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Application of Radiomics in Vesselness Analysis of CT Angiography Images of Stroke Patients

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Abstract. Development of vascular collaterals in a lesion area is one of the key factors that determine not only the choice of treatment for ischemic stroke (IS) patients, but also outcome and therapy effectiveness. The main method for examining the vessels' ramification is CT angiography (CTA). CTA analysis may be improved by incorporating filters designed to extract more features about vessels and quantify their level of development. This work suggests the usage of radiomics methods in the analysis of vesselness measure calculated from CTA images. Vesselness measurement is based on the analysis of the Hessian matrix with a few modifications dictated by practical aspects of this issue. The developed algorithm was implemented as a filter that generates a new 3D image, every voxel of which has the probability of belonging to a vessel-like structure. Further analysis of the distribution of vesselness in the lesion area and in the intact contralateral area was conducted with the methods from the open library PyRadiomics. A set of radiomics features was calculated. Preliminary analysis on a sample of 30 IS patients showed the presence of significant differences between afflicted and intact hemispheres.

Keywords. Collaterals, imaging biomarkers, ischemia, tomography

1. Introduction

Ischemic stroke (IS) is one of the leading causes of death and disability in the world [1]. The outcome of IS depends not only on the timeliness of the reperfusion therapy but also on the intensity of collateral flow [2]. The absence of well-developed collaterals leads to an increase in the volume of necrotized tissue and to a decrease in the effectiveness of treatment [3]. In daily practice, CT angiography (CTA) is used as the main method for visualizing of vascular anatomy. However, it is very common among radiologists to analyse CTA images manually, resulting in subjectivity of the assessment. Cutting-edge methods of image processing, including vesselness calculation algorithms, may be of help in addressing this problem, by providing an automatic measure of collateral status.

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Vesselness calculation involves assessment of the probability of each voxel belonging to a vessel-like structure [4]. According to literature, there is a possibility of using vesselness to resolve some clinical challenges in treatment of IS patients [5-7]. Currently, most of studies include analysis of variables based only on the volume of vessel-like structures, but not on their spatial behavior and other characteristics. At the same time, one of the most perspective directions of modern medicine is the analysis of radiological images, specifically radiomics [8-10]. It allows extracting numerous features including those that describe shape and texture from radiological images. So, in the line with the above, the aim of the presented work was the application of radiomics methods in the analysis of vascular behavior calculated from the CTA images of the patients with IS.

2. Methods

This pilot study included data of 30 patients (74 years old (IQR 57-80), 18 males, 12 females) admitted to the N.V. Sklifosovskiy Scientific Research Institute of Emergency Care with IS in the territory of the middle cerebral artery (up to 5 hours from stroke onset). The examination of the patients was performed with multi-slice CT-scanner (GE Medical Systems), with pixel spacing of 0.44 x 0.44 mm, and slice thickness of 0.5 mm. We used CTA images obtained on the admission of a patient to the hospital, and images from non-enhanced CT conducted on the second day after IS onset, when the ischemic region was already visible as a hyperdensive area. The last ones were used for contouring of the regions of interest (ROI) that was conducted by two radiologists (Figure 1, A). Each of them had more than 20 years of experience.

Brain normalisation was conducted to build a symmetrical area and to transfer both areas (with damaged and intact brain tissues) onto the CTA series (Figure 1, B and D). It was performed with the set of instruments described in the Advanced normalisation tools (ANTS) [11] that allowed coregistration of a brain to a template image using linear affine and warp transformations.

Then, CTA images were processed through the vesselness filter (Figure 1, C). The vesselness calculation was based on the following key concept: if we look at every voxel of a 3D image and evaluate the function of the derivative of intensity along three orthonormal directions, then it is possible to establish criteria for a voxel belonging to a tubular structure. The mathematical representation of this is the Hessian matrix calculation with second-order partial derivatives, and the assessment of its three eigenvalues λ_1, λ_2, λ_3 sorted in ascending order [4]. This method successfully identifies vessels, but it causes a decline of vesselness value in vessel bifurcation points. To address this issue, [7] proposed using λ_p as a regularized value, which is computed depending on the maximal value of λ_3.

Based on the latter, we developed a vesselness filter, but made some changes to adaptation to further clinical research work. First, as the original CT images are noisy, it was necessary to smooth them to make them better suited for vessel analysis. The minimisation of noise is determined by the size of vessels that we are looking for and by the resolution of the CT scanner (0.7-1.4 mm). Thus, we applied the Gaussian filter with σ=0.7 mm. This allowed us to determine the Hessian matrix more robustly while keeping information about small vessels. Second, we adapted the approach proposed in [7] to λ_p regularization. λ_p depends on the maximal value of λ_3 throughout an image. In this case, even if we have a fairly smooth image with relatively meagre vascularity, we find a lot of vessel-like structures. So, the results of vesselness analysis for different images and patients are not comparable. To avoid this, we decided to exclude the dynamic nature of λ_p and fix the maximum value of λ_3 at 400 HU/mm$_2$. The filter was implemented in our previously developed platform for medical images analysis [12].

The initial CTA images of 30 patients were processed through it, and new 3D images were generated. Each voxel has a vesselness value which measures the similarity of the voxel to a vessel-like structure. As the total sum of vessel-like voxels is very sensitive to the threshold of vesselness, we decided to implement the calculation of other features of the filtered images, describing other morphometric and distribution aspects of vesselness. The open library PyRadiomics was used to calculate 75 features of damaged and intact areas [13-14]. They included first-order statistics (FO) and second-order statistics which were based on analysis of the grey-level co-occurance (GLCM), grey-level size zone (GLSZM), and grey-level run-length (GLRLM) matrices.

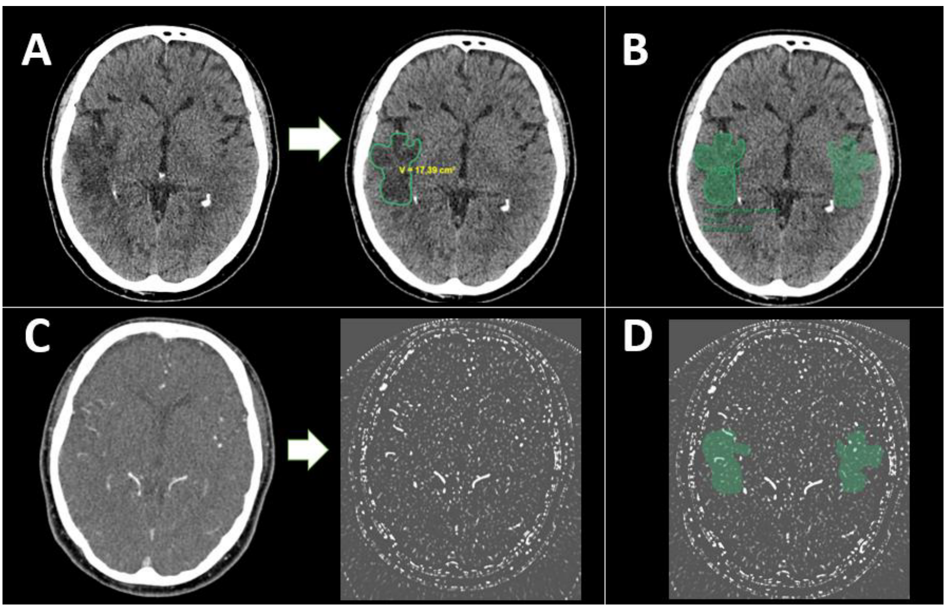

Figure 1. Scheme of the image processing for the calculation of radiomics features of vesselness (A – semiautomatic segmentation of ROI with damaged tissue on non-enhanced CT, B – automatic segmentation of ROI in the intact area, C – Application of vesselness filter on CTA images, D – copy of two ROIs to the filtered CTA images)

3. Results

Comparative analysis of 75 features in damaged and intact areas of 30 patients showed the presence of statistically significant differences in 57 parameters ($p<.05$, the Wilcoxon signed-rank test). For 48 of them these differences were highly significant ($p <.001$). We evaluated their relative change against the intact side to select the most informative features. It the confidence interval of a feature's relative change contained zero, the feature was excluded. Thus, the following list of features with the most pronounced and stable changes was formed (Table 1).

Table 1. The magnitude of the features' relative change in comparison with intact area.

Feature Group	Feature Name	Relative change	P-value
FO	Energy	↓ 79.3 (IQR 12.3-91.0) %	<<0.001
	Variance	↓ 79.6 (IQR 11.1-91.2) %	<<0.001
	Entropy	↓ 34.9 (IQR 11.1-91.2) %	<<0.001
GLCM	Contrast	↓ 81.4 (IQR 21.9-47.7) %	<<0.001
	Difference Variance	↓ 81.5 (IQR 21.0-91.0) %	<<0.001
	Joint Entropy	↓ 34.5 (IQR 23.3-47.3) %	<<0.001
GLRLM	High Grey Level Run Emphasis	↓ 72.0 (IQR 10.0-84.6) %	<<0.001
GLSZM	Large Area Emphasis	↑ 133.2 (IQR 10.9-228.1) %	<<0.001
	Size-Zone Non-Uniformity	↓ 71.9 (IQR 14.9-84.9) %	<<0.001
	Zone Variance	↑ 133.1 (IQR 10.9-228.0) %	<<0.001

As you can see in the table 1, the damaged areas show a decrease in energy and variance as a result of reduction in the number of vessel-like voxels. GLCM features indicated a decrease in the homogeneous patterns in the image. Changes in size-zone non-uniformity and zone variance of GLSZM reflect the fact that the distribution of zones with the same intensity level was modified in the damaged ROIs.

4. Discussion

One of the most effective ways to improve the quality of treatment for IS patients is to implement the advanced technologies of intellectual analysis and image processing into interpretation of the results of neuroimaging examinations. Assessment of the collateral status on the CTA allows predicting effectiveness of revascularization surgeries and long-term outcome of a clinical case, hence providing the decision support in the choosing of the treatment tactics for patients.

In this work we detected a large difference between damaged and intact areas in 10 features describing vesselness behavior. An interesting aspect of these preliminary results was that some of these features indirectly described the volume of vascular tree or a number of bright voxels (e.g., energy, variance, root mean squared), but others outlined the homogeneity of regions of interest (e.g., entropy, contrast of GLCM, size-zone non-uniformity and zone variance of GLSZM).

It is important to note that with the application of radiomics methods to the initial images of CTA it is difficult to explain whether the discovered differences in the features are caused by the changes in vessels or in the brain tissue. At the same time, the physiological interpretation of the images resulting from the use of the vesselness filter is simpler as all changes are only related to voxels of vessels.

Limitations to this study include its retrospective design and a small sample size. Also, we didn't have a control group to investigate the behavior of the features for healthy people. In the future work we will try to address these limitations.

5. Conclusion

In this paper, we presented a method of quantitative assessment of collaterals based on the analysis of vesselness measure. The suggested procedure includes the calculation of vesselness with an algorithm developed by Jerman et al, modified by using Gaussian filters and fixing the maximum value of λ_3. The result of the application of the vesselness filter is proposed to analyse with the radiomics methods, effectively investigating not only the volumetric characteristics of vesselness, but also the pattern of its distribution. Comparison analysis of extracted features of vesselness between the afflicted and the intact ROIs had shown that there are significant differences in a number of parameters. This makes it possible to develop clinically relevant measures for assessment of collaterals and prediction of treatment outcomes in further work.

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References

[1] V.L. Feigin, B. Norrving, G.A. Mensah, Global Burden of Stroke, Circulation research 120 (3) (2017), 439-448.

[2] C. Zerna, G. Thomalla, B.C.V. Campbell, J. Rha, M.D. Hill, Current practice and future directions in the diagnosis and acute treatment of ischaemic stroke, Lancet 392(10154) (2018), 1247-1256.

[3] S.A. Sheth, N. Sanossian, Q. Hao, S. Starkman, L.K. Ali, D. Kim, N.R. Gonzalez, S. Tateshima, R. Jahan, G.R. Duckwiler, J.L. Saver, F. Vinuela, and D.S. Liebeskind, Collateral flow as causative of good outcomes in endovascular stroke therapy, Journal of neurointerventional surgery 8 (2016), 2-7.

[4] A.F. Frangi, W.J. Niessen, K.L. Vincken and M.A. Viergever, Multiscale vessel enhancement filtering, Medical Image Computing and Computer-Assisted Intervention 1496 (1998), 130-137.

[5] A.M.M. Boers, R.S. Barros, I.G.H. Jansen, C.H. Slump, D.W.J. Dippel, A. van der Lugt, W.H. van Zwam, Y.B.W.E.M. Roos, R.J. van Oostenbrugge, C.B.L.M. Majoie, H.A. Marquering, Quantitative Collateral Grading on CT Angiography in Patients with Acute Ischemic Stroke, Molecular Imaging, Reconstruction and Analysis of Moving Body Organs, and Stroke Imaging and Treatment. RAMBO 2017, CMMI 2017, SWITCH 2017. Lecture Notes in Computer Science, 10555 (2017). 176-184.

[6] A.M.M. Boers, B.R. Sales, I.G.H. Jansen, O.A. Berkhemer, L.F.M. Beenen, B.K. Menon, D.W.J. Dippel, A. van der Lugt, W.H. van Zwam, Y.B.W.E.M. Roos, R.J. van Oostenbrugge, C.H. Slump, C.B.L.M. Majoie, H.A. Marquering, Value of Quantitative Collateral Scoring on CT Angiography in Patients with Acute Ischemic Stroke, American journal of neuroradiology 39(6) (2018), 1074-1082.

[7] T. Jerman, F. Pernus, B. Likar and Z. Spiclin, Enhancement of Vascular Structures in 3D and 2D Angiographic Images, IEEE Transactions on Medical Imaging 35 (2016), 1-1.

[8] J. Park, H. Kim, Radiomics as a Quantitative Imaging Biomarker: Practical Considerations and the Current Standpoint in Neuro-oncologic Studies, Nuclear Medicine and Molecular Imaging. 52 (2018), 99-108.

[9] S. Rizzo, F. Botta, S. Raimondi, D. Origgi, C. Fanciullo, A.G. Morganti, M. Bellomi, Radiomics: the facts and the challenges of image analysis, European radiology experimental. 2 (2018). doi: 10.1186/s41747-018-0068-z

[10] W. Qiu, H. Kuang, J. Nair, Z. Assis, M. Najm, C. McDougall, B. McDougall, K. Chung, A.T. Wilson, M. Goyal, M.D. Hill, A.M. Demchuk, and B.K. Menon, Radiomics-based intracranial thrombus features on CT and CTA predict recanalization with intravenous alteplase in patients with acute ischemic stroke, American Journal of Neuroradiology. 40(1) (2019), 39-44.

[11] B.B. Avants, N. Tustison, G. Song, Advanced normalization tools (ANTS). Release 1.5, 2011.

[12] D. Dolotova, V.Donitova, I.Arhipov, F. Sharifullin, T. Zagriazkina, B. Kobrinskii, A. Gavrilov, "A Platform for Collection and Analysis of Image Data on Stroke, Studies in Health Technology and Informatics. 262 (2019), 308-311.

[13] https://pyradiomics.readthedocs.io. Last access: January 10, 2020.

[14] J.J.M.van Griethuysen, A. Fedorov, C. Parmar, A. Hosny, N. Aucoin, V. Narayan, R.G.H. Beets-Tan, J.C. Fillon-Robin, S. Pieper, H.J.W.L. Aerts, Computational Radiomics System to Decode the Radiographic Phenotype, Cancer Research 77(21) (2017), e104–e107.