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T2*-Weighted Imaging Enables Excellent Interobserver Concordance but Should Not Be Considered as Sole Gold Standard Imaging for Hemorrhagic Transformation Classification after Thrombolysis

Jochen B. Fiebach^a, Georg Bohner^b

^aCenter for Stroke Research Berlin, Department of Neurology, and ^bDepartment of Neuroradiology, Charité Centrum 6, Charité Universitätsmedizin Berlin, Berlin, Germany

Renou et al. [1] reported inter- and intrarater reading reproducibility for the diagnosis of postthrombolysis hemorrhagic transformation. The definition they used has been described by Fiorelli et al. [2] in conjunction with the European Cooperative Acute Stroke Study 1 and has been used in the European Cooperative Acute Stroke Study 2 and the Safe Implementation of Thrombolysis in Stroke-Monitoring Study [3, 4]: 'HI was defined as a petechial infarction without space-occupying effect, and PH was defined as a hemorrhage (coagulum) with mass effect' [2]. However, an MRI-specific adaptation of this definition of HI (hemorrhagic infarction) and PH (parenchymal hematoma) appearance on different MRI imaging types is lacking.

Based on imaging examination from a group of 43 thrombolized patients, Renou et al. [1] tested the consistency of CT and MRI reports provided by 6 different readers. The κ values in non-contrast CT were lower than that reported by Fiorelli et al. [2], showing that excellent trained and motivated readers do not necessarily come to the same classification. More than a decade of CT hardware and software development did not lead to improvement in HI assessment.

Based on the observation that reproducibility was excellent with T2*GRE, the authors suggested considering this MRI sequence as an alternative. However, this seems hard to advocate, as Renou et al. [1] did not follow the definition they initially quoted. On MRI 'some haematomas, particularly PH1, don't seem to induce mass effect, especially when the HT is situated far from the ventricles'. This description reflects that confluent hypointensities on T2*GRE do not necessarily represent hematomas (fig. 1). The blooming effect of signal loss on T2*-weighted images could contribute to a shift from HI1 to HI2 and to a misclassification of HI2 in the PH group. A shift from HI1 to HI2 was acknowledged by the authors and upward grading was described in a study on 12 HT patients by Arnould et al. [5].

Considering T2*GRE as a new gold standard cannot be recommended based on the current results presented by Renou et al. The lack of intermodality comparison does not allow an evaluation of the accuracy of both modalities. If comparison had been done, the limited number of patients with PH would have obviated a clinically relevant confidence level. Screening MRI in clinical trials

Fig. 1. T2*-weighted image shows hypointense mass in thalamus and lentiform nucleus. CT examination performed 3 h after MRI shows HI2, which is in line with findings on FLAIR and DWI.

saves placebo patients X-ray administration without any clear benefit and provides dedicated patient selection. MR imaging at 24–36 h as surrogate parameter for safety after investigational medical product administration or new endovascular treatment should be used with caution. Mass effects caused by extended infarction combined with some HI2 could be misinterpreted as PH and would lead to falsely increased rates of ‘symptomatic bleeding’ in new therapies.

With the increasing availability of 3T systems with a high sensitivity to hemosiderin deposits on T2*-weighted imaging, the risk of false-positive PH diagnosis increases even more. Therefore, combining FLAIR, DWI and T2*GRE for the detection and characterization of HI seems appropriate and should be considered to value all aspects of imaging pattern: shape of abnormal areas, signal intensity on different types of image and the time course of signal alteration in relation to initial symptom onset.

References

- Renou P, Sibon I, Tourdias T, Rouanet F, Rosso C, Galanaud D, Drier A, Coudert M, Deltour S, Crozier S, Dormont D, Samson Y: Reliability of the ECASS radiological classification of post-thrombolysis brain haemorrhage: a comparison of CT and three MRI sequences. *Cerebrovasc Dis* 2010;29:597–604.
- Fiorelli M, Bastianello S, von Kummer R, del Zoppo GJ, Larrue V, Lesaffre E, Ringleb AP, Lorenzano S, Manelfe C, Bozzao L; ECASS I Study Group: hemorrhagic transformation within 36 hours of a cerebral infarct: relationships with early clinical deterioration and 3-month outcome in the European Cooperative Acute Stroke Study I (ECASS I) cohort. *Stroke* 1999;30:2280–2284.
- Berger C, Fiorelli M, Steiner T, Schäditz WR, Bozzao L, Bluhmki E, Hacke W, von Kummer R: Hemorrhagic transformation of ischemic brain tissue: asymptomatic or symptomatic? *Stroke* 2001;32:1330–1335.
- Wahlgren N, Ahmed N, Dávalos A, Ford GA, Grond M, Hacke W, Hennerici MG, Kaste M, Kuelkens S, Larrue V, Lees KR, Roine RO, Soinne L, Toni D, Vanhooren G; SITS-MOST Investigators: Thrombolysis with alteplase for acute ischaemic stroke in the Safe Implementation of Thrombolysis in Stroke-Monitoring Study (SITS-MOST): an observational study. *Lancet* 2007;369:275–282.
- Arnould MC, Grandin CB, Peeters A, Cosnard G, Duprez TP: Comparison of CT and three MR sequences for detecting and categorizing early (48 h) hemorrhagic transformation in hyperacute ischemic stroke. *AJNR Am J Neuroradiol* 2004;25:939–944.

Jochen B. Fiebach
Center for Stroke Research Berlin, Department of Neurology
Charité Universitätsmedizin Berlin
Hindenburgdamm 30, Room 1252, DE-12200 Berlin (Germany)
Tel. +49 30 8445 4088, Fax +49 30 8445 2066
E-Mail jochen.fiebach@charite.de