

**ORIGINAL ARTICLE****Correlation Between Slit Lamp Examination and Anterior Segment Optical Coherence Tomography for the Evaluation of Central Infectious Corneal Perforation**

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**ABSTRACT**

**Background:** The aim of this work is to compare slit lamp (SL) examination and anterior segment optical coherence tomography (AS-OCT) for the evaluation of central infectious corneal perforation.

**Methods:** This observational study included 50 eyes of 50 patients with central infectious corneal perforation. Each eye was subjected to both examination modalities, SL and AS-OCT, for the pre-treatment and post-treatment examinations.

**Results:** The progress of healing started from day 7, 5 eyes (10%) appeared to be healed by SL, and only 3 (6%) appeared to be healed by OCT. All eyes appeared to be healed in the 1st month, 39 (78%) of them appeared to be healed by OCT and 45 eyes (90%) appeared to be healed by the 2nd month, the final healed eyes were 46 (92%) at the 3rd month. The first appeared to be healed is the corneal epithelium as seen by both SL and OCT after one month, corneal stroma appeared to be entirely healed in the first month by SL but by OCT, 39 eyes (78%) healed by the first month and the rest 11 (22%) had partial healing by OCT. In the third month, 46 eyes (92%) had complete callous formation as seen by OCT and the rest 4 eyes (8%) had partial or incomplete healing.

**Conclusions:** AS-OCT is a reliable non-invasive tool for the evaluation of corneal perforation and its progression of healing. It was superior and more accurate than SL in the assessment of corneal perforation as it provides information on wound healing and the surrounding tissue in layers that can detect any surprise that can not be seen by the slit lamp.

**Keywords:** Infectious keratitis, corneal perforation, Slit lamp examination, AS-OCT.

**INTRODUCTION**

Many factors that cause corneal melting can lead to corneal perforation, a potentially fatal consequence. In addition to trauma when penetrating injuries happen, other causes include microbial keratitis, ocular surface disease, and autoimmune illnesses. In order to restore globe integrity and reduce the risk of secondary problems such as endophthalmitis, choroidal haemorrhage, and glaucoma, it is linked with severe ocular morbidity and demands immediate surgery. The literature has reported a variety of therapeutic approaches, with multi-staged procedures being needed to facilitate visual restoration. While non-infectious etiologies include autoimmune illness and ocular surface conditions, infectious perforation can develop as a result of bacterial, fungal, viral, or parasite infection [1]. Using slit-lamp microscopy, the corneal tissue healing area may be difficult to assess [2]. When examining anterior segment

pathology involving the cornea, AS-OCT is incredibly helpful [3]. In cases of corneal damage, AS-OCT is particularly helpful for determining the area of the true stromal thickness and healing tissue [4].

Higher axial resolution pictures were made possible by the advancement of OCT from time domain to spectral domain. A noninvasive, in vivo cross-sectional picture of the ocular surface and corneal structure can be obtained using AS-OCT devices, with resolutions ranging from less than 5 μm (ultra-high-resolution) to greater than 5 μm (high-resolution) [5].

The purpose of this study is to compare between SL and AS-OCT in evaluating infectious central corneal perforation pre-treatment and post-treatment as well as during the follow-up period.

**METHODS**

This is a prospective clinical and comparative study conducted between October 2022 till February 2023 at the Ophthalmology Department,

Zagazig University Hospitals, Egypt. The Institutional Review Board (IRB) at the faculty of medicine, Zagazig University approved the study protocol, which adhered to the tenets of the Declaration of Helsinki, and written informed consent was obtained from all participants before participation. Approval of IRB was considered under the number of 9711-15-7-2022.

The study included patients of more than 18 years of age (both sexes included) seeking for treatment of infectious (bacterial, viral, and fungal) central corneal perforation. Exclusion criteria were other forms of keratitis than infectious, underlying autoimmune disease, sterile or surgical perforation.

Patients who agreed to be enrolled in the study and provided informed consent, were examined by use of SL (group 1), then examined by AS-OCT (group 2). The treated eyes were examined weekly by the two modes (SL & OCT) for one month and monthly for 3 months.

Initial examination included the patient's medical history, specifically the history of contact lens wear, ocular trauma, the duration and type of treatment before the first visit, measurement of corrected distance visual acuity, slit lamp biomicroscopy, corneal photography, and pachymetry for measuring the corneal thickness by ultrasound or Pentacam. The parameters evaluated during slit-lamp examination included the localization and extent of corneal ulcer diameter, the site and extent of infiltrate, and extent and localization of corneal vascularization.

Identification of organisms was done by scraping of ulcer site for direct smears and cultures, then samples were sent to the laboratory for the differentiation of the micro-organisms before the treatment. Complete healing was defined as complete closure of corneal perforation with formed anterior chamber together with complete resolution of infectious keratitis.

**AS-OCT** Spectral domain OCT (SD-OCT), The Nidek RS-3000 Advance (NIDEK Inc., USA) was used in the study with a resolution of a 1.9 mm scan depth, and an 870 nm average wavelength [6,7]. This AS-OCT device has been used to capture the corneal OCT images pre-treatment and during the treatment follow-up period (3 months).

### **Statistical analysis**

The collected data were coded, entered, presented and analyzed by computer using a data base software program, Statistical Package for

Social Science (SPSS) version 20. Mean  $\pm$  SD, chi-square and t-test were used for determination of significance (P value). P <0.05 is considered significant.

### **RESULTS**

The study constitutes 50 eyes of 50 patients of infectious corneal perforation. They were 35 males (70%) and 15 females (30%). The vast majority of eyes had BCDVA less than 0.1 by decimal values 45 (90%), while the rest 5 eyes (10%) had BCDVA more than 0.1 by decimal values. The mean age was  $42.8 \pm 8.35$  years. The mean perforation size was  $2.75 \pm 1.58$  mm<sup>3</sup> as shown in **table (1)**.

Regarding causative micro-organisms, bacterial infection was the most common 26 (52%), followed by fungal keratitis in 18 eyes (36%) and the least were viral and parasitic keratitis 4 (8%) and 2 (4%), respectively (**table 2**). Regarding the risk factors and etiology, trauma was the most common 32 eyes (64%), corneal erosion or ulcer in 10 (20%) of eyes, neglected infection in 5 eyes (10%), and only 2 eyes (4%) and 1 (2%) were due to contact lens wear and surgical foreign body removal, respectively (**table 3**).

The progress of healing started from day 7, 5 eyes (10%) appeared to be healed by SL, only 3 (6%) of them was healed by OCT. All eyes appear to be healed in the 1st month, 39 (78%) of them appeared to be healed by OCT and 45 eyes (90%) appeared to be healed by the 2nd month, the final healed eyes were 46 (92%) at the 3rd month (**table 4**).

Delayed healing after one week was presented in 45 eyes (90%) and 47 eyes (94%) by SL and OCT, respectively, while complete healing occur after the first month by SL but by AS-OCT 11 eyes (22%) were not healed completely. Of them, 5 eyes (10%) had incomplete healing in the 2nd month, they became 4 (8%) by the 3rd month which were partially healed (**table 5**).

The first corneal layer that appeared to be healed was the corneal epithelium as seen by both SL and OCT after one month, corneal stroma appeared to be healed completely in the first month by SL but by OCT, 39 eyes (78%) healed by the first month and the rest 11 (22%) had partial healing by OCT. On the third month, 46 eyes (92%) had complete callous formation as seen by OCT and the rest 4 eyes (8%) had partial or incomplete healing (**table 6**).

**Table 1:** Patients’ characteristics of the study population.

	Patients with corneal perforation	
	No.	Percent (%)
Males	35	70.0
Females	15	30.0
Total	50	100
BCDVA > 0.1 (decimal)	5	10.0
BCDVA < 0.1 (decimal)	45	90.0
	<b>Mean ± SD</b>	
Age (years)	42.8 ± 8.35	
Mean ± SD	18 – 66	
Range		
Perforation size (mm <sup>3</sup> ):	2.75 ± 1.58	
Mean ± SD	0.86 – 4.35	
Range		

BCDVA: Best corrected distant visual acuity.

**Table 2:** Causative micro-organisms of corneal perforation.

Causing organism	Number	Percent (%)
Bacterial	26	52.0
Fungal	18	36.0
Parasitic	2	4.00
Viral	4	8.00
Total	50	100

**Table 3:** Etiology of corneal perforation in our study.

Etiology	Number (50)	Percent (%)
Direct trauma	32	52.0
Contact lens wearers	2	36.0
Entropion corneal erosion	10	4.00
Surgical removal or foreign body	1	8.00
Neglected infection	5	100

**Table 4:** Timing of healing of the corneal perforation.

Timing	Group (1)		Group (2)		Significance	
	No.	%	No.	%	$\chi^2$	P
3 days	0	0.00	0	0.00		
7 days	5	10.0	3	6.00	19.57	0.000*
1 month	50	100	39	78.0	1.934	0.023*
2 months	50	100	45	90.0	1.864	0.046*
3 months	50	100	46	92.0	1.856	0.047*

$\chi^2$  = Chi square test, \*p <0.05 = statistically significant.

**Table 5:** Delayed treatment of corneal perforation during the follow-up period.

Delayed treatment	Group (1)		Group (2)		Significance	
	No.	%	No.	%	$\chi^2$	P value
7 days	45	90.0	47	94.0	0.717	0.142
1 month	0	0.00	11	22.0	2.951	0.000*
2 months	0	0.00	5	10.0	2.417	0.001*
3 months	0	0.00	4	8.00	2.246	0.001*

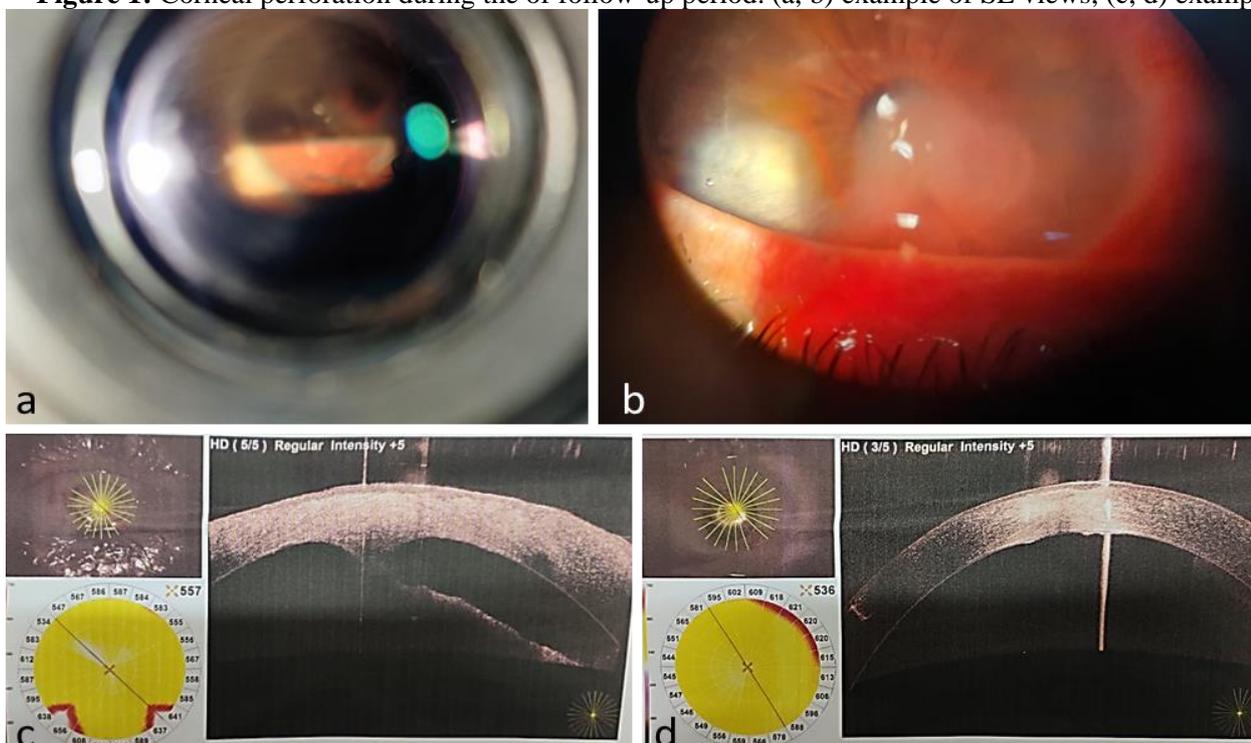
$\chi^2$  = Chi square test, \*p <0.05 = statistically significant.

**Table 6:** Progress of healing of corneal perforation during the follow-up period.

Progress of healing	SL		AS-OCT		Significance	
	No.	%	No.	%	$\chi^2$	P value
<b>After one month</b>						
Corneal epithelium	50	100	50	100	0.000	1.000
Corneal stroma	50	100	39	78.0	1.934	0.023*
Partial callous formation	0	0.00	11	22.0	2.951	0.000*
Complete callous formation	50	100	39	78.0	1.934	0.023*
<b>After three months</b>						
Corneal epithelium	50	100	50	100	0.000	1.000
Corneal stroma	50	100	46	92.0	1.856	0.047*
Partial callous formation	0	0.00	4	8.00	2.246	0.001*
Complete callous formation	50	100	46	92.0	1.856	0.047*

$\chi^2$  = Chi square test, \*p < 0.05 = statistically significant.

**Figure 1:** Corneal perforation during the of follow-up period. (a, b) example of SL views, (c, d) example of



AS-OCT pictures showing corneal layer details.

**DISCUSSION**

A corneal perforation is an urgently treatable ocular problem. Foreign objects, bacterial keratitis, and immunological conditions can all result in corneal perforations [8]. A variety of eye issues, such as hyphema, microhyphema, an ill-shaped iris, a shallow anterior chamber, and impaired visual acuity, can result from corneal perforation [9].

The purpose of treating corneal perforations is to bring back the integrity of the globe and promote repair of the defect so that the cornea can be used for future vision therapy [10].

Regardless of the underlying cause, a breakdown of the corneal epithelium is the

primary pathologic mechanism of a corneal ulceration. The purpose of medical care is to either promote re-epithelialization through the use of preservative-free lubricants, to prevent or treat an infection through the use of effective antimicrobial, antiviral, or antifungal therapy, or to reduce inflammation through individualized treatment plans for each distinct etiology [11].

No intraocular foreign bodies were found during the slit-lamp test. Clinical and AS-OCT analysis of the corneal full-thickness tear suggested that it was likely caused by a sharp needle piercing the cornea rather than an impact damage from a piece of glass, metal, or wood. In these circumstances, AS-OCT is advantageous

[12]. In the present study we aimed to compare between SL and AS-OCT for the evaluation of infectious central corneal perforations.

According to the study, the most frequent cause of corneal perforation was bacterial keratitis. This was demonstrated by earlier research, which discovered that the majority of cases of infectious keratitis are caused by bacterial keratitis [13–15]. The virulence factors and enzymes secreted by the bacterial cells vary depending on the kind of infecting bacterium [16], which also affects the clinical findings of bacterial corneal ulcer and perforation [17]. The most frequent bacteria found in infected corneal ulcers are *Pseudomonas aeruginosa* and *Staph. aureus* [18]. Whereas the latter is an anaerobic Gram-positive coccus that is found in the pharynx as well as on the skin, including the perineum and water, the former is a Gram-negative bacterium that is prevalent in the natural environment, including soil.

By triggering an innate immune response, bacterial infection causes PMNs to be recruited to the infection site. The infiltrated PMNs subsequently release IL-1, which, as was already explained, is also secreted as an alarmin by injured epithelial cells. The host's response to bacterial infection, especially that linked to corneal ulcer, is significantly regulated by IL-1. By encouraging corneal fibroblasts to produce chemokines like IL-8 that prolong PMN infiltration in the cornea, IL-1 partially contributes to the loss of corneal tissue [14,19].

Fungal keratitis (FK) represents the second most common keratitis responsible for corneal perforation. The most common genera isolated from filamentous fungal keratitis cases are *Fusarium* spp. and the aspergilli [20], followed by the dematiaceous fungi—a heterogenous group of fungi characterized by melanin-production and pigmentation—*Curvularia* spp. being the most commonly reported genus from this group [21,22]. Without the use of a slit lamp, these clinical signs can be seen with a simple torch, either with or without loupes, together with a blue filter and fluorescein test strips. It is possible to separate the various causing agents to some extent by performing a more thorough inspection with a slit-lamp biomicroscope; fungal keratitis is more likely if there are serrated margins, increased slough (dead epithelial tissue), and/or colour other than yellow [23]. The extensive use of contact lenses, including bandage lenses, and the use of topical steroids are both implicated in an increase in incidence over time in industrialized nations [24,25].

According to **Barrientez et al.** [26], corneal lacerations and perforations frequently result from comparable events and can be distinguished by the level of injury. Corneal perforation is frequently induced by corneal trauma. In contrast to corneal perforations, when the lesion enters the endothelium, corneal lacerations affect the stroma of the cornea.

Both SL and OCT were used in this investigation to show that corneal epithelium recovered more quickly than stroma. **Kamil and Mohan's** [27] evidence supports this. In this study, corneal epithelium healed faster than stromal healing as detected by both SL and OCT. This was proved by **Kamil and Mohan** [27]. The epithelium undergoes a complete turnover in about a week [28], which was similar to our results. Coordination of different cytokines and growth factors is necessary for the process of epithelial repair [29]. The interactions between the corneal epithelium and stroma are mediated by these growth factors and cytokines. The basement membrane mediates interactions between stromal and epithelial cells. These interactions bring up keratocyte apoptosis, activation, and trans-differentiation into myofibroblasts, which are stromal responses [27]. This improvement in corneal stromal and epithelial repair was seen by SL and verified by OCT. Corneal epithelial wound healing and accompanied stromal-epithelial interactions. Once the corneal epithelium is injured, epithelial cells lose adhesions, change shape, proliferate, and migrate rapidly to cover the defect. EGF (epidermal growth factor) is the primary pathway initiating cell migration and proliferation [27]. It is helped by insulin-like growth factor (IGF), insulin, transforming growth factor  $\beta$  (TGF $\beta$ ), and platelet-derived growth factor (PDGF) [29].

After treatment, AS-OCT revealed that the corneal wound had closed and the corneal edoema had diminished. It also provided precise data on anterior chamber depth and corneal thickness. As previously described [30], AS-OCT proved a useful method for noninvasively observing wound form and identifying the presence of intracorneal foreign items.

When an FB in the cornea or the AC is detected, imaging such as AS-OCT should be taken into account in order to determine its location, size, and composition, to learn the condition of the surrounding ocular structures, and to track the healing process following surgical repair [31]. Depending on the kind of foreign body, AS-OCT has varying levels of reflectivity. Glass foreign entities are well defined and have

little internal reflectivity, but metal and wood foreign bodies have considerable anterior reflectivity and shadowing, respectively [30].

The detection of anterior chamber (AC) inflammation in uveitis using anterior segment OCT imaging is another application [32]. This inflammation can be seen as hyperreflective patches in the AC, as was the case in our patient at the 1-week post-operative visit. [32].

AS-OCT enables non-invasive rapid imaging of ocular tissue at various depths, allowing for accurate assessment of foreign body characteristics and evaluation of full-thickness perforation [30]. This is true even though high resolution slit-lamp biomicroscopy at magnifications of 10–25 (and up to 100) is clinically reliable for visualizing the cornea.

A stromal scar and epithelial thickening were seen, according to a previous study that looked at the repair of corneal wounds caused by foreign bodies of iron [33]. A low-intensity shadow was also seen, which was believed to represent a piece of the iron foreign body that had been missed by slit-lamp biomicroscopy. The urgency of removing a foreign body depends on its nature, and metallic foreign entities need to be removed quickly [34]. Corneal foreign body imaging offers details on the position, size, and depth of foreign bodies. By routine slit-lamp biomicroscopic examination, AS-OCT can also detect unexpected lesions in situations of ocular damage that are undetectable or challenging to notice [35].

In order to plan surgical removal, AS-OCT offers crucial information regarding the Descemet's membrane integrity and the place of entry of a foreign body. Foreign bodies were removed via the anterior route when Descemet's membrane was intact and the scar at the point of foreign body entry was known; however, when Descemet's membrane was breached and the point of entry had healed, the foreign body was removed via the anterior chamber using an air tamponade. When a foreign body was removed through the anterior chamber, no sutures were used, which prevented any astigmatic effects [30]. AS-OCT is a non-invasive technique for quick imaging of ocular tissue at different depths that accurately tracks wound healing for the best results [34].

In some circumstances, corneal thinning may be suspected when the corneal perforation heals. In such circumstances, AS-OCT is incredibly helpful since it enables quantitative evaluation of the remaining corneal thickness and flags the possibility of an additional approaching perforation [30]. If the defect is less than 2 mm,

cyanoacrylate glue and a bandage can be utilized to treat the corneal tissue loss [36].

## CONCLUSIONS

AS-OCT is a reliable non-invasive tool for evaluation of corneal perforation and its progression of healing. It was superior and accurate than SL for evaluation of corneal perforation as it provides information of the wound healing and the surrounding tissue in layers that can detect any surprise cannot be seen by slit lamp.

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