Anterior Segment Optical Coherence Tomographic Angiography Assessment of Acute Chemical Injury

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• PURPOSE: To compare routine clinical examination with optical coherence tomography angiography (OCTA) for the assessment of limbal conjunctival ischemia following a chemical burn.

• SETTING: Validity analysis.

• METHODS: We assessed 10 participants (15 eyes) with an acute chemical injury. Clinical photographs were used to determine the extent of any limbal conjunctival epithelial defect and ischemia. These were compared with the extent of limbal ischemia identified on OCTA images of the ocular surface. Quantitative and longitudinal analysis using the OCTA software were also performed. Correlations with visual outcome were sought using clinical and OCTA-derived variables.

• RESULTS: The extent of clinically determined limbal ischemia was less than that identified with OCTA (2.3±3.6 clock hours vs 5.1±4.2 clock hours, $P =$ .003), which in turn was less than the size of limbal conjunctival epithelial defect (7.3±5.1 clock hours, $P = $ .03). Longitudinal OCTA analysis showed that mean vessel area increased by 0.2%±0.1% during the study, corresponding to a rate of vascular recovery of 0.9 mm^2/d. Significant correlations were found between visual outcome at 3 months and limbal conjunctival fluorescein staining ($r = 0.67$, $P = $ .006), and limbal conjunctival ischemia on OCTA ($r = 0.76$, $P = $ .001).

• CONCLUSIONS: OCTA can objectively identify and monitor the recovery of limbal ischemia following an acute ocular chemical injury. OCTA confirms that limbal ischemia is usually more extensive than is suggested by clinical examination, and the former is highly correlated with visual outcome. OCTA therefore is a useful tool in the management of ocular chemical injury.   (Am J

A CHEMICAL BURN CAN CAUSE RAPID AND PERMAnent damage to the anterior segment of the eye. The mechanisms of injury include tissue denaturation, inflammation, ischemia, and the loss of corneal limbal epithelial stem cells (LESCs).[1] Grading systems have been developed to guide clinical management and provide a prognosis.[2–6] An important component of these is an assessment of the radial extent of any epithelial defect or vascular closure at the corneoscleral limbus (limbal ischemia), which are thought to reflect the likelihood of LESC loss and subsequent corneal opacity. Assessment of limbal ischemia is typically based on the subjective appearance of limbal vasculature on slit-lamp examination, but currently no standard criteria exist and the assessment is subject to observer error. Unlike the retina, dye-based angiography of the ocular surface has not been fully established. Thus, an objective and easily available method to document the presence or absence of flow within the limbal vasculature could make grading more reliable.

Optical coherence tomography angiography (OCTA) is a rapid, noninvasive imaging technique that can identify the anatomy of ocular vasculature based on the measurement of erythrocyte flow.[7,8] It has been adopted as an alternative to conventional dye-based angiography in the assessment of retinal and optic disc vasculature.[7,8] OCTA has also been used to image the iris vasculature,[9,10] corneal neovascularization,[9,11] and most recently the normal conjunctival and intrascleral vascular anatomy.[12]

In this study, we have used OCTA to evaluate the extent of limbal ischemia following an acute chemical injury, looking at both the conjunctival and intrascleral vessels, and compared these results with subjective clinical grading. We have also used OCTA in a pilot longitudinal study to estimate the rate of conjunctival revascularization.

METHODS

THIS PROSPECTIVE COHORT STUDY WAS APPROVED BY THE Moorfields Eye Hospital Institutional Ethics Committee

(ROAD15/063) and we adhered to the principles of the Declaration of Helsinki. Consecutive individuals who attended with an ocular chemical burn were recruited after they had received acute medical treatment, and informed consent was obtained. Exclusion criteria were a presentation delayed for more than 1 week after the initial injury, absence of a conjunctival epithelial defect demonstrable after application of 2% fluorescein, or initial treatment that included placing an amniotic membrane graft over the ocular surface.

We recorded details of the causative chemical agent (eg, acid or alkali), best-corrected visual acuity (BCVA) with glasses if worn, and any treatment that had been given. All participants had a slit-lamp examination with color photography with and without fluorescein. Two experienced ophthalmologists (R.M.K.S. and S.J.T.) assessed the photographs subsequently and documented the size of the conjunctival epithelial defect (identified by fluorescein staining) and any limbal or conjunctival ischemia (identified by conjunctival blanching) according to the classification published by Dua et al.[4] Conjunctivalization at 3 months was assessed as late staining following topical application of fluorescein.[13]

OCTA images were obtained by 2 of the authors (S.S.M.F. or S.K.D.) using the technique described previously.[9] Images were captured with the split-spectrum amplitude decorrelation angiography algorithm on the AngioVue OCTA system (Optovue, Fremont, California, USA) with an adaptor lens mounted for anterior segment imaging. Each scan was performed with axial resolution of 5 μm with a beam width of 22 μm and a light source centered on 840 nm. The instrument captures consecutive B-scans containing 304×304 A-scans at 70 000 scans per second in a slow transverse, which constructs a 3-dimensional scan cube in approximately 3-4 seconds.[7] To bring the limbal conjunctival vasculature into focus, the machine was carefully positioned 2-4 cm from the ocular surface, and the focal length of the system was manually adjusted until a clear image was obtained. To capture 360 degrees of limbal conjunctival vasculature, OCTA scans (6 × 6-mm-volume cubes) were obtained in the 4 quadrants of limbal conjunctiva (superior, inferior, temporal, and nasal) of each affected eye. In this study, the lack of a detectable vascular signal on OCTA imaging was considered to represent vascular nonperfusion, henceforth termed ischemia. The extent of ischemia at the corneoscleral limbus was assessed and determined in clock hours. An estimate of the total area of ischemia was calculated using the software provided by the OCTA system. The depth of vessels and also ischemia were determined using the en face mode of the OCTA software, which provides a cross-sectional reference image during analysis to allow segmentation of superficial conjunctival and deeper intrascleral blood vessels.

Two different software modes were used to capture the images: OCTA designed for retinal vasculature (AngioRetina) was used in the first 12 eyes of 7 patients, whereas the 3 eyes of the remaining 3 patients were imaged with an OCTA mode designed to image corneal vessels—a software that the manufacturer stated to have an anterior segment focus but was only available to the authors toward the end of the study. We included the latter software to allow assessment of its usability in the setting of acute chemical injury.

Both the AngioRetina and the cornea imaging modes provide automatic image processing with the internal software, with the quality of the images reported as the signal strength index. For images captured by retinal mode, the software was able to provide a quantitative estimate of the vessel area density within each image after the conjunctival area in the image had been identified manually. The percentage of vascularized area was then calculated by dividing the total vascular area on OCTA by the total conjunctival area identified in each image. Longitudinal changes in vessel density were then assessed by subtracting the percentages between the initial and final assessment of each patient. Images were exported in PNG format for comparison with the clinical estimate of limbal ischemia and conjunctival involvement.

Comparisons were made between the size of the epithelial defect at the corneoscleral limbus and the extent of limbal ischemia estimated from OCTA imaging. We also compared the extent of ischemia estimated from clinical examination and OCTA. Statistical analysis was performed using SPSS, version 22 (IBM Corp, Armonk, New York, USA). Correlations between the area of ischemia identified by OCTA and the area identified by clinical observation were determined with Spearman ρ, with coefficient <0.3 categorized as weak, 0.3-<0.7 as moderate, and ≥0.7 as strong correlations. The degree of agreements between OCTA and clinical observation were determined using a 2-way mixed intraclass correlation coefficient (ICC). Agreement is categorized as fair (ICC = 0.40-0.59), good (ICC = 0.60-0.74), and excellent (ICC = 0.75-1.00). A P value <.05 was considered statistically significant.

RESULTS

• **PATIENT DEMOGRAPHICS AND CLINICAL SEVERITY OF CHEMICAL INJURY:** We examined 15 eyes of 10 individuals. Table 1 summarizes the demographics and clinical findings. Patient 9 was unable to undergo OCTA assessment in the right eye due to extreme photophobia and pain despite usage of topical anesthesia, and this eye was excluded from further analysis. Eleven of the 15 eyes had alkali burns and 4 acid burns, but for simplicity the results for the 2 groups were combined. All subjects were male, with a mean (±standard deviation) age at presentation of 31.8±14.7 years. The mean spectacle BCVA at presentation was 0.3±0.3 logMAR (range: –0.1 to 0.8 logMAR). On clinical examination, the extent of the conjunctival

Case No.	Eye	Chemical Agent	BCVA at Presentation	Other Findings	Clinical Limbal Features (Clock Hours) Epithelial Defect	Blanching	Ischemia on OCTA (Clock Hours)	RH[a]	Dua[b]	BCVA at 3 Months	Clinical Feature at 3 Months
1	OD	Acid	0.20		5	0	4	I	III	0.00	
	OS	Acid	0.20		5	0	5	I	III	0.00	CPC: Nasal 2′
2	OS	Alkali	0.30	Pseudomembrane	12	7	12	IV	VI	0.30	CPC: Inferior 3′
3	OD	Alkali	0.20		0	1	0	II	I	0.20	
4	OD	Alkali	0.60		12	0	9	I	VI	0.80	12′ CPC
	OS	Alkali	0.80	Pseudomembrane	12	0	8	I	VI	0.60	12′ CPC
5	OD	Acid	0.00		0	0	0	I	I	0.00	ASC
	OS	Acid	0.80		12	12	12	IV	VI	0.80	PED
6	OD	Alkali	0.00		5	4	4	III	III	0.00	
	OS	Alkali	−0.10	Raised IOP, anterior subcapsular cataract	12	6	9.5	IV	VI	0.80	PED
7	OD	Alkali	0.00		0	0	3	I	I	0.00	
	OS	Alkali	0.20		0	0	0	I	I	0.00	
8	OD	Alkali	0.60		12	4	6	III	VI	0.20	Inferonasal 1′ CPC
9	OD	Alkali	0.50	Pseudomembrane/ symblepharon	12	0	N/A	I	VI	0.00	Inferior 3′ CPC
	OS	Alkali	0.50		9	0	0	I	IV	−0.10	Inferior 3′ CPC
10	OD	Alkali	0.60		8	0	0	I	IV	0.00	

Patient 4 has a background of retinitis pigmentosa resulting in reduced central vision. Patient 9 was unable to undergo OCTA assessment owing to compliance issues.

ASC = anterior subscapsular cataract; BCVA = best corrected visual acuity (in LogMAR); OCTA = optical coherence tomographic angiography; RH = Roper-Hall classification[2]; Dua = Dua's classification[4]; OD = oculus dexter; OS = oculus sinister; CPC = conjunctivalization of peripheral cornea (2′ = 2 clock hours); ASC = anterior subscapsular cataract; PED = persistent epithelial defect; IOP = intraocular pressure; N/A = not available.

[a]Roper-Hall classification ranges from I-IV.
[b]Dua classification ranges from I-VI.

epithelial defect at the corneoscleral limbus was 7.3±5.1 clock hours. Categorizing this clinical finding with the classification of Dua and associates,[4] the median severity of the chemical injury was grade IV (range I-VI). A limbal conjunctival epithelial defect was not observed in 4 eyes.

• OCTA IMAGING CHARACTERISTICS: OCTA images were successfully acquired on the day of injury in 10 eyes. The remaining 5 eyes, which presented late to our specialist clinic, were imaged within 5 days of the chemical injury. The mean signal strength index score for the 12 eyes examined with the retinal mode was 29.7±9.6, compared to 58.9±15.6 for the 3 eyes imaged with the corneal mode. Conjunctival edema did not appear to affect the detection of vascular flow with OCTA (Figures 1 and 3).

• COMPARISON BETWEEN EPITHELIAL DEFECT AND ISCHEMIA MEASURED BY OCTA: OCTA showed that 11 (73.3%) of the 15 eyes had evidence of limbal ischemia, including 1 eye that did not have fluorescein staining at OCTA assessment that was done 4 days after injury. In 3 of the remaining 4 eyes, limbal conjunctival staining was not observed clinically, while 1 eye had 8 clock hours of limbal conjunctival staining but no ischemia was identified on OCTA. The mean extent of the ischemia of all 15 eyes was 5.1±4.2 clock hours (Figure 1), which was significantly less than the extent of the epithelial defect ($P = .03$). This observation was independent of the size of the lesions, as there was a strong and statistically significant correlation between the 2 measurements ($r = 0.82$, $P < .001$). There was also excellent ICC agreement (ICC = 0.86, 95% confidence interval 0.53-0.96, $P < .0001$).

• COMPARISON OF LIMBAL ISCHEMIA ESTIMATED BY CLINICAL EXAMINATION AND OCTA: With 1 exception, the estimate of the extent of limbal ischemia on clinical examination (2.3±3.6 clock hours) was significantly less than that found on OCTA (5.1±4.2 clock hours, $P = .003$), indicating that clinical examination usually underestimates the extent of vascular closure (Figure 2). The absence of a significant correlation or agreement between OCTA and clinical estimates of limbal ischemia
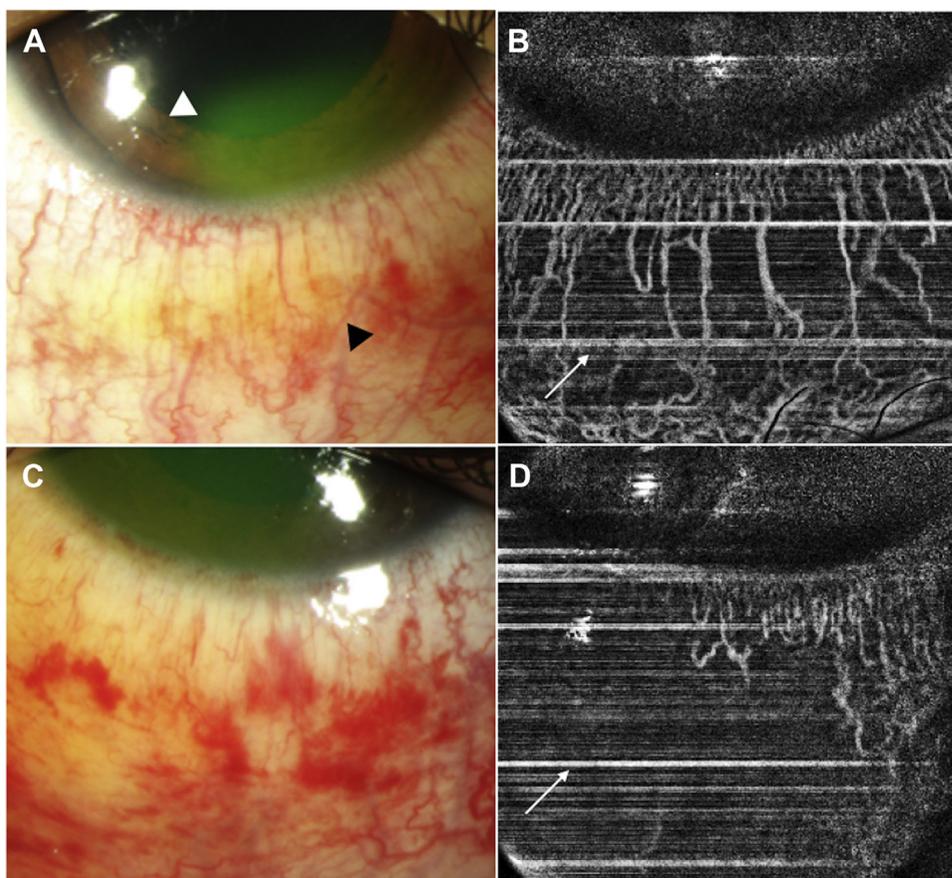
FIGURE 1. Patient 1 at presentation, showing a similar clinical appearance in both eyes but with a different pattern of vascular flow with optical coherence tomography angiogram (OCTA). In the right eye (A), despite a corneal epithelial defect (white arrowhead), the adjacent limbal vascular arcades appear to be intact in both color and OCTA images (B). There are areas of conjunctival ischemia peripheral to the corneoscleral limbus, and an episcleral vessel was also affected (black arrowhead). In the left eye (C), there is a complete corneal epithelial defect, and OCTA identifies extensive areas of limbal ischemia that were otherwise difficult to detect on color images (D). The horizontal white lines in the OCTA images are motion artifacts (white arrows).

($r = -0.33$, $P = .23$; ICC $= -0.07$, $P = .61$), confirms the variability inherent in clinical estimates of limbal ischemia.

• OCTA QUANTITATIVE ANALYSIS OF THE TOTAL AREA OF ISCHEMIA: Using an inbuilt software, semiautomated quantitative analysis was performed on the images obtained with the OCTA retinal mode in 12 eyes. Of these 12 eyes, 9 had limbal ischemia, and all had varying degrees of bulbar ischemia. Combining the data, the mean area of limbal and bulbar conjunctival surface analyzed was 77.1 ± 37.7 mm^2. Ocular surface ischemia ranged from 10.1% to 60.3% of the total conjunctival surface, with a mean of $51.2\% \pm 6.2\%$. We could not obtain quantitative data with the OCTA corneal mode because of software limitations.

• OCTA DEPTH ANALYSIS: Superficial conjunctival and the deeper intrascleral vessels could be differentiated in 5 of the 15 eyes (Figure 4). In 3 eyes, there was flow within the intrascleral vessels beneath the area of superficial ischemia, while in the remaining 2 eyes there was intrascleral ischemia directly beneath areas of conjunctival ischemia but the adjacent vessels were perfused (Figure 5). In the other 10 eyes, images obtained from tissue deeper than the conjunctival layer was of poor quality and were therefore excluded from further analysis.

• OCTA LONGITUDINAL ANALYSIS: Five patients (8 eyes) were available for a repeat examination between 7 and 21 days (mean 11.0 ± 7.0 days) after their initial assessment, allowing reassessment of the conjunctival vasculature. There was no evidence of any major reduction in the area of ischemia suggestive of reversal of vascular spasm. In all eyes, there was evidence of early recovery of vascular flow in areas of conjunctiva that were previously ischemic (Figure 6). Using the estimate provided by the software, OCTA vessel area density (ie, area of an image occupied by conjunctival vessels of any sort) increased by $0.2\% \pm 0.1\%$ between the 2 observations, with a rate of increase
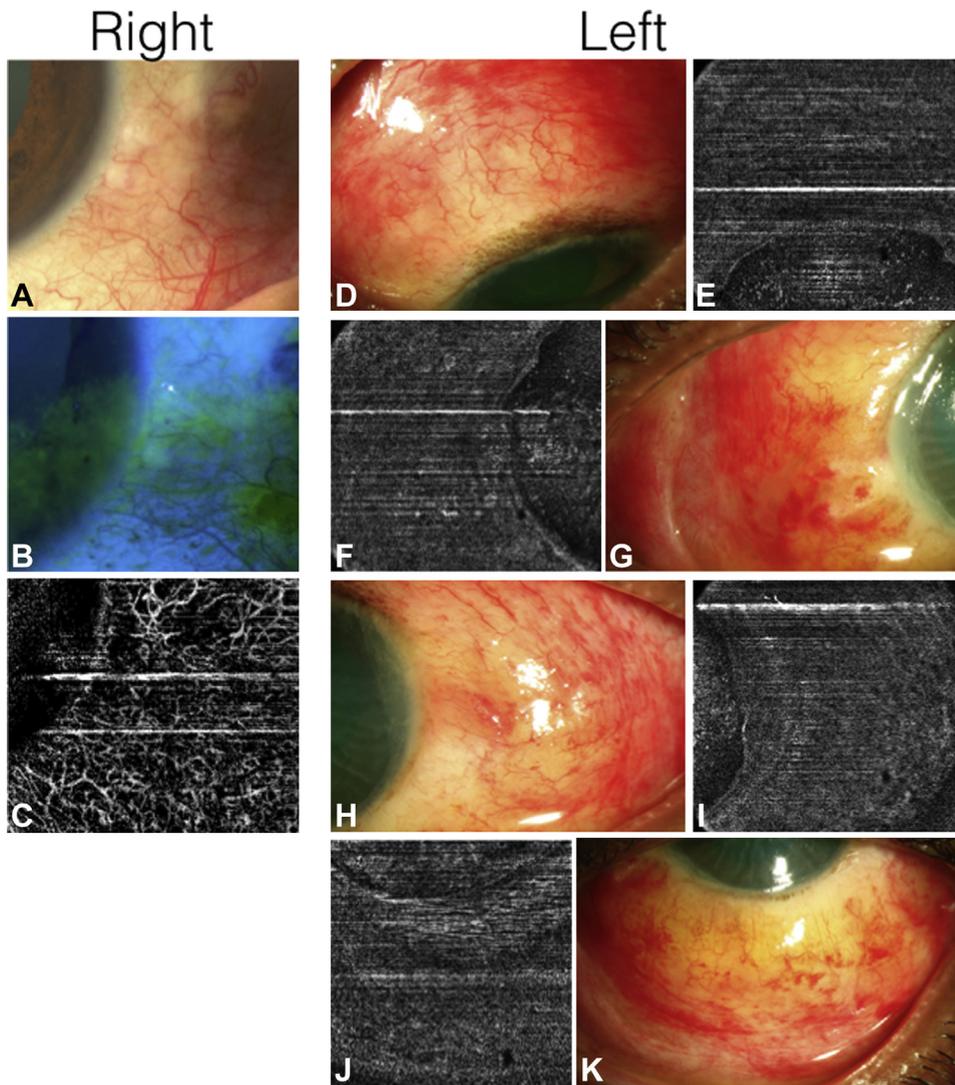
FIGURE 2. Clinical photographs and OCTA images in case 5. The right eye showed an area of conjunctival injection (A) with fluorescein staining at the corneoscleral limbus (B), but relatively normal vascular perfusion was demonstrated on OCTA (C). In contrast, the left eye had extensive limbal conjunctival damage with complete limbal and bulbar conjunctival ischemia, and no detectable vascular signal on OCTA in all 4 quadrants (D, E: superior; F, G: nasal; H, I: temporal; J, K: inferior). OCTA = optical coherence tomography angiogram.

in vessel area density of 0.03% (0.9 mm^2) per day after the initial chemical injury.

• **CORRELATION WITH VISUAL OUTCOME:** Relationships between visual outcome at 3 months and a number of factors were sought. The results are summarized in Table 2. After statistical adjustments, significant correlations were found between final BCVA and the extent of fluorescein staining on clinical photographs ($r = 0.67$, $P = .006$) and the extent of limbal conjunctival ischemia on OCTA in clock hours ($r = 0.76$, $P = .001$). Furthermore, we found that in the 9 patients with evidence of limbal stem cell failure (identified by late fluorescein stain of the corneal epithelium at final assessment), the affected areas corresponded to areas of severe limbal ischemia on OCTA (data not shown).

DISCUSSION

IN THIS STUDY, WE HAVE CONFIRMED THAT OCTA CAN RELIABLY image blood flow within the conjunctival vessels, permitting the documentation of areas of ischemia following chemical injury. In a proportion of eyes, OCTA could also detect ischemia of the intrascleral vessels, giving an estimate of the depth of the injury. The extent of limbal conjunctival ischemia determined by OCTA often differed from other clinical estimates; however, the former was found to best correlate with the final visual outcome after chemical injury.

Chemical or thermal burns cause rapid denaturation of the tissue of the ocular surface. Epithelial loss and vascular closure (ischemia) are both important clinical signs that
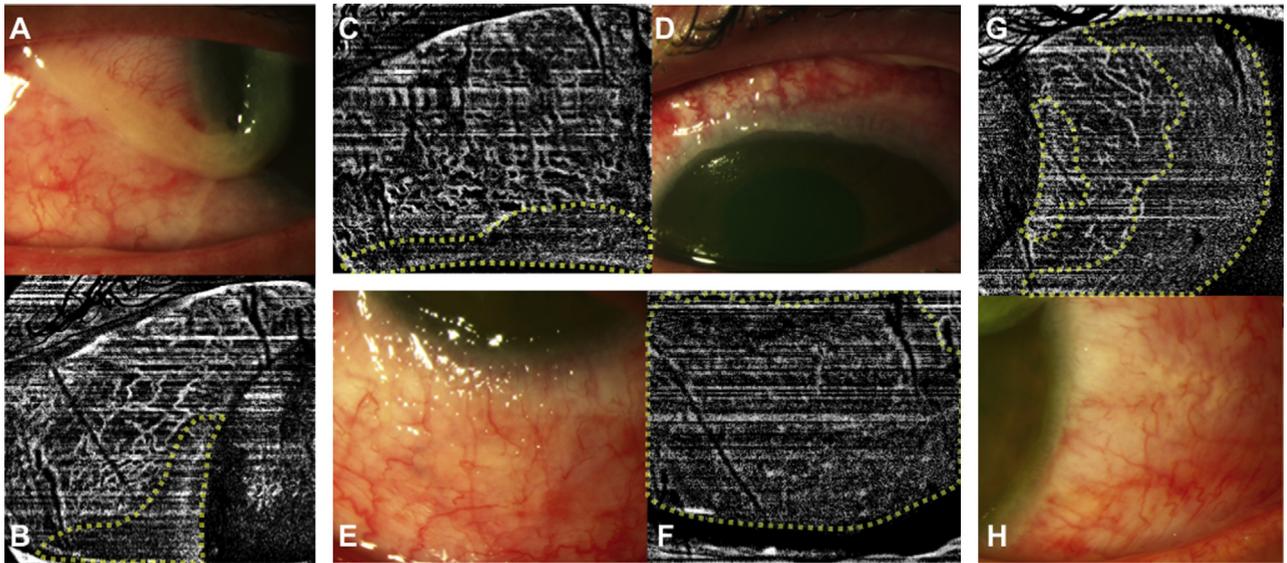
FIGURE 3. Left eye of patient 4 at presentation with color and corresponding OCTA images of the 4 quadrants of limbal and bulbar conjunctiva (A, B: nasal; C, D: superior; E, F: inferior; G, H: temporal). Note the extensive limbal and bulbar conjunctival nonperfusion identified by OCTA (highlighted areas) in areas where vessels appeared to be present in the color images. OCTA = optical coherence tomography angiogram.
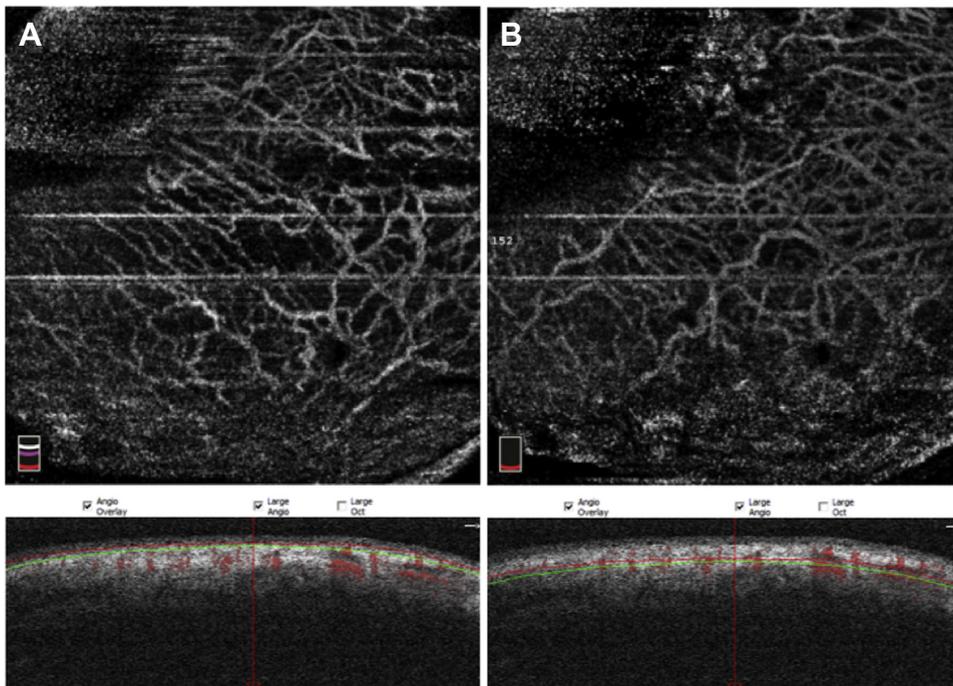

FIGURE 4. En face OCTA images showing superficial conjunctival (A) and deeper intrascleral vasculature (B) in the normal right eye of patient 3. The lower images demonstrate the level of OCTA segmentation of the ocular surface vasculature, indicated by the red and green horizontal lines. OCTA = optical coherence tomography angiogram.

reflect the severity of the injury. Both are associated with irreversible loss of LESC, which can lead to limbal stem cell deficiency, conjunctival overgrowth on the cornea, and visual loss. It is not known whether the extent of an epithelial defect or ischemia at the corneoscleral limbus best reflects permanent LESC damage. An epithelial defect may only involve the superficial tissue and not include the deeper limbal stem cell crypt, in which case normal
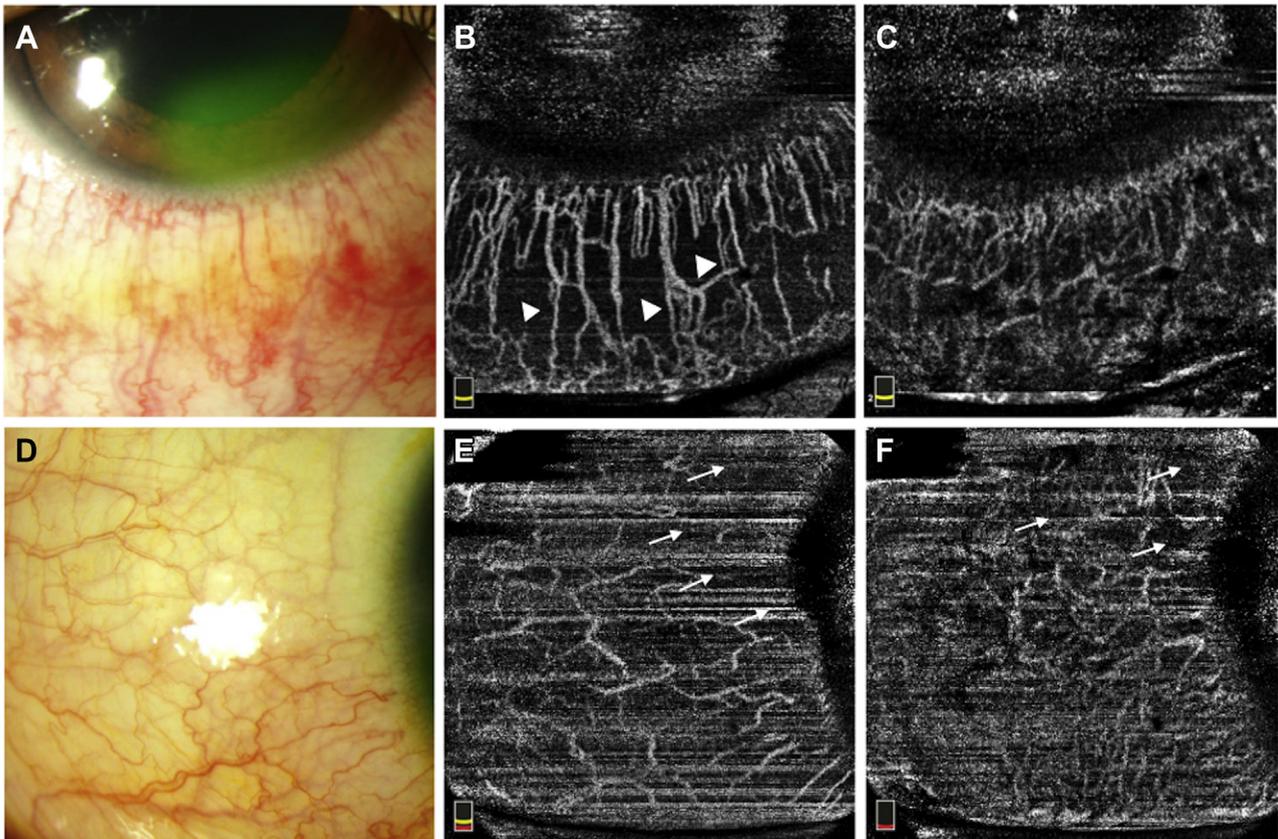
FIGURE 5. Top row: patient 1 color photograph (A) and OCTA images of the conjunctival (B) and intrascleral vasculature (C). Although there were areas of conjunctival ischemia (white arrowheads), the intrascleral vessels were intact, reflecting the superficial nature of the injury. Bottom row: images from patient 6, who suffered a severe chemical injury. Although the vessels in the color photograph appear normal (D), both the conjunctival (E) and the intrascleral vasculature (F) at the supratemporal corneoscleral limbus appeared ischemic on OCTA (arrows). OCTA = optical coherence tomography angiogram.

reepithelialization will occur.[14,15] Clinical estimation of the extent of limbal ischemia is largely subjective and could be highly variable between different examiners.[16] Blood vessels may also have a relatively normal appearance despite vascular stasis, which can only be distinguished by dynamic studies. Therefore, an objective method to accurately delineate the full extent and depth of limbal conjunctival vascular nonperfusion may provide a more accurate prognosis.[2,4,6]

Dye-based angiography has been used to image the vasculature of the anterior segment[17–20] and identify conjunctival ischemia after chemical burns.[21] Kuckelkorn and associates used fluorescein angiography (FA) to delineate the area and depth of tissue ischemia, and they also observed that the extent of injury could be greater than that suggested by the clinical appearance.[21] However, owing to the rapid fluorescein transit time, booster injections were needed to fully assess a region of interest, with image degradation from leakage of fluorescein into the tissue.[21] Low-dose fluorescein injection, in which the dye is bound to albumin, reduces vascular leakage, but this has not been used to assess chemical burns.[18] Indocyanine

green angiography has also been used to image the anterior segment, although these studies were directed to the effect of inflammation on the marginal corneal vascular arcades[20] or pathologic corneal neovascularization rather than chemical injury.[11,19]

High levels of agreement between OCTA and FA have been demonstrated in studies assessing macular vasculature.[8,22] Advantages of OCTA include its ability in generating high-contrast, well-defined images of the retinal microvasculature without any obscuration from dye leakage–related hyperfluorescence.[7] Furthermore, images obtained by OCTA could be segmented and quantitatively analyzed so that individual layers of vasculature could be separately assessed. OCTA could also be performed more rapidly with no systemic risks or side effects compared with dye-based angiography. Limitations of OCTA include the fact that it could not assess vessel permeability and leakage, and that OCTA could be affected by shadow and motion artifacts similar to dye-based angiography.[7,23] Nevertheless, there is now a growing body of evidence demonstrating the usefulness of this technology.
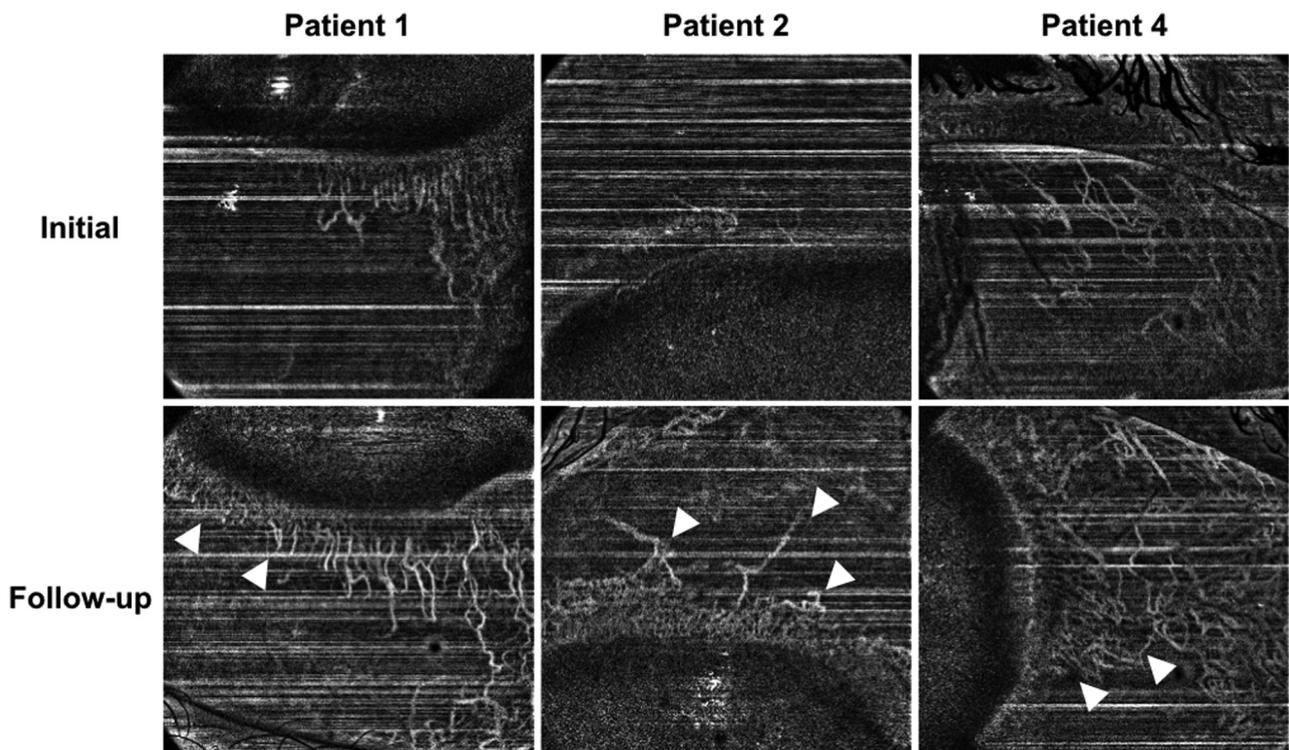
FIGURE 6. Longitudinal changes on OCTA in 3 patients after chemical injury. When compared to the OCTA images obtained at presentation, follow-up OCTA scans showed new vascular flow signals in limbal and conjunctival areas that were previously nonperfused (arrows). OCTA = optical coherence tomography angiogram.

TABLE 2. Correlations Between Clinical Factors and Final Visual Outcome 3 Months After Chemical Injury

Factors	Pearson r	P Value
Limbal conjunctival fluorescein staining	0.67	.006
Clinically determined limbal ischemia	0.54	.04
Roper-Hall classification	0.53	.04
Dua classification	0.58	.02
OCTA-determined limbal conjunctival ischemia	0.76	.001

Statistical significance after Bonferroni adjustment is defined as $P < .01$.
OCTA = optical coherence tomographic angiography.

A number of reports have described the use of OCTA in the anterior segment.[9–12] The appearance of normal conjunctival vasculature has been described by our group previously.[9] Recently, Akagi and associates used swept-source OCTA to identify both the normal conjunctival and intrascleral vasculature.[12] In this study, we were able to identify the normal vasculature in unaffected areas of limbal conjunctiva (shown in Figures 1 and 2), as well as areas of ischemia. The latter was similar in appearance to previous reports using fluorescein angiography to investigate chemical burns on the ocular suface.[21]

We found other advantages of OCTA in the assessment of ocular chemical burn. In this study, OCTA imaging was able to detect vascular flow despite the presence of conjunctival edema and hemorrhages, as shown in Figures 1 and 3. This contrasts with OCTA studies in the posterior segment, in which masking effects by retinal edema and hemorrhages were reported.[24] The reason behind the discrepancy is uncertain. The severity of chemical injuries suffered by our consecutive cohort of patient ranged from mild to severe, and therefore selection bias toward less edema was unlikely. Otherwise, the differences may be because the conjunctival vascular flow is higher, the caliber of the vasculature is larger, or that the conjunctival vessels are more superficial in relation to surrounding tissues compared to retinal vessels. Future comparative studies using dye-based angiography could help confirm the presence of absence of masking effects.

Excellent agreement was found between limbal ischemia determined by OCTA and conjunctival epithelial defect

identified by fluorescein staining clinically; however, the OCTA findings did not agree with clinical estimates of limbal ischemia. The latter could be because we used clinical photographs to assess clinical signs, thus unable to dynamically assess vascular flow, and may have underestimated the full extent of limbal conjunctival ischemia. Furthermore, the detection of vascular pattern by OCTA is dependent on vascular flow (or more precisely, erythrocyte movement within the blood vessels). Areas with very slow blood flow, for example, in the setting of conjunctival vasospasm, therefore may not be detected by OCTA and appear as ischemic instead.[8] However, we did not observe dramatic changes of conjunctival vasculature on OCTA after a relatively short follow-up, suggesting that reversible vasospasm did not exert significant influence on our data.

It has been shown that the extent of limbal epithelial defect could predict clinical outcomes after chemical burn better than relying on signs of limbal ischemia.[4,25] However, although we found that visual outcome at 3 months correlates well with limbal conjunctival fluorescein staining ($r = 0.67$), it was superseded by OCTA estimation of limbal ischemia ($r = 0.76$). We also noted that areas of limbal stem cell failure corresponded to OCTA-determined areas of severe limbal ischemia. OCTA therefore improves visualization of the limbal conjunctival vasculature, making it a more reliable sign useful for prognostication and treatment. It is interesting that the severity grading of either Roper-Hall or Dua classifications did not correlate with visual outcome in this study, suggesting that precise measures of the extent of limbal damage may be more informative instead. Gupta and associates have previously shown that the Dua classification is better associated with the clinical outcome at 1 year than the traditional Roper-Hall classification.[25] They noted that there was a positive correlation between the Dua classification and the formation of symblepharon, but a similar relationship was not found with visual outcome. Future comparison with dye-based angiography with longer follow-up would help to determine the precision of OCTA and its ability in prognostication after chemical burn injuries.

Repeat OCTA examinations were easy to perform, suggesting that this is a suitable noninvasive method for longitudinal monitoring of vascular recovery. Indeed, we were able to provide an estimate area of vascular reperfusion after an ocular chemical burn using OCTA. However, we are cautious in our interpretation, because the lack of image registration would negatively influence the precision of our assessment. We nevertheless believe it is a development that should be further explored. En face OCTA potentially provides an additional dimension to the assessment of a chemical injury as, in a minority of eyes, we could distinguish the deeper intrascleral vessels. Although this may not be a more sensitive marker of LESC loss than clinical estimates of superficial limbal ischemia, it may be an index of more severe damage leading to iris atrophy, cataract, secondary ocular hypertension, or hypotony. Future studies are required to confirm our findings.

The limitations of this study include the small patient cohort, the limited follow-up, and the lack of correlation of the acute clinical signs to long-term ocular surface changes, although the latter may also reflect the inadequacies of current grading systems. In addition, the study has only 1 image grader assessing all the images, and therefore an element of subjective bias may have influenced our results. Further studies on OCTA-outcome correlation and intergrader agreement would help to clarify these issues. The majority of the images were captured with the retinal mode of OCTA, so some estimates of vessel area and density may be inaccurate because of software calibration. Nevertheless, we found that the difference between the AngioRetina and the cornea modes of OCTA was primarily the signal strength index. Although the cornea mode could provide better-quality images, the retinal mode OCTA provides quantitative data that was unavailable in the cornea mode. As such, AngioRetina is currently our preferred mode of image acquisition.

In summary, we report the application of OCTA to assess ischemia following an acute ocular chemical injury. Our results show that OCTA may give a more reliable and objective record of areas of vascular nonperfusion compared to clinical assessment, as well giving an estimate of the depth of the vascular damage. As such, the use of OCTA may help refine the prognosis after injury, enable monitoring of revascularization during healing and the documentation of the effect of treatment.

REFERENCES

1. Wagoner MD. Chemical injuries of the eye: current concepts in pathophysiology and therapy. *Surv Ophthalmol* 1997;41(4): 275–313.

2. Roper-Hall MJ. Thermal and chemical burns. *Trans Ophthalmol Soc U K* 1965;85:631–653.

3. Pfister RR. Chemical injuries of the eye. *Ophthalmology* 1983; 90(10):1246–1253.

4. Dua HS, King AJ, Joseph A. A new classification of ocular surface burns. *Br J Ophthalmol* 2001;85(11):1379–1383.

5. Bagley DM, Casterton PL, Dressler WE, et al. Proposed new classification scheme for chemical injury to the human eye. *Regul Toxicol Pharmacol* 2006;45(2):206–213.

6. Harun S, Srinivasan S, Hollingworth K, Batterbury M, Kaye S. Modification of classification of ocular chemical injuries. *Br J Ophthalmol* 2004;88(10):1353–1354. author reply 1354-1355.

7. Spaide RF, Fujimoto JG, Waheed NK, Sadda SR, Staurenghi G. Optical coherence tomography angiography. *Prog Retin Eye Res* 2018;64:1–55.

8. Jia Y, Wei E, Wang X, et al. A review of optical coherence tomography angiography (OCTA). *Ophthalmology* 2015;1(1):5.

9. Ang M, Sim DA, Keane PA, et al. Optical coherence tomography angiography for anterior segment vasculature imaging. *Ophthalmology* 2015;122(9):1740–1747.

10. Williams BK, Di Nicola M, Ferenczy S, Shields JA, Shields CL. Iris microhemangiomatosis: clinical, fluorescein angiography, and optical coherence tomography angiography in 14 consecutive patients. *Am J Ophthalmol* 2018;196:18–25.

11. Ang M, Cai Y, Macphee B, et al. Optical coherence tomography angiography and indocyanine green angiography for corneal vascularisation. *Br J Ophthalmol* 2016;100(11): 1557–1563.

12. Akagi T, Uji A, Huang AS, et al. Conjunctival and intrascleral vasculatures assessed using anterior-segment optical coherence tomography angiography in normal eyes. *Am J Ophthalmol* 2018;196:1–9.

13. Muthusamy K, Tuft SJ. Iatrogenic limbal stem cell deficiency following drainage surgery for glaucoma. *Can J Ophthalmol* 2018;53(6):574–579.

14. Shortt AJ, Secker GA, Munro PM, Khaw PT, Tuft SJ, Daniels JT. Characterization of the limbal epithelial stem cell niche: novel imaging techniques permit in vivo observation and targeted biopsy of limbal epithelial stem cells. *Stem Cells* 2007;25(6):1402–1409.

15. Dua HS, Shanmuganathan VA, Powell-Richards AO, Tighe PJ, Joseph A. Limbal epithelial crypts: a novel anatomical structure and a putative limbal stem cell niche. *Br J Ophthalmol* 2005;89(5):529–532.

16. Kam K, Patel C, Nikpoor N, Yu M, Basu S. Limbal ischemia: reliability of clinical assessment and implications in the management of ocular burns. *Indian J Ophthalmol* 2019;67(1):32.

17. Easty DL, Bron AJ. Fluorescein angiography of the anterior segment. Its value in corneal disease. *Br J Ophthalmol* 1971; 55(10):671–682.

18. Meyer PA, Watson PG. Low dose fluorescein angiography of the conjunctiva and episclera. *Br J Ophthalmol* 1987;71(1): 2–10.

19. Kirwan RP, Zheng Y, Tey A, Anijeet D, Sueke H, Kaye SB. Quantifying changes in corneal neovascularization using fluorescein and indocyanine green angiography. *Am J Ophthalmol* 2012;154(5):850–858.e2.

20. Zheng Y, Kaye AE, Boker A, et al. Marginal corneal vascular arcades. *Investig Ophthalmol Vis Sci* 2013;54(12):7470–7477.

21. Kuckelkorn R, Remky A, Wolf S, Reim M, Redbrake C. Video fluorescein angiography of the anterior eye segment in severe eye burns. *Acta Ophthalmol Scand* 1997;75(6): 675–680.

22. Nobre Cardoso J, Keane PA, Sim DA, et al. Systematic evaluation of optical coherence tomography angiography in retinal vein occlusion. *Am J Ophthalmol* 2016;163: 93–107.e6.

23. Ma J, Desai R, Nesper P, Gill M, Fawzi A, Skondra D. Optical coherence tomographic angiography imaging in age-related macular degeneration. *Ophthalmol Eye Dis* 2017;9. 1179172116686075.

24. Kashani AH, Chen C-L, Gahm JK, et al. Optical coherence tomography angiography: a comprehensive review of current methods and clinical applications. *Prog Retin Eye Res* 2017; 60:66–100.

25. Gupta N, Kalaivani M, Tandon R. Comparison of prognostic value of Roper Hall and Dua classification systems in acute ocular burns. *Br J Ophthalmol* 2011;95(2):194–198.