Development of an Imaging System for the Objective Assessment of Conjunctival Hyperemia

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Background & Purpose

Conjunctival hyperemia is a key symptom of allergic conjunctivitis and is an important endpoint in clinical efficacy and safety trials. Most current methods for assessing hyperemia are highly subjective and inconsistent from site to site. The purpose of this study was to develop a software suite, the Imaging System for Ocular Surface (ISOS; Alcon Laboratories, Inc), to objectively and automatically quantify conjunctival hyperemia.

Methods: Subjects and Conditions

- Images were obtained from 13 subjects with a history of allergic conjunctivitis upon exposure to ragweed
- Images from baseline, postexposure, and posttreatment (various therapies) were captured from each subject at dozens of prespecified time points over 7 visits
- Allergen exposure conditions included:
  - Conjunctival Allergen Provocation Testing (CAPT)
  - Environmental Exposure Chamber (EEC)

Methods: Manual Grading

- Ocular redness in the nasal and temporal conjunctiva were assessed separately in both eyes
- Hyperemia was graded at the following magnifications:
  - Live in the clinic, at 3x
  - In 10x images, by 3 separate graders per image
  - In 25x images, by 1 expert grader
- Hyperemia at 10x and 3x was graded by using a scale with descriptive anchors and photographic anchors (shown below), similar to a validated scale[1]

Grade	Image Anchor	Description
0		None / Normal
0.5		
1		Mild
1.5		
2		Moderate
2.5		
3		Severe
3.5		
4		Extremely Severe

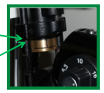
Anchor images are reprinted from Reference 1 with permission.

- Hyperemia at 25x was graded on the same scale, but by using the following parameters:
  - Vessel surface area
  - Average vessel diameter
  - Reduction of white surface areas due to emergence of episcleral vasculature and dilation of conjunctival vessels
  - Injection close to the limbus

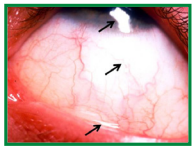
Methods: Slit Lamp Photography

Images were captured from nasal and temporal aspects with a Haag-Streit BX-900 slit lamp equipped with a Canon digital camera, with the following settings and modifications:

- Slit: wide open, setting 8
- Camera: perpendicular to the ocular surface
- Aperture: 4 (depth of field)
- Lamp: tilted 40º to the camera/viewing angle
- Light filters and diffusers:
  - Illumination polarizing filter, set at 90º to an image path polarizing filter
  - Illumination holographic diffuser

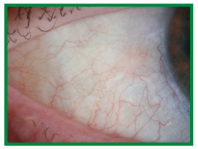


Without Polarized Filters



Specular Reflections (arrows)

With Polarized Filters

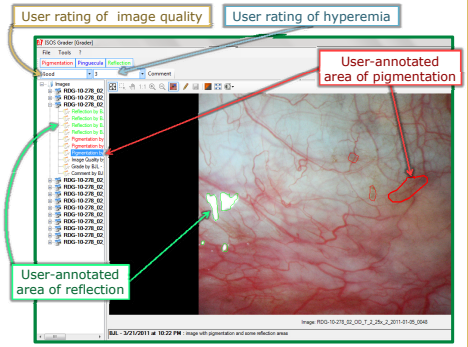


Matte Illumination

Methods: Software Development

ISOS consists of a suite of software components:

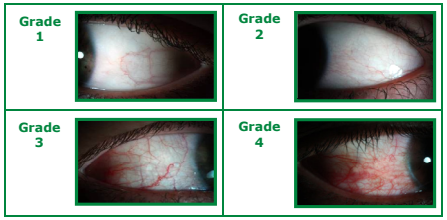
- **An image acquisition interface**
- **A data synchronizer**, which allows users to upload images to a secure server
- **A manual image grading interface**, where users can annotate images and grade hyperemia:



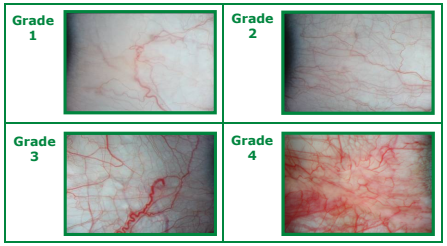
- **An automatic image processor** that detects vessels and computes a set of 50 shape and densitometry measurements, including:
  - Vessel surface area
  - Maximum vessel diameter
  - Average vessel diameter
- **An image reviewing interface** that allows users to easily compare manual and automatic measurements

Results: Manual Grading of Images

- >2000 images from 10x magnification were manually graded by 3 graders each to aid with software validation
  - Intra-grader consistency analyses are ongoing
  - Sample grade assignments are shown below

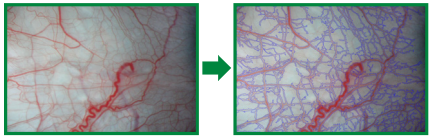


- >2000 images from 25x magnification were manually graded by 1 expert grader to aid with software development; sample grades are shown below



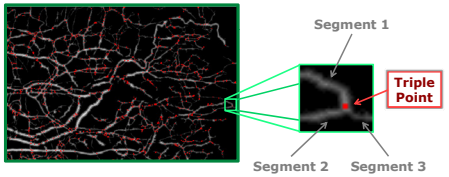
Results: Automatic Image Processing

- The automated image processing algorithm optimized the detection of the vessels and applied a skeletonization transform to allow measurement of vessel diameter and number of branch points



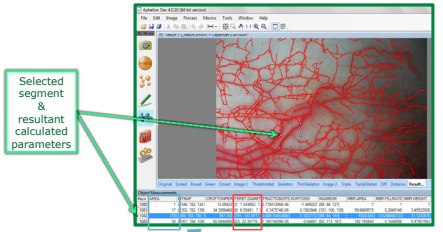
Grade 3, 25x — Skeletonized Vessels

- Automatic analysis detected "triple points" (intersections) to quantify vessel ramification (arborization):

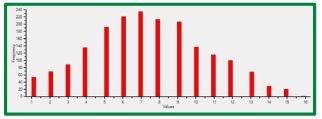


Results: Vessel Parameters

- Calculations were returned for each vessel segment:



- Automatic measurements yielded a variety of factors that were not evident to clinical observers, including:
  - vessel area
  - vessel diameter
  - total vessel length
  - vessel density (vessel area/total area), and
  - other shape factors
- Measurements could be plotted as histograms, as shown below for vessel segment radius:



Maximum Vessel Segment Radius, Pixels

- Image transformation, vessel detection, and parameter calculation required only a few seconds per image.

Discussion & Conclusions

- **Discussion:**
  - Preliminary results from this pilot study indicated that the ISOS suite can objectively measure changes in conjunctival hyperemia.
  - Only a few automated techniques for the assessment of hyperemia have been reported;[2,3] neither method yielded any information about vessel morphology
- **Conclusions:** These tools for the grading of conjunctival hyperemia are fast, reliable, accurate, not prone to human bias, and return information about vessels that was not available with other automated methods.

References & Disclosures

1. Schulze MM, Jones DA, Simpson TL. *Optom Vis Sci* 2007;84:976–983.
2. Wolffsohn JS. *Br J Ophthalmol* 2004;88:1434-14388.
3. Sorbara L, et al. *Contact Lens Anterior Eye* 2007:30:53-59.

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MJT, RO, GW, JW, DL, and AN are employees of Alcon.
RO and GW are named as inventors in the patent application.

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