QUANTITATIVE ANALYSIS OF RETROILLUMINATION IMAGES

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SUMMARY

We have developed a semi-automated image processing system for analysis and evaluation of retroillumination images. This paper describes methods used to compensate for illumination variations in the images, separation of data into cataractous and non-cataractous portions, how quantitative measurements are made and how they assess the pathological condition. In addition to the traditional area measurement, this system computes the net integral of density and several measurements involving the location of the opacity in relation to the pupillary margin. The computer measures of area, integral of density, area centrality, weighted area, density centrality and weighted density provide more data than previously described systems. Data produced by this interactive and automated system can be used in studies of posterior subcapsular and cortical cataracts, and to study the effect of these opacities on vision.

The goal of our work has been the development of computer-based instrumentation for use in the study of ocular pathology. The combination of reproducibility, speed, ease of operation, and relative ease at letting the operator/ophthalmologist interact with the computer can significantly enhance analysis of ophthalmic images. Our main emphasis has been computer-based algorithms specifically designed around the anterior eye segment and studies of cataracts. There are a number of devices used to observe cataracts, each requiring customised software tailored around the information content observed with that device. The methods previously described for the Scheimpflug, for example, provide a valuable assessment of nuclear cataracts.[1] In fact, the Scheimpflug has been described as one of the best devices for studying nuclear cataract.[2] In this article, we examine retroillumination imaging in the study and assessment of posterior subcapsular (PSC) and cortical opacities.

The difficulties in automatic assessment of retroillumination images are many, the most notable being the uneven illumination in the images. Sparrow *et al.*[3] noted that the variability can include photographic variability and flash intensity, variability between photographic systems, variability of the light source for CCD cameras, variability of the amount of light entering the eye through different-sized pupils, and variability in the amount of light reflected off the retina. The variability has been measured and documented by Chylack *et al.*[4] who found a high measured variance with repeated image capture using the Neitz-CTR camera. Improvements have been made to the device to raise the quality of image capture. Kawara and Obazawa[5] pointed out a technique utilising polarising filters to help eliminate the corneal reflection. More recently, fixation lights have been used to increase reproducibility of the

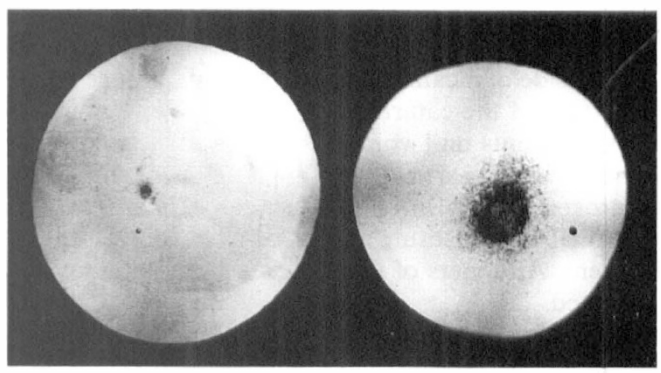

Fig. 1. *The image on the left shows one type of uneven illumination occurring with the Oxford retroillumination system. This type of uneven illumination is characterised by the 'light bulb' effect seen on the upper right-hand portion of the image. The photograph on the right shows the aberrant and more characteristic 'Maltese cross' pattern found commonly with retroillumination systems. This image is from a Neitz-Kawara retroillumination system.*

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image capture.[2] Despite these improvements, images produced by the current retroillumination devices contain significant background variations. Fig. 1 shows several examples of uneven illumination. Removal of these variations is left to the realm of rigorous computer-based image processing.

Several automated and semi-automated techniques for analysis of retroillumination images have been published in the literature.[3,6–12] Each of these describes techniques for analysis of images as well as the measurements found useful in describing cataract pathology. Nearly all retroillumination image analysis studies make the assumption that there is a direct correlation between area, or size, of the cataract and the extent of cataract pathology. Some of these studies have also measured a type of density function.[3,4] It is clear that an assessment of cataract using a retroillumination image should include measures of area and density. We have extended this by obtaining the density measure through methods not previously used. Additionally, we present a measure of how centrally located the density and area measures are with respect to the pupillary margin.

ACQUISITION OF IMAGES

In principle, our software was designed to handle retroillumination images from any source. There are, however, some restrictions that must be placed on the data quality before analysis should be done. Low-quality data will result in inaccurate image analysis. A major source of data error is under- or over-exposure of images. Adjusting the system gain can help to prevent many of these cases. The image should also contain reasonably good contrast, meaning that the range of intensity values should be fairly wide. Currently, our software does not handle *severe* gradients in the background illumination level. In general, this might be described as the background on any side of a cataract being the same grey level as a portion of the cataract.

All patients and volunteers for data seen in this article were participants in a clinical protocol approved by the intramural research board of the National Eye Institute and each gave full informed consent. All tenets of the Helsinki Declaration were followed.

We acquire images with the Oxford CCD retroillumination system (Marcher Enterprises, UK). Images are currently transferred from the host PC to a Macintosh Quadra computer (Apple Computer Inc., CA, USA). Upon transfer from the PC to the Macintosh, we properly scale the data into square pixels. We have devised several histogram-based tests to ascertain the image quality. The current software supplied by Marcher provides no feedback to the operator on the image quality. It is, therefore, a current goal of ours to acquire images directly with a frame grabber on the Macintosh. Doing this will allow on-line exposure tests and will greatly enhance the quality of the data acquired. Fig. 2 shows types and examples of feedback which can help lead tc production of higher-quality data.

USER INTERFACE

Our software development involved modifications to the public domain NIH-Image program. This is a Macintosh-based image processing package. The unmodified NIH-Image software is available to download via internet anonymous file transfer protocol at zippy.nimh.nih.gov [128.231.98.32]. The software was developed by Wayne Rasband of the National Institutes of Health (E-mail address: wayne@helix.nih.gov). The program has a full graphical user interface including the standard Macintosh menubar, tool icons, and numerous image processing operations. Fig. 3 shows the application as it appears during use, along with a typical cataract image ready for evaluation.

SEGMENTATION AND IDENTIFICATION OF CATARACT

The principal factor which hinders identification of cataract is the uneven illumination described above. Applying a simple threshold to segment the image into cataract and non-cataractous portions does not function well. The general model for the threshold segmentation algorithm depends upon the image being inherently bimodal in nature.[13,14] This is not the case with retroillumination images, since background levels can rise to grey levels corresponding to cataract. Several authors have devised ingenious methods to compensate for this by dividing the lens into small regions, or a grid network.[10,11] Utilising this method allows for a regional identification which is not greatly disrupted by a global (image-wide) distortion pattern or uneven illumination. Each of these authors reports success in analysing images by these methods.

Before we segment our images, we use a two dimensional rolling-ball background subtraction routine to correct uneven background levels.[15] Similar routines have been described and applied to retroillumination images by the Nuffield Laboratory of Ophthalmology in England.[16] For each pixel in the image, software extends out from that point and computes what the background level actually should be. After the image is corrected, it is segmented into cataractous and non-cataractous areas. Applying these reproducible computer algorithms is considered a necessary first step leading to cataract identification. The Macintosh computer, the graphical user interface and our software provide a number of image editing tools, including a freehand

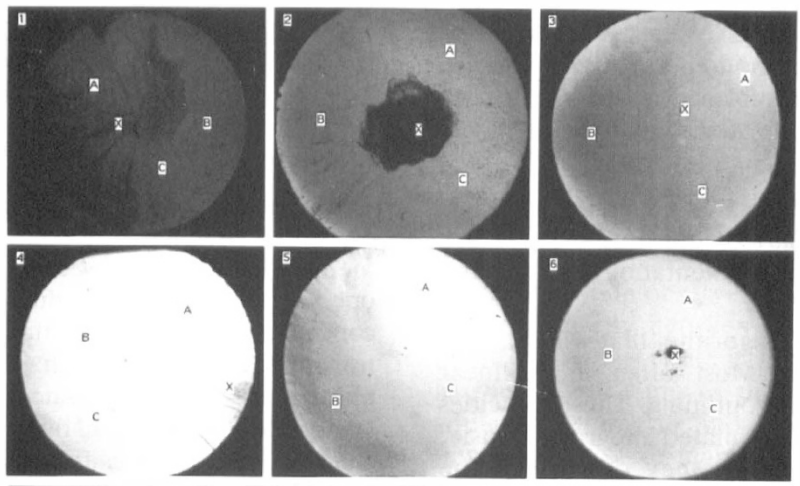

Image number	1	2	3	4	5	6
Histogram max minus min.	50	99	104	147	188	156
Background level at point A	218	171	117	28	42	101
Background level at point B	212	195	200	61	179	143
Background level at point C	218	163	162	92	107	116
Max gradient (%) between points ABC	2.8	19.6	70.9	228.5	326.2	41.5
Value of cataract at point X	236	250	182	109	-	216

Fig. 2. *Types and examples of feedback which can help in the production of higher-quality data. The points labelled A, B and C are arbitrary background test points. The X in each image is a point which is cataractous. Image 1 is visibly poor and the testing shows only 50 grey levels in the data. Image 2 appears acceptable to the eye; however, the cataract data seem underexposed at level 250 (black) and the entire image still has fewer than 100 grey levels. Image 3 has a gradient severe enough that some of the background points are higher in value than the cataract. Image 4 appears acceptable to the eye but testing reveals a substantial gradient. Image 5 has a gradient visible to the eye and very severe (326%). Image 6 is an acceptable image. It has a wide range of values, only a moderate gradient and very good separation of cataractous pixel levels from the background pixel levels. Acceptable parameter levels for each image differ and can depend upon factors within the image as well as on the severity of the cataract.*

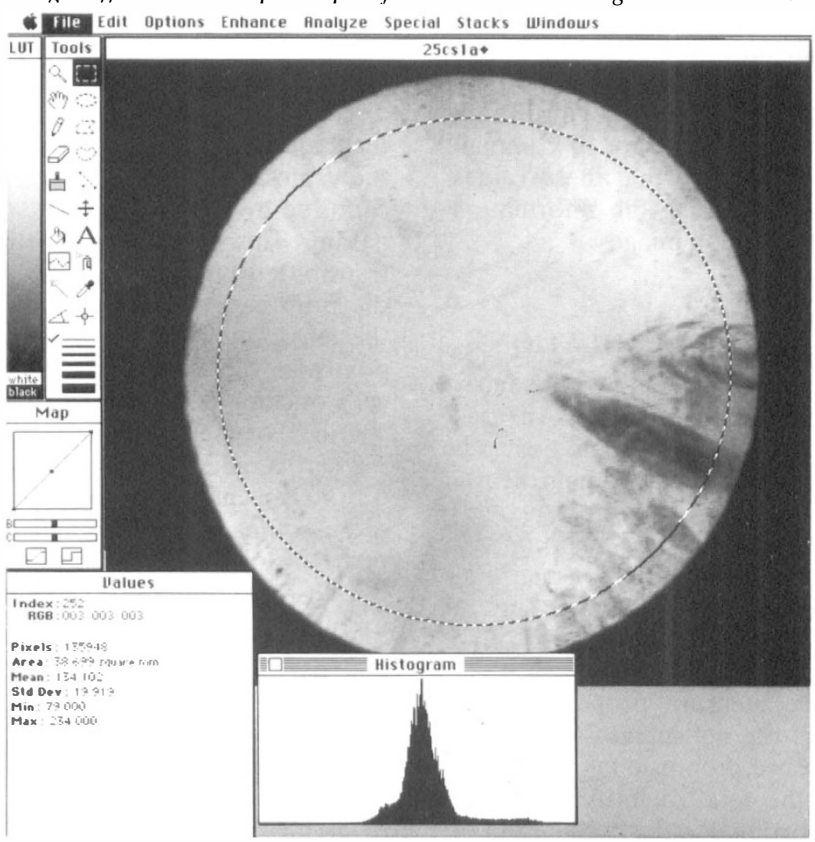

Fig. 3. *Our application as it appears during use, showing a typical cataract image ready for evaluation. The region of interest used for analysis is seen within the image.*

outliner, eraser and magnifier. We allow the operator to interact with the computer at this point and perform additions and subtractions of areas with these tools. Our philosophy for allowing editing is as follows:

1. We do not consider isolated vacuoles, retrodots and waterclefts as part of our study. These are often identified by the segmentation software and need to be deleted.
2. There is no computer algorithm that will segment every image exactly. Most often, faint linear opacities need manual outlining. These opacities tend not to affect the calculated integrated density value by much; however, they do add to the overall cataract area measurement.
3. Software can not differentiate between cortical and PSC opacities. A manual override can let the operator exclude PSC opacities when studying cortical opacities, and vice versa.
4. Manual tracing by experienced operators has been demonstrated to be reproducible.[6]

Other software which locates or identifies the cataract has been the main emphasis of literature involving retroillumination images.[10,11,16] It has been our goal to extend beyond the identification stage. As retroillumination imaging is improved, and the background subtraction routines become specially designed around the problems and conditions of these images, identification of cataract will become an easier task. Simple identification of cataract in an image leaves us with an incomplete assessment of the pathological condition which we are studying. To fill this void, we have developed software to compute several additional values. We feel that these values are the next step in fully utilising the information content seen in retroillumination images.

INTEGRATED DENSITY CALCULATION

Once the cataract in an image is identified it is fairly easy to measure an area of the disease. An area measure alone is insufficient because some opacities are quite dark (dense) while others remain nearly clear or transparent. We must therefore extend beyond area measures and try to quantify the density of the opacity. The computation or measurement of a density value must be done in such a manner that the values used correlate with the underlying pathology. The logarithmic optical density scale is a scientific measure proportional to concentration. Likewise, the net integral of density value is a scientific measure proportional to mass. It is our hypothesis that the total quantity (mass) of cataract is directly proportional to the net integral of optical densities. The principles of densitometry provide this basis.[17] By Beer's law, the density of a point is the log ratio of incident light upon it and transmitted light through it:

$$\mathrm{OD}[i,j] = \log_{10}\left(\frac{I_0[i,j]}{I[i,j]}\right)$$

There are several standard methods used to find the density of an object or a point on an image. The first method is commonly used in instrumentation developed for densitometry. Scanning densitometers have controlled or known illumination levels and measure transmitted light through an object such as a photographic negative. Since both the incident and transmitted light are known quantities, the device can then compute this ratio directly. With regard to retroillumination, a pure ratio technique is impossible since we can not measure the retroilluminated light, on a two-dimensional basis, immediately before it passes through the lens optics. Were a lens removed, it would be possible to pass a controlled or known illumination level through the lens capsule, then to measure light transmitted through it. This method of computing densities has been done with the isolated chick lens.[18] The second technique to determine density of a point involves correlating data to known optical densities by using a set of standards, such as a neutral density step tablet. Some instruments provide these standards internally in the optical path of the instrument. Unfortunately, the background illumination level in a retroillumination image may vary by such a large amount that the error could make such a correlation useless.

Despite the limitations described above, we have discovered a method which allows us to use the ratio technique to calibrate an image into densities. Half the values needed for the ratio are the actual values captured by the video camera/frame grabber combination. This would be the light which has been transmitted through the lens. The other portion of the ratio is defined as retroilluminated light before the lens optics. Instead of measuring this light, the pointwise values of light can be determined analytically or computationally by a background subtraction routine. For each pixel in the image, software extends outward a radius and computes what the background for that specific point would be.[15] The calculated OD of any point in the two-dimensional image is based upon the log scaling of the unmodified image divided by the background level found by this routine. For example:

$$\text{Calculated OD } [i,j] = \log_{10}\left(\frac{\text{Pixel } [i,j]}{\text{Background } [i,j]}\right)$$

The integral of cataract density values can then be computed as the sum of density values for the opacity or as mean calculated OD value multiplied by the number of cataractous pixels. This value represents the integral of cataract densities in the lens:

$$\text{Net integral of cataract} = \sum_{i=1}^{n} \text{OD}[i, j] = n \times \bar{\mu}$$

where n is the number of pixels considered cataract and $\bar{\mu}$ is the mean of these pixels in calculated OD units.

CENTRALITY AND WEIGHTED MEASURES OF THE OPACITY

The task of correlating how and why an opacity causes visual disability is more complex than using methods such as Snellen acuity, contrast sensitivity and area of the opacity.[19] There is a clear need for tests and measurements which more closely evaluate the degree of pathology as well as the effects of the disease. The integrated density value is one way to measure the opacity. Although this degree of density will probably correlate well with degree of disability, location of the opacity might also contribute to visual disability. It is a hypothesis of ours that centrally located opacities will affect vision to a larger extent than peripheral opacities. The central region of the lens is the most vital portion because the middle contains the optical focal point. In addition to this, central areas of the lens will be the portions which focus light onto the macula under all lighting conditions.

An attempt to model how crucial the centre of the lens (or an image of it) might be, must take into account sources of error. It is likely that there is some error (a spatial disparity) in assuming that the centre of the dilated pupil seen in a retroillumination image corresponds to the focal point of the lens. Retroillumination images are captured when light from the device reflects near the optic nerve and produces a good view when observed from the frontal plane. A spatial disparity between the image and the focal point of the lens could easily increase and decrease as the operator moves the optical instrumentation while attempting to find a suitable image. For our purposes the error margin is unknown, but fixation lights help in producing consistent and higher-quality images.[2,20] Further contributors of error might include improper frontal plane acquisition of the image (such as a tilt in the relationship of the eye to the optics), saccadic movements, difficulties in dilation of the pupil, ability of the patient to look around the opacity, and other factors. Since it is impossible to measure all error sources with our model, the centre of the dilated pupil seen in each retroillumination image serves only as an approximation.

Our basic model for computing centrality values overcomes many of the error sources described

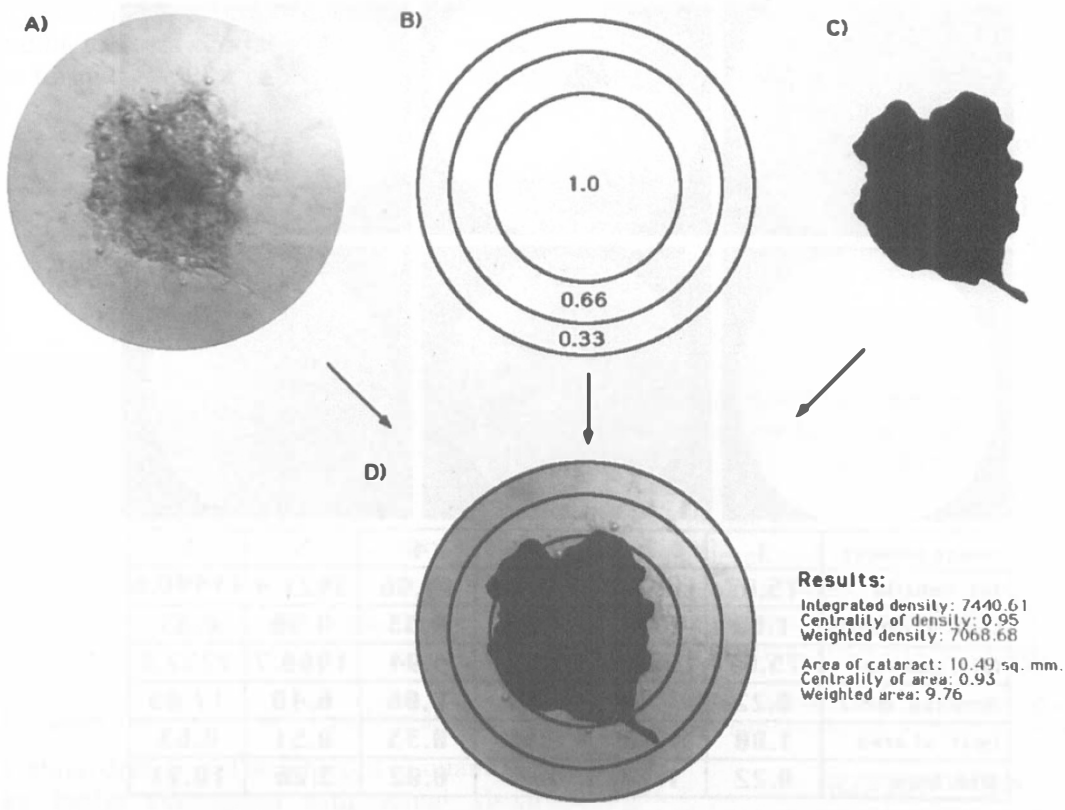

Fig. 4. *A graphical representation of the centrality function. Image A contains the data to be measured. Image B shows the regional weighting factors which define how central the opacity is. Each of the regions contains one-third the total area. Image C shows a mask of pixels which are cataractous. Finally, image D is an overlay of images A-C.*

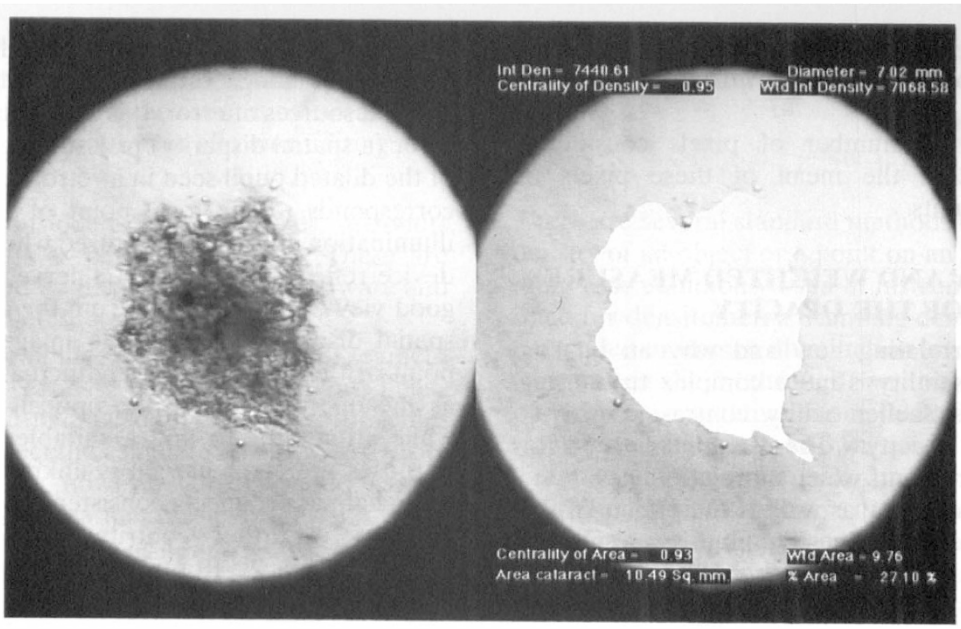

Fig. 5. *The operator is presented with an original image and an analysed image after running the software. The original image input data are seen on the left. The fully analysed image and results, as presented to the physician/operator, are seen on the right.*

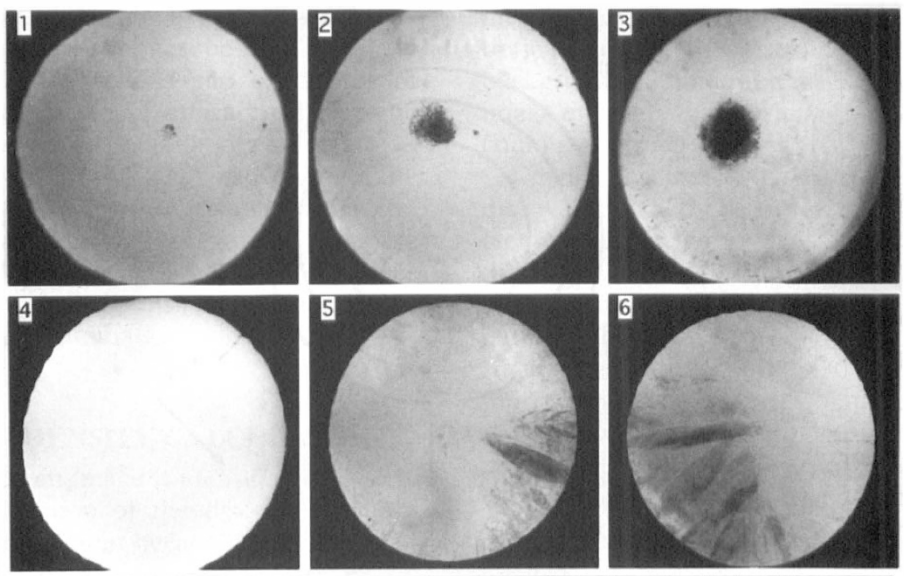

Image number	1	2	3	4	5	6
Int. Density	75.07	1980.0	7353.6	14.96	3921.4	11480.6
Cent. of density	1.00	1.00	1.00	0.33	0.50	0.63
Wtd. density	75.07	1980.0	7353.6	4.94	1960.7	7232.8
Area (sq. mm.)	0.22	1.79	3.55	0.06	6.40	17.00
Cent. of area	1.00	1.00	0.98	0.33	0.51	0.63
Wtd. area	0.22	1.79	3.48	0.02	3.26	10.71

Fig. 6. *Across the top of the figure are posterior subcapsular images in varying grades from faint to severe. Below this are cortical opacities with a similar pattern of pathology. The table at the bottom shows the analysis results for all the images. Note how centrality differs greatly between PSC and cortical cataract. Image 6 shows up as a large cataract but not highly dense. Image 3 is much smaller in area than image 6 but is more central and is very dense. The weighted density for image 3 is therefore higher in value than that of image 6.*

above. The model divides the lens into three areas, each of which corresponds to one-third of the total area studied. The total area for our studies encompasses a 7 mm diameter circle placed at the approximate centre of the lens. The 7 mm diameter circular area is used even when dilation makes the pupil larger than this. A 7 mm diameter area is associated with a widely dilated pupil, or highly scotopic conditions.[21] The first measurement area extends out from the centre until one-third the total area is reached. The first region is therefore fairly large in diameter (4 mm). It will undoubtedly include portions of the lens which focus light on the macula even if a fairly large spatial disparity exists. The 4 mm diameter is also the approximate size of a normal adult pupil in ordinary room light, or usual photopic diameter.[22] This region will have the largest effect on vision and will therefore be assigned a high value for what we call a weighting factor. This weighting factor represents an assignment or value or usefulness to a particular region in the image. Peripheral regions of the lens receive a small but still existent (non-zero) weight. Fig. 4 helps explain the concept of centrality.

Weighting factors are multiplied by the regional percentage of total area or total density, then summed to produce an overall rating for the lens. As a first test of our centrality model, we apply a stepwise linear decrease in weighting factors. The weighting factors used are 1.0, 0.66 and 0.33 corresponding to areas central to peripheral respectively. The formula used for centrality of area can be shown as:

$$\text{Centrality of area} = \sum_{n=1}^{3} \frac{\text{Cataract in region } n}{\text{Total cataract}} \times \text{Regional weighting factor}$$

Similarly, density centrality can be calculated as:

$$\text{Centrality of density} = \sum_{n=1}^{3} \frac{\text{Density in region } n}{\text{Total}} \times \text{Regional weighting factor}$$

Centrality of area and density are useful measures relating to location of the opacity. In addition to these two values, weighted values for area and density are also calculated. This is done by multiplying the centrality values by the corresponding measure of area or density:

$$\text{Weighted area} = \text{Cataractous area} \times \text{Centrality of area}$$

and:

$$\text{Weighted density} = \text{Integrated density} \times \text{Centrality of density}$$

The weighted density and weighted area quantities may have better correlation with actual visual disability than area and density alone.

It is likely that the model can be improved with sufficient testing and perhaps modelled more closely to physiological events. For example, we could describe the innermost ring as an area associated with photopic vision. A cataract in this inner area might be associated with and correlate well with visual disability during photopic conditions. Outer rings might be associated with scotopic conditions. Despite our model being a developing model, the type of values produced by it may present a new and useful numerical quantity to assess how the opacity disrupts or affects vision. It is felt that this represents a new step in the evaluation of cataract pathology.

PROGRAM OUTPUT AND RESULTANT DATA

When the operator finishes running the analysis software, a side-by-side view of the original data and analysed image with results are presented. Fig. 5 shows an image before and after analysis. Resultant data from the analysed image can then be saved into a database and spreadsheet for later retrieval and statistical analysis. To demonstrate the ability of the software in producing meaningful results, Fig. 6 shows a series of images with results. This six-image data set covers posterior and cortical opacities as well as a wide range of pathological conditions. Complete details concerning the effectiveness of the system are currently under evaluation for presentation.

CONCLUSION

We have described a theoretical basis for assessing cataract pathology via computerised analysis and measurement. These measurements differ from both the traditional ocular assessments (visual acuity, contrast sensitivity) and the standard single quantity measured by other retroillumination analysis systems (area). The system described by us produces five additional values from the retroillumination image which may help to assess the state of cataract pathology. The area measure describes how widely spread the disease is. The integrated density value, by theory, correlates with a measure of mass performed on the cataractous region of the lens. The two centrality measures provide useful information as to how location of an opacity may affect or interfere with vision. Weighted area and density show promise for correlation of the opacity with other visual function testing. Taken together, the system described is useful in the evaluation of a patient on a single visit basis; alternatively the information can be numerically tracked for the sake of a longitudinal (visit to visit) study.

Key words: Densitometry, Image processing, NIH-image, Ophthalmic instrumentation, Retroillumination.

REFERENCES

1. Vivino MA, Chintalagiri S, Trus B, Datiles M. Development of a Scheimpflug slitlamp camera system for quantitative densitometric analysis. Eye 1993; 7:791–8.
2. Brown NAP, Bron AJ, Sparrow JM. Methods for

evaluation of lens changes. Int Ophthalmol 1988; 12:229–35.
3. Sparrow JM, Brown NAP, Shun-Shin GA, Bron AJ. The Oxford modular cataract image analysis system. Eye 1990;4:638–48.
4. Chylack LT, Rosner B, Cheng HM, *et al.* Sources of variance in the objective documentation of human cataractous change with Topcon SL-45 and Neitz-CTR retroillumination photography and computerised image analysis. Curr Eye Res 1987;6:1381–90.
5. Kawara T, Obazawa H. A new method for retroillumination photography of cataractous lens opacities. Am J Ophthalmol 1980;90:186–9.
6. Datiles MB, Podgor MJ, Sperduto RD, *et al.* Measurement error in assessing the size of posterior subcapsular cataracts from retroillumination photographs. Invest Ophthalmol Vis Sci 1989;30:1848-54.
7. Hanna KJ, Tarassenko L. Tracking cataract by the four-line method. Image Vis Comput 1989;7:57–62.
8. Mayer H. Application of digital image analysis in cataract retroillumination photography. Ophthalmic Res 1987;19:266–70.
9. Maclean H, Taylor CJ. An objective staging for cortical cataract *in vivo* aided by pattern-analysing computer. Exp Eye Res 1981;33:597–602.
10. Wolfe JK, Chylack LT. Objective measurement of cortical and subcapsular opacification in retroillumination photographs. Ophthalmic Res 1990;22(Suppl 1):62–7.
11. Miyauchi A, Mukai S, Sakamoto Y. A new analysis method for cataractous images taken by retroillumination photography. Ophthalmic Res 1990;22(Suppl 1):74–7.
12. Kawara T, Obazawa H. Quantitative evaluation of cataractous lens opacities with retroillumination photography. Jpn J Clin Ophthalmol 1979;33;21–6.
13. Gonzalez RC, Wintz P. Digital image processing, 2nd ed. Reading Mass.: Addison-Wesley, 1987.
14. Ridler TW, Calvard S. Picture thresholding using an iterative selection method. IEEE Trans Syst Man Cybernet 1978;8:630–2.
15. Sternberg S. Biomedical image processing. IEEE Comput 1983;16:22–34.
16. Harris ML, Hanna KJ, Shun-Shin GA, Holden R, Brown NAP. Analysis of retroillumination photographs for use in longitudinal studies of cataract. Eye 1993; 7:572-7.
17. Waser J. Quantitative chemistry. New York: Benjamin, 1964:226–9.
18. Babizhayev MA, Zhukotskii AV, Sologub AA. Image analysis of the lens opacities induced in developing chick embryo by glucocorticoid. Exp Eye Res 1992;55:521–37.
19. Brown NAP. The morphology of cataract and visual performance. Eye 1993;7:63–7.
20. Brown NAP. The Oxford retro-illumination cataract recording camera: a new instrument. J Audiovis Media Med 1988;11:58–60.
21. Newman M. Visual acuity. In: Moses RA, editor. Adler's physiology of the eye: clinical application, 6th ed. St Louis: CV Mosby, 1975:501.
22. Moses R. The iris and the pupil. In: Moses RA, editor. Adler's physiology of the eye: clinical application, 6th ed. St Louis: CV Mosby, 1975:332.