18.3
Chloroquine Maculopathy

Kellner and colleagues demonstrated that FAF imaging may show distinct alterations in patients taking chloroquine/hydroxychloroquine medication [9]. A pericentral ring of increased intensity was present in patients with mild changes. More advanced stages showed a more mottled appearance with levels of increased and decreased intensity in the pericentral macula (Fig. 18.3). Electrophysiology is thought to remain the most sensitive tool to diagnose early chloroquine maculopathy. However, FAF imaging appears to be more sensitive than fundus photograph or fluorescein angiography in detecting toxic alterations at the level of the RPE.

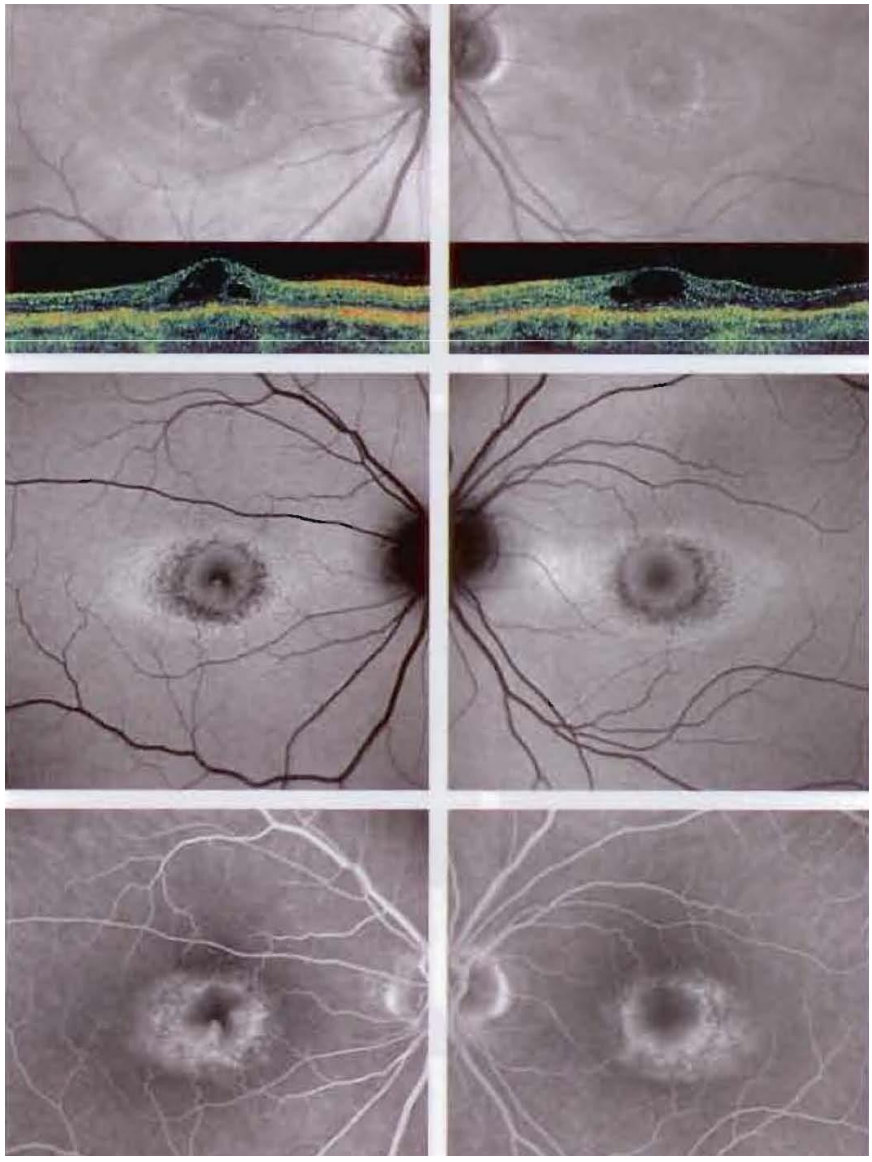

Fig. 18.3. Reflectance, optical coherence tomography (OCT), fundus autofluorescence (FAF), and late-phase fluorescein angiography images of a 51-year-old woman with chloroquine maculopathy. FAF imaging shows a mottled pattern of increased and decreased intensities in the pericentral retina and further levels of increased intensity toward eccentricity. In the fovea itself, a cystoid macula edema is present in both eyes, showing irregular levels of increased autofluorescence.

Preface

It has been known for many years from histopathological studies that autofluorescence is present in the retinal pigment epithelium (RPE) due to the presence of lipofuscin. The demonstration that the excitation spectrum of the "orange-red" fluorophores extends into the visible range indicated that imaging of lipofuscin was accessible to in vivo excitation. However, in vivo recording in humans of autofluorescence using spectrophotometric techniques and imaging with a scanning laser ophthalmoscope are relatively recent.

It is believed that the level of autofluorescence represents a balance between accumulation and clearance of lipofuscin. Accumulation of fluorescent material in the RPE reflects the level of metabolic activity, which is largely determined by the quantity of photoreceptor outer segment renewal. Abnormally high levels are thought to be due to RPE cell dysfunction or to the RPE's being subjected to an abnormal metabolic load as occurs in Stargardt disease, in which the discs contain abnormally high levels of N-retinylidene-N-retinylethanolamine (A2-E). Evidence of clearance is derived from the observation that outer retinal degeneration is associated with decreased autofluorescence. This could be due to a variety of factors. There appears to be constant degradation of residual bodies in the RPE. There is evidence of photodegradation of A2-E, and in addition, long-term phagolysosomes may be discharged from the RPE cells into the extracellular space.

It is now clear that autofluorescence imaging is useful for diagnosis in patients with visual loss and that certain inherited disorders have distinctive patterns of change. Perhaps more important is the ability to assess the state of the RPE/photoreceptor complex in ageing. Until recently the only index of ageing was the state of Bruch's membrane as indicated by the number, size, and distribution of drusen. It is now possible to assess changes in the RPE, and it has been recognised for some years that the RPE plays a crucial role in the pathogenesis of age-related macular disease (AMD). It has been shown that the pattern of autofluorescence varies among patients. However, there is marked symmetry between the eyes of those with bilateral early AMD, implying that autofluorescence characteristics reflect the risk factors, whether genetic or environmental. Furthermore, it is believed that geographic atrophy is preceded by focal increases in autofluorescence, and this belief has given rise to concepts regarding pathological processes in this form of late disease. Lipofuscin is a free radical

generator when illuminated with blue light. It also acts as a surfactant that causes leakage of membranes and a rise in the pH of phagolysosomes, with consequent predictable loss of activity of degradative enzymes. In turn, lack of recycling from phagosomes may result in lack of material for outer segment renewal and photoreceptor cell death. Of perhaps the greatest importance is the ability to verify the integrity of the RPE/photoreceptor complex prior to treatment of choroidal neovascularisation such that the likely therapeutic outcome may be determined. This can be verified on the basis of autofluorescence imaging. If it is shown that therapeutic benefit can be predicted by autofluorescence imaging, it should become a routine part of the management of such cases, particularly in light of the therapeutic results of the new biological agents.

The value of autofluorescence imaging to clinical practice has been shown beyond any doubt, although, as with many new techniques, the clinical value of the technique has yet to be fully understood. It gives information that is of major clinical importance but is not yet accessible by any other technique.

In this book the principles of autofluorescence imaging are explained, the scope of the technique is summarised, and its application in clinical practice is illustrated. It is hoped that this information will help make the technique more widely available and of greater value to the clinician.

London, Juli 2007
Alan C. Bird

I. Emerging Development in Ocular Imaging

OCT was first introduced in 1991 by Huang et al as a high-resolution, non-invasive in-vivo ophthalmic imaging technique. It is analogous to an ultrasound, but instead of measuring sound echoes, it detects echo time delays of light. The best choice depends on your specific needs. Commercially available devices are listed in Table 3.

The Stratus OCT (Carl Zeiss) is based on time domain detection technology and has a slow acquisition speed, leading to loss of true retinal topography.

The Spectral domain or Fourier domain (the terms are used interchangeably) has high acquisition speed, so it preserves true retinal topography and allows for better delineation of pathology.

All seven spectral/Fourier domain OCT's offer physicians better image quality and more comprehensive and accurate data sets.

The Heidelberg Spectralis® HRA + OCT is the most complete for research in a retinal practice. It has simultaneous fluorescein angiography and 3-D Spectral Domain OCT, autofluorescence ICG and active eye tracking to obtain consistent follow up imaging positioning.

Table 3: Commercially Available OCT Devices

Company	Name of Device	Speed (scan/sec)	(A- Axial Resolution µm)
Bioptigen	3D SDOCT	20,000	~6
Carl Zeiss Meditec	Cirrus HD-OCT	27,000	~5
Heidelberg Engineering	Spectralis HRA + OCT	40,000	~7
OPKO Instrumentation/OTI	Spectral OCT/SLO	27,000	~5-6
Optopol/Reichert	SOCT Copernicus	25,000	~6
Optapol/Reichert	SOCT Copernicus HR	50,000	~3
Optovu	RTVue-1000	20,000	~5
TOPCON	3D-OCT 1000	20,000	~5

Our practice has the Heidelberg Spectralis® HRA and OCT. We have been utilizing it for two years. Our clinical experience with our patients has proven to be invaluable in making difficult diagnostic evaluations.

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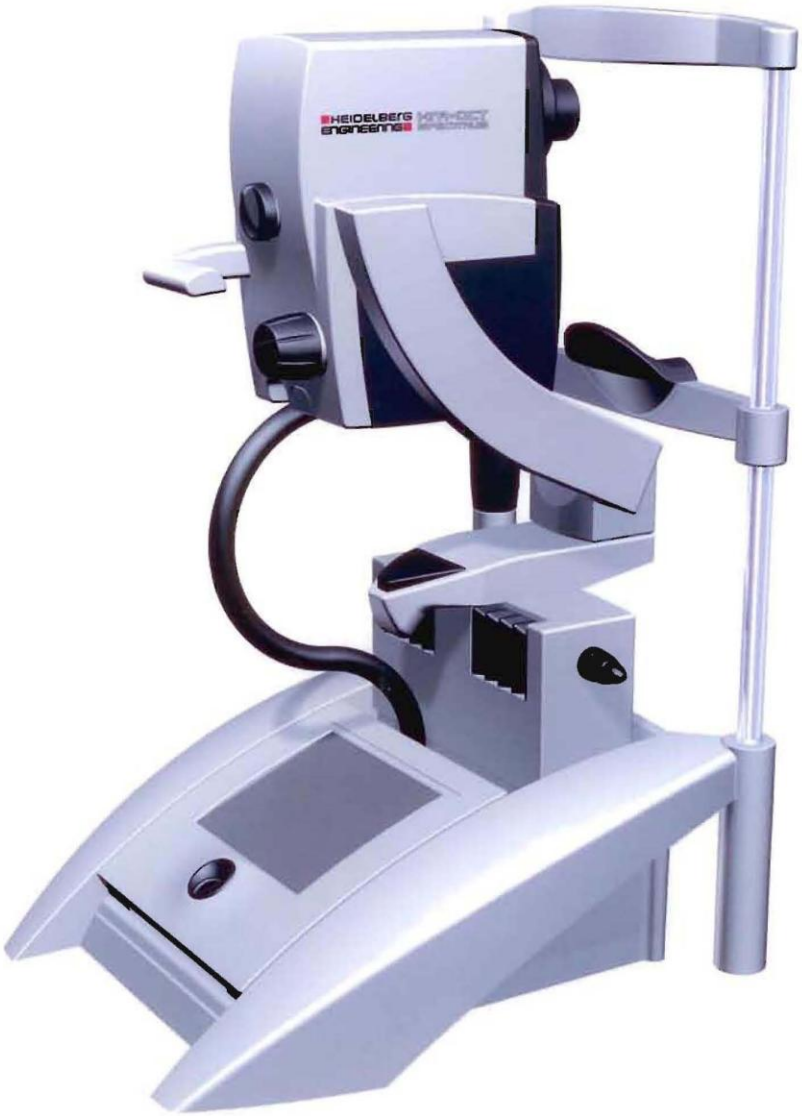

HRA SPECTRALIS

HRA+OCT SPECTRALIS

OCT SPECTRALIS