CHAPTER 3

AIM OF THE THESIS

Although the morphology of ARM has been described in detail, the pathogenesis is still poorly understood. Several important questions remain to be answered in order to develop new prevention and treatment strategies.

Although the most striking associated factor for ARM is age, it is still not clear whether ARM is an exaggeration of the normal aging process (in other words an advanced stage of a deteriorative process that takes place in all eyes\textsuperscript{1}), or a fundamentally different disease-entity. All major signs of ARM increase with advancing age, but only in some individuals they progress to the stage of functional loss or cell death.\textsuperscript{1} A well-known mechanism of cell death and subsequent atrophy is apoptosis. To address this topic, we studied the presence of apoptosis in the aging retina in the second part of this thesis. The RPE appears to play a vital role in the development of ARM. The expression of the apoptosis–regulating protein Fas-ligand on RPE is hypothesized to have an inhibitory effect on human neovascularization\textsuperscript{64} by inducing apoptosis of active vascular endothelial cells. Therefore, we investigated whether Fas-ligand expression on RPE cells is associated with the stage of ARM and with age.

Focussing on neovascular AMD the question remains what factors trigger neovascular capillaries to develop from the choroid. It is acknowledged that growth factors are important in initiation and development of CNV. VEGF seems to play a central role in neovascular AMD,\textsuperscript{144,145,159-166} however other growth factors are probably required in addition. Thus, in the third part of this thesis, we focus on the Insulin-like Growth Factor pathway in neovascular AMD. IGF-I is associated with ocular angiogenesis in animal models,\textsuperscript{177,178} it has direct angiogenic effects,\textsuperscript{170,173} and modulates the expression and effects of VEGF\textsuperscript{156,178} Finally, in order to assess the effects of treatments, we describe the histopathological findings of radiotherapy on neovascular AMD.