Recent research [1] demonstrated that HT was more likely to occur when ischemic regions with very low cerebral blood volume (vCBV) had been hypoperfused. It is hypothesized that reperfusing tissue that suffered from vCBV condition (accompanied with a possible damage to endothelial cells) is likely to result in HT. Since the HT can have detrimental effects on final neurological and functional outcome, predicting the tissue that could go on to HT would be valuable information for the stroke neurologists to have early on to augment treatment decisions. Here, we present a novel tool that has been integrated into our RAPID pipeline [2, 3] and can automatically (Fig. 1) – without any user-interaction and within a few minutes after the imaging – deliver information about tissue that is likely to undergo HT.

METHODS — To predict the HT region, the patient first undergoes a standard MRI imaging protocol for acute stroke, including a diffusion-weighted MRI (DWI); SE-EPI, TR = 4-10s, TE = 60-100ms, matrix 128×128, FOV 24cm, at 1.5-3T; and a dynamic-susceptibility-contrast perfusion MRI (PWI): GRE-EPI, TR = 1.2-2s, TE = 20-40ms, FA = 60-80°, matrix 128×128, FOV 24cm, at 1.5T-3T, 40-80 time frames, with 0.1mmol/kg gadolinium tracer bolus. The DWI image (b=0, isotropic b=1000) and raw PWI (T2*-weighted) images are then DICOM-pushed from the MRI scanner to a RAPID processing node [2, 3] where the DSC-MRI perfusion data are post-processed to obtain maps of quantitative perfusion parameters including CBV, and where the DWI and PWI are co-registered. Next, the PWI anatomic images are mirrored about a P/A axis and spatially coregistered with the unmirrored originals. The obtained spatial transformation matrix is then applied to the CBV images to obtain estimates of contralateral CBV values. Large vessels are then removed from both original and mirrored CBV maps by thresholding based on the median CBV value, and both volumes are spatially smoothed afterwards. Estimates of CBV relative to contralateral hemisphere (rCBV) are obtained as a ratio between the original and A/P mirrored CBV maps. Ultimately, ischemic regions (based on ADC threshold ADC < 600×10−6 mm²/s [2, 3]) that also manifest rCBV < 0.25 are considered predictors for HT. Very small regions (<1ml) of predicted HT are considered artifacts and ignored. For purposes of this study, we tested the HT prediction on 19 cases from DEFUSE2 multi-center trial that showed good baseline and follow-up imaging and manifested reperfusion in the originally hyperperfused regions. Cases that had complications during mechanical thrombectomy (e.g. vessel perforation) were excluded from the analysis, as well as non-reperfusing patients. Presence of HT was assessed on 5-day T2 FLAIR images.

RESULTS — Fig. 2a and 2b show example cases where baseline CBV, ADC and the HT prediction maps are compared to final stroke outcome assessed on the follow-up FLAIR imaging. As can be seen, the hemorrhage was likely to occur only in tissue that has both low CBV and was reperfused. Those ischemic regions that do not have significantly reduced CBV or do not reperfuse usually do not suffer from hemorrhage. In the evaluated patient group, the presented approach for prediction of HT resulted in 5 true positives, 11 true negatives, 2 false positive and 1 false negative (Cohen’s κ = 0.65, sensitivity = 83%, specificity 86%, accuracy 84%, $p = 0.01$, positive predictive value 71%, negative predictive value 92%, positive likelihood ratio 5.4). DISCUSSION — We present a novel tool for a fully automated prediction of HT in acute ischemic stroke. Information provided by this tool can be valuable for stroke treatment decisions and has potential implications for actual stroke treatment. The information about HT might serve e.g. as guidance for the regions at which mechanical thrombectomy should focus on or which it should avoid (i.e. deliberate partial thrombectomy). The reliability and robustness of this tool in clinical routine strongly depends on the quality of the underlying DWI and PWI data (noise, motion-related artifacts, etc.), as well as on time elapsed since vCBV onset. In terms of predicted HT volume, it appears that the final 5-day FLAIR hemorrhage lesions tend to be larger than volumes predicted from baseline CBV. We speculate that this is caused by hemorrhage- and/or stroke-related edema present in 5-day scans.


ACKNOWLEDGEMENTS — NIH (5R01EB002711, 5R01EB008706, 3R01EB008706, 5R01EB006526, 5R21EB006860, 2P41RR09784), Lucas Foundation, Oak Foundation.