

Semi-automatic detection of cerebral microbleeds on clinical 3.0T T2*-weighted images using the radial symmetry transform

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Introduction: To date, the standard for detection of cerebral microbleeds (CMBs) is visual rating with validated visual rating scales on T2*-weighted scans [1,2]. This process is time-consuming and has limited reproducibility. Since interest in CMBs is increasing rapidly, because they are associated with vascular disease and dementia [1,3-5], there is a rising need for semi-automated detection of CMBs. Semi-automated detection is likely to improve rating quality and decrease rating time.

Recently, several methods have been published addressing semi-automated detection of CMBs. The methods of Barnes *et al.* [6] and Seghier *et al.* [7] were evaluated on clinical 1.5T T2*-weighted GRE scans. Both methods have a relatively low specificity, requiring 5-15 minutes human rater time to censor false positives. In a previous study [8], we have shown that using the radial symmetry transform (RST) results in much fewer false positives, which require only two minutes of human rater time to censor them. This research was carried out on non-clinical dual-echo 7.0T gradient echo data.

In the present paper, we present a proof-of-principle experiment of the use of the RST for semi-automated microbleed detection on clinically available (single echo) 3.0T T2*-weighted data.

Methods and materials: For this study, five patients referred to the memory clinic of the University Medical Center Utrecht with CMBs on an MRI scan were included. Written informed consent was given by all patients. The patients underwent a 3.0T MR exam, including a 3D T2*-weighted sequence (TR/TE = 1635/20 ms), with an acquired voxel size of 0.99x0.99x3.0 mm³, and a 3D T1-weighted turbo field echo MR sequence (TR/TE = 8/4 ms).

Two experienced raters independently scored all scans visually according to the Microbleed Anatomical Rating Scale (MARS) [2]. The cases on which both raters disagreed were evaluated in a consensus meeting with a third rater to obtain a final scoring. In total, 22 microbleeds were found in the five patients.

First, a binary mask of gray and white matter was obtained from the T1-weighted scan, using unified segmentation as implemented in SPM8 [9]. The probabilistic mask was thresholded at a level of 93% to create the binary mask and rigidly registered to the T2*-weighted scan. Within this mask, the intensity values of the T2*-weighted sequence were normalized to a range of [0,255], using the 5th and 95th percentiles of the histogram as lower and upper bound, respectively.

For the automatic detection of microbleeds, two stages involving the RST were applied. The RST is a technique that utilizes image gradients and orientations to find the center of mass of spherical objects in a scan [10]. During the first stage, a 3D RST was applied on the T2*-weighted scan with parameters that were heuristically determined to be optimal for this type of scan. Processing was performed within the binary gray and white matter mask, since that is where microbleeds occur. Thresholding on the radial symmetry value resulted in a list of potential CMB locations. The full details of the implementation are described in our previous study [8]. During the second stage, a small region of interest around each potential CMB was selected automatically. A slab of 12mm thickness was created using minimum intensity projection (minIP) and a 2D RST was computed. If the radial symmetry value in the second stage at the location of the potential CMB did not exceed a heuristically determined threshold, it was discarded as a potential CMB. This procedure is derived from the manual rating process, in which a rater checks for 2D hypointense spherical objects on a minIP representation of the scan. On minIP, microbleeds show up as dark round spots, while typical false positives (such as small vessels) are displayed as elongated structures.

In the experiments that were performed, one rater was presented with the results of the method. The number of false positives present in the results was assessed together with the time to visually censor the false positives. When CMBs were detected by the RST that were not present in the original visual rating, they were added to the ground truth if the rater confirmed them as true microbleeds.

Results: In total, 107 potential microbleeds were detected in the five patients, on average 21.4±8.0 (mean±sd) potential CMBs per patient. Among these potential CMBs, 16 true positives (present in the original visual rating) were found, 91 false positives, and 2 extra positives that were not present in the original visual rating, but were marked as potential CMB and confirmed as true CMB by the rater. The rater required 11.5 minutes to censor all detected microbleeds (2.5±1.5 minute per patient). Six microbleeds were not detected by the method (false negatives). Computation of the algorithm took about 1 minute per patient, using a standard single-core workstation.

In total, 24 microbleeds were detected: 22 in the original visual rating and 2 extra positives found by the method. The method had a sensitivity of 75.0%, whereas the original visual rating had a sensitivity of 91.7%.

Discussion: Detecting potential cerebral microbleeds using the radial symmetry transform on 3.0T MR scans, with a low number of false positives, seems feasible. The method outperforms previously published methods in terms of specificity, since significantly less human rater time is required to censor false positives afterwards. In terms of sensitivity, the method of Barnes performs better with a sensitivity of 81.7%. Sensitivity on the number of microbleeds was not provided by Seghier.

The algorithm used in this study was a slightly adapted version of that used in [8]. The original method consisted only of one stage, performing a 3D RST. However, owing to the anisotropic voxel size of a 3.0T scan, the 3D radial symmetry of a microbleed was not as prominent as on a 7.0T scan with isotropic voxels. This caused too much false positives after the first stage (in total 425 for the five patients), demanding additional processing to remove them. By locally computing a minIP at potential CMB locations and computing a 2D RST, it was possible to significantly improve the specificity without losing too much sensitivity (one TP was lost).

References: [1] S.M. Greenberg *et al.* *Lancet Neurol.* 2009;8:165-174 [2] S.M. Gregoire *et al.* *Neurology* 2009;73:1759-1766 [3] J.M. Wardlaw *et al.* *Stroke* 2006;37:2633-2636 [4] M.W. Vernooij *et al.* *Neurology* 2008;70:1208-1214 [5] C. Cordonnier *et al.* *Brain* 2007;130:1988-2003 [6] S.R. Barnes *et al.* *Magn. Reson. Imaging* 2011;29:844-852 [7] M.L. Seghier *et al.* *PLoS One* 2011;6:e17547 [8] H.J. Kuijff *et al.* *NeuroImage* 2011;in press [9] J. Ashburner *et al.* *NeuroImage* 2005;25:839-851 [10] G. Loy *et al.* *IEEE Trans. Pattern Anal. Mach. Intell.* 2003;25:959-973

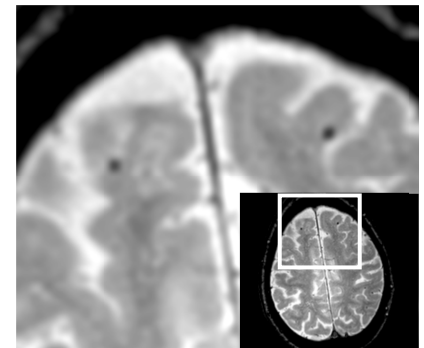


Figure 1: Two microbleeds as seen on a transverse slice of a 3.0T T2*-weighted scan.

Table 1: Microbleeds detected during visual rating (upper), by the RST (middle), and the overview (bottom).

Participant:	1	2	3	4	5	
Visual ^a	Number of microbleeds detected					Total
Total (VT)	10	2	3	3	4	22
Automatic ^b	Number of locations found					Total
Total	27	21	28	8	23	107
TP	8	0	3	2	3	16
EP	1	0	1	0	0	2
FP	18	21	24	6	20	89
Overview ^c	Number of microbleeds					Total
VT+EP	11	2	4	3	4	24
FN	2	2	0	1	1	6

^a Number of microbleeds detected during visual rating.

^b Total of detected locations: true positives (TP), extra positives (EP) and false positives (FP). EPs were detected by the RST, but not during visual rating.

^c Overview combining visual total (VT) and EP, together with the false negatives (FN).