Imaging System for Ocular Surface:
Objective Assessment of Conjunctival Hyperemia

M. Tort[1], B. Lay[2], R. Danno[2], R. Ornberg[1], G. Williams[1], F. Soong[3], A. Salapatek[3]

[1]Alcon Research Ltd, Fort Worth, TX
[2]ADCIS, Saint-Contest, France
[3]Cetero Research, Mississauga, ON, Canada

Purpose

Conjunctival hyperemia is a key sign of allergic conjunctivitis and is an important endpoint in clinical efficacy and safety trials. Most methods for assessing hyperemia are highly subjective and are inconsistent from site to site. The purpose of this study was to develop a software suite that could objectively and automatically quantify conjunctival hyperemia resulting from patient's allergic responses.

Methods

13 subjects with a history of allergic conjunctivitis upon exposure to ragweed were selected. They were examined over 7 visits, during which their eyes were exposed to allergen using Conjunctival Allergen Provocation Testing (CAPT) or an Environmental Exposure Chamber (EEC) model. Images from baseline, post-exposure, and post-treatment (various therapies) were captured from each subject at dozens of pre-specified time points, with various magnifications, resulting in a total of about 5000 images.

The Imaging System for Ocular Surface (ISOS; Alcon) consisted of a modified slit lamp and a suite of software components designed to capture and store patient data and images, and to perform automated image analysis of conjunctival blood vessel morphology. Software components consisted of:

- ✓ An image acquisition interface;
- ✓ A data synchronizer to upload images and patient data to a secure database server;
- ✓ An interface used by experts to manually grade the level of allergic response, independently from one another. The grading values ranged between 0 and 4:

| 0 | 1 | 2 | 3 | 4 |
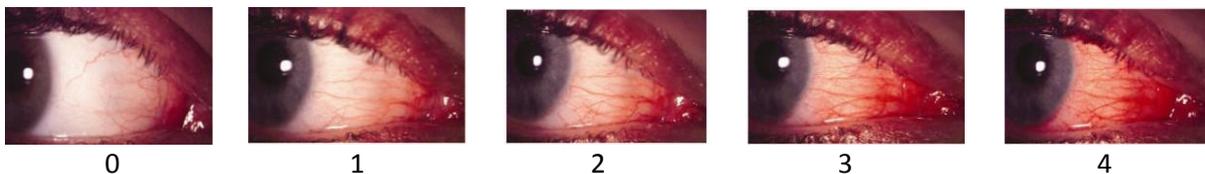
Anchor images are reprinted with permission from: Schulze MM, Jones DA, Simpson TL. Optom Vis Sci 2007;84:976–983

- ✓ An image processing software computing measurements on images and storing the measurements into the database;
- ✓ An interface to review results and query image properties and measurement values. A capability to register images of the same visit and patient for different time points was added to the software, with the ability to generate movies.

The automated image processing algorithm optimized the detection of the vessels, working on the full-resolution images that were shot at 25x magnification, and applied a skeletonization transform to allow accurate measurements of vessels, including vessel density, total length, number of triple

points, mean diameter, etc. The limbus was also detected to refine these measurements, and to compute the vessel density in the limbus neighborhood to mimic manual grading.

Original 25x image
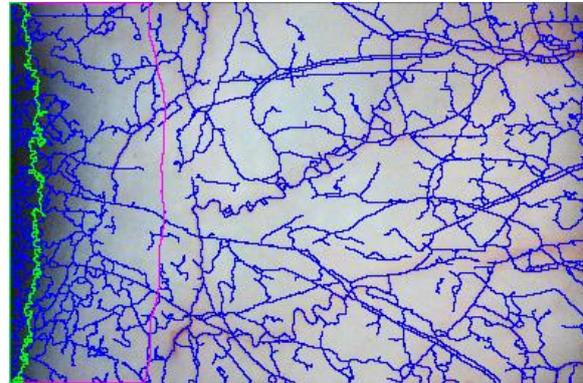
25x Image with vessel detection, limbus and limbus neighborhood

Measurements were input into a classification system to determine the most pertinent measurements and to train a classifier to reproduce the experts grading.

Results

The system was successfully used to obtain and analyze conjunctival images from 13 participants with a history of allergic conjunctivitis following exposure to allergen. Automated measurements yielded a variety of parameters that were not evident to a clinical observer, including vessel area, vessel diameter, total vessel length, vessel density (vessel area/total area), color intensity statistics, number of branch points (also called triple points or ramification points), and the length and tortuosity of individual vessel branches. Image transformation, vessel detection, and parameter calculation required only a few seconds per image.

Statistical analyses revealed that vessel density was highly correlated to manual grading.

Conclusion

Preliminary results from this pilot study indicated that the ISOS suite could objectively measure parameters of conjunctival hyperemia. These tools for assessing conjunctival hyperemia were fast, reliable, accurate, and not prone to human bias.

This study showed that image analysis could dramatically help in developing a full classification system that includes acquisition, manual grading and data mining.

It is planned to have a follow-up study with more patients in the fall 2012.