English Summary
The aim of the thesis is to present a neuroimaging perspective of pathological ageing especially focusing on vascular aspects.

In chapter 2, various disorders causing dementia are discussed, as well as the usefulness of several neuroimaging modalities for their diagnosis. It is stressed that a large proportion of patients may have a combination of degenerative and vascular pathology in the brain. New functional magnetic resonance (MR) and molecular imaging techniques are also discussed, as well as future perspectives concerning their potential benefit.

Chapter 3 focuses on medial temporal lobe atrophy (MTA), a structural neuroimaging feature suggestive of Alzheimer’s pathology. A new linear measurement to assess MTA on magnified coronal high-resolution T1-weighted images is proposed, the fimbriosubicular distance. By using this measurement, it is possible to evaluate the hippocampal sulcus width, whose enlargement is associated with MTA in Alzheimer’s disease.

In chapter 4, three studies on vascular dementia are presented. These studies were derived from baseline data of patients fulfilling the clinical and neuroimaging parts of the National Institute of Neurological Disorders and Stroke (NINDS) – Association Internationale pour la Recherche et l’Enseignement en Neurosciences (AIREN) criteria for probable vascular dementia, with central assessment of the neuroimaging criteria at the Image Analysis Centre (VU University Medical Centre, Amsterdam, the Netherlands) according to published operational definitions.

Chapter 4.1 corresponds to a study comparing the sensitivity of T2-weighted images (T2-WI) with fluid-attenuated inversion recovery (FLAIR) images to depict thalamic lesions. The study showed that the sensitivity of T2-WI to depict thalamic
lesions is far superior to FLAIR images and, for this reason, FLAIR should not be used as the only MR sequence to detect thalamic lesions in patients suspected of having vascular dementia.

**Chapter 4.2** corresponds to a study about the prevalence and clinical relevance of infratentorial abnormalities in vascular dementia. Focal infratentorial vascular lesions were found to be especially frequent among patients with small vessel disease and were associated with basal ganglia and thalamic lesions. Midbrain and cerebellar atrophy were also present in a minority of patients. Only midbrain atrophy was found to be associated with cognitive impairment, and the association persisted after correction for abnormalities representing degenerative and vascular supratentorial pathology. These findings suggest that the midbrain may contribute to cognition independently of the supratentorial structures, and that assessment of midbrain atrophy should perhaps be a factor to take into account in future studies on brain aging and dementia. It is conceivable that midbrain atrophy may represent concomitant Alzheimer’s pathology, and that its occurrence in the periaqueductal gray matter may explain the association between midbrain atrophy and cognitive impairment by disruption of mesencephalic connections.

A study designed to investigate the relative contribution of cerebrovascular disease and MTA to cognitive impairment in a large sample of patients with vascular dementia is presented in **chapter 4.3**. The study showed that both MTA and the occurrence of large vessel vascular dementia were independently associated with general cognitive and executive dysfunction, while small vessel disease seemed to be related to worse executive functioning, especially in patients without considerable MTA. Again, the results of this study point to the possibility that both the occurrence of MTA in patients fulfilling diagnostic criteria for vascular dementia and its association with cognitive impairment are attributable to concomitance of Alzheimer’s pathology.
Finally, chapter 5 corresponds to a study of a sub-sample of the Leukoaraiosis and Disability (LADIS) study. The LADIS study is a prospective, longitudinal, multicentre European study on the role of WMH as an independent predictor for transition to disability in nondemented elderly subjects. The study presented in the thesis explored the relation between the degree of WMH and cerebral blood flow (CBF) by means of pulsed arterial spin labelling (PASL), a new functional MR perfusion-weighted technique. In this study, absolute values of CBF were determined and an association was found between lower CBF measurements and higher grades of WMH, indicating that subjects with diffuse confluent white matter lesions have approximately 20% lower CBF than subjects with punctiform or beginning confluent lesions.

In conclusion, most of the work presented in this thesis reflects that brain atrophy and cerebrovascular disease currently are the two most important characteristics in the evaluation of dementia by means of neuroimaging. In the future, it is expected that neuroimaging techniques will detect neuropathology and its morphofunctional consequences even before the occurrence of substantial brain atrophy, which in conjunction with clinical evaluation, will enable to do earlier diagnoses, as well as to better monitor the potential benefit of treatment.