The Lens Opacities Classification System III

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- Objective.—To develop the Lens Opacities Classification System III (LOCS III) to overcome the limitations inherent in lens classification using LOCS II. These limitations include unequal intervals between standards, only one standard for color grading, use of integer grading, and wide 95% tolerance limits.

- Design and Results.—The LOCS III contains an expanded set of standards that were selected from the Longitudinal Study of Cataract slide library at the Center for Clinical Cataract Research, Boston, Mass. It consists of six slitlamp images for grading nuclear color (NC) and nuclear opalescence (NO), five retrolumination images for grading cortical cataract (C), and five retrolumination images for grading posterior subcapsular (P) cataract. Cataract severity is graded on a decimal scale, and the standards have regularly spaced intervals on a decimal scale. The 95% tolerance limits are reduced from 2.0 for each class with LOCS II to 0.7 for nuclear opalescence, 0.7 for nuclear color, 0.5 for cortical cataract, and 1.0 for posterior subcapsular cataract with the LOCS III, with excellent interobserver agreement.

- Conclusion.—The LOCS III is an improved LOCS system for grading slit-lamp and retrolumination images of age-related cataract.

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The Lens Opacities Classification System II (LOCS II) was introduced in 1989,1 was validated by other investigators in 1989 and 1991,2,3 and has been used in epidemiologic studies of the natural history of age-related cataract. It has also been compared with objective means of measuring cataract type and cataract growth,4 used to evaluate the effects of cataract on visual function,5,6 adopted in clinical trials of antacataract and potentially cataractogenic7 drugs or diseases,8 and compared with other systems of cataract classification.9-12 The LOCS II is a simple classification system based on a set of standard color photographic transparencies of cortical cataract (C), nuclear opalescence (NO), posterior subcapsular cataract (P), and nuclear color (NC) that can be used as references to classify lens opacities at the slit-lamp or in standardized lens photographs.

Although LOCS II has proven valuable in several clinical research applications, it does have several limitations: (1) The scale for NC grading is small and coarse. (2) The guidelines for color grading are not linked to parameters of color (ie, hue, purity, and luminance) and have been difficult to teach to others. (3) The early stages of nuclear cataract (NO in the LOCS II system) are underrepresented. (4) The scaling intervals on all scales are unequal, only indirectly related to objective measurements, and often too broad to allow delineation of small changes in cataract severity. (5) The scale for P grading underrepresents early P change, and the extent of the cataract in two of the standards is difficult to define. (6) The 95% tolerance limits are large because LOCS II grading employs an integer scale.

We have attempted to rectify these deficiencies in the LOCS II by developing LOCS III. We have (1) expanded the scale for NO grading from three steps (using one standard reference) to six steps (with five standards); (2) linked the subjective scaling of NO to two objective measures of color (purity and the Commission Internationale de l'Éclairage [CIE] X chromaticity coordinate [1931 scale]) and confirmed that the ranking by eye and by fast spectral scanning colorimetry are concordant; (3) expanded the scale for NO so that the early stages of nuclear cataract are better represented; (4) established objective bases for the selection of the interval steps for the grading of different cataract features; (5) used equal scaling intervals for measuring NO and NC and intervals between the reference standards for the grading of C and P that are based on a monotonic function; (6) expanded the lower end of the P scale to better represent the early stages of P formation; and (7) used the decimal rather than integer grading to reduce the size of the 95% tolerance limits.

Recently, Bailey et al13 and others14,15 have shown that adopting a finer grading system can have substantial advantages. Grading in finer incremental steps lowers the observed concordance (ie, the frequency of perfect agreement between independent observers), but it can dramatically increase the sensitivity to change in the parameter or characteristics being assessed. Finer scales may be easily adopted in cataract grading by decimalizing the scale so that the observer interpolates in 0.1-unit steps between the standard photographic reference images that represent integer values. This type of grading system has been incorporated into LOCS III.

We believe the LOCS III will find useful application in long-term studies of age-related changes and short-term clinical trials of antacataract drugs and drugs with cataractogenic potential. The purpose of this article is to describe LOCS III and to illustrate some of its features.

MATERIALS AND METHODS
Selection of LOCS III Standard Images
For NO and NC.—From the large library of Lens Opacities Case-Control Study II photographs at the Center for Clinical Cataract Research, Boston, Mass, we selected 3×3-cm color transparencies (Ektachrome ASA 200, Arch Ophthalmol—Vol 111, June 1993

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The grader decides in which interval the unknown image falls; the severity of the opacity must be more than that in the lower standard and less than or equal to that in the next higher standard. Each interval between adjacent reference standards is imagined to be divided into 10 equal parts, each being 0.1 of an interval unit. For each cataract type or for NC, higher grading scores indicate greater severity. The scale ranges from 0.1 (clear or colorless) to 5.9 (very opaque or brownish in cases of NO and NC). A decimal grade, using 0.1-unit intervals, is then assigned to the opacity. The decimal grade should reflect the position of the unknown in the standard interval; for example a grade of 2.5 would mean that the severity of the cataract is judged to be midway between standards 2 and 3. If the severity of the cataract is equal to that in standard image 3, the grade is 3.0. If it is less than that shown in standard image 3 but more than midway through the interval, the score would range from 2.0 to 2.9. Similarly, a score of 1.1 to 2.0 is assigned if the cataract is greater than that in standard 1, but less than or equal to that shown in standard 2. The most severe cataract shown in the reference standards is 5 for C and 6 for NC and NO. The highest score for each grade should be 5.9 and 6.9, respectively. Thus, the assigned score ranges from 0.1 to 5.9 or 6.9.

To Grade NO.—Nuclear opalescence is graded by comparing the colored slit-lamp image to be graded with the standard nuclear images (standards 1 through 6). The average opalescence of the entire nucleus in the lens being evaluated is compared with that of the opalescence in each of the standards. The grader then assigns a decimal grade to reflect the position of the unknown within the appropriate standard interval. For example, if the average opalescence of the unknown is slightly greater than standard 1 but definitely less than standard 2, the grader might assign a grade of 1.2. For grading purposes, the nuclear area extends between the anterior and posterior surfaces of the lens, and the opalescence is measured at the edge of the nucleus. This technique is applied to each slice of the lens, and the central area, the equatorial area, and the periphery are graded separately. The central area is graded by comparing the nuclear images with the standard 1 through 6 in the NO column. The equatorial area is graded in the same manner. The peripheral area is graded by comparing the nuclear images with the standard 1 through 6 in the NO column. The central area is graded by comparing the nuclear images with the standard 1 through 6 in the NO column.

Fig. 2.—Relationship between grades of nuclear color (NC) with the subjective Lens Opacities Classification System III and two objective measures: purity and the X chromaticity coordinate of the 1931 Commission Internationale de l'Eclairage (CIE). The relationship between the subjective measure and the two objective measures is highly linear.
may range from 0.1 to 5.9. Opacities visible only in the posteriorly focused image are graded as cortical if they are closer to the periphery than to the center of the pupil unless they are connected to a central opacity. In this case, the entire opacity is graded as P. Isolated water cloths, vacuoles, retrodisks, lamellar separations, and sutural opacities are ignored (not graded). If, however, such irregularities are clustered and organized into discrete arrays, they should be graded as C. In many retroillumination images, the peripheral portions of the image manifest soft, radially oriented areas of variable contrast—almost like very soft opacities; these zones lack the sharp, discrete edges of most cortical opacities. These soft hazy zones of the image range cannot be used to grade these areas consistently.

To Grade P.—Only posteriorly focused retroillumination images are used in grading P. The area of the opacity in the lens being graded is compared with that in standards 1 through 5. The second interval selected should bracket the opacity of the ungraded image. The assigned decimal grade should reflect the location of the cataract in the interval; the assigned score may range from 0.1 to 5.9. Opacities visible only in the posteriorly focused image are graded as P if they are closer to the center than to the periphery of the area.

Evaluating the LOCS III System

Selection of Photographs to Test LOCS III.—One hundred sixty sets of cataract images were identified from the slide library of the Center for Clinical Cataract Research to represent the range of cataract types and severities based on their LOCS II classifications. Each set included three photographs: one 35-mm color slide-lamp transparency of a cross-sectional view of the nuclear region of the lens and two black-and-white retroillumination images, one focused on the anterior lens at the pupillary plane and one on the posterior lens capsule. For the black-and-white photographs, a flash intensity of 3, illumination aperture of 8 mm, and lens aperture of 7 are used. These images are used to grade C and P. For the color transparency, the beam of the slit lamp is oriented 45° to the line of vision, and the camera is focused in the center of the nucleus. The illumination aperture is set at 4 mm; the slit-lamp width at 0.2 mm; and the flash intensity at 3. The beam is tall enough to just overlap the margins of the pupil. One takes the film using an ASA speed of 200. The color images are used to grade NO and NC. A slit-lamp image is also useful in identifying the anterior-posterior location of opacities seen in retroillumination photographs.

Grading of Test Photographs.—The slides were coded by a technician, arranged in random sequence, placed into slide carousels, and projected onto a large screen for grading. For grading NO and NC, the color slit-lamp image was projected for grading C and P, the two retroillumination images and a slit-lamp image were projected. Between experimental sessions a technician rearranged the slide sequence into a new random order. In each experimental session, either NO and NC or C and P were graded. The relevant LOCS III standard images were continuously projected onto the same large screen and were maintained at the same magnification as the slide being graded. Six sessions were needed for the judgment and retest sessions for NO/NC and C/P groups of slides. Grading sessions were typically separated by 1 to 2 weeks.

Each set of slides was graded by the same two experienced graders. Each grader wrote a score on a separate standardized form; the two graders then compared scores and arrived at a consensus score that was recorded on a third standardized form.

Method of Analysis.—We analyzed the repeatability of LOCS III gradings and estimated the 95% tolerance limits for defining change. For each photograph and for each characteristic, two grades may be compared (either grades from each observer in the same session or grades from different sessions determined by the same observer). The discrepancy or difference between the two scores can be simply calculated. The distribution of these discrepancies is then plotted, and the SD of the discrepancy distribution provides a measure of the reproducibility of the grading. We defined change as a difference greater than ± 0.5 grading errors. The approximate 95% tolerance limits are useful specification of the distribution of grading errors. They were calculated as the next highest increment above the 95th percentile of discrepancy values. These limits become clinically useful as the established tolerance limits for defining change. If the difference between sequential observations exceeds these 95% tolerance limits, it is assumed that a change has occurred. If the discrepancy between sequential measures does not exceed the tolerance limits, it is assumed there has been no significant change in the condition. Assuming no bias (the tendency to obtain consistently higher or consistently lower values, either between observers or between sessions), the distribution of discrepancies should have a mean of 0, and the SD should have a relatively symmetrical distribution of discrepancies.

RESULTS

The results are presented in the Table. For each of the four cataract types, the table shows the mean difference, the median difference, the SD of difference, and the 95% tolerance limits for the five different comparisons for observer 1 and 2, values for observers 1 and 2 were compared with those obtained at session 2. For consensus, values determined by both observers were averaged and then compared for the two sessions. For sessions 1 and 2, values obtained by observer 1 were compared with those obtained by observer 2. For NO, the between-sessions 95% tolerance limits were 0.7 for observer 1 and 1.0 for observer 2, and the between-observer tolerance limits were 0.7 and 0.8 at sessions 1 and 2, respectively. For
### LENS OPACITIES CLASSIFICATION SYSTEM III (LOCS III)

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**Fig 5**—The LOCS III standards. This set of standards is prepared as a set of slides for grading standardized photographic images of opacity. The five or six individual standard slides for the cataract type or nuclear color being graded are projected at the same size as the slides of unknown opacity. NO1 to NO6 and NC1 to NC6 are the standards for nuclear opalescence and nuclear color, respectively. C1 to C5 are the standards for cortical cataract, and P1 to P5 are the standards for posterior subcapsular cataract.

NC, the between-session limits were 0.7 and 0.8 for observers 1 and 2, respectively, and the between-observers tolerance limits were 0.6 at both sessions 1 and 2. For C, the between-sessions tolerance limits were 0.7 for observers 1 and 2, and the between-observers tolerance limits were 0.6 for session 1 and 0.5 at session 2. Finally, for P, the between-sessions tolerance limits were 0.9 for observers 1 and 2, and the between-observers tolerance limits were 0.4 for both sessions 1 and 2.

**COMMENT**

The LOCS III, with its expanded sets of reference photographs and decialized grading, is easier to use and provides more sensitive grading than LOCS II when applied to photographic images of cataracts. A fuller analysis of the benefits of decialized grading systems has been presented elsewhere, but the 95% tolerance limits for all of the LOCS III classes are much smaller (0.4 to 1.0) than the 95% tolerance limits for LOCS II, which uses integer increments only. For each category of cataract or for NC, the LOCS II tolerance limits are at best 2.0. Because sequential observations do not show 95% concordance, the level of concordance required for the 95% tolerance limit would be 1.0.13

For each category (NO, NC, C, and P), LOCS III has some specific advantages over LOCS II. For grading NO, the rescaling has achieved approximately equal intervals between each reference standard, and there are more standards for evaluation of the early stages of NO. Removal of inconsistent variations in color over the range of NO standards makes judgments about the severity of NO much more straightforward. Improved opalescence grading may offer opportunities to assess in vivo basic age-related biochemical processes such as protein aggregation, and there is evidence that NO, as judged using LOCS II, is correlated to some aspects of visual dysfunction (e.g., contrast sensitivity loss). 21

In LOCS II, there was only one reference standard for NC, making assessment of NC the most subjective of all the judgments in LOCS II. A much broader array of standard reference images in LOCS III greatly facilitates the assignment of NC grades.

In the past, grading brunescence has not always been considered important. However, there is evidence that increased NC may be related to contrast sensitivity dysfunction.21 In addition, grading NC is necessary if one is to assess the protective effect of lens pigments against short-wave-length visible and long-wave-length UV light. There is also a well-known but poorly quantified clinical relationship between NC and ease of nuclear phacomelulysation.

Nuclear opalescence and NC are correlated. 22 23 In one analysis, 22 33% of the variability in NO grading (using LOCS II) was due to variations in NC. If one is to isolate the effect of opalescence on visual function and define the relationship between NO and other biologic phenomena, one must be able to isolate and eliminate the variability in opalescence grading due to color in statistical analyses using regression models. Therefore, it is important to grade NC as well as NO.

For grading C, the reference standards in LOCS III are the same as those used in LOCS II. The standards are separated by intervals that increase...
monotonically when measured with the computerized objective method of assessing cataract area, OPAC, and are easy to use. We have changed the instructions for using cortical standards in LOC5 III to reduce between-session variability. We have determined that much of the variability is due to variability in the contrast of the peripheral parts of the cortical region in nearly clear lenses. The areas of variable contrast are sometimes graded as opacity and at other times graded as clear. The instructions for LOC5 III specify that only sharply defined areas of cortical opacity are to be graded; the soft hazy areas should be ignored.

With respect to grading P, LOC5 III standards are considerably improved from those of LOC5 II. Standards illustrating early P have clearly defined, sharp borders that make estimation of area more straightforward. Furthermore, the number of standards has increased, with a systematic increase in the area of P between standards; these features contribute to improved P grading. Irregular and stellate opacities would be assessed by estimating the area of a circle that would be occupied by the cataract, much in the same way that we form a mental aggregate of multieentric cortical opacities, and the circular surrogate would be compared with the discoid opacities in the P standards. The outliers in P grading occurred when large Ps with very vague borders coexisted with advanced NO or C. Inevitably, some portions of mixed cataracts will not be clearly imaged and delineation of the extent of each portion of the cataract will not be clear to the grader. We doubt that a new approach to grading will alter this situation.

We have investigated the use of grids and templates to measure Cs and Ps and demonstrated that results with these tools are similar to results obtained using OPAC. We continue to use OPAC regularly for objective analysis of C and P. However, we believe that there is still a place for the use of subjective systems in evaluating cataract because much of the hardware and software required for objective analysis is expensive and not readily available.

Alternative methods of grading involve adjustment of beam width of the slit lamp to measure the vertical and horizontal limits of Ps; consideration of the circumferential extent of C, which is advocated in the Wilmer system; and a percentage/grid approach, which is used in the Wisconsin system. We chose to adopt deci-
ract classification systems in that its
intervals have been determined by objec-
tive measures of cataract applied to a
vast array of candidate images. When
the images were ranked according to
their objective measurements, no sub-
jective inconsistencies in ranking were
apparent. In other words, objective
methods ably rank a series of images in
a manner perfectly acceptable to the
eye. It should not be surprising, there-
fore, to find a high correlation between
the subjective grades and corresponding
objective scores derived from the
same photographs. The LOCS II
standards were selected using subjective
criteria alone, and although recent anal-
yses indicate that increasing LOCS II
grades of NO, NC, C, and P are associ-
ated with increasing corresponding
objective scores, there is considerable
overlap. Few have sought to make di-
rect correlations between frequently
used cataract classification systems23
and objective measures of cataract. One
study by Adamsom et al24 demonstrated
good correlation between clinical
gradings and digital analysis of NO and
C. With LOCS III, we have a subjective
system that gives results comparable to
the objective systems in NC and the
three cataract types (NO, C, and P).
Thus, we believe LOCS III is a subjec-
tive system that gives results compar-
able to those of objective methods.
There may be concern that objective and
subjective systems for quantifying cataract
measure completely different features
of the cataractogenic process. Our
results with the subjective and objective
aspects of LOCS III suggest that the
grader's eye and the objective sensors
are assessing essentially the same
features in an image. Thus, LOCS III may
be useful also in evaluating new objec-
tive systems of cataract quantification.

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