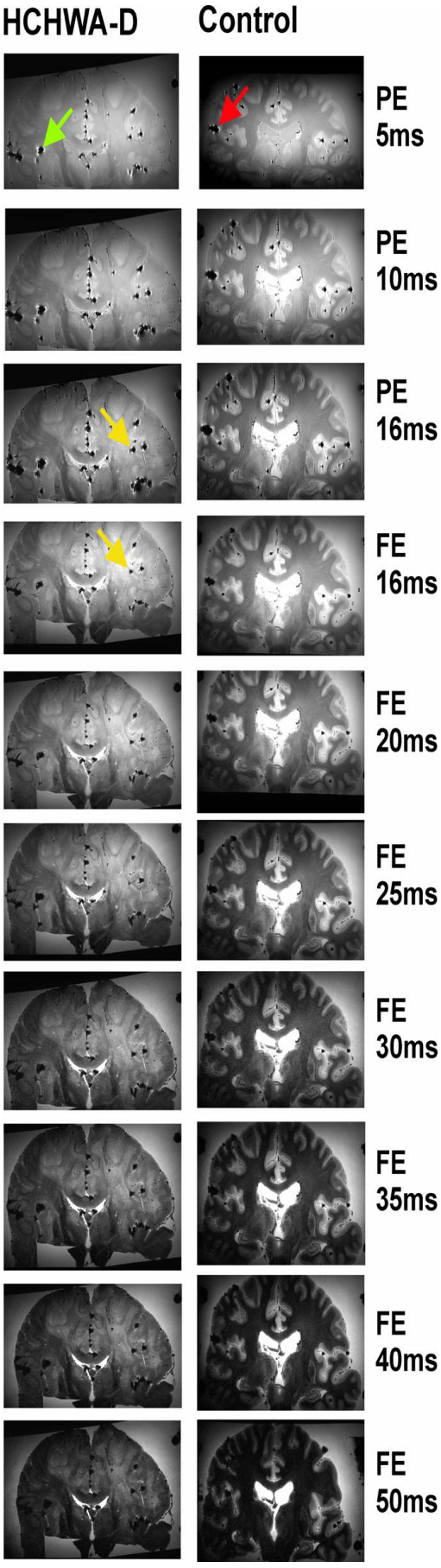
High Field Amyloid Imaging.

S. van Rooden[1], M. van Osch[2], W. Teeuwisse[2], R. Nabuurs[2], L. van der Weerd[2], M. van Buchem[2], and J. van der Grond[2]
[1]Radiology LUMC, Leiden, Netherlands, [2]Radiology LUMC, Netherlands



Introduction

Alzheimer's Disease (AD) is characterized neuropathologically by extracellular amyloid plaques and intracellular neurofibrillary tangles. These changes are associated with progressive neuronal loss and resultant cerebral atrophy. Tau deposition is thought to begin in the entorhinal cortex and progress to involve the hippocampus before affecting the cortex more widely, whereas amyloid plaque formation additionally targets inferior frontal areas. Although in the last decades many neuroradiological characteristics of AD have been revealed on MRI, the unique hallmark of AD (amyloid plaques) remained MRI invisible. Nonetheless, these amyloid decompositions, which contain misfolded peptides called amyloid beta (Aβ), are of interest since they are formed in the brain many years before the clinical signs of Alzheimer's are observed. Unfortunately, by now, no medical tests are available to diagnose Alzheimer's disease conclusively pre-mortem. Still, there is ample evidence in mice that amyloid plaques can be identified in vivo at relatively high field strengths (≥7T), however, no in vivo human data are currently present. The introduction of whole body high field MRI systems has potentially opened the opportunity to visualize amyloid plaques on susceptibility weighted imaging (SWI) based on MR contrasts primarily caused by amyloid plaques itself without the use of external markers. However, the optimization of SWI protocols is difficult because of the uncertainty of the presence of amyloid plaques in suspected AD. The specific aim of the study was to find optimal acquisition parameters to visualize the amyloid burden in the cortex and small microbleeds throughout the brain.

Materials and Methods

To investigate the 'behaviour' of amyloid plaques on SWI at 7T we investigated brain specimen of deceased patients who had hereditary cerebral haemorrhage with amyloidosis–Dutch type (HCHWA-D) and compared them with brain specimen of deceased patients without any neurological deficit. HCHWA-D is an autosomal dominant form of severe cerebral amyloid-angiopathy, characterized by recurrent hemorrhagic strokes and dementia form of hereditary cerebral hemorrhage with amyloidosis. It has been shown previously that the vascular amyloid deposits were related to the beta-protein associated with Alzheimer disease [van Duinen]. The advantage of the HCHWA-D model is that all mutation carriers have a severe vascular amyloid burden. All samples were investigated on a whole body 7T scanner (7T Achieva, Philips Medical Systems) using the NOVA Medical 16 channel head coil. Gradient echo-3D acquisition parameters: TR 60ms, flip angle 10°, NSA 2, FOV 180x99x11mm (FHxRLxAP), matrix 600x333x37 resulting in a nominal isotropic 300μ voxel which was reconstructed on 180μ resolution (reconstruction matrix 960). We varied echo times from 5ms, 10ms and 16ms; all partial echo (PE), up to 16ms, 20ms, 25ms, 30ms, 35ms, 40ms and 50ms; all full echo (FE).

Results

An example of ex vivo data set of a deceased HCHWA-D patient (left column) and a patient without any neurological deficit (right column) is shown in the left figure (window settings fixed). Susceptibility artefacts caused by air bubbles caught deep inside sulci could easily be recognized in both examples. Changes in TE did not have a large effect on the size of the field distortion caused by air bubbles (red arrow), whereas field distortions caused by intra cerebral haemorrhage demonstrated increased field distortion with increasing echo time (green arrow). Increasing echo time did not allow the detection of new lesions, but did result in a clear reduction in signal to noise (see figure). Very short echo times (5ms or 10ms) did result in an underestimation of the number of field distortions, i.e. small accumulations of iron in microbleeds or in amyloid plaques were not recognized. An echo time of 16ms combined both good susceptibility weighted contrast as well as a relatively good signal to noise. Partial echoes resulted in larger visual field distortions than full echoes (yellow arrow). However, the advantage of full echoes is the possibility of using phase information to create enhanced contrast between tissues with different susceptibilities [Haacke].

Conclusion

Gradient echo brain imaging at high field strengths offers excellent possibilities to visualize small distortions of the magnetic field, offering the potential to detect amyloid plaques. A multi-echo approach may be useful to differentiate between distortions caused by air bubbles and iron accumulation.

References

van Duinen, S.G. et al. Hereditary cerebral hemorrhage with amyloidosis in patients of Dutch origin is related to Alzheimer disease. Proc. Nat. Acad. Sci. 1987, 84: 5991-5994.

Haacke EM et al. Susceptibility weighted imaging (SWI). Magn Reson Med. 2004 Sep;52(3):612-618