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# Determining Degenerative from Vascular Dementia Using Optical Coherence Tomography Biomarkers for Tomography and Angiography

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## Abstract

The majority of cases of cognitive impairment in elderly persons are caused by Alzheimer's disease and vascular dementia. These two basic types of dementia, which include several subcategories, frequently overlap, and in some cases, a conclusive diagnosis may only be made after death. This affects the standard of treatment for these individuals as well as how tailored therapies are created for them. The non-invasive imaging technique known as Optical Coherence Tomography Angiography (OCTA), which is used to see the retinal layers and veins, has shown promising findings in the research of several neurological disorders, including dementia. This study seeks to concisely summarise the current state of knowledge and offer important insight into new patterns of OCTA biomarker values in vascular dementia and Alzheimer's disease. The inner retinal layer thickness might be a biomarker that is preferentially affected in degenerative dementia, including Alzheimer's, whereas the outer-layer thickness as a whole justifies attention as a potential vascular dementia biomarker. According to the current literature, vessel density seems to be a common biomarker for both forms. Further research should be done on radial peripapillary capillary density as a biomarker especially connected to vascular dementia.

**Keywords:** Alzheimer's • Biomarkers• Neurodegeneration • Small vessel disease • Vascular cognitive impairment

## Introduction

Degenerative dementia is an umbrella term for the two primary diseases that account for the vast majority of dementia cases, which are steadily increasing and are mostly represented by Alzheimer's Disease (AD) and Vascular Dementia (VaD) [1]. Despite having separate underlying pathophysiological mechanisms, there is a non-negligible overlap that makes it difficult to differentiate between the two and, as a result, to take fast and effective action. Invasive, costly, and time-consuming methods that are less useful in a routine clinical environment may be necessary to identify abnormal proteins such as Amyloid beta (A) and tau (), as well as sensitive and specific magnetic resonance imaging (MRI) results, to support either diagnosis.

The non-invasive technology known as Optical Coherence Tomography Angiography (OCTA) enhances the high-resolution imaging capabilities of structural OCT by offering the opportunity to retrieve quantitative and repeatable information on the retinal microvasculature in addition to its anatomical characteristics. It quickly became clear that it has numerous and important uses in ophthalmology, connecting the data from OCT and fluorescein angiography. But the technology is also swiftly demonstrating its relevance in the study of several neurological and neuro-ophthalmic disorders, such as multiple sclerosis, optic neuritis, and dementia [2]. In this review, we assess the data on OCTA biomarker levels in patients with a diagnosis of either vascular or degenerative dementia, identify emerging patterns, and identify potential research topics of interest. The findings of this review may help other researchers in this field with their work and planning. Even though we do not intend to claim that we have done an exhaustive analysis of the literature already in existence, great care has been taken to ensure an accurate and objective presentation of the consensus on the topics under study so that this brief review is an accurate reflection of the state of the art in the field.

### OCTA in alzheimer's disease

One of the main causes of dementia globally, Alzheimer's Disease (AD) is a neurological condition. Because it interferes with cognitive functions, thinking ability, language, and attention, and eventually changes their behavior and personalities, it has significant effects on the quality of life for those who are afflicted. In extreme circumstances, it may be fatal. The development of extracellular A plaques and intracellular beta-proteins in the cortical and limbic brain regions is the pathophysiological process underlying AD. Only after death can AD be definitively confirmed by locating neurofibrillary tangles and A plaques in these regions of the brain. The consensus appears to be that patients with AD show an increase in the Foveal Avascular Zone (FAZ), as well as a decrease in the superficial parafoveal and the whole-Vessel Density (VD), even though OCTA is a relatively new imaging modality and its application in dementia is still being investigated [3]. In one of the initial investigations on the subject, Jiang et al. demonstrated that, in comparison to controls, AD patients had significantly lower VD in both the superficial (SCP) and Deep Capillary Plexus (DCP). Subsequent research has confirmed these findings [4]. The evaluation of the FAZ as a potential biomarker for AD has also yielded some encouraging results, with research pointing to an expansion of this region in those with the disease. The formation of plaques in the retina in a way similar to processes affecting the brain is the pathogenic mechanism that has been postulated to explain these observations. More specifically, it appears that retinal hypoxia is a result of Vascular Endothelial Growth Factor (VEGF) binding to A and its confinement in the plaques, as well as the deposition of A proteins in the internal vessel walls, which results in vascular occlusion, decreased blood flow, and, ultimately, retinal hypoxia. The majority of studies comparing the thickness of the Retinal Nerve Fiber Layer (RNFL) and the Ganglion Cell-inner Plexiform Layer Complex (GC-IPL) in AD patients with those in healthy controls have found that the former group exhibits notable thinning in these regions compared to the latter. For instance, even though AD causes a decrease in the mean RNFL globally, the superior quadrant appears to be the region that is most clearly impacted. A few research, nevertheless, have not been able to support these conclusions. Given that AD is a stage of established dementia, meaning that the patient's health has already been significantly compromised at the time of diagnosis, researchers have also given attention to the prodromal stage of the illness, also known as Mild Cognitive Impairment (MCI). When compared to controls, an MCI group had considerably less parafoveal SCP VD, according to Zhang et al. A recent prospective study also found that MCI patients have a noticeable reduction of VD in the DCP. This is consistent with Jiang et alfindings who discovered a lower VD in the superonasal quadrant of the DCP. In a study by Querques et al., a dynamic vessel analyzer and OCTA were used to quantitatively examine the retinal vessels of patients with MCI and AD. The reaction amplitude and arterial dilation in the MCI group were found to be reduced, but there was no discernible difference in the OCTA values between the groups. Researchers found that the A-positive group had increased VD in all locations, with no changes found in the FAZ area, in a monozygotic twin's preclinical AD investigation. The majority of research concurs that RNFL thickness is significantly lower in the MCI group as compared to controls. Additionally, a few studies have found a substantial difference between AD and MCI in the thickness of the retina. Studies on peripapillary vasculature have produced contradictory results, it seems. Although Zabel et al. showed no statistically significant differences between the AD group and healthy controls, Lahme et al. did show a lower Radial Peripapillary Capillary (RPC) VD in AD patients. Lastly, Zhang

et al. discovered no variations in the RPC values between the MCI group and controls. Therefore, more investigation is required to accurately identify particular OCTA parameters that may be able to identify early forms of AD. As various studies have been able to show, choroidal thickness is a useful biomarker for AD and exhibits considerable thinning in these individuals when compared to controls. These findings' underlying pathophysiological mechanisms are not yet fully understood. However, it appears that similar to what happens in AD brains, the buildup of A in the choroid triggers inflammatory responses, and complement activation, and finally results in choroidal vascular angiopathy.

Deep learning and artificial intelligence are continually altering medicine and how we understand some diseases. The retinal vasculature can be analyzed in terms of its fractal dimensions using a retinal OCTA segmentation database (ROSE) in conjunction with an OCTA network. Despite being a novel approach, the outcomes seem promising because scientists have already found substantial differences between healthy controls and AD patients.

### OCTA in vascular dementia

Due in part to its overlap with other dementia syndromes, such as AD, Vascular Cognitive Impairment and Dementia (VCID), also known as Vascular Dementia (VaD), is the second most prevalent cause of cognitive impairment and a difficult diagnosis. Executive, visuospatial, and/or memory problems, among other cognitive features, are included in the diagnosis of VaD, which is primarily clinical. Vasco- allopathy, which includes hypertension, hyperlipidemia, and diabetes, is strongly associated with brain ischemia and degeneration through many pathways. The MRI signs of this illness include white matter lesions or hyperintensities (WML/WMH), lacunar infarcts, microinfarcts, cerebral microbleeds, and hemorrhages [5]. The examination of the retina's vasculature may reveal brain pathology since the retina is thought of as an extension of the cerebral tissue. As a result, OCTA is perfectly suited for non-intrusively observing the functional microvascular changes that VaD is likely to exhibit. Given that it correlates with the Fazekas scale but not with the presence of pathologic (A, ) proteins in the Cerebrospinal Fluid (CSF), it has been shown that the flow density of the inner retinal layers may be a useful biomarker in separating vascular from degenerative dementia. In addition to Wang et alresults that the VD of the SCP correlates with both WMHs and cognitive scores in patients with Cerebral Small-Vessel Disease (CSVD), a comprehensive study by Zhang et al. also identified a connection between WMHs and lower VD values [6]. The temporal RPC plexus of patients with Subcortical Vascular Cognitive Impairment (SVCI), a subtype of VaD, has lower Capillary Density (CD) values than that of healthy subjects, according to research. The findings are consistent with the possible utility of this OCTA measure as a distinguishing biomarker because the researchers showed that the CD values of the temporal and superior RPC quadrants were lower in the SVCI subgroup than in AD patients. Additionally, they discovered a negative relationship between the RPC density and the CSVD score, a factor that is crucial for cognitive decline in VaD. Patients with CSVD had lower VD levels in their temporal macular SCP and RPC plexuses than healthy controls, according to a different study. The potential of OCTA as an early biomarker is highlighted by another recent study that found VD to be significantly reduced in the DCP and RPC of healthy (i.e., cognitively normal) subjects with higher Fazekas scores as well. The discovery that lower Vessel Skeleton Density (VSD), a measure of the perfused retina in OCTA images, is correlated with worse clinical (lower visuospatial and executive cognitive functions) and anatomical findings in patients with the Small-vessel Disease (SVD) support the idea that retinal microcirculation parameters might serve as biomarkers in VaD. Particularly, MRI results about cerebral perfusion and reactivity as well as executive and visuospatial cognitive processes were discovered to be adversely affected. Additionally, it seems that cognitive function and SCP density are related. A thinning of the choroid and electrophysiology consistent with outer retinal dysfunction was seen in one case report of a patient with post-stroke VaD, which is contrasted with the inner retinal disease purportedly linked with AD [7]. It appears that the expansion of cerebral hypoperfusion to the choroidal circulation is the underlying pathophysiological process. We still need to do more research to fully understand this case, though.

VaD and Cerebrovascular Disease (CVD) are intricately related, hence research on hereditary CVD has made sense in the hunt for pertinent retinal biomarkers. Indeed, reduced VD in the DCP, an impaired RPC plexus, and even choroidal thinning have all been discovered to be related to Cerebral Autosomal Dominant Arteriopathy with Subcortical Infarcts and Leukoencephalopathy (CADASIL) [8]. Similar to this, another study contends that macular VD OCTA characteristics may serve as early indicators for Fabry disease since they anticipate cardiac abnormalities that may occur before cognitive decline [9].

Clancy et al. are doing a comprehensive analysis of the variables influencing the CSVD load in patients with mild stroke as part of an ambitious continuing cohort research. Patients undergo an OCTA as well as another test. It is hoped that the findings of this study will clarify the connection between retinal imaging and the risk of developing VaD and establish its diagnosis [10].

## Conclusions

OCT and OCTA are imaging modalities that are used regularly by all ophthalmologists in their work and have become crucial to understanding the retina and choroid. OCT has so far been used by neurologists to diagnose neurological diseases including multiple sclerosis. Therefore, the purpose of this review is to call attention to yet another potential use for this developing technology. Data indicate that certain OCT/OCTA findings may overlap in AD and VaD, notwithstanding the paucity of research that has been done. However, it appears that some OCTA markers offer intriguing targets for additional study in this area. This review seeks to provide an overview of the most recent information and may provide a guide for future work, such as the investigation of OCTA as a tool for tracking changes over time in a variety of neurodegenerative illnesses.

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