The spectrum of cortical microinfarcts; a post-mortem classification study with 7Tesla MRI

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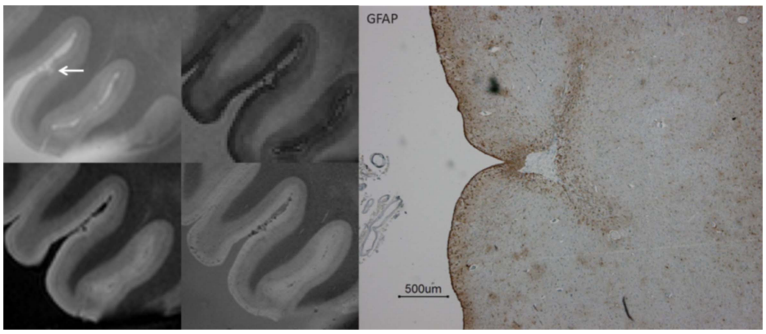
TARGET AUDIENCE – Clinicians, neuroradiologists, neurpathologists, neuroscientists.

PURPOSE – Cerebral microinfarcts are common neuropathological findings in the aging human brain.[1,2] They have been related to small vessel disease and show a strong correlation with cognitive decline. Due to their small size they go undetected on conventional MRI. Recently, it has been shown that cortical microinfarcts can be visualised in vivo with high-field 7Tesla MRI.[3] This finding was verified with post-mortem MRI, also at 7Tesla. That study focused on one type of intracortical microinfarcts on MRI. Most likely, there are different types of microinfarcts, possibly with different causes. The current study was designed to determine which types of cortical microinfarcts can be captured with 7Tesla post-mortem brain MRI.

METHODS – Brain specimens of fifteen patients with Alzheimer and/or vascular pathology were selected from the UMC Utrecht neuropathology department. Three 10 mm-thick coronal brain slices were selected per patient and subjected to post-mortem MRI. Scans were acquired overnight on a whole-body 7Tesla MR system (Philips Healthcare) with a volume transmit and 32-channel receive head coil (Nova Medical). The standard protocol, optimized for post-mortem scanning, included a 3D FLAIR, a 3D TSE, a 3D T1 (all with 400 µm isotropic acquired resolution), and a 3D T2* weighted sequence (180 µm isotropic acquired resolution). After scanning, all intra- and juxtacortical focal abnormalities ≤5mm, possibly due to ischemia or microhemorrhage, were dissected and subjected to histological and immunohistochemical analysis. Regions with no apparent MRI abnormalities were sampled as control areas. These samples were taken from white matter regions, cortical regions, basal ganglia, and hippocampus.

RESULTS – The patients had a mean age at death of 76.4 (SD 7.5) years. On the obtained post-mortem MR images 35 focal abnormalities (median 1.5, range 0 – 10 per patient) were detected and subjected to histopathological examination. Twenty-one abnormalities were located intracortically and 14 juxtacortically. Intracortically, histopathology identified 12 focal MR abnormalities as microinfarct. Six could not be retrieved, 2 were due to post-mortem tissue damage, 1 proved to be tissue alteration. Juxtacortically, histopathology identified 2 MR abnormalities as microhemorrhages. Three could not be retrieved, and 9 proved to be abnormal perivascular spaces. Thirteen additional intracortical microinfarcts were found upon histopathological examination, of which only one in the control samples. Overall, the following 6 different microvascular lesion types could be identified. Intracortically: gliotic microinfarct (*Figure 1*), cavitated microinfarct, recent microinfarct, microinfarct with hemorrhagic components. Juxtacortically: microhemorrhage, abnormal perivascular space.

Table 1. MR characteristics of 4 subtypes of intracortical microinfarcts.



Type	FLAIR	T2	T1	T2*
Gliotic	Hyper	Hyper	Hypo / hyper	Hypo / hyper
Cavitated	Hypo with hyper rim	Hyper	Hyper	Hypo
Recent	Hypo	Hypo	Hyper	Hypo
Hemorrhagic	Hypo	Hypo	Hypo	Hypo

Figure 1. Intracortical gliotic microinfarct. This subtype always appeared hyperintense on T2 and FLAIR, and either hypo- or hyperintense on T1 and T2*. Standard histological examination identified this type as a delineated region of tissue pallor, accompanied by neuronal death and gliosis. This lesion is GFAP positive, indicating the presence of astrogliosis.

DISCUSSION – With high resolution post-mortem MRI 6 different microvascular lesion types could be identified, with different MR characteristics. Microinfarcts could be divided into 4 subtypes (*Table 1*). Future studies should look into the causes of microinfarcts, which might differ between subtypes. Location within the cortex, which can easily be assessed on high resolution post-mortem MRI, should also be taken into account. Noteworthy, no juxtacortical microinfarcts, neither on MRI nor on histopathological examination, could be identified in this study.

CONCLUSION – Post-mortem MRI at 7Tesla is a useful tool to distinguish type and location of cortical microvascular pathology. Using this approach we can now study the underlying mechanisms of intracortical microinfarcts to better understand their role in aging and dementia.

REFERENCES – [1]Smith EE et al. Cerebral microinfarcts: the invisible lesions. *Lancet Neurol* 2012. [2]Brundel M et al. Cerebral microinfarcts: a systematic review of neurpathological studies. *JCBFM* 2012. [3]Van Veluw SJ et al. In vivo detection of cerebral cortical microinfarcts with high-resolution 7T MRI. *JCBFM* 2013.