Prediction of Stroke Infarct Growth Rates by Baseline Perfusion Imaging

Stroke

CLINICAL AND POPULATION SCIENCES

Prediction of Stroke Infarct Growth Rates by Baseline Perfusion Imaging

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BACKGROUND AND PURPOSE: Computed tomography perfusion imaging allows estimation of tissue status in patients with acute ischemic stroke. We aimed to improve prediction of the final infarct and individual infarct growth rates using a deep learning approach.

METHODS: We trained a deep neural network to predict the final infarct volume in patients with acute stroke presenting with large vessel occlusions based on the native computed tomography perfusion images, time to reperfusion and reperfusion status in a derivation cohort (MR CLEAN trial [Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands]). The model was internally validated in a 5-fold cross-validation and externally in an independent dataset (CRISP study [CT Perfusion to Predict Response to Recanalization in Ischemic Stroke Project]). We calculated the mean absolute difference between the predictions of the deep learning model and the final infarct volume versus the mean absolute difference between computed tomography perfusion imaging processing by RAPID software (iSchemaView, Menlo Park, CA) and the final infarct volume. Next, we determined infarct growth rates for every patient.

RESULTS: We included 127 patients from the MR CLEAN (derivation) and 101 patients of the CRISP study (validation). The deep learning model improved final infarct volume prediction compared with the RAPID software in both the derivation, mean absolute difference 34.5 versus 52.4 mL, and validation cohort, 41.2 versus 52.4 mL ($P<0.01$). We obtained individual infarct growth rates enabling the estimation of final infarct volume based on time and grade of reperfusion.

CONCLUSIONS: We validated a deep learning-based method which improved final infarct volume estimations compared with classic computed tomography perfusion imaging processing. In addition, the deep learning model predicted individual infarct growth rates which could enable the introduction of tissue clocks during the management of acute stroke.

GRAPHIC ABSTRACT: A graphic abstract is available for this article.

Key Words: deep learning ■ infarction ■ ischemic stroke ■ perfusion imaging ■ reperfusion

Acute ischemic stroke treatment aims at salvaging the hypoperfused tissue by recanalizing the occluded artery by intravenous thrombolysis or endovascular treatment (EVT). For years, expected time of symptom onset to treatment determined eligibility for these therapeutic regimens.[1–3] Recent trials have provided evidence for efficacy of EVT after imaging-based selection in patients presenting outside of the conventional time windows of stroke onset.[4,5]

Perfusion imaging, most commonly computed tomography perfusion (CTP), can aid in identifying the potentially salvageable tissue (ie, penumbra) calculated by subtracting the irreversibly damaged ischemic core from the hypoperfused lesion volume.[6–8] The currently clinically

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Nonstandard Abbreviations and Acronyms

CTP	computed tomography perfusion imaging
DL	deep learning
EVT	endovascular treatment
HIR	hypoperfusion intensity ratio
MAD	mean absolute volumetric differences
mTICI	modified Thrombolysis in Cerebral Infarction
rCBF	relative cerebral blood flow

available software programs calculate different perfusion parameters by using a deconvolution technique.[9,10] In the clinical trials DEFUSE 3 (Endovascular Therapy Following Imaging Evaluation for Ischemic Stroke), SWIFT-PRIME (Solitaire With the Intention for Thrombectomy as Primary Endovascular Treatment), DAWN (Diffusion Weighted Imaging or Computerized Tomography Perfusion Assessment With Clinical Mismatch in the Triage of Wake Up and Late Presenting Strokes Undergoing Neurointervention) and EXTEND (Extending the Time for Thrombolysis in Emergency Neurological Deficits), a relative cerebral blood flow (rCBF) <30% determined the ischemic core volume and a delay to the maximum of the residue function (Tmax) exceeding 6s identified the critically hypoperfused tissue.[4,5,11,12] Patients were selected for inclusion in these trials based on a predefined mismatch pattern of core and perfusion lesion estimates.[13,14] However, the calculated maps depend on the software program used and can still require human input to distinguish artifacts from real perfusion deficits.[10] In addition, this deconvolution technique is inherently sensitive to noise and, therefore, improving the current perfusion algorithms or even use deconvolution-free summary parameters is the aim of current research.[15–17] Machine learning is an alternative to estimate tissue fate in patients with ischemic stroke.[18–20] The current classification of tissue into penumbra and core relate to the moment of scanning and does not project the rate of infarct evolution which can be useful in transfer settings. The rate of infarct growth varies greatly between patients and is among other things dependent on the collateral circulation.[21,22] The hypoperfusion intensity ratio (HIR), which ranges between 0 and 1, obtained at baseline with perfusion imaging correlated with actual infarct growth rates and a HIR value <0.5 suggested infarct growth rates below 5 mL/h.[23] A better insight in the individual growth prediction could influence logistics regarding both transfer of patients as well as time metrics in comprehensive stroke centers.

We previously developed a deconvolution free algorithm based on deep learning (DL) to predict tissue status directly from CTP source images.[24] The aim of this study was to compare final infarct volume estimation accuracy between a deep neural network and a classic deconvolution/thresholding analysis. Additionally, we aimed to provide individual lesion growth rates in patients with a large vessel occlusion and correlate these estimations to the HIR.

METHODS

The data that support the findings of this study are available from the corresponding author upon reasonable request.

The local institutional review boards from all participating institutions approved the original studies.

DL Model

We trained a deep neural network to predict final infarct size in patients with acute ischemic stroke with large vessel occlusions in the anterior circulation.[2] We refer to the original paper for the full technical details of the DL model.[24] To summarize, the network was trained based on the CTP source images from patients included in the MR CLEAN trial (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; the derivation cohort) in a voxelwise classification approach. Four clinical parameters were added to the DL model: time of symptom onset to imaging, time to recanalization, modified Thrombolysis in Cerebral Infarction (mTICI) scores at the end of the procedure and the persistence of the arterial occlusion on CT angiography at 24 hours. The output of the DL model provides the probabilities of infarction per voxel. The predicted final infarct volumes are calculated by taking the sum of all probabilities and multiply this result with the volume per voxel (Figure 1). Upon request, we added the MI-CLAIM (Minimum Information About Clinical Artificial Intelligence Modeling) checklist to the Data Supplement as a quality check.[25]

Validation of the Final Infarct Volume Prediction

We compared the performance of the DL model in predicting the final infarct volume in 2 cohorts of patients to a clinically validated CT perfusion software package (ie, RAPID; iSchemaView, Menlo Park, CA) which uses a deconvolution/thresholding approach.[9] The DL model was internally validated in a

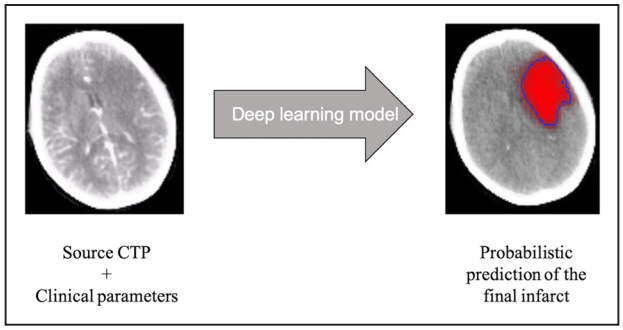

Figure 1. Example of the probabilistic prediction made by the deep learning model using the native perfusion images and clinical parameters.
The red (online) voxels represent the probabilistic prediction of the final infarct by the deep learning model and the blue (online) line depicts the actual final infarct. CTP indicates computed tomography perfusion.

5-fold cross-validation in the derivation cohort (MR CLEAN).[2] The cohort was randomly split in 5 subcohorts, and the model was trained 5× on the subjects of 4 subcohorts and evaluated based on the predictions for the subjects in the other subcohort.[24] As a result, we obtained predictions for each subject by a model that was not trained on that subject. Here, the DL model was validated externally in an independent dataset from the CRISP study (Computed Tomographic Perfusion to Predict Response to Recanalization in Ischemic Stroke).[26]

We used the manually delineated lesions (from the original study) at follow-up CT scan on day 5 (or when not available at 24 hours) in the MR CLEAN study to define the gold standard for the final infarct volumes. For the CRISP study, these final volumes had been determined by the core lab based on the fluid attenuated inversion recovery images of day 5.[27,28] The same slice coverage as for the initial CTP scan was considered for the calculation of the final infarct volume.

The DL model can predict the final infarct volume for any hypothetical level of achieved reperfusion. Inherently, the deconvolution/thresholding approach can predict the final infarct only in the absence of reperfusion (baseline hypoperfused lesion volumes serves as a proxy for the final infarct volume) or if complete reperfusion is achieved (where the baseline infarct core will equal the final infarct volume). Poor and intermediate reperfusion status will result in an infarct volume which cannot be estimated by the deconvolution/thresholding approach. To address this issue, we excluded patients with intermediate reperfusion when comparing baseline predictions versus actual final infarct volumes for both models. Successful reperfusion was defined as a mTICI scale 2b or 3 in patients who underwent EVT; poor (mTICI, 1) or intermediate reperfusion (mTICI, 2a); and no reperfusion in patients with a final mTICI of 0 and in addition patients without EVT in whom CT angiography at 24 hours showed a persistent large vessel occlusion. In patients with successful reperfusion, the core volume at baseline, defined as the area with a reduction of the rCBF below 30%, served as the prediction of the final infarct volume. In patients without reperfusion, the hypoperfused lesion volume, delineated by Tmax maps with a delay of >6s, was regarded as the predicted final infarct volume.[5,7,29] These thresholds have been used in many clinical trials for patient selection for reperfusion therapy and are implemented by RAPID software as the default output maps.[5,11] We visually inspected all the perfusion maps and manually corrected the arterial input function when automatic selection failed.

Evaluating the ischemic core with CTP remains challenging and although the threshold of a rCBF <30% is clinically relevant and validated, the mean absolute volumetric differences (MAD) between the CTP versus acute diffusion weighted imaging core volume is the smallest when using a threshold of 38%.[7] Therefore, in an exploratory analysis, we calculated final infarct volumes in patients with reperfusion based on the rCBF threshold of 38%.

Growth Prediction and Association With Collateral Grades in CRISP

We computed infarct volumes as predicted by the DL model at different time points after imaging and with various grades of reperfusion in the validation sample of the CRISP study. Based on these data, we calculated the mean lesion growth rates per 60 minutes for patients in a time window between imaging and reperfusion of 30 to 180 minutes with simulated mTICI scores. We only show results for clinically relevant mTICI scores of 2a, 2b, or 3.

We obtained the HIR as a marker of collateral status, which is defined as the proportion of Tmax >6s volume with Tmax >10s.[30] HIR correlates well with the quality of collateral circulation determined by angiography.[30] We investigated the association between the HIR and predicted lesion growth in patients with a target mismatch profile similar as has been reported for actual growth in patients during transfer to a comprehensive stroke center.[23] This target mismatch profile was defined according to DEFUSE 3 criteria as a core volume below 70 mL, an absolute difference in Tmax >6s minus core volume of at least 15 mL and a ratio of the Tmax >6s lesion over the core volume of 1.8 or higher.[5]

Statistical Analysis

Characteristics of the 2 study populations were compared with a χ^2 test for categorical variables and with the Mann-Whitney *U* test for continuous variables.

We calculated MAD between the predicted and the gold standard final infarct volumes. These volume errors were compared between the DL model versus RAPID software by the Wilcoxon signed-rank test.

Receiver operating characteristic curves are depicted for HIR values to discriminate between slow and fast predicted rates of lesion growth with optimal sensitivity and specificity. Following the definitions of a previous publication, the cut off for slow versus fast infarct growth was set to 5 mL/h.[23] The optimal HIR threshold to separate slow and fast lesion growth was calculated by the Youden index. In addition, we compared the difference in median lesion growth between patients with good and poor collateral circulation with the Mann-Whitney *U* test.

R software was used for statistical analysis.[31] *P* values below 0.05 were considered significant.

RESULTS

Demographics

We included 127 of the 500 patients randomized in the MR CLEAN trial. Reasons for exclusion were: absence of baseline CTP (231), insufficient quality of baseline CTP (42), incomplete information on reperfusion status (59), and lack of follow-up noncontrast CT (41). For the external validation, we could analyze 104 of the 190 patients enrolled in CRISP. Most patients (84) were excluded since follow-up fluid attenuated inversion recovery at day 5 was unavailable, and in 2 patients the CTP data was of insufficient quality (Figure I in the Data Supplement). We manually selected the arterial input function in 4 patients. Clinical and imaging characteristics of the included patients are listed in the Table. Patients from the CRISP dataset were older, had smaller baseline core volumes, presented later after symptom onset for CTP imaging, had shorter imaging to reperfusion time windows, and higher reperfusion rates. CRISP was a cohort study of patients undergoing EVT and the MR CLEAN trial was a

Table. Demographic Data

	MR CLEAN (n=127)	CRISP (n=104)	*P* value
Age	63 (52–73)	68 (57–76)	0.01
Gender, female	63 (50%)	52 (50%)	1
NIHSS D0	17 (14–21)	18 (12–21)	0.36
Time of symptom onset to CTP, min	171 (110–233)	273 (154–406)	<0.01
Time of CTP to recanalization, min	163 (136–217)	142 (106–174)	<0.01
Core volume RAPID, mL	14.1 (0–39.9)	7.6 (0–20.3)	0.01
mTICI score 2b–3*	48 (38%)	87 (84%)	<0.01
Final infarct volume, mL	51.0 (21.3–112.5)	52.0 (25.7–109.0)	0.80

Data are median (IQR) or n (%). CTP indicates computed tomography perfusion; IQR, interquartile range; MR CLEAN, Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands; mTICI, modified Thrombolysis in Cerebral Infarction; and NIHSS, National Institutes of Health Stroke Scale.

*For MR CLEAN in 48 of 75 patients (64%) randomized to the interventional arm the mTICI score was 2b–3.

randomized controlled trial in which half of the patients did not receive EVT. This at least partially explains the lower rates of successful reperfusion in patients included from the MR CLEAN trial.

Validation of Final Infarct Volume Prediction

For the internal validation of the MR CLEAN study, we could include 48 patients (36%) with successful and 60 patients (44%) without reperfusion to assess the baseline prediction of the final infarct size in comparison to RAPID software. When comparing the final infarct estimation in these 108 patients based on the RAPID analysis of the baseline CTP versus the actual infarct volume the MAD was 52.4 mL (SD, 49.8). The DL model provided a better estimate of the final infarct with a MAD of 34.5 mL (SD, 29.4; $P<0.01$; Figure 2A, Table I in the Data Supplement).

In 19 patients with intermediate reperfusion from the MR CLEAN study, the MAD for the DL model versus the actual final infarct volume was 36.7 mL (SD, 38.3). This result did not differ from the group with complete or no reperfusion ($P=0.64$).

In the external validation of the CRISP study, we documented successful reperfusion in 87 patients (84%) and no reperfusion in 5 (5%). In this independent cohort of 92 patients, the MAD between baseline and actual final infarct volume was also smaller (41.2 mL [SD, 55.4]) for the DL model compared with the prediction by the RAPID software (52.4 mL [SD, 58.3]; $P<0.01$; Figure 2B, Table I in the Data Supplement). Bland-Altman plots for

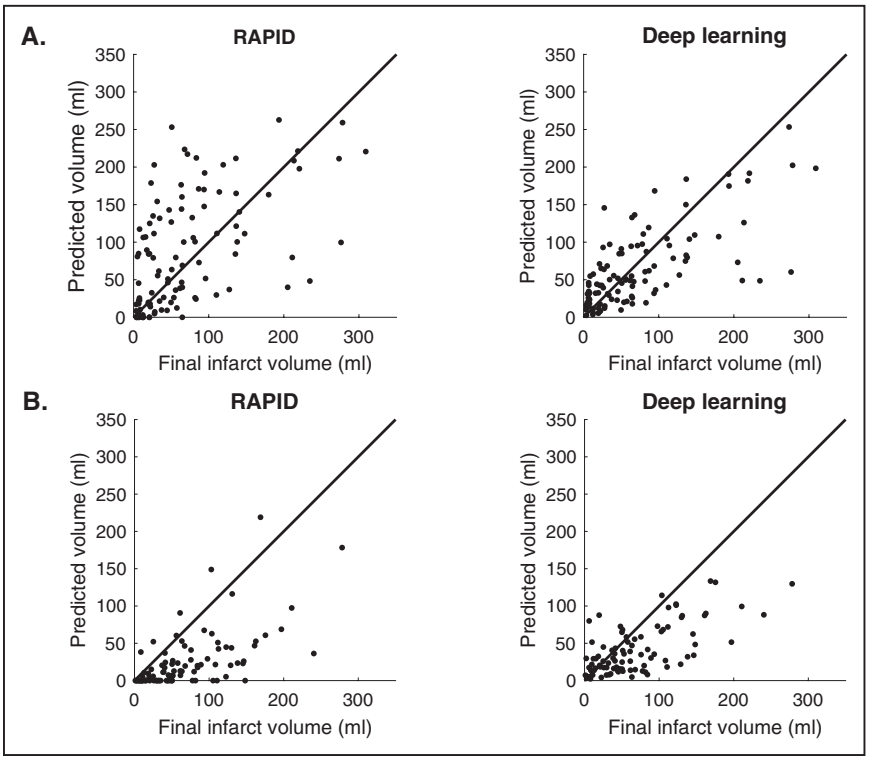

Figure 2. Overiew of the predicted final infarct volumes.
A, Internal validation: Scatterplots for predicted volumes (mL) for the MR CLEAN (Multicenter Randomized Clinical Trial of Endovascular Treatment for Acute Ischemic Stroke in the Netherlands) population (n=108). **B**, External validation: Scatterplots for predicted volumes (mL) for the CRISP population (n=92). Black line depicts the identity line.

the internal and external validation sets are depicted in Figure II in the Data Supplement.

In an exploratory analysis of the CRISP dataset, we applied a different rCBF threshold of 38% to calculate the core volume (ie, the predicted final infarct volume in reperfused patients) with the RAPID software. This resulted in a lower MAD (42.2 mL [SD, 54.5]) for the calculations by the automated RAPID software. At this threshold, both the DL model and RAPID software performed similarly in predicting the final infarct volume (*P* value for difference in MAD, 0.3).

In the CRISP dataset, 12 patients presented with intermediate reperfusion and the MAD for the DL model versus the final infarct volume was 58.5 mL (SD, 63.5). This difference was comparable to the group with complete or no reperfusion (*P*=0.46).

Individual Growth Modelling

Based on the information of the baseline CTP, the DL model can provide infarct growth rates in individual patients. With the input of a particular reperfusion status (mTICI 2a, 2b, or 3) at a chosen time point after imaging, the model is able to estimate the corresponding final infarct volume. The evolution of infarct growth can be presented in a graph and transformed in a movie to provide clinicians with an interactive visualization. In Figures 3 and 4, we show examples of such growth predictions for different patients (Movies I and II in the Data Supplement).

We calculated the HIR and projected mean lesion growth rates per hour for patients who presented with a target mismatch profile (n=98, 94%). Figure 5A depicts the receiver operating characteristic curve of the HIR as a predictor of patients with fast (>5 mL/h) versus slow infarct growth rates (≤5 mL/h). The Youden index revealed an optimal threshold of 0.36 to discriminate between these 2 growth patterns. In patients with a HIR <0.36, the median lesion growth rate was lower (2.7 mL/h) compared with patients with a HIR ≥0.36, in whom the median growth rate was 8.5 mL/h (*P*<0.01; Figure 5B). In Figure III in the Data Supplement, the scatterplot between HIR and predicted infarct growth rate is depicted.

DISCUSSION

We present a DL model to predict final infarct volumes at baseline based on CTP images and reperfusion status in patients with an acute ischemic stroke caused by a large vessel occlusion. The model improved estimations of final infarct volumes in 2 independent cohorts compared with a clinically validated automated software. This DL model provided infarct growth rates for individual patients, and we replicated a correlation between the HIR and these growth rates.

The randomized clinical trials of EVT in the extended time window included patients in whom tissue status was known based on CTP or MR imaging, underscoring the importance of more advance neuro-imaging compared with only noncontrast CT and CT angiography.[4,5] Although software packages to identify core and penumbra are clinically validated, limitations of the classic deconvolution technique are well described in the literature and current research focuses on more advanced learning approaches. Previously published DL models made use of the different perfusion parameters obtained by deconvolution as input parameters or the output derived from

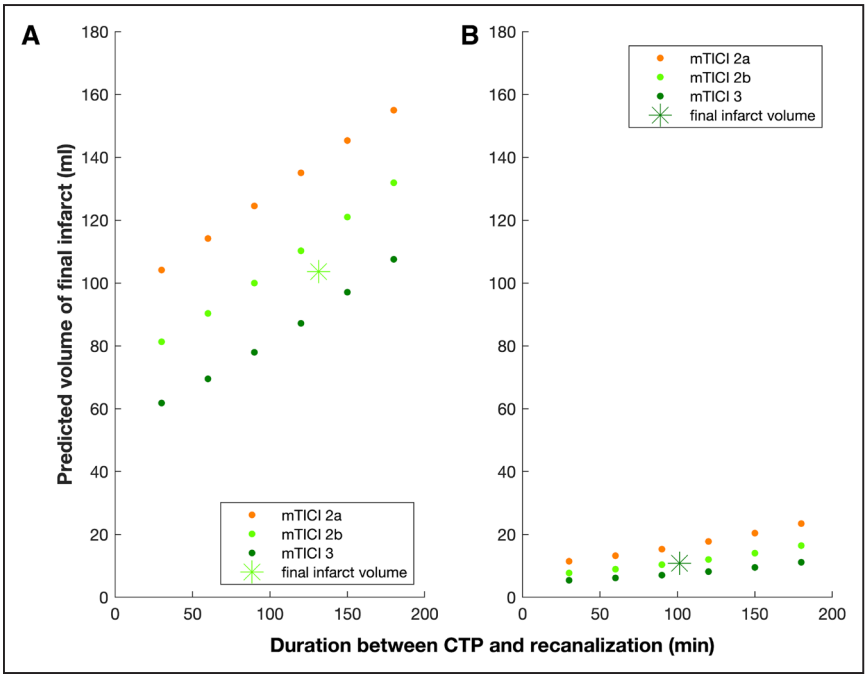

Figure 3. Examples of infarct growth prediction curves.
A, Patient with a mean infarct growth of 18.3 mL/h. The final infarct volume was 104 mL. Recanalization was performed 131 min after computed tomography perfusion (CTP) with a modified Thrombolysis in Cerebral Infarction (mTICI)=2b. **B**, Patient with a mean infarct growth of 2.3 mL/h. The final infarct volume was 10.8 mL. Recanalization was performed 101 min after CTP with a mTICI=3.

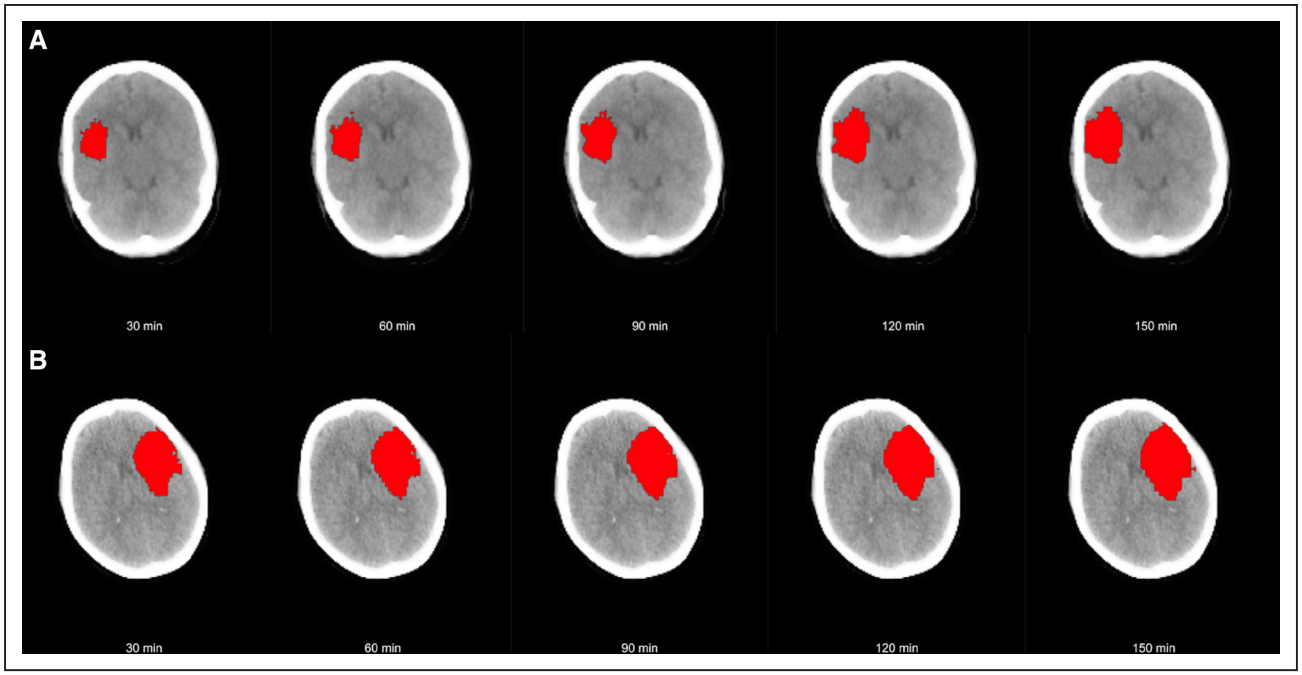

Figure 4. Final infarct volumes for complete reperfusion as predicted by the deep learning model.
The predicted final infarct volumes are illustrated in red (online) at different time points. Patient A had a mean infarct growth of 9.6 mL/h and patient B of 12.8 mL/h. Corresponding movies can be found in Movies in the Data Supplement.

deconvolution as ground truth.[18,32–35] Our model is completely free of deconvolution by using the source perfusion images as input and the final infarct as ground truth, which is a great advantage. In previous research, we showed that source perfusion scans as input parameters outperformed perfusion parameters derived from deconvolution in predicting final infarct volume.[24]

CTP imaging reveals infarcted and hypoperfused brain tissue based on hemodynamic changes resulting from the occlusion of an artery. A decrease in the CBF has been validated as the most accurate prediction of the ischemic core with a threshold of a rCBF <38%. Calculations of core volumes based on this threshold will occasionally overestimate the infarcted tissue, potentially resulting in the exclusion of candidates for EVT. In clinical practice, preventing overcalling of the infarcted tissue is favored over accuracy and, therefore, the more strict threshold of a rCBF <30% was introduced in the

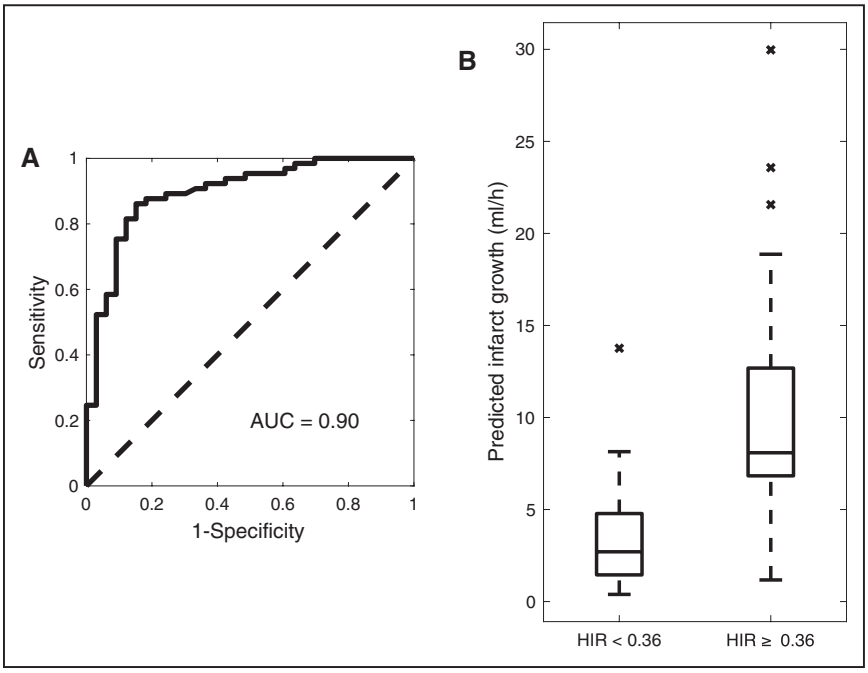

Figure 5. Association between the hypoperfusion intensity ratio (HIR) and predicted infarct growth.
A, Receiver operating characteristics curve for HIR to predict lesion growth of 5 mL/h in patients with the target mismatch profile in CRISP (n=98). Youden index=0.36. **B**, Boxplots for the predicted infarct growth (mL/h) depending on a HIR <0.36 (n=36) vs ≥0.36 (n=62; P<0.01). AUC indicates area under the curve.

RAPID software to determine core.[7] The perfusion lesion volume (ie, the area in the brain which is critically hypoperfused) is derived from the Tmax parameter revealing delays above 6s.[36] In patients with successful reperfusion, the ischemic core obtained at baseline frequently equals the final infarct volume and in patients without reperfusion the estimated perfusion lesion volume acts as a prediction for the final infarct size.[12] Any intermediate reperfusion status will result in stroke sizes between the baseline core and perfusion lesion volumes, but accurate prediction is unobtainable from conventional CTP analyses. Therefore, the comparison of the MAD between volumes acquired by conventional CTP-based automated software versus the actual final infarct could only be determined in the group of patients with and without reperfusion (ie, not in patients with intermediate reperfusion).

The DL model produced lower MADs in both the MR CLEAN and CRISP study compared with the RAPID software, one of the most commonly used perfusion software programs that is based on a classic deconvolution/thresholding technique. One of the advantages of the DL model might be the integration of the timing of the imaging related to the onset of symptoms and to the timing of recanalization. However, we do admit that the mean absolute differences remain quite large which is a known challenge in estimating infarct volumes at baseline, likely due to the inherent limitation of the current perfusion imaging.[17]

We performed an exploratory analysis comparing the DL to the RAPID analysis with the rCBF <38% threshold. This analysis underscored the previous findings of a more accurate prediction with this threshold since the MAD was no longer different between the 2 methods.

In the group with intermediate reperfusion, we could only investigate the performance of the DL model which revealed similar volumetrical differences to the group with complete or no reperfusion.

An important advantage of the DL approach is the possibility to predict the final infarct volume in different scenarios for both time to recanalization and mTICI scores. In addition, we created individual growth rates which can be visualized in graphs and movies displaying the evolution of the infarct. This tissue clock can guide physicians in several decisions like the indication to repeat neuroimaging in transfer patients and may encourage teams in comprehensive stroke centers during EVT procedures to improve time metrics. Models predicting infarct growth rates can also be of importance in future trials with neuroprotective agents. The most optimal patients will be those with substantial infarct growth in the therapeutic time window between imaging and reperfusion. Patients with slow infarct growth rates are not likely good candidates for these neuroprotective treatments since considerable infarct growth between imaging and reperfusion is not expected.[37,38] In a previous study, collateral status, as assessed by the HIR at baseline, correlated with actual infarct growth rates calculated based on 2 neuroimaging studies before and after transfer of patients to a comprehensive stroke center.[23] With our model, we identified a similar association between the HIR and the predicted lesion growth rate, which may represent an indirect confirmation of the growth prediction model. The suggested threshold of 0.36 closely approximates the threshold of 0.4 as predictor of collateral status defined on digital subtraction angiography and infarct growth in the original article that introduced the HIR.[30] This analysis was limited to patients with a target mismatch profile, which might have led to an exclusion of the fast growers. Therefore, validation in a cohort of consecutive stroke patients with large vessel occlusions would be of interest to increase the heterogeneity in perfusion profiles.

A general limitation of a DL model is the difficult interpretation of the origin of the individual results. One can only interpret the probabilities of the final infarct prediction, but not how they are exactly calculated by the DL model. Furthermore, our results are only applicable to patients with similar characteristics as in the described study population. Further research is warranted in other cohorts as for instance in patients with posterior stroke.

Another limitation of our study is the lack of a uniform method to quantify the final infarct volume. In the derivation cohort, we determined the final infarct on noncontrast CT imaging 5 days after stroke onset and if unavailable we used the 24-hour noncontrast CT. The latter may be suboptimal since in a substudy of MR CLEAN some infarct growth occurred after 24 hours.[27] Therefore, previously we evaluated the 2 methods as measurement of the final infarct volumes and found no difference in performance of the DL model.[24] In the validation cohort, we delineated final infarct volumes on the day 5 fluid attenuated inversion recovery to enable a more accurate volumetric approach, since early MRI can result in underestimation especially in patients who do not reperfuse.[28,39] Another limitation is the lack of a gold standard to validate the calculated lesion growth rates. In MR CLEAN and CRISP, patients did not undergo 2 neuro-imaging studies before reperfusion therapy hampering measurements of actual growth rates. Furthermore, hemorrhagic transformation may also contribute to infarct growth. The similar association with the HIR and our predicted infarct growth rates compared with the actual infarct growth found in a smaller study could serve as an indirect validation of our model.[23]

Conclusions

We validated an innovative DL approach to predict final infarct volumes directly from the CT source perfusion images in a large independent dataset of patients with acute large vessel ischemic strokes. The model can

derive individual infarct growth rates which could become part of clinical routine in both primary and comprehensive stroke centers.

ARTICLE INFORMATION

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Disclosures

Dr Marquering reports co-founder and shareholder of Nico-lab outside the submitted work. Dr Roos reports stock ownership of Nico-Lab outside the submitted work. Dr Majoie reports grants from CVON (Netherlands Cardiovasculair Research Initiative)/Dutch Heart Foundation, grants from European Commission, grants from Dutch Health Evaluation Program, grants from Stryker, and grants from TWIN Foundation (Toegepast Wetenschappelijk Instituut voor Neuromodulatie) outside the submitted work; and is shareholder of Nico-lab. Dr van der Lugt reports grants from Angiocare BV, grants from Covidien/EV3, grants from Medac GmbH/Lamepro, grants from Stryker, grants from Penumbra, and grants from Dutch Heart Foundation during the conduct of the study; grants from stryker, grants from Medtronic, grants from penumbra, grants from cerenovus, and grants from thrombolytic science Inc outside the submitted work. Dr Lansberg reports grants from National Institutes of Health during the conduct of the study. Dr Albers reports equity interest in iSchemaView, owner of RAPID software which is used in this study. Dr Christensen reports equity interest in iSchemaView, owner of RAPID software which is used in this study. Dr Dippel reports grants from Dutch Heart Foundation, grants from AngioCare BV, grants from Covidien/EV3, grants from MEDAC Gmbh/LAMEPRO, grants from Penumbra Inc, grants from Top Medical/Concentric, grants from Stryker, during the conduct of the study. Dr van Zwam reports personal fees from Cerenovus and personal fees from Stryker during the conduct of the study. Dr Robben reports grants from Flanders Innovation and Entrepreneurship (VLAIO [Agency for Innovation and Entrepreneurship]) during the conduct of the study; in addition, Dr Robben has a patent to Patent for automatic arterial input function selection pending. Dr Lemmens is a senior clinical investigator for Fund for Scientific Research-Flanders (FWO: 1841918 N), reports a grant from FWO Flanders (G049620N) and institutional support for consultancy by iSchemaView. The other authors report no conflicts.

Supplemental Material

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