Incremental nature of anterior eye grading scales determined by objective image analysis

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Aim: To use previously validated image analysis techniques to determine the incremental nature of printed subjective anterior eye grading scales.

Methods: A purpose designed computer program was written to detect edges using a 3 × 3 kernel and to extract colour planes in the selected area of an image. Annunziato and Efron pictorial, and CCLRU and Vistakon-Synoptik photographic grades of bulbar hyperaemia, palpebral hyperaemia roughness, and corneal staining were analysed.

Results: The increments of the grading scales were best described by a quadratic rather than a linear function. Edge detection and colour extraction image analysis for bulbar hyperaemia ($r^2 = 0.35–0.99$), palpebral hyperaemia ($r^2 = 0.71–0.99$), palpebral roughness ($r^2 = 0.30–0.94$), and corneal staining ($r^2 = 0.57–0.99$) correlated well with scale grades, although the increments varied in magnitude and direction between different scales. Repeated image analysis measures had a 95% confidence interval of between 0.02 (colour extraction) and 0.10 (edge detection) scale units (on a 0–4 scale).

Conclusions: The printed grading scales were more sensitive for grading features of low severity, but grades were not comparable between grading scales. Palpebral hyperaemia and staining grading is complicated by the variable presentations possible. Image analysis techniques are 6–35 times more repeatable than subjective grading, with a sensitivity of 1.2–2.8% of the scale.

METHODS

A purpose designed computer program was written (Labview and Vision Software, National Instruments, Austin, TX, USA) to objectively quantify changes in ocular physiology from stored image files of the anterior eye, using the techniques previously found to be most repeatable and robust to changes in luminance (fig 1):28

- Colour extraction: the relative intensity of the red, green, and blue colour planes was extracted and the ratio of red (for hyperaemia) or green (for staining) to overall intensity calculated.
- Edge detection: each pixel was compared to its neighbours and spatial filters used to alter pixel values with respect to variations in light intensity of their neighbourhood. Non-linear Sobel and Robert 3 × 3 filter kernels were used as previously identified.29 The number of pixels highlighted by a 15/256 greyscale threshold was divided by the total area to give the percentage of area detected as containing edges.

To examine the incremental nature of the Annunziato, Efron (Millennium Edition),4 and Vistakon-Synoptik grading scales, the printed images of bulbar hyperaemia,
palpebral hyperaemia (also referred to as papillary conjunctivitis), and corneal staining extent were scanned at 600 dpi stored in tagged image format (TIFF) and analysed. Vistakon-Synoptik palpebral conjunctivitis images were analysed selecting the palpebral hyperaemia and the area with reflections separately to distinguish between hyperaemia and roughness. Original 700×525 pixel JPEG images of bulbar hyperaemia, lid redness, and roughness (white light and sodium fluorescein) and corneal staining extent from the CCLRU grading scale were analysed. Compression of a non-glossy TIFF image into the high quality JPEG format of the CCLRU grading scale was found to not significantly affect the image analysis techniques used. An area of approximately 90 000 pixels (about 6.0 mm²) covering the area of interest was outlined manually three times for each scale grade.

Statistical analysis
Analysis of variance was used to examine overall effects and Tukey’s pairwise multiple comparison test to assess individual differences between scale grades. The results were fitted using linear ($y = mx+c$) and quadratic ($y = ax^2+bx+c$) functions, with the variance assessed by Pearson’s Product Moment Correlation. Image analysis discrimination was described by the standard deviation of repeated measures divided by the scale range.

RESULTS
Bulbar hyperaemia, palpebral hyperaemia roughness, and corneal staining grade images were best described by a quadratic rather than linear or other curve fitting functions (table 1). Edge detection and red colouration significantly differed with increasing bulbar hyperaemia scale grades ($p<0.001$), although for the Annunziato and Vistakon-Synoptik scales, the edge detection increments were smaller between higher grades (fig 2).

Red colouration increased with increasing palpebral hyperaemia scale grades ($p<0.001$), although the increments between grades were less regular with photographic scale (CCLRU and Vistakon-Synoptik) grades. However, for palpebral hyperaemia edges detected increased with the Efron scale ($F = 131.0, p<0.001$), decreased with the CCLRU scale ($F = 1.6×10^5, p<0.001$) and despite varying between grades, did not progress incrementally in the Annunziato ($F = 306.5, p<0.001$) and Vistakon-Synoptik ($F = 49.4, p<0.001$) scales (fig 3).

Palpebral roughness in photographic scales depicted by reflections (CCLRU and Vistakon-Synoptik) showed a general increase in edges detected and red colouration with increasing scale grades, although the increments between grades were non-uniform ($p<0.001$). Palpebral roughness depicted by fluorescein staining viewed with cobalt blue illumination through a Wratten filter (CCLRU), resulted in an increase in edges detected ($F = 264.2, p<0.001$) and a decrease in green colouration ($F = 778.9, p<0.001$) with increasing scale grade, although the highest grade shows an apparent decrease in severity (fig 4).

Green colouration increased with increasing corneal staining scale grade for the Annunziato ($F = 5763.8, p<0.001$) and Efron ($F = 1.3×10^7, p<0.001$) scales, but decreased with the CCLRU scale ($F = 306.5, p<0.001$) and did not progress incrementally with the Vistakon-Synoptik scale ($F = 665.9,$
p<0.001). Edges detection showed a general increase with increasing corneal staining grade (p<0.001), although there was not a systematic incremental change (fig 5).

The variability between repeat highlighting of the bulbar conjunctiva, palpebral conjunctiva and corneal area was generally small (table 2). There was no significant difference in discrimination between edge detection and colour extraction for each of the grading scales (2.8 (SD 3.8)% v 1.2 (SD 2.5)%, p = 0.15).

**DISCUSSION**

Validated image analysis techniques of edge detection and colour extraction showed that bulbar hyperaemia, palpebral hyperaemia roughness, and corneal staining grade images were quadratic rather than linear in nature. This results in the lower end of the scale being more sensitive (a smaller change between grades) than the upper end of the scale. As most eyes only have minimal hyperaemia and corneal staining this approach to grading scale design could be considered appropriate, but could lead to errors if clinicians interpolate between scale grade images to improve sensitivity. For example, if a clinician decides an eye had bulbar hyperaemia halfway between grade 0 and grade 1 on the Efron Millennium edition grading scale, they would note a grade of 0.50, whereas the grade identified by image analysis is 0.48 (using the quadratic fit of scale grade [x] against edge detection [y] = 2.5x^2+8.0x+3.9, r^2 = 0.99). Obviously the difference is only slight and could not be considered of clinical significance. However if the linear nature of grades 0–4 was followed by the clinician (y = 20.6x−9.4, r^2 = 0.99) the interpolated subjective grade would be 0.84. Although the difference is again within the variability of clinical grading and relative change will govern clinical decision making, individual grading strategies will increase the variance between individuals, and hence

Figure 3  Edge detection (filled symbols) and relative red colouration (open symbols) with grading scale images of palpebral hyperaemia. Error bars = 1 SD.

Figure 4  Edge detection (filled symbols) and relative red/green colouration (open symbols) with grading scale images of palpebral roughness. Error bars = 1 SD.

Figure 5  Edge detection (filled symbols) and relative green colouration (closed symbols) with grading scale images of corneal staining. Error bars = 1 SD.
decrease the statistical power of clinical research studies or the ability of clinicians to monitor small changes over time.

Edge detection techniques are local rather than global in nature and examine the surrounding pixels to determine the presence of edges (vessels or areas of staining). Colour extraction has face validity and examines global relative colouration (red for hyperaemia and green for staining). Both techniques were strongly correlated with increasing bulbar hyperaemia scale grades, although for higher grades the Annunziato and Vistakon-Synoptik scales rely on an increase in red colouration in isolation, rather than in combination with an increased number of blood vessels. As with the other scales analysed, grades are not comparable between grading scales as has previously been shown objectively. Hence clinicians should note the grading scale used when grading on clinical records.

Palpebral hyperaemia scale images were well described by colour extraction techniques. However, although all the scales are in agreement that red colouration increases with scale grade, with pictorial scales (Efron and Annunziato) blood vessels become more prominent with initial scale grades and are then replaced by increasing severity of papillae (both identified by edge detection). In comparison, blood vessels vary in prominence between photographic scale grades (CCLRU and Vistakon-Synoptik). Palpebral roughness in photographic scales was depicted by reflections (CCLRU and Vistakon-Synoptik) or by fluorescein staining viewed with cobalt blue illumination through a Wratten filter (CCLRU). The intensity, incidence angle, and type of illumination will affect the reflections as well as the apparent size and shape of the papillae, and therefore the non-uniform change with increasing photographic scale intensity may be expected. Highlighting the papillae with fluorescein would appear a more appropriate method for determining palpebral roughness as previously described, causing an increase in edges detected and a decrease in the fluorescein coverage, despite an apparent decrease in severity with the highest CCLRU scale grade. Further investigation of the palpebral response to stimuli such as antigens, toxic chemicals, and mechanical effects is required to determine whether the

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<th>Correlation ($r^2$) between image grade and edge detection or relative colouration image analysis for the Annunziato, Efron, CCLRU, and Vistakon-Synoptik grading scales</th>
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<th>Table 2</th>
<th>Image analysis standard deviation (SD) of repeated measures and discrimination (SD of repeated measures divided by the scale range) of edge detection (% coverage) and relative colouration (%) for the Annunziato, Efron, CCLRU, and Vistakon-Synoptik grading scales</th>
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<tr>
<td>Corneal staining</td>
<td>Annunziato 0.08 0.01 0.6 0.4</td>
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response is similar and how it should be best depicted or photographed for grading purposes.

Staining can differ in intensity (dependent on factors such as the amount of fluorescein instilled, tear film production and drainage, depth of the wound), area, shape, and segmentation. Therefore an epithelial scratch, punctate staining, and confluent ulceration could all have similar intensity of green colouration and edge detected area. All the staining (extent) scales analysed, except the Vistakon-Synoptik scale, depicted more than one type of staining and therefore assessing the ability of image analysis measures to determine the severity of staining is complicated. A general increase in edges detected with increasing scale grade was seen in all the scales analysed, although the change in green colouration was more variable. However, image analysis would have merit in monitoring changes in individual patients with time and the computer could also count the number of segments identified (to identify between punctate and confluent type staining), provide a ratio of the longest to the shortest axis (to give an indication of shape) in addition to the measures of edges detected (a stable indicator of area) and green colouration (stain intensity).

The image analysis techniques were highly repeatable for both pictorial and photographic scale grades, having a 95% confidence interval of between 0.02 (colour extraction) and 0.10 (edge detection values) units (on a 0–4 scale). Compared with reported values of clinician subjective grading variability using these grading scales, image analysis techniques are approximately 6–35 times more repeatable, with a sensitivity of 2.8 to 1.2% of the scale (respectively). This study again highlights the high repeatability of image analysis techniques and their ability to assess a range of indicators of anterior ocular physiology.

The occasional apparent reversal in severity in several of the scales could arise from deficiencies in the scale images, such as the lack of an appropriate photographic image taken with similar perspective and illumination or from scale designers considering a range of feature characteristics to assess the grade of an image. Image analysis of a particular feature may require the assessment of a number of characteristics to provide a more simplistic condition grade, comparable with (although having better repeatability and sensitivity than) subjective techniques. There has been much discussion and debate in the literature concerning the merits and relative difficulties of constructing photographic versus pictorial grading scales, with the suggestion that painted grading scales, although not as realistic as photographs, allow more control in depicting incremental increases in severity that are clear and unambiguous to the clinician. This study generally supports the notion that pictorial grading scales have more incremental increases between grades than photographic scales, although image analysis cannot assess the realism of an image. In the future, image analysis techniques could allow grading of real time or stored images and comparison with population norms without incurring the limitation of photographic or pictorial subjective grading.

In conclusion, the printed grading scales analysed were quadratic in nature, having a higher sensitivity for grading features of low severity. Grading features such as palpebral hyperaemia, palpebral roughness, and corneal staining is complex and there is a compromise between the simplicity of a single scale and the ability to fully describe and monitor changes in the feature. Edge detection and colour extraction image analysis techniques are highly repeatable and offer the potential for more repeatable and sensitive grading than using printed subjective grading scales.

REFERENCES

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