Differential Macular Morphology in Patients with RPE65-, CEP290-, GUCY2D-, and AIPL1-Related Leber Congenital Amaurosis

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PURPOSE. To evaluate genotypic and macular morphologic correlations in patients with RPE65-, CEP290-, GUCY2D-, or AIPL1-related Leber congenital amaurosis (LCA) using spectral-domain optical coherence tomography (SD-OCT).

METHODS. SD-OCT macular scans were performed in 21 patients, including 10 with RPE65, 7 with CEP290, 3 with GUCY2D, and 1 with AIPL1 mutations. An image processing software was used to manually draw segmentation lines by three observers. Lamellar structure was evaluated based on the number of retinal layers on segmented images. Total retinal thickness was measured at the central macular and perifoveal areas by using an automated algorithm.

RESULTS. All three patients with GUCY2D mutations (age range, 20–53 years) retained six retinal layers with visible photoreceptor inner/outer segment juncture (PSJ). However, the preservation of lamellar structures did not parallel better visual acuity. Patients with other mutations had poorly defined PSJ and disorganized retinal lamellar structures, where only one to three retinal layers could be observed. Patients with CEP290 mutations tended to have retention of the outer nuclear layer at the fovea and macular thickening, especially at younger ages. In patients with RPE65 (age range, 20–71 years) and AIPL1 mutations (age, 22 years), macular thickness was markedly decreased. Disorganization of retinal lamellar structures in the RPE65 group trended toward a worsening with increasing age.

CONCLUSIONS. Variations of macular microstructures were observed among LCA patients with different genotypes. Disorganization of retinal lamellar structure was generally age related. Preservation of retinal microanatomic structures may not be associated with better visual acuity. (Invest Ophthalmol Vis Sci. 2010;51:2608–2614) DOI:10.1167/iovs.09-3734

Leber congenital amaurosis (LCA) is clinically described as a group of early-onset photoreceptor cell degenerations. It is usually inherited in an autosomal recessive fashion and characterized by severe impairment of visual function and nystagmus early in life. Affected individuals may have a normal-appearing fundus at an initial stage, which may be followed by retinal pigment clumping and vascular attenuation. Other fundus findings—for instance, retinal flecks, macular coloboma-like lesions, and chorioretinal atrophy—may be observed. Marked reduction or absence of retinal function measured by an electroretinogram (ERG) is characteristic. Enophthalmos, ocudigital phenomenon, cataract, keratoconus, and hyperopia have also been described.

LCA is a genetically heterogeneous disease. To date, plausible disease-causing variations have been reported in 14 genes: AIPL1, CEP290, CRB1, CRX, GUCY2D, IMPDH1, LCA5, LRAT, MERTK, RD3, RDH12, RPE65, RPGRIP1, and TULP1. Mutations in these genes account for approximately 70% of all cases of LCA. The most prevalent mutated genes are CEP290 (15%) and GUCY2D (12%).

Interest in LCA has recently been increasing since the reports of preliminary success in phase 1 studies of gene-directed therapy in LCA patients with RPE65 mutations. Gene-directed therapy is eventually likely to be applicable for LCA patients with other genetic mutations as well. Although there is an overlap of phenotypic expressions between different genotypes, phenotypic trends in patients with the same genotype have been described for at least some mutations. In this study, we evaluated possible correlations between macular microstructure and various LCA genotypes for patients with mutations in RPE65 (retinal pigment epithelium-specific 65-kDa protein), CEP290 (centrosomal 290-kDa protein, also known as NPHP6), GUCY2D (guanylate cyclase 2D, also known as RETGC), or AIPL1 (arylhydrocarbon interacting receptor protein-like 1) genes, detected by spectral-domain-optical coherence tomography (SD-OCT). These types of studies are important for at least two reasons: one is to probe anatomic differences between the various LCA genotypes to understand the disease phenotypes better. Another reason is to evaluate the possibilities of viable retinal structures, including photoreceptors, to aid in predicting the potential for therapeutic success.

MATERIALS AND METHODS

Patients

Included in this study were 21 patients (38 eyes) with a diagnosis of LCA and plausible disease-causing variations in either the RPE65,
CEP290, GUCY2D, or AIPL1 genes. A diagnosis of LCA was based on ocular history, fundus examination, and electrophysiological and visual field examinations. The patients, whose names were listed in a genetic database, participated after receiving a telephone invitation. The study was conducted in the Electrophysiology and Inherited Retinal Disease unit at the Illinois Eye and Ear Infirmary. All patients were examined by two authors (SP, GAF). The study procedures adhered to the tenets of the Declaration of Helsinki and were approved by an institutional review board at the University of Illinois Medical Center. Informed consent or assent was obtained from all participants or their legal guardians.

Genetic Testing
DNA was extracted from peripheral blood leukocytes by procedures previously described.\textsuperscript{15,17} Polymerase chain reaction (PCR) assay, single-strand conformational polymorphism (SSCP) analysis, and denatured high-pressure liquid chromatography wave analysis (DHPLC; Transgenomic, Inc., San Jose, CA), followed by automated bidirectional direct sequencing (model 3100; Applied Biosystems, Inc., [ABI], Foster City, CA) for genetic screening techniques. Some of the mutations were initially identified by the LCA mutation chip Asper Ophthalmics, Tartu, Estonia) and confirmed by sequencing.

Ocular Examination and Functional Tests
Data collection included date of birth, sex, race, onset of visual impairment, presence of nystagmus, progression of symptoms, medical and ophthalmic histories, genetic testing results, and pedigree information. All patients underwent a comprehensive ocular examination, including retinoscopic refraction, best corrected visual acuity (BCVA) measurement using either a Snellen projection chart or a Feinbloom Distance Test Chart for the Partially Sighted (Designs for Vision, Inc., Ronkonkoma, NY), slit lamp biomicroscopy, Goldmann applanation tonometry, and diluted fundus examination with direct and indirect ophthalmoscopy. Color fundus photographs were obtained on all patients. Sixteen patients had a visual field evaluation using Goldmann perimetry, and 12 patients underwent ERG testing obtained by either of two procedures previously described.\textsuperscript{18,19} The recording techniques adhered to an international standard for clinical electrophysiological measurements.\textsuperscript{20} ERG measurements were compared with either 90% tolerance limits or with a proportionate range obtained from a normally sighted control population.

Optical Coherence Tomography and Image Segmentation
SD-OCT imaging was performed with a commercially available instrument (RTVue Model-RT100 ver. 3.5; Optovue Inc., Fremont, CA). Most of the patients were very poorly sighted and unable to see an internal fixation target provided by the instrument. For image acquisition, these patients were asked to direct their gaze in a direction to facilitate visualization of their maculae. Macular scans were generated using the radial lines protocol, which provided 12 radial 6-mm scans. Scan acquisition time required for each of the radial lines scans was 0.27 seconds. The scans had a depth resolution of 5 \( \mu \text{m} \)/pixel and a spatial resolution of 6 \( \mu \text{m} \)/pixel.

All patients had various degrees of nystagmus, and, as a result, scans with the foveal depression at the center of the image were occasionally difficult to obtain. All 12 scans obtained in each patient were reviewed by one observer (SP), and the best-quality image from each eye was selected for analysis. The selected images from different patients did not necessarily have the same radial orientation. Images were saved in TIF format and the contrast was adjusted by using the same threshold levels. Three observers (SP, RZ, ML) independently reviewed each selected image to evaluate retinal lamellar structures. Segmentation lines were manually drawn by the three observers with image-processing software (ImageJ; available at http://rsb.info.nih.gov/ij, developed by Wayne Rasband and provided in the public domain by National Institutes of Health, Bethesda, MD). Segmentation lines were drawn by the observers based on the presence of visible changes in light reflected from different retinal layers. Sample images acquired in normal control eyes that clearly displayed six retinal layers (retinal nerve fiber layer, ganglion cell–inner plexiform layers, inner nuclear layer, outer plexiform layer, outer nuclear layer (ONL)+photoreceptor inner segment, and photoreceptor outer segment) were also used to standardize segmentation technique among observers. Lamellar structure was evaluated based on the number of retinal layers depicted on segmented images.

Total retinal thickness analysis was also performed based on the segmented images by using a dedicated software program (Matlab; The Mathworks, Inc., Natick, MA). Thickness was measured based on the separation between segmentation lines representing the internal limiting membrane (ILM) and the retinal pigment epithelium (RPE). Thickness profiles were generated from measurements obtained at 100-\( \mu \text{m} \) intervals along 6-mm radial line scans.

Data Analysis
The number of segmented retinal layers was tabulated by each observer. Results from each image were reported based on an exact agreement between at least two of three observers. Agreement among two and three observers was present in 24 and 14 images, respectively. None of the images were excluded because of an inconsistency among all three observers.

For quantitative total retinal thickness analysis, the foveal center was identified at the location on the thickness profile with the minimum thickness. Retinal thicknesses in the central macular and perifoveal areas were calculated by averaging 9 and 18 measurements on thickness profiles, respectively. The central macular area was 800 \( \mu \text{m} \) in diameter, centered at the foveal center. The perifoveal area was defined as an 800-\( \mu \text{m} \)-width ring surrounding the central macular area. Measurements obtained based on image segmentation by three observers were averaged. The results were compared with values from eight visually normal subjects (control group; 16 eyes) whose ages ranged between 34 and 68 years (mean, 55 \pm 11). Thickness measurements in the control group were made by an automated algorithm.\textsuperscript{21} Values from vertical and horizontal scans in both eyes were averaged. All comparisons were made in a by-person analysis where an average thickness of the two eyes in each patient was used for analysis. Mean thicknesses in the central macular and perifoveal areas of the patients’ eyes were compared with those of control eyes by unpaired Student’s \( t \)-test. Statistical significance was considered at \( P < 0.05 \).

RESULTS
Patients’ Characteristics
This study evaluated 21 LCA patients (38 eyes) with different gene mutations, including 10 patients (18 eyes) with RPE65 mutations, 7 (13 eyes) with CEP290 mutations, 3 (6 eyes) with GUCY2D mutations, and 1 (1 eye) with AIPL1 mutations. The mean age of all patients was 36.2 \pm 16.9 years (range, 5–71 years). The median age was 49 (range, 20–71 years), 31 (range, 5–44 years), and 33 (range, 20–53 years) years in patients with RPE65, CEP290, and GUCY2D mutations, respectively. Sixty-two percent were female, and 86% were Caucasian. Patients’ visual acuity and their genetic testing results are shown in Table 1.

Eighteen (86%) patients reported progressive visual loss, whereas the other three patients (two with GUCY2D and one with CEP290 mutations) had markedly poor vision early in life without a noticeable subjective degree of progression. None of the patients felt that their vision had improved at any point. Twelve patients had undergone ERG testing, and all these patients had a nondetectable ERG.

Findings on ocular examination and SD-OCT testing in patients with RPE65, CEP290, and GUCY2D mutations are shown in Table 2. None of the seven patients with CEP290...
mutations (age range, 5–44 years) had a lens opacity, whereas eight (89%; age range, 29–61 years) of nine patients with RPE65 mutations had various degrees of posterior subcapsular cataract, excluding one patient who underwent cataract surgery in both eyes. Fundus examination showed that all three patients with GUCY2D mutations had grossly normal-appearing maculae, even though they had markedly impaired vision. In the 10 patients with RPE65 mutations, a bull’s eye maculopathy was seen in 3 (age range, 20–31 years), who retained some reading ability, and the other 7 (age range, 39–71 years) had geographic atrophic macular lesions. Patients with CEP290 mutations had various degrees of macular changes, from a blunted foveal reflex to bull’s eye maculopathy. Optic disc drusen were observed in two patients with CEP290 mutations.

Image Segmentation Analysis

Patients with GUCY2D Mutations. All three patients with GUCY2D mutations retained retinal lamellar structures, displaying six retinal layers (retinal nerve fiber layer, ganglion cell+inner plexiform layers, inner nuclear layer, outer plexiform layer, ONL+photoreceptor inner segment, and photoreceptor outer segment), similar to observations in normal con-

![Macular OCT images from visually normal subjects (A, B), GUCY2D mutant (C–F), and CEP290 mutant (G–L) patients.](https://iovs.arvojournals.org/)

**Figure 1.** Macular OCT images from visually normal subjects (A, B), GUCY2D mutant (C–F), and CEP290 mutant (G–L) patients. (A) An OCT image of a normal subject shows organization of retinal microstructures with well-defined photoreceptor inner/outer segment juncture (PSJ; arrows), and (B) six identifiable lamellar layers (retinal nerve fiber layer, ganglion cell+inner plexiform layers, inner nuclear layer, outer plexiform layer, ONL+photoreceptor inner segment, and photoreceptor outer segment; from top to bottom). (C) Pre- and (D) postsegmented OCT images of a 20-year-old GUCY2D-mutant patient also show retention of six lamellar structures with visible, ill-defined PSJ (arrows). (E, F) Similar findings in a 53-year-old patient with GUCY2D mutations. (G) Pre- and (H) postsegmented OCT image of a 17-year-old patient with CEP290 mutations shows three identified lamellar layers with preservation of the ONL centrally. (I, J) Such preservation was less prominent in a 31-year-old patient. (K) An OCT image of a patient without an IVS26+1655 A>G sequence variation does not show preservation of the ONL. (L) Inner retinal cystlike lesions (arrowbeads) were observed in a 17-year-old patient.
trol eyes (Figs. 1A–F). Photoreceptor inner/outer segment juncture (PSJ) was visible throughout the macular scan in all three patients (age range, 20–53 years), although they were less well-defined than those of visually normal eyes.

Patients with CEP290 Mutations. Unlike patients with GUCY2D mutations, the retinas of those with CEP290 mutations could be clearly segmented into only three layers (Figs. 1G–J). The outer retinal layer, which in normally sighted subjects predominately corresponds to the ONL, was notably preserved at the central macular area in six of seven patients, but was thinner than normal from the perifoveal area centrifugally. Such preservation tended to decline with an increase in the patients’ age and was observed in all six patients who had the same mutation (IVS26+1655A>G) in the CEP290 gene. In these six patients, PSJ was poorly defined in the central macula, but was invisible in the periphery. Another patient with a different plausible disease-causing variation (IVS34-3del1bpC) in CEP290 did not have the characteristic preservation of the outer retinal layer.

### Table 1. Visual Acuity and Genetic Testing Results of Leber Congenital Amaurosis Patients

<table>
<thead>
<tr>
<th>Patient No./Age</th>
<th>Gene</th>
<th>Sequence Variations</th>
<th>Better Eye VA</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/20</td>
<td>GUCY2D</td>
<td>Ser981 delTtC homozygous</td>
<td>LP</td>
</tr>
<tr>
<td>2/33</td>
<td>GUCY2D</td>
<td>Leu954Pro &amp; Ser981 delTtG compound heterozygous</td>
<td>LP</td>
</tr>
<tr>
<td>3/53</td>
<td>GUCY2D</td>
<td>Thr312Met and Arg795Trp compound heterozygous</td>
<td>20/400</td>
</tr>
<tr>
<td>4/5</td>
<td>CEP290</td>
<td>IVS26+1655 A&gt;G and Gln1654 del2CAA compound heterozygous</td>
<td>LP</td>
</tr>
<tr>
<td>5/14</td>
<td>CEP290</td>
<td>IVS26+1655 A&gt;G heterozygous</td>
<td>20/40</td>
</tr>
<tr>
<td>6/17</td>
<td>CEP290</td>
<td>IVS26+1655 A&gt;G and Arg1926Stop compound heterozygous</td>
<td>20/60</td>
</tr>
<tr>
<td>7/51</td>
<td>CEP290</td>
<td>IVS26+1655 A&gt;G heterozygous</td>
<td>HM</td>
</tr>
<tr>
<td>8/32</td>
<td>CEP290</td>
<td>IVS34+5 del11tC compound heterozygous</td>
<td>LP</td>
</tr>
<tr>
<td>9/35</td>
<td>CEP290</td>
<td>IVS34+5 del11tG compound heterozygous</td>
<td>HM</td>
</tr>
<tr>
<td>10/44</td>
<td>CEP290</td>
<td>IVS26+1655 A&gt;G heterozygous</td>
<td>10/120</td>
</tr>
<tr>
<td>11/20</td>
<td>RPE65</td>
<td>Lys354 ins1tgA &amp; Ala393Glu compound heterozygous</td>
<td>20/70</td>
</tr>
<tr>
<td>12/29</td>
<td>RPE65</td>
<td>Lys354 ins1tgA &amp; Ala393Glu compound heterozygous</td>
<td>10/600</td>
</tr>
<tr>
<td>13/51</td>
<td>RPE65</td>
<td>Gly40Ser &amp; His182Tyr compound heterozygous</td>
<td>5/350</td>
</tr>
<tr>
<td>14/59</td>
<td>RPE65</td>
<td>Gly40Ser &amp; His182Tyr compound heterozygous</td>
<td>5/350</td>
</tr>
<tr>
<td>15/49</td>
<td>RPE65</td>
<td>Tyr239Asp heterozygous</td>
<td>HM</td>
</tr>
<tr>
<td>16/49</td>
<td>RPE65</td>
<td>IVS1-5 G&gt;A homozygous</td>
<td>NLP</td>
</tr>
<tr>
<td>17/50</td>
<td>RPE65</td>
<td>Asn321 ins1bp ins &amp; Arg124Stop compound heterozygous</td>
<td>HM</td>
</tr>
<tr>
<td>18/53</td>
<td>RPE65</td>
<td>IVS1-5 G&gt;A homozygous</td>
<td>LP</td>
</tr>
<tr>
<td>19/61</td>
<td>RPE65</td>
<td>Gly146 del1ltG &amp; Gln102Stop compound heterozygous</td>
<td>LP</td>
</tr>
<tr>
<td>20/71</td>
<td>RPE65</td>
<td>Arg124Stop heterozygous</td>
<td>2/600</td>
</tr>
<tr>
<td>21/22</td>
<td>AIPL1</td>
<td>Trp277Stop exon 6 homozygous</td>
<td>LP</td>
</tr>
</tbody>
</table>

HM, hand motion; LP, light perception; NLP, no light perception; VA, visual acuity.
† Morimura H, et al.15, patient 9190.

### Table 2. Phenotype-Genotype Associations among Leber Congenital Amaurosis Patients with GUCY2D, CEP290 and RPE65 Mutations

<table>
<thead>
<tr>
<th>Phenotypes</th>
<th>GUCY2D (n = 3; Age Range, 20–53 y)</th>
<th>CEP290 (n = 7; Age Range, 5–44 y)</th>
<th>RPE65 (n = 10; Age Range, 20–71 y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General eye examination</td>
<td>Median VA in the better seeing eye</td>
<td>LP</td>
<td>HM</td>
</tr>
<tr>
<td>Refraction</td>
<td>Hyperopia</td>
<td>Hyperopia (83%)</td>
<td>Hyperopia (70%), Hyperopia (30%)</td>
</tr>
<tr>
<td>Cataract</td>
<td>Variable</td>
<td>None</td>
<td>PSC (89%)*</td>
</tr>
<tr>
<td>Fundus examination</td>
<td>Optic disc pallor</td>
<td>33%</td>
<td>57% (optic disc drusen 29%)</td>
</tr>
<tr>
<td>Vascular attenuation</td>
<td>100%</td>
<td>Reduced foveal reflex; bull’s eye maculopathy</td>
<td>100%</td>
</tr>
<tr>
<td>Macula</td>
<td>Normal-appearing</td>
<td>Peripheral pigment clumping; granular hypopigmentary changes</td>
<td>Peripheral pigment clumping; diffuse hypopigmentary changes and pigment clumping</td>
</tr>
<tr>
<td>Periphery</td>
<td>Absent to mild granular pigmentary changes</td>
<td>Peripherally clumped; granular hypopigmentary changes</td>
<td>Early: geographic atrophic lesions</td>
</tr>
<tr>
<td>SD-OCT findings</td>
<td>Numbers of layers†</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>PSJ visibility</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Cystic changes</td>
<td>No</td>
<td>May be present (43%)</td>
<td>No</td>
</tr>
<tr>
<td>Characteristics</td>
<td>Retained lamellar structures</td>
<td>Preservation of ONL at the fovea with distorted inner retina</td>
<td>Disorganized lamellar structures</td>
</tr>
<tr>
<td>Age-related changes</td>
<td>Relatively minimal</td>
<td>Thinning of central ONL</td>
<td>Progressive disorganization of lamellar structures</td>
</tr>
</tbody>
</table>

CF, count fingers; HM, hand motions; LP, light perception.
* Excludes one patient who underwent cataract surgery.
† Based on segmentation agreement among at least two of three observers (visually normal eye had six layers).
not show the preservation of the ONL nor any visible PSJ in
the central macular area (Fig. 1K).

Furthermore, cystlike macular lesions were identified in
three (43%) of the seven patients with CEP290 mutations. The
cystic changes were located proximal to the ONL (Fig. 1L).

**Patients with RPE65 or AIPL1 Mutations.** In our cohort,
the patients with RPE65 or AIPL1 mutations had more disorga-
nized lamellar structures than did the patients with CEP290 or
GUCY2D mutations. Only one to three retinal layers could be
clearly identified (Fig. 2). Also, the PSJ was not clearly visible
throughout the macular scans. Cystlike lesions were not seen in
any of these patients. Disorganization of retinal lamellar structures
tended to worsen with an increase of the patients’ age (Fig. 3).

**Macular Thickness Analysis**

Mean macular thickness in the central macular and perifoveal
areas of patients from each group are shown in Table 3.
Compared with visually normal control subjects, patients with
RPE65 had significantly thinner retinas in both the central
macular (P < 0.0001) and perifoveal (P < 0.0001) areas. In
patients with CEP290 and GUCY2D mutations, there was no
significant difference in the central macular thickness (P >
0.50) compared with control eyes; however, significant thin-
ing in the perifoveal area was observed in both mutations
(P = 0.02 and 0.01 for the CEP290 and GUCY2D groups,
respectively). A decrease in macular thickness in both areas
tended to be age-related in all three genotypes. Patients with
CEP290 mutations were likely to have a thickened macula at a
younger age, whereas older patients showed more thinning in
the macula. Among the patients with RPE65 mutations, no
statistically significant differences in retinal thickness were
observed between those with (patients 11-13) and without
(patients 14-20) bull’s eye maculopathy in either the central
macular (P = 0.72) or perifoveal (P = 0.15) areas.

**DISCUSSION**

A previous retinal histopathologic study of an 11.5-year-old
GUCY2D-mutant LCA patient reported the presence of rods
and cones in the macula, in the absence of outer segments. The thickness of the inner nuclear layer was normal, but a thinning of the ganglion cell layer was observed.22 Macular SD-OCT results in our patients with GUCY2D mutations demonstrated a similar preservation of retinal lamellar structures with a visible PSJ. This finding is consistent with a previously published observation in a 31-year-old Italian patient with GUCY2D mutations.23 We did not find significant differences in retinal microstructures among the patients whose ages ranged from 20 to 53 years. Although this group of patients retained good retinal lamellar structures, their visual acuity was markedly impaired. This dichotomy in structural-functional relationships appears to characterize the LCA retinas with markedly impaired. This dichotomy in structureal–functional impairment of visual acuity. All the patients with CEPT290 mutations (all had an IVS26+1655 A>G sequence variation retained the ONL in the central macula, although it was less apparent with increasing age. However, another patient (number 8) with a different sequence variation had a markedly thin foveal center without a well-defined ONL. Inner retinal structures in CEPT290 mutation-bearing patients were distorted. Three patients with CEPT290 mutations (all had an IVS26+1655 A>G sequence variation) were found to have cystlike lesions in the inner retina.

Several previous TD-OCT studies showed that young RPE65-mutant LCA patients (age ≥25 years) may present with preserved retinal lamellar architecture.25–27,29 However, the thickness of the ONL may be reduced. This photoreceptor cell loss was not clearly related to age.26 Although most of our patients with an RPE65 mutation were older than those in previous studies,25–27,29 our results showed that, using higher resolution SD-OCT scans, preservation of lamellar structures and the PSJ was not appreciated, even in a 20-year-old RPE65-mutant patient. The macular lamellar architecture was appreciably distorted and tended to worsen with an increase in the patients’ age. This observation may imply that heterogeneity of phenotypic expression is present, even in patients with different variations in the same gene, as also seen in CEPT290-mutant patients. Nonetheless, in fact, our patients with an RPE65 mutation had a higher median age than did those with other mutations. This may also, in part, contribute to our finding a higher prevalence of lens opacity in this genetic subtype.

Although an automated image segmentation algorithm was reported to be useful for an evaluation of thickness profiles in eyes with well-preserved lamellar architectures,31 it did not accurately segment the retina into different layers in those with disorganized lamellar structures in any of our LCA patients in this study. We found that manual segmentation was more reliable; however, it was also more time-consuming. Because our patients were very poorly sighted, with various degrees of nystagmus, well-centered images were difficult to obtain that could ensure an accurate measurement of macular thickness. However, the findings from our image acquisitions provide useful comparative data among different genetic subtypes of LCA.

This study demonstrates that SD-OCT macular imaging is a potentially useful method of differentiating certain patients with different genotypes. Preservation of retinal microanatomic structures may not be associated with better visual acuity. Nevertheless, such preservation, for instance, of lamellar architectures in GUCY2D-mutant patients, and of ONL in the central macula in CEPT290-mutant cases, may have an impact on determining the potential success rate for future gene-directed therapy. Studies that focus only on structures or function of outer retinal layers, where current treatment options are targeted, may not be sufficient to predict the effectiveness of such treatments.

References


