

# Optical Coherence Tomography of the Retina

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**Figure 1.** The Helmholtz ophthalmoscope (circa 1851), a groundbreaking invention in the history of ophthalmology.

**A**lthough the question of why the pupil is black had attracted the attention of writers dating back to the time of Ancient Rome, it was not until 1851 that Herman Ludwig von Helmholtz unlocked the door to the back of the eye by inventing the Augenspiegel, or ophthalmoscope (Fig. 1). Von Helmholtz's groundbreaking invention enabled examination of both normal and diseased eyes. It also allowed drawings to be made of the fundus. The first images of the retina were useful to physicians for communicating both normal and unusual findings to their colleagues.<sup>1</sup>

In 1961, another milestone in examination techniques was achieved with the development of fluorescein angiography,<sup>2</sup> a technique which detects relative leakage of intravenous fluorescein sodium dye from diseased or damaged blood vessels. The development of fluorescein angiography dramatically improved our understanding of retinal vascular diseases by al-

lowing doctors to image the normal and diseased vasculature in the fundus.

Cross-sectional examination of the eye was limited to microscopic examination of excised specimens until the invention of the slit lamp by Gullstrand in 1921. With some modifications of the focusing lenses, examination of the macula is also possible with the slit-beam technique. An addition to retinal exam in the 1950s and early 1960s was the development of ophthalmic ultrasound, which provides two-dimensional imaging of the retina, but at a lower resolution than is possible with optical devices.

Today, the introduction of optical coherence tomography (OCT) to the ophthalmic armamentarium is rapidly changing the world of retinal examination. The use of low-coherence interferometry provides information on relative reflectivity and on the location of ocular structures. It allows non-invasive, cross-sectional imaging of the macula at high resolution, with

no need to ascertain the existence of vascular leakage before rendering a diagnosis of disease.

The emergence of OCT has shed new light on the participation of non-vascular structures in many retinal disease processes. OCT studies have demonstrated fibrotic bands within the vitreous gel, the vitreoretinal interface, the structures within the retina, and the subretinal tissues. Better understanding of the relationship of the posterior segment structural components will likely change the diagnostic grouping of diseases and the treatment of retinal conditions.

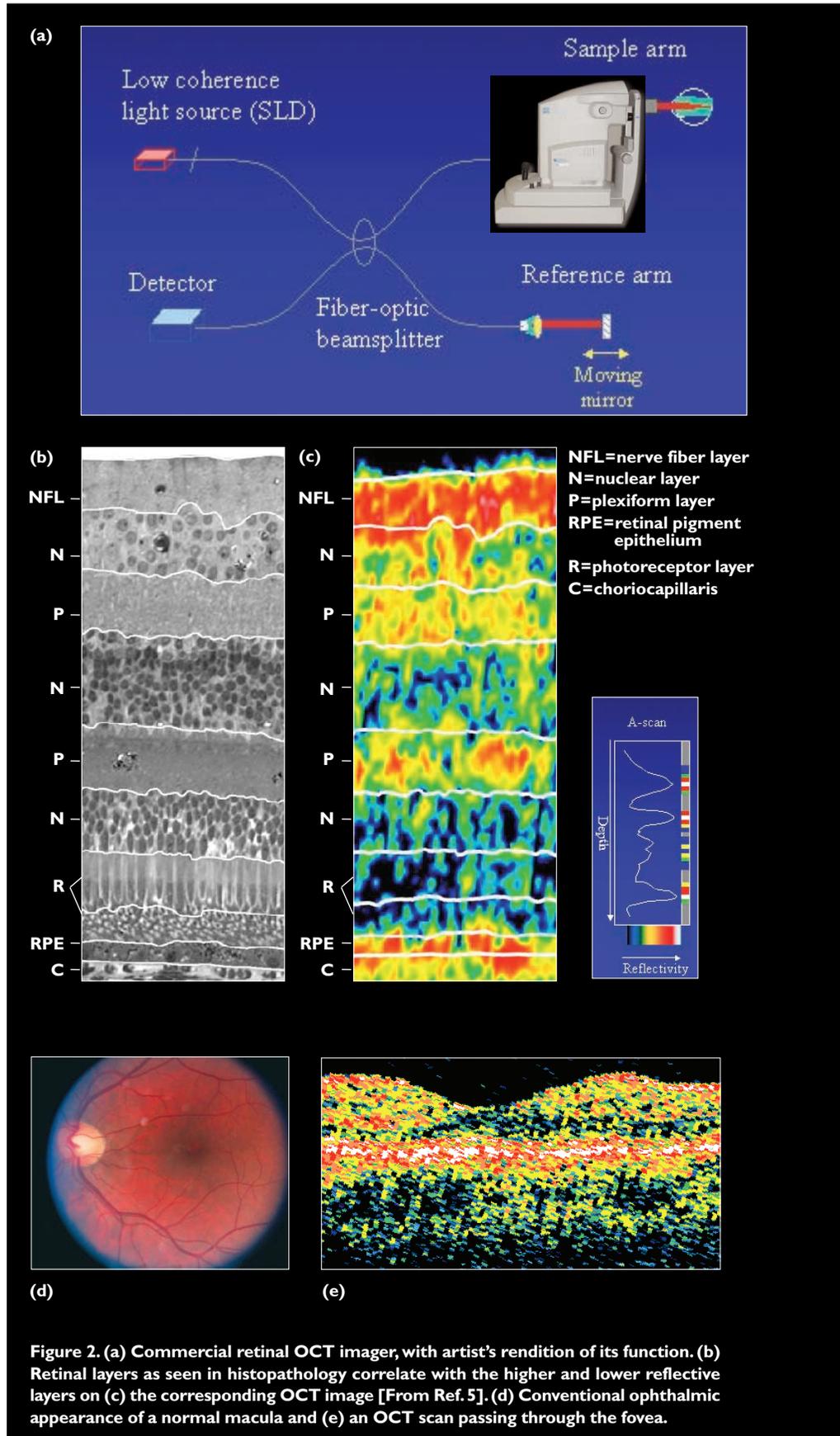
**OCT applied to retinal imaging**

In OCT imaging of the retina, low-coherence light from a superluminescent diode (SLD) source is coupled into a fiber-optic Michelson interferometer. Infrared light at 843 nm is divided at a coupler into reference and sample paths. Light retroreflected from a variable reference delay is combined in the coupler with the light backscattered from the subject's eye. A photodiode detects temporal information from the interference signal, which is then processed, and a longitudinal profile similar to an ultrasound A-scan is obtained.<sup>3</sup> Different layers of the posterior pole of the eye reflect and scatter light in different ways, yielding both longitudinal and lateral spatial information as well as information on reflectivity. Cross-sectional images are built from a sequence of single longitudinal reflectivity profiles obtained by scanning the probe beam across the retina. Today's commercial scanners acquire 100 longitudinal A-scans in 1-2.5 sec.<sup>3,4</sup>

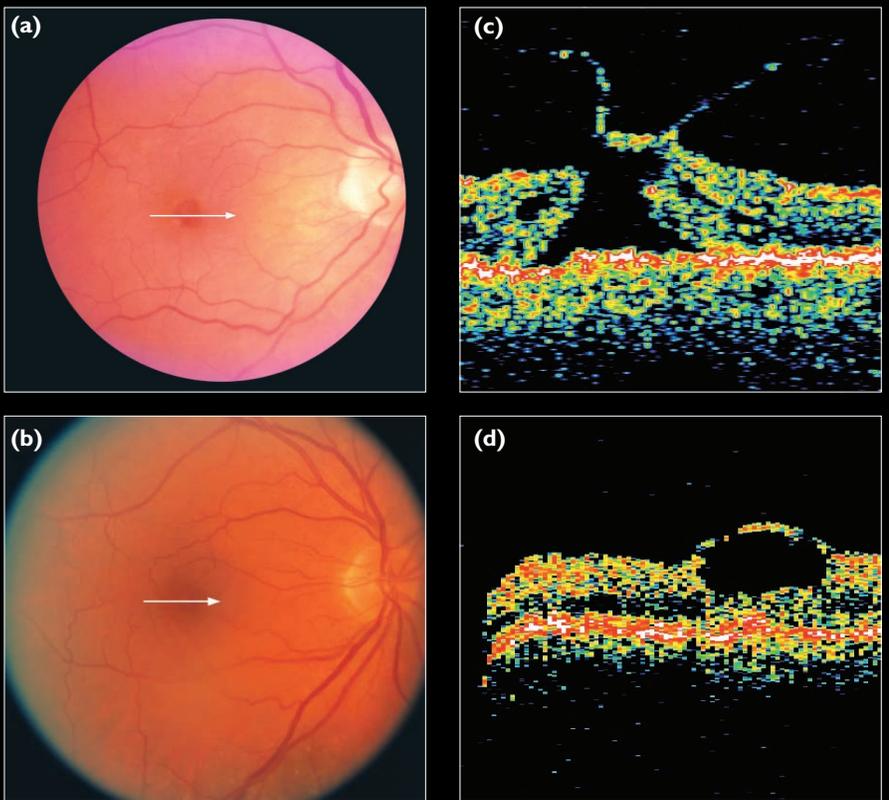
**Imaging the normal retina**

Light at 843 nm is minimally absorbed by the vitreous and anterior structures in the visual pathway, thus allowing the signal energy necessary to reach the layers of the retina (Fig. 2). OCT is useful for finding abnormalities within these layers, which have contrasting structure and reflectivity. Higher reflectivity appears to correlate with horizontally oriented layers, such as the nerve-fiber layer and the plexiform layers. Lower reflectivity correlates with nuclei and vertical structures, such as photoreceptors.<sup>5</sup>

Scientists' ability to analyze OCT images is causing a major shift in our understanding of the interaction, in retinal dis-



**Figure 2. (a) Commercial retinal OCT imager, with artist's rendition of its function. (b) Retinal layers as seen in histopathology correlate with the higher and lower reflective layers on (c) the corresponding OCT image [From Ref. 5]. (d) Conventional ophthalmic appearance of a normal macula and (e) an OCT scan passing through the fovea.**



**Figure 3. OCT in macular holes and cysts. (a) Color fundus photograph of a full-thickness macular hole. (b) OCT imaging through the fovea of the same patient showing evidence of tangential traction. (c) Color fundus photograph of a macular cyst. (d) OCT scan through the fovea demonstrating the outline of the cyst.**

ease, of the vitreous gel, the retina, and the subretinal tissue. Next we will describe several applications of OCT in the vitreous, the retina, and the subretinal space.

**Imaging vitreoretinal disorders**

In the normal aging eye, the vitreous body liquifies and may eventually separate from the retina. This posterior vitreous separation may be incomplete, creating sites of vitreoretinal adhesion. OCT has recently been used to demonstrate the normal evolution of vitreous separation in the posterior pole.<sup>6</sup> With OCT, researchers have also identified vitreous adhesions and the role they play in the development of macular diseases such as macular hole, cystoid macular edema, and diabetic retinopathy.<sup>7</sup> Prior to OCT, it was thought that macular holes evolved secondary to tangential traction along the retinal surface. The advent of OCT has allowed ophthalmologists to recognize the more important action of anteroposterior forces.<sup>8</sup>

It can be difficult to differentiate small, round, central foveal lesions, such as mac-

ular cysts, full-thickness macular holes, and partial-thickness macular holes. Differentiation is important, since the treatments for these lesions differ. Imaging in cross section clearly shows the difference between the lesions. OCT imaging has also been useful in objectively demonstrating hole closure postoperatively.<sup>9</sup>

Cystoid macular edema (CME), the thickening of the retina with fluid-filled cysts, can be the end result of many different eye diseases—diabetic retinopathy, inflammatory disease, or macular degeneration. The thickening can result either from leakage of fluid from abnormal blood vessels or from traction by the vitreous gel.

Subtle degrees of CME are difficult to diagnose clinically: fluorescein angiography is often used to look for leaking blood vessels and fluorescein dye pooled in the cysts [see Fig. 4(a)]. When CME is caused by structural, nonvascular factors, OCT can show both the structure and the location of intraretinal cysts, thus allowing doctors to diagnose specific cases of edema.<sup>10</sup> One disadvantage of OCT is that it

does not show leaking blood vessels; fluorescein angiography does.

OCT can show the height of retinal thickening [extrapolated to estimate volume, see Fig. 4(b)]. It can also be used to monitor the volume of edema, and thus the effectiveness of treatment. Several studies have found that the decrease in central vision is proportionate to the extent of macular thickening.<sup>11,12</sup>

The use of OCT has helped identify CME in a higher number of cases of otherwise unexplained vision loss by identifying nonvascular, structural causes. Fluorescein angiography still has a role, however, in identifying leaking vasculature in this disease, as well as in treatment. Management of many cases of CME may require assessment using both OCT and fluorescein angiography.

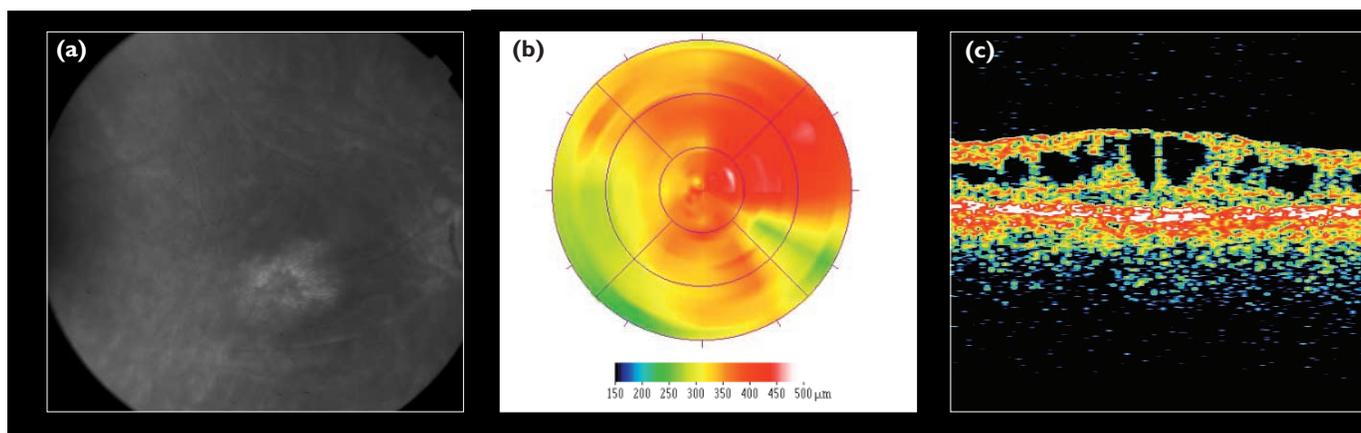
Age-related macular degeneration (AMD) is the leading cause of legal blindness in individuals 65 years of age or older in western societies. Many treatment modalities are being tried, with different rates of success. In the wet or neovascular subgroup, most treatment is directed at subretinal neovascularization, the cause of the majority of serious vision loss in these patients.

Fluorescein angiography has been the mainstay in the diagnosis of neovascular AMD. Some aspects of this disease, however, can only be shown using OCT imaging. In particular, doctors have found OCT useful in assessing:

- the state of the vitreoretinal interface and sites of attachment to the macula;
- intraretinal pathology in terms of thickness and the presence of intraretinal cysts;
- the subretinal space for neovascularization, geographical atrophy, and the presence of blood or fluid.

We have recently documented intraretinal morphology associated with neovascular AMD. In a study of 61 patients with AMD, retinal edema associated with loss of vision was present in 46% of patients with subfoveal neovascularization.<sup>13</sup> Recently, we have also shown a correlation between vitreous attachment to the macula and the development of tears in the retinal pigment epithelium (RPE) over subfoveal neovascularization.<sup>14</sup>

The use of optical cross-sectional imaging has allowed us to identify new fac-



**Figure 4. OCT in cystoid macular edema (CME).** (a) Fluorescein angiography demonstrates vascular leakage and dye in cysts. (b) Composite analysis of multiple OCT images quantifies retinal thickness, (c) individual, cross-sectional OCT scan shows detailed structure of cysts.

tors causing vision loss in patients with AMD. These findings may one day lead to new treatments for this serious disease.

In summary, OCT imaging of the retina marks a shift from our traditional view of macular disease to improved cross-sectional documentation of pathology involving the posterior vitreous, retina, and subretinal structures. OCT also has improved our understanding of the causes of macular diseases. Yet the research is still at a relatively early stage and there is much ground left to cover.

The first commercial unit, released in 1996, is still in use, despite its limitations: if the subject does not remain immobile for 1-2.5 sec, motion artifacts can be generated during image acquisition; reflections from microstructures of importance, such as the RPE, cannot be identified at current resolution levels of 10-15  $\mu\text{m}$ .

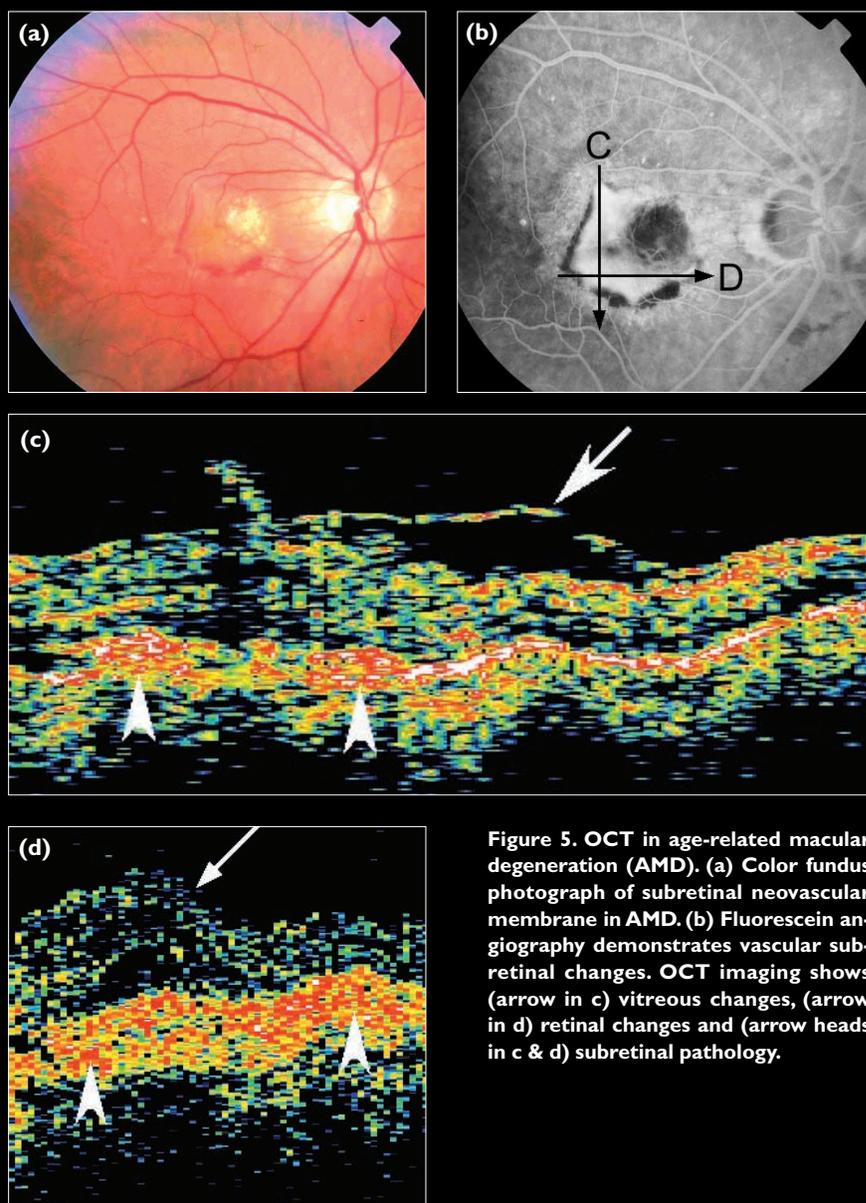
Researchers are striving to develop systems with higher resolution as well as faster image-acquisition time. These are just two of the many opportunities being pursued to expand on the information available from this optical technology.

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*The references to this article appear on p. 60, OPN's reference page.*

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**Figure 5. OCT in age-related macular degeneration (AMD).** (a) Color fundus photograph of subretinal neovascular membrane in AMD. (b) Fluorescein angiography demonstrates vascular subretinal changes. OCT imaging shows (arrow in c) vitreous changes, (arrow in d) retinal changes and (arrow heads in c & d) subretinal pathology.