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Automated detection of cerebral microbleeds in patients with traumatic brain injury

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ABSTRACT

In this paper a Computer Aided Detection (CAD) system is presented to automatically detect Cerebral Microbleeds (CMBs) in patients with Traumatic Brain Injury (TBI). It is believed that the presence of CMBs has clinical prognostic value in TBI patients. To study the contribution of CMBs in patient outcome, accurate detection of CMBs is required. Manual detection of CMBs in TBI patients is a time consuming task that is prone to errors, because CMBs are easily overlooked and are difficult to distinguish from blood vessels.

This study included 33 TBI patients. Because of the laborious nature of manually annotating CMBs, only one trained expert manually annotated the CMBs in all 33 patients. A subset of ten TBI patients was annotated by six experts. Our CAD system makes use of both Susceptibility Weighted Imaging (SWI) and T1 weighted magnetic resonance images to detect CMBs. After pre-processing these images, a two-step approach was used for automated detection of CMBs. In the first step, each voxel was characterized by twelve features based on the dark and spherical nature of CMBs and a random forest classifier was used to identify CMB candidate locations. In the second step, segmentations were made from each identified candidate location. Subsequently an object-based classifier was used to remove false positive detections of the voxel classifier, by considering seven object-based features that discriminate between spherical objects (CMBs) and elongated objects (blood vessels). A guided user interface was designed for fast evaluation of the CAD system result. During this process, an expert checked each CMB detected by the CAD system.

A Fleiss' kappa value of only 0.24 showed that the inter-observer variability for the TBI patients in this study was very large. An expert using the guided user interface reached an average sensitivity of 93%, which was significantly higher ($p = 0.03$) than the average sensitivity of 77% (sd 12.4%) that the six experts manually detected. Furthermore, with the use of this CAD system the reading time was substantially reduced from one hour to 13 minutes per patient, because the CAD system only detects on average 25.9 false positives per TBI patient, resulting in 0.29 false positives per definite CMB finding.

1. Introduction

To determine the severity of Traumatic Brain Injury (TBI) and patient prognosis, the Glasgow Coma Scale (GCS) together with the assessment of large hemorrhages and fractures seen on Computed Tomography (CT) are widely used. The GCS is a neurological scale to determine the level of consciousness of a patient. Using three measures; motor response, verbal performance, and eye opening, a scale between 3 and 15 is determined, where 3 indicates deep unconsciousness of a patient (Teasdale and Jennett, 1974). The prognostic precision of these two assessments is low, most likely because less acute damage such as diffuse axonal injury is not evaluated. Therefore research is focusing on Magnetic Resonance (MR) imaging to identify prognostic markers which are less or not visible on CT scans, such as Cerebral Microbleeds (CMBs). CMBs are thought to be related to Diffuse Axonal Injury (DAI) and to clinical prognosis (Werring, 2011). Studies evaluating the clinical

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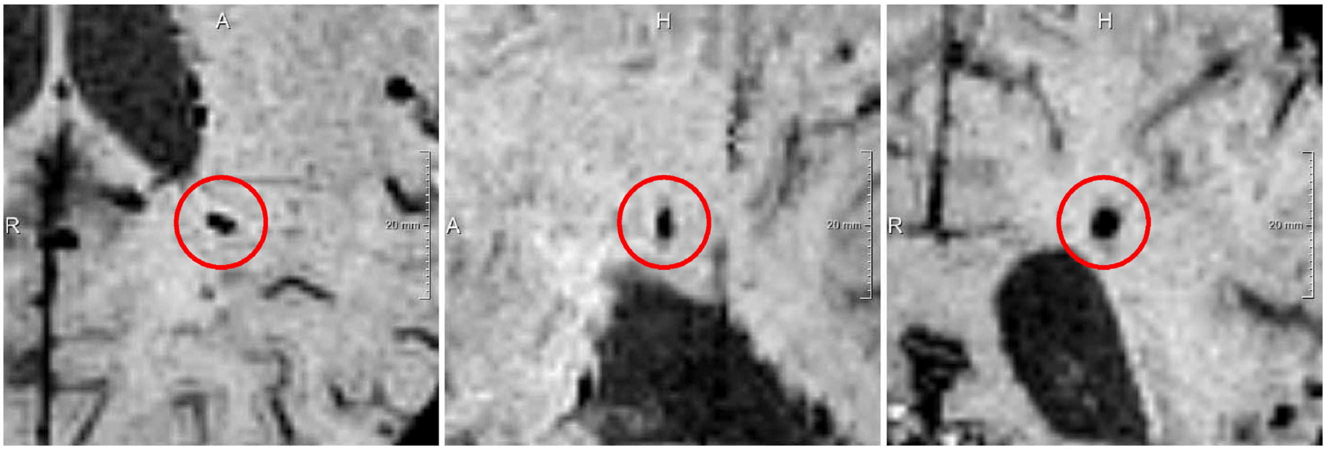

Fig. 1. Example of a CMB on an SWI scan. From left to right: axial, sagittal and coronal view.

and prognostic value of the individual location and size of CMBs in TBI do not exist, mainly due to the amount of time required to exhaustively annotate every CMB in a TBI scan.

CMBs are hemosiderin deposits in the brain caused by leakage of small blood vessels. CMBs can be detected on both T2* GRE and Susceptibility Weighted Imaging (SWI) scans, where it has been shown that the sensitivity of SWI outperforms the sensitivity of T_2* GRE imaging in finding CMBs (Geurts et al., 2012; Nandigam et al., 2009; Tong et al., 2003; Cheng et al., 2013; Liu et al., 2014). On an SWI scan CMBs appear as spherical hypointense lesions and are considered to have a diameter smaller than ten millimeters (Greenberg et al., 2009). Fig. 1 shows an example of a single CMB on an SWI scan, Fig. 2 shows a TBI patient with many CMBs.

The observer variability for the detection of CMBs is large (Geurts et al., 2012; Kuijf et al., 2012). Additionally, manual detection of CMBs is a time consuming task, which can take more than one hour per TBI patient. A Computer Aided Detection (CAD) system can alleviate these drawbacks. Several CAD systems have been developed for the detection of CMBs in other patient populations (stroke patients Seghier et al., 2011; Dou et al., 2016), Alzheimer patients Barnes et al., 2011; Fazlollahi et al., 2014, patients with arterial disease Kuijf et al., 2012, patients with radiation damage Bian et al., 2013, and the elderly Ghafaryasl et al., 2012), but to the authors knowledge this is the first CAD system designed for TBI patients. These existing CAD systems report several false positive (FP) detections per CMB. Since the number of CMBs in our TBI patient population is a factor larger than what is commonly seen in the population for which these systems were designed, these CAD systems would result in large amounts of false positive detections. This would reduce the possible time gain that could be achieved with the use of a CAD system compared to manual annotation, as it would require extensive manual false positive reduction.

In this paper we present a CAD system that automatically detects CMBs in TBI patients.

2. Material and methods

A schematic overview of our work is given in Fig. 3. In short, a preprocessing step was performed to identify the brain, the different modalities were registered, the bias field was corrected and the images were normalized. Next, a voxel classifier identified CMB candidates. Subsequently false positive detections were removed by a second, object-based, classifier taking the shape of the detected CMBs.

candidates into account. Next, four experiments were performed. First, the observer variability was measured. Second the CAD system was optimized. Third, the optimized CAD system was manually evaluated by a neuroradiologist. Last, the performance of the CAD system was compared to the annotations of six independent experts.

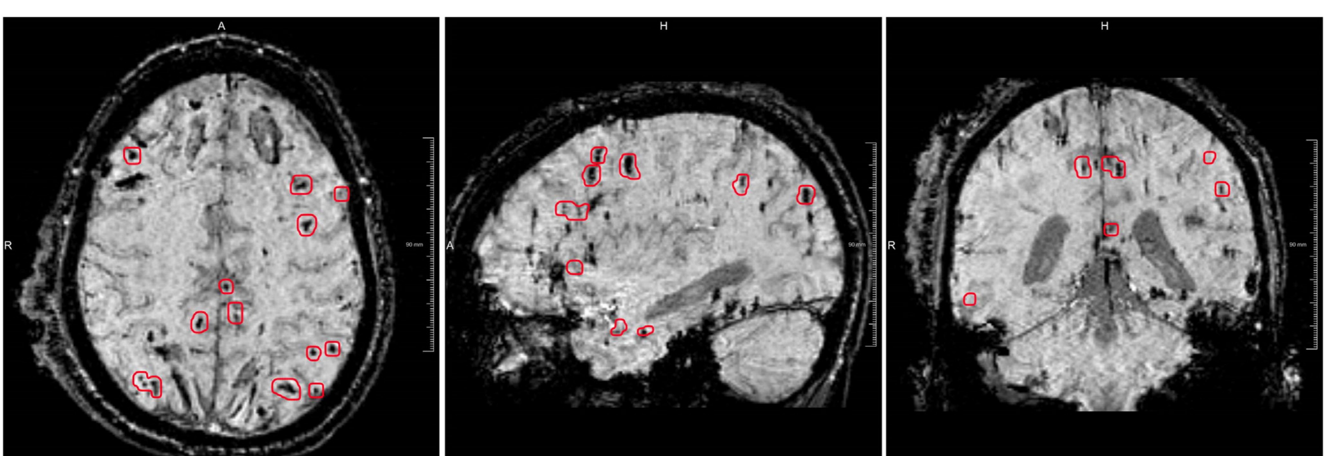

Fig. 2. Example of a TBI patient with many CMBs encircled in red and two large hemorrhages located bifrontal. From left to right: axial, sagittal and coronal view. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)