

Analysis of Ocular Surface Tumours and Lesions by High-definition Anterior-segment Optical Coherence Tomography

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ABSTRACT

Introduction: High resolution AS-OCT (Anterior segment- Optical coherence tomography) is an imaging modality predominantly used in tertiary ophthalmologic centres to diagnose and characterise various ocular surface tumours as well as an adjunct to monitor treatment response.

Objective: The objective of this study was to evaluate the utility of AS-OCT for ocular surface tumours.

Methodology: This was a prospective cohort study of patients done at a tertiary care hospital in Nepal over one year from 2023 August to 2024 July. A consecutive sampling was done in the patients aged 18 years and older who were suspected of having ocular surface tumours and lesions during the study period. Demographic data, slit lamp biomicroscopic examination including size, site and morphology of tumour and AS-OCT using High Definition Zeiss Cirrus 6000 were carried out for all patients enrolled. Diagnosis was based on clinical evaluation and AS-OCT features. Those patients suspected of malignancy surgical excision and their histopathology was analysed.

Result: Among the 110 enrolled patients, the median age was 50 (range: 18–87) years. Of them, 63 (57%) were female and 47 (43%) were male. A total of 5 (4.5%) participants had bilateral involvement. Based on clinical picture and AS-OCT features, 84 eyes (73.04%) were diagnosed to have ocular surface squamous neoplasia (OSSN), 18 eyes (15.65%) with conjunctival nevus and two eyes (1.73%) were suspected to have melanoma. Histopathology of 80 eyes who underwent surgical excision, OSSN of various grades in 86% eyes was the most common diagnosis followed by conjunctival melanoma in 3%.

Conclusion: Though HPE is a gold standard for diagnosing ocular surface tumours, AS-OCT can provide a non-invasive optical biopsy. Additional research in AS-OCT is needed to increase the sensitivity and specificity of accurately diagnosing ocular surface lesions.

Key words: Anterior segment optical coherence tomography; ocular surface squamous neoplasia; ocular surface tumours; primary acquired melanosis.

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INTRODUCTION

A high definition AS-OCT (Anterior segment-Optical coherence tomography) is an upcoming imaging modality useful to diagnose and characterise various ocular surface lesions present at different layers of conjunctiva and cornea (Tran AQ et al., 2019). It can also be used as an adjunct to monitor treatment response and assess for recurrence of ocular surface tumours. One study showed that high resolution AS-OCT can even detect subclinical OSSN which can be used to detect a very early recurrence (Venkateswaran et al., 2021b). It is considered a non-invasive optical biopsy for suspected ocular surface tumours of both epithelial and subepithelial lesions wherein chemotherapy can be started based on the clinical and AS-OCT features without doing a biopsy (Karp et al., 2019).

This is the landmark study in Nepal for ocular oncology, carried out at a tertiary care center to describe the utility of AS-OCT for various ocular surface tumours and lesions. It aimed to investigate whether this established imaging modality could be translatable and comparable with clinical diagnosis alone and with the histopathology diagnosis of ocular surface tumours and lesions.

METHODOLOGY

This was a prospective cohort study of patients carried out from August 2023-July 2024 at the Ocular Oncology clinic of Tilganga Institute of Ophthalmology, Kathmandu, Nepal. A consecutive sampling was done to include the adult patients aged 18 years and older who presented with various ocular surface tumours and clinically undifferentiated lesions, during

the study period. The inflammatory conditions of ocular surface were excluded from the study. Informed and written consent was taken in the local language. Patient's data was DE identified and no full face photographs was taken. Ethical approval for the study was obtained from Nepal Health Research Council in July 2023 with ref number 191-2023.

Demographic data were collected from the patients included in the study. Then a slit lamp biomicroscopic examination including size (in mm and clock hours of limbus), site (conjunctiva, limbus or cornea) and morphology (colour, surface, margin, feeder vessels) of the lesion was done and documented. Clinical photograph of the eye involved was taken with mobile phone. AS-OCT using High Definition Zeiss Cirrus 6000 were carried out for all patients enrolled. The final clinical diagnosis was done based on clinical evaluation and AS-OCT features. Those patients suspected of malignancy, surgical excision was carried out and their histopathology was analysed.

RESULT

In this study, 110 patients were enrolled, among which 63 (57%) were females and 47 (43%) males. The most common age group in this study were young adults in the age group of 18 to 30 years old; median age of the enrolled patients being 50 years (range 18-87 years). The rest of the age groups have been tabulated (Table 1). Five (4.5%) patients had bilateral disease; with two of them were patients of xeroderma pigmentosum. Hence, a total of 115 eyes were taken for the study.

On examination, the lesion was present solely on conjunctiva in 37 (32%) eye cornea in 17

(15%) while 61 (53%) eyes had lesions on both conjunctiva and cornea. Nasal bulbar conjunctiva was the commonest quadrant involved, in 66 (57.3%) eyes followed by temporal bulbar conjunctiva in 35 (30.4%) and superior bulbar conjunctiva in six (5.2%).

Morphologically, the lesions were velvety in 56 (48.6%) eyes, leucoplakic in 33 (28.6%), and brown mass was in 17 (14.7%) eyes. Lesions were associated with feeder vessel in 52 (45.2%) cases (Table 2).

Table 1: Age group.

Age group (Years)	Frequency (Percent)
18-30	27 (24.6)
31-40	12 (10.9)
41-50	20 (18.2)
51-60	19 (17.3)
61-70	16 (14.5)
71 and above	16 (14.5)
Total	110 (100)

Table 2: Morphology of the lesions.

Morphology	Frequency (Percent)
Gelatinous	8 (7.0)
Leukoplakic	10 (8.7)
Leukoplakic,feeder vessels	6 (5.2)
Leukoplakic, gelatinous	6 (5.2)
Leukoplakic,gelatinous,feeder vessel	1 (0.9)
Leukoplakic,nodular,feeder vessel	10 (8.7)
Nodular,gelatinous	1 (0.9)
Pigmented lesion	16 (13.9)
Pigmented lesion,feeder vessel	1 (0.9)
Velvety	18 (15.7)
Velvety,feeder vessel	15 (13)
Velvety,gelatinous,feeder vessel	4 (3.5)
Velvety,nodular	4 (3.5)
Velvety,nodular,feeder vessel	15 (13.0)
Total	115 (100.0)

Based on clinical picture and AS-OCT features, 84 eyes (73.04%) were diagnosed to have ocular surface squamous neoplasia (OSSN), 18 eyes (15.65%) with conjunctival nevus and two (1.73%) eyes were suspected to have melanoma. Rest of the AS-OCT assisted clinical diagnosis is has been tabulated (Table 3). A suspicious case of melanoma on clinical and AS-OCT was found to be having nevus (Figure 1).

Among 115 eyes, surgical excision of the lesion was done in 80 eyes as they were suspicious of the malignancy. Among them, the most common diagnosis on histopathology was OSSN in 69 (86%) eyes, granuloma in four (5%) cases, melanocytic nevus and melanoma in two (2.5%) each. Squamous cell papilloma, hamartoma and orchronosis in one (1.3%) each. An example of matching ASOCT features with histopathology of an OSSN case is shown (Figure 2).

Table 3: Anterior segment optical coherence tomography assisted clinical diagnosis.

Benign lesions	Frequency (Percent)
Nevus	18 (15.65)
Primary Acquired Melanosis	1 (0.86)
Malignant lesion	
OSSN*	84 (73.04)
Melanoma	2 (1.73)
Lymphoma	1 (0.86)
Inflammatory /infectious	
Granuloma (1), episcleritis (3), Rhinosporidiosis (2), phlycten (2)	8 (6.95)
Degenerative	
Pterygium	1 (0.86)

*One case of OSSN was with intraocular extension

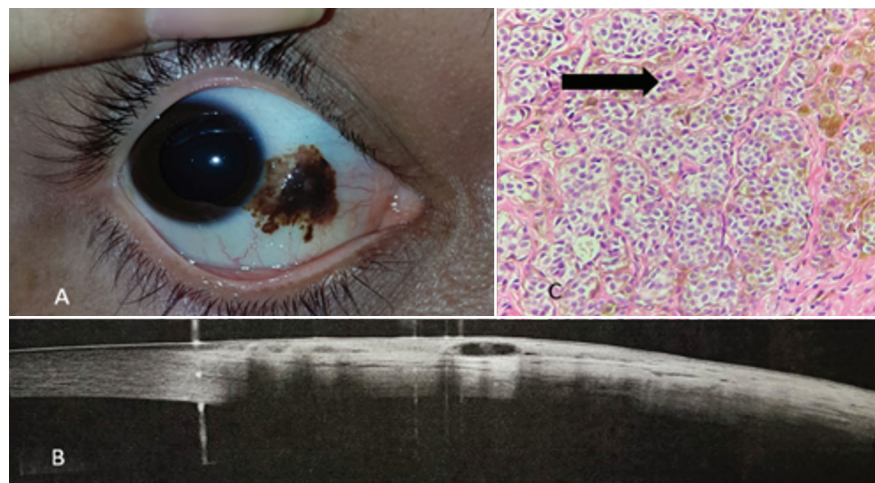


Figure 1: Intraocular melanocytic nevus: A, Brown pigmented, irregular lesion in the nasal bulbar conjunctiva; B, Subepithelial lesion with heterogeneous appearance with presence of cystic spaces casting significant shadowing; the overlying epithelium is irregular with areas of thickening and thinning, no abrupt transition; C, Hematoxylin and eosin stain (HE) X100 magnification. Dermis shows nests of nevoid cells with cytoplasmic melanin pigmentation, oval nucleus and conspicuous nucleolus (black arrow showing aggregates and sheets of nevoid cells).

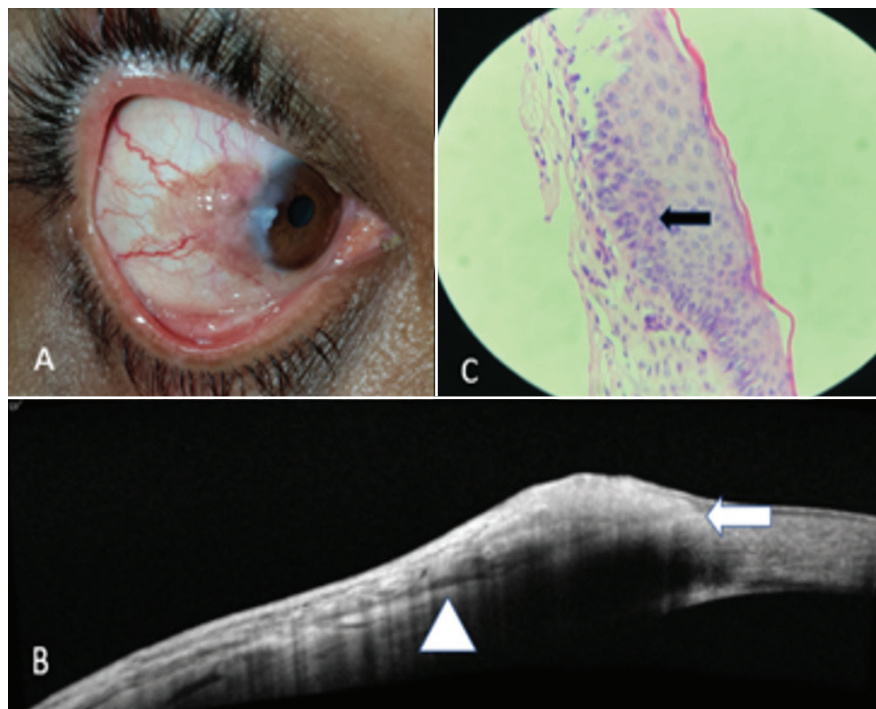


Figure 2: Conjunctival intraepithelial neoplasia grade II: A, A pink gelatinous conjunctival mass with feeder vessels and extending to temporal limbus; B, Hyperreflective and irregular thickened epithelium with abrupt transition (shown by white arrow), with clear demarcation line (shown by white arrow head); HE stain X100 magnification. Hyperplastic stratified squamous epithelium showing loss of polarity and nuclear atypia involving lower half.

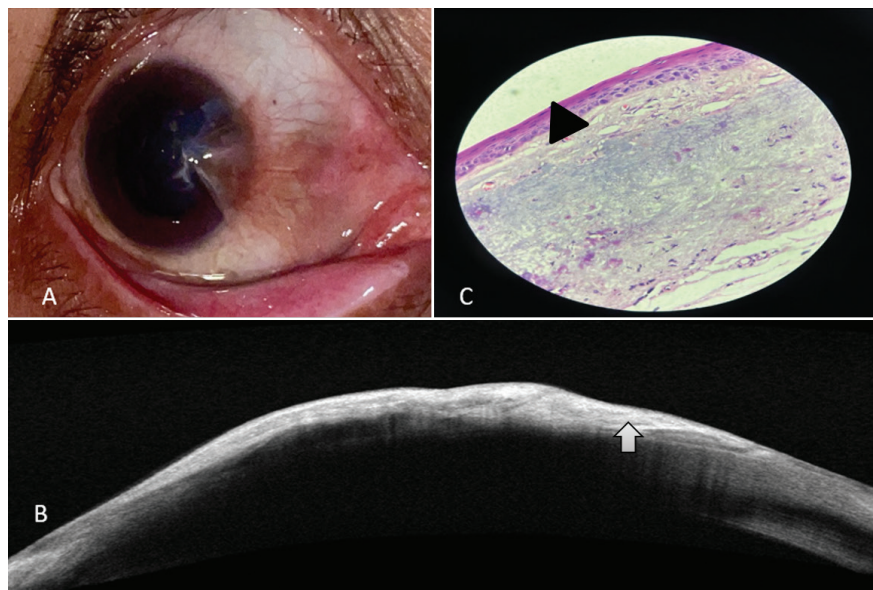


Figure 3: Pterygium: A, Pinkish, raised, fleshy, triangular-shaped mass encroaching the cornea; Grade II Pterygium; B, Subepithelial mass with relatively homogenous hyper reflective structure; epithelium is hyper reflective without significant thickening or transition line (arrow); C, HE stain X 400 magnification. Conjunctival epithelium and underlying fibrous stroma with solar elastosis. (arrow head).

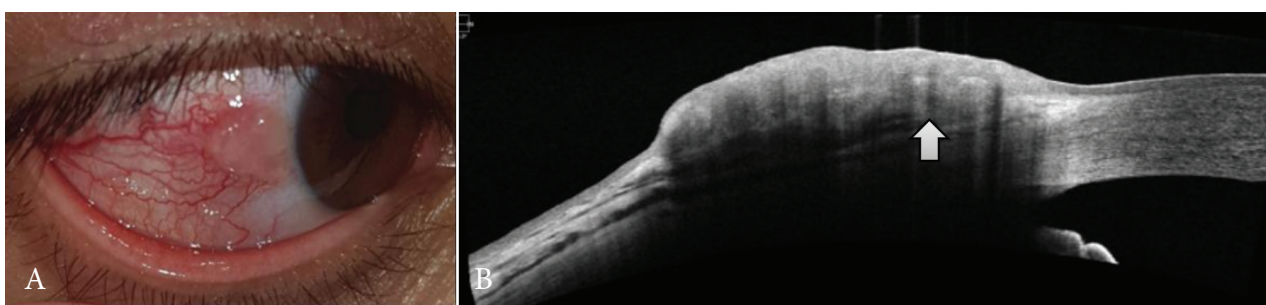


Figure 4: Conjunctival granuloma: A, Pinkish, gelatinous, elevated mass with feeder vessels on the temporal bulbar conjunctiva; B, Iso to hyperreflective, irregular thickening of epithelium with multiple circular or nummular intraepithelial hyporeflective lesions (arrow) on AS-OCT.

DISCUSSION

Optical coherence tomography (OCT) is an excellent technology for imaging various parts of the eye. Today, available OCT technology is capable of producing imagery with high resolutions of 3.5–5 μm or less (Venkateswaran et al., 2021b). The AS-OCT is highly useful for detecting and monitoring several pathologies of the cornea and conjunctiva, such as OSSN, pterygia, pingueculae, dry eye disease, corneal dystrophy and more. It provides fast, noninvasive and high-resolution imaging of the ocular surface that can be easily interpreted by novice clinicians. HR-OCT is particularly valuable for diagnosing and managing OSSN.

On AS-OCT, OSSN can be identified as thickened, hyper-reflective epithelium with an abrupt transition from normal to abnormal tissue. Additionally, one study showed that high resolution AS-OCT can detect subclinical OSSN (Venkateswaran et al., 2021b). It is especially useful for monitoring progression of OSSN treatment with topical chemotherapy. It can also help find tumour margins before during surgical excision (Karp et al., 2019). In subtle cases, OSSN can be difficult to detect when present with other ocular surface pathologies such as pannus, pterygia, pinguecula and scarring. As such, HR-OCT serves as an ‘optical biopsy’ (Karp et al., 2019). It is fast, non-invasive and presents virtually no discomfort to the patient.

There were 110 patients enrolled in the study. The median age of presentation in the study is 50 years, ranging from 18 years to 87 years. Most of the cases were within the age group of 18-30 years (27, 24.5%) followed by 41-50

years (20, 18.2%), 51-60 years (19, 17.27%), 61-70 years (16, 14.55%), 71 years and above (16, 14.55%), 31-40 years (12, 10.91%). The mean age of present study is higher than the studies done by Shields et al., and Lee et al., but consistent with the studies done by Shrestha et al., Shrestha et al., 57 (63%) were females and 43 (47%) were males. The number of affected females in our study is slightly higher than other studies (Thomas et al., 2014; Shrestha et al., 2022) but similar to a study done in Nepal (Shrestha et al., 2019). Single eye involvement was seen in 104 (94.5%) and both eyes were involved in six (5.5%). Most common presenting complaint was the growth of mass (77, 100%), which could be because patients present late and also as this is a tertiary eye care center, patients are referred here for treatment of the “mass in the eye”. Similarly, the most common presenting symptom was mass growth in other studies done in Nepal as well (Shrestha et al., 2022; Shrestha et al., 2019). While in other studies patients also presented with symptoms like watering, redness, blurring of vision (Thomas et al., 2014; Vempuluru et al., 2021). Duration of symptoms ranged from a few months to years before presenting to us. The commonest site involved was nasal bulbar conjunctiva (41, 51%) followed by temporal bulbar conjunctiva (22, 28%) which is similar to other studies (Shrestha et al., 2022; Shrestha et al., 2019). In this study the most common morphology was velvety mass while in a study done by Xu et al., most common morphology was a red gelatinous tumour with feeder vessel (Xu et al., 2012). In a study done by Vempuluru et al., most cases presented with a nodular, non-pigmented mass with feeder vessel (Thomas et al., 2014). In present study feeder vessels was present in 45.2% of total lesions.

High resonance-Optical coherence tomography (HR-OCT) helps in the diagnosis and management of OSSN. The typical AS-OCT findings include thickened, hyperreflective epithelium and an abrupt transition from healthy to diseased epithelium (Karp 2017; Yim et al., 2018; Shrestha et al., 2022). The authors took the same three points to diagnose OSSN as in other studies. Epithelial changes like OSSN are also seen in epithelial hyperplasia, granular dystrophy, nevus and granulation tissue (Thomas et al., 2014) while subepithelial changes are seen in chronic inflammation, lymphoma and arteriovenous malformation (Thomas et al., 2014) This mirrors the morphological findings seen on histopathology. Studies have shown that distinctive AS-OCT findings allow for the diagnosis of OSSN in the setting of co-existing ocular surface diseases, including pterygia, ocular rosacea, Salzmann's nodular degeneration, and limbal stem cell deficiency (Nanji et al., 2015; Atallah et al., 2017). In current study AS-OCT findings of pterygium were hyper reflective epithelium with abrupt transition and possible focal thickening; with irregular subepithelial lesion which is similar to study done by Venkateswaran N et al where AS- OCT of pterygia showed hyperreflective epithelium with dense subepithelial layer (Venkateswaran et al., 2021a). Episcleritis showed mildly hyper-reflective epithelium with minimal thickening and no transition in our study. Nevus showed hypo reflective homogenous thickened epithelium with multiple cystic spaces, back shadowing with intact sclera in our study which is similar to the study done by Venkateswaran et al and Shields et al., (Venkateswaran et al., 2021a; Shields et

al.,2011). The PAM showed normal thickness of epithelium with hyper reflectivity which is similar to the study done by Venkateswaran et al., (Venkateswaran et al., 2021a). AS-OCT is a noninvasive diagnosis modality that can be performed in the clinical setting. AS-OCT can be used to guide medical management of OSSN as well as inflammatory lesions with apparent clinical resolution but continue to show subclinical disease (Tran et al., 2019). Monitoring for tumour resolution with AS-OCT can also potentially prevent overuse of topical chemotherapeutic agents and steroids which can lead to ocular toxicity.

The differences between AS-OCT and HPE diagnosis include the fact that in HPE, the description can be to the details of the layers. It would be interesting if in the future AS-OCT it can provide such description. Perhaps in the future of studying of future of newer generation perhaps we can get the AS-OCT to distinguish Conjunctival and Corneal Intraepithelial Neoplasia 1,2,3 also can be described in detail. It is unique to have this study for Nepali population as AS-OCT features have not yet been reported from Nepal and most of the cases of OSSN are getting mixed up for inflammatory diagnosis.

CONCLUSION

AS-OCT can provide a non- invasive optical biopsy in ocular surface tumours as well as subepithelial lesions. Though HPE is a gold standard for diagnosing ocular surface tumours, AS-OCT can, not only be used for diagnosis but also can be used in post- surgical cases for ongoing monitoring of recurrence potential

cases especially in the case of Nepal where OSSN is the commonest ocular tumour and there are limited expertise. Since OSSN is more common than we think it is important not to miss the diagnosis by clinical judgment alone and utilise AS-OCT wherever indicated.

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