

The Evolution of Confocal Scanning Laser Ophthalmoscopy

Many disparate elements came together to create this modern imaging technology.

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In the years since its introduction, confocal scanning laser ophthalmoscopy (cSLO) has revolutionized our ability to visualize the posterior pole of the eye. With its ability to capture images of the retina with a high degree of spatial sensitivity, cSLO has improved our ability to diagnose and follow patients with glaucoma, macular degeneration, and other diseases of the posterior segment.

But how did this technology come to be? The invention of cSLO is the culmination of research spanning centuries in disparate fields. Its creation required the coming together of multiple concepts, including photography, digital photography, ophthalmoscopy, scanning laser technology, angiography, and confocality. This article takes a timeline approach to explain how these disparate concepts came together to produce the technology that today provides clinicians and researchers with an unprecedented clear vision of the back of the eye.

EARLY DEVELOPMENTS

1569: The first existing reference to a “camera” of a sort is by the Venetian philosopher and mathematician Daniele Matteo Alvise Barbaro (Figure 1). In his book *La pratica della prospettiva*, he described the concept of the “camera obscura,” in which a lens projects an image into a darkened room. This was one of the ideas that led to the development of cameras and photography as we now know them.



Figure 1. Daniele Barbaro

1726: The evolution of photography proceeded slowly. The next advance in photographic technology took place almost 2 centuries later, when the German physicist Johann Heinrich Schultz made the first attempt to capture an illuminated image permanently. He described how silver nitrate mixed with chalk darkened when exposed to light.

1822: The 19th century saw a flowering of research and technological advances leading to the development of photography and ophthalmoscopy. In this year, a complete technique for ophthalmoscopy was first described, in Latin, by the Czech anatomist and physiologist Jan Evangelista Purkinje.

1824: Just 2 years later, the French inventor Nicéphore Niépce (Figure 2) took the world’s first known photograph, using a pewter plate. He subsequently partnered with his countryman Louis Daguerre to develop further refinements of photographic technique.



Figure 2. Nicéphore Niépce

A FLOOD OF INNOVATION

1829-1839: A flurry of activity leading to the development of the ophthalmoscope took place during the decade of the 1830s. The German physicist and physiologist Ernst Wilhelm Ritter Von Brücke, as well as Kussmaul, Cumming, and Babbage, worked on and

developed aspects that helped lead to the creation of the direct ophthalmoscope.

1850: But of course it was the great German physician and scientist Hermann Ludwig Ferdinand von Helmholtz (Figure 3) who invented the direct ophthalmoscope. Helmholtz is also remembered for other contributions to modern ophthalmology, from descriptions of the optics of the eye to theories of vision, spatial perception, and color vision.



Figure 3. Hermann von Helmholtz

1871: Adolf Von Bayer, the German chemist, founder of the pharmaceutical firm Bayer and a future winner of the Nobel Prize in chemistry, synthesized fluorescein dye for the first time in this year. Its first application in ophthalmology was described 10 years later by the German bacteriologist Paul Ehrlich, who used fluorescein to study the flow of the aqueous humor in humans.

1886: The first photography of the human fundus in vivo was published by the Americans W.T. Jackman and J.D. Webster¹ in 1886, and in the same time period Lucien Howe² was the first to be able to focus the images. A challenge at this time was how to illuminate the interior of the eye. Howe reported that, when illumination was supplied by a Bunsen burner, “the heat was so intense that we had to use topical cocaine to keep the patient from twisting in pain.”²

THE 20TH CENTURY

1925: Modern ophthalmoscopy and photography of the fundus began with the development of the fundus camera by the Swedish ophthalmologist J.W. Nordenson³ and its production by Carl Zeiss between 1925 and 1932. Illumination of the interior of the eye was still a problem at this time. The back of the eye reflects only 10% of the light that enters the eye, and the developers used an unstable carbon arc lamp as a source of light for this early fundus camera.

1930: The illumination problem was rectified with the invention of the stroboscopic flash by the American engineer Harold Edgerton, better known as “the man who stopped time” because his innovation led to the introduction of high-resolution photography.

1953: Edgerton’s electronic flash photography was coupled with a fundus camera for the first time by Wilber Rucker and Kenneth Ogle of the Mayo Clinic.⁴

1957: Confocal microscopy, an imaging technique used to increase optical contrast and resolution in microscopy, is a predecessor to cSLO. It allows the creation of 3-D structures from the images obtained. The concept of confocal microscopy was patented in this year by the American mathematician Marvin Minsky, also known as the father of artificial intelligence. The principles of confocal microscopy that he formulated at the Massachusetts Institute of Technology later evolved into the combination of confocal microscopy and scanning laser ophthalmoscopy that led to cSLO.

1961: Fluorescein angiography (FA) was described by Harold Novotny and David Alvis.⁵ Alvis, a student at the time, was the first subject in which the technology was applied. Their publication was initially rejected by the *American Journal of Ophthalmology* but was subsequently accepted and published by *Circulation*.

1975: The digital camera was invented at Kodak Laboratories by Steven Sasson. The first digital camera weighed 3.6 kg and had a resolution of 0.01 megapixels (10,000 pixels). It took 23 seconds to record an image and 23 seconds more to send it to a TV monitor.

1979: Scanning laser ophthalmoscopy, the use of a laser to illuminate and image a small area of the retina, was invented in this year by Robert H. Webb, a physicist at Massachusetts General Hospital and researcher at Schepens Eye Research Institute.⁶

1987: Topcon introduced digital photography integrated into a fundus camera for the first time.

1991: Huang and colleagues⁷ at Harvard and the Massachusetts Institute of Technology described optical coherence tomography (OCT), a noninvasive method of imaging the posterior wall of the eye in cross-sectional segments. The original time-domain OCT produced 2-D images analogous to ultrasonic imaging or to “in vivo histopathology.”

1992: Heidelberg Engineering developed the first angiographer using cSLO (HRA Classic).

1995: Microsoft introduced Windows (Microsoft) software for managing images from digital cameras.

2007: The integration of all the elements discussed above finally came in 2007 with introduction of the Spectralis HRA + OCT (Heidelberg Engineering), combining spectral-domain (SD) OCT with cSLO angiography.

The high resolution of this technology is achieved thanks to point-by-point illumination of every part of the retina. The point-by-point illumination and high resolution are possible because of the speed of the laser and because of the principle of confocality, which means that illumination of a specific point is registered exclusively, filtering out all other rays projected at different depths in the retina.

The Spectralis also integrates a second element, which is the possibility to use OCT with cSLO to produce different types of simultaneous images. cSLO can produce infrared, fluorescein, indocyanine green, and autofluorescence images, and any of these can be combined with SD-OCT.

CONCLUSION

This timeline shows how many different efforts of human intelligence, through several centuries, have been united and integrated in a high technology solution to give physicians the ability to look deep in the pathological process of disease and to develop better diagnostics and therapeutic strategies. Individually, each contribution of invention and discovery has its own unique history of effort and challenges, success and disappointments in the professional and personal spheres of each of these great men. Certainly they would never have had an idea that all their work would feed into the development of SD-OCT technology. It is clear now in hindsight, however, that the most important impact of these individual developments is in the benefits that patients have received through the use of this technology. ■

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