Correlation between the graft-host junction of penetrating keratoplasty by anterior segment-optical coherence tomography and the magnitude of postoperative astigmatism

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Purpose: This study aimed to evaluate the alignment pattern of the graft-host junction after penetrating keratoplasty (PK) by anterior segment-optical coherence tomography (AS-OCT) and to correlate this pattern with the magnitude of postoperative astigmatism. **Methods:** This retrospective observational study was carried out on forty patients who underwent PK from February 2013 to August 2014. AS-OCT was performed, and the graft-host junctions were classified into well-apposed junction, malapposed junction, and equally apposed junction. Mal-apposition is subdivided into gap and protrusion. The correlations between clinical characteristics, wound profiles from the AS-OCT, and the magnitude of postoperative astigmatism by Sirius camera (Costruzione Strumenti Oftalmici [CSO], Florence, Italy (CSO, Sirius), were analyzed. **Results:** Graft-host junctions from forty patients were analyzed; 18 eyes had well-apposed junctions, ten eyes had malapposed junctions, and 12 had equally apposed junctions. The mean cylinder was $-9.44 \pm -4.00D$ in well-apposed group, $-13.40 \pm -5.01D$ in malapposed group, and $-4.67 \pm -0.94D$ in equally apposed group. Alignment pattern of the graft-host junction by AS-OCT can explain the postoperative astigmatism (P = 0.123). **Conclusion:** The alignment pattern of the graft-host junction by AS-OCT can explain the postoperative astigmatism after PK where it correlates significantly with the magnitude of astigmatism.



Key words: Anterior segment-optical coherence tomography, corneal topography, graft–host junction, penetrating keratoplasty, postoperative astigmatism

The precise apposition at the graft–host junction is an important goal of penetrating keratoplasty (PK) and is also a prognostic factor affecting the surgical outcome.^[1] Postoperative astigmatism still remains an important cause of low vision after PK. Astigmatism after PK can be caused by many factors including misalignment between the graft and host.^[2,3] Hence, evaluation of the graft–host junction is important in the management of post-PK patients.

Owing to the recent development of optical coherence tomography (OCT), high-resolution anterior segment (AS) images can be obtained and applied in the diagnosis of various corneal disorders.^[4,5]

There are few studies that analyzed the wound profile after PK using AS-OCT.^[6-8] In this study, we evaluated alignment pattern of the graft–host junction by AS-OCT and correlated it with the postoperative astigmatism.

Methods

This study was done on forty patients. We retrospectively reviewed the clinical records of patients who underwent PK at Cairo University Hospital from February 2013 to August 2014 and were followed up for more than 1 year. The studied preoperative data included age at the time of surgery, sex, and the preoperative corneal pathology. All patients underwent full

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ophthalmologic examinations including best-corrected visual acuity (BCVA), refraction, slit-lamp bio-microscopy, intraocular pressure (IOP), evaluation of the graft-host interface using AS-OCT, and evaluation of postoperative astigmatism by Costruzione Strumenti Oftalmici (CSO) topographer.

Patients who had combined surgery such as amniotic membrane transplantation or limbal transplantation were excluded from the study. We also excluded the patients when it was difficult to acquire high-quality images because of poor cooperation.

Surgery was performed by experienced surgeons under general anesthesia. The suturing technique consisted of 16–18 bite interrupted or continuous sutures, according to the surgeon's decision. A 10-0 nylon monofilament suture was used in all cases.

Anterior segment-optical coherence tomography imaging technique

AS-OCT was done using Optovue RTVue model RT100 (Optovue, Inc., Fremont, CA, USA). A corneal adopter

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module which produced telecentric scanning for AS imaging using either a wide-angle or high-magnification adaptor lens was used. Evaluation was performed 1 month after all corneal sutures were removed. The patients were asked to look straight at a fixation target within the device. A single experienced examiner scanned four high-resolution optical sections at 45° interval, showing eight graft–host junctions using raster scan pattern. The scan pattern included 17 parallel line scans, 2–10 mm in length and 1–6 mm in width.

A single trained examiner masked to the clinical data of the patients interpreted the OCT images. Each graft–host interface was categorized according to alignment patterns of the corneal internal side as follows: well-apposed junction if the corneal internal side was aligned precisely without disconnection [Fig. 1], gap if the Descemet's membrane and the inner stroma of the donor and recipient were not connected, but were aligned [Fig. 2], and protrusion if the Descemet's membrane and the stroma protruded toward the anterior chamber (AC) [Fig. 3].



Figure 1: Anterior segment-optical coherence tomography image using raster scan evaluating graft-host junction in the superior quadrant showing precisely aligned corneal internal side without disconnection (well apposition)

The distribution of alignment patterns in each section was evaluated. The eyes were classified into the well-apposed junction, malapposed junction, and equally apposed junction according to the most frequent alignment pattern among the eight cross sections. We considered the graft–host junction of the eye as well apposed if more than four sections were aligned precisely without disconnection, malapposed if more than four sections showed gapping or protrusion, and equally apposed if each of the four sections showed the same alignment pattern (four sections are malapposed and the other four sections are well apposed).

We evaluated the graft-host disparity by calculating the corneal thickness difference between the donor and recipient each at a point 1 mm away from a line where the donor and recipient met among the eight cross sections and we calculated the average of them [Fig. 4].

Patient age, sex, BCVA by spectacles, IOP, spherical equivalent, postoperative topographic astigmatism, and central corneal thickness were compared between alignment



Figure 2: Anterior segment-optical coherence tomography image using raster scan evaluating graft–host junction in the inferior quadrant showing disconnected Descemet's membrane and the inner stroma of the graft–host junction (gapping)



Figure 3: Anterior segment-optical coherence tomography image using raster scan evaluating graft-host junction showing protrusion of the stroma and the Descemet's membrane toward the anterior chamber (protrusion)



Figure 4: Anterior segment-optical coherence tomography image using manual caliber for calculation of the graft–host thickness disparity

groups. Correlation between the alignment pattern of wound interface and the magnitude of postoperative astigmatism was evaluated.

Corneal astigmatism was evaluated using CSO Sirius topographer (Costruzione Strumenti Oftalmici, Florence, Italy), which uses a combination of a Placido disk and a rotating Scheimpflug camera to measure the anterior and posterior corneal surfaces and the corneal thickness across the whole cornea.

Statistical analysis

Data were coded and entered using the statistical package Statistical Package for the Social Science (SPSS Inc., Chicago, IL, USA) version 22. Data were summarized using mean, standard deviation, and range for quantitative data and using frequency (count) and relative frequency (percentage) for categorical data. Comparisons between quantitative variables were done using the nonparametric Kruskal–Wallis and Mann–Whitney tests. Correlations between quantitative variables were done using Spearman's correlation coefficient. P < 0.05 was considered statistically significant.

Results

Forty patients who fulfilled the inclusion criteria were identified. The mean age of patients at the time of the study was 41.4 ± 13.40 years (range; 16–62 years). The mean spherical equivalent was 2.2 ± 1.66 (range: -2-+7.00). The mean postoperative flatter corneal meridian was 32.85 ± 2.56 D. The mean postoperative steeper corneal meridian was 41.95 ± 6.89 D. The mean astigmatic error was -9.00 ± -4.00 D. The mean IOP was 16.65 ± 2.32 mmHg, and the mean central corneal thickness was 528.75 ± 46.77 µm.

The indications of PK were bullous keratopathy (four eyes, 10%), corneal dystrophy (two eyes, 5%), keratoconus (six eyes, 15%), leukoma adherent (four eyes, 10%), and leukoma nonadherent (24 eyes, 60%).

There were no statistically significant differences in age, BCVA by spectacles, spherical equivalent, postoperative astigmatism, IOP, and central corneal thickness between different etiological groups [Table 1].

The distribution of the alignment pattern was not significantly different between the preoperative diagnosis groups (P = 0.082). The keratoconus group showed a higher

incidence of malapposed junction (66.7%) whereas the most frequent type of alignment pattern in the other groups was well-apposed junction (85% in corneal dystrophy, 60% in bullous keratopathy, and 52% in leukoma group).

Eyes were classified according to the most frequent alignment pattern among the eight cross sections. Eighteen (45%) eyes had well-apposed junctions, 10 (25%) eyes had malapposed junctions, and 12 (30%) had equally apposed junctions. Eyes with malapposed junction were subdivided into four (10%) gapping and six (15%) protrusion.

The mean cylinder was $-9.44 \pm -4.45D$ in well-apposed group, $-13.40 \pm -5.01D$ in malapposed group, and $-4.67 \pm -0.94D$ in equally apposed group. Alignment pattern of the graft–host junction correlated statistically significantly with the magnitude of astigmatism (*P* = 0.034) [Fig. 5].

The mean thickness disparity at the wound interface was $44 \pm 10.14 \ \mu\text{m}$ in well-apposed group, $70 \pm 8.58 \ \mu\text{m}$ in malapposed group, and $60 \pm 12.58 \ \mu\text{m}$ in equally apposed group.

We found that the graft-host disparity correlates statistically significantly with the graft-host junction pattern (P = 0.002).



Figure 5: Correlation between alignment pattern of the graft–host junction and the magnitude of astigmatism in the different alignment groups

Table 1: Comparison between different corneal diseases

	Mean±SD						
	Bullous keratopathy	Corneal dystrophy	Keratoconus	Leukoma adherent	Leukoma nonadherent	Р	
Age	58.00±5.66	47.00±0.0	25.67±6.66	32.00±22.6	43.67±10.5	0.068	
BCVA (logMAR)	0.80±0.40	0.73±0.46	0.50 ± 0.49	0.65±0.46	0.57±0.48	0.152	
SE	4.50±2.12	4.50±0.0	5.67±3.79	5.50±0.71	5.00±1.21	0.889	
K1	32.00±2.83	45.0±0.0	34.0±6.08	34.50±9.19	33.58±5.50	0.596	
K2	40.5±0.71	55.0±0.0	51.0±5.29	41.50±3.54	38.92±5.2	0.051	
Cylinder (D)	-8.5±-0.54	-10.0±0.0	-17.67±-3.7	-7.0±-1.66	-5.34 ± -0.2	0.123	
IOP (mmHg)	16.5±2.12	17.1±0.0	16.3±2.0	18.0±0.1	16.5±2.78	0.851	
CCT (µm)	563.5±79.9	488±0.0	524±36.5	560±42.4	522±46.8	0.581	

BCVA: Best-corrected visual acuity, SE: Spherical equivalent, IOP: Intraocular pressure, CCT: Central corneal thickness, SD: Standard deviation, LogMAR: Logarithm of the minimum angle of resolution, K1: Postoperative flatter corneal meridian, K2: Postoperative steeper corneal meridian

Comparisons of various parameters between the well-apposed group, malapposed group, and equally apposed group were summarized in Table 2.

We found that the more the number of malapposed sections, the higher the magnitude of postoperative astigmatism, however it was statistically insignificant [Table 3].

Anterior chamber-angle by anterior segment-optical coherence tomography

The angle of the AC was evaluated. It was open in 28 eyes (70%). There was peripheral anterior synechiae (PAS) in 12 eyes (30%). All patients with PAS had normal IOP. There was no statistically significant difference between both groups (P = 0.473).

Discussion

Corneal astigmatism after PK is a common complication that can prevent a good visual outcome in an eye with a clear graft and an otherwise healthy visual system. It arises from many causes related to the recipient cornea:^[9] trephination of the donor material, trephination of the recipient bed, suturing of the donor cornea to the recipient bed, excessive or uneven suture tension, graft–host misalignment, and irregular wound healing.^[10-12]

It is easy to detect external misalignment during surgery. However, external misalignment does not mean necessarily that the inner edges of the wound are well apposed; in many cases, the endothelial side is not well apposed.^[6,7] With the development of AS-OCT as an important modality for evaluation of the different corneal conditions, the graft–host junction could be evaluated easily.

In a study done by Kaiserman *et al.* on 27 eyes, they reported that the internal graft–host malapposition is relatively common and associated with increased astigmatism and IOP, and they also found that keratoconus patients had significantly more graft steps. They also reported that graft oversizing increased the size of malapposition, while the internal gapes or steps significantly reduced graft–host touch. They handled the eight images obtained from each eye as eight different data, so it is inconclusive whether the statistical results are really significantly different.^[6]

Jhanji *et al.* also conducted a similar study and categorized the alignment pattern into the two groups, step and ledge. Since they did not evaluate the characteristics of each alignment group, it was difficult to know whether the alignment pattern after PK affects the postoperative outcome or not.^[7]

Sung *et al.* conducted a similar study and evaluated the wound profile of post-PK eyes and the factors related to the wound alignment pattern. The alignment pattern of wound interface after PK differed according to the clinical diagnosis and was significantly associated with spherical equivalent and keratometric astigmatism.^[8]

In our study, we evaluated the wound profile of postkeratoplasty eyes using AS-OCT and correlated its pattern with the postoperative refractive and topographic astigmatism.

We found, similar to the previous reports, that among the malapposed junctions, protrusion was the most common misalignment type as it represented 60% of malapposed junction group. The result might be explained by the curling up of large donor on the wound interface. In addition, the tendency for stromal overgrowth induced by incomplete contact between the donor and recipient may affect the wound profile.^[8,13]

In contrast to the previous reports,^[6,8] the distribution of the alignment pattern was not statistically significantly different between the preoperative diagnosis groups (P = 0.082). However, the keratoconus group showed a higher incidence of malapposed junction (66.7%) which is similar to the other studies. This can be explained by the thickness mismatch between the thin peripheral part of recipient cornea and thick donor graft.

Thickness disparity at the wound interface was statistically significantly different between the alignment groups (P = 0.002). It was lowest in the well-apposed group and highest in the malapposed group.

Similar to the previous report,^[8] we found statistically significant difference in the postoperative astigmatism between different alignment groups. The malapposed group showed statistically significant higher mean astigmatic error than that of the other groups (P = 0.034), while the equally apposed group showed the least mean astigmatic error. This might be

	Mean±SD						
	Well apposed	Malapposed	Equally apposed				
Age	42.00±15.39	50.00±11.5	38.5±12.31	0.567			
Sex (male/female)	12:04	9:11	3:01	0.13			
BCVA (logMAR)	0.57±0.43	0.78±0.45	0.46±0.5	0.12			
SE	2.17±2.17	1.7±2.82	2.58±1.7	0.652			
K1 (D)	29.56±5.94	28±4.62	28.5±5.76	0.755			
K2 (D)	43.33±4.65	45±7.85	37.0±6.32	0.005			
Cylinder (D)	-9.44±-4.45	-13.40±-5.01	-4.67±-0.94	0.034			
CCT (µm)	514.56±36.4	551.2±40.7	531.33±58	0.128			
IOP (mmHg)	17.00±0.35	16.3±2.5	18±0.15	0.840			
Thickness disparity (µm)	44±10.14	70±8.58	60±12.58	0.002			

Table 2: Comparison of various parameters between the different alignment groups of anterior segment-optical coherence tomography

SE: Spherical equivalent, K1: Postoperative flatter corneal meridian, K2: Postoperative steeper corneal meridian, BCVA: Best-corrected visual acuity, IOP: Intraocular pressure, CCT: Central corneal thickness, SD: Standard deviation, LogMAR: Logarithm of the minimum angle of resolution

Table 3: Correlation between the number of malapposed	
sections per eye and the magnitude of astigmatism	

Number of sections	Mean cylinder	SD	Ρ
5 sections	-8.00	-2.17	0.336
6 sections	-9.57	-3.64	
7 sections	-10.14	0	
8 sections	-13.80	-4.61	

SD: Standard deviation

explained by the presence of equal sections of both malapposed and well-apposed junctions which might neutralize the effect of each other.

However, we did not find statistically significant difference in the spherical equivalent between the different alignment groups as other factors rather than the influence of astigmatism such as the axial length and lens status might have affected the spherical equivalent (P = 0.652).

Regarding topographic astigmatism, our results suggested that the alignment state has significant effect on cylindrical power. We used Scheimpflug keratometer (CSO, Sirius) in the assessment of postkeratoplasty astigmatism to get more accurate correlation, while previous studies used manual keratometer whose range of measurements is limited within 3 mm of the central cornea and does not include the posterior corneal surface.

Our study has several limitations. Our study population had patients with selected underlying diseases and the number of patients in each group was relatively small, thus the results may not be applicable to all post-PK cases. In addition, we did not exclude the effect of the degree of graft oversize as not all the eyes had the same degree of graft oversize and this might have had effect on the results. We recommend a large-scale study on various preoperative clinical diagnoses to understand the alignment patterns of the wound interface after PK.

Conclusion

The alignment pattern of the graft–host junction by AS-OCT can explain the postoperative astigmatism after PK where it correlates significantly with the magnitude of astigmatism.

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Conflicts of interest

There are no conflicts of interest.

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