Non-contact Confocal Microscopy of the Tear Film in Unoperated Eyes

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ABSTRACT

PURPOSE: The NIDEK ConfoScan4 (CS4) is a digital scanning slit confocal microscope. The corneal structure and tear film can be viewed, magnified, measured, and photographed at magnifications up to 500×, in vivo, in a noninvasive manner. The objective of this study was to evaluate and illustrate various conditions related to dry eye using the CS4 confocal microscope with the 20× noncontact lens.

METHODS: The CS4 was used to evaluate the natural tear film in 58 eyes of 29 patients with normal examinations, allergic conjunctivitis, nonspecific conjunctivitis, and dry eyes. In a subset of this patient population, subjective and objective findings were used to classify mild, moderate, and severe dry eye disease states. The usefulness of confocal microscopy as an objective tool to diagnose and manage different tear film-related ocular disease was also evaluated.

RESULTS: The differences in tear film composition were visible using confocal microscopy. Photographs demonstrate confocal noncontact 20× microscopy as a diagnostic tool.

CONCLUSIONS: Noncontact confocal microscopy is a valuable tool in the diagnosis and treatment of dry eye syndrome and other ocular states such as allergic and nonspecific conjunctivitis. It provides a simple and effective way to observe, classify, and treat the tear film. As investigators visualize and learn more, understanding of this structure will continue to improve. [J Refract Surg. 2007;xx:xxx-xxx.]

The CS4 (ConfoScan4; NIDEK Technologies Srl, Padova, Italy) is a digital scanning slit confocal microscope. It enables the practitioner to view, magnify, measure, and photograph the structures of the cornea and tear film at 250× to 500×, in vivo, in a noninvasive way. The 20× noncontact lens was used in this study. This lens has a working distance of 12 mm and magnification of 250× (on a 15" monitor at 1024×768 resolution). The field of view is 460×690 μm. Previous studies have indicated that noncontact confocal microscopy allows visualization of the tear film and ocular surface, which appears to be relevant to its physiological state.1,2

Dry eye syndrome is a disorder of the tear film due to tear deficiency or excessive tear evaporation, which causes damage to the interpalpebral ocular surface and is associated with symptoms of discomfort. Approximately 14.4% of the US population aged 48 to 91 years has dry eye syndrome.1 This figure, in conjunction with US census data,2 indicates that approximately 15 million people in the United States between the ages of 48 and 91 years suffer from dry eye. It is a common presentation for the patient seeking refractive surgery or reduced dependence on contact lenses.

The tear film is the first refracting surface. Its proper function is essential to contrast sensitivity and visual acuity.3 The outer lipid layer prevents evaporation and stabilizes the tear film. The aqueous component is a complex mixture of proteins, mucins, electrolytes, cytokines, and growth factors. It provides moisture and proper nutrient balance. Mucins provide viscosity and stability during the blink cycle and promote even distribution of tear film across the corneal surface.

Noncontact confocal microscopy was used to investigate morphological differences between normal, mild, moderate, and severe dry eyes. An additional subset of five patients was evaluated using this technology for the diagnosis of infectious and allergic conjunctivitis.

PATIENTS AND METHODS

This study comprised 58 eyes of 29 patients that underwent tear film evaluation with 20× noncontact confocal microscopy using the CS4. The natural tear film was evaluated in patients with normal examinations, allergic conjunctivitis, nonspecific conjunctivitis, or dry eyes. The usefulness of confocal microscopy as an objective tool to diagnose and manage different tear film–related ocular disease was also evaluated. In a subset of this patient population, subjective and objective findings were used to classify mild, moderate, and severe dry eye disease states. Measures included history, the ocular surface disease index, uncorrected visual acuity, best spectacle-corrected visual acuity (BSCVA), low contrast visual acuity, tear production, and conjunctival staining. The individual examinations were reviewed and classified by the investigators.

RESULTS

Of the 29 patients, 10.3% (n=3) were classified as normal. 37.9% (n=11) had mild dry eye syndrome, 37.9% (n=11) had moderate dry eye syndrome, and 13.8% (n=4) had severe dry eye syndrome. Of these, a subgroup comprising 10 patients was tested for BSCVA, low contrast visual acuity, and tear break-up time. Thirty percent
(n=3) were classified as having mild dry eye syndrome, 50% (n=5) as having moderate dry eye syndrome, and 20% (n=2) as having severe dry eye syndrome.

In the mild dry eye syndrome group, average BSCVA was 20/20, average low contrast visual acuity was 20/60, and average tear break-up time was 10.16 seconds. In the moderate dry eye syndrome group, average BSCVA was 20/20, average low contrast visual acuity was 20/40, and average tear break-up time was 6.0 seconds. In the severe dry eye syndrome group, average BSCVA was 20/25, average low contrast sensitivity was 20/40, and average tear break-up time was 3.75 seconds. The ocular surface disease index was assessed on a scale of 0 to 100, with higher scores representing greater disability. Scores were calculated from 12 questions the patients answered to assess ocular symptoms, whether problems with their eyes limited their ability to perform common tasks, and how their eyes felt under different environmental conditions. Patients assessed each question on a 0- to 4-point scale that ranged from “None of the time” to “All of the time.” The mean score was 40.5 (median=37.5; range: 12.5 to 84.1).

Changes in the tear film of patients with mild (Fig 1), moderate (Fig 2), and severe dry eye syndrome (Fig 3) were easily differentiated with confocal microscopy. These findings were consistent with the objective findings of tear break-up time and ocular surface disease index scores; however, BSCVA and low contrast visual acuity showed no consistency in helping determine classification. Because of the high magnification of the confocal microscope, it is easy to see the lipid layer of the tear film as well as individual cells such as epithelial cells, macrophages (Fig 4), and eosinophils (Fig 5).

In normal and mild dry eyes, early decompensation of the outer lipid layer is observed. As the eye progresses to moderate dry eye syndrome, more proteinaceous debris, break-up of the lipid layer, and early desquamation of epithelial cells are seen. Severe dry eye disease demonstrates more desquamated cells and lack of continuity of the tear film. In conjunctivitis, the diagnosis of acute, allergic, and nonspecific conjunctivitis can be determined by evaluating the inflammatory cell types of the tear film such as lymphocytes, eosinophils, and macrophages. These findings, corroborated with clinical subjective and objective findings, allowed the CS4 to be used as an adjunctive tool for the management of patients.

**DISCUSSION**

Noncontact confocal microscopy is a valuable tool in the diagnosis and treatment of a variety of tear film-related conditions. This pilot study was performed to show the clinical use of evaluating the tear film with additional objective findings using the NIDEK CS4. Classification systems of normal, mild, moderate, and severe dry eye–related disease may be derived from
these preliminary findings using CS4 technology; however, more formal studies are required.

These findings will provide the framework for more formalized evaluation of a variety of treatments for dry eye–related diseases and conjunctivitis. Confocal microscopy provides a simple and effective way to observe, classify, and treat the tear film. As we learn more and can visualize more, our understanding of this structure will continue to improve.

REFERENCES

Figure 4. Conjunctivitis demonstrating a macrophage (red arrow). Figure 5. Allergic conjunctivitis demonstrating an eosinophil (red arrow). Note the horseshoe-shaped double nuclei.