

Highlighting the need for worldwide collaboration on cerebral microbleeds: the Microbleeds International Collaborative Network

*Microbleeds International Collaborative Network**

We were interested and encouraged to read the recent letter calling for international collaborations on the topic of cerebral microbleeds (CMBs) ([http://www.thelancet.com/journals/laneur/article/PIIS1474-4422\(16\)30124-7/fulltext](http://www.thelancet.com/journals/laneur/article/PIIS1474-4422(16)30124-7/fulltext)). Key questions remain about the clinical relevance of CMBs, particularly regarding their potential role as a marker of bleeding-prone arteriopathies and intracerebral haemorrhage risk in patients treated with antithrombotic agents following ischaemic stroke or TIA.^{1,2} We agree that single-centre studies are unlikely to fully answer all of the important scientific questions about CMBs; international collaboration is essential to increase the scale of data available, maximizing scientific and statistical power. Collaborative research networks relating to CMBs have developed over recent years.³ We wish to raise awareness of the recently established Microbleeds International Collaborative Network, which arose from two large multicentre inception cohort studies addressing the key question of whether CMBs are associated with increased bleeding risk on oral anticoagulants in patients following ischaemic stroke or TIA: Clinical Relevance of Microbleeds in Stroke (CROMIS-2; <https://www.ucl.ac.uk/cromis-2>, and <https://clinicaltrials.gov/ct2/show/NCT02513316>) and Intracerebral Hemorrhage Due to Oral Anticoagulants: Prediction of the Risk by Magnetic Resonance (HERO; <http://heropub.pic.es>; <https://clinicaltrials.gov/ct2/show/NCT02238470>). Together, CROMIS-2 and HERO have successfully recruited over 2500 patients from over 110 hospitals in the UK and Spain, and will report their first results in 2017. The teams leading these observational studies, together with investigators leading other relevant study groups and cohort studies worldwide, have established a Microbleeds International Collaborative Network. We aim to undertake high quality large-scale robust pooled analyses relating to CMBs that are free from biases, including selective inclusion and outcome reporting. With these aims in mind, our first project is a systematic review and individual patient data meta-analysis of the clinical relevance of CMBs in patients with TIA and ischaemic stroke (the prospectively registered protocol is published at: http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42016036602). This project is conducted according to the PRISMA-IPD standards for reporting systematic reviews and individual patient data meta-analyses. We held a successful investigator workshop at the European Stroke Organisation Conference in Barcelona, May 2016, with input from 16 groups from 14 countries worldwide, who worked to finalize the protocol and set timelines. Following this workshop, our team has access to data from over 10000 individuals (Table); we warmly welcome other investigators to contribute to expanding this research effort.

Important work is also needed to standardize acquisition sequences, lesion definition and measurement, and post-processing of neuroimaging markers of small vessel disease. Members of the Microbleeds International Collaborative Network thus work closely with large-scale international harmonization initiatives including STRIVE⁴ and COEN.⁵

Large-scale collaborative systematic reviews and pooled analyses will provide the strongest evidence to incorporate CMB imaging into clinical practice, including precise estimates of the ischaemic stroke and intracerebral haemorrhage risks associated with antithrombotic (antiplatelet and anticoagulant) drug exposure in patients with CMBs. The Microbleeds International Collaborative Network endorses the need for global collaboration on CMBs and small vessel disease research more widely; full, open communication and collaboration are essential to avoid unplanned duplication of effort. We look forward to working with other researchers worldwide to tackle the many outstanding research questions relating to CMBs.

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