Fundus Autofluorescence Imaging

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Core Messages

- With the advent of confocal scanning laser ophthalmoscopy, fundus autofluorescence (FAF) intensity and distribution can be recorded in vivo
- FAF imaging gives information over and above conventional fundus photography and fluorescence angiography and is a noninvasive diagnostic tool for evaluating age- and disease-related alterations of the retinal pigment epithelial (RPE) layer
- The FAF signal derives from fluorophores in lipofuscin granules within the RPE cell cytoplasm, with A2-E being a dominant fluorophore
- RPE lipofuscin accumulates with age and represents a common downstream pathogenetic pathway in various monogenetic and complex retinal degenerations
- Absorbing structures anterior to the RPE including retinal vessels and macular pigment as well as lack of autofluorescent material in RPE atrophy are associated with a decreased autofluorescence signal
- Topographic patterns of abnormal FAF may vary considerably in eyes with similar manifestations on funduscopy. Therefore, FAF imaging allows for more precise phenotyping
- For age-related macular degeneration it has been shown that particular FAF phenotypes have an impact on disease progression
- Findings of FAF imaging in retinal degenerations underscore the pathophysiological relevance of potentially toxic properties of excessive lipofuscin accumulation in the RPE
- Visualizing metabolic changes in RPE cells may be helpful for monitoring novel interventional strategies aimed at slowing accumulation of toxic lipofuscin compounds
- High-resolution cSLO fundus autofluorescence imaging now allows for visualization of the polygonal RPE cell monolayer with delineation of individual cells in vivo

2.1 Introduction

2.1.1 Advances in Ocular Imaging: Visualization of the Retinal Pigment Epithelial Cell Layer

Retinal pigment epithelial (RPE) cells possess numerous functions which are essential for normal photoreceptor function. The RPE cell monolayer has also been implicated in various retinal diseases [1, 21, 51, 57]. Given the close anatomical relationship to layers posterior and anterior to the RPE cell monolayer, postmitotic RPE cells are involved in disease processes even if the specific cause originates, e.g. from cells of the neurosensory retina or the choroid. Given the crucial role in retinal disease, various attempts have been made to visualize the RPE in the living eye. While fluorescence angiography mainly detects secondary effects such as alterations in the outer blood-retinal barrier, resolution, e.g. of ultrasonography or optical coherence tomography, was insufficient to visualize the cellular elements. With the advent of confocal scanning laser ophthalmoscopy, which was initially developed by Webb et al. [56], it is now possible to record fundus autofluorescence (FAF) and its spatial distribution in vivo (Fig. 2.1). Therefore FAF imaging represents a diagnostic, noninvasive tool for evaluating the RPE during ageing and in ocular disease. As shown by spectrometric findings by Delori et al. [17], the FAF signal mainly derives from RPE lipofuscin. Methodological developments with higher resolution now even allow for delineation of individual RPE cells in the human eye. Spaide has described a method by which autofluorescence photographs can be obtained using a fundus camera-based system [50].

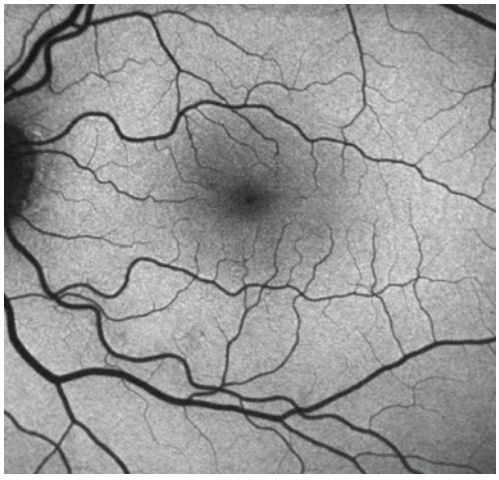

Fig. 2.1. FAF mean image of a 59-year-old male patient with normal topographic distribution of FAF intensity. Absorption by macular pigment and by retinal vessels results in decreased FAF signal intensitiy

2.1.2 Lipofuscin Accumulation in the RPE Cell: A Common Downstream Pathogenetic Pathway

An essential function of postmitotic RPE cells is the lifelong phagocytosis of shed photoreceptor outer segment discs and degradation with subsequent release of degraded material at the basal cell side, where it is normally cleared by the choriocapillaris. With age lipofuscin accumulates in the lysosomal compartment [17, 23]. It is also known to present a common pathogenetic pathway in various monogenetic and complex retinal diseases and is associated with photoreceptor degeneration. Although the mechanisms of lipofuscinogenesis are incompletely understood, there is strong evidence that oxidative damage plays an important role, with antioxidant deficiency or oxidant conditions being of importance [2, 4, 15].

Several lines of evidence indicate that lipofuscin is not an inert by-product but